Electronic Supplementary Material (ESI) for Chemical Communications

Cu(I)-Catalyzed Intramolecular Oxidative C–H Amination of 2-Aminoacetophenones: a Convenient Route toward Isatins

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Supporting Information

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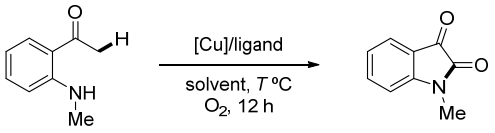
General. All reactions were conducted under an oxygen atmosphere on a dual-manifold Schlenk line unless otherwise mentioned and in oven-dried glass wares. All solvents were dried according to known methods and distilled prior to use.[1] 2-Aminoacetophenones **1** were synthesized according to the literature procedures.[2] Other reagents were commercially available and used as purchased.

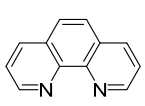
Table. Optimization Studies for the Formation of *N*-Methylisatin 2a.[a]



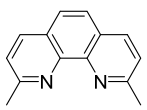
1a **2a**

entry	[Cu]/L, mol%[b]	Cu source	ligand	solvent	yield %[c]
1	10	$Cu(OAc)_2$	bpy	DMSO	12
2	10	$Cu(OH)_2$	bpy	DMSO	20
3	10	CuO	bpy	DMSO	5
4	10	Cu_2O	bpy	DMSO	trace
5	10	CuCl	bpy	DMSO	3
6	10	$CuCl_2$	bpy	DMSO	10
7	10	CuBr	bpy	DMSO	13
8	10	CuI	**L1**	DMSO	70
9	10	CuI	**L2**	DMSO	27
10	10	CuI	**L3**	DMSO	85
11	10	CuI	**L4**	DMSO	86
12	10	CuI	dppe	DMSO	69
13	10	CuI	TMEDA	DMSO	47
14	10	CuI	bpy	DMF	68
15	5	CuI	bpy	DMF	22
16	20	CuI	bpy	DMF	67
17	20	CuI	bpy	DMF	59[d]
18	10	CuI	bpy	DMF	31[e]
19	10	CuI	bpy	DMAc	65
20	10	CuI	bpy	*o*-DCB	47
21	10	CuI	bpy	*o*-xylene	26
22	**10**	**CuI**	**bpy**	**DMSO**	**91 (89)**[f]
23	–	–	–	DMSO	N.R.

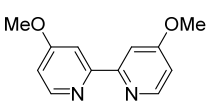
[a] Unless otherwise mentioned, all reactions were carried out using **1a** (0.3 mmol), CuI, ligand in 0.6 mL solvent. [b] The ratio of Cu source and ligand was 1:1. [c] Yields were determined by the ^1H NMR integration method using CH_2Br_2 as the internal standard. [d] 1.2 mL DMF was used. [e] Reaction was carried out for 120 °C. [f] Isolated yield. bpy = 2,2'-bipyridine. DMAc = *N,N*-dimethylacetamide. *o*-DCB = *o*-dichlorobenzene.



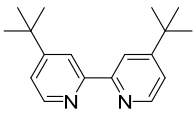
L1



L3

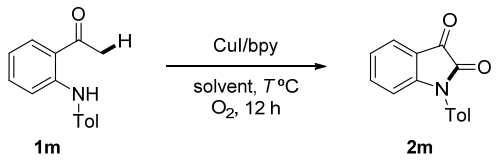


L2



L4

Table. Optimization Studies for the Formation of *N*-Tolylisatin 2m.[a]

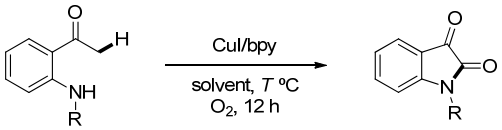


1m **2m**

entry	CuI/bpy, mol%[b]	solvent	yield %[c]
1	10	DMF	trace
2	10	DMSO	trace
3	10	*o*-xylene	74
4	10	Ph-Cl	73
5	10	*o*-DCB	75
6	10	2-ethoxyethanol	complicated
7	10	AcOH	complicated
8	10	*o*-DCB	66[d]
9	10	*o*-DCB[e]	66
10	5	*o*-DCB	72
11	**10**	***o*-DCB**	**77 (72)**[f,g]
12	–	*o*-DCB	N.R.

[a] Unless otherwise mentioned, all reactions were carried out using **1m** (0.3 mmol) in 0.6 mL solvent. [b] The ratio of Cu source and ligand was 1:1. [c] Yields were determined by the ^{1}H NMR integration method using CH_2Br_2 as the internal standard. [d] Reaction was carried out for 120 °C, 24 h. [e] 1.2 mL *o*-DCB was used. [f] Reaction was carried out for 3 h. [g] Isolated yield.

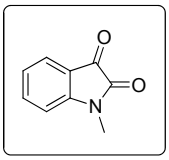
General Procedure for the Copper-Catalyzed Synthesis of Isatines:



1 **2**

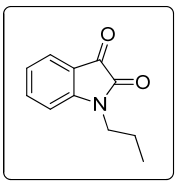
A sealed tube containing CuI (0.030 mmol, 10.0 mol%), 2,2'-bipyridine (10.0 mol%) was evacuated and purged with oxygen gas three times. Then, DMSO or *o*-DCB (0.6 mL), 2-aminoacetophenone **1** (0.30 mmol), were sequentially added to the system via a syringe under an oxygen atmosphere and the reaction mixture was allowed to stir at 140 °C for 3-12 h. When the reaction was completed, the mixture was cooled and diluted with CH_2Cl_2 (10 mL). The mixture was filtered through a Celite and silica gel pads and washed with EA (50 mL). The combined filtrate was concentrated and the residue was purified by a silica gel column using hexane–EtOAc as eluent to give pure **2a** in 89%.

1-Methylindoline-2,3-dione (2a)



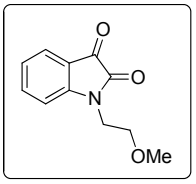
red solid; **m.p.** 121 – 122 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 – 7.59 (m, 2H), 7.14 (td, *J* = 7.4, 0.8 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 3.26 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.2, 158.0, 151.2, 138.3, 124.9, 123.6, 117.1, 109.9, 26.0; **IR** (neat, cm^{-1}): 1728, 1606, 1469, 1327, 1112, 1089; **HRMS** (EI^+) calcd for $C_9H_7NO_2$: 161.0477, found: 161.0474.

1-Propylindoline-2,3-dione (2b)



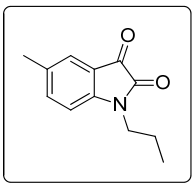
red solid; **m.p.** 66 – 68 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.61 – 7.57 (m, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 3.70 (t, *J* = 7.2 Hz, 2H), 1.75 (sextet, *J* = 7.4 Hz, 2H), 1.00 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.5, 158.1, 150.9, 138.3, 125.2, 123.5, 117.4, 110.1, 41.6, 20.5, 11.2; **IR** (neat, cm^{-1}): 2962, 1728, 1614, 1471, 1342, 1128, 1093; **HRMS** (EI^+) calcd for $C_{11}H_{11}NO_2$: 189.0790, found: 189.0785.

1-(2-Methoxyethyl)indoline-2,3-dione (2c)



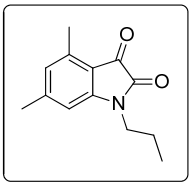
red solid; **m.p.** 75 – 76 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.60 – 7.56 (m, 2H), 7.10 (td, *J* = 8.0, 0.8 Hz, 1H), 7.05 (dd, *J* = 8.4, 0.8 Hz, 1H), 3.91 (t, *J* = 5.4 Hz, 2H), 3.66 (t, *J* = 5.4 Hz, 2H), 3.34 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.3, 158.3, 151.4, 138.2, 125.0, 123.5, 117.4, 111.0, 69.8, 58.9, 40.3; **IR** (neat, cm^{-1}): 2929, 2894, 2832, 1743, 1614, 1471, 1344, 1118, 1093; **HRMS** (EI^+) calcd for $C_{11}H_{11}NO_3$: 205.0739, found: 205.0738.

