Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Palladium Catalyzed Acetoxylation of Benzylic C-H Bonds Using a Bidentate Picolinamide Directing Group

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Support Information

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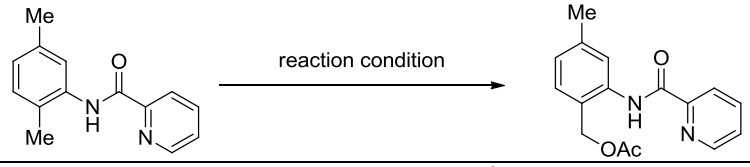
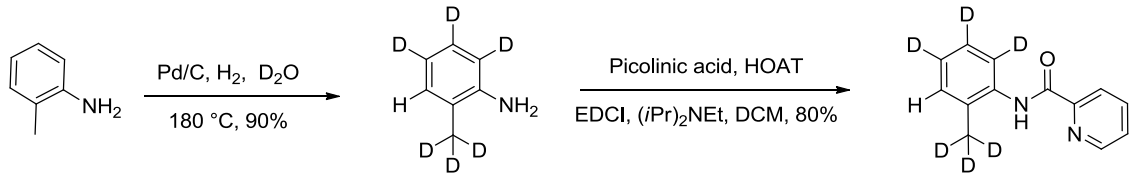
Condition screening



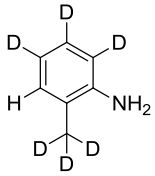
entry	cat	solvent	T (^{o}C)	additive	time (h)	conv. (%)[b]
1	--	DCE	110	--	24	N.R.
2	$Fe(acac)_3$	DCE	110	--	24	N.R.
3	$Ni(acac)_2$	DCE	110	--	24	N.R.
4	$Cp(Ph_3P)_2RuCl$	DCE	110	--	24	N.R.
5	$[RhCp^*Cl_2]_2$	DCE	110	--	24	N.R.
6	$[Cp^*Rh(CH_3CN)_3]$ $(SbF_6)_2$	DCE	110	--	24	N.R.
7	$[Ir(OCH_3)(C_8H_{12})]_2$	DCE	110	--	24	N.R.
8	$[Rh(OAc)_2]_2$	DCE	110	--	24	N.R.
9	$Pd(OAc)_2$	DCE	110	--	24	40
11	$Pd(OAc)_2$	Toluene	110	--	24	50
12	$Pd(OAc)_2$	DMF	110	--	24	25
13	$Pd(OAc)_2$	PivOH	110	--	24	30
14	$Pd(OAc)_2$	Toluene/HOAc (1ml/0.2ml)	110	--	24	50
15	$Pd(OAc)_2$	*t*-AmOH	110	--	24	N.R.
16	$Pd(OAc)_2$	Toluene	110	Li_2CO_3	24	48
17	$Pd(OAc)_2$	Toluene	110	KOAc	24	N.R.
18	$Pd(OAc)_2$	Toluene	110	KF	24	29
19	$Pd(OAc)_2$	Toluene	110	KOH	24	N.R.
20	$Pd(OAc)_2$	Toluene	110	$KHCO_3$	24	N.R.
21	$Pd(OAc)_2$	Toluene	110	Na_2CO_3	24	27
22	Pd(OAc)2	Toluene	110	K_2CO_3	24	27
23	$Pd(OAc)_2$	Toluene	110	AgOTf	24	N.R.
24	$Pd(OAc)_2$	Toluene	110	AgOAc	24	36
25	$Pd(OAc)_2$	Toluene	110	$AgPF_6$	24	N.R.
26	$Pd(OAc)_2$	Toluene	110	$AgClO_4$	24	N.R.
27	$Pd(OAc)_2$	Toluene	110	$AgSbF_6$	24	N.R.
28	$Pd(OAc)_2$	Toluene	130	--	24	52
29	$Pd(OAc)_2$	Toluene	110		24	50
30	$Pd(OAc)_2$	Toluene	90	--	24	20
31	$Pd(OAc)_2$	Toluene	70	--	24	N.R.
32	$Pd(OAc)_2$	Toluene	50	--	24	N.R.
33	$Pd(OAc)_2$	Toluene	110	--	1	10
34	$Pd(OAc)_2$	Toluene	110	--	4	20
35	$Pd(OAc)_2$	Toluene	110	--	8	33
36	$Pd(OAc)_2$	Toluene	110	--	16	40
37	$Pd(OAc)_2$	Toluene	110	--	48	72

[a] Reaction condition: substrate (22.6 mg, 0.1 mmol, 1equiv.), $PhI(OAc)_2$ (64 mg, 0.2 mmol, 2 equiv.) additive (0.1 mmol, 1 equiv.) and cat. (0.01 mmol, 0.1 equiv.) were placed in a seal tube. The reaction vessel was degassed/backfilled with argon three times and the solvent (0.5 mL) was added. The reaction mixture was placed in an oil bath (T ˚C) and stirred for indicate time. [b] The conversion was calculated by GC-MS using biphenyl as internal standard. [c] Isolated yield.

KIE Experiment for Isotope Effect

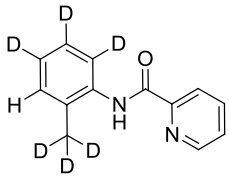


***d*^{6}-o-toluidine**



o-Toluidine (214 mg, 2 mmol, 1 equiv) and Pd/C (42 mg, 20% wt%) were placed in a sealed tube, D_2O (12 mL) was added. The reaction vessel was degassed and flushed with H_2 three times. The tube was capped and heated to 180 ˚C for 24 hour. The catalyst was by filtering through Celite. The solution was extracted with DCM. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concertrated to give *d*^{6}-*o*-toluidine (203 mg, 90%) as a colorless oil. The product was directly used for the next steo without further purifaction.

Compound *d*^{6}-1j

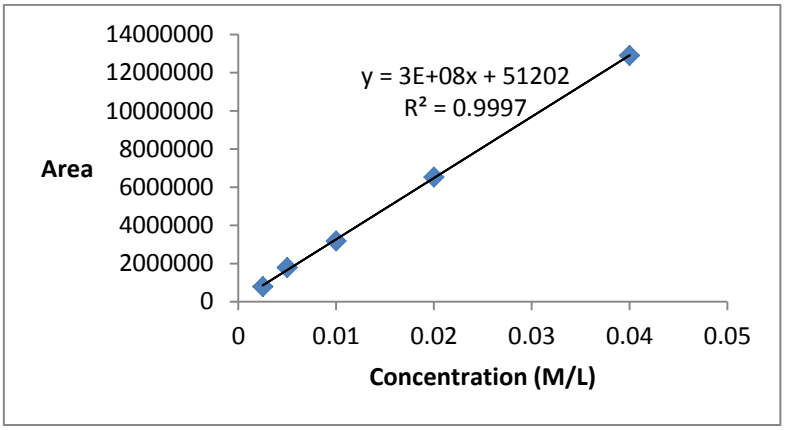


d^6-*o*-toluidine (812 mg, 4 mmol, 1 equiv) and 2-Picolinic acid (0.73 g, 6 mmol, 1.5 equiv) were dissolved in DCM (25 mL). HOAT (0.59 g, 4.4 mmol, 1.1 equiv) and EDCI (0.84 g, 11 mmol, 1.1 equiv) were added sequentially, followed by (*i*Pr)$_2$NEt (1.55 g, 12 mmol, 3 equiv). The reaction mixture was stirred at rt for 24 h. washed using sat. $NaHCO_3$, and extracted with DCM three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel flash column chromatograph (EtOAc:Hexane = 1:10) to give compound ***d*^{6}-1j** (697 mg, 80%). R_f = 0.3 (Hexane/EtOAc = 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.64 (d, *J* = 3.9 Hz, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 7.92 (t, *J* = 7.7 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.25 (d, *J* = 14.6 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ161.87, 150.21, 148.08, 137.59, 135.94, 130.29, 127.90, 126.63, 126.35, 124.25, 122.33, 121.06, 16.85.

Stardard Concertation Curve of *d*^{6}-2j

The ethanol solution (1 mL) of ***d*^{6}-2j** (0.0025 M/L, 0.05 M/L, 0.01 M/L, 0.02 M/L, 0.04 M/L) were prepared, and the absorption area of ***d*^{6}-2j** (0.0025 M/L, 0.05 M/L, 0.01 M/L, 0.02 M/L, 0.04 M/L) were masured under follow condition: Ethanol/n-Hexane = 40/60, flow rate = 1.0 mL/min, λ = 271 nm, retention time: 3.6 min (***d*^{6}-2j**).

Concertration (***d*^{6}-2j**)	Absorption Area
0.0025	783369
0.05	1578382
0.01	3177289
0.02	6525472
0.04	12895330



With 1j as substrate

Five parallel reactions were performed side-by-side as the following: Compound **1j** (21.6 mg, 0.1 mmol, 1 equiv), $PhI(OAc)_2$ (64 mg, 0.2 mmol, 2 equiv) and $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.1 equiv) were weighted into a Schlenk tube, which was capped using a rubber septum. The reaction tube was degassed and backfilled with argon three times. Toluene (1 mL) was added via a syringe. The reaction mixture was sitrred at 110 ˚C for the below indicated time. The solvent was removed under vacuum. The solvent was removed under vacuum. the crude was dissolved in ethanol (1 mL). the absorption area of **2j** was determined by HPLC. And then the conversion of the acetoxyaltion of **1j** was caulated by comparing the absorpition area with stardard concertration curve.

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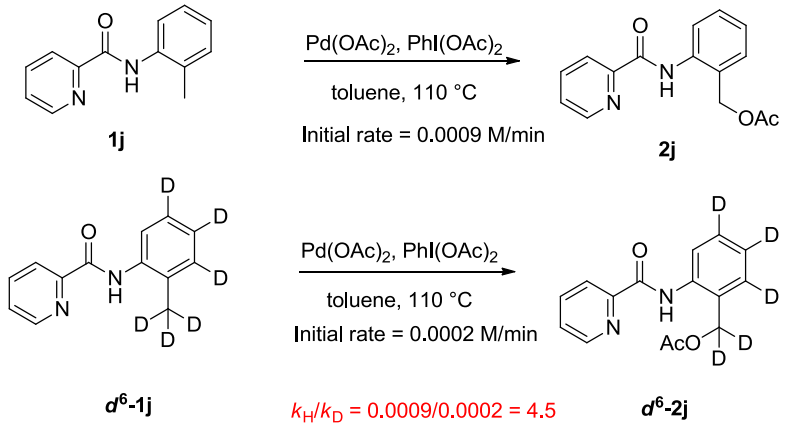
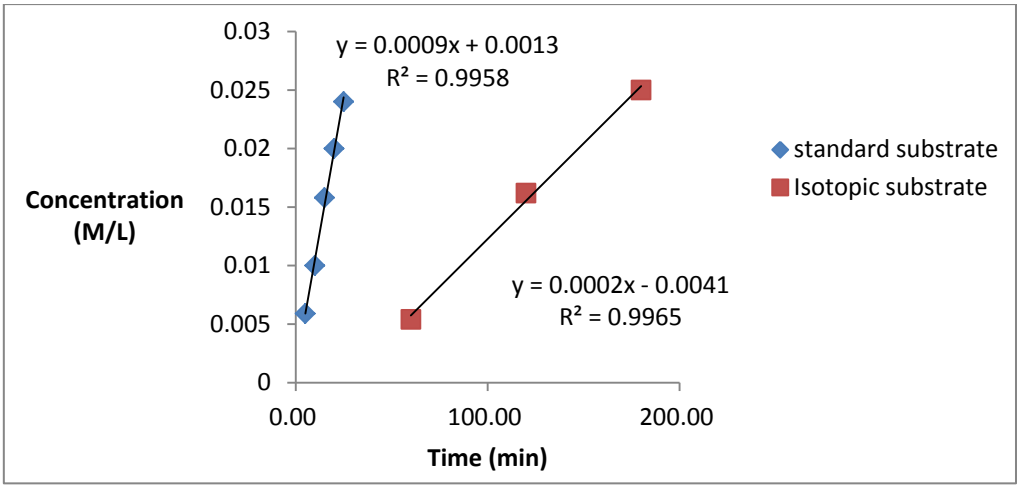
Time (min)	Concertration (M/L)
5	0.0059
10	0.01
15	0.0158
20	0.02
25	0.024

With d^6-1j as substrate

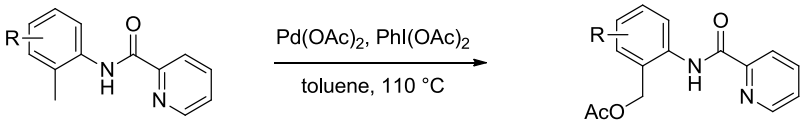
Three parallel reactions were performed side-by-side as the following: Compound ***d*^{6}-1j** (11.4 mg, 0.05 mmol, 1 equiv), $PhI(OAc)_2$ (32 mg, 0.1 mmol, 2 equiv) and $Pd(OAc)_2$ (1.2 mg, 0.005 mmol, 0.1 equiv) were weighted into a Schlenk tube, which was capped using a rubber septum. The reaction tube was degassed and backfilled with argon three times. Toluene (1 mL) was added via a syringe. The reaction mixture was sitrred at 110 ˚C for the below indicated time. The solvent was removed under vacuum. the crude was dissolved in ethanol (1 mL). the absorption area of d^6-**2j** was determined by HPLC. And then the conversion of the acetoxyaltion of ***d*^{6}-1j** was caulated by comparing the absorpition area with stardard concertration curve.

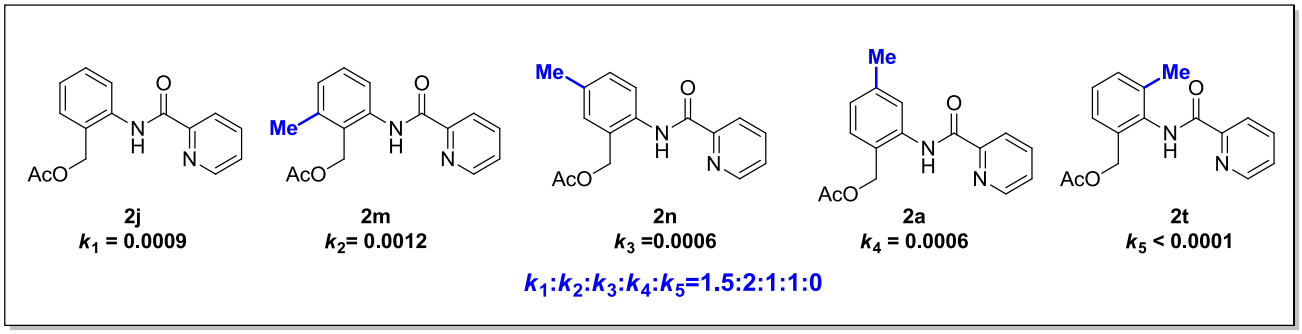
Time (min)	Concertration (M/L)
60	0.0054
120	0.0162
180	0.025





Rate Constants of Substrates with an Additional Methyl at Different Positions.

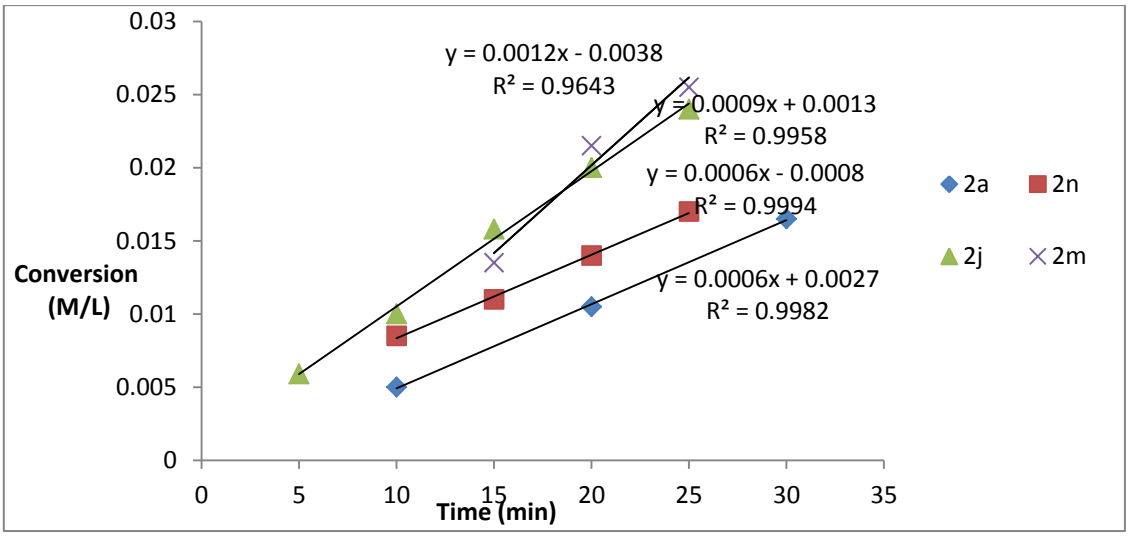




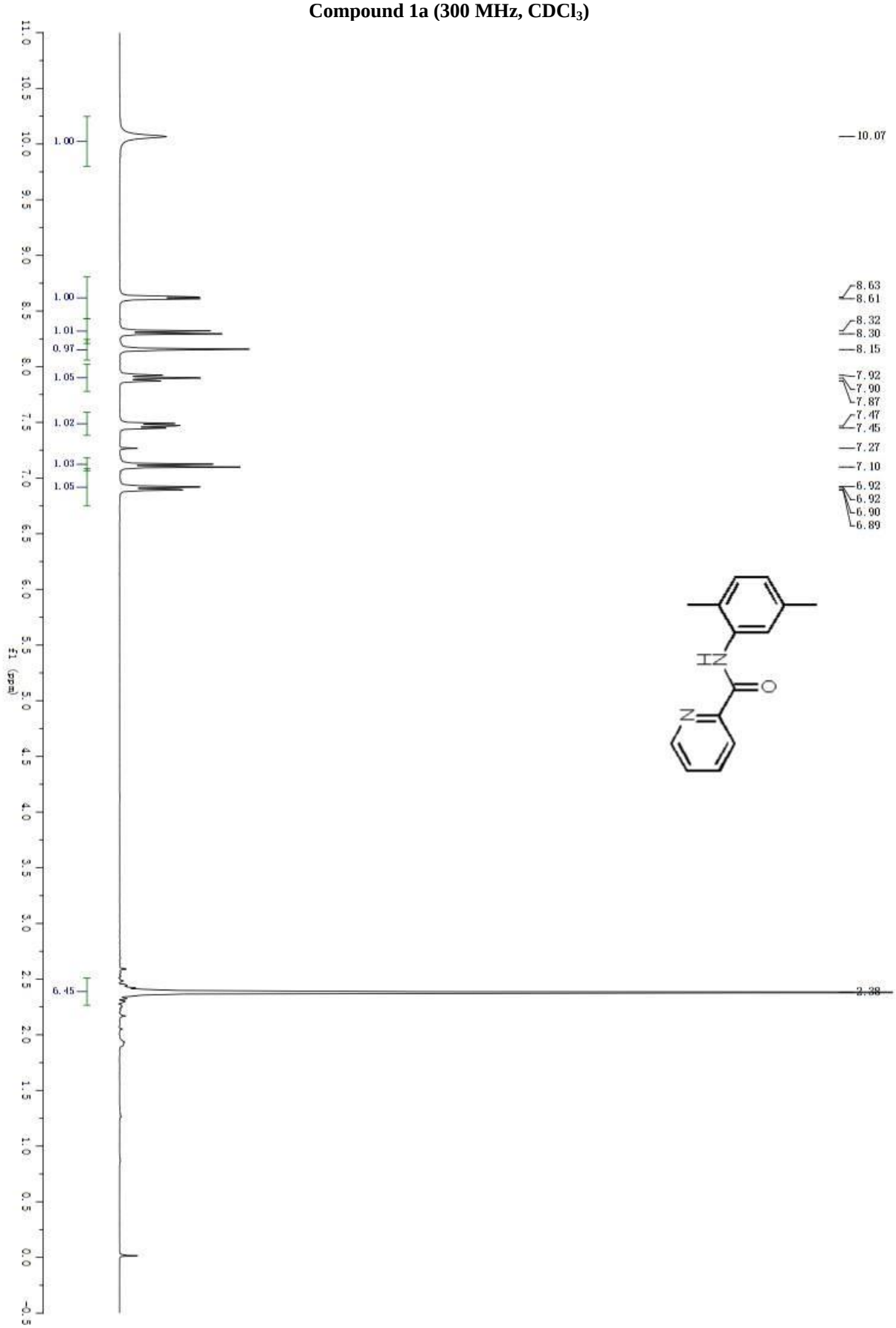
The rate constant was determined similarly as described above.

Time (min)	Concertration (M/L)				
	2a	**2j**	**2m**	**2n**	**2t**
5		0.0059			N.R.
10	0.005	0.01		0.0085	N.R.
15		0.0158	0.0135	0.011	N.R.
20	0.0105	0.02	0.0215	0.014	N.R.
25		0.024	0.0255	0.017	N.R.
30	0.0165		0.0375	0.022	N.R.

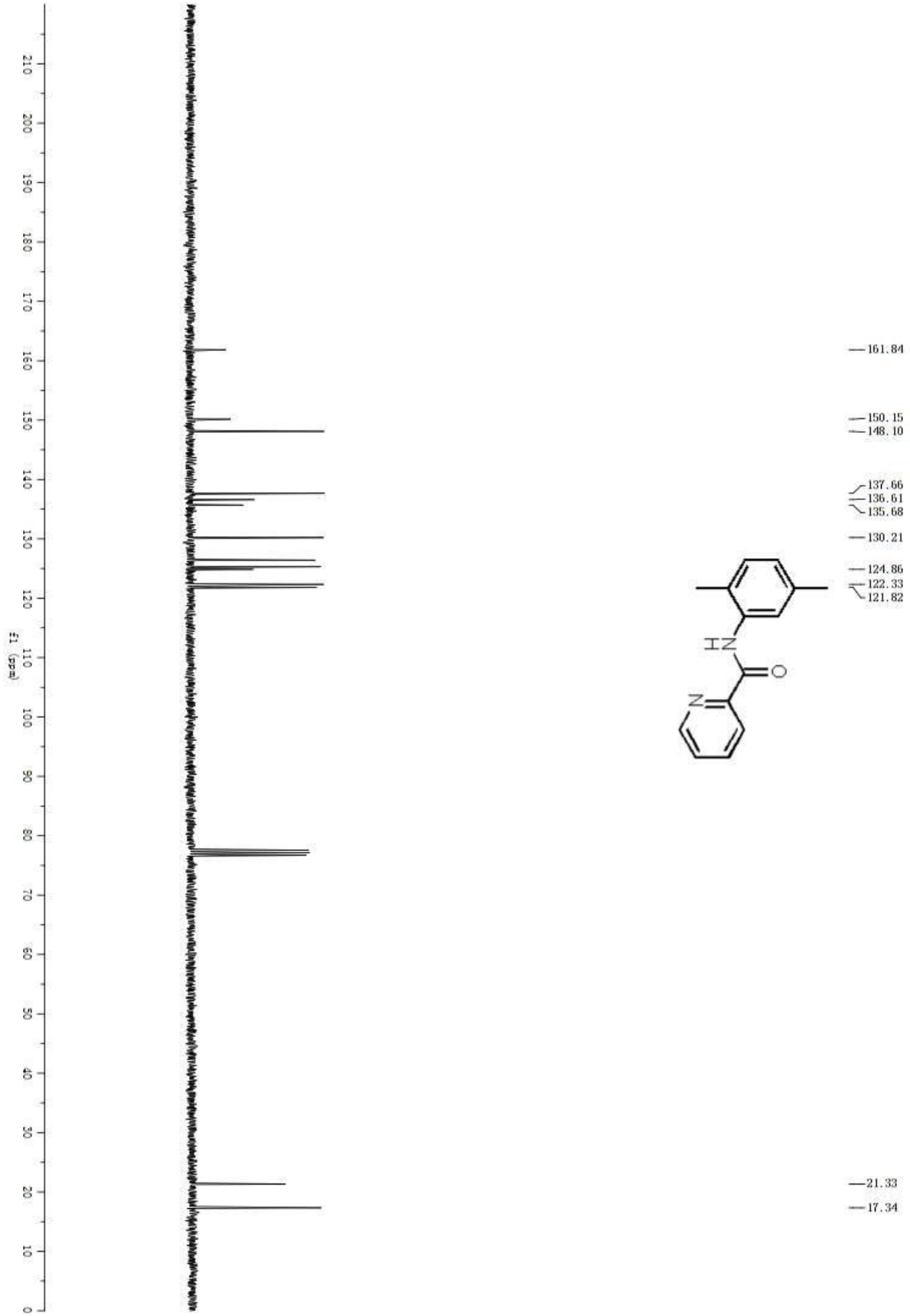
35					N.R.
40	0.021				N.R.
45					N.R.
50	0.024				N.R.
55					N.R.
60	0.0275				N.R.



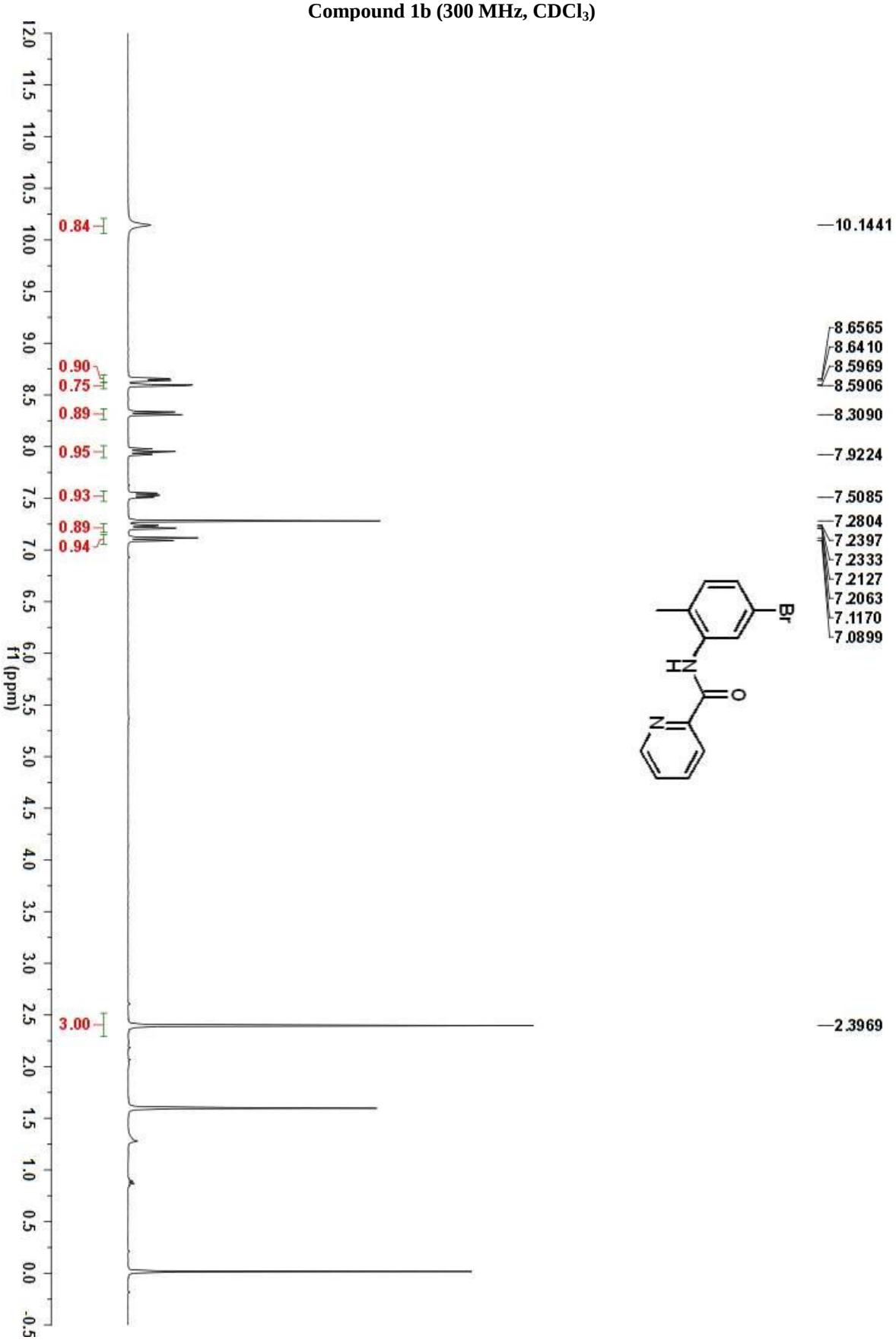
Compound 1a (300 MHz, $CDCl_3$)



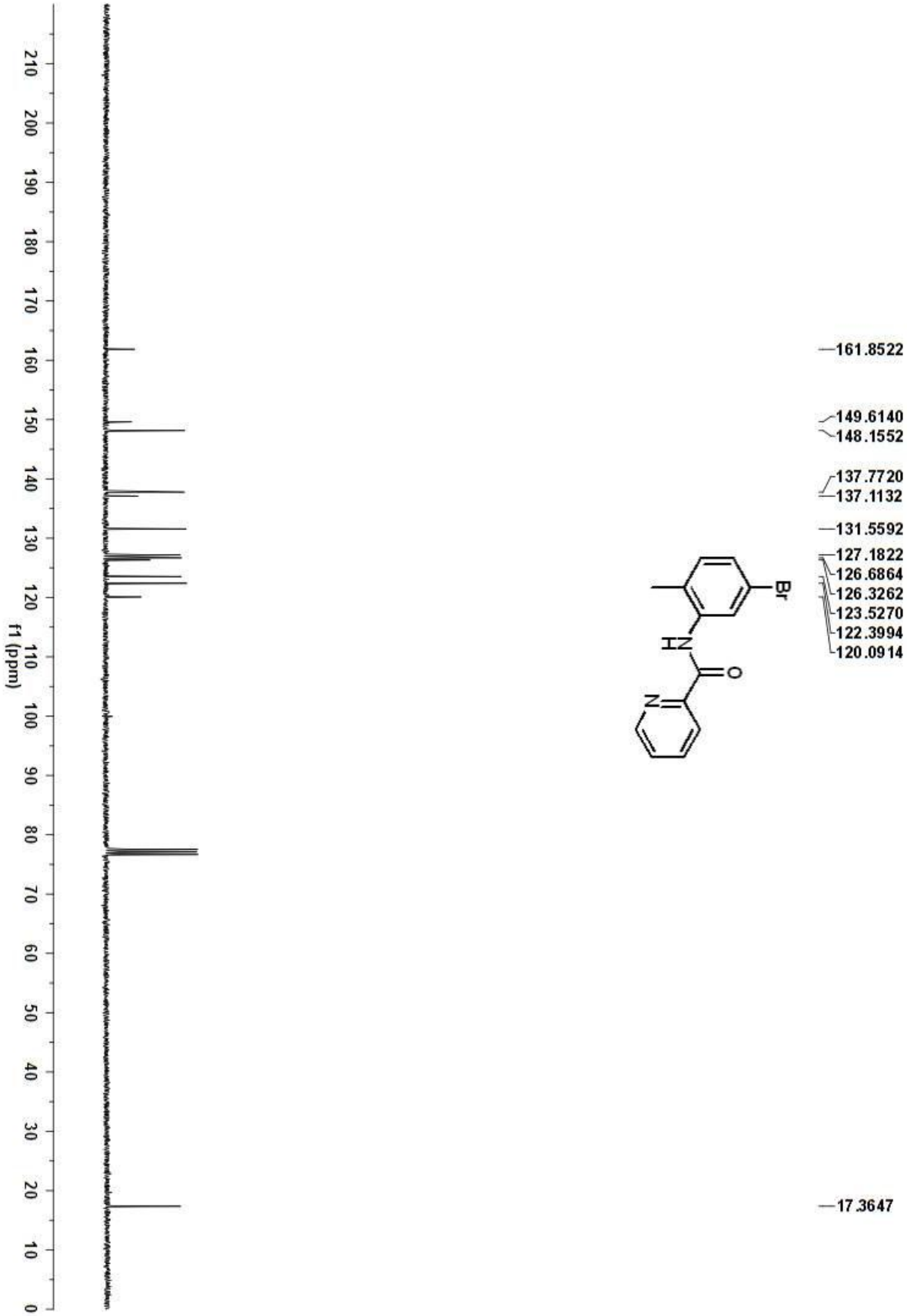
Compound 1a (75 MHz, $CDCl_3$)



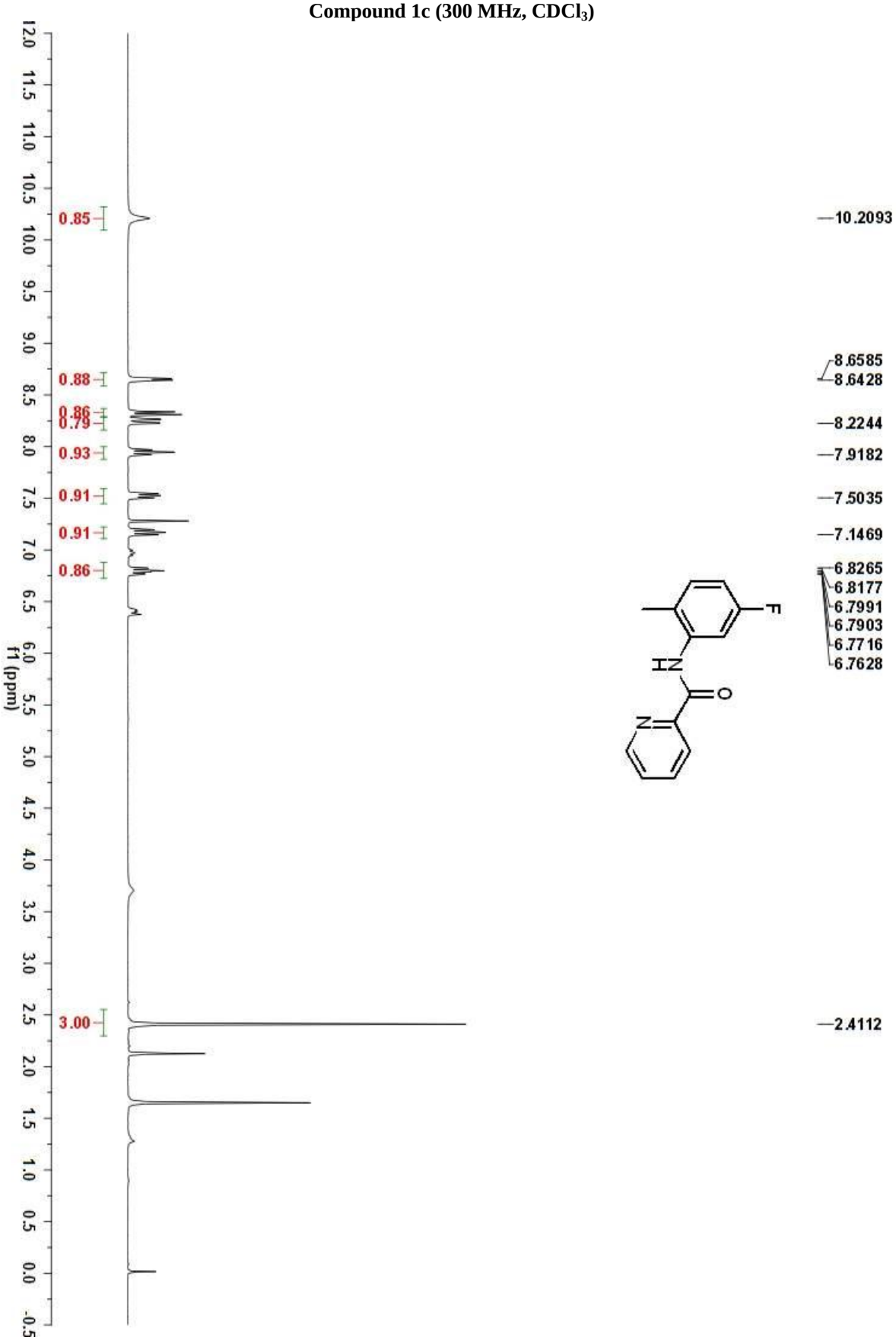
Compound 1b (300 MHz, $CDCl_3$)



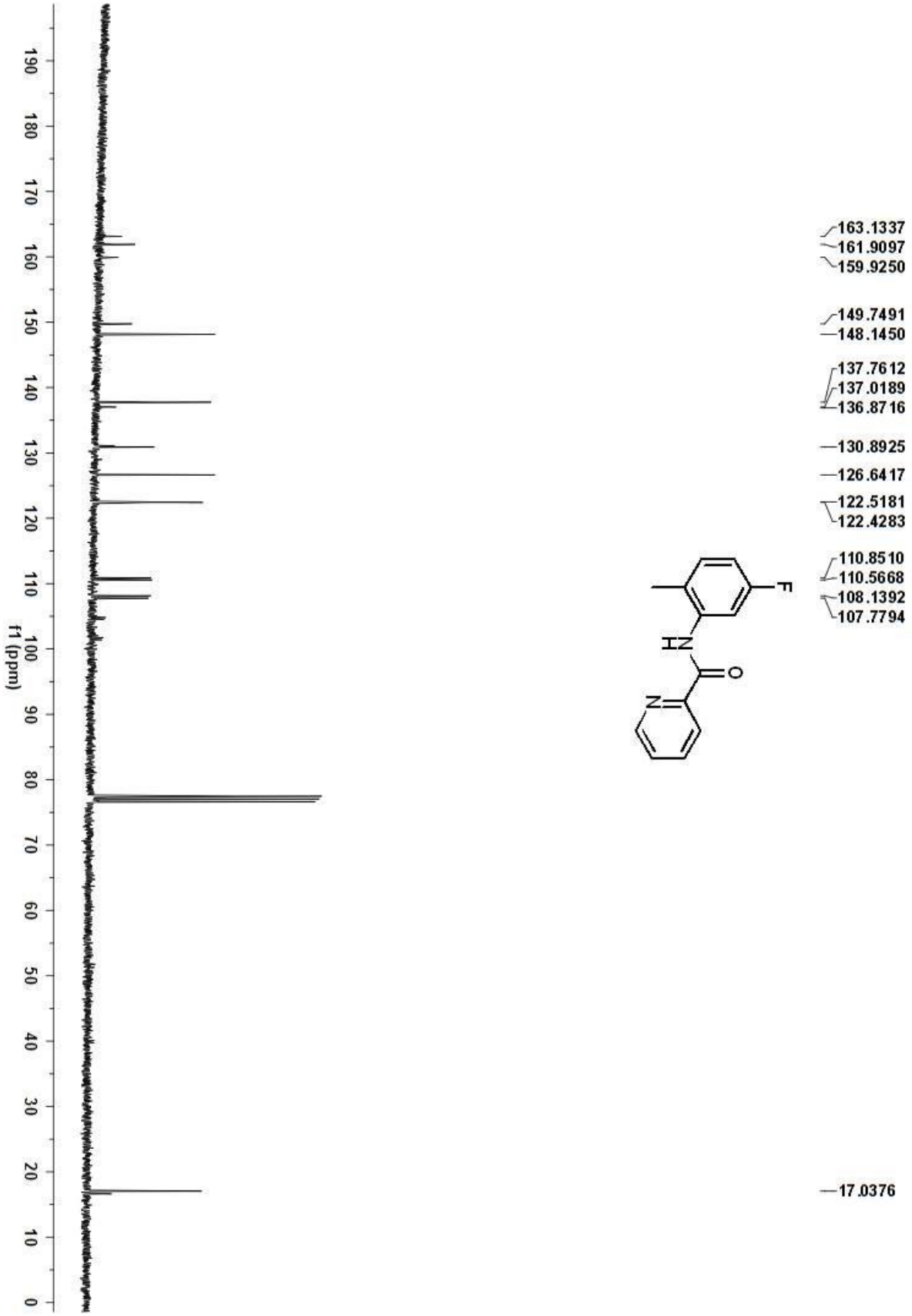
Compound 1b (75 MHz, $CDCl_3$)