5-Methyl-1-propylindoline-2,3-dione (2d)



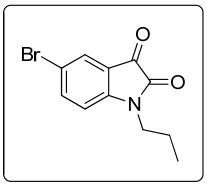
red solid; **m.p.** 78 – 79 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41 – 7.37 (m, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 3.67 (t, *J* = 7.2 Hz, 2H), 2.33 (s, 3H), 1.73 (sextet, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.8, 158.2, 148.8, 138.6, 133.3, 125.6, 117.4, 110.0, 41.7, 20.53, 20.50, 11.2; **IR** (neat, cm^{-1}): 2966, 2875, 1730, 1619, 1492, 1344, 1207, 1122; **HRMS** (EI^+) calcd for $C_{12}H_{13}NO_2$: 203.0946, found: 203.0949.

4,6-Dimethyl-1-propylindoline-2,3-dione (2e)



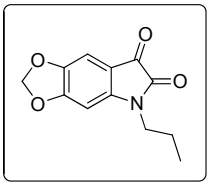
red solid; **m.p.** 110 – 112 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.68 (d, *J* = 0.8 Hz, 1H), 6.50 (s, 1H), 3.65 (t, *J* = 7.2 Hz, 2H), 2.52 (s, 3H), 2.38 (s, 3H), 1.72 (sextet, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.2, 158.7, 151.3, 149.6, 141.0, 126.3, 113.5, 108.2, 41.4, 22.6, 20.6, 17.8, 11.2; **IR** (neat, cm^{-1}): 3056, 2962, 2875, 1731, 1616, 1596, 1456, 1261, 1149; **HRMS** (EI^+) calcd for $C_{13}H_{15}NO_2$: 217.1103, found: 217.1100.

5-Bromo-1-propylindoline-2,3-dione (2f)



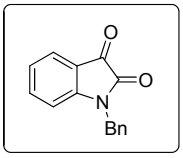
red solid; **m.p.** 124 – 125 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 – 7.68 (m, 2H), 6.82 (dd, *J* = 8.0, 0.8 Hz, 1H), 3.69 (t, *J* = 7.4 Hz, 2H), 1.73 (sextet, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.3, 157.3, 149.7, 140.4, 127.9, 118.5, 116.2, 111.9, 41.8, 20.4, 11.2; **IR** (neat, cm^{-1}): 3079, 2971, 2873, 1736, 1606, 1465, 1432, 1330, 1178, 1116; **HRMS** (EI^+) calcd for $C_{11}H_{10}BrNO_2$: 266.9895, found: 266.9873.

5-Propyl-5*H*-[1,3]dioxolo[4,5-*f*]indole-6,7-dione (2g)



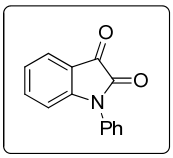
dark red solid; **m.p.** 130 – 131 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.03 (s, 1H), 6.43 (s, 1H), 6.06 (s, 2H), 3.62 (t, *J* = 7.4 Hz, 2H), 1.70 (sextet, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 180.9, 159.1, 156.5, 150.7, 144.2, 110.2, 104.8, 102.6, 93.2, 41.7, 20.7, 11.2; **IR** (neat, cm^{-1}): 2925, 1720, 1610, 1475, 1245, 1118, 1031; **HRMS** (EI^+) calcd for $C_{12}H_{11}NO_4$: 233.0688, found: 233.0686.

1-Benzylindoline-2,3-dione (2h)



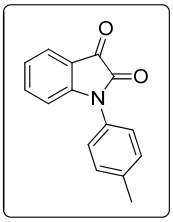
red solid; **m.p.** 122 – 123 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.48 (td, *J* = 8.0, 1.2 Hz, 2H), 7.36 – 7.30 (m, 4H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 4.94 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.1, 158.2, 150.6, 138.3, 134.4, 128.9, 128.0, 127.3, 125.2, 123.7, 117.5, 110.9, 43.9; **IR** (neat, cm^{-1}): 3454, 3029, 1731, 1612, 1471, 1349, 1176, 1002; **HRMS** (EI^+) calcd for $C_{15}H_{11}NO_2$: 237.0790, found: 237.0789.

1-Phenylindoline-2,3-dione (2l)



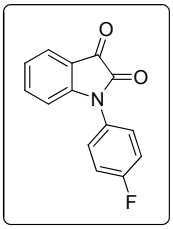
red solid; **m.p.** 128 – 129 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.58 – 7.52 (m, 3H), 7.47 (d, *J* = 6.8 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.8, 157.2, 151.5, 138.3, 132.8, 129.9, 128.7, 125.9, 125.5, 124.2, 117.4, 111.2; **IR** (neat, cm^{-1}): 3060, 1739, 1608, 1498, 1465, 1365, 1301, 1193, 929; **HRMS** (EI^+) calcd for $C_{14}H_9NO_2$: 223.0633, found: 223.0625.

1-(*p*-Tolyl)indoline-2,3-dione (2m)



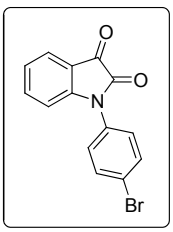
red solid; **m.p.** 131 – 132 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.0, 157.4, 151.8, 138.9, 138.3, 130.5, 130.1, 125.7, 125.4, 124.1, 117.3, 111.2, 21.2; **IR** (neat, cm^{-1}): 2919, 1737, 1612, 1515, 1465, 1365, 1299, 1180, 1093, 927; **HRMS** (EI^+) calcd for $C_{15}H_{11}NO_2$: 237.0790, found: 237.0789.

1-(4-Fluorophenyl)indoline-2,3-dione (2n)



red solid; **m.p.** 222 – 224 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.28 – 7.23 (m, 2H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H); **^{13}C NMR** (100 MHz, DMSO-d_6): δ 182.7, 161.4 (d, *J* = 243.9 Hz), 157.6, 151.2, 138.0, 129.6, 129.0 (d, *J* = 9.3 Hz), 124.7, 123.7, 117.6, 116.7 (d, *J* = 22.5 Hz), 110.7; **IR** (neat, cm^{-1}): 1735, 1606, 1508, 1461, 1361, 1288, 1182, 1097; **HRMS** (EI^+) calcd for $C_{14}H_8FNO_2$: 241.0539, found: 241.0537.

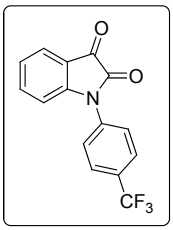
1-(4-Bromophenyl)indoline-2,3-dione (2o)



red solid; **m.p.** 169 – 170 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72 – 7.68 (m, 3H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.3, 157.1, 151.0, 138.4, 133.1, 131.8, 127.5, 125.7, 124.5, 122.4, 117.5, 110.7; **IR** (neat, cm^{-1}): 1737, 1610, 1494, 1465,

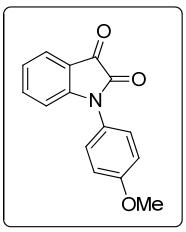
1363, 1294, 1180, 1012, 925; **HRMS** (EI^+) calcd for $C_{14}H_8BrNO_2$: 300.9738, found: 300.9743.

1-(4-(Trifluoromethyl)phenyl)indoline-2,3-dione (2p)



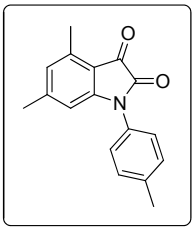
red solid; **m.p.** 171 – 173 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.74 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.62 – 7.57 (m, 3H), 7.23 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.0, 157.0, 150.6, 138.4, 136.1, 130.5 (q, *J* = 32.8 Hz), 127.0 (q, *J* = 3.6 Hz), 126.0, 125.8, 124.7, 123.5 (q, *J* = 270.8 Hz), 117.5, 111.1; **IR** (neat, cm^{-1}): 3095, 1743, 1606, 1469, 1373, 1317, 1160, 1114, 925; **HRMS** (EI^+) calcd for $C_{15}H_8F_3NO_2$: 291.0507, found: 291.0502.

1-(4-Methoxyphenyl)indoline-2,3-dione (2q)



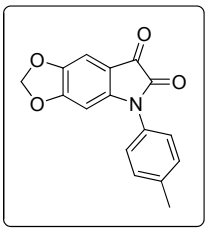
red solid; **m.p.** 155 – 156 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.8 Hz, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 7.6 Hz, 1H), 3.87 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 183.1, 159.6, 157.6, 152.0, 138.3, 127.4, 125.4, 125.3, 124.1, 117.4, 115.2, 111.1, 55.5; **IR** (neat, cm^{-1}): 2917, 2840, 1731, 1608, 1513, 1465, 1297, 1251, 1184, 1027; **HRMS** (EI^+) calcd for $C_{15}H_{11}NO_3$: 253.0739, found: 253.0736.

4,6-Dimethyl-1-(*p*-tolyl)indoline-2,3-dione (2r)



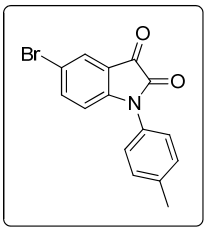
red solid; **m.p.** 156 – 157 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.8 Hz, 2H), 7.27 – 7.25 (m, 2H), 6.72 (s, 1H), 6.44 (s, 1H), 2.58 (s, 3H), 2.43 (s, 3H), 2.30 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.6, 158.1, 152.3, 149.7, 141.3, 138.7, 130.43, 130.39, 126.9, 126.1, 113.6, 109.3, 22.7, 21.2, 18.1; **IR** (neat, cm^{-1}): 2921, 2852, 1747, 1731, 1614, 1513, 1363, 1276, 1164, 941; **HRMS** (EI^+) calcd for $C_{17}H_{15}NO_2$: 265.1103, found: 265.1106.

5-(*p*-Tolyl)-5*H*-[1,3]dioxolo[4,5-*f*]indole-6,7-dione (2s)



dark red solid; **m.p.** 180 – 182 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.23 (m, 2H), 7.09 (s, 1H), 6.37 (s, 1H), 6.05 (s, 2H), 2.42 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 180.2, 158.4, 156.4, 151.5, 144.7, 138.8, 130.5, 130.1, 125.9, 110.3, 104.5, 102.6, 94.2, 21.2; **IR** (neat, cm^{-1}): 2917, 1737, 1716, 1610, 1469, 1382, 1253, 1232, 1157, 1039, 945; **HRMS** (EI^+) calcd for $C_{16}H_{11}NO_4$: 281.0688, found: 281.0689.

5-Bromo-1-(*p*-tolyl)indoline-2,3-dione (2t)