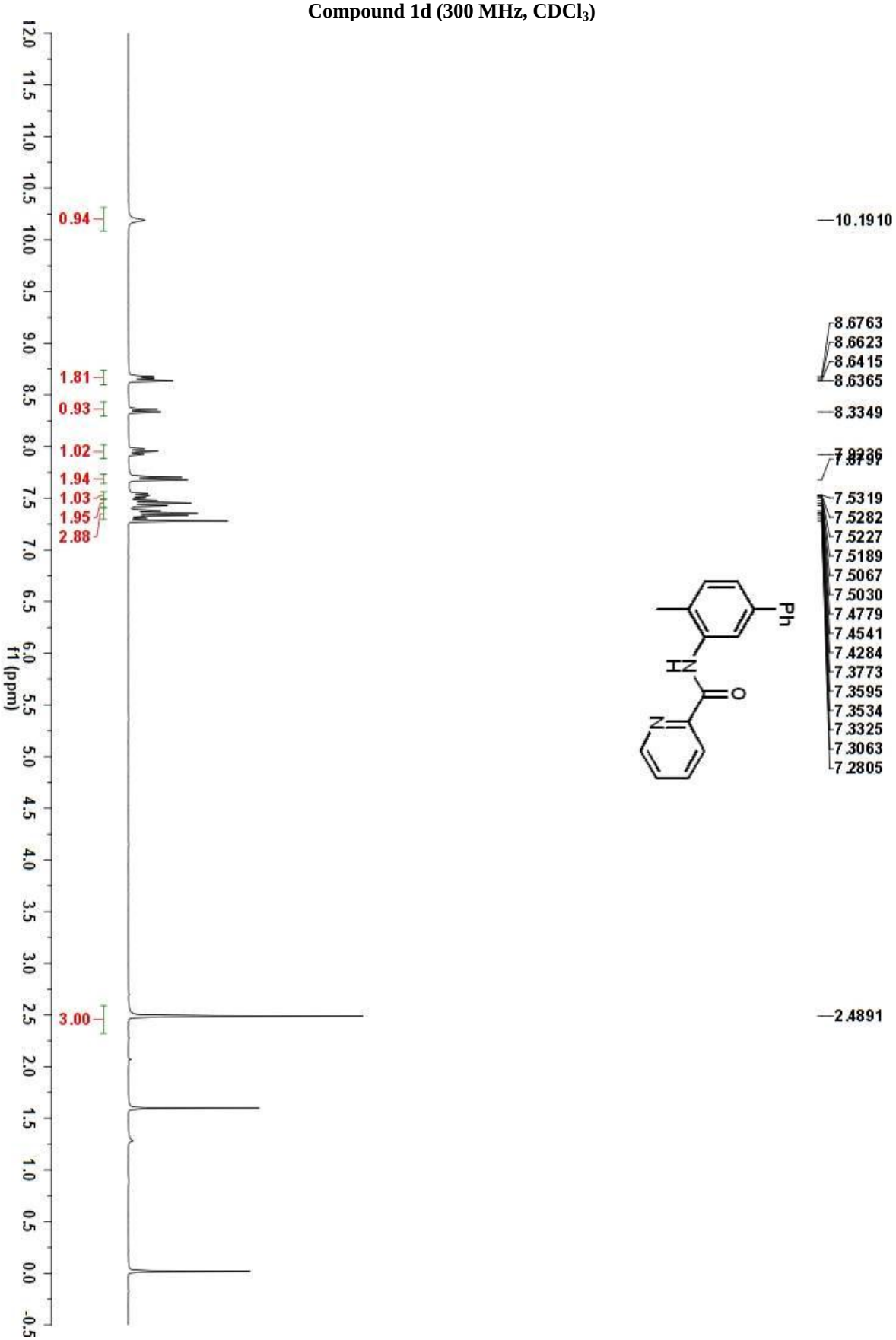
Compound 1c (300 MHz, $CDCl_3$)



Compound 1c (75 MHz, $CDCl_3$)



Compound 1d (300 MHz, $CDCl_3$)



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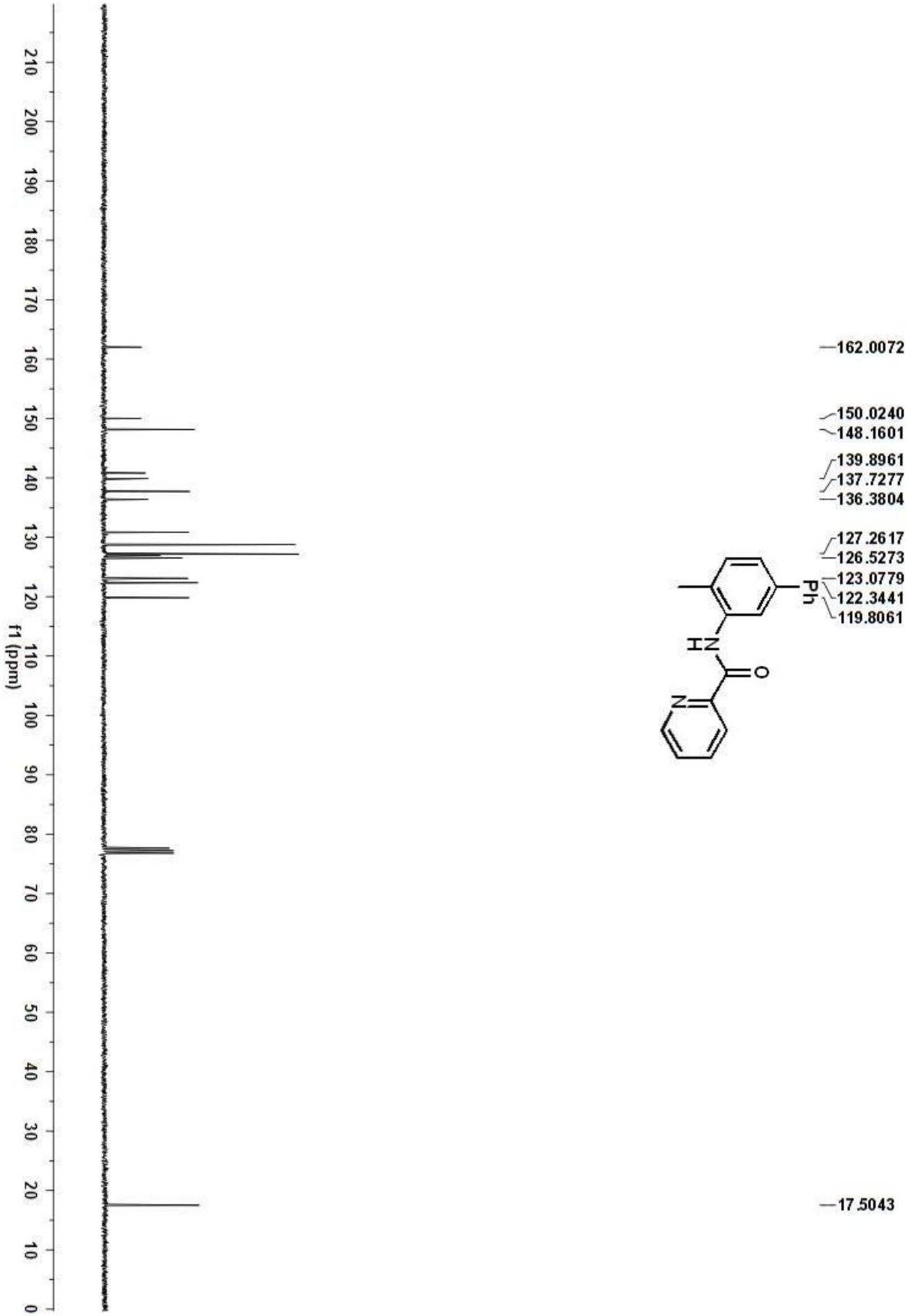

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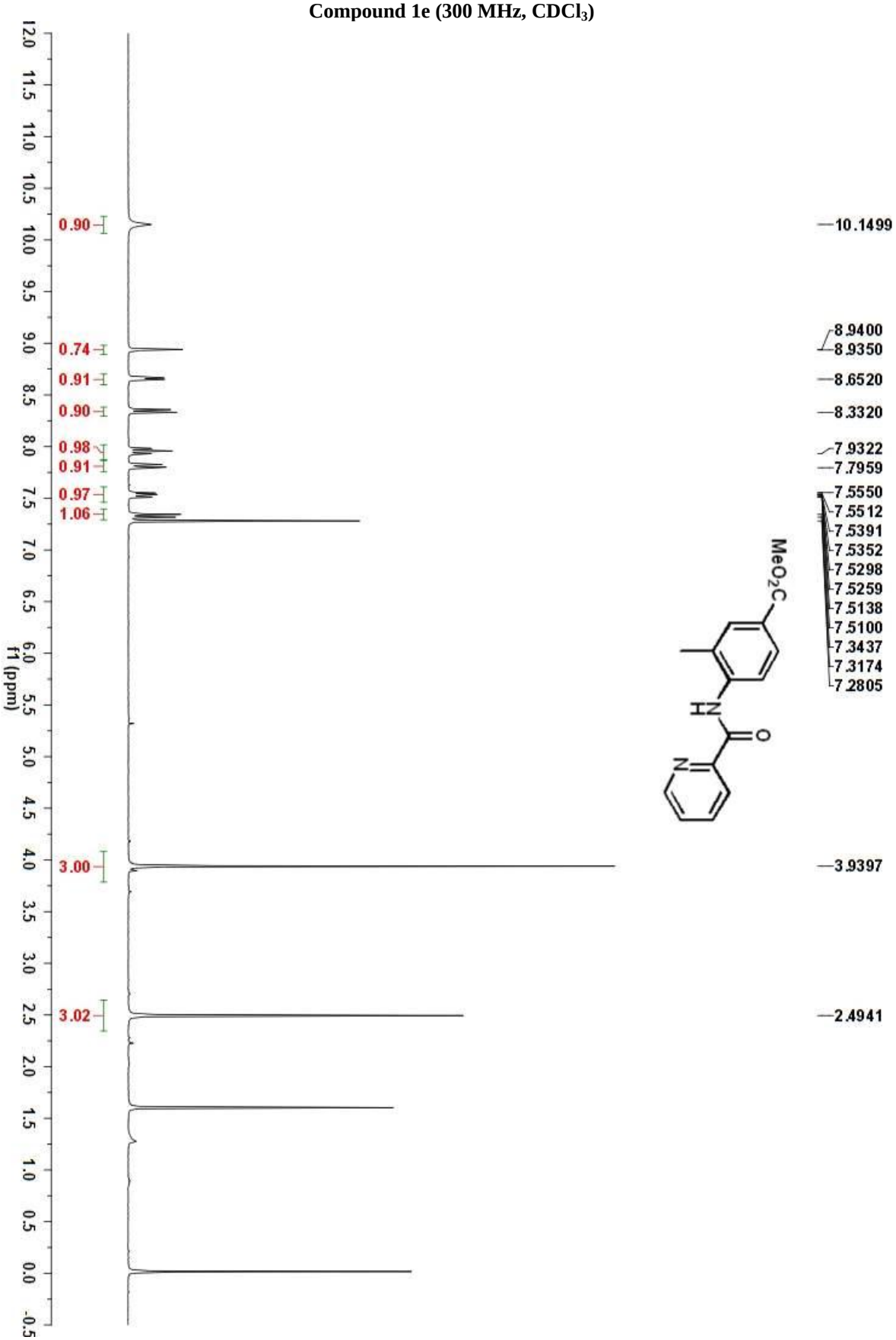
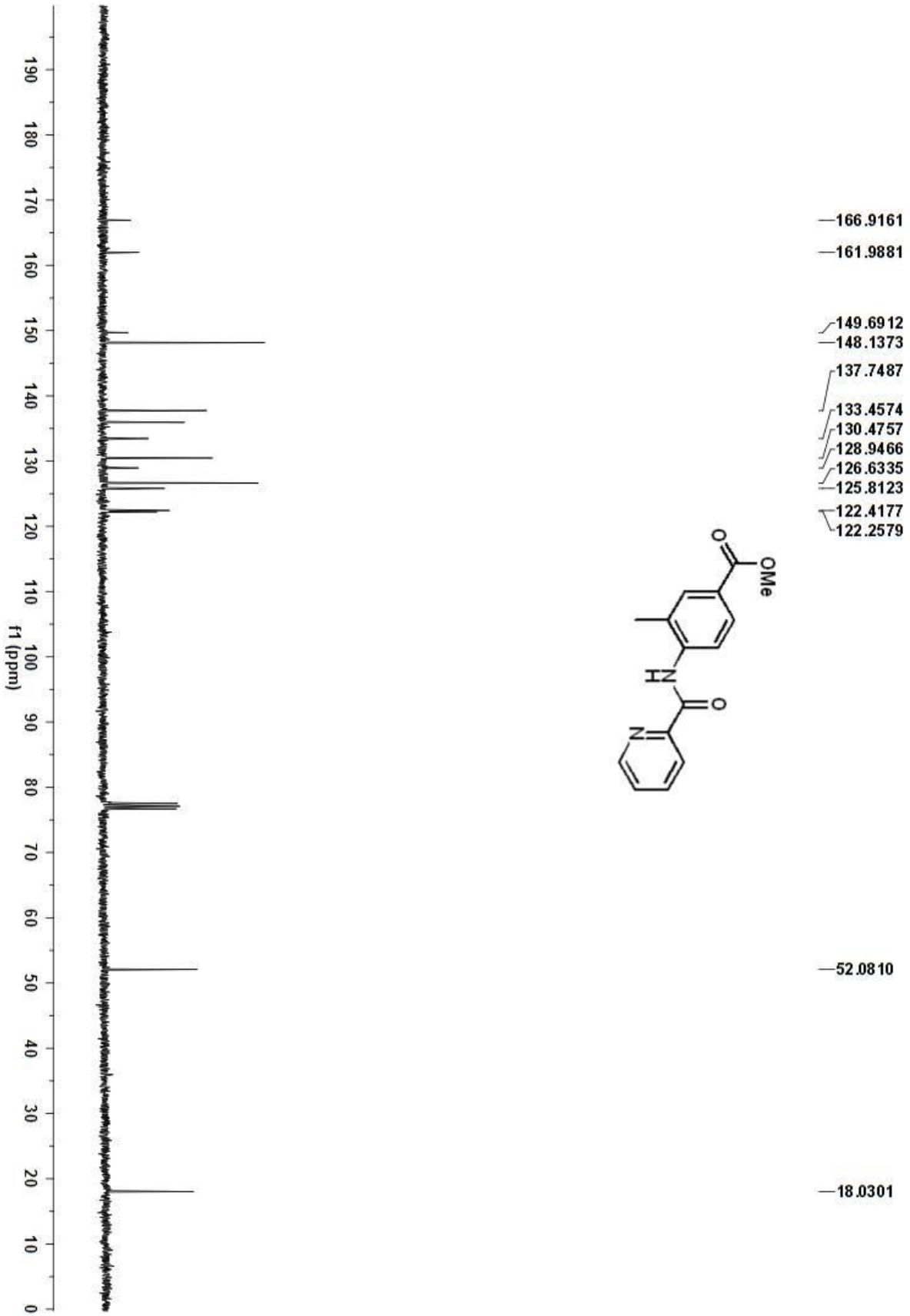


Compound 1e (75 MHz, $CDCl_3$)



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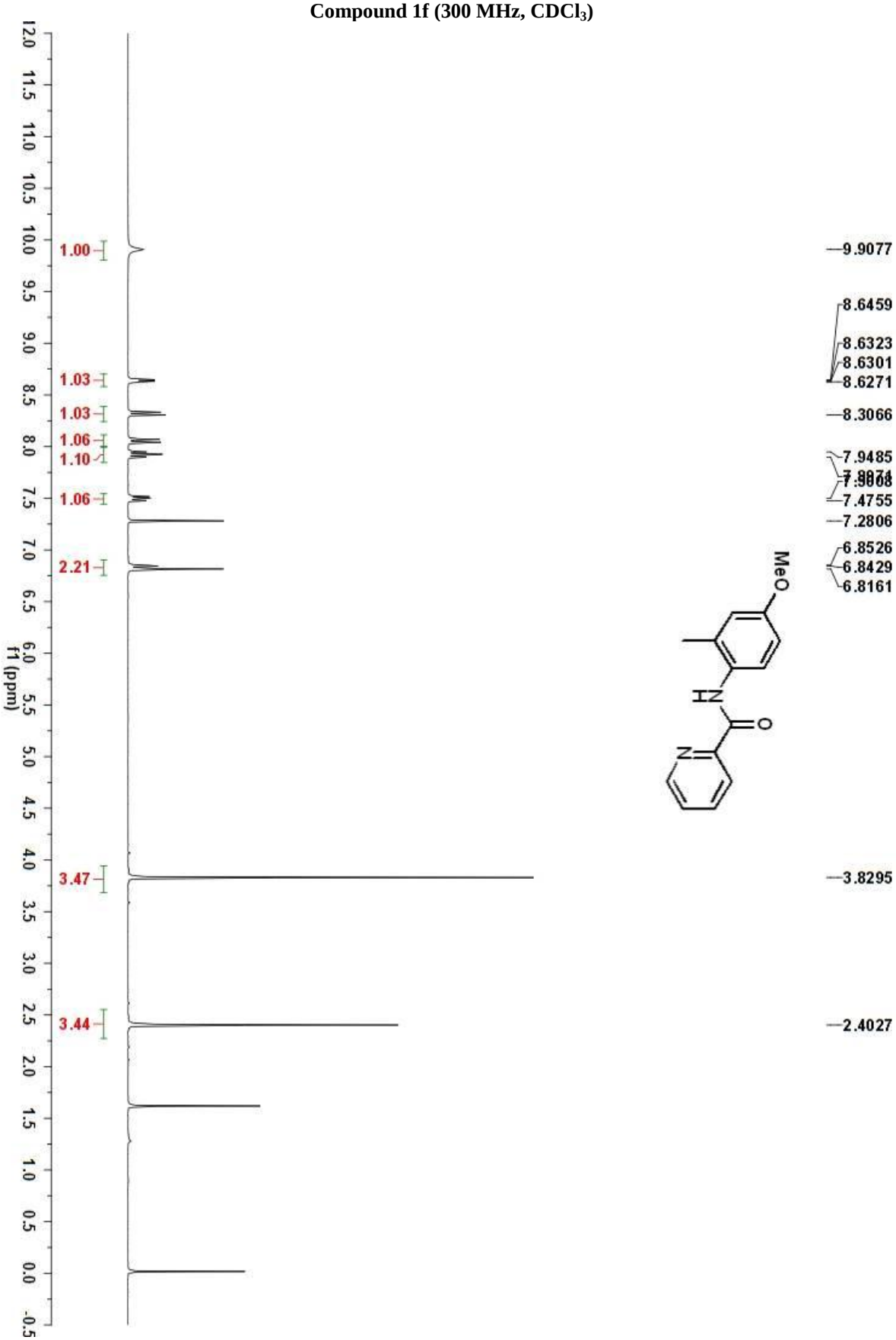

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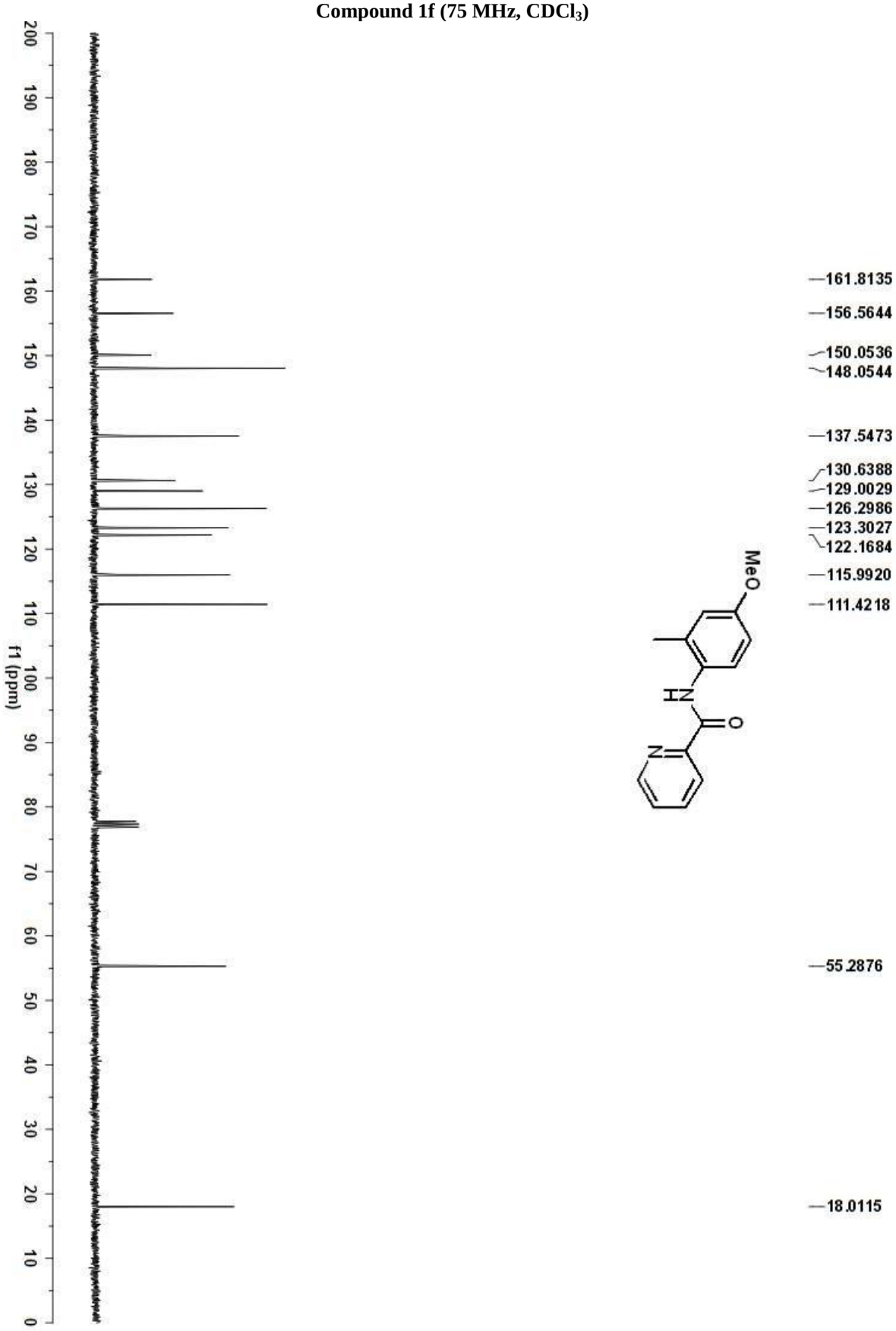

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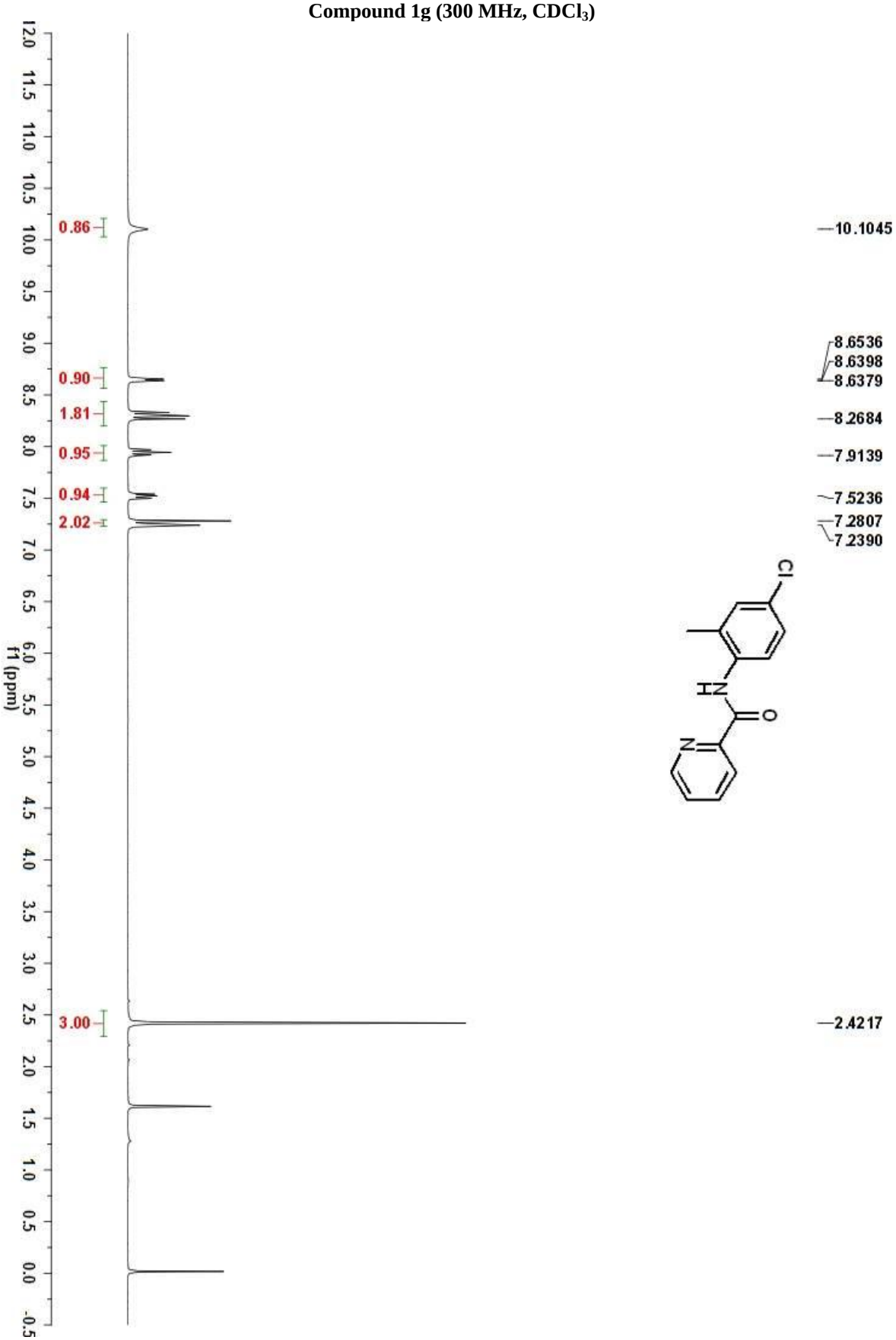

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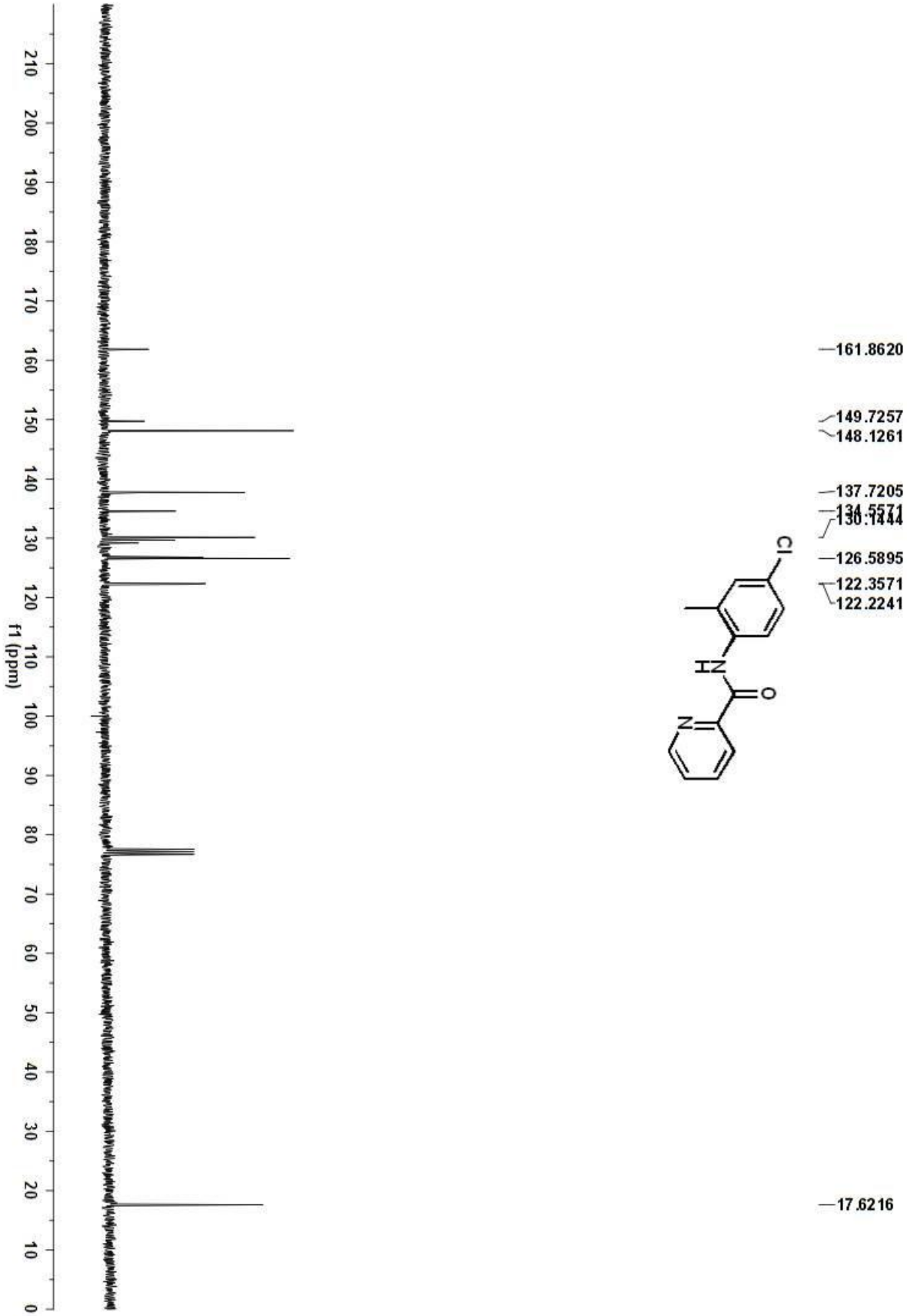

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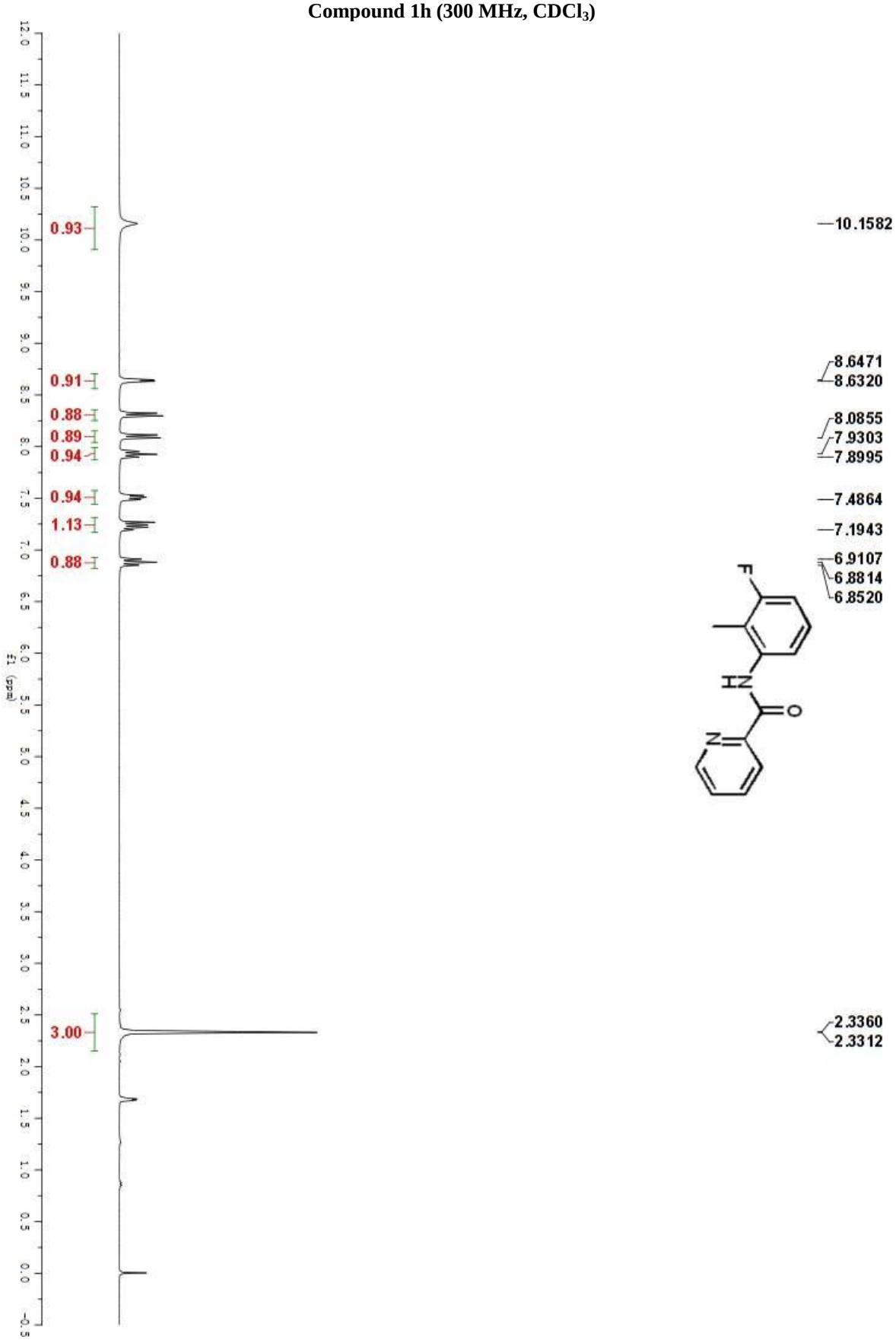

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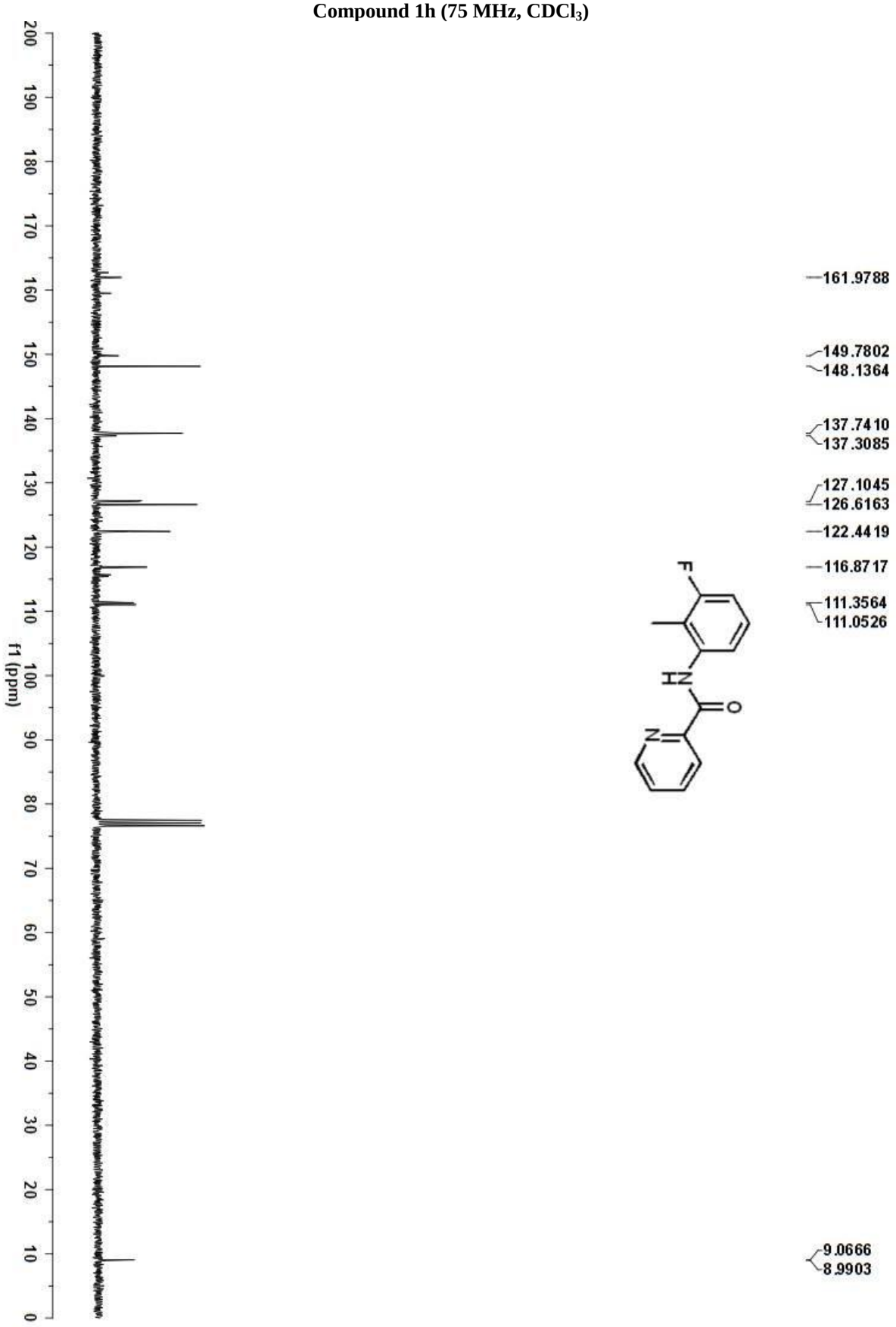

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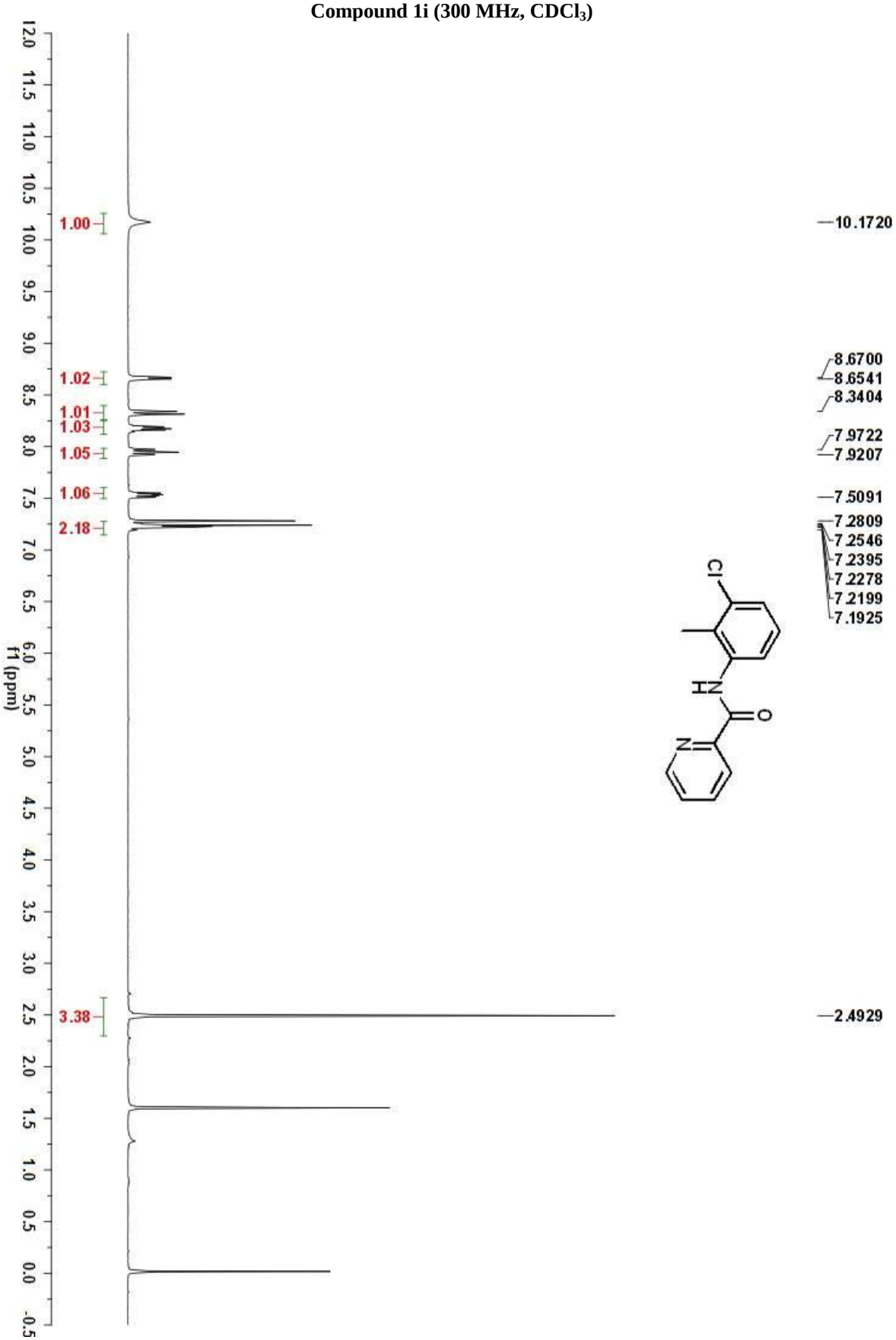

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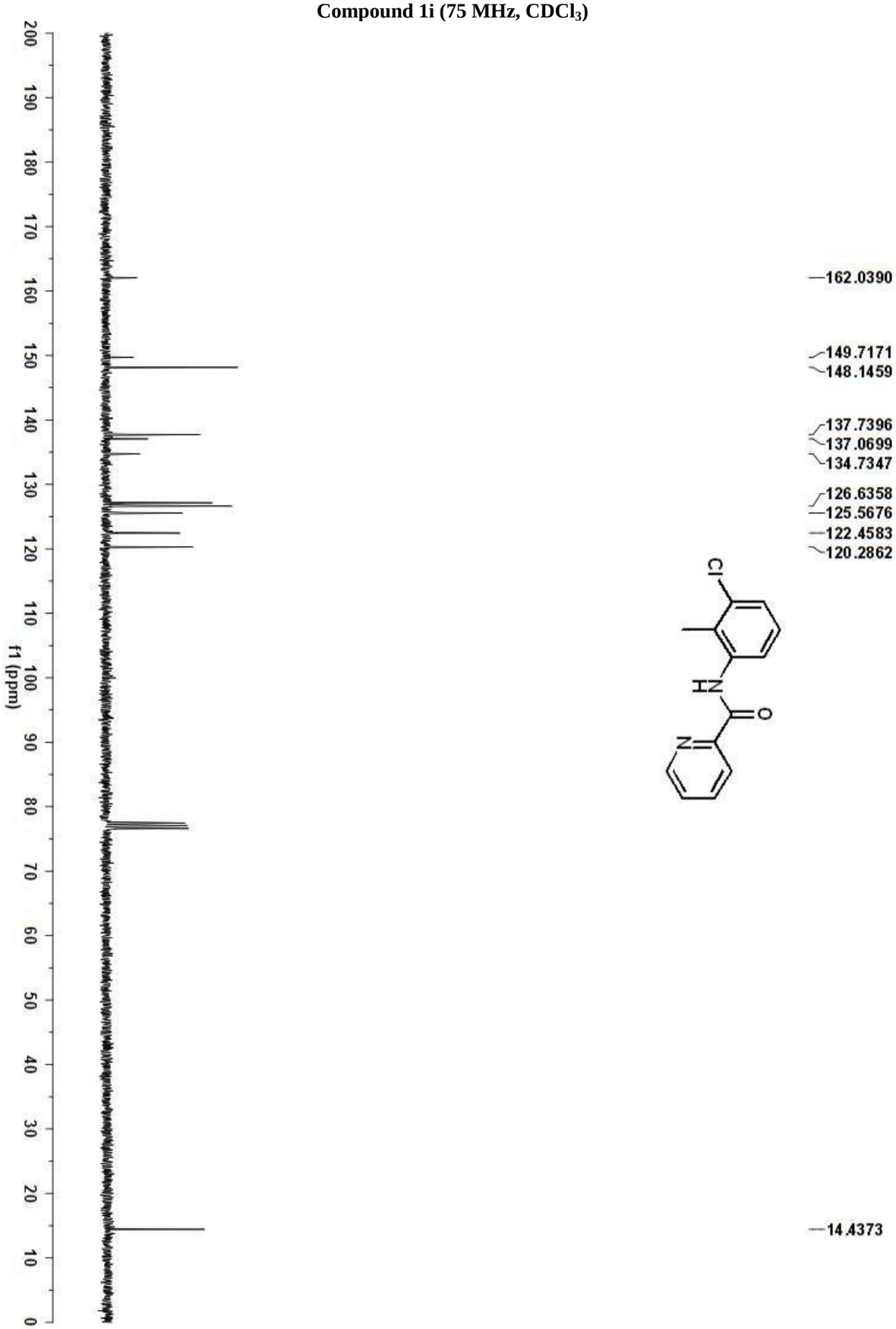

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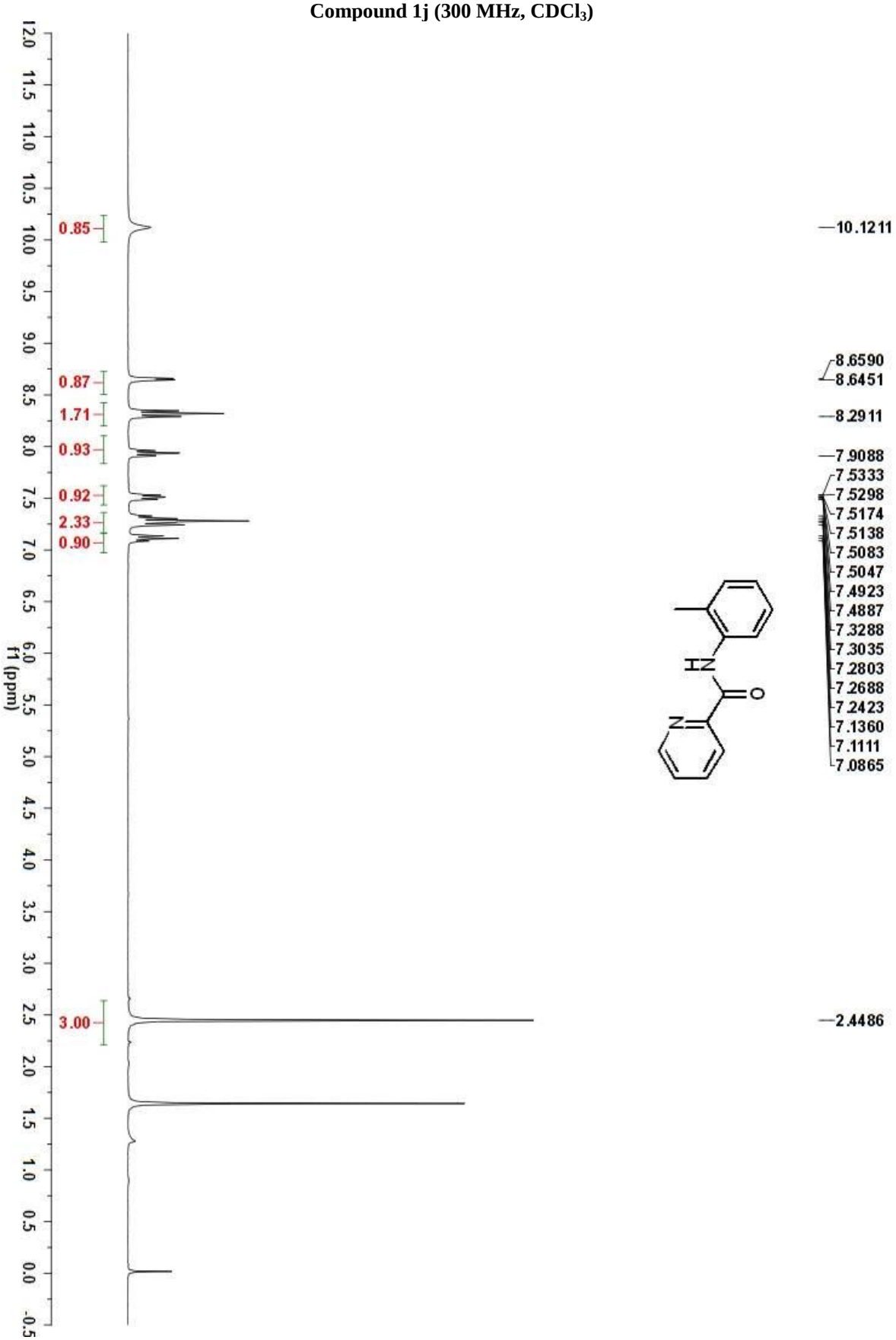

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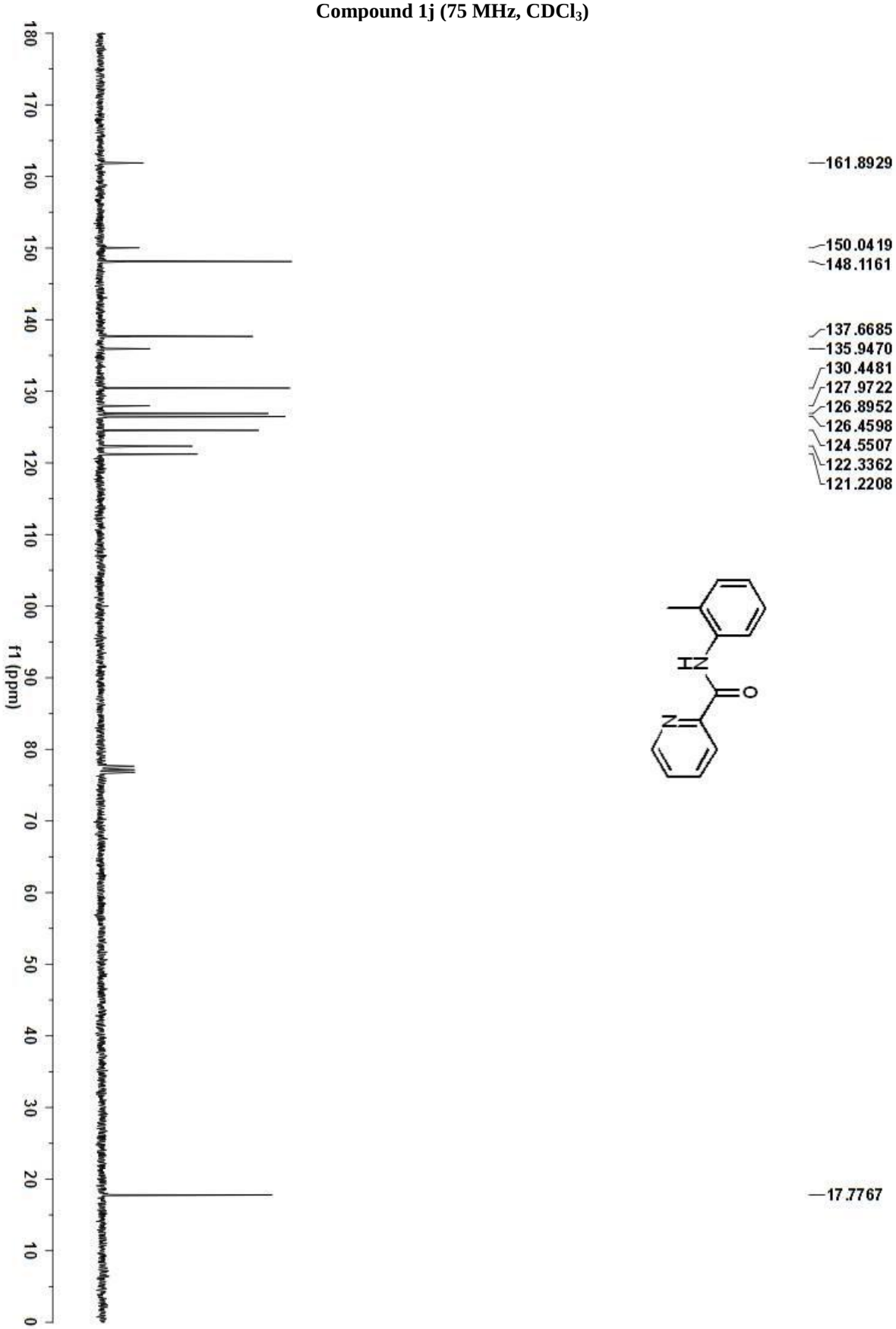

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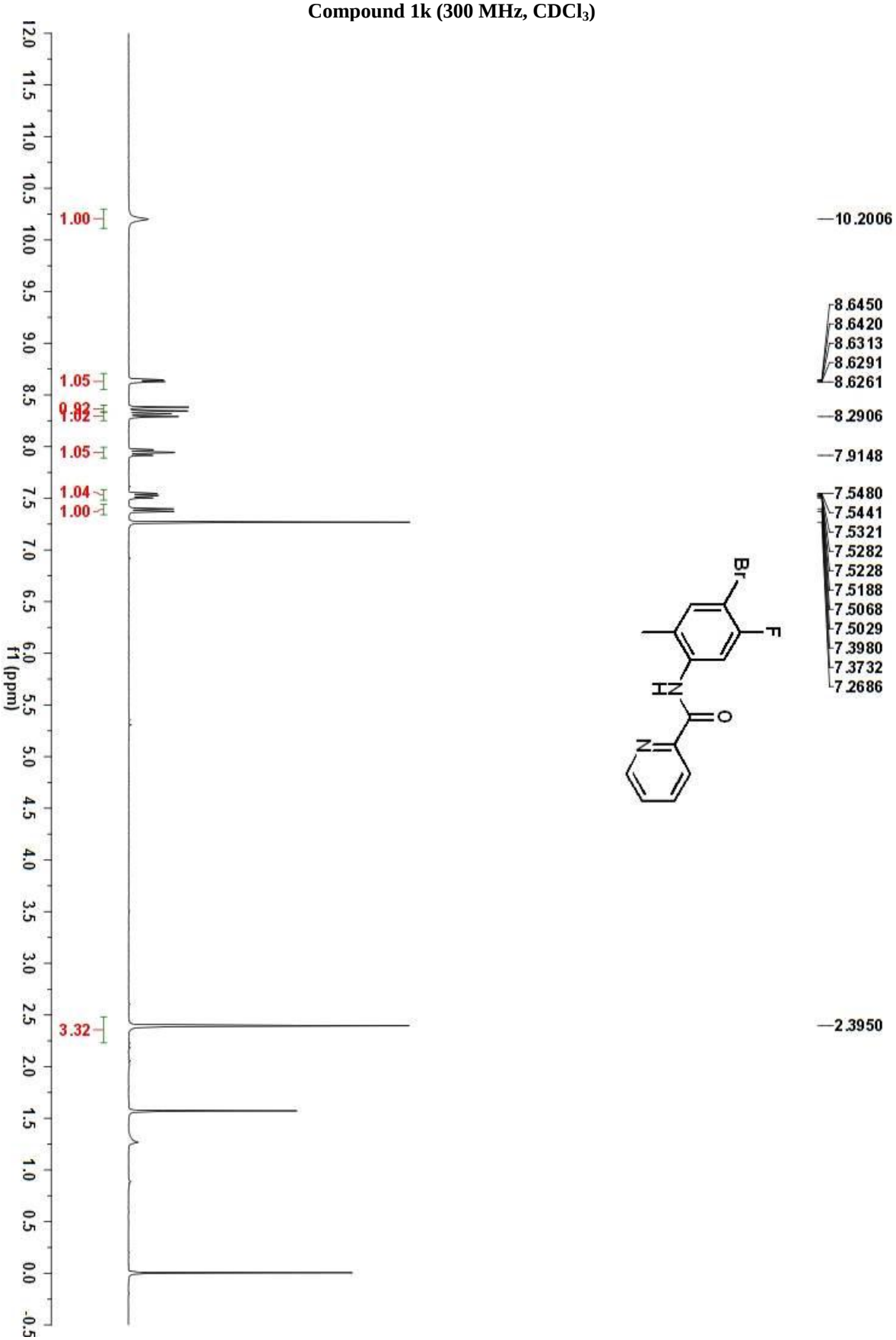

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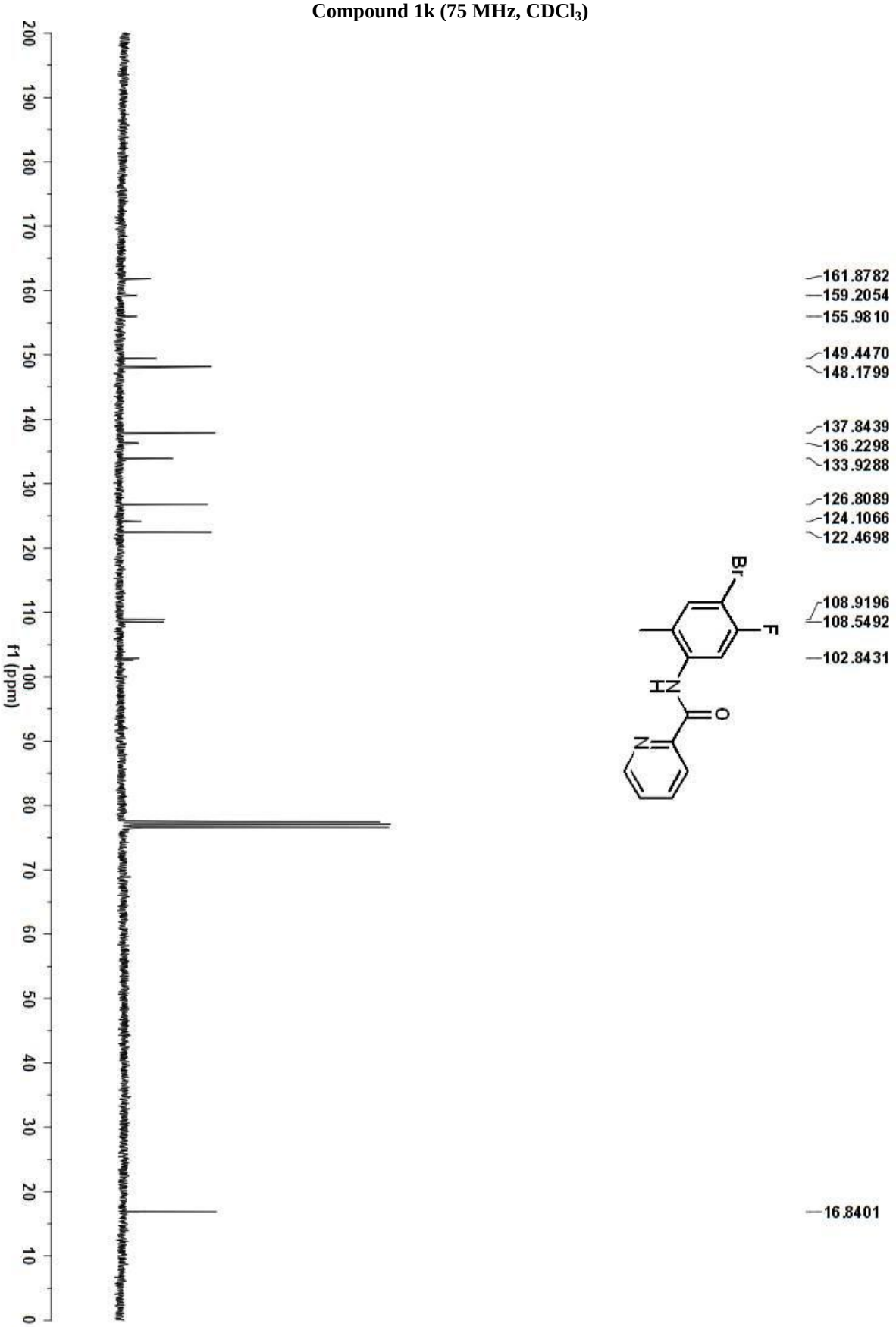

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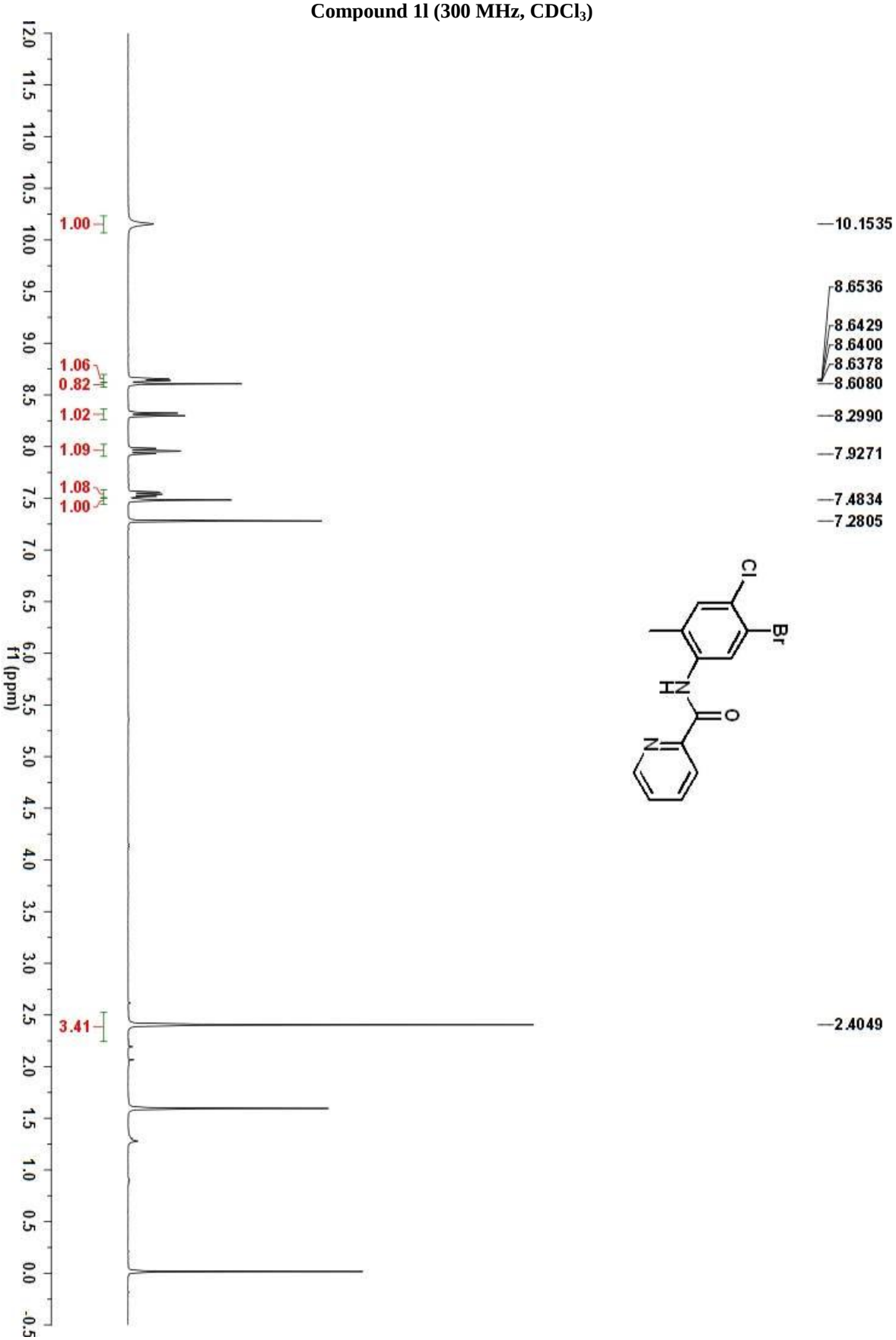

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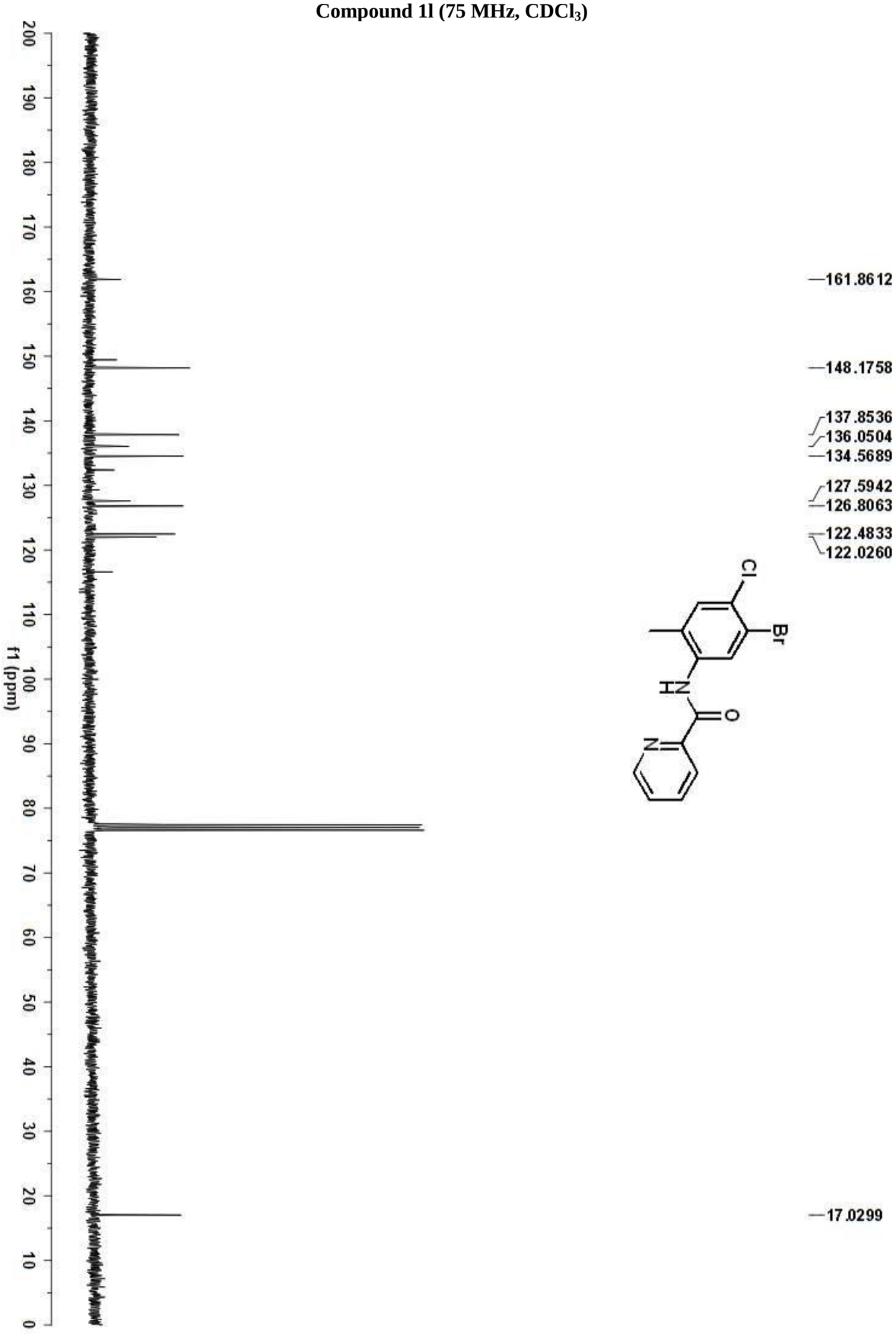

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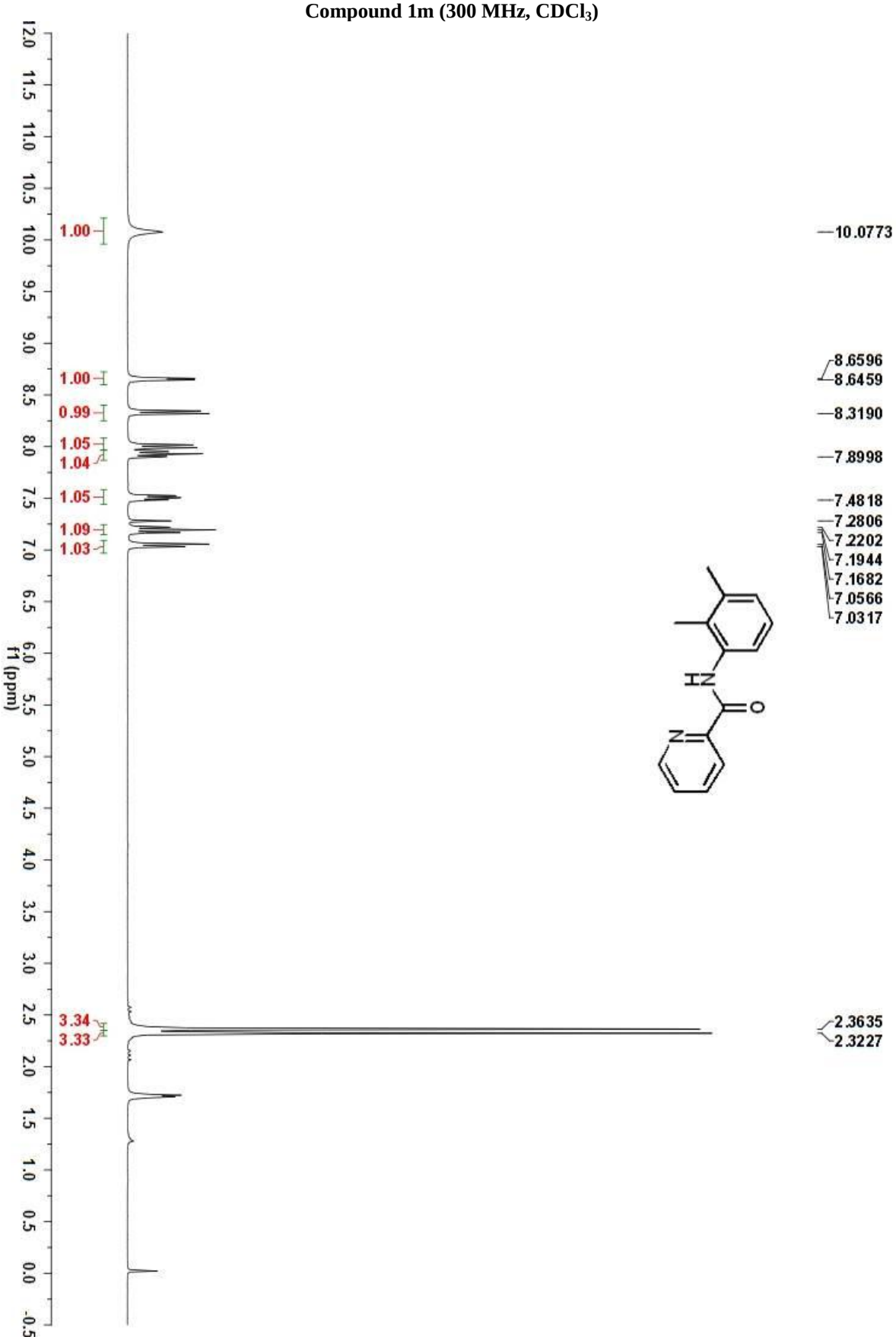

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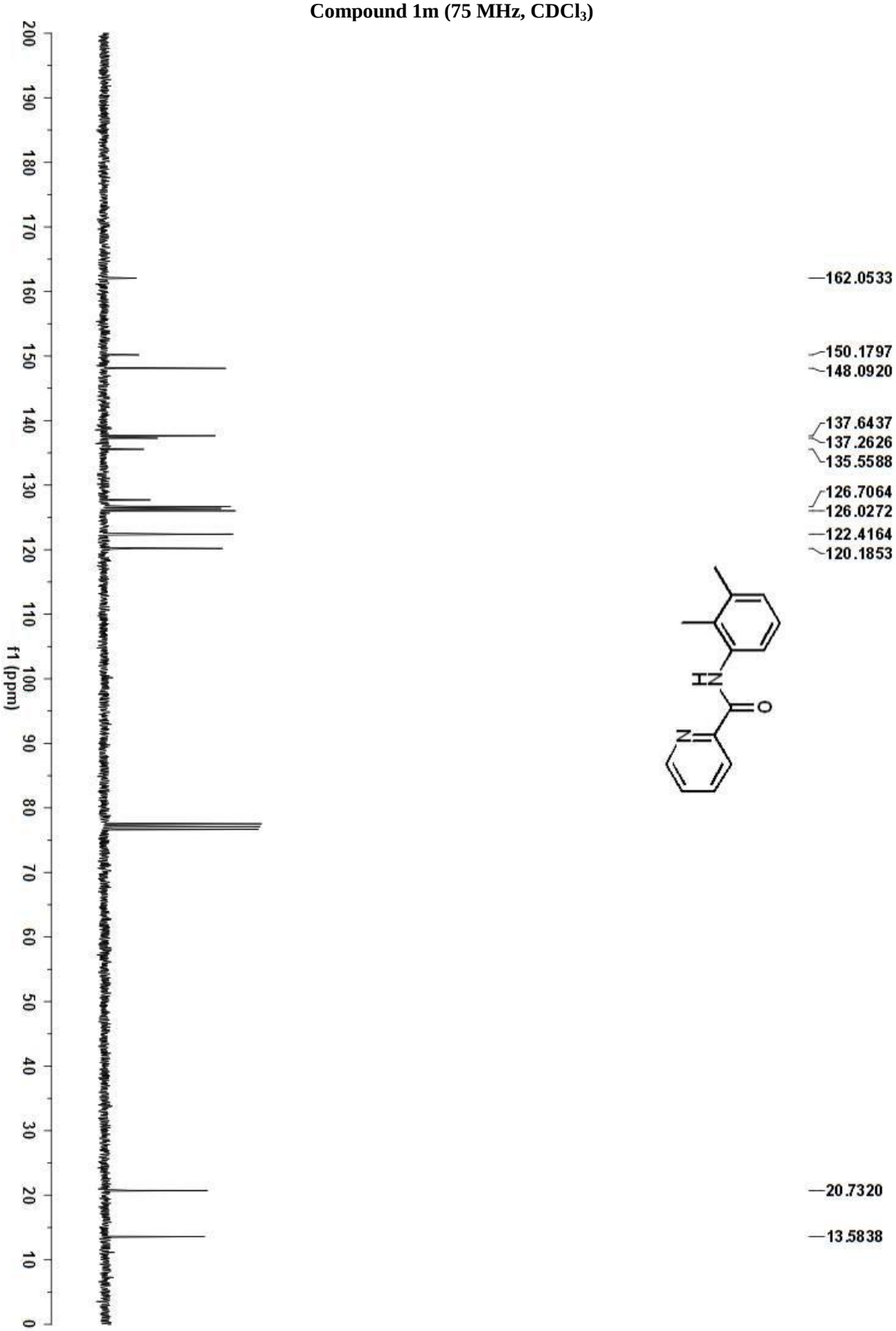
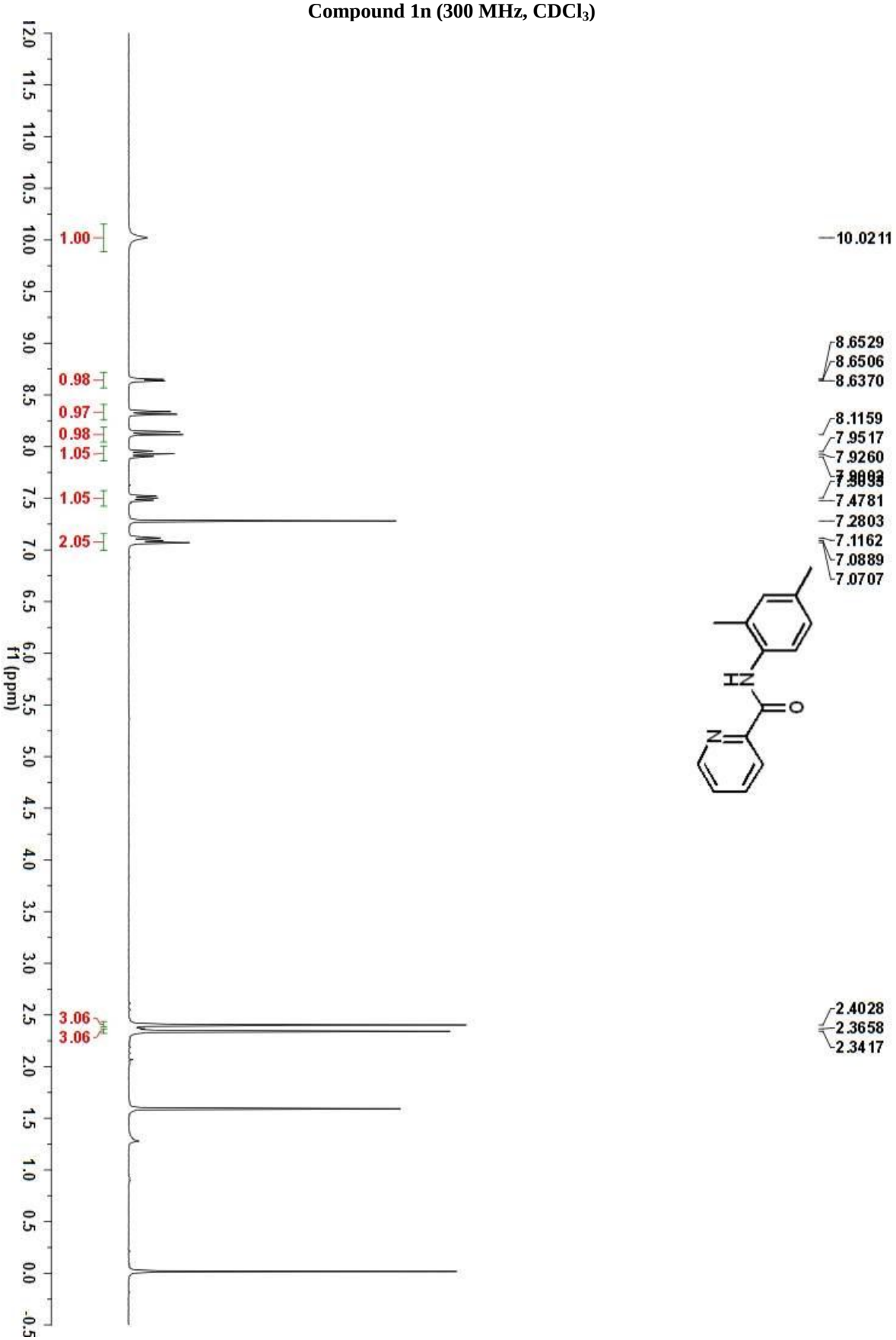
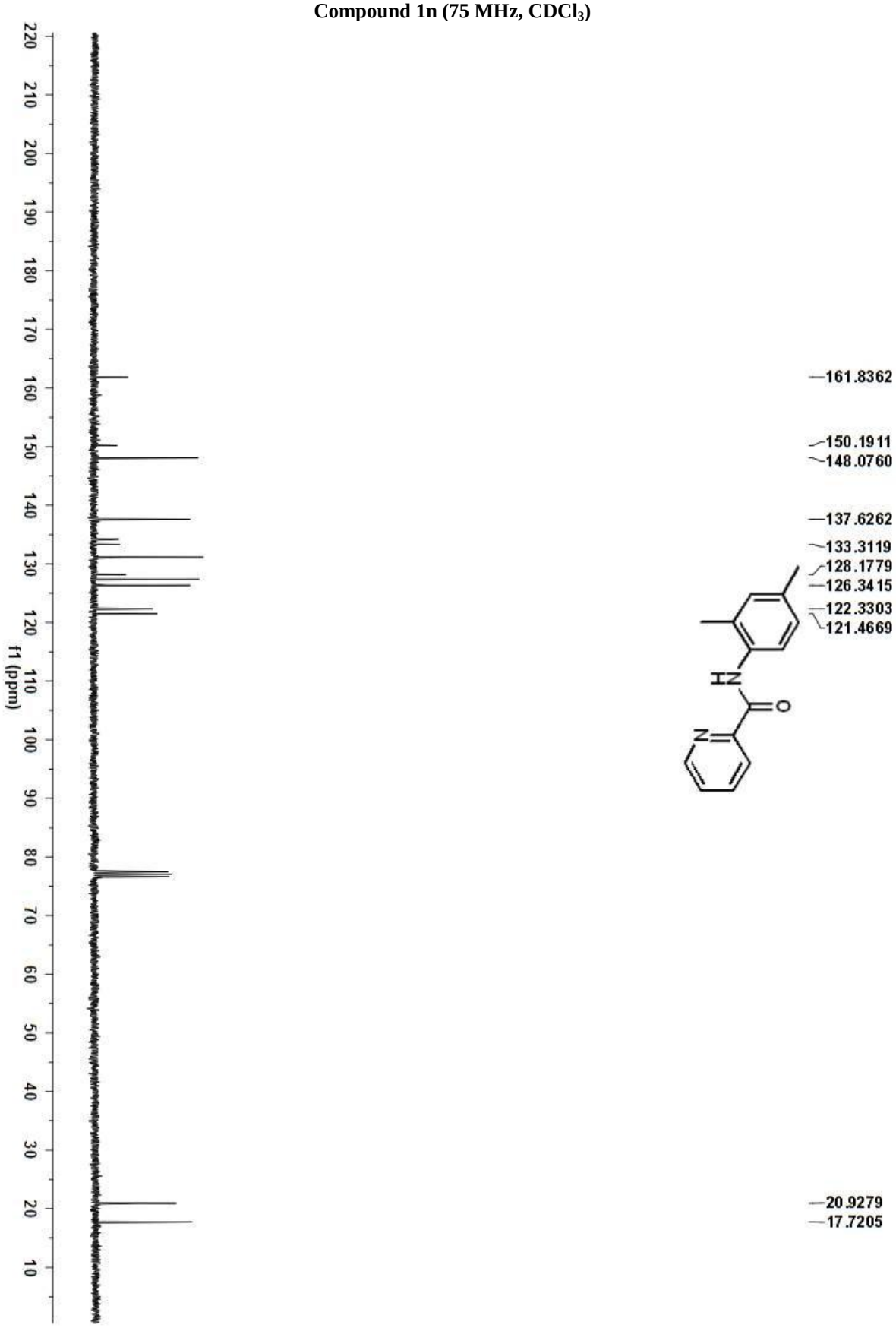


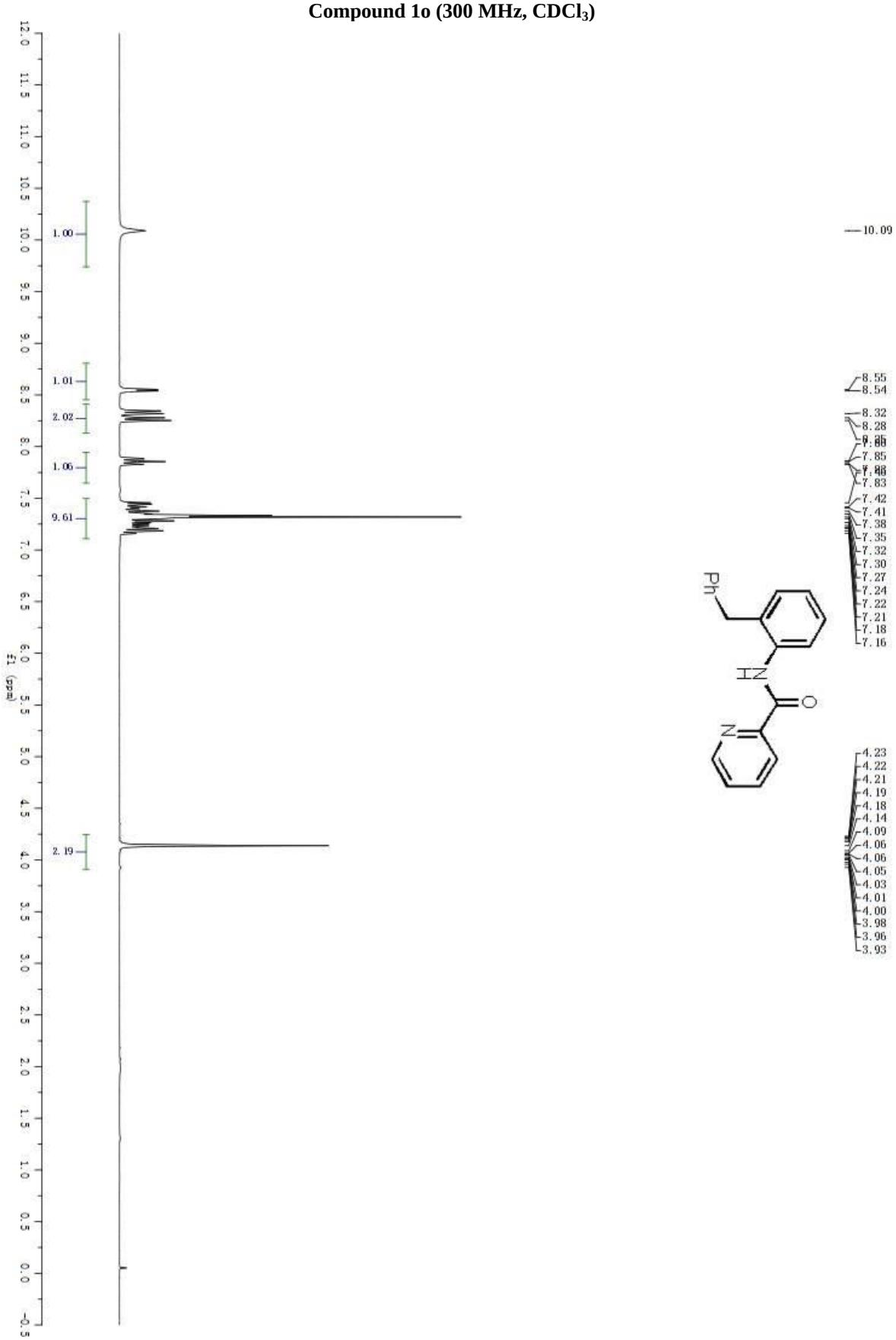
Compound 1n (300 MHz, $CDCl_3$)