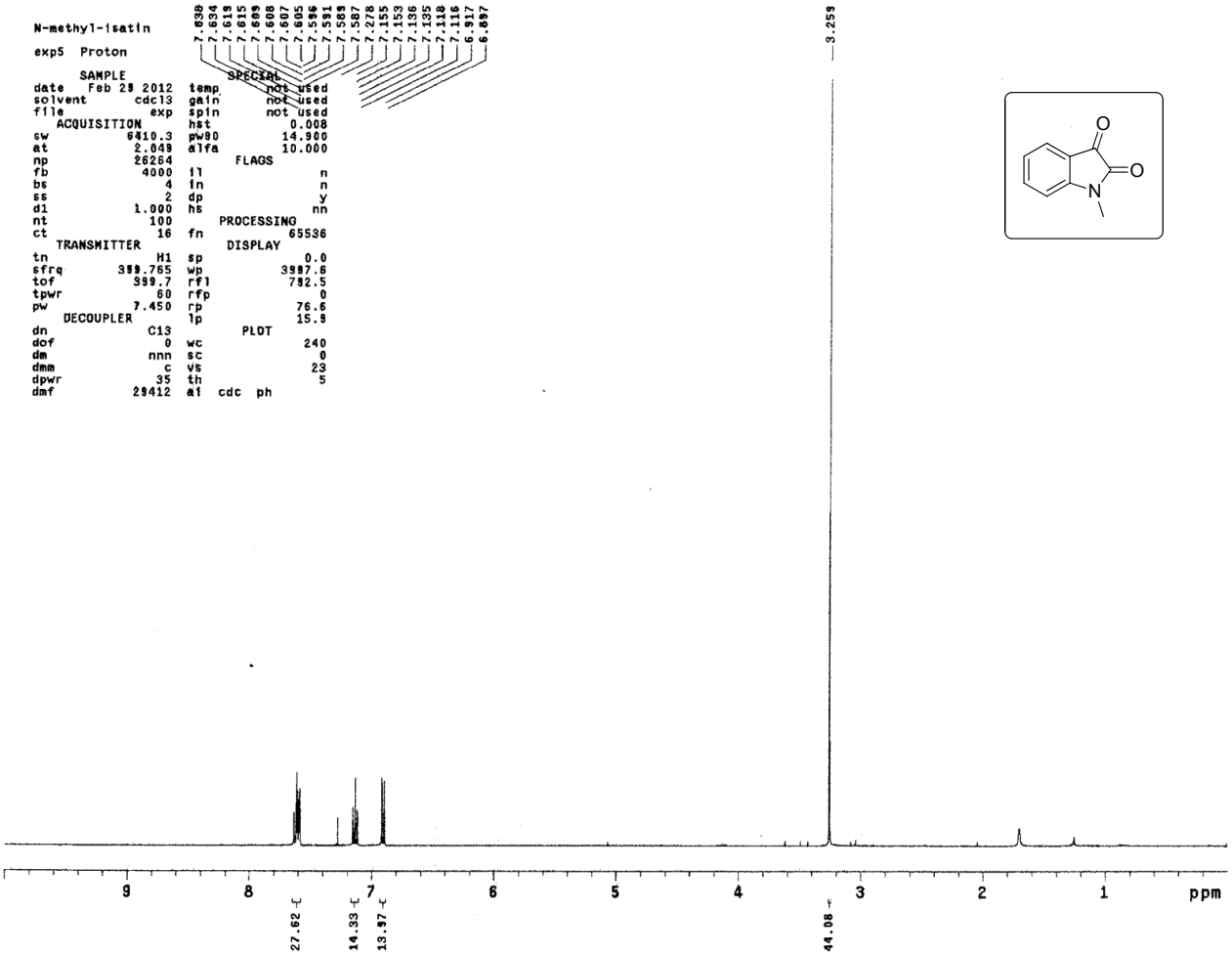


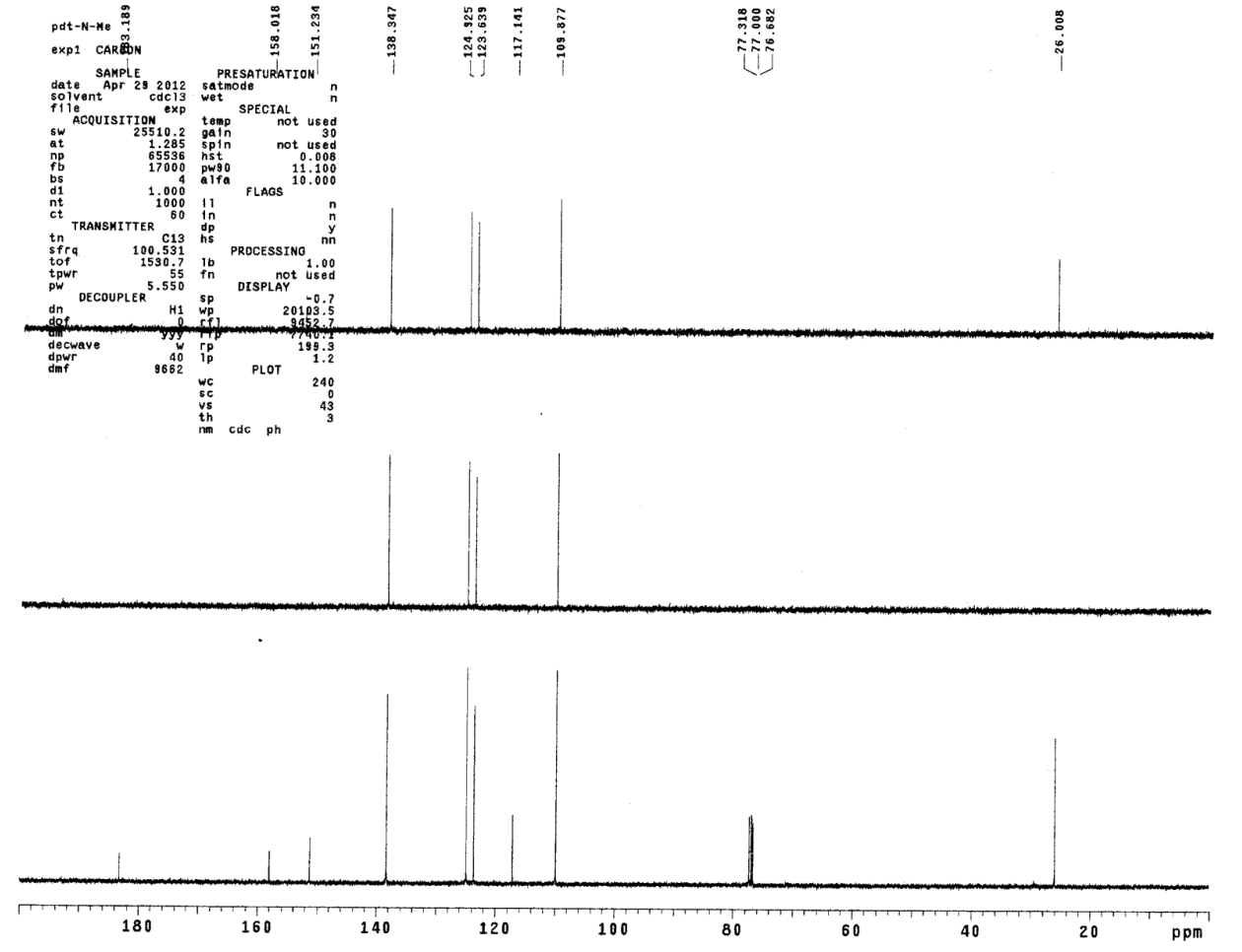
red solid; **m.p.** 192 – 194 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 2.0 Hz, 1H), 7.63 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 2H), 7.27 – 7.25 (m, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 181.9, 156.6, 150.6, 140.5, 139.3, 130.7, 129.8, 128.1, 125.7, 118.6, 116.9, 113.0, 21.2; **IR** (neat, cm^{-1}): 2923, 1745, 1604, 1467, 1436, 1290, 1189, 1122; **HRMS** (EI^+) calcd for $C_{15}H_{10}BrNO_2$: 314.9895, found: 314.9890.

References:

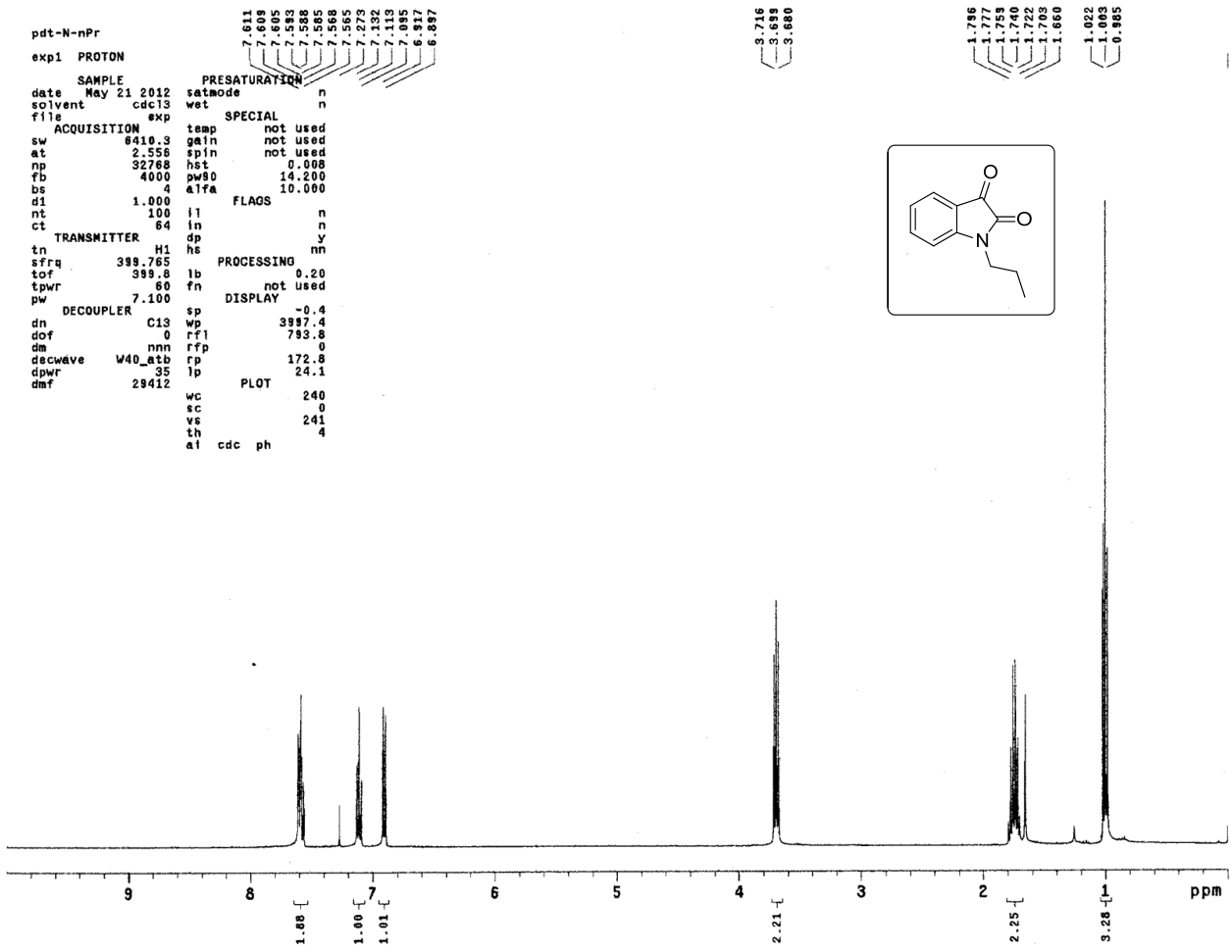
1. Perrin, D. D.; Armarego, W. L. F. *In Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.
2. Sugasawa, T.; Toyoda, T.; Adachi, M.; Sasakura, K. *J. Am. Chem. Soc.* **1978**, *100*, 4842.