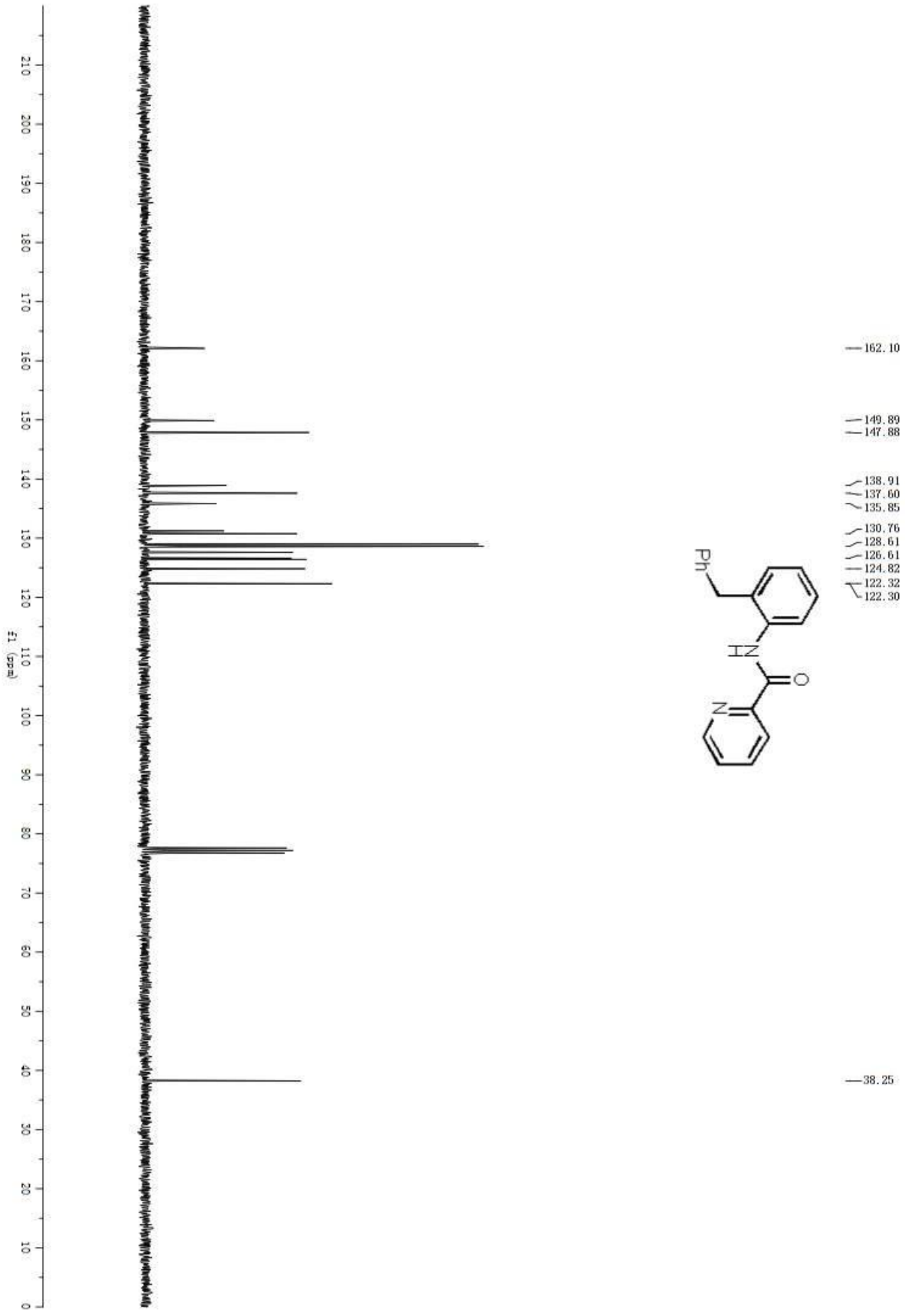
Compound 1n (75 MHz, $CDCl_3$)



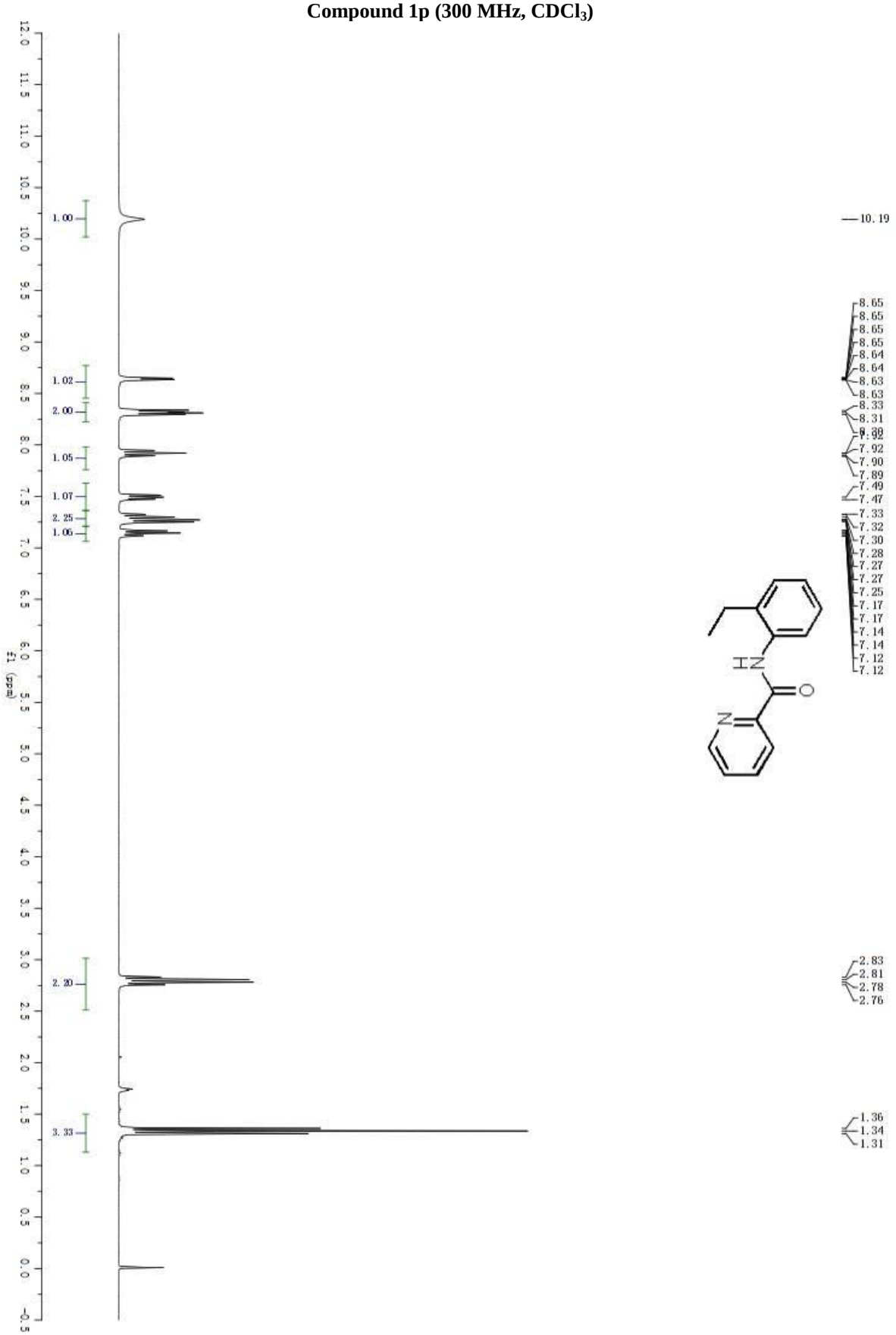
Compound 1o (300 MHz, $CDCl_3$)



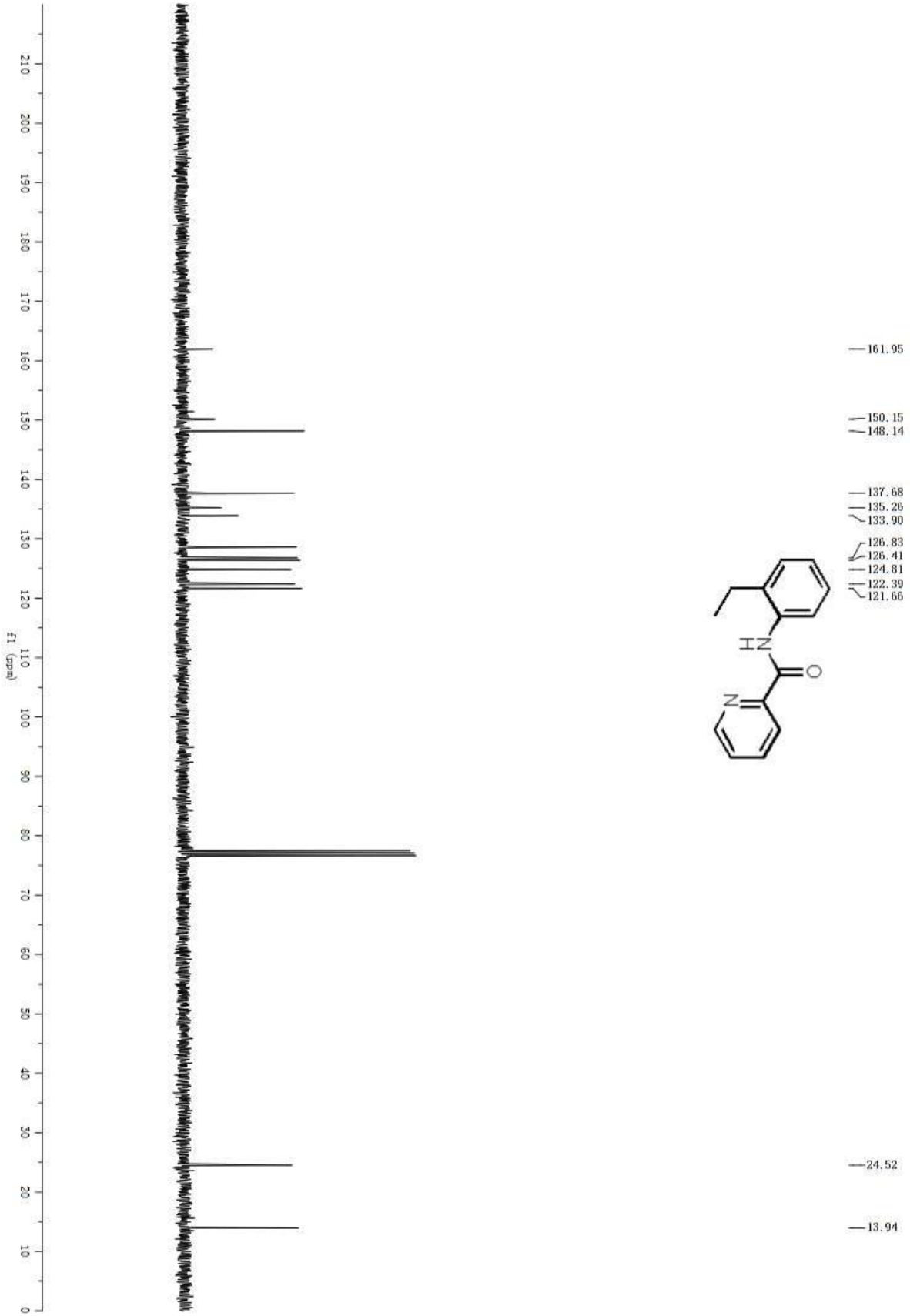
Compound 1o (75 MHz, $CDCl_3$)



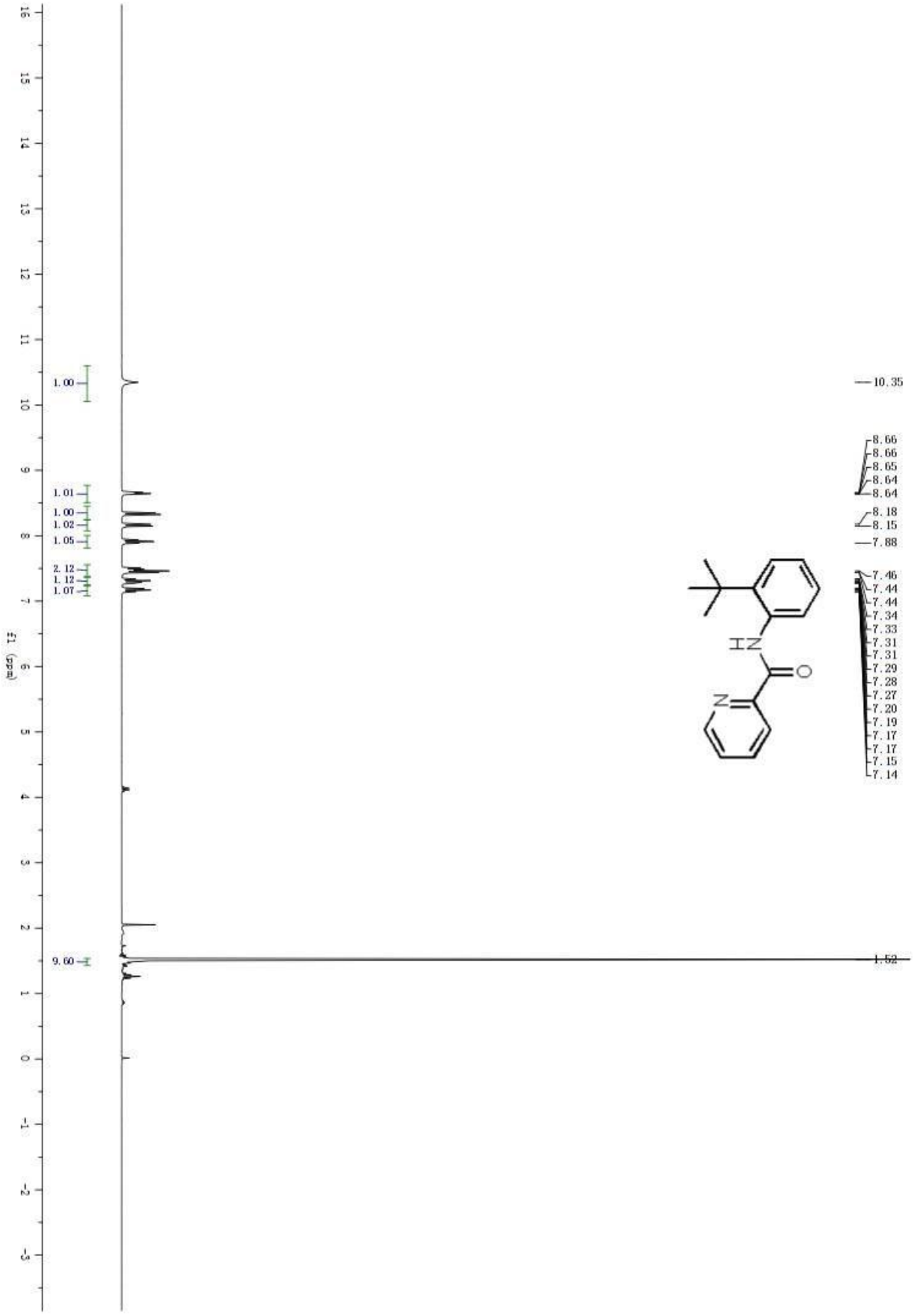
Compound 1p (300 MHz, $CDCl_3$)



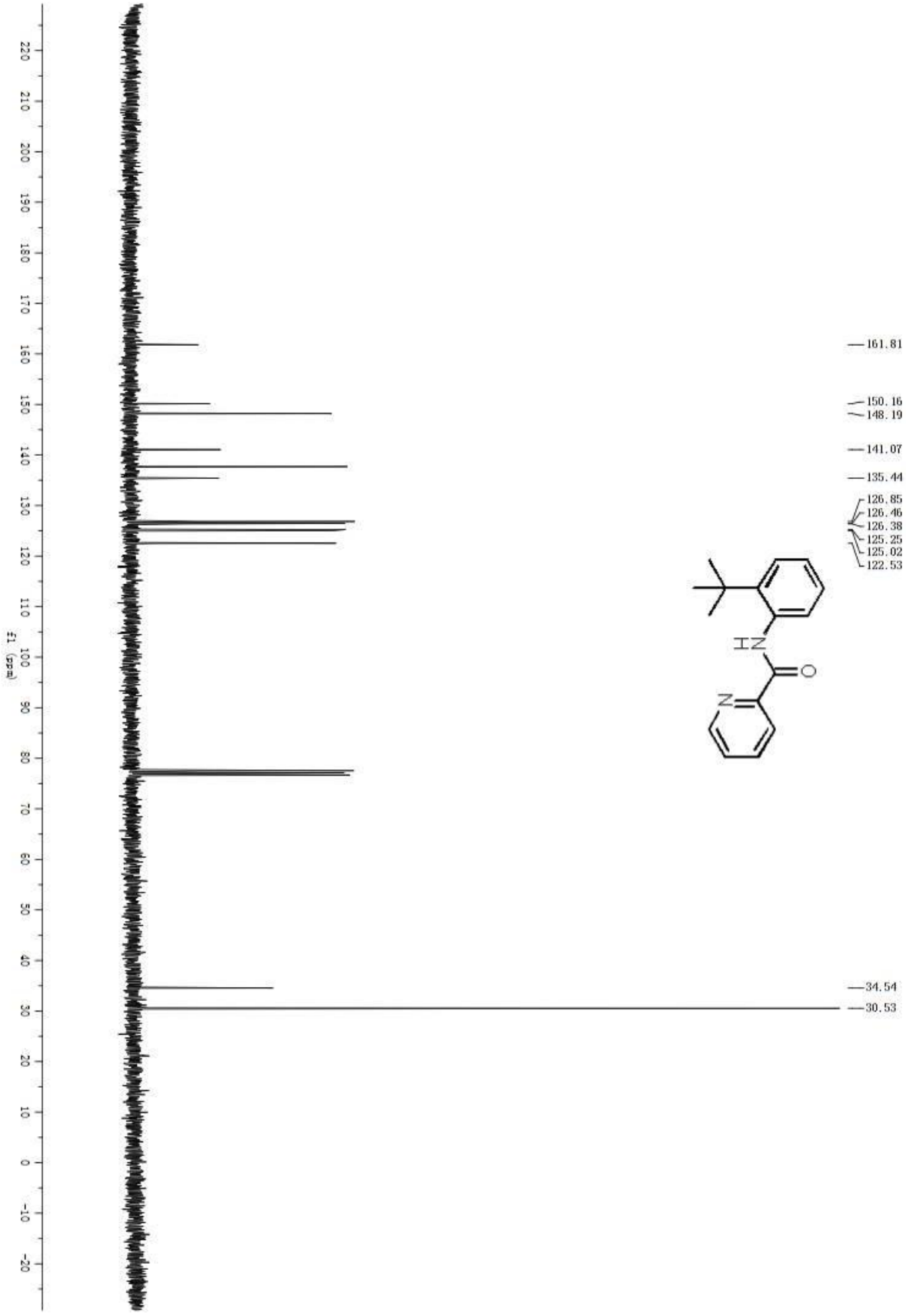
Compound 1p (75 MHz, $CDCl_3$)



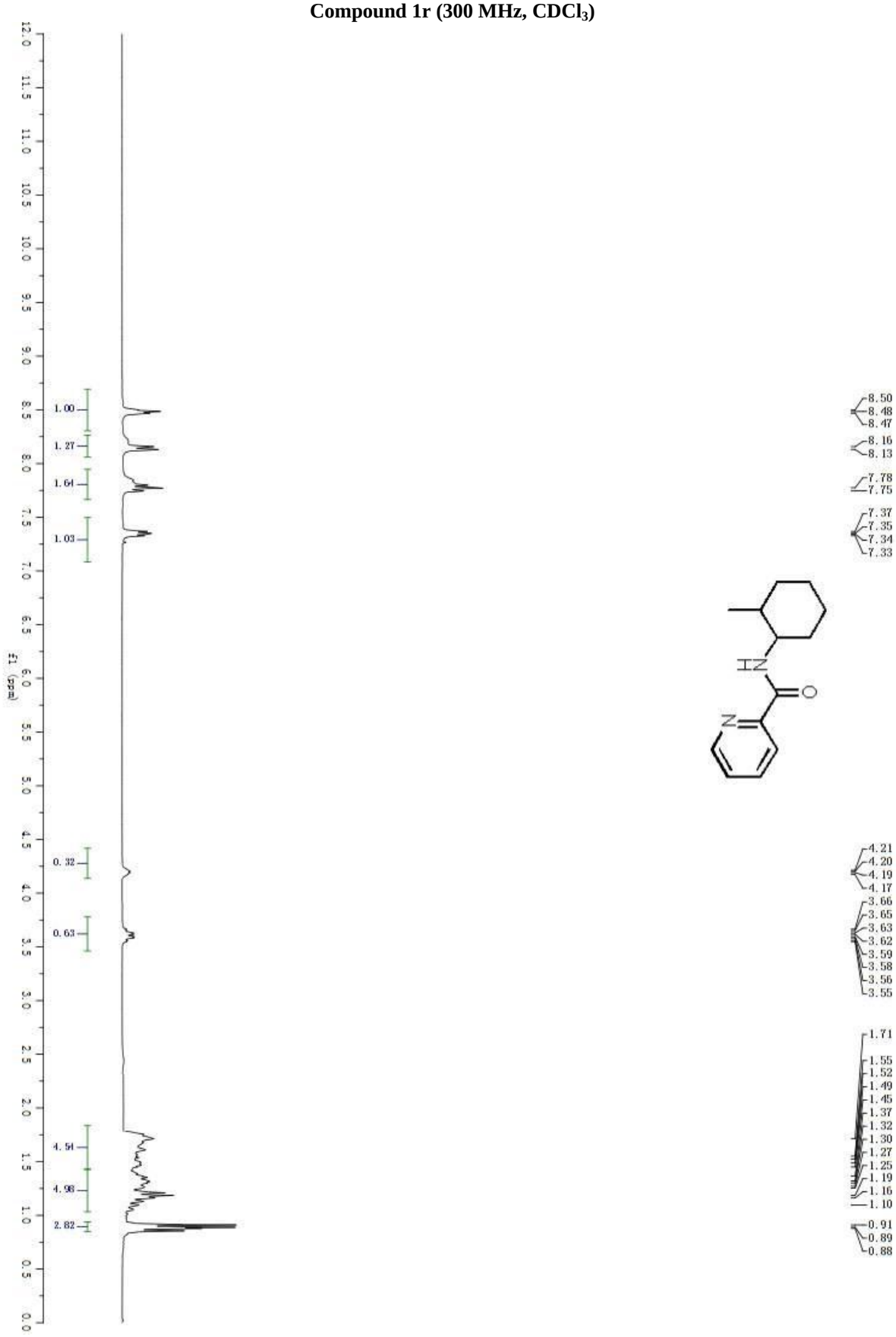
Compound 1q (300 MHz, $CDCl_3$)



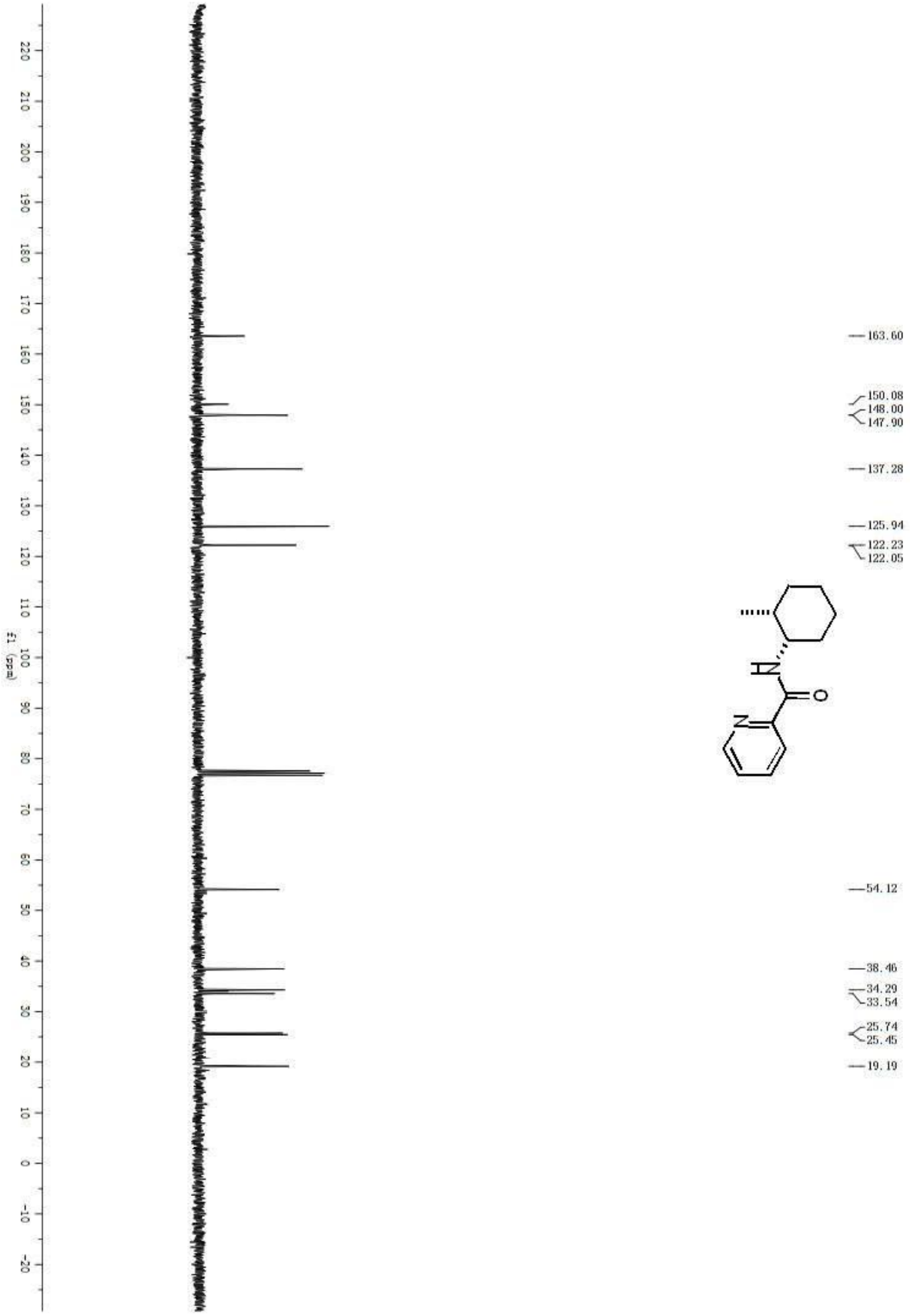
Compound 1q (75 MHz, $CDCl_3$)



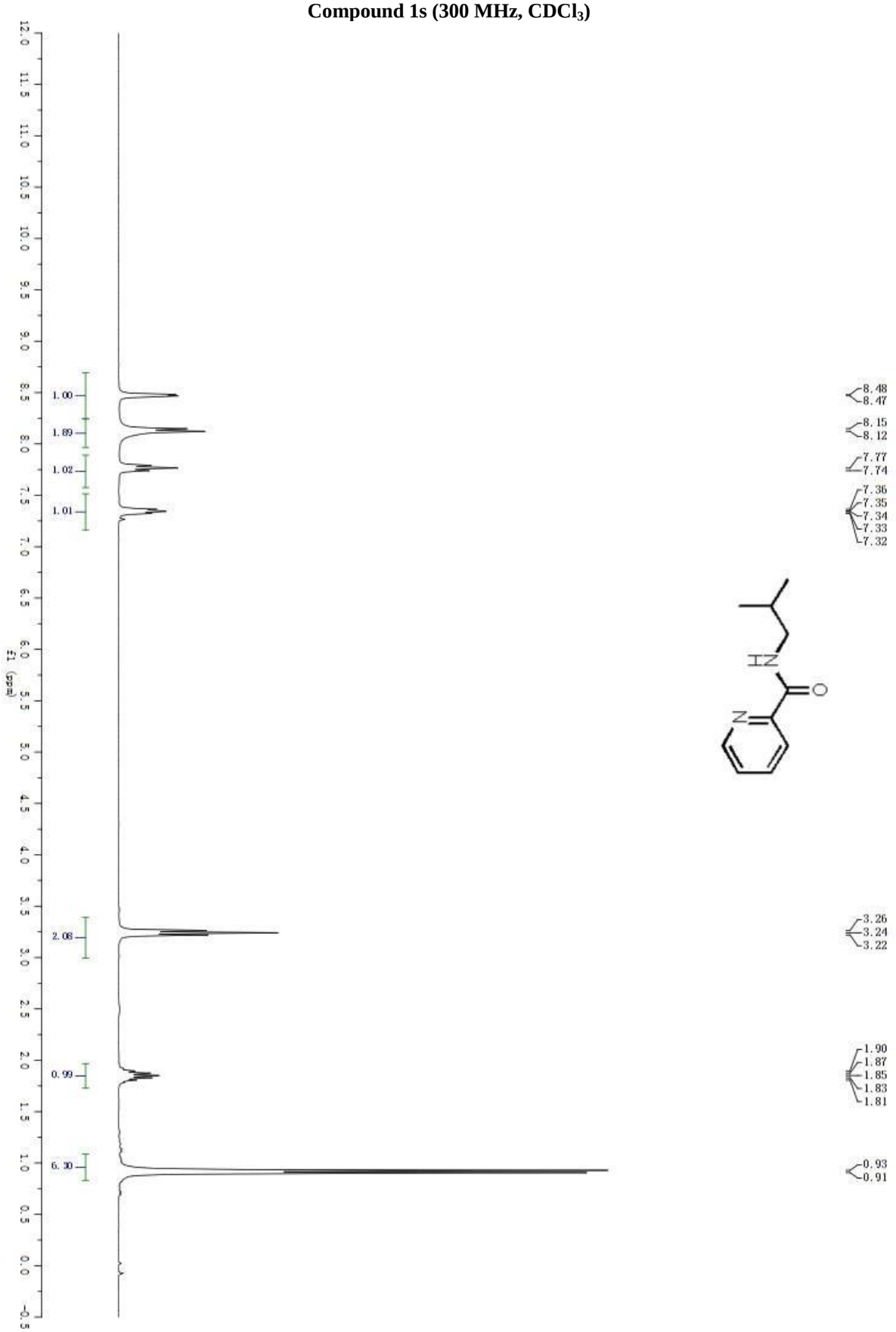
Compound 1r (300 MHz, $CDCl_3$)



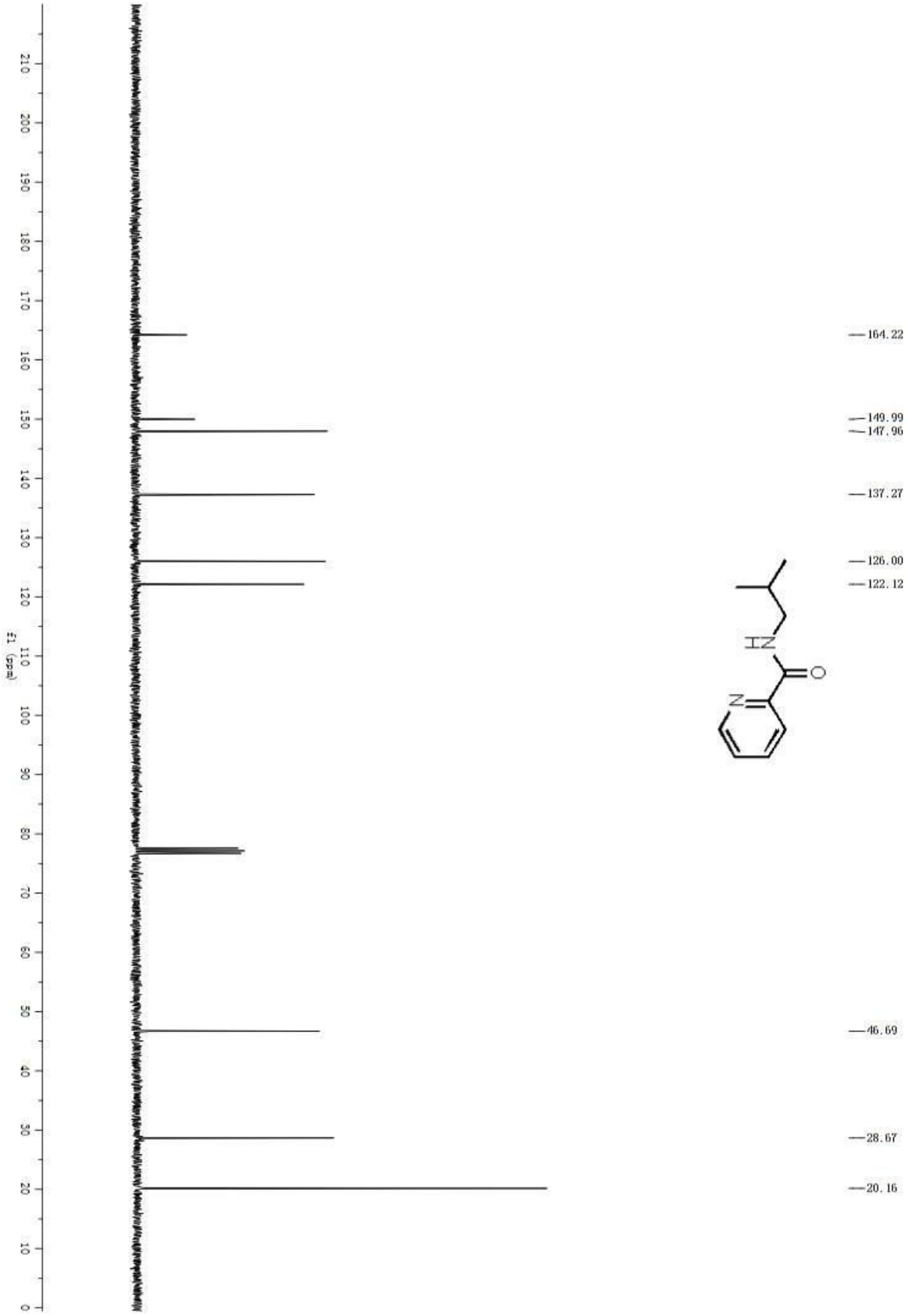
Compound 1r (75 MHz, $CDCl_3$)



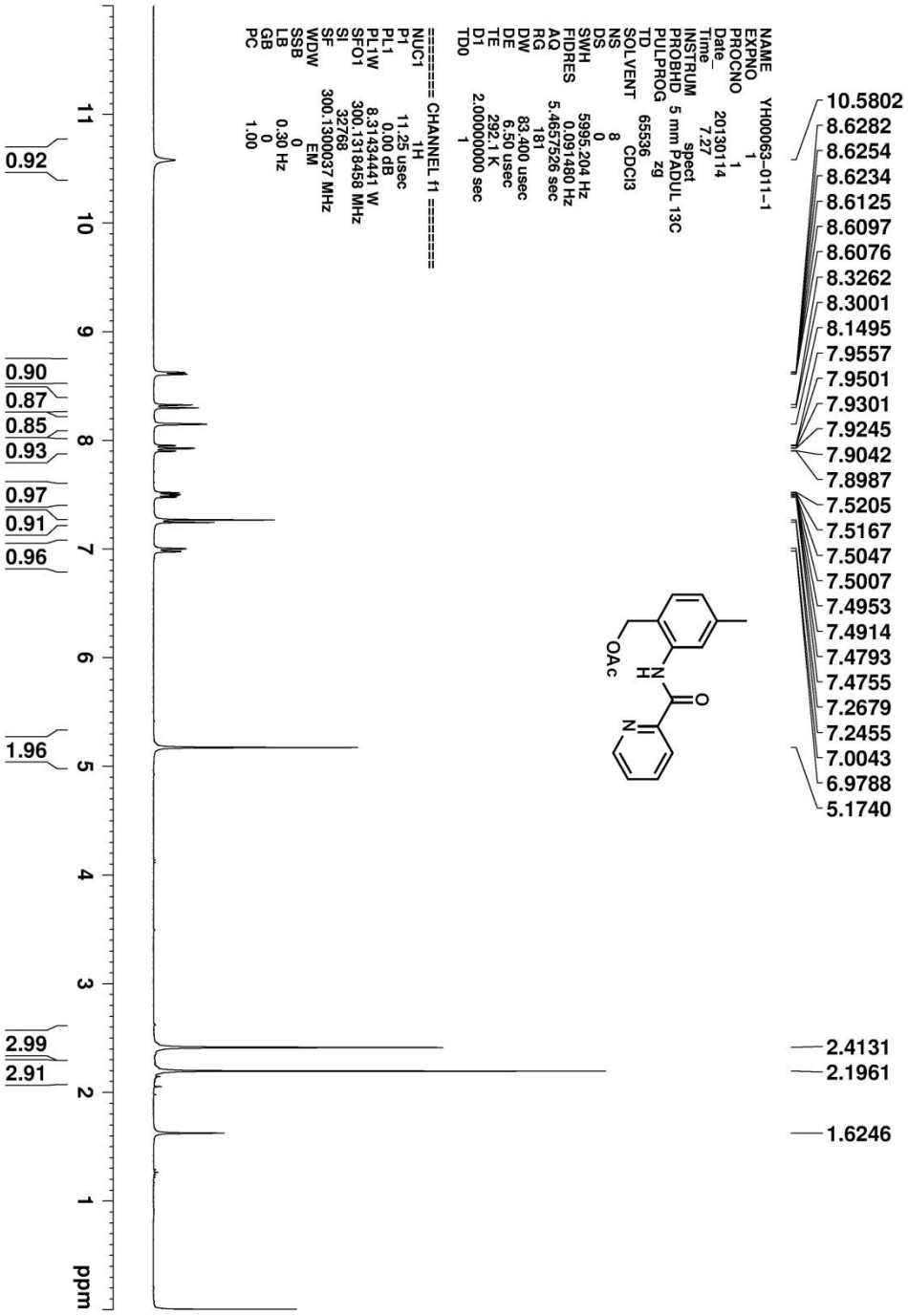
Compound 1s (300 MHz, $CDCl_3$)



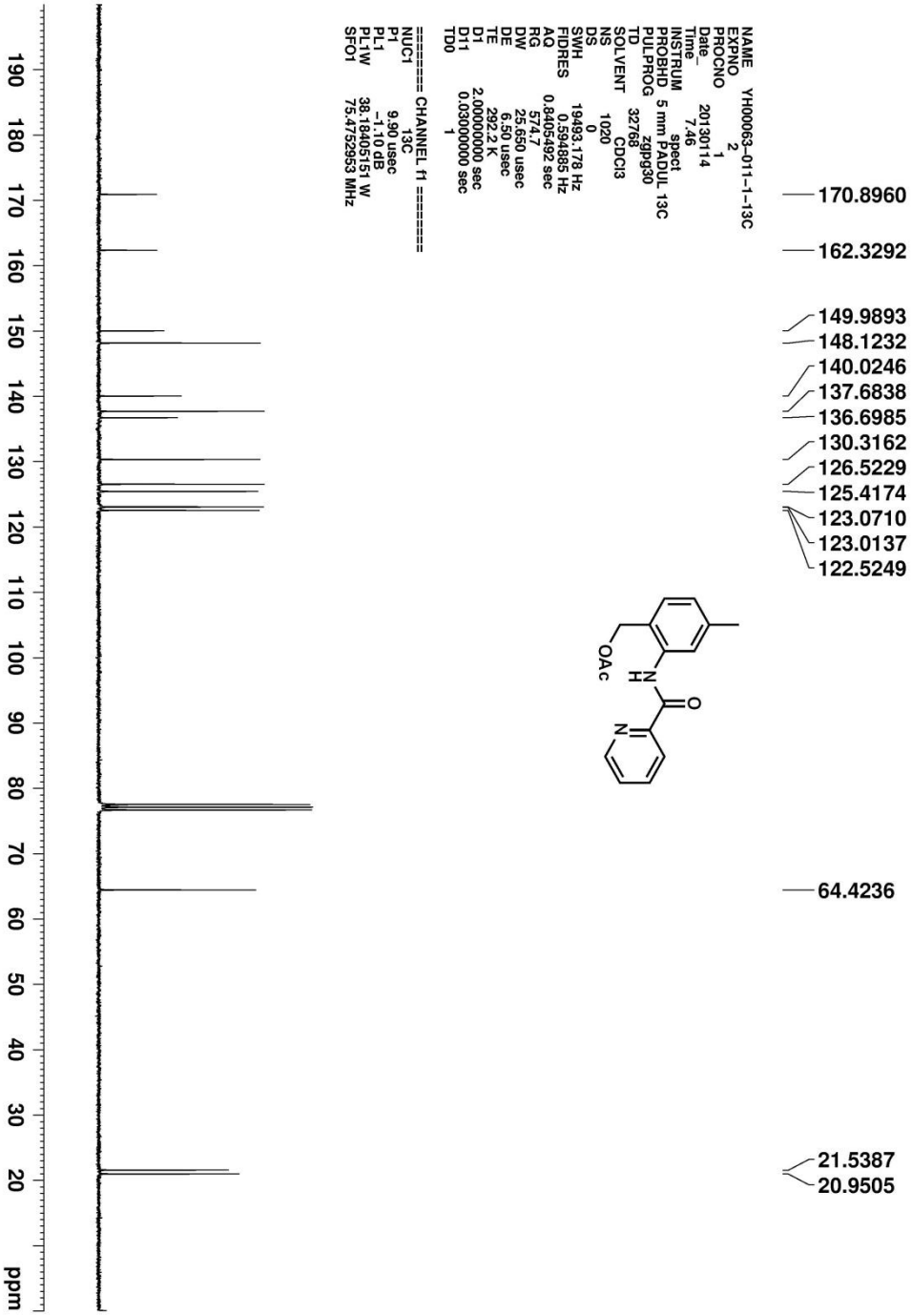
Compound 1s (75 MHz, $CDCl_3$)



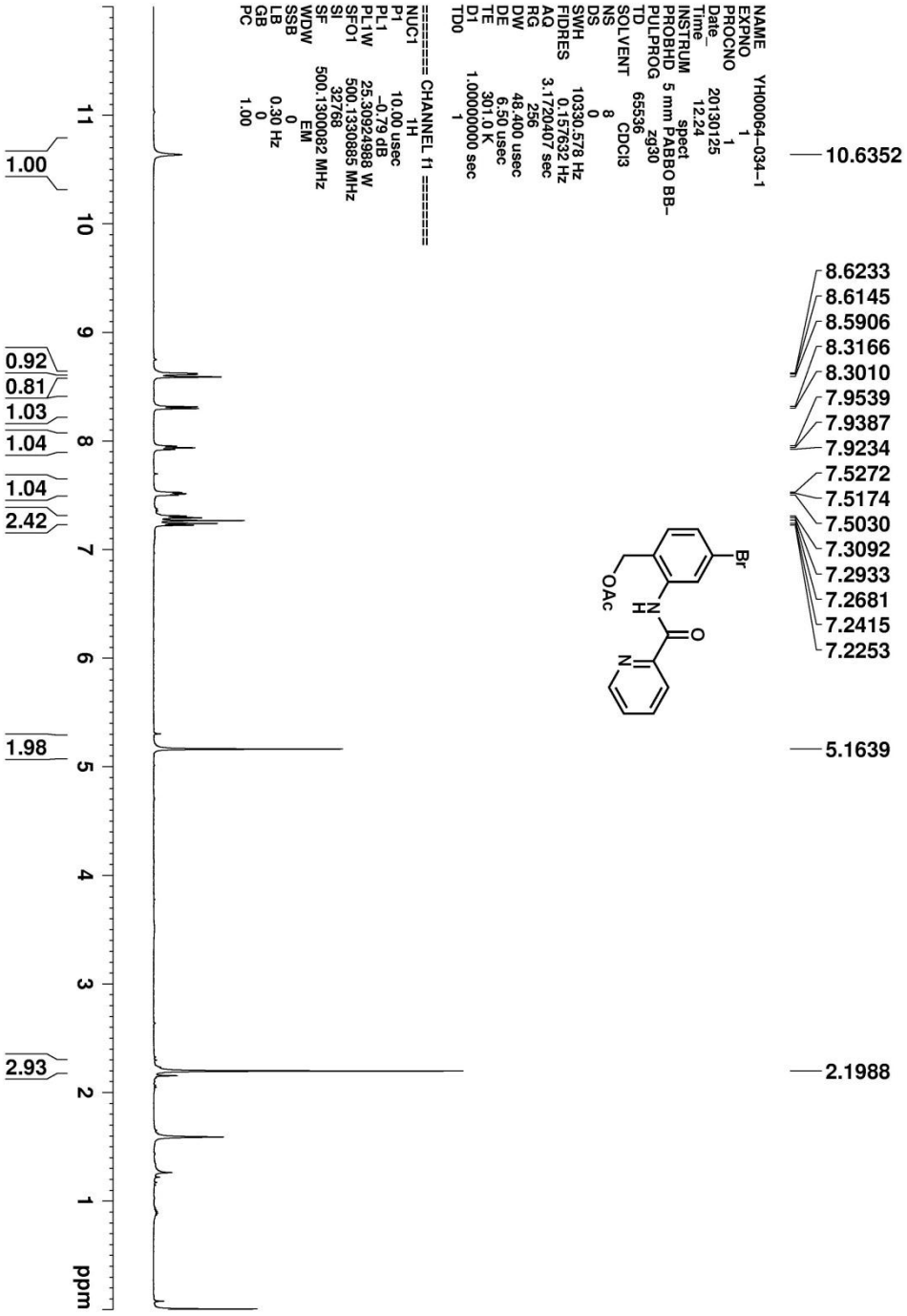
Compound 2a (300 MHz, $CDCl_3$)



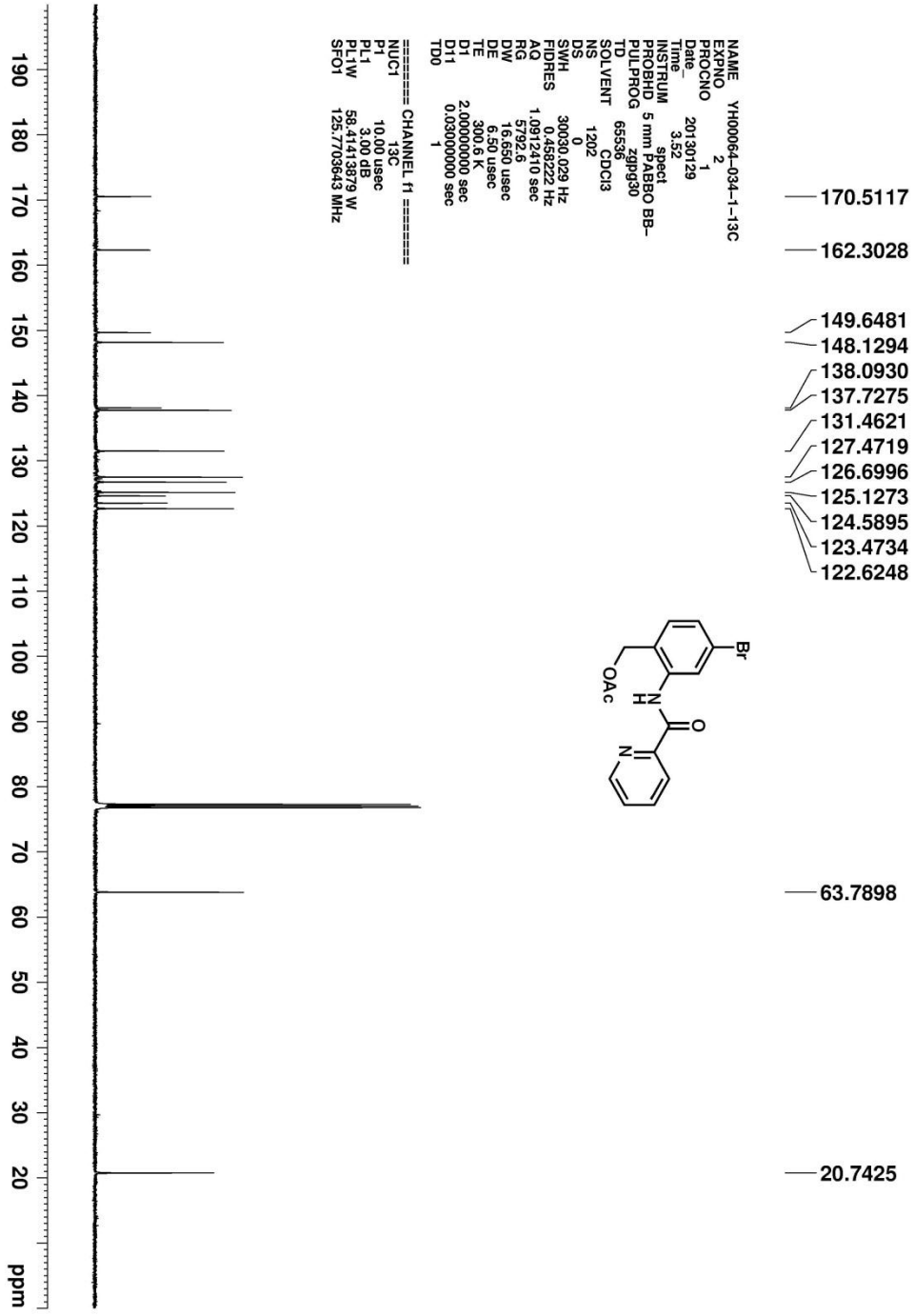
Compound 2a (75 MHz, $CDCl_3$)



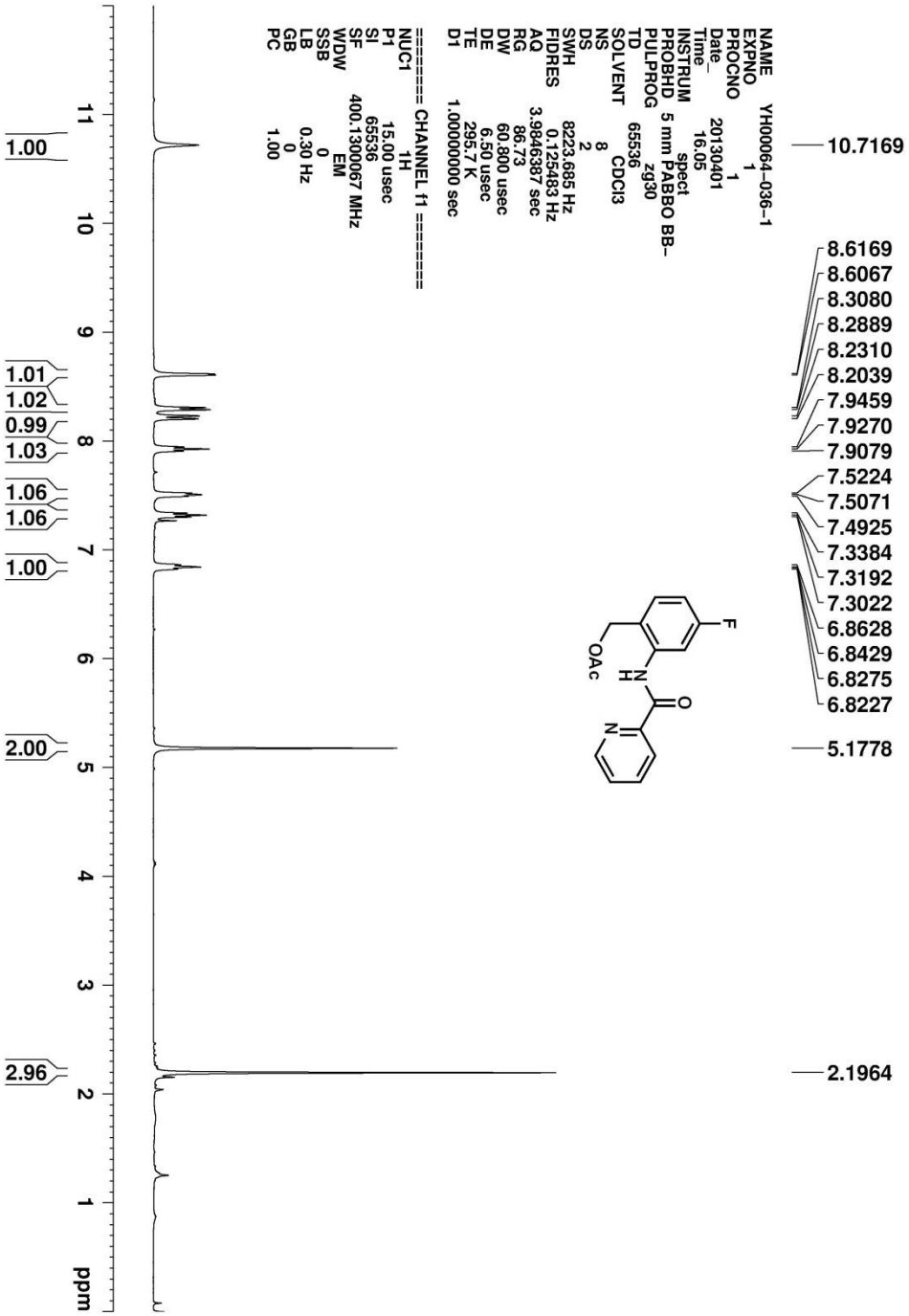
Compound 2b (500 MHz, $CDCl_3$)



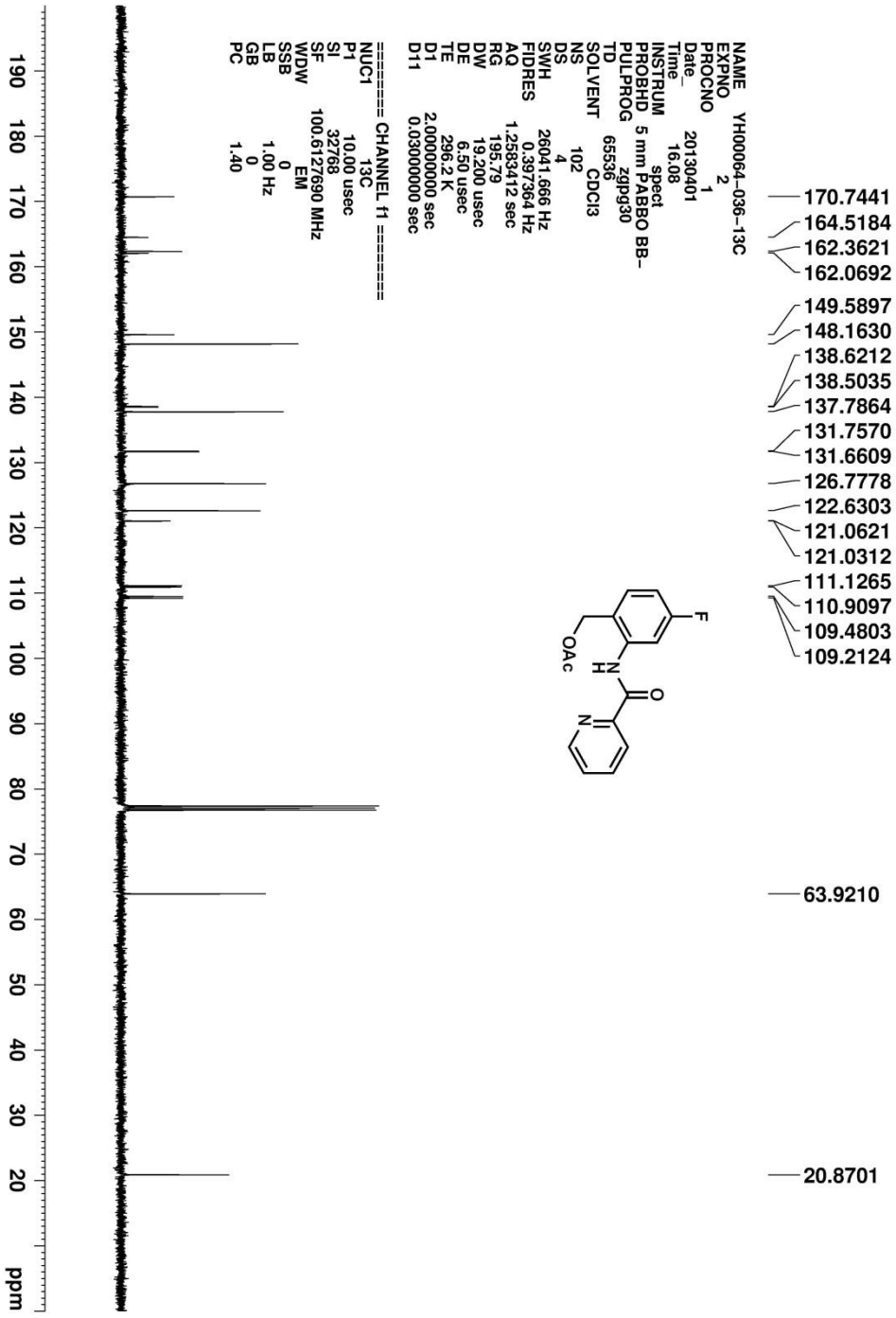
Compound 2b (125 MHz, $CDCl_3$)



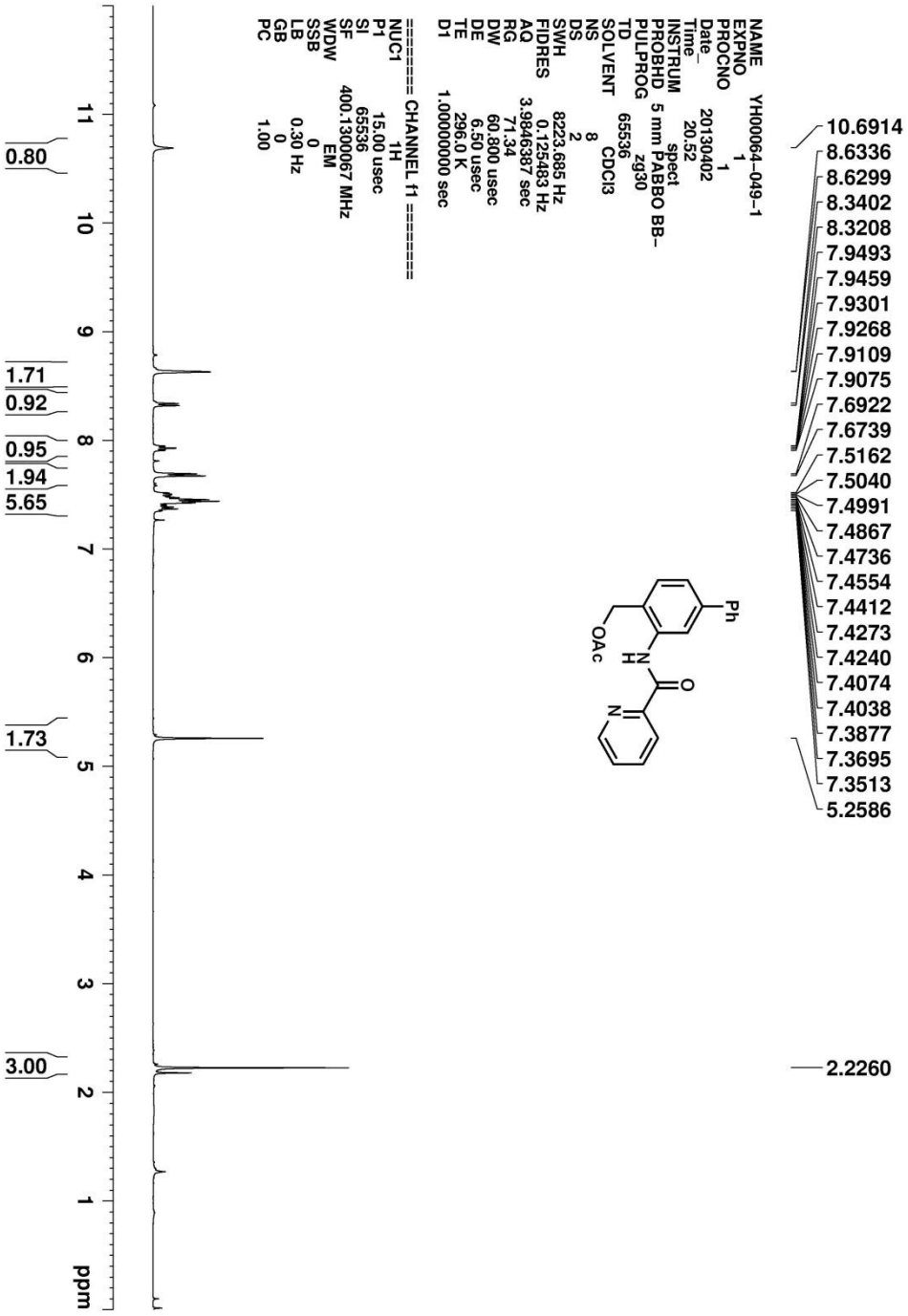
Compound 2c (400 MHz, $CDCl_3$)



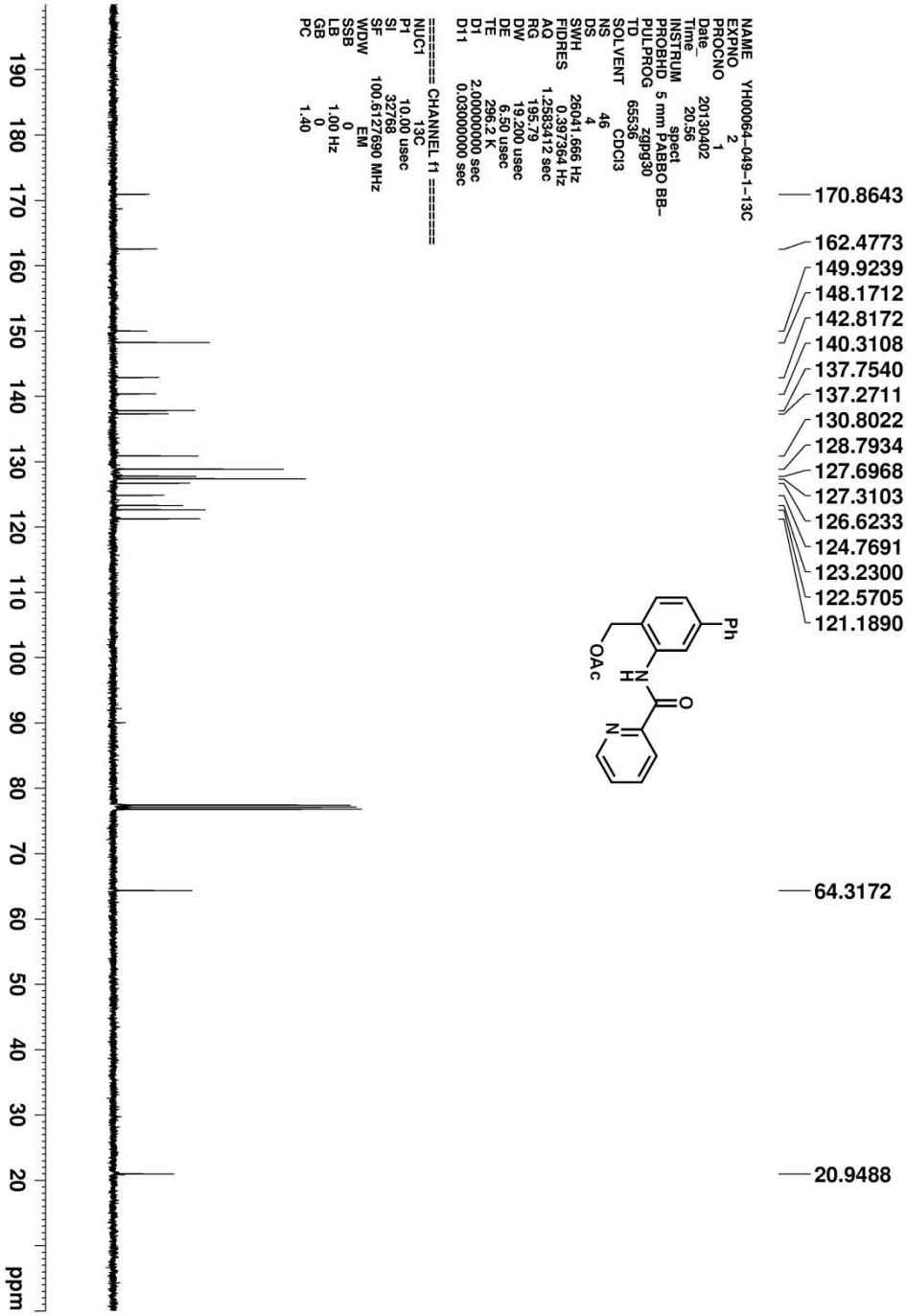
Compound 2c (100MHz, $CDCl_3$)



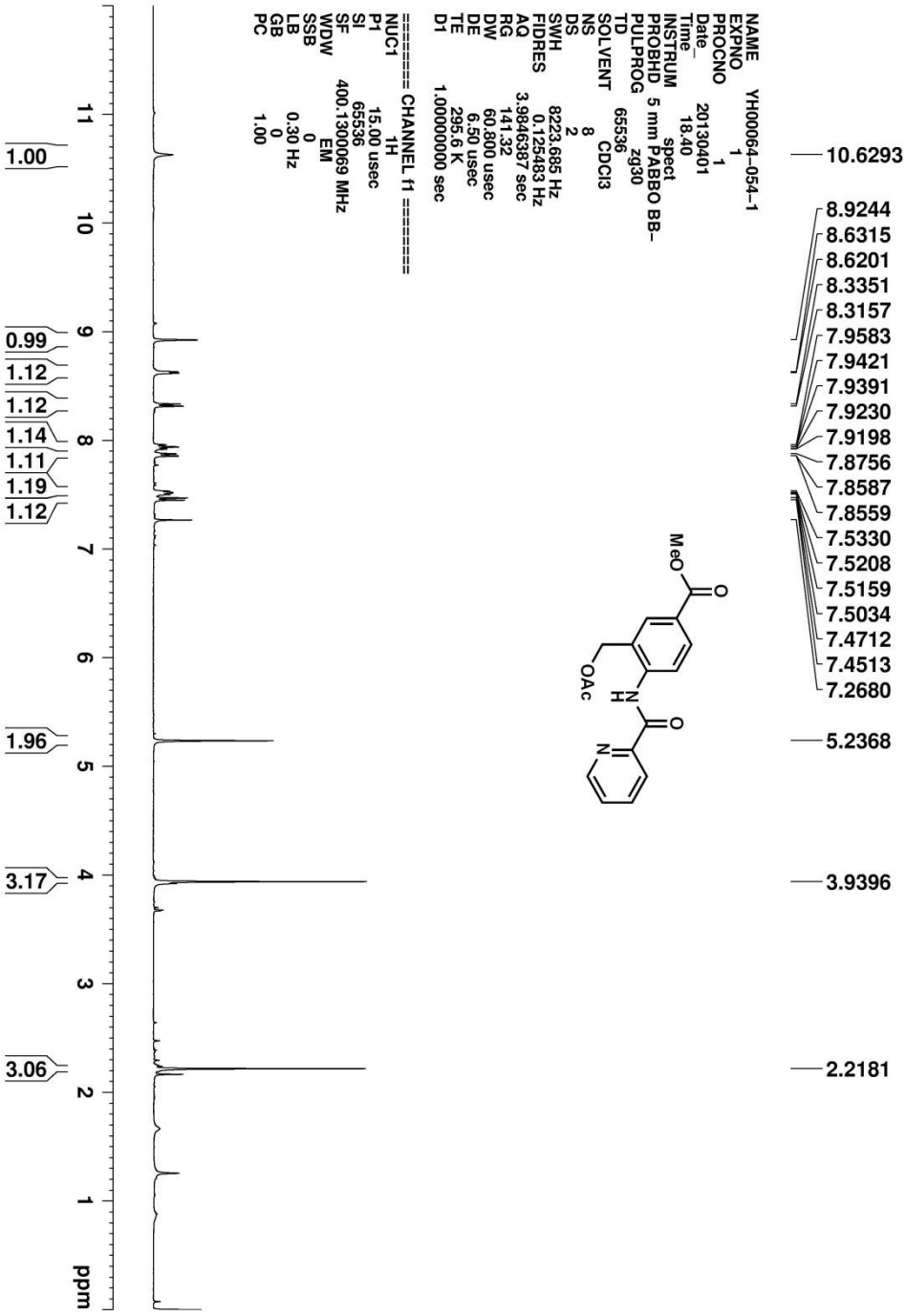
Compound 2d (400MHz, $CDCl_3$)



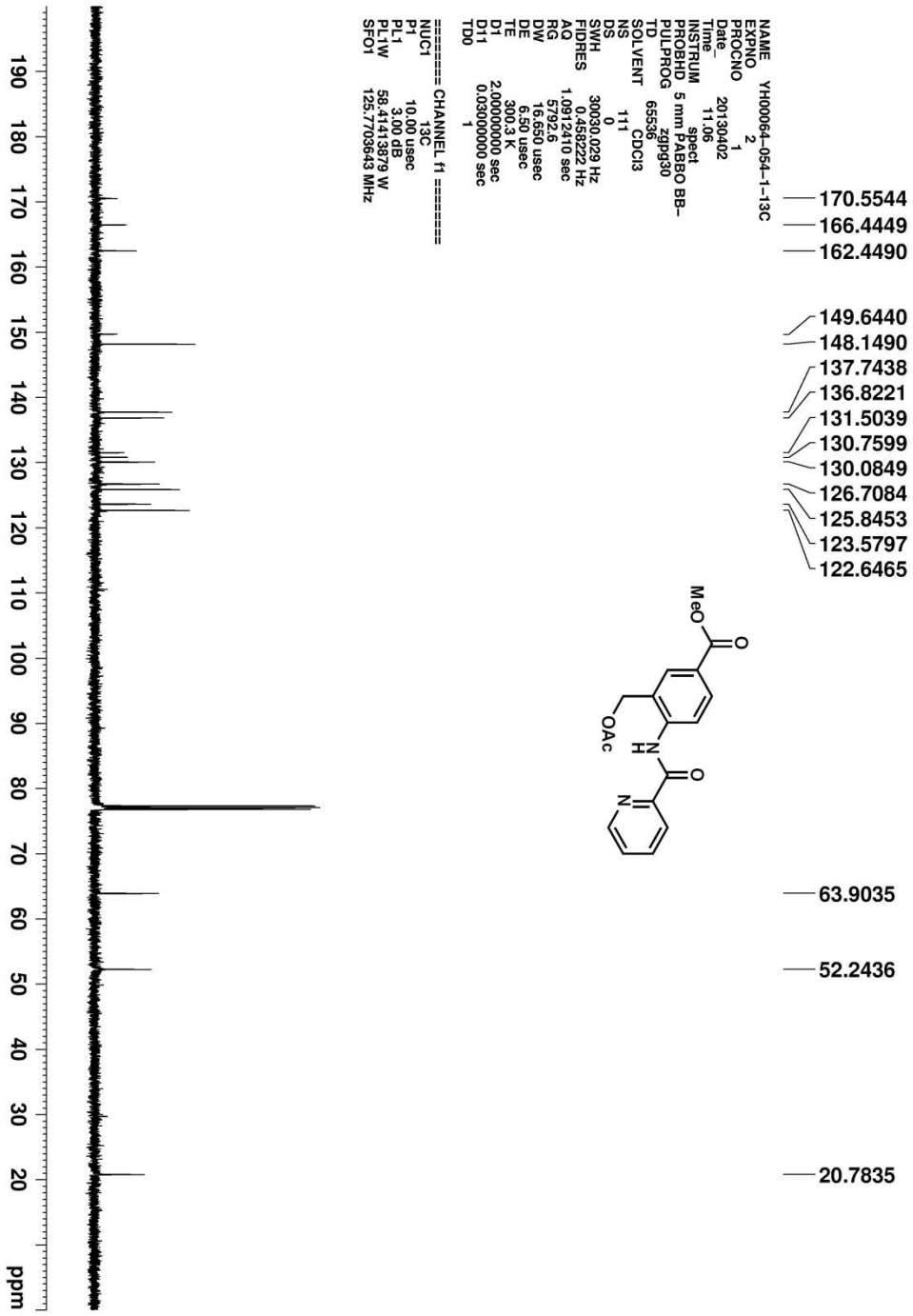
Compound 2d (100 MHz, $CDCl_3$)



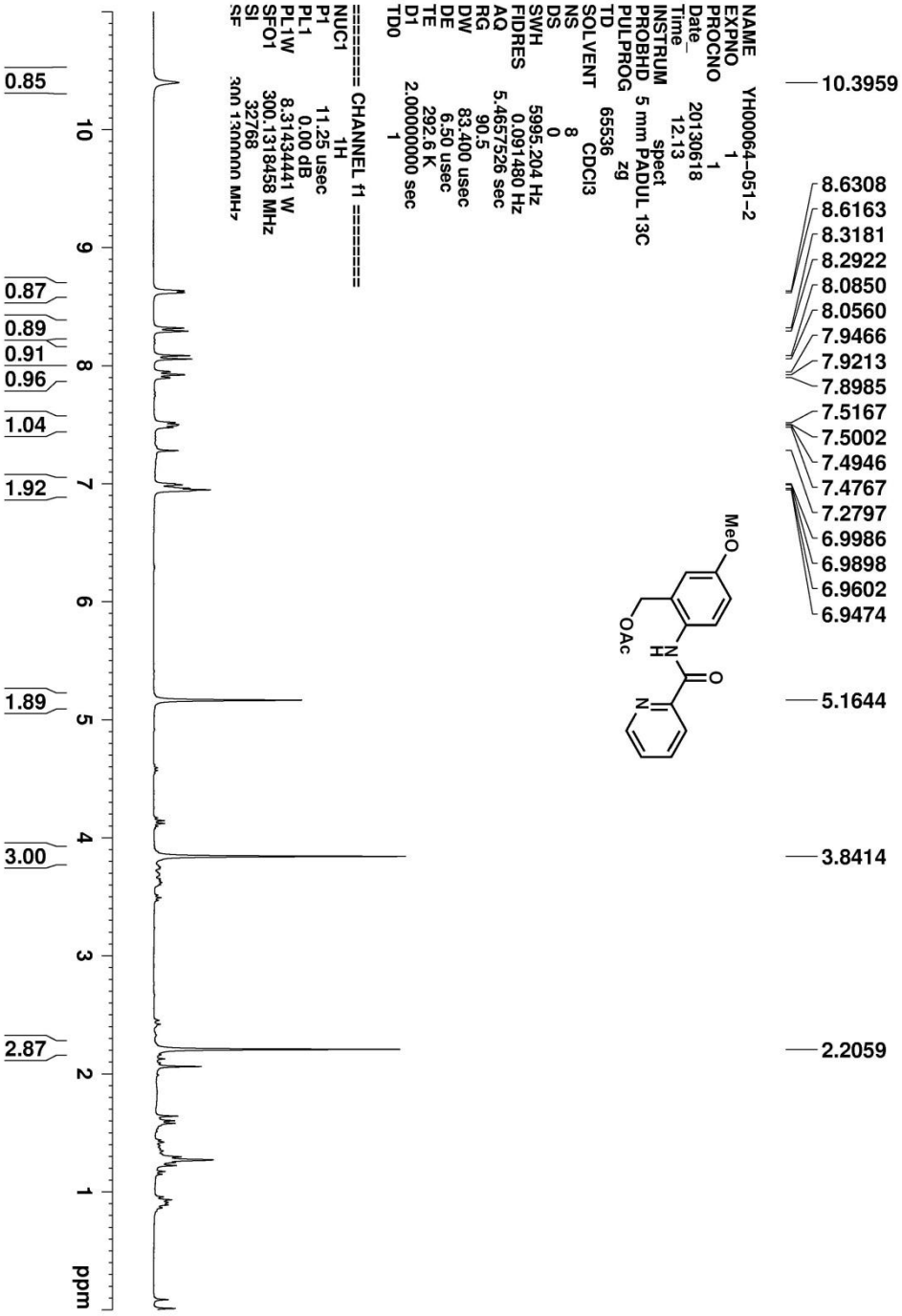
Compound 2e (400 MHz, $CDCl_3$)



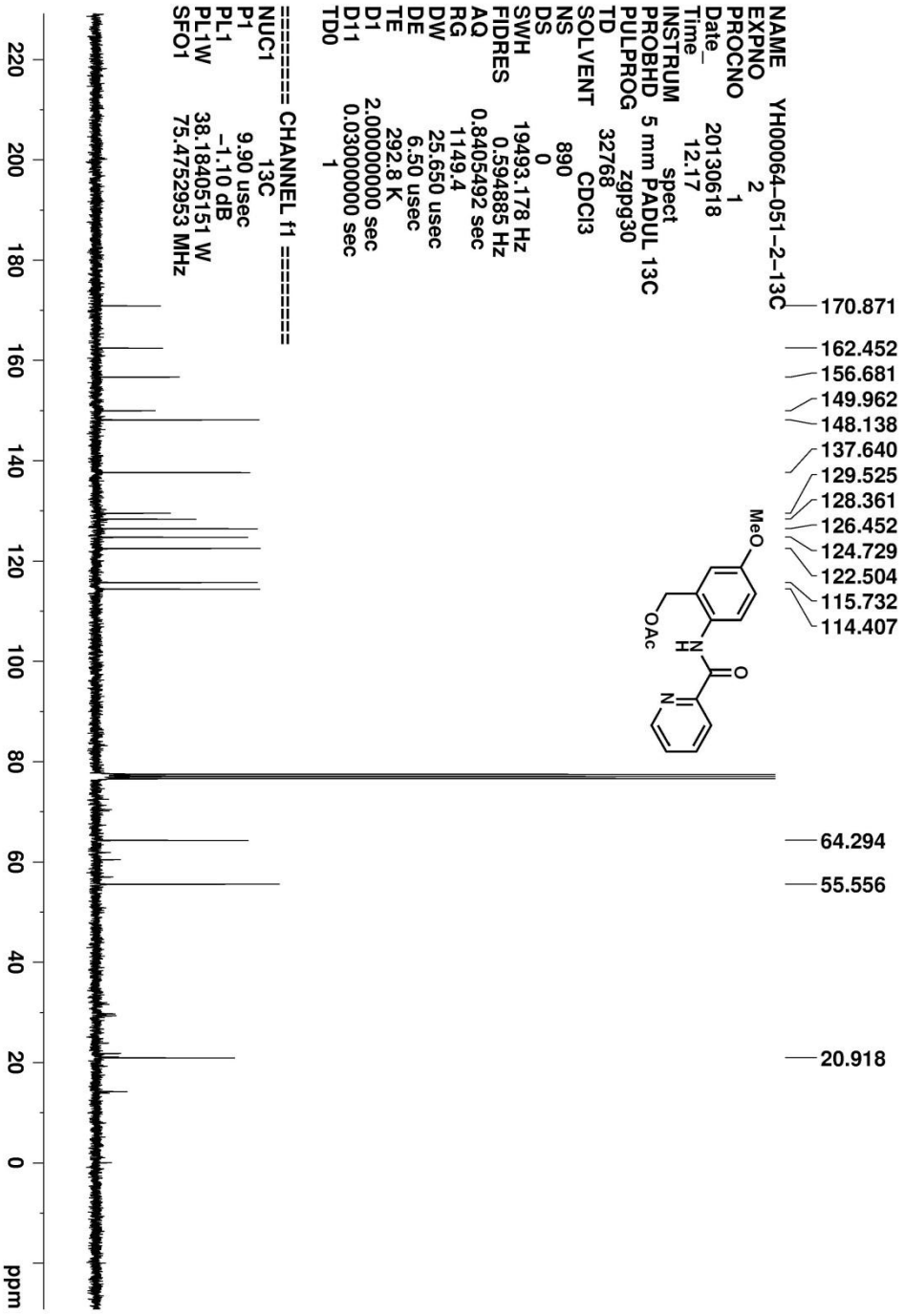
Compound 2e (125 MHz, $CDCl_3$)