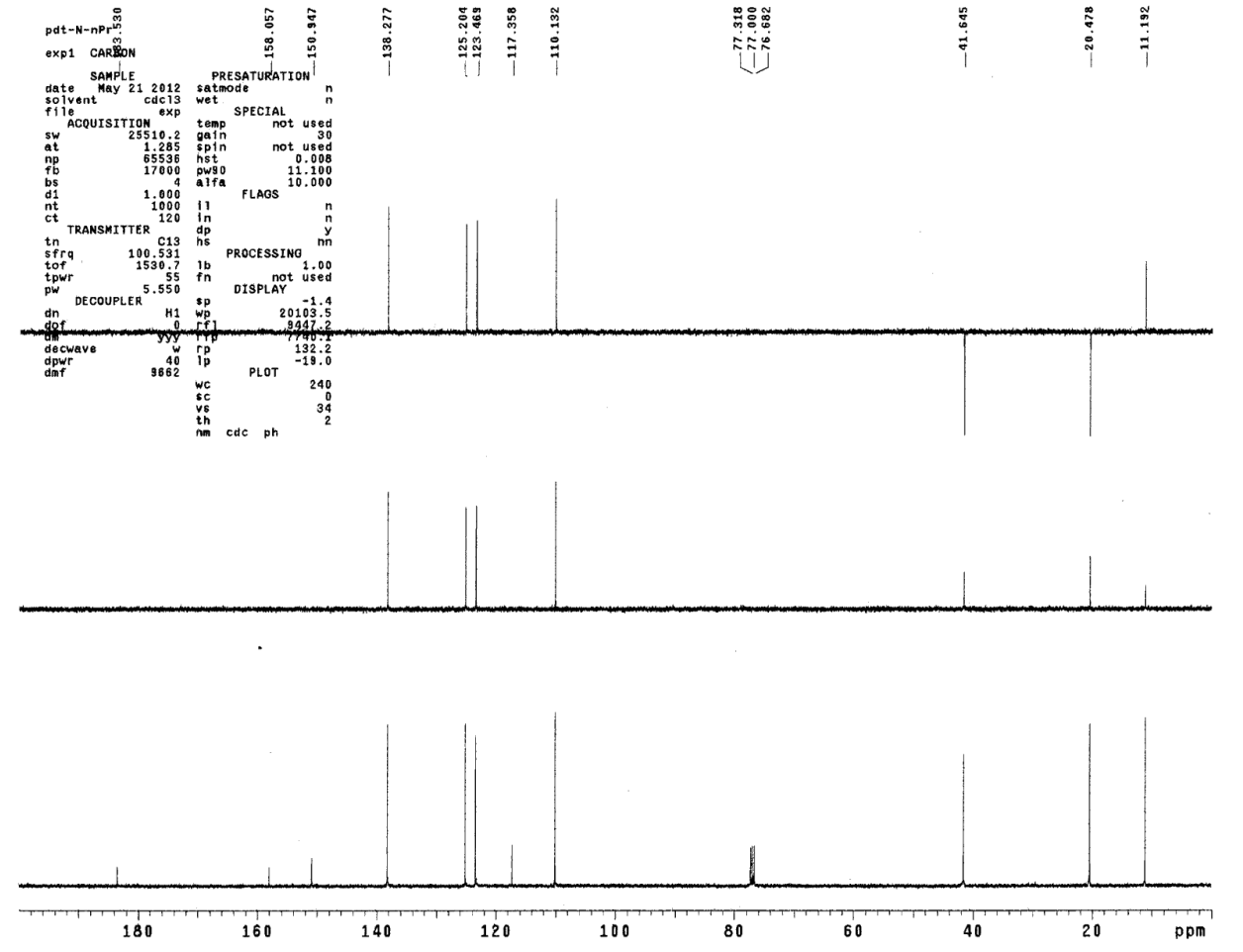
^{1}H and ^{13}C NMR spectra of compound **2a**