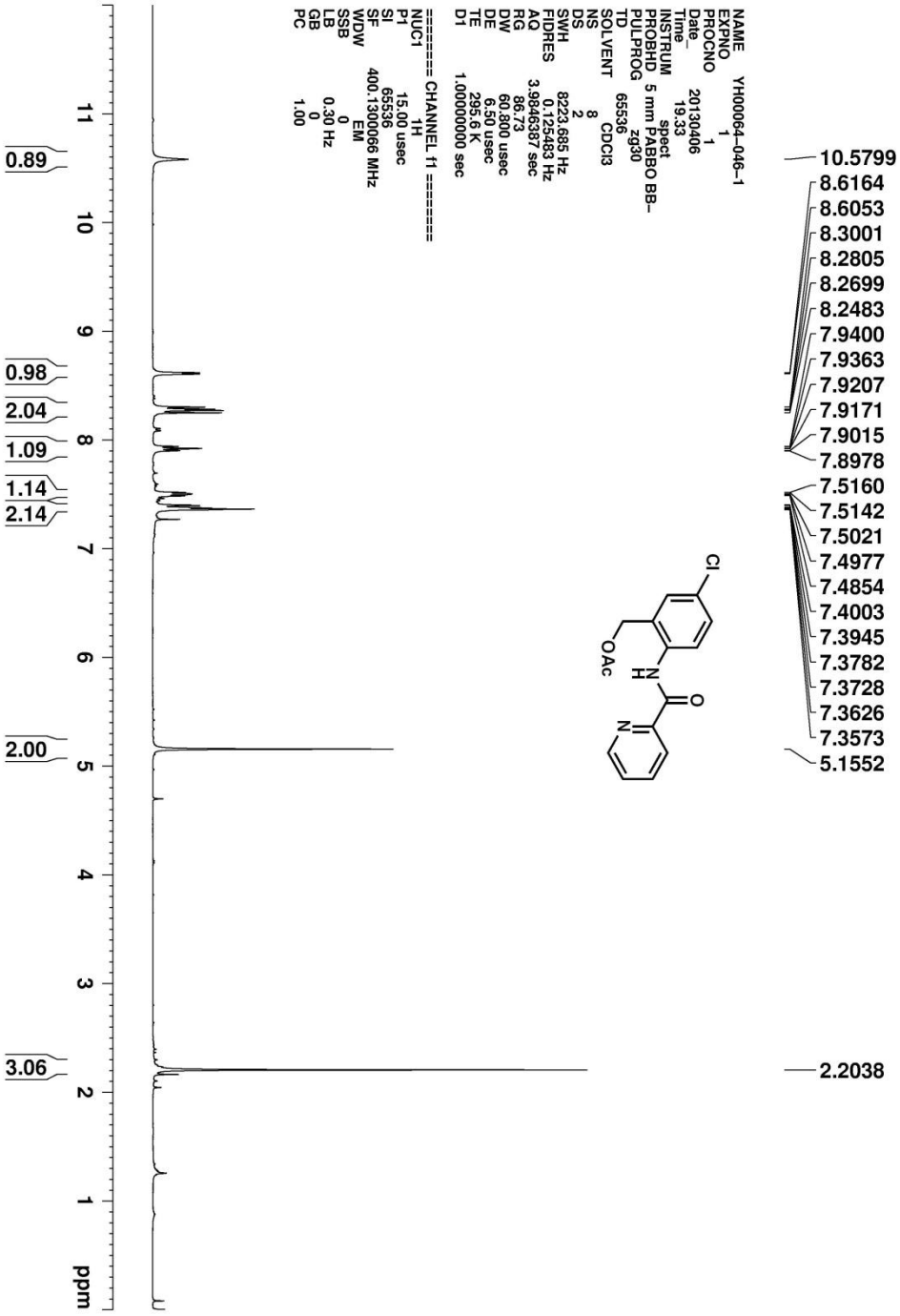
Compound 2f (300 MHz, $CDCl_3$)



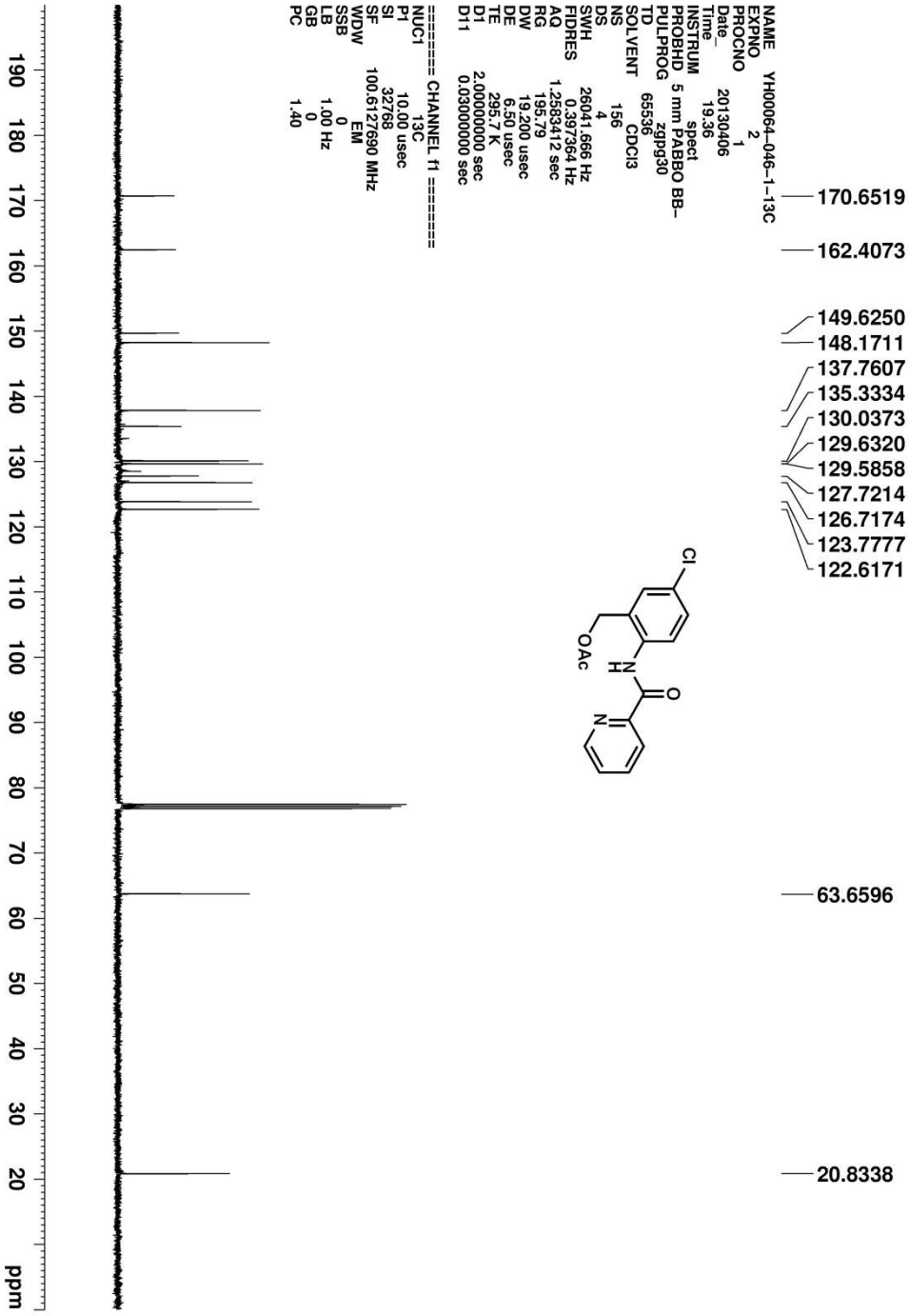
Compound 2f (75 MHz, $CDCl_3$)



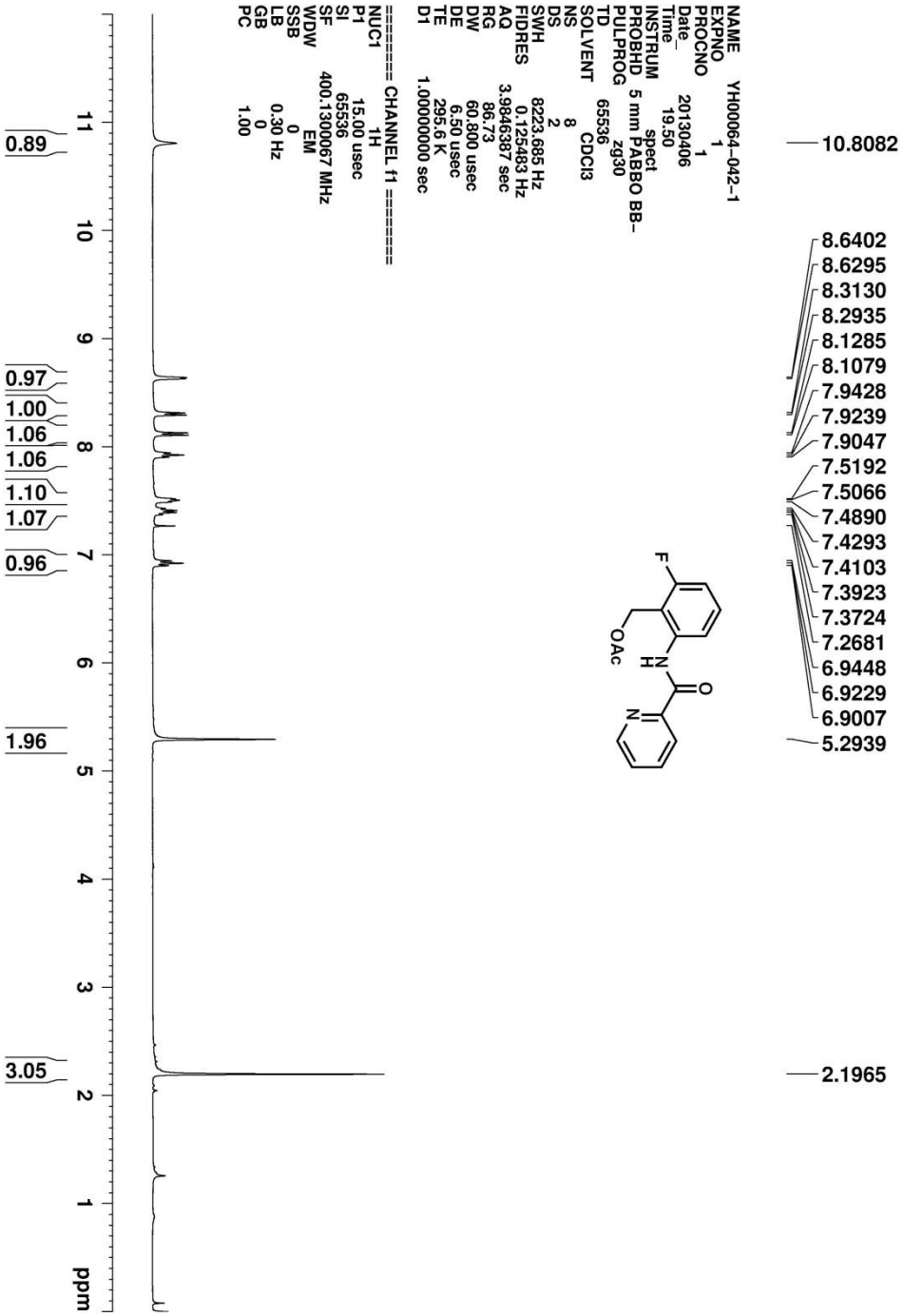
Compound 2g (400 MHz, $CDCl_3$)



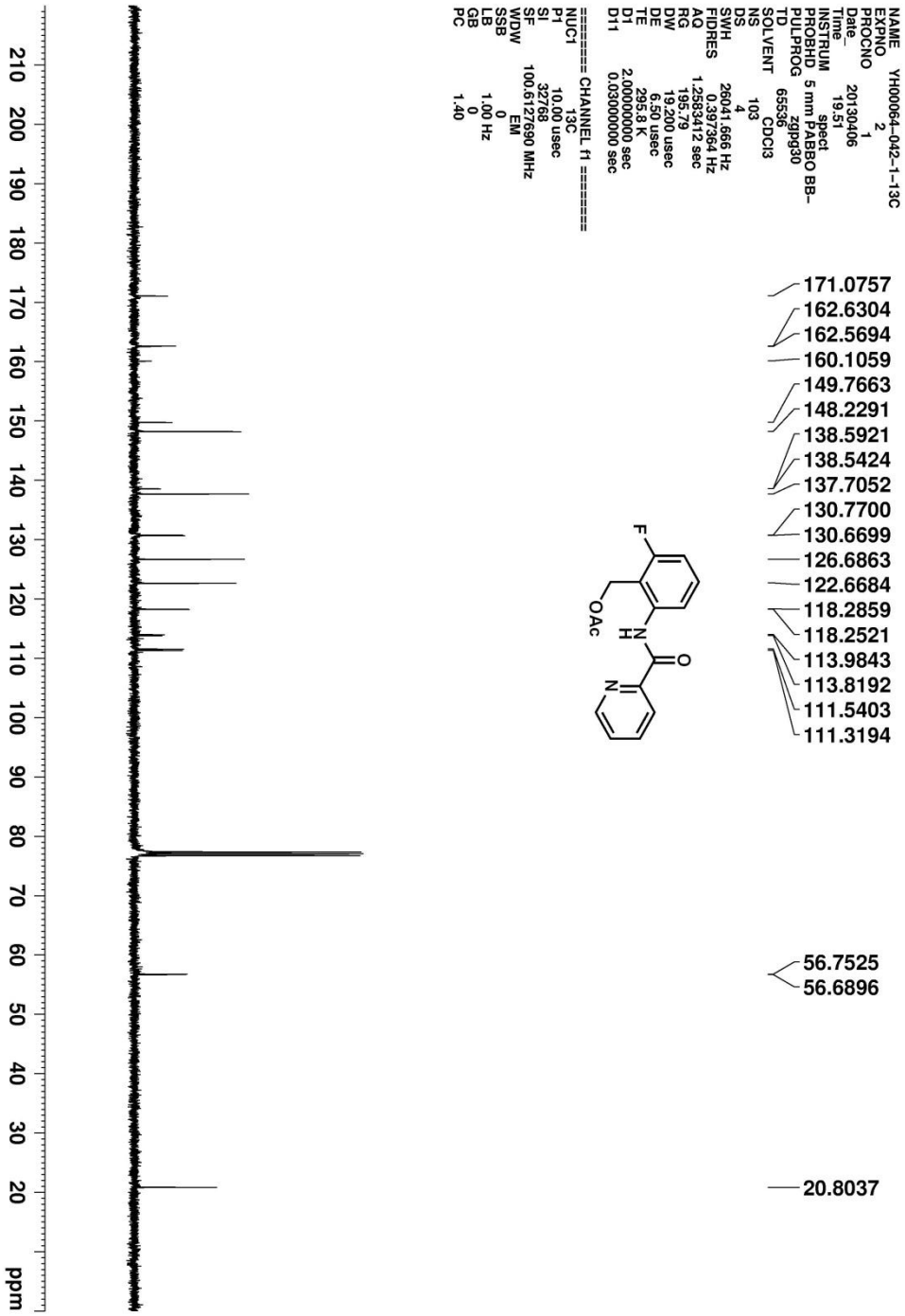
Compound 2g (100MHz, $CDCl_3$)



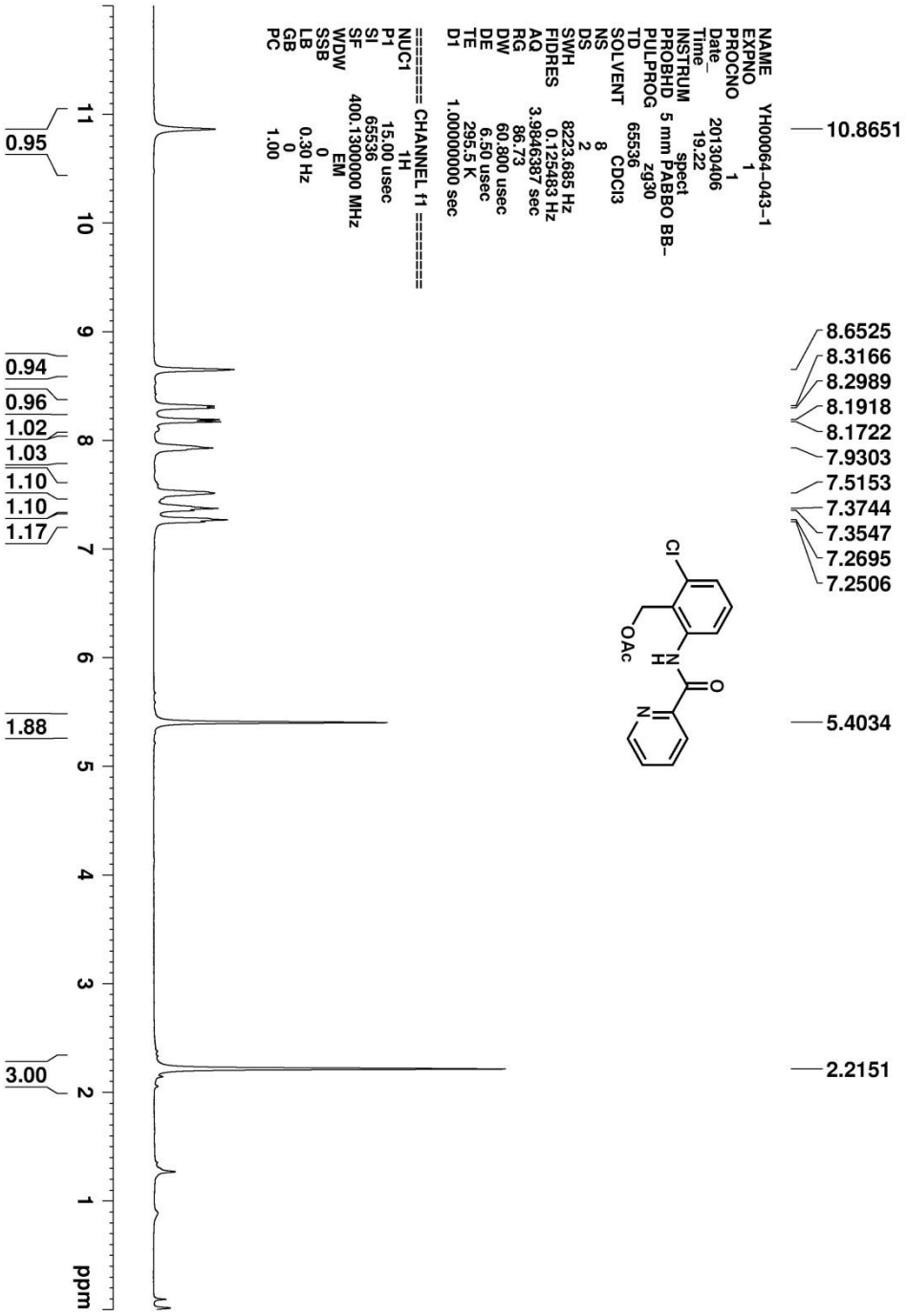
Compound 2h (400 MHz, $CDCl_3$)



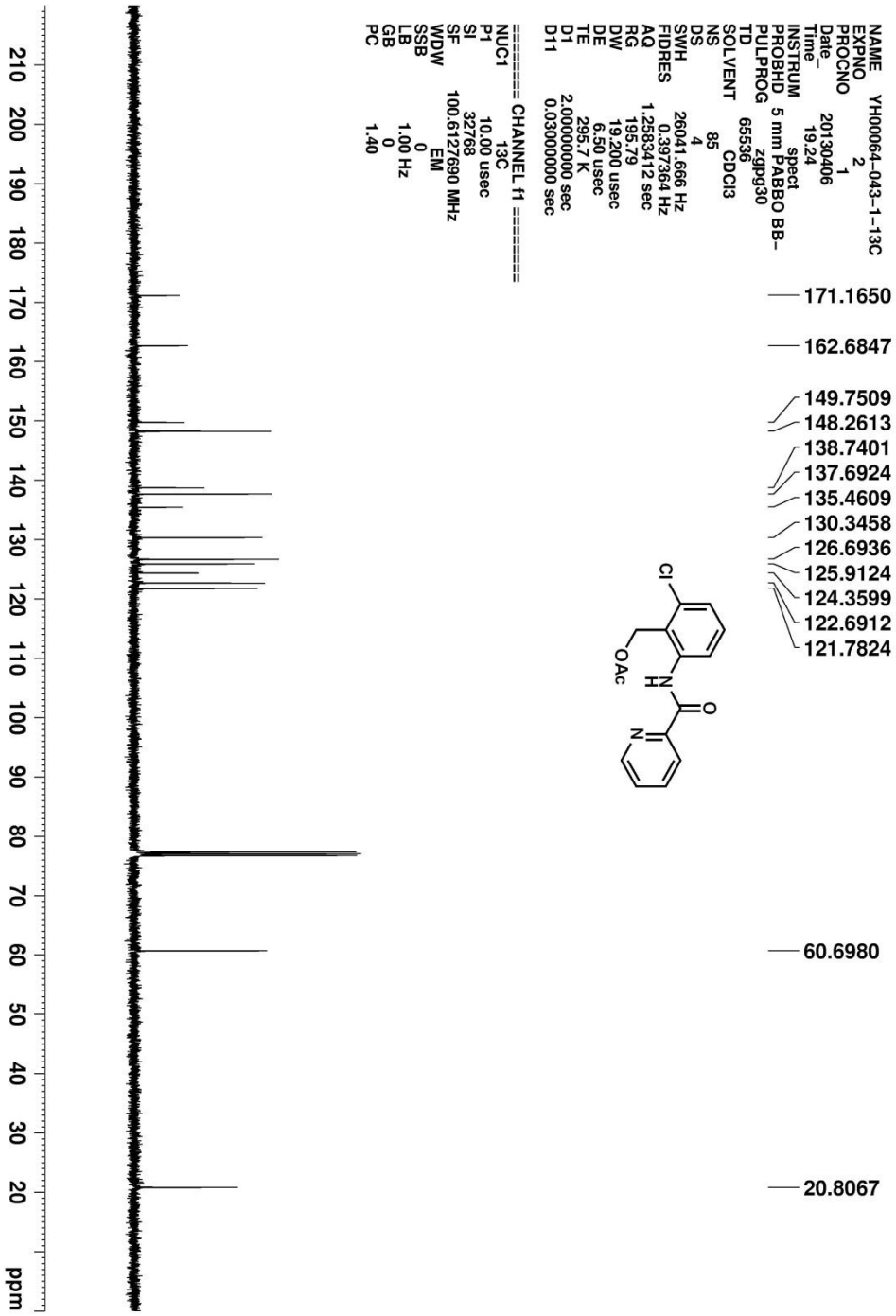
Compound 2h (100 MHz, $CDCl_3$)



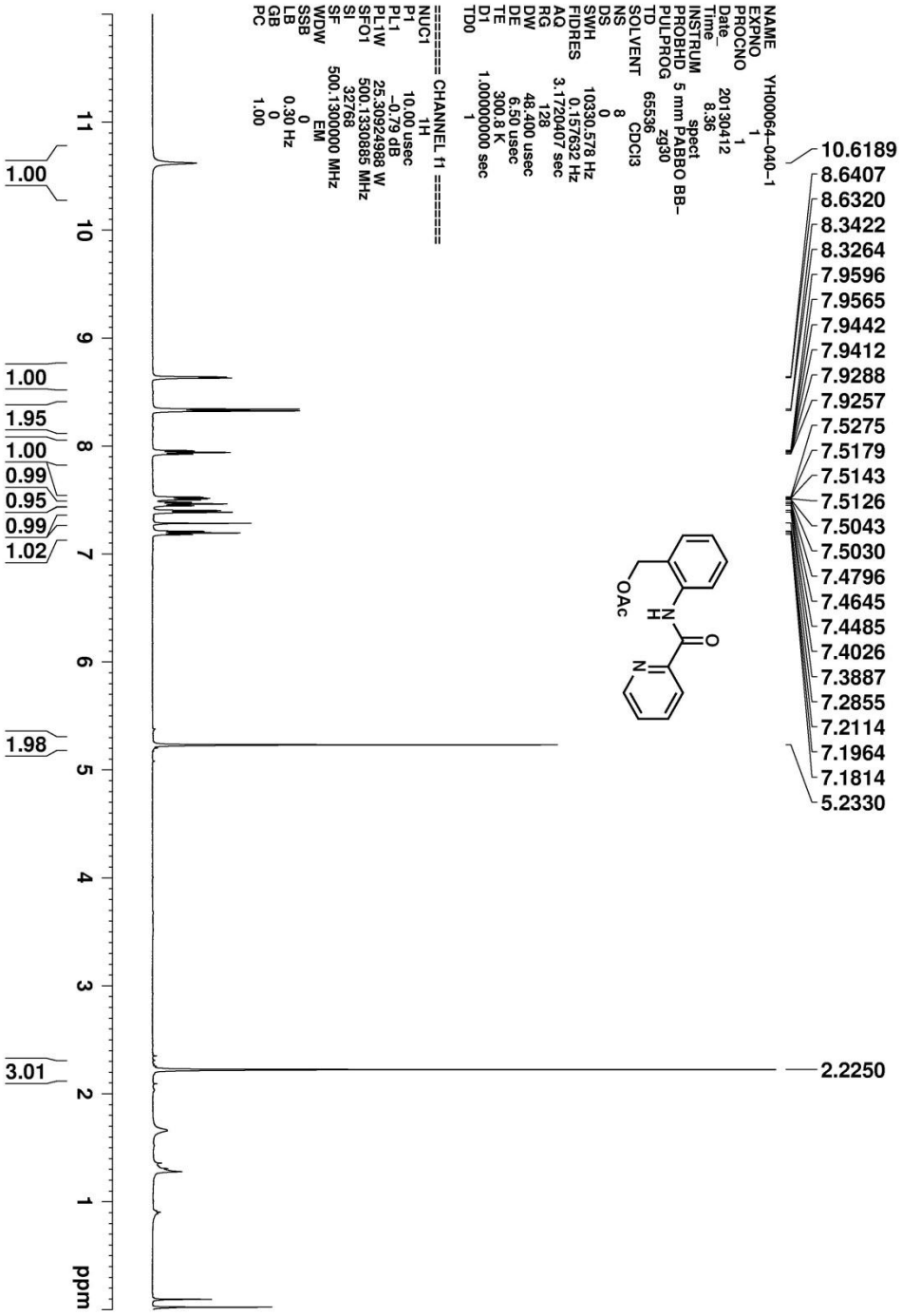
Compound 2i (400 MHz, $CDCl_3$)



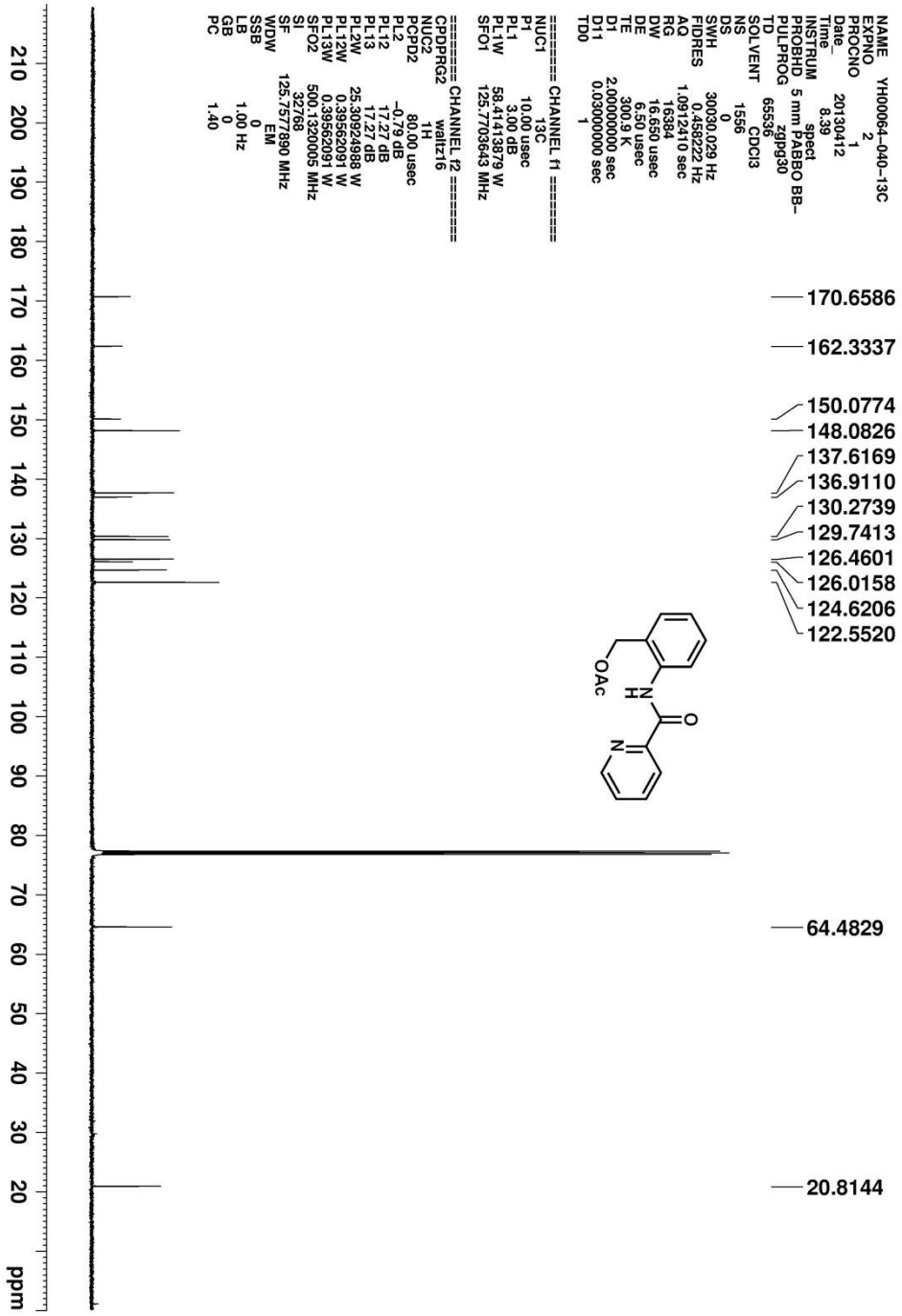
Compound 2i (100 MHz, $CDCl_3$)



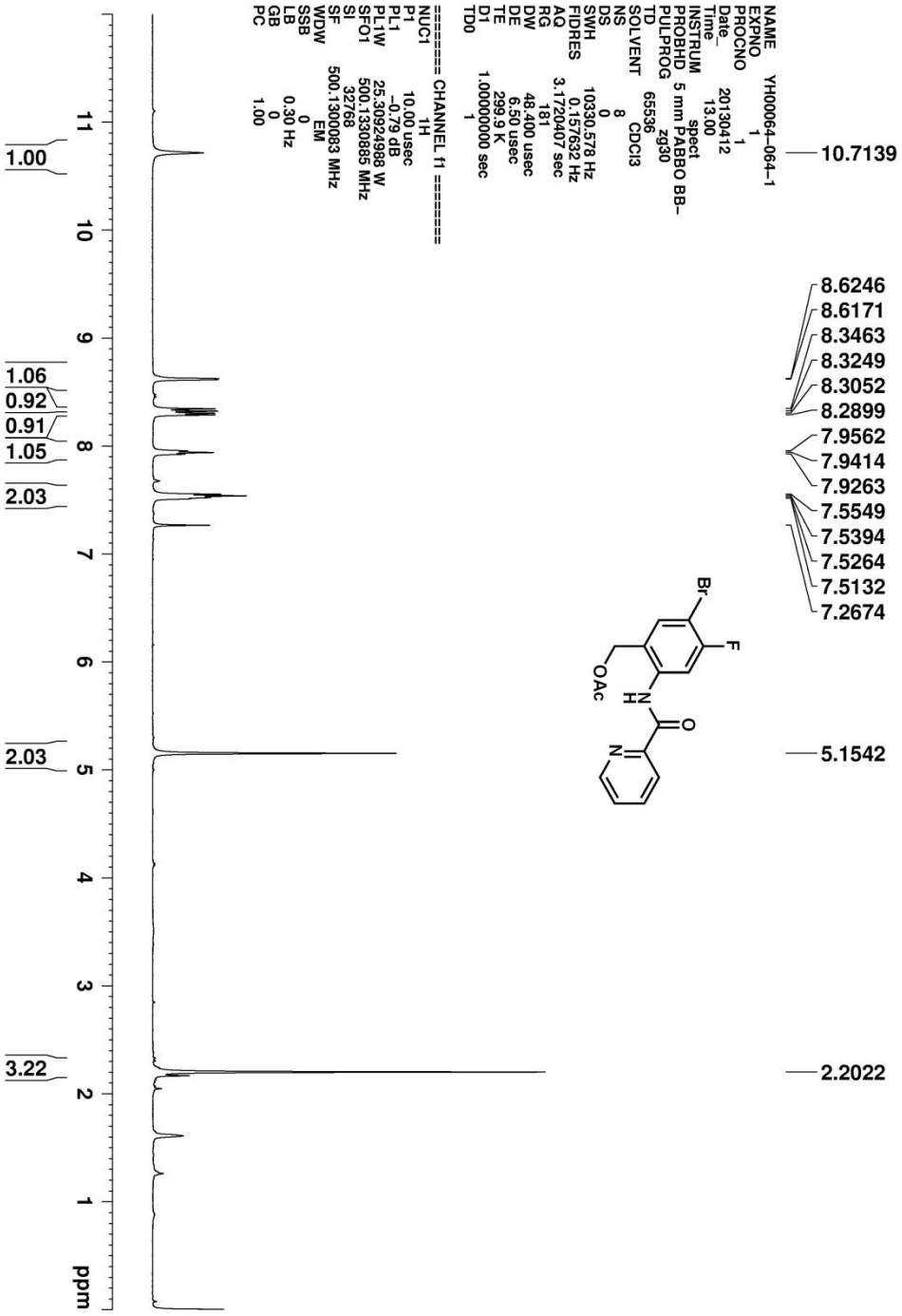
Compound 2j (500 MHz, $CDCl_3$)



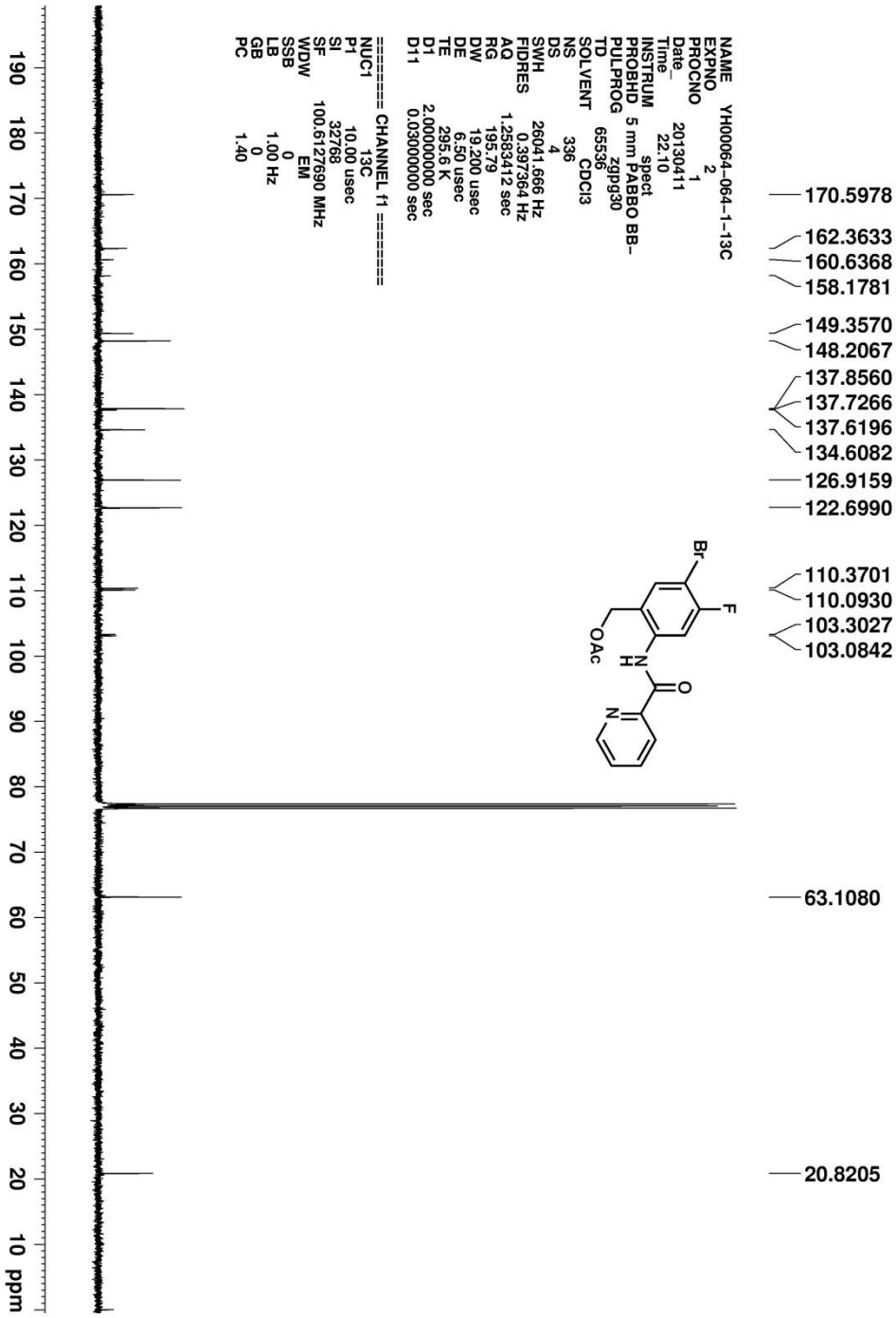
Compound 2j (125 MHz, $CDCl_3$)



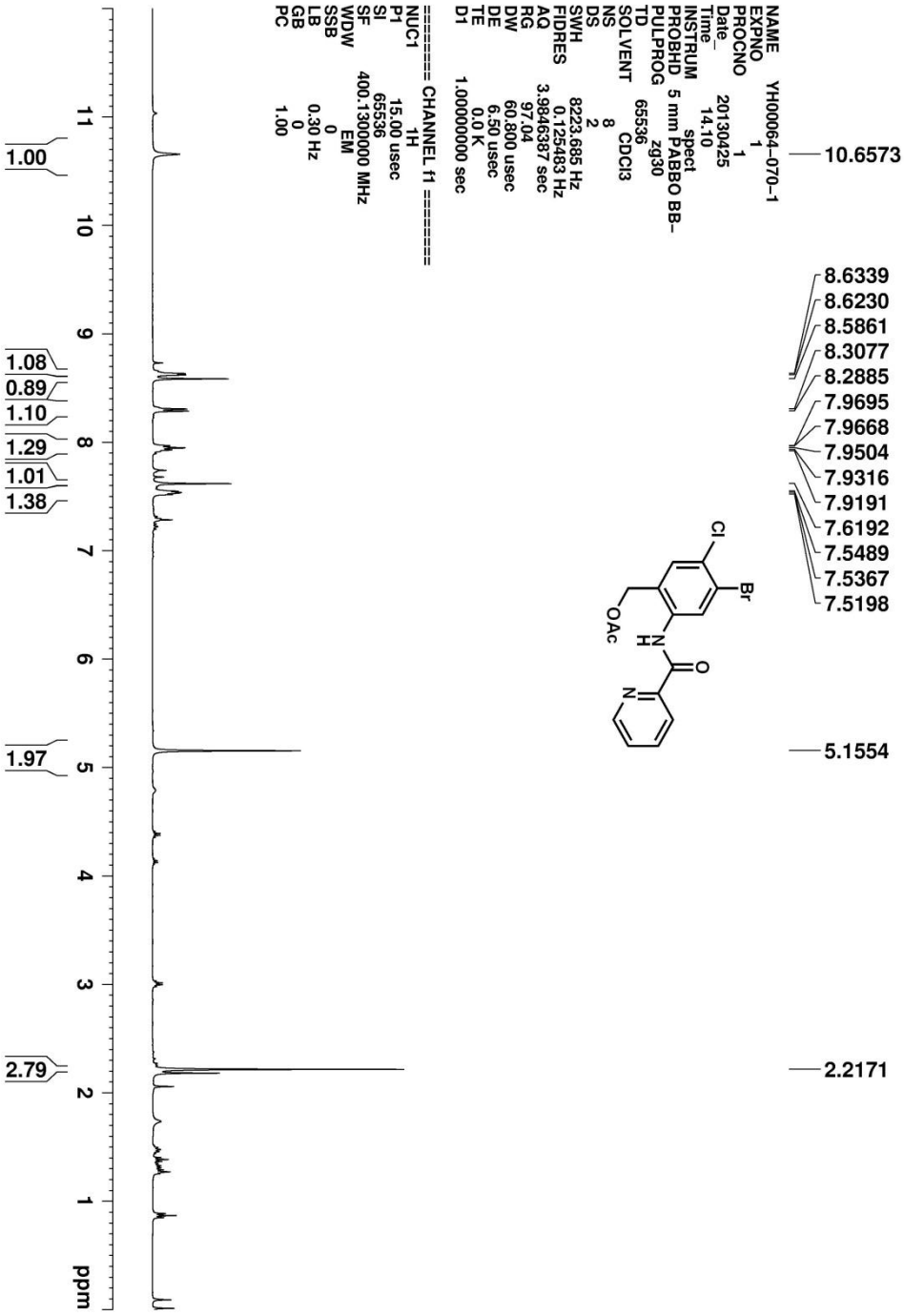
Compound 2k (500 MHz, $CDCl_3$)