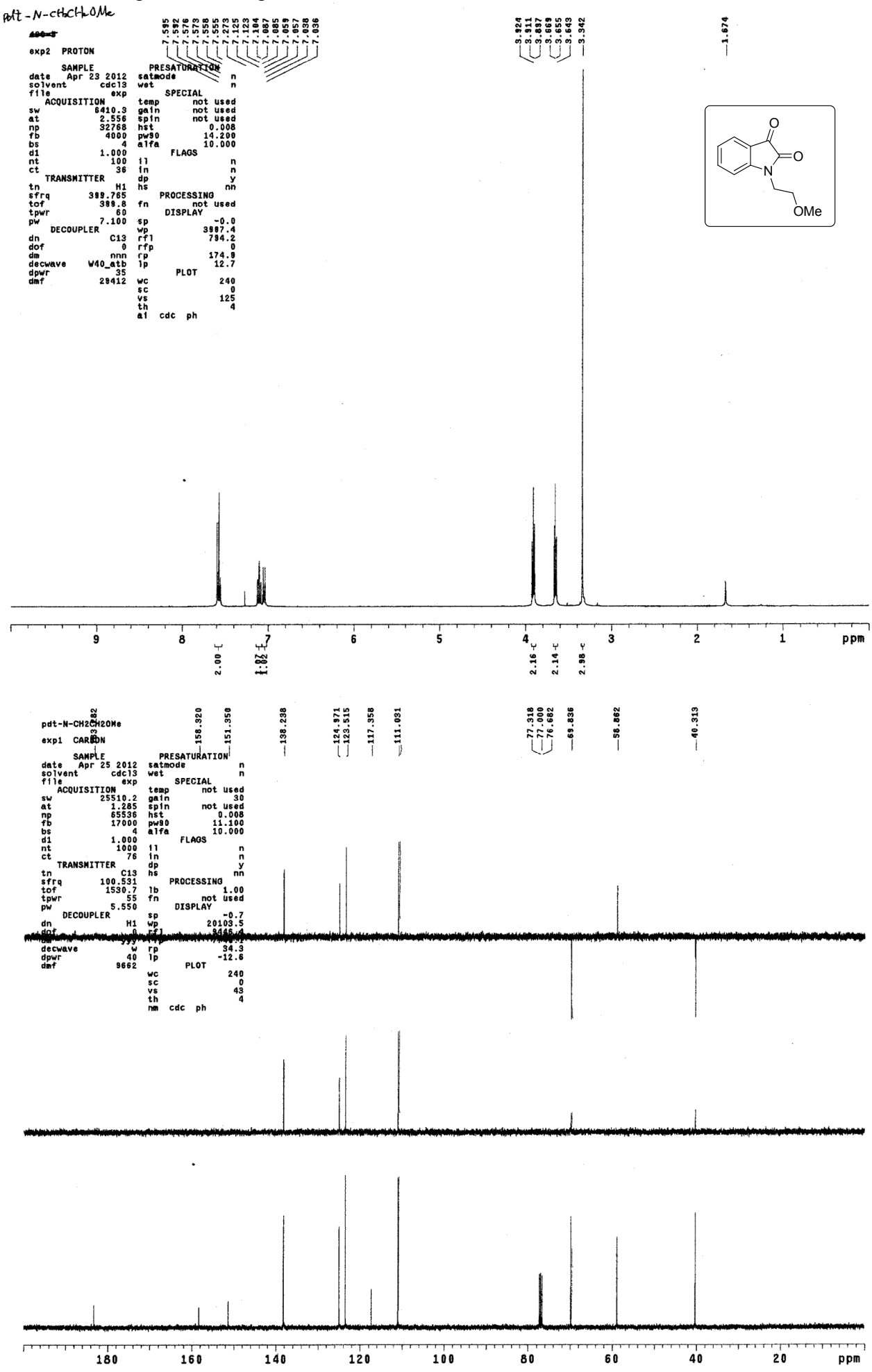


^{1}H and ^{13}C NMR spectra of compound **2b**

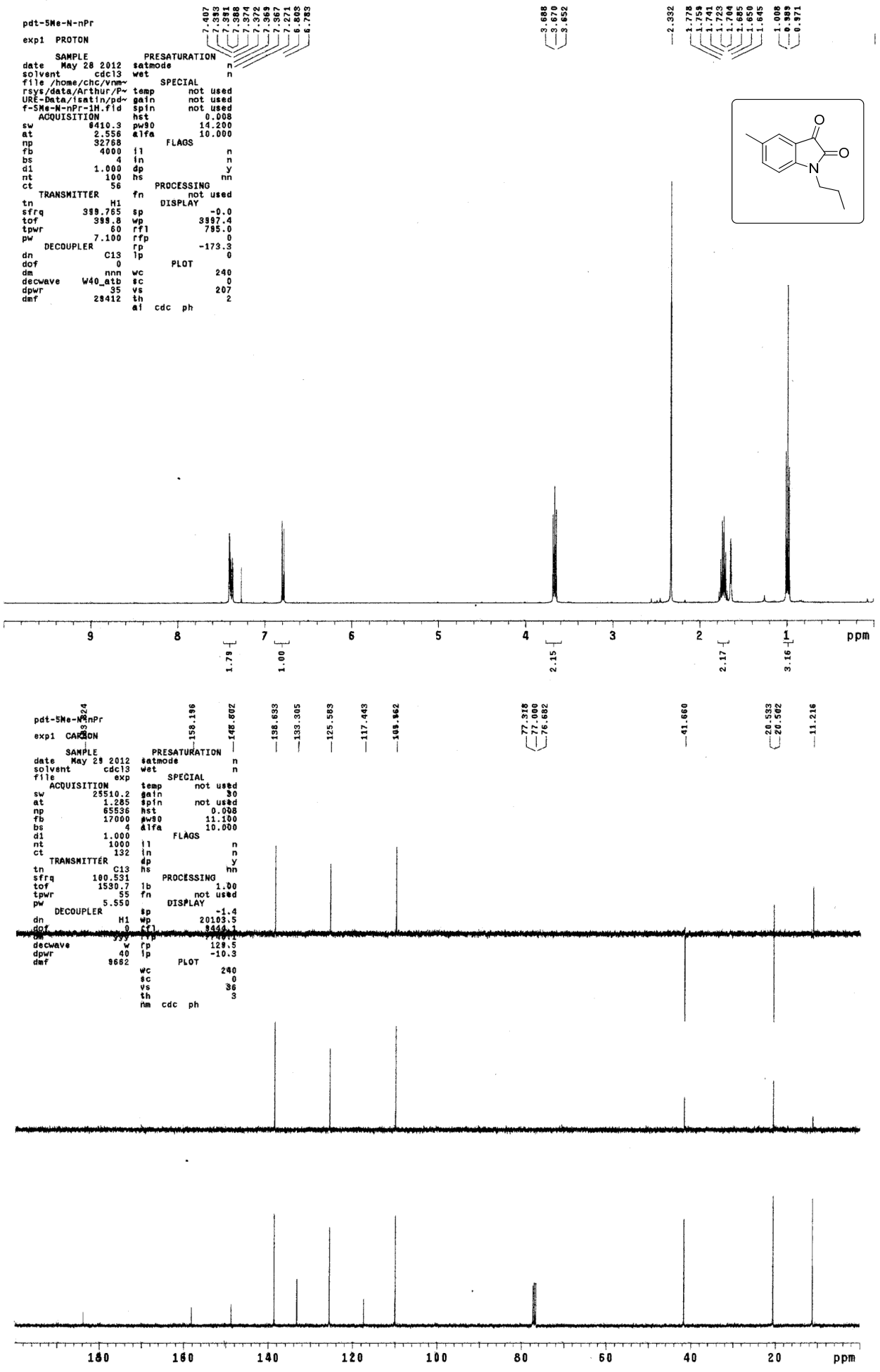




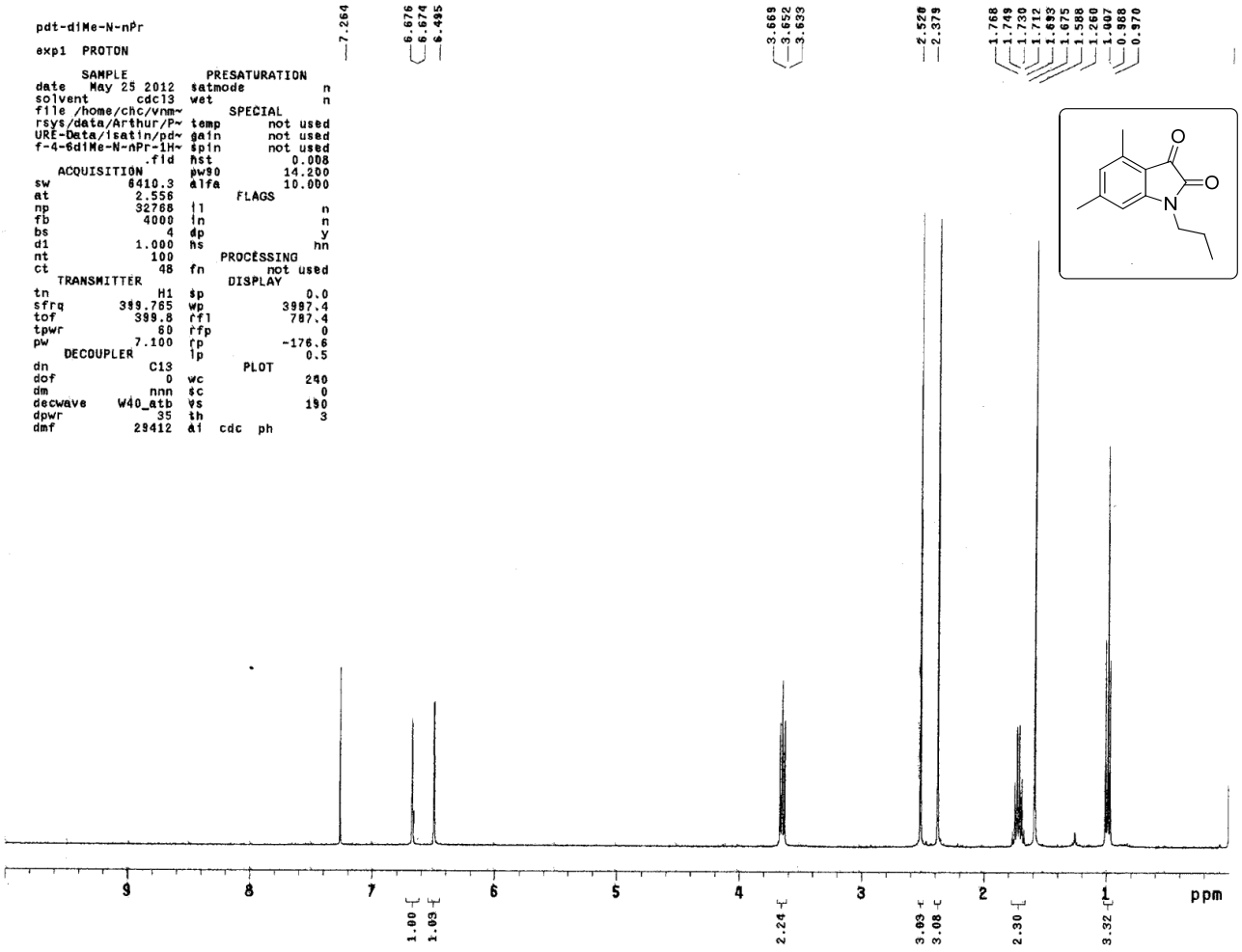
^{1}H and ^{13}C NMR spectra of compound **2c**

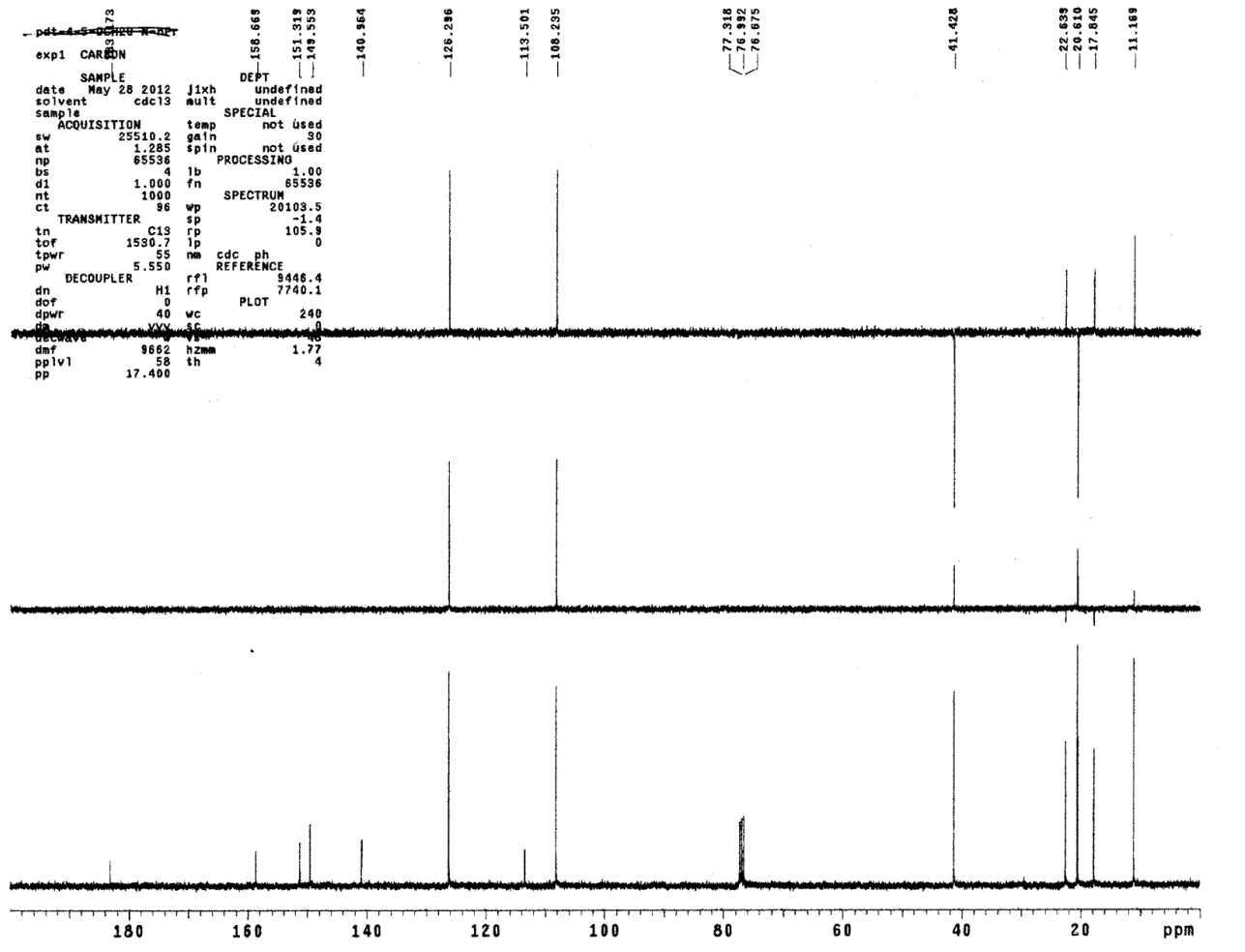


^{1}H and ^{13}C NMR spectra of compound **2d**

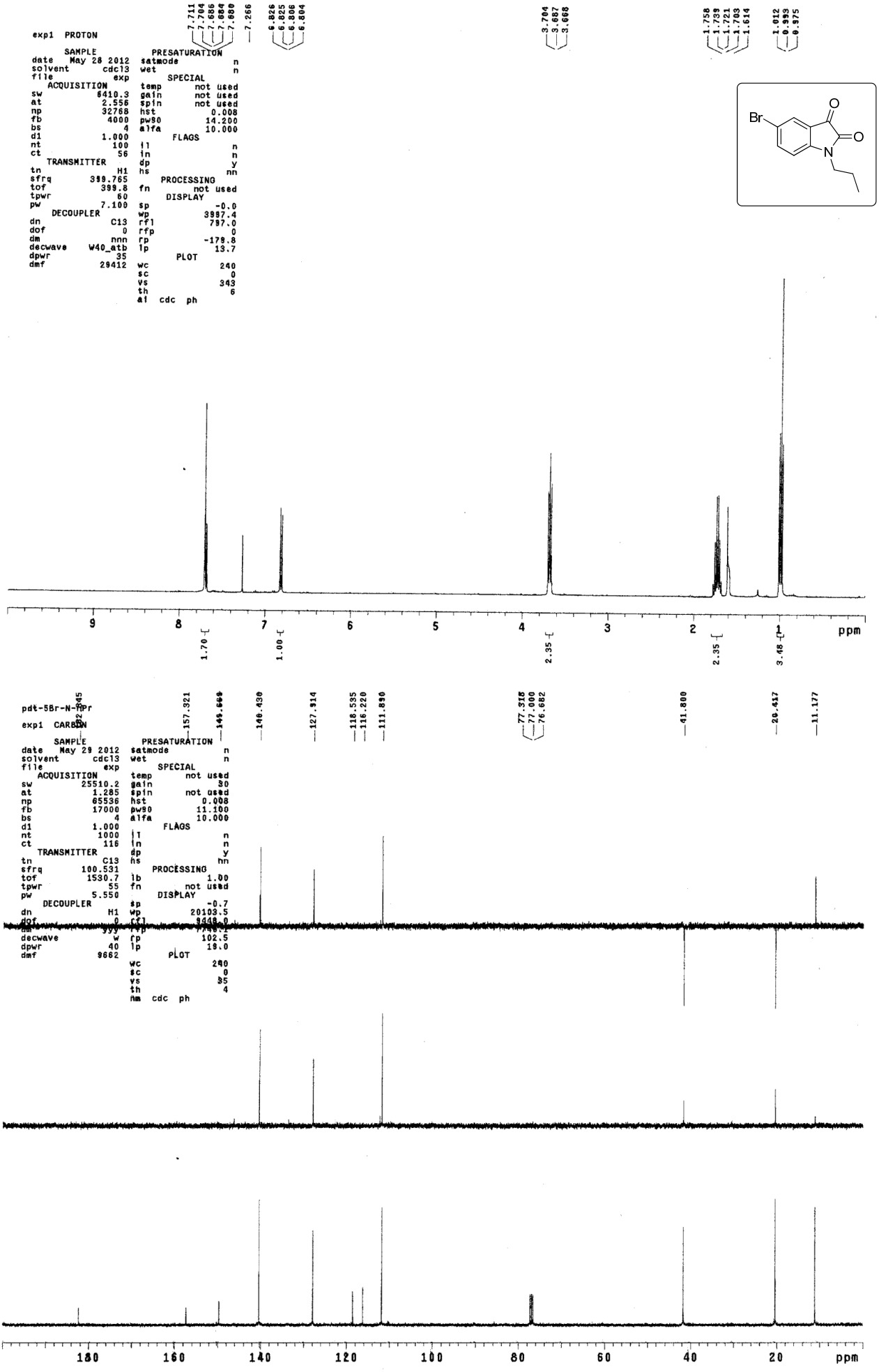


^{1}H and ^{13}C NMR