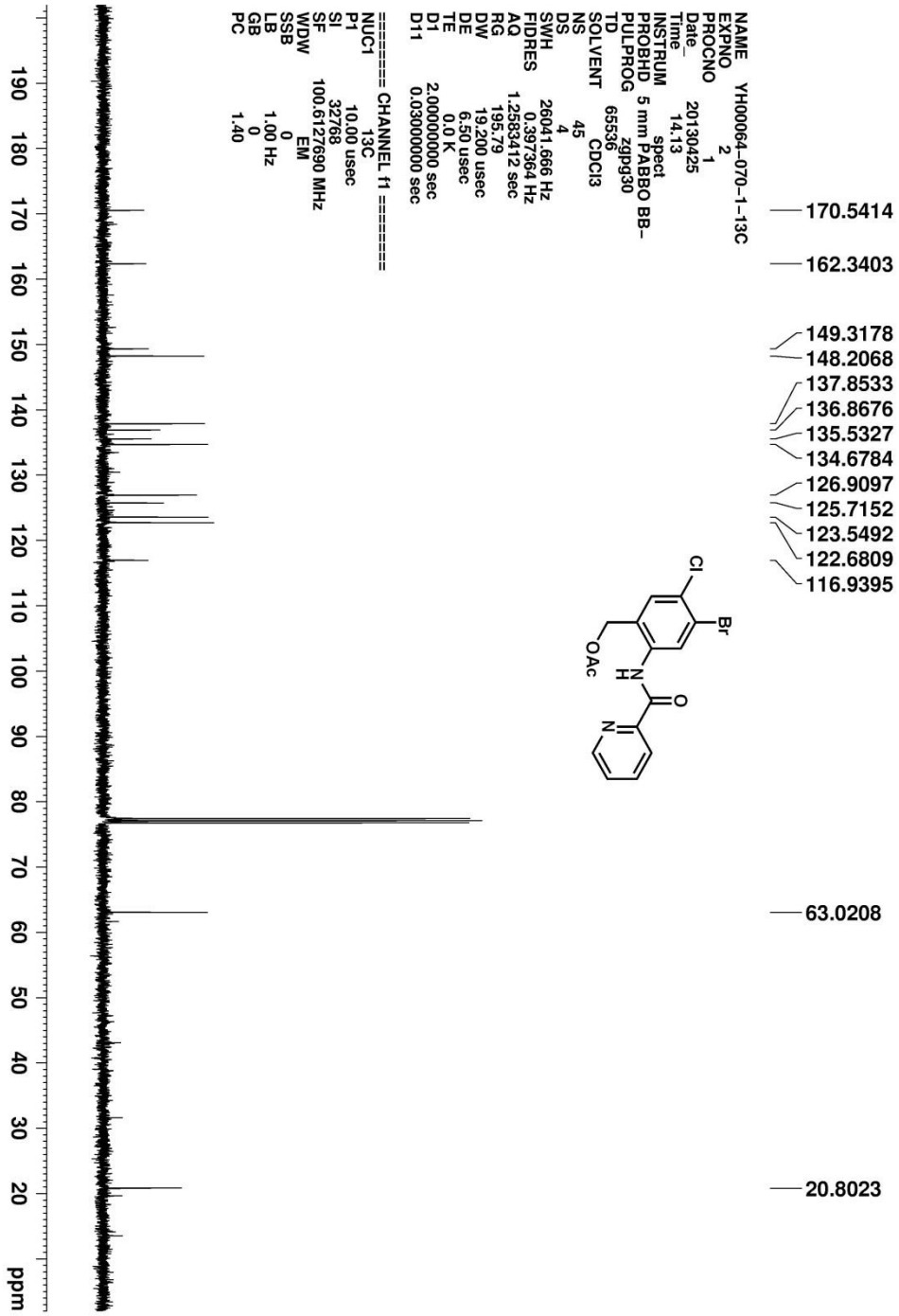
Compound 2k (100MHz, $CDCl_3$)



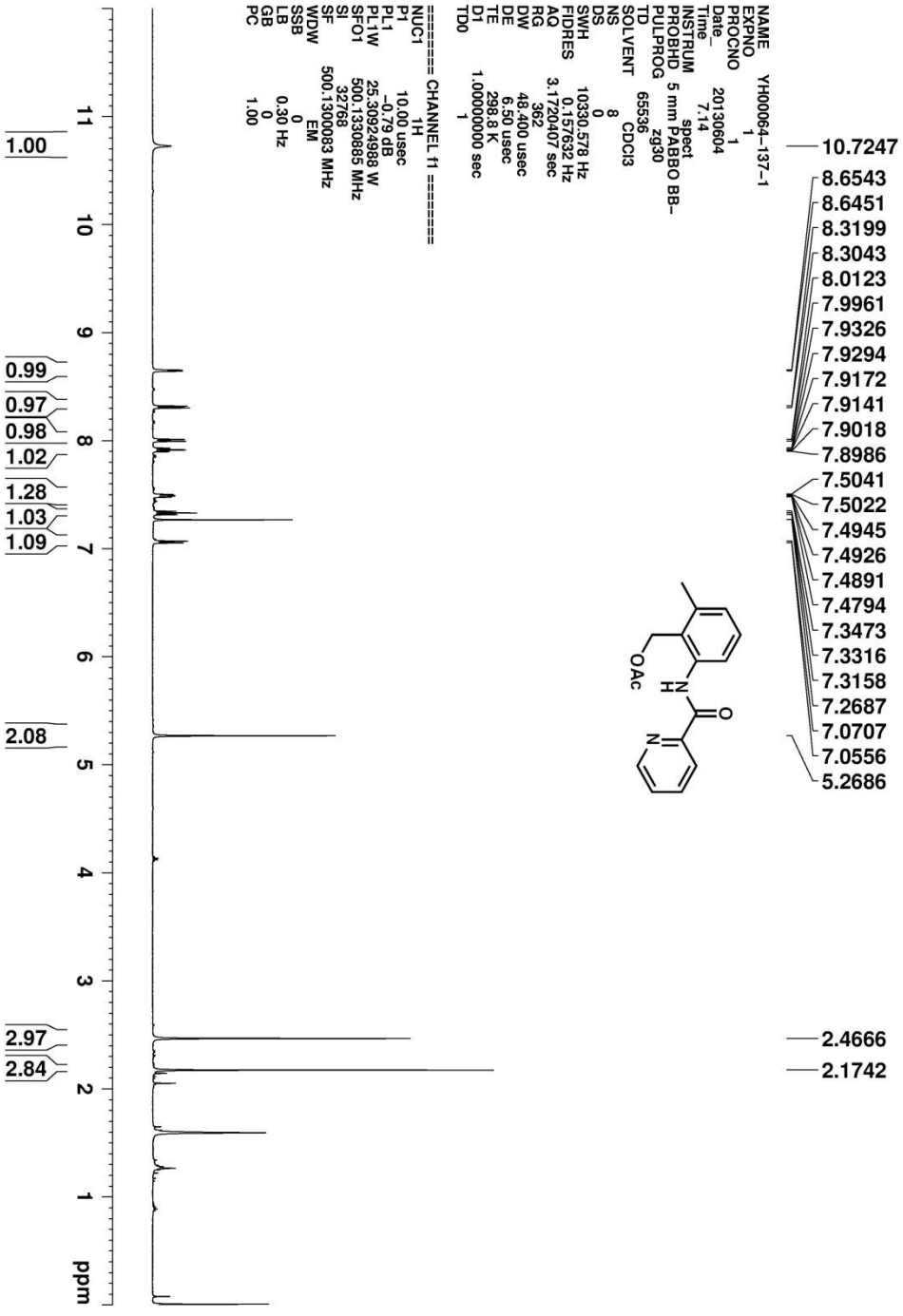
Compound 2l (400 MHz, $CDCl_3$)



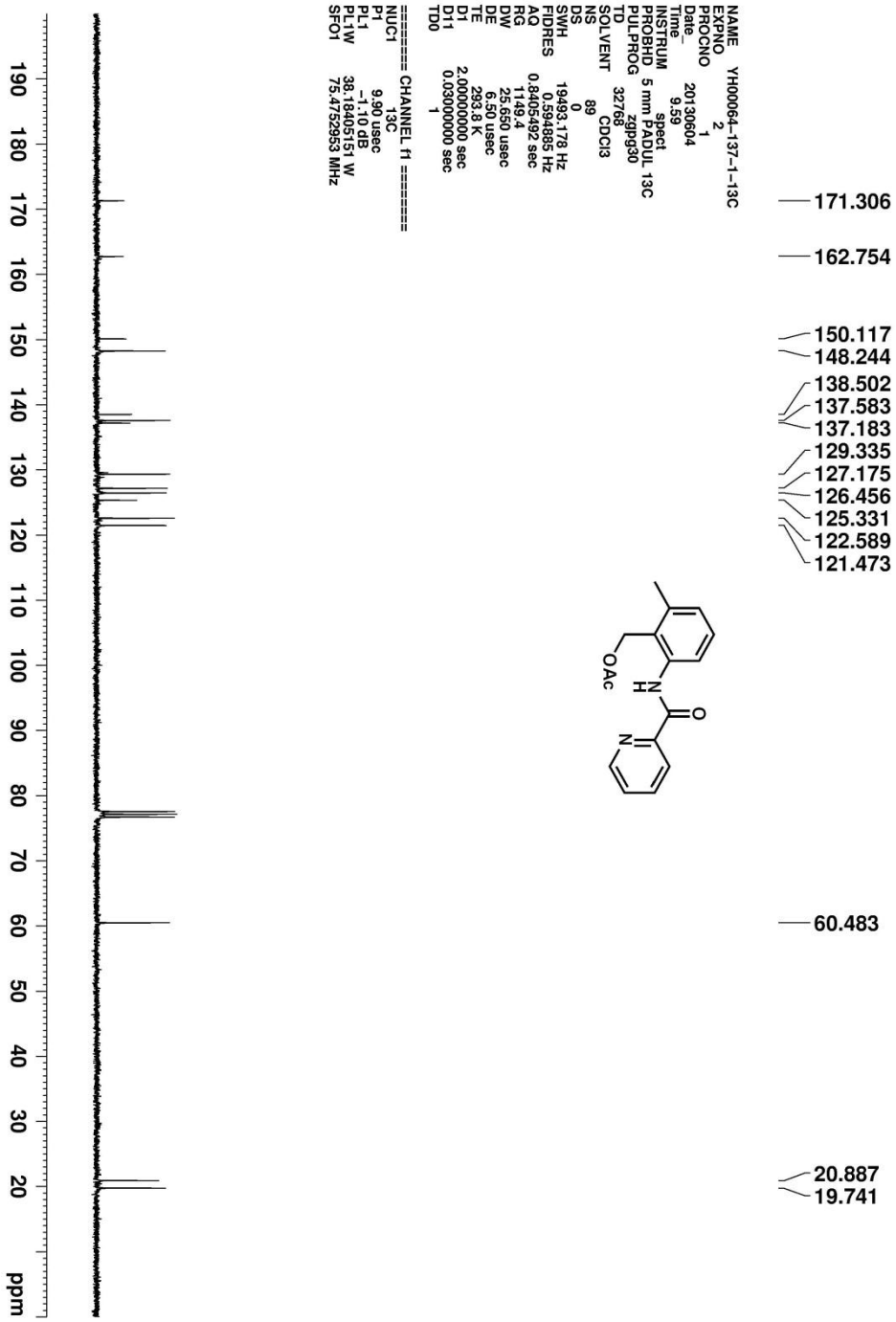
Compound 2l (100 MHz, $CDCl_3$)



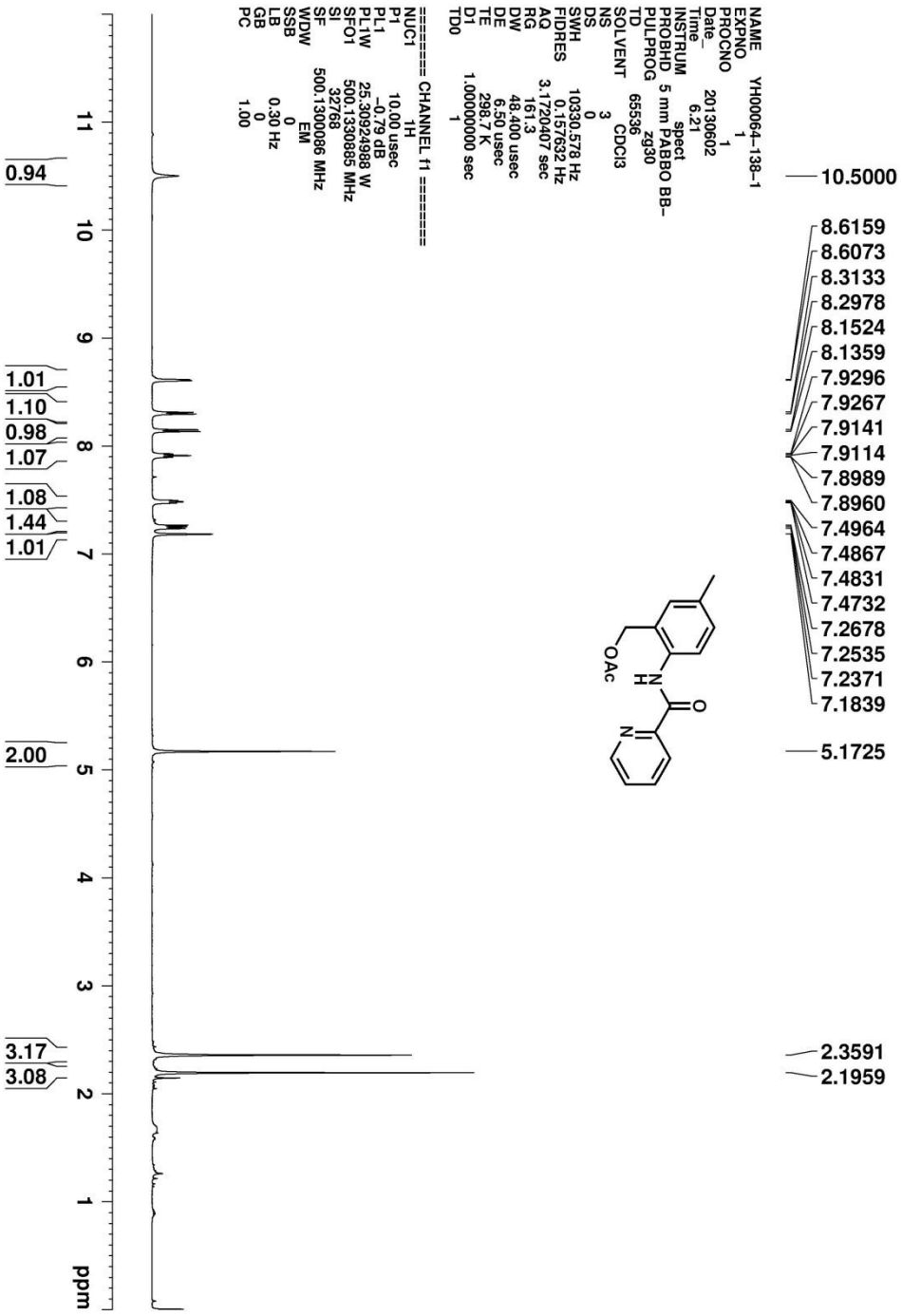
Compound 2m (500MHz, $CDCl_3$)



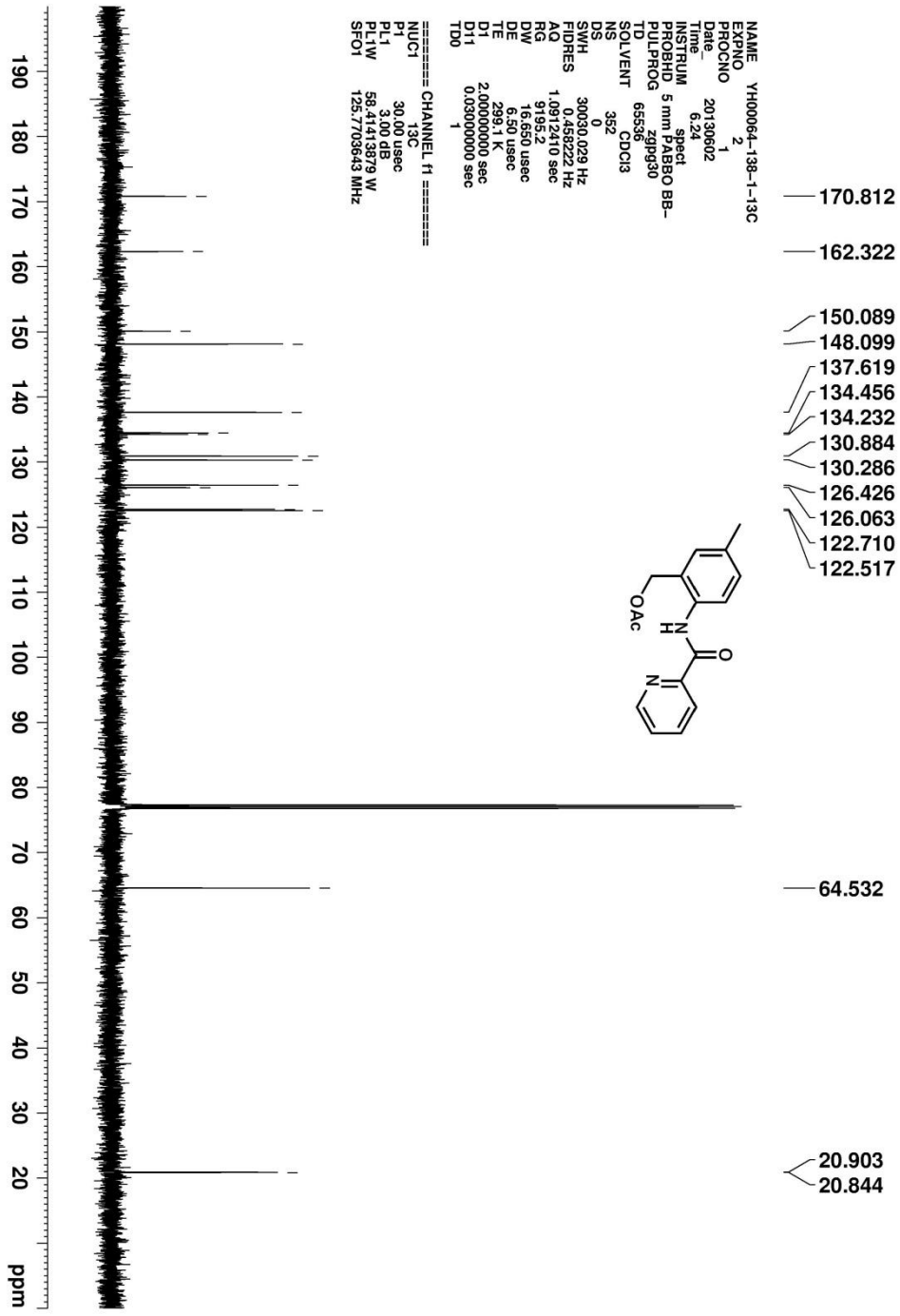
Compound 2m (75MHz, $CDCl_3$)



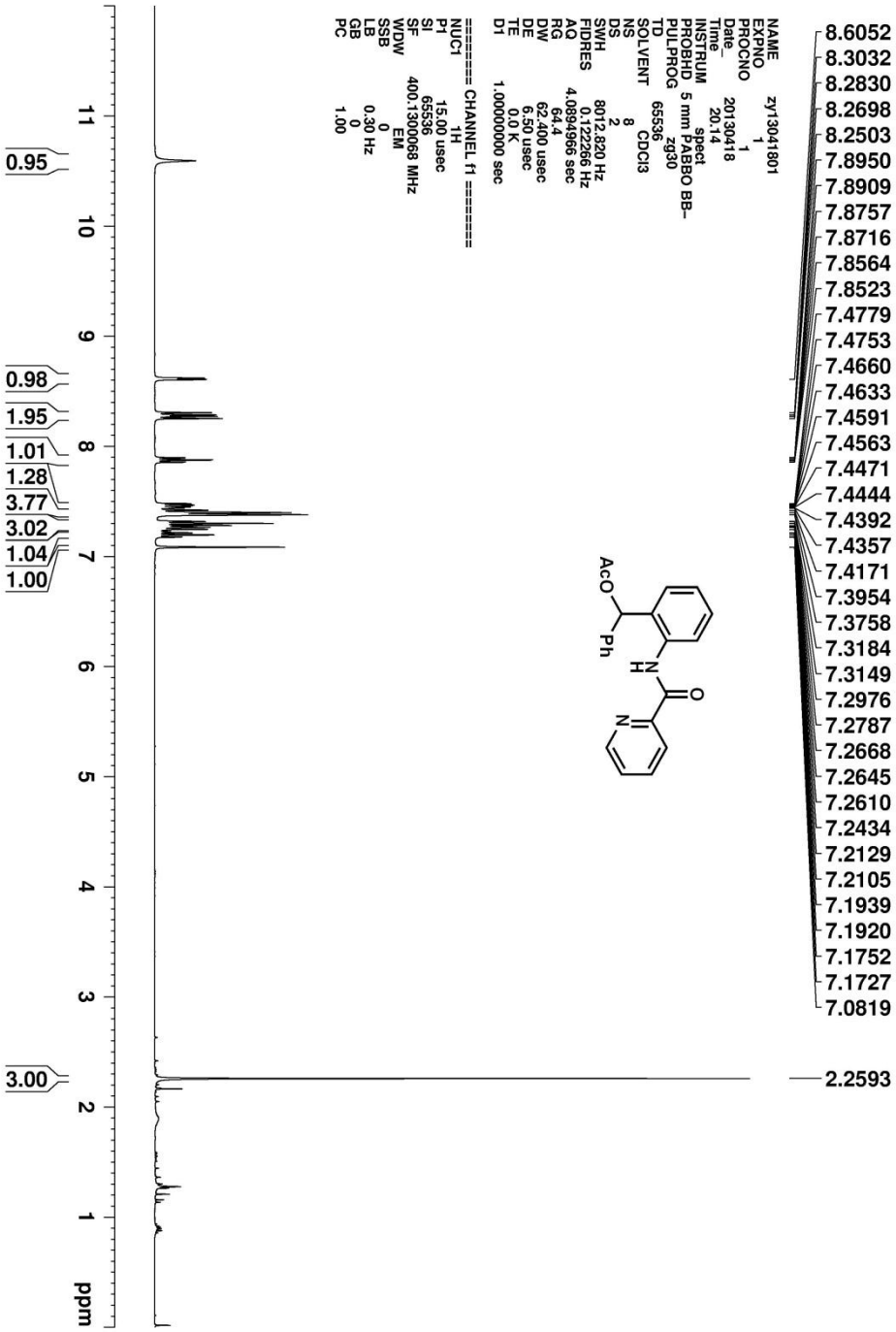
Compound 2n (500MHz, $CDCl_3$)



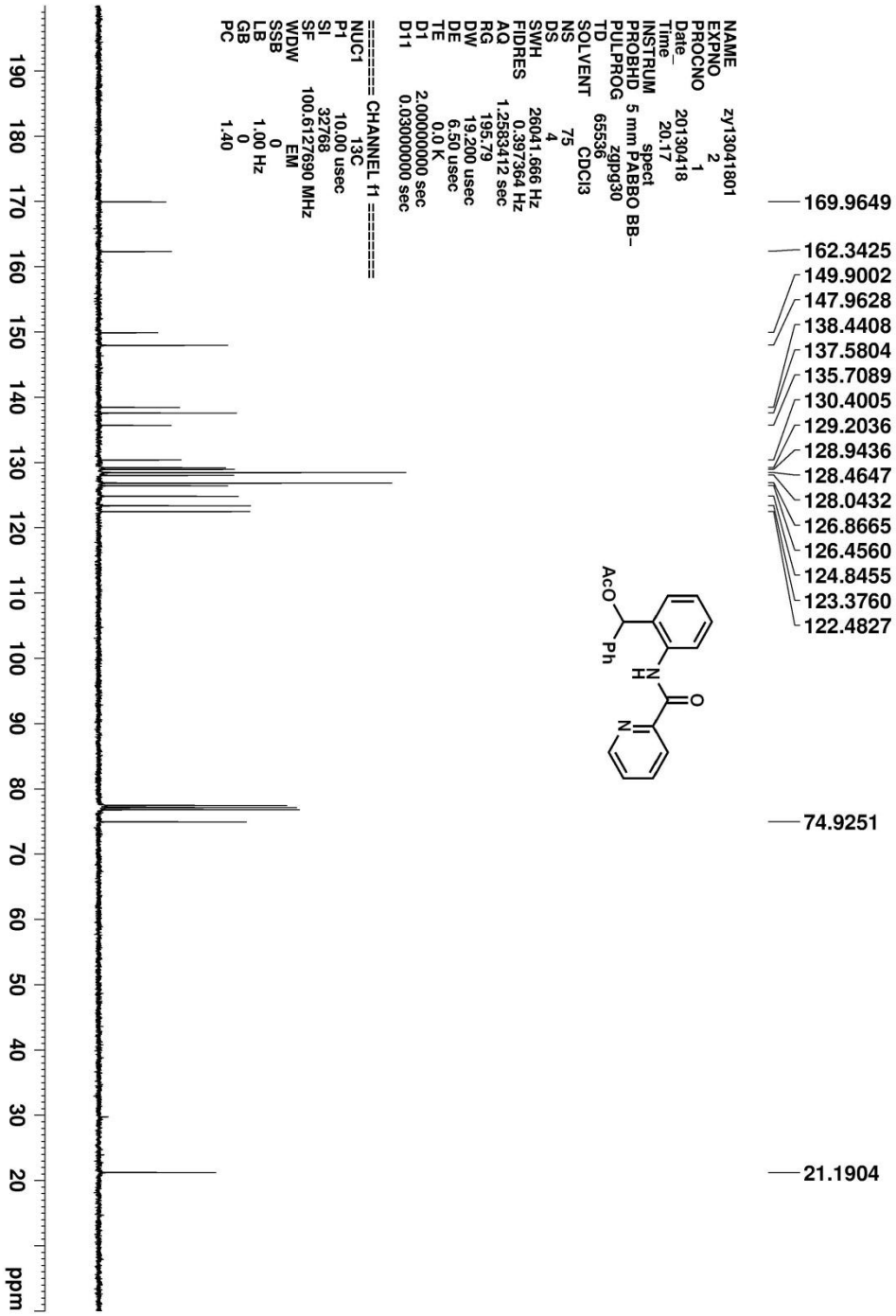
Compound 2n (125 MHz, $CDCl_3$)



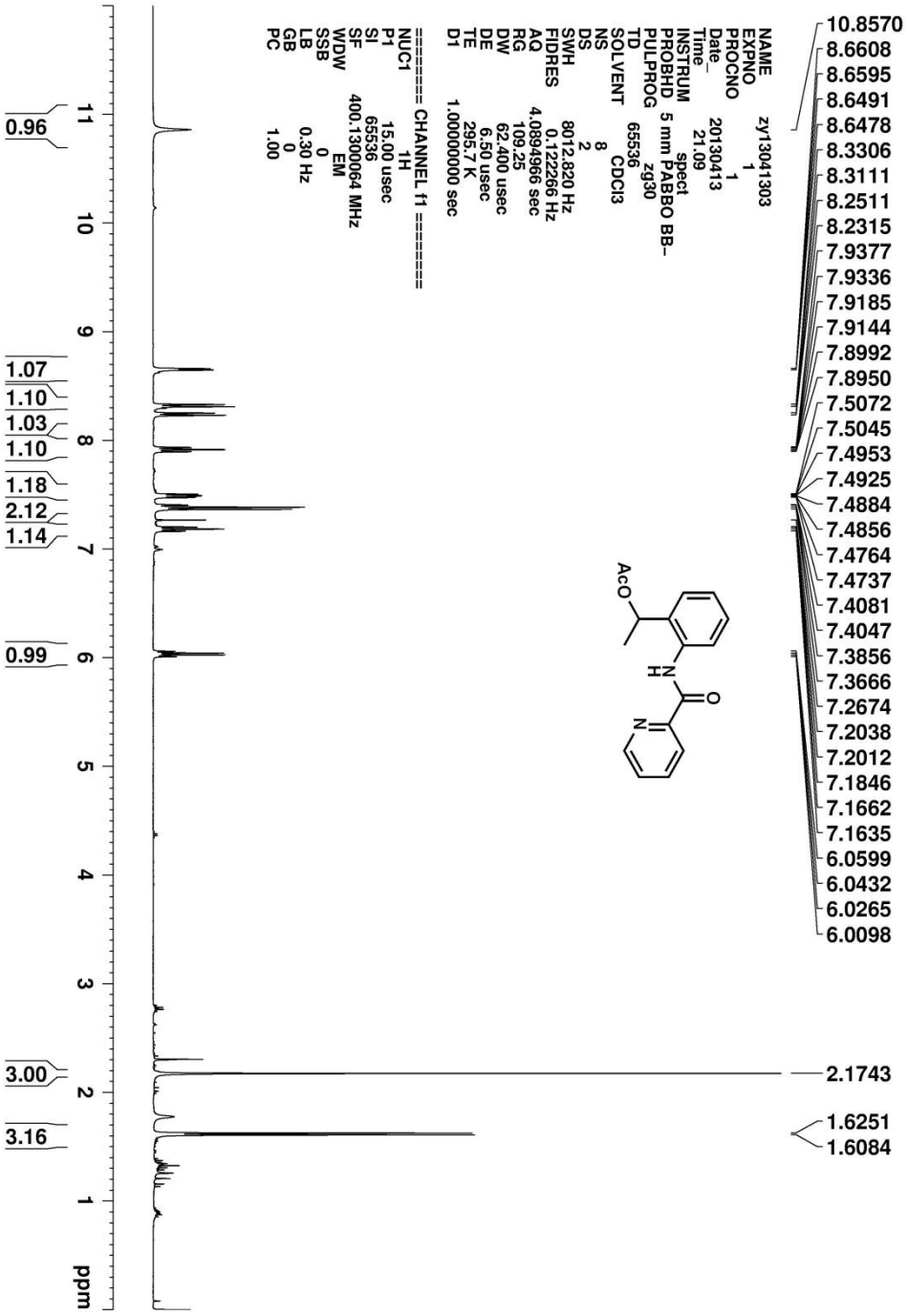
Compound 2o (400 MHz, $CDCl_3$)



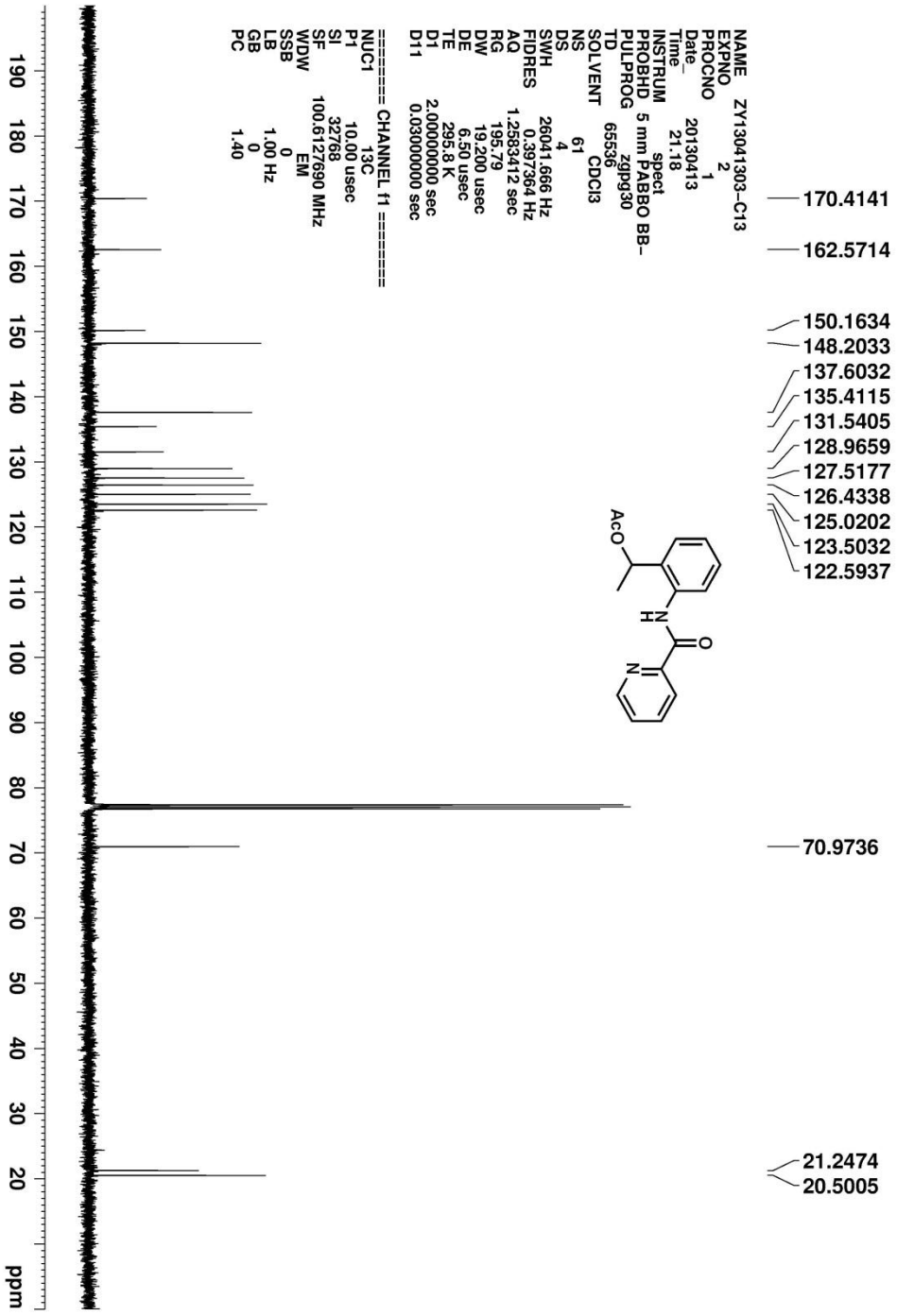
Compound 2o (100 MHz, $CDCl_3$)



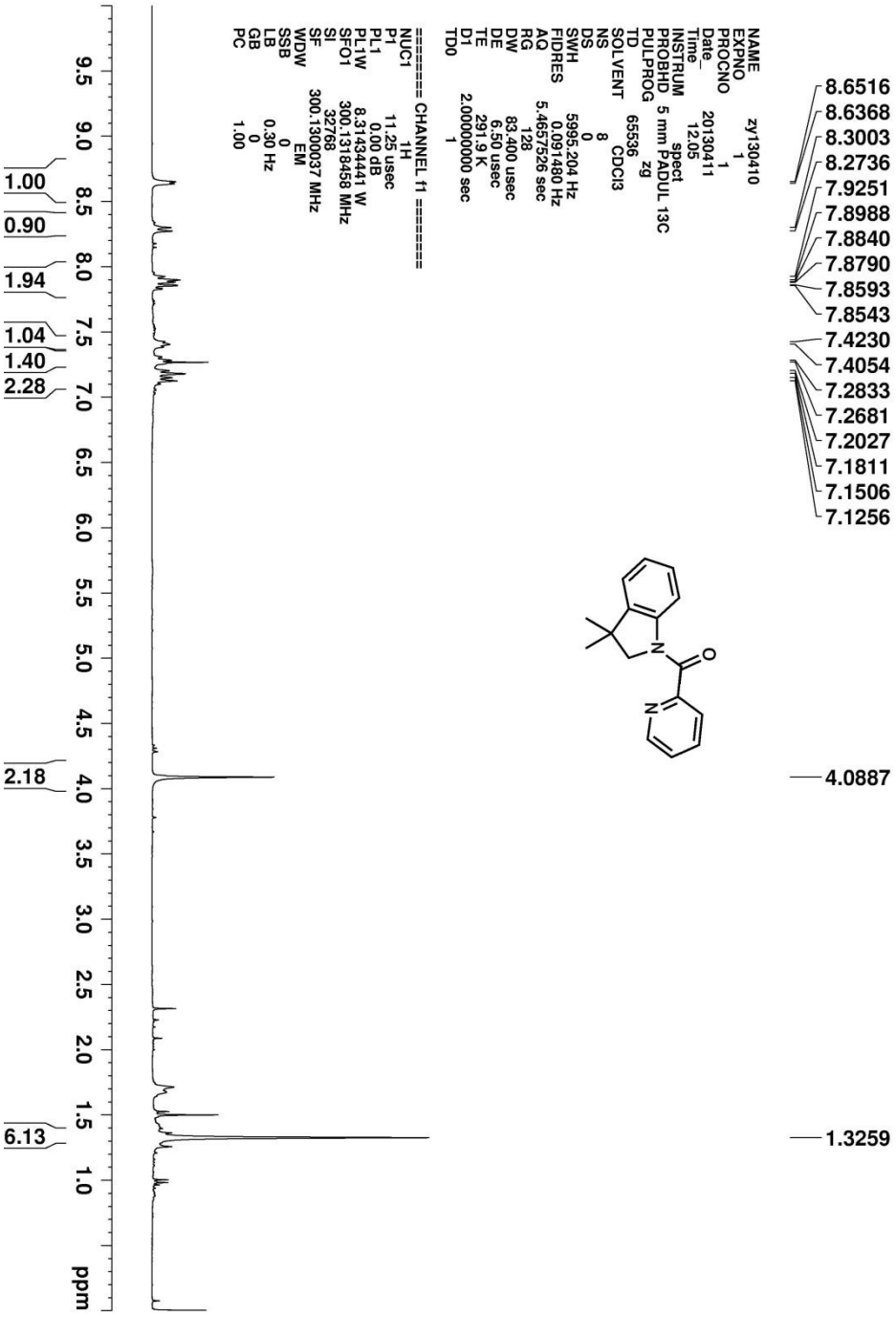
Compound 2p (400 MHz, $CDCl_3$)



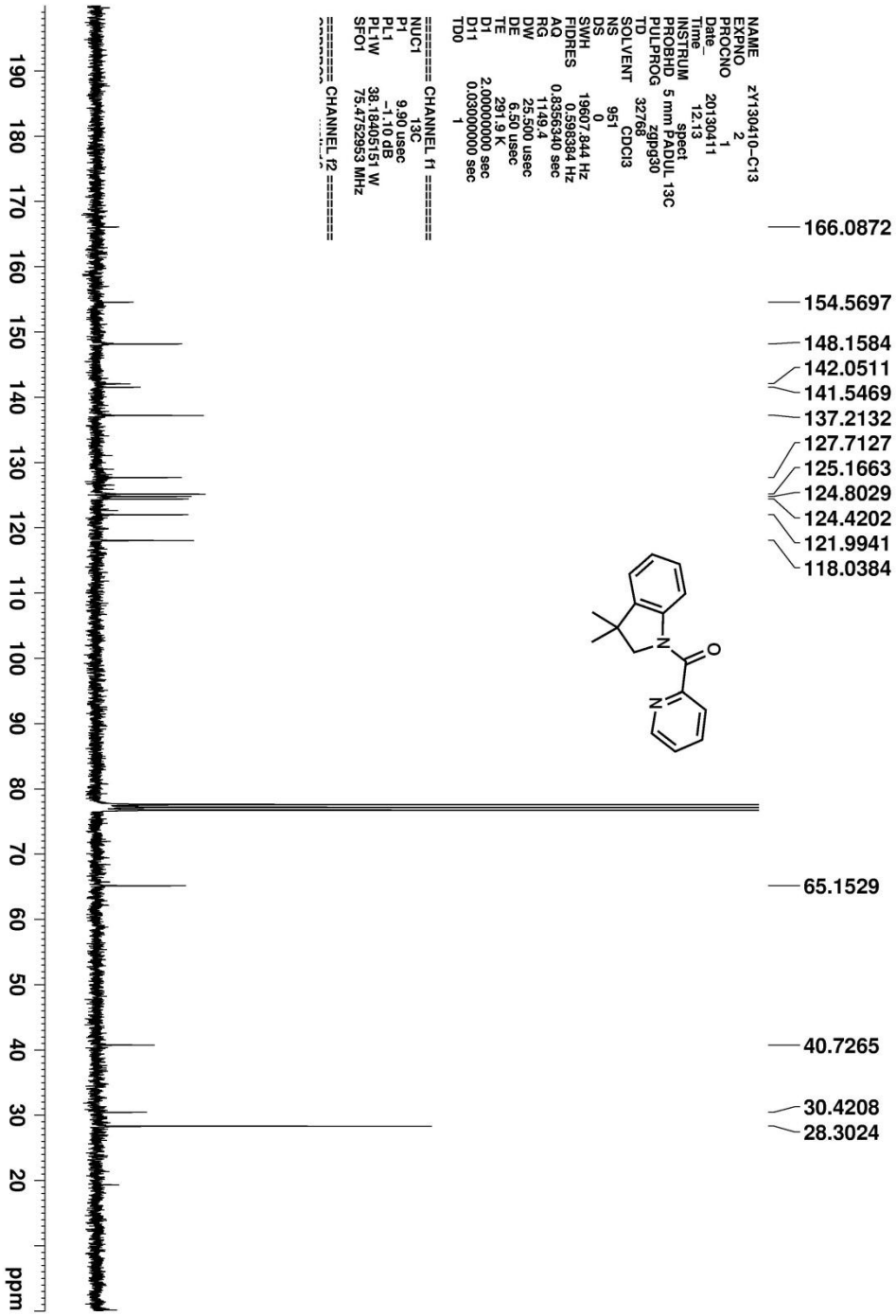
Compound 2p (100 MHz, $CDCl_3$)



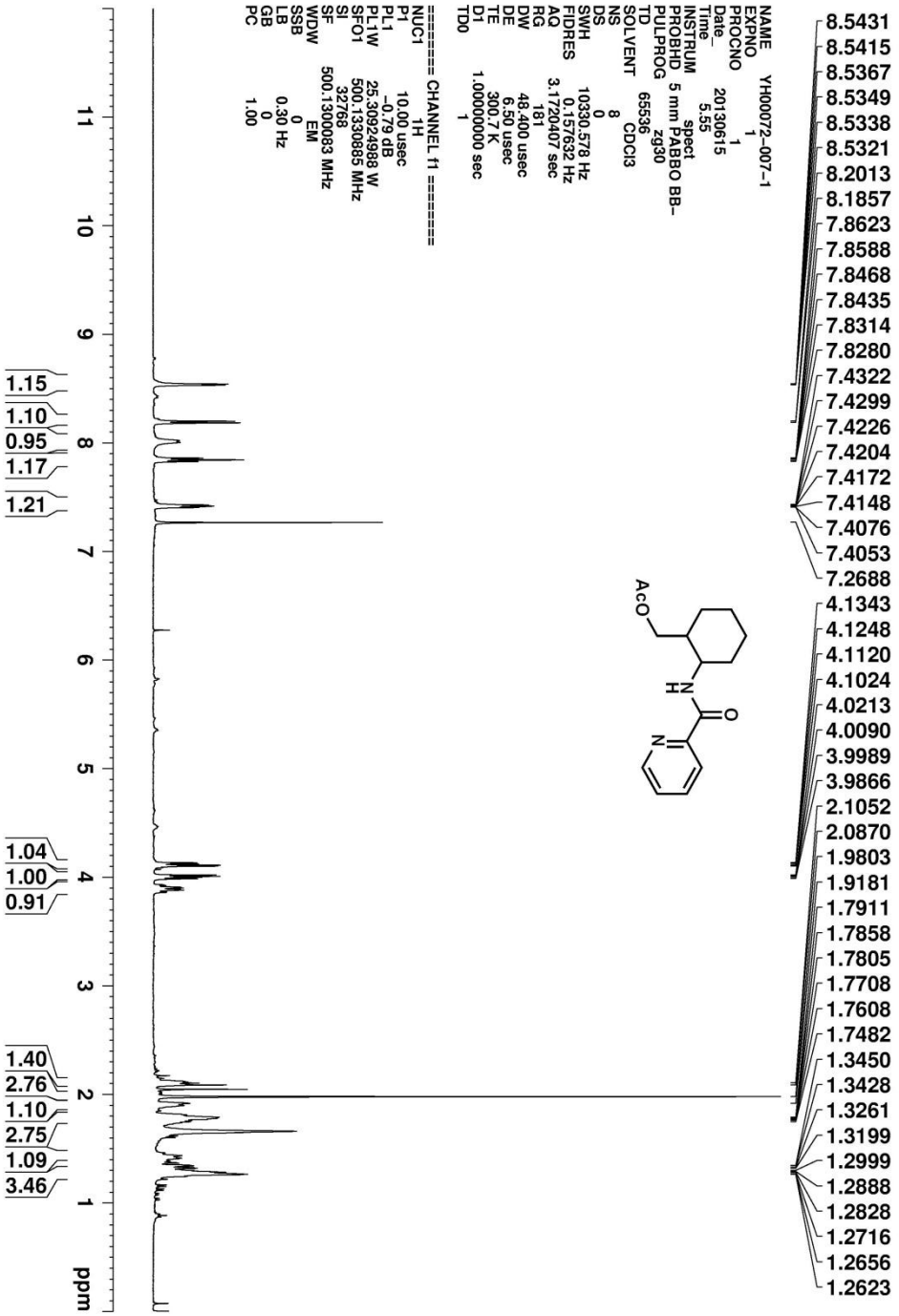
Compound 2q (300 MHz, $CDCl_3$)



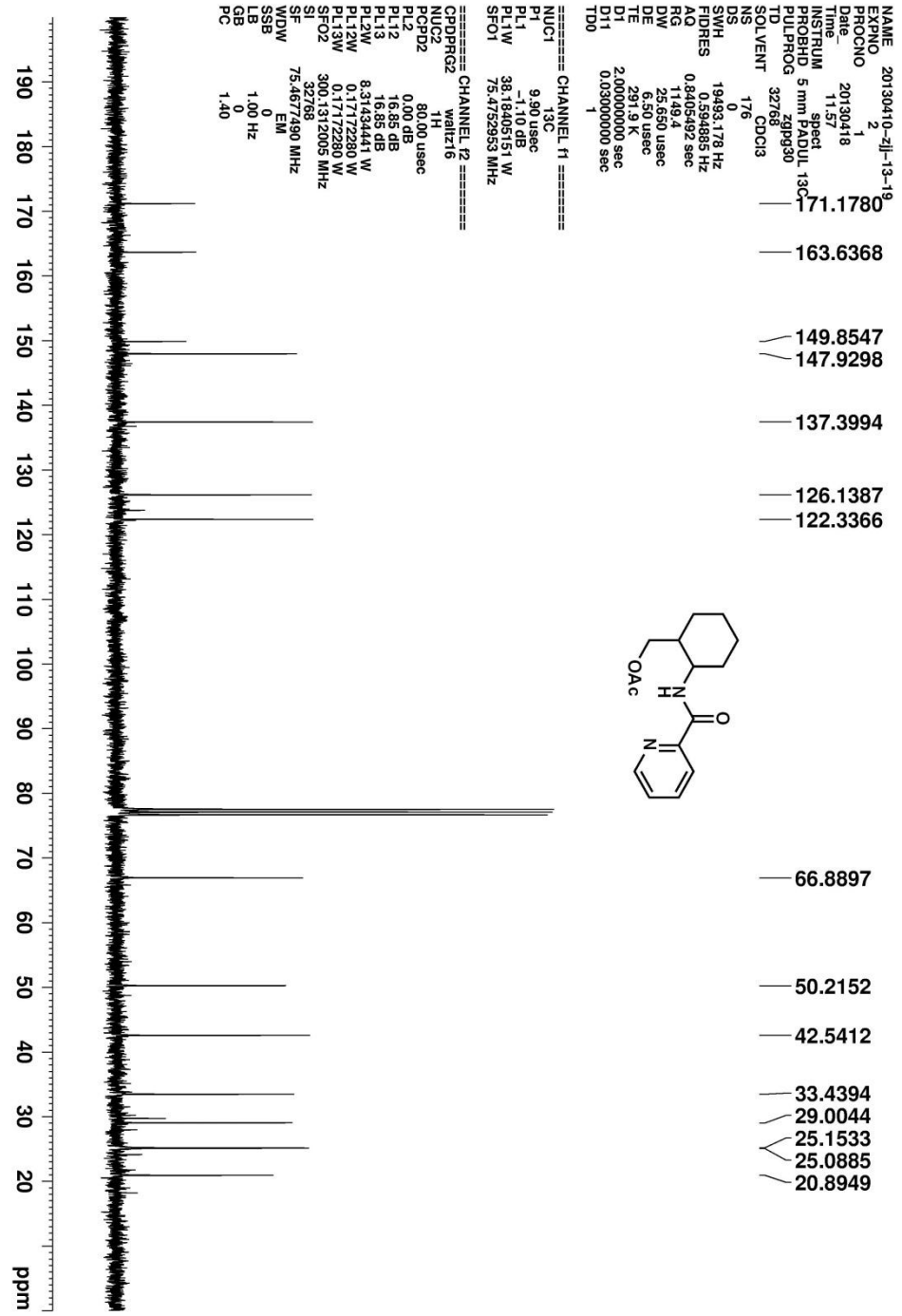
Compound 2q (75 MHz, $CDCl_3$)



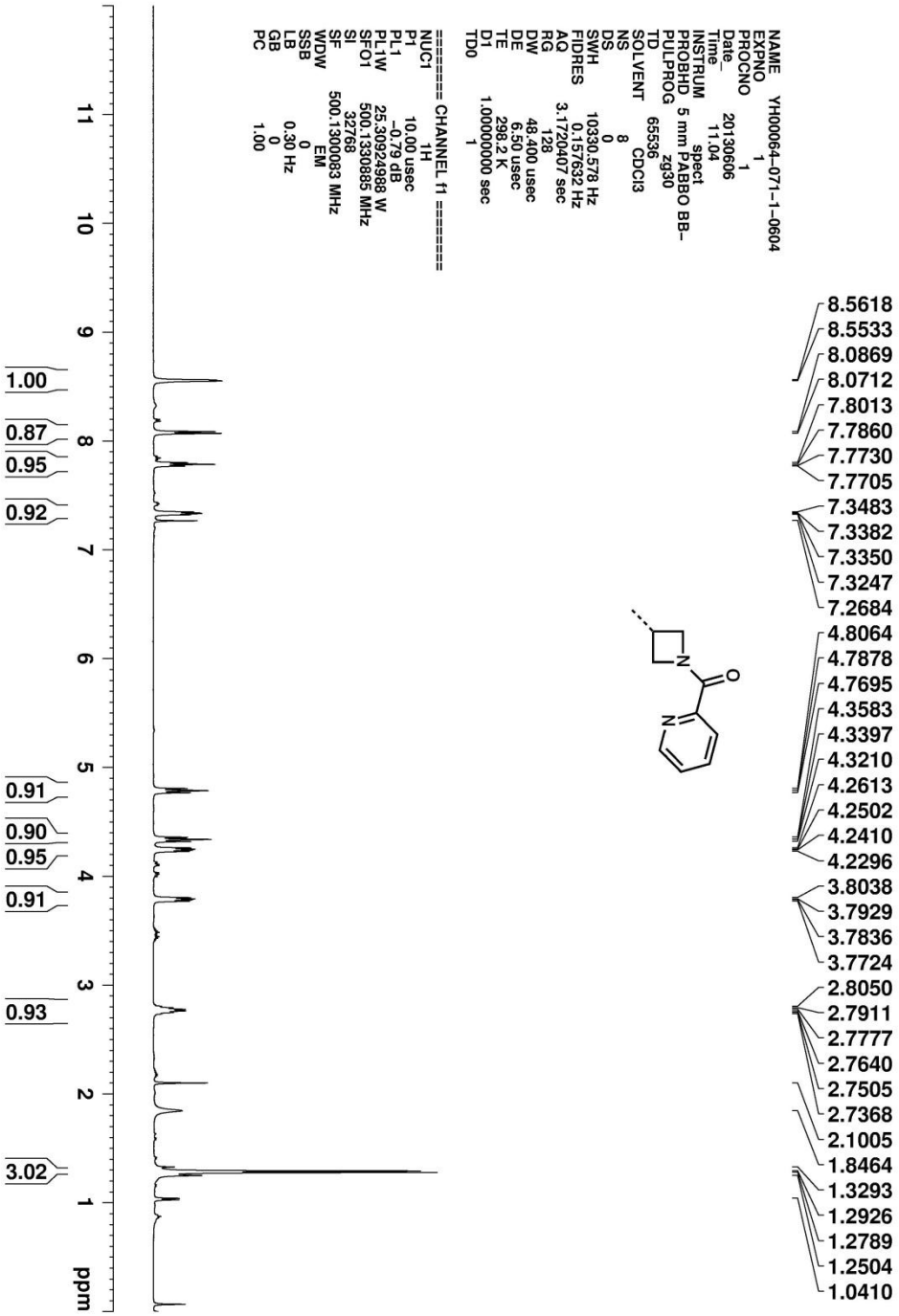
Compound 2r (500 MHz, $CDCl_3$)



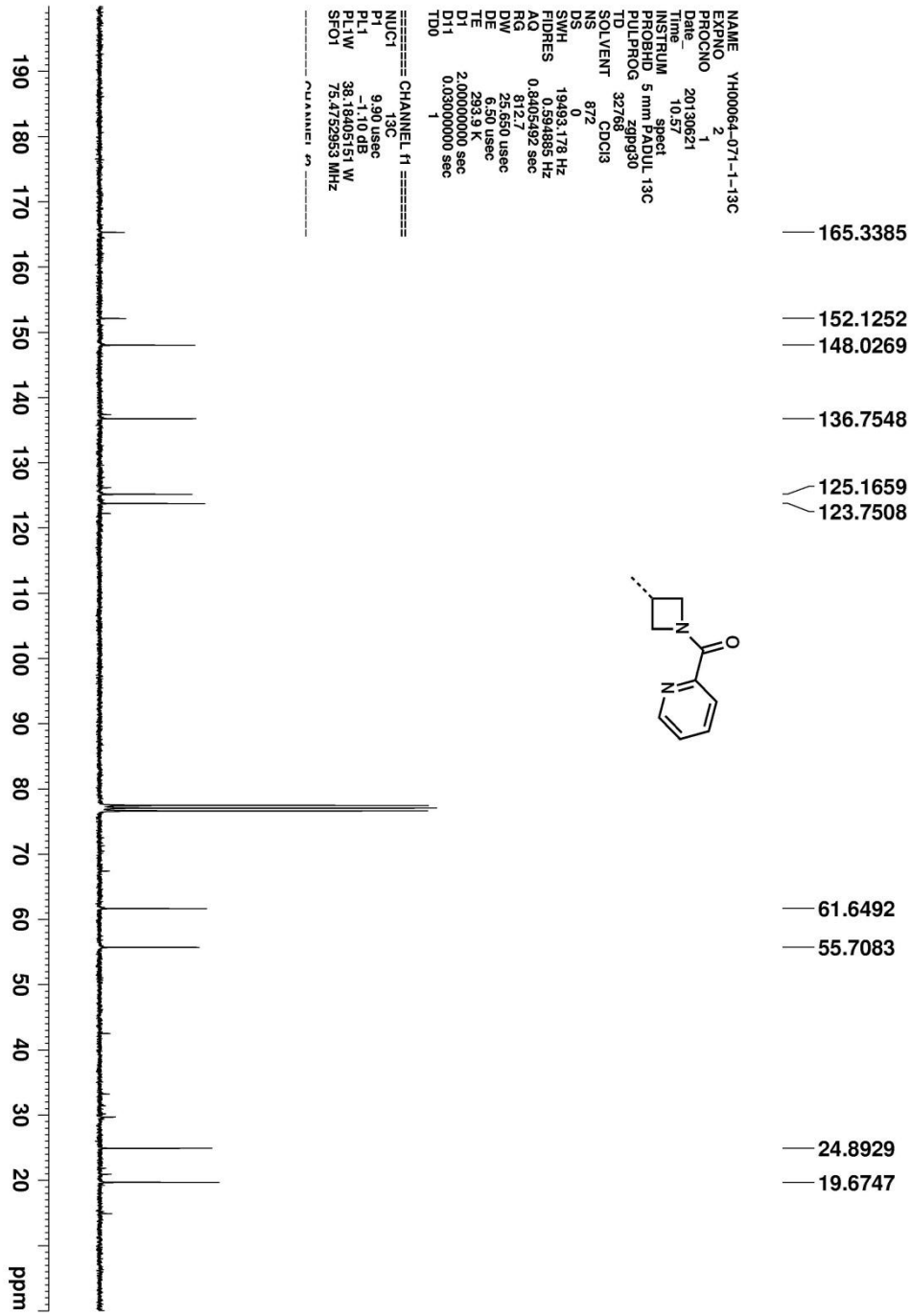
Compound 2r (75 MHz, $CDCl_3$)



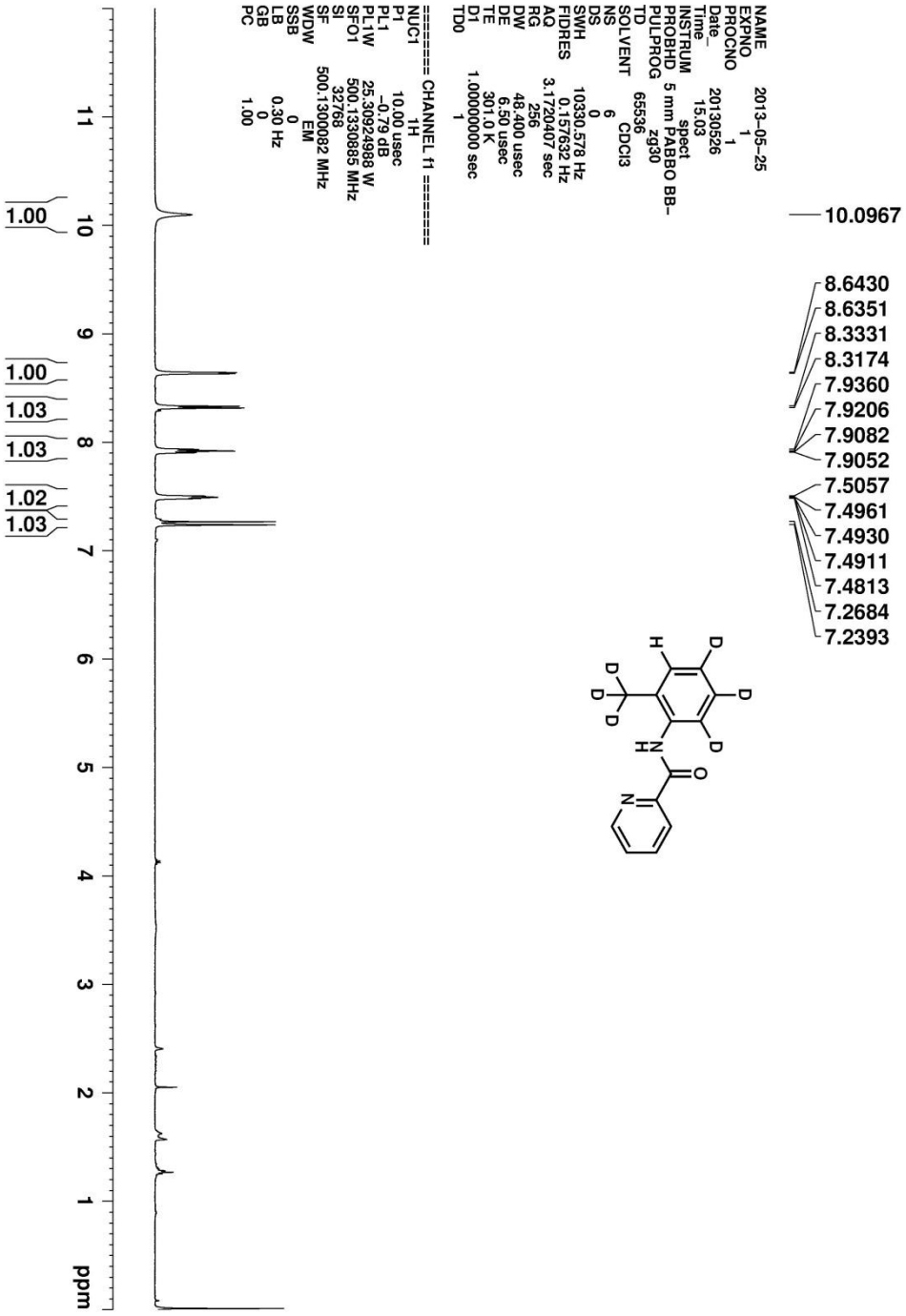
Compound 2s (500 MHz, $CDCl_3$)



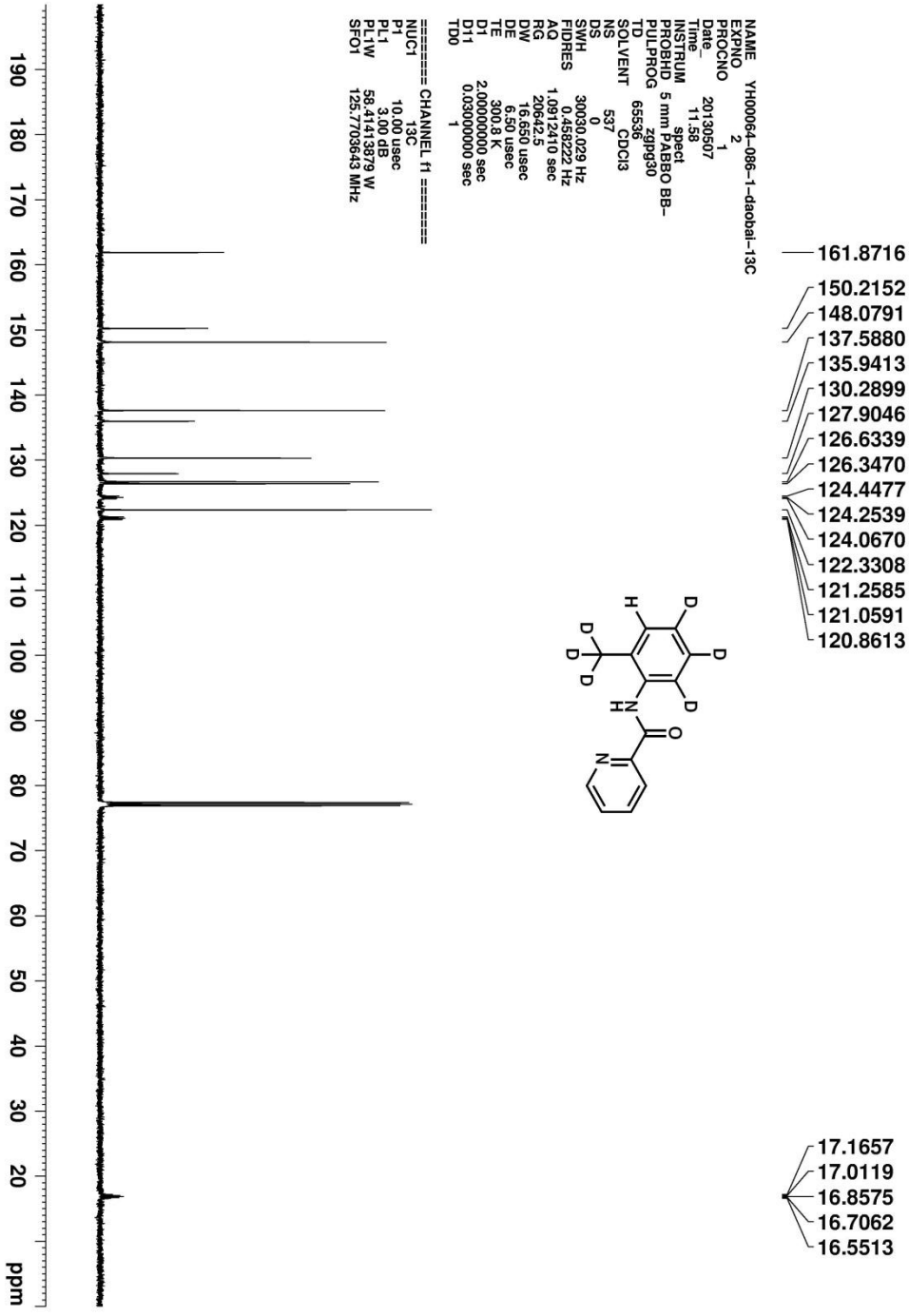
Compound 2s (75 MHz, $CDCl_3$)



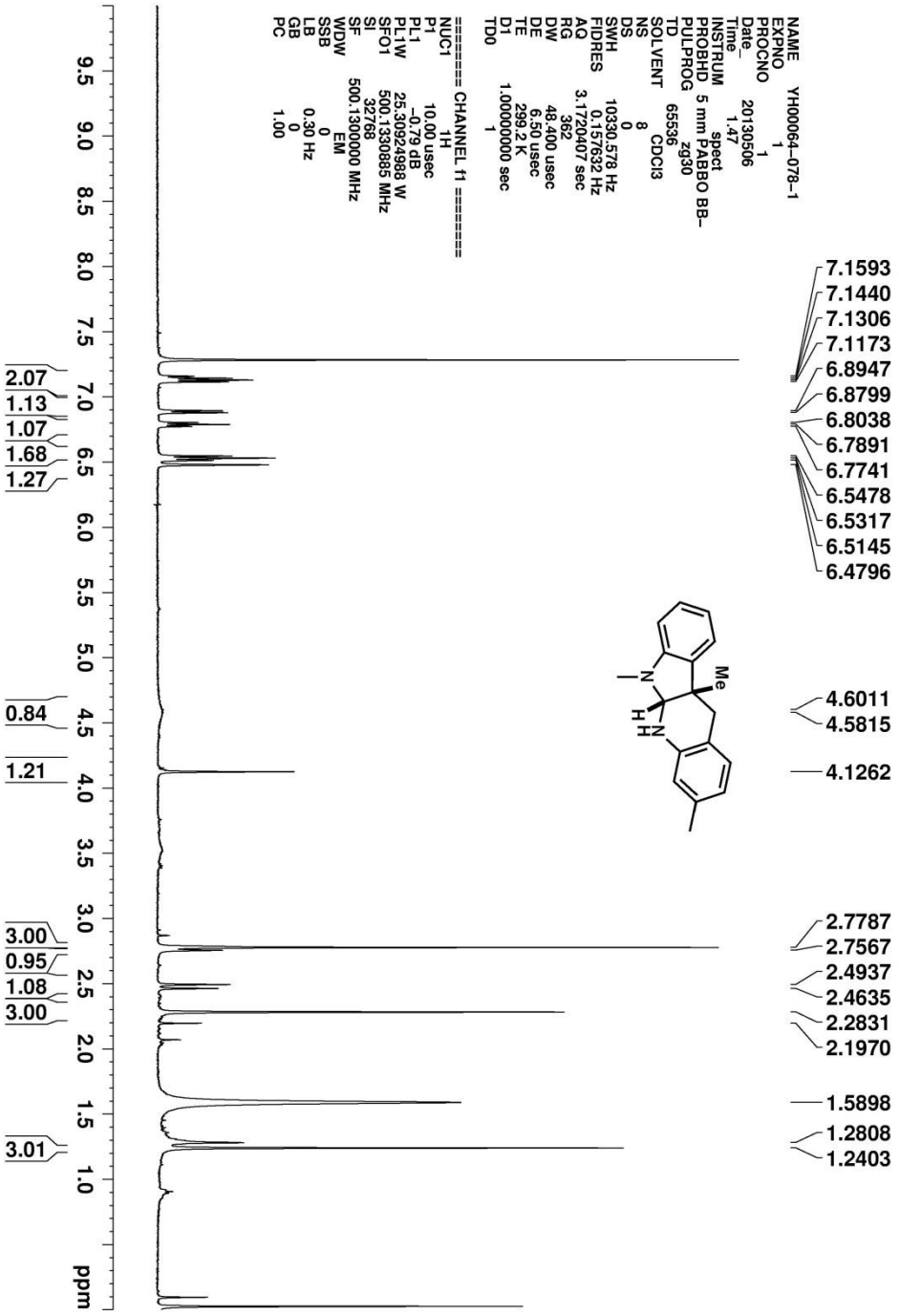
Compound d^6-1j (500 MHz, $CDCl_3$)



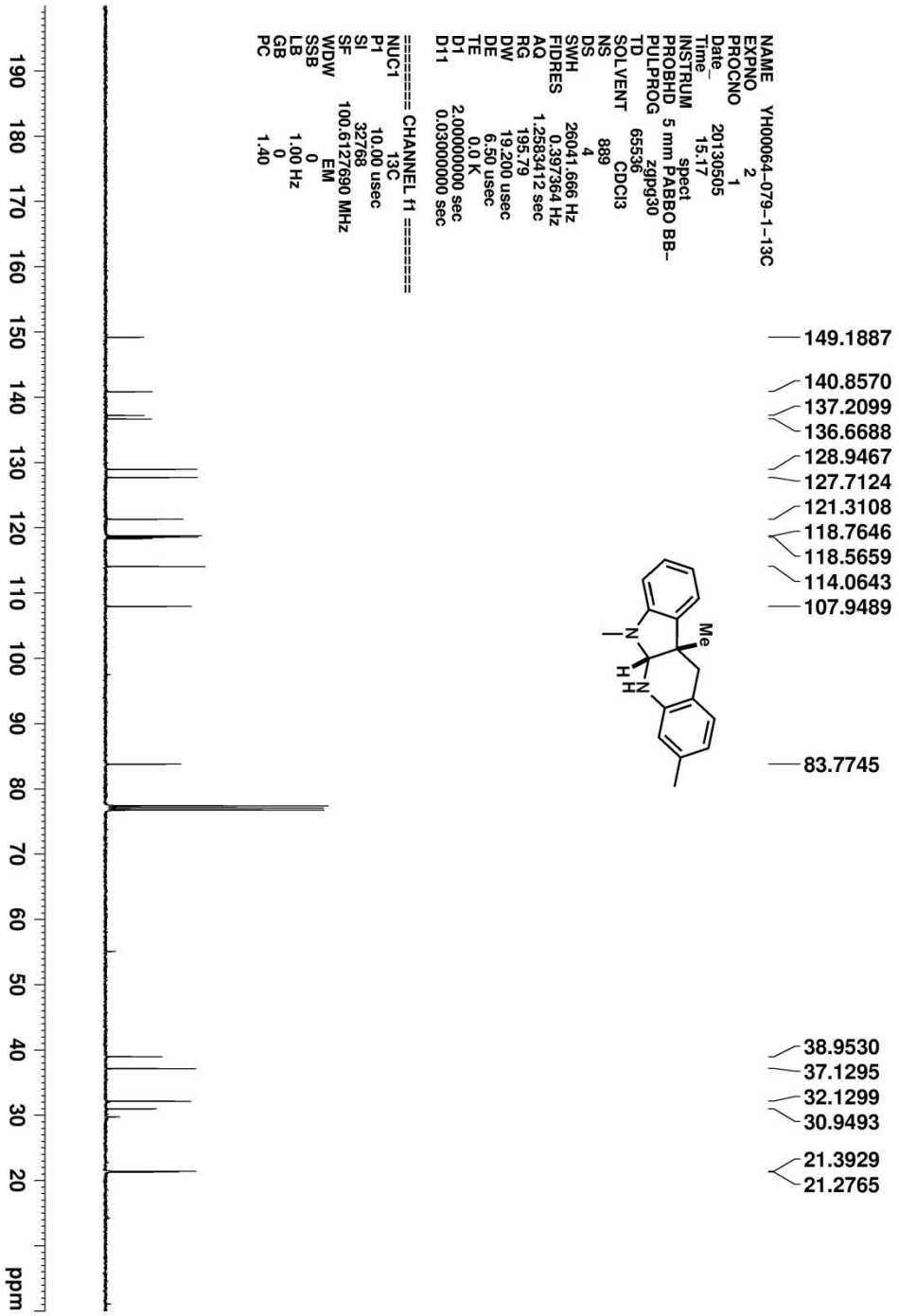
Compound d^6-1j (125 MHz, $CDCl_3$)



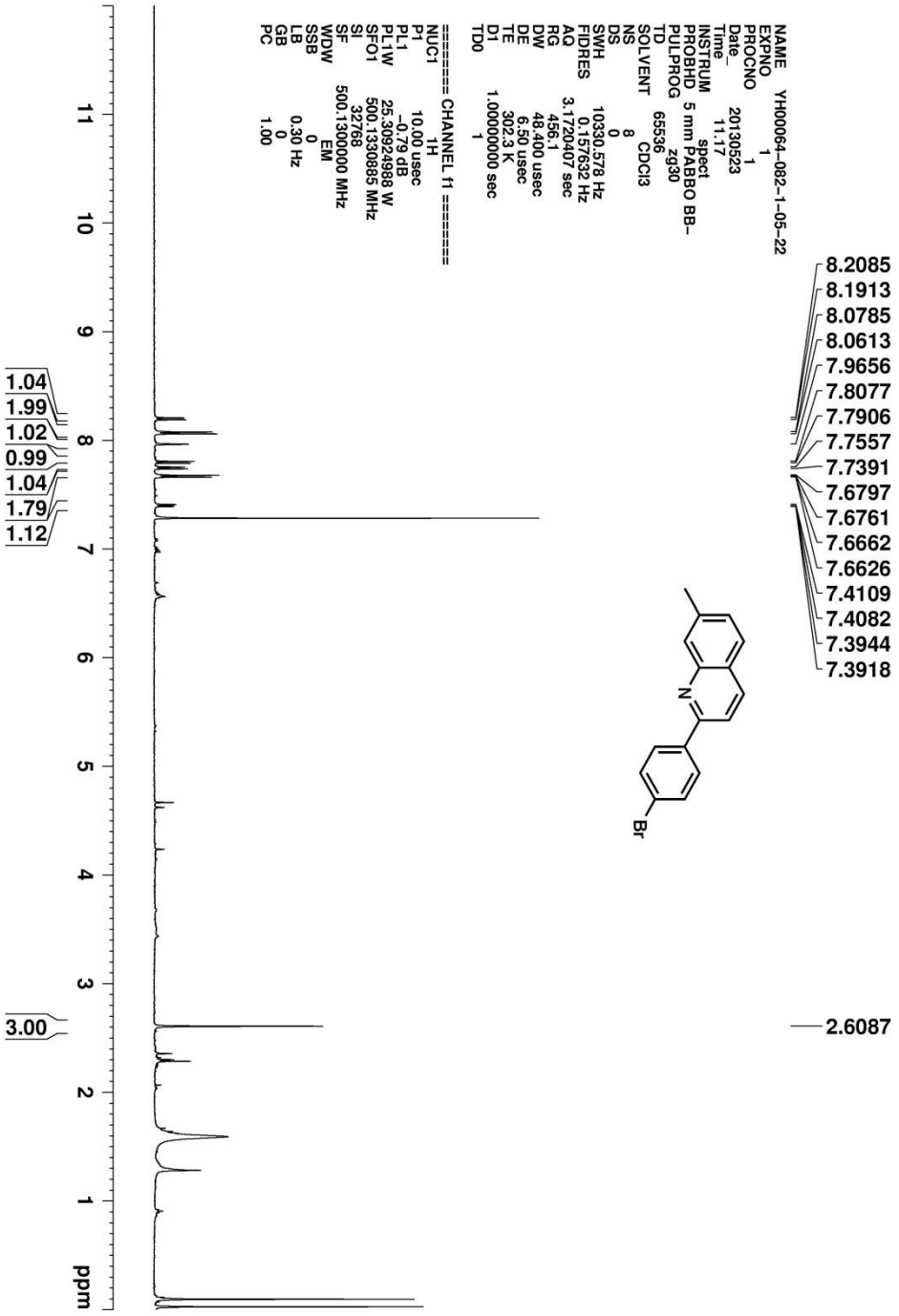
Compound 4a (500 MHz, $CDCl_3$)



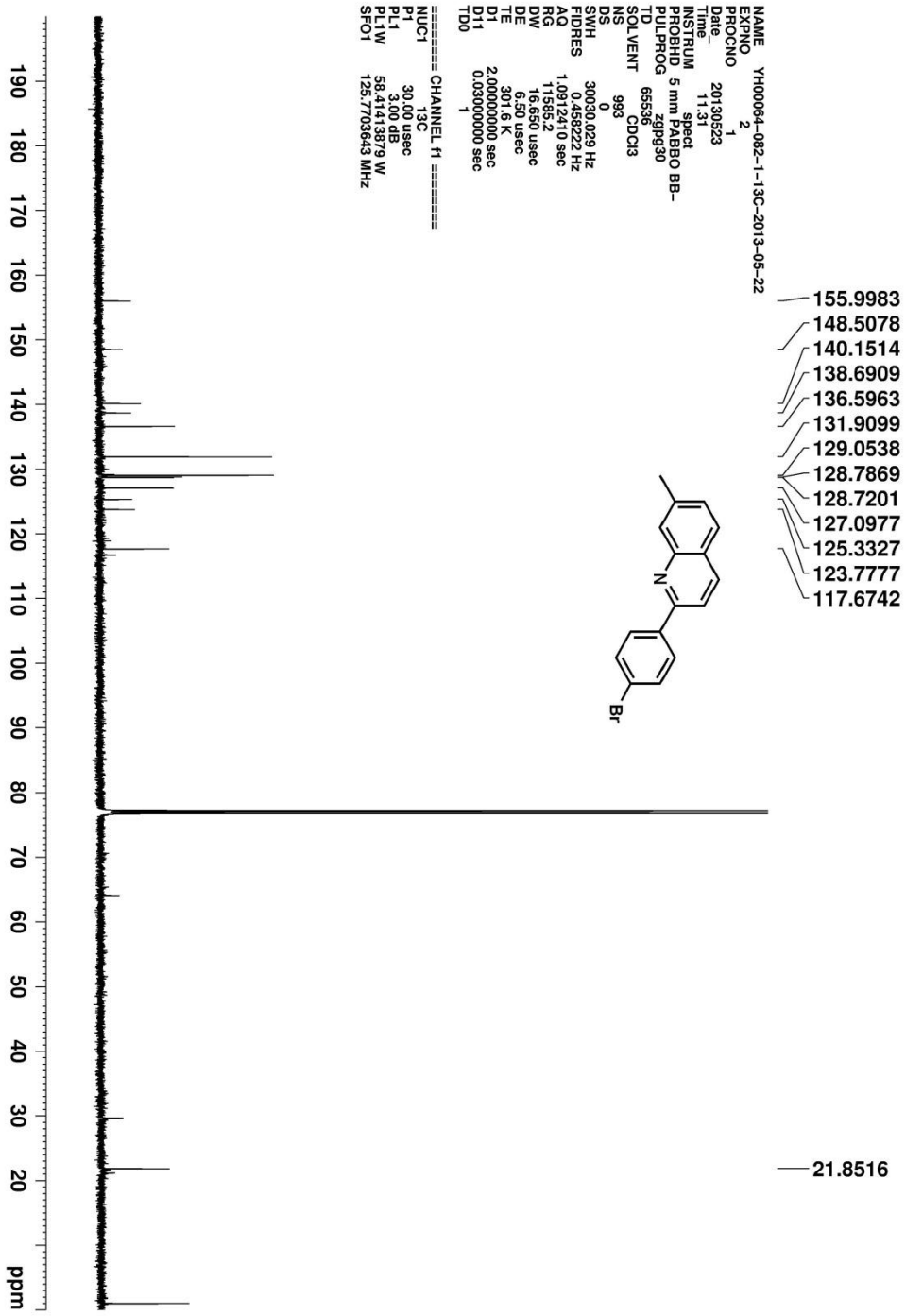
Compound 4a (100 MHz, $CDCl_3$)



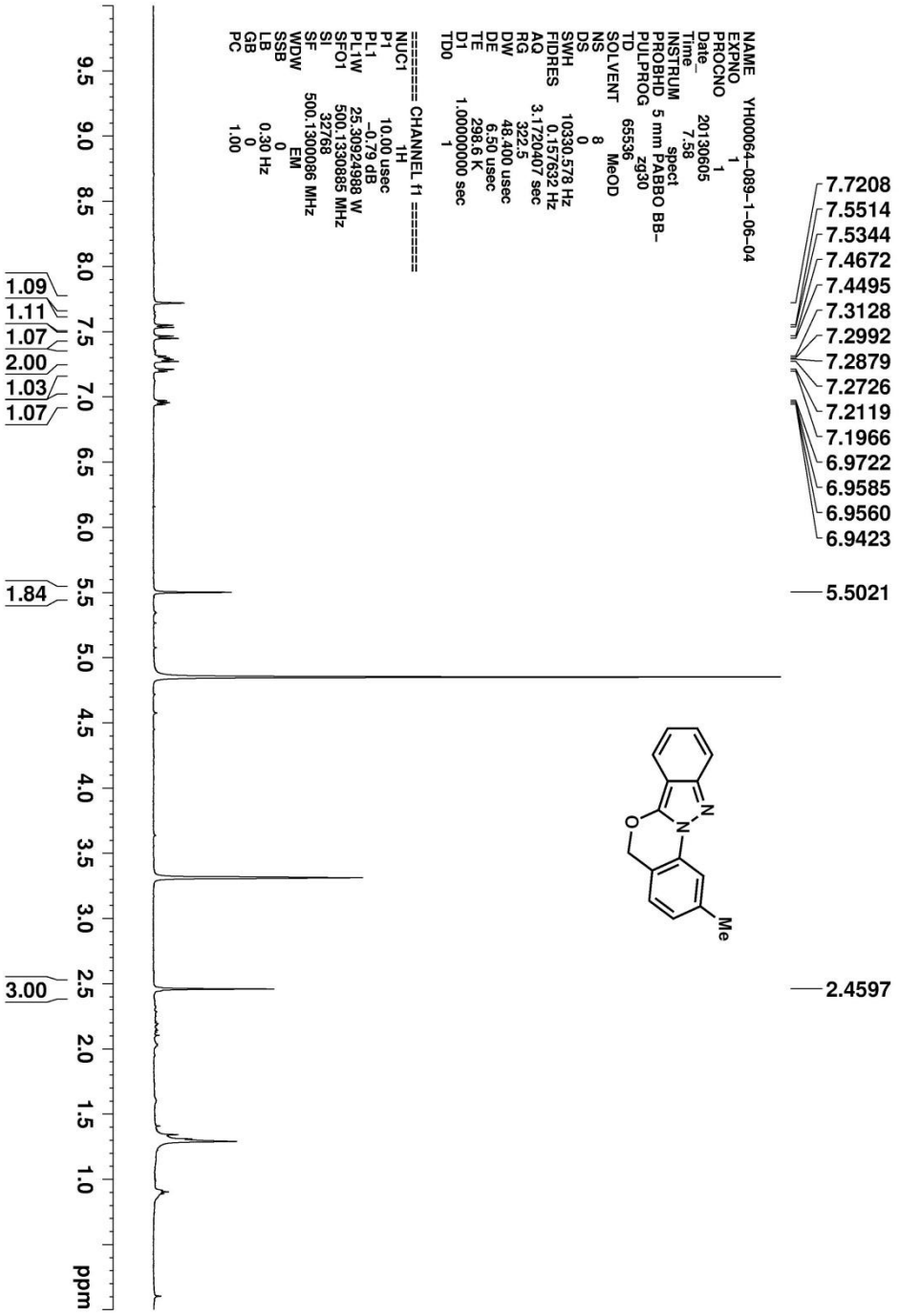
Compound 5a (500 MHz, $CDCl_3$)



Compound 5a (125 MHz, $CDCl_3$)



Compound 6a (500 MHz,MeOD)



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Compound 6a (75 MHz, MeOD)