spectra of compound **2e**

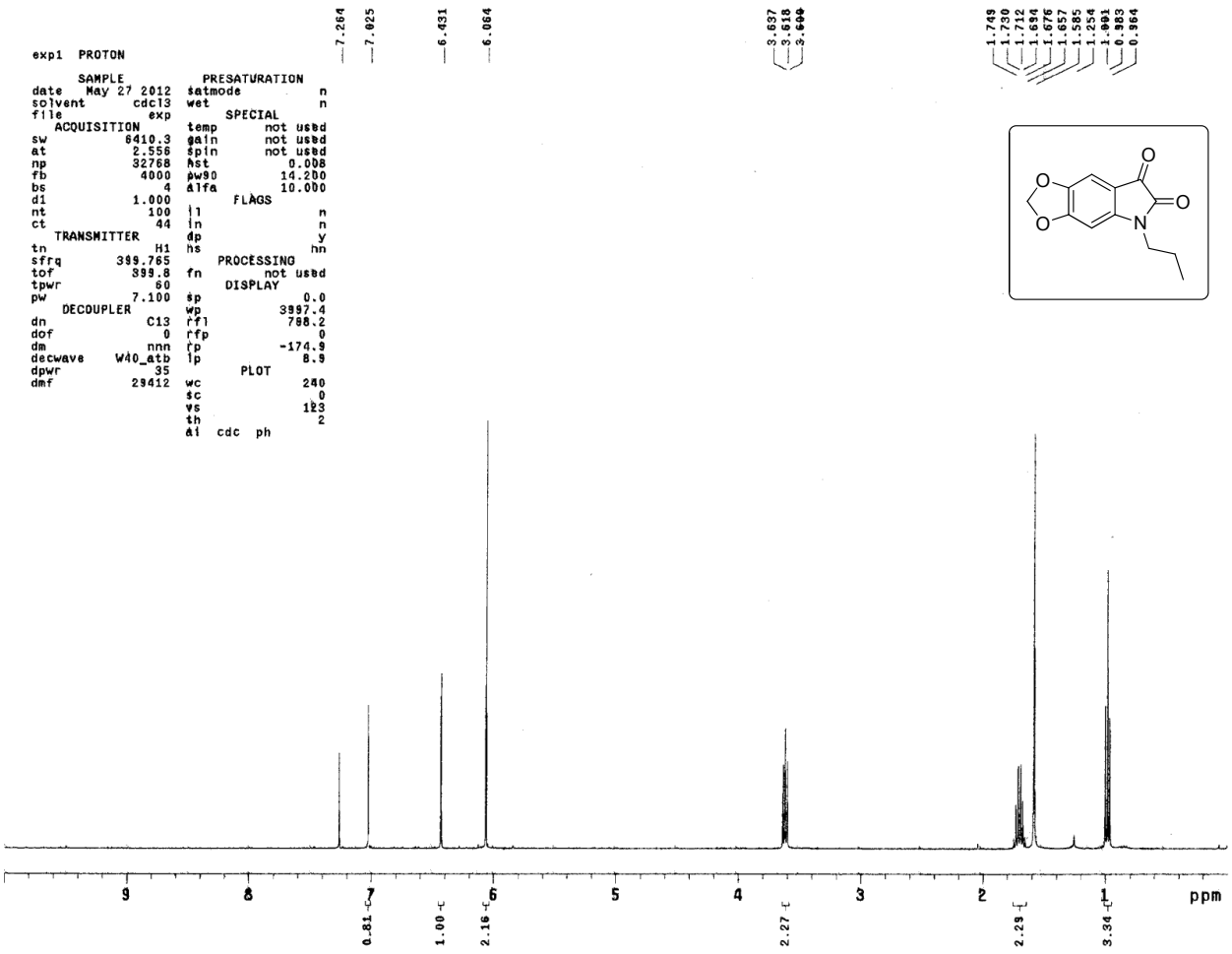


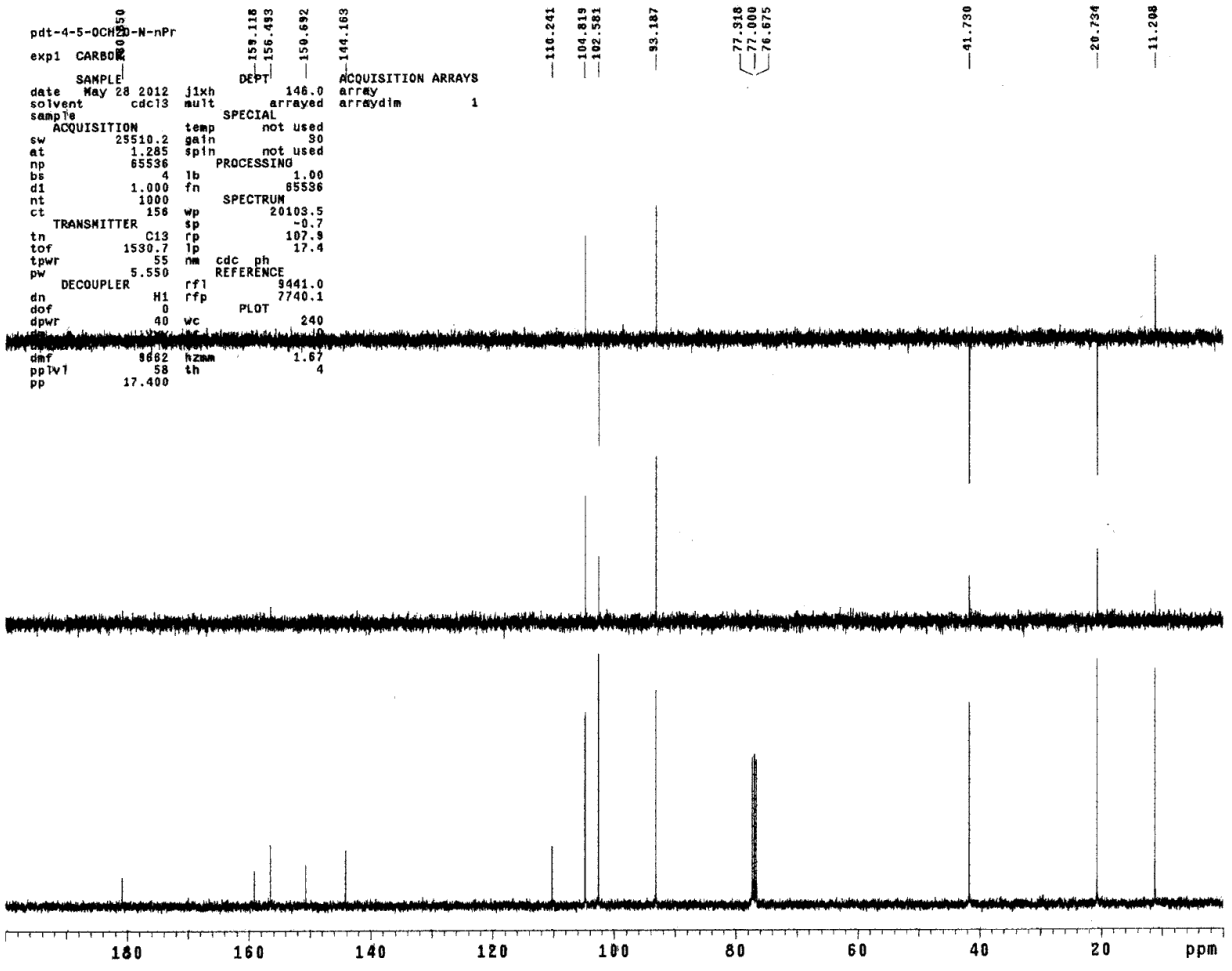


^{1}H and ^{13}C NMR spectra of compound **2f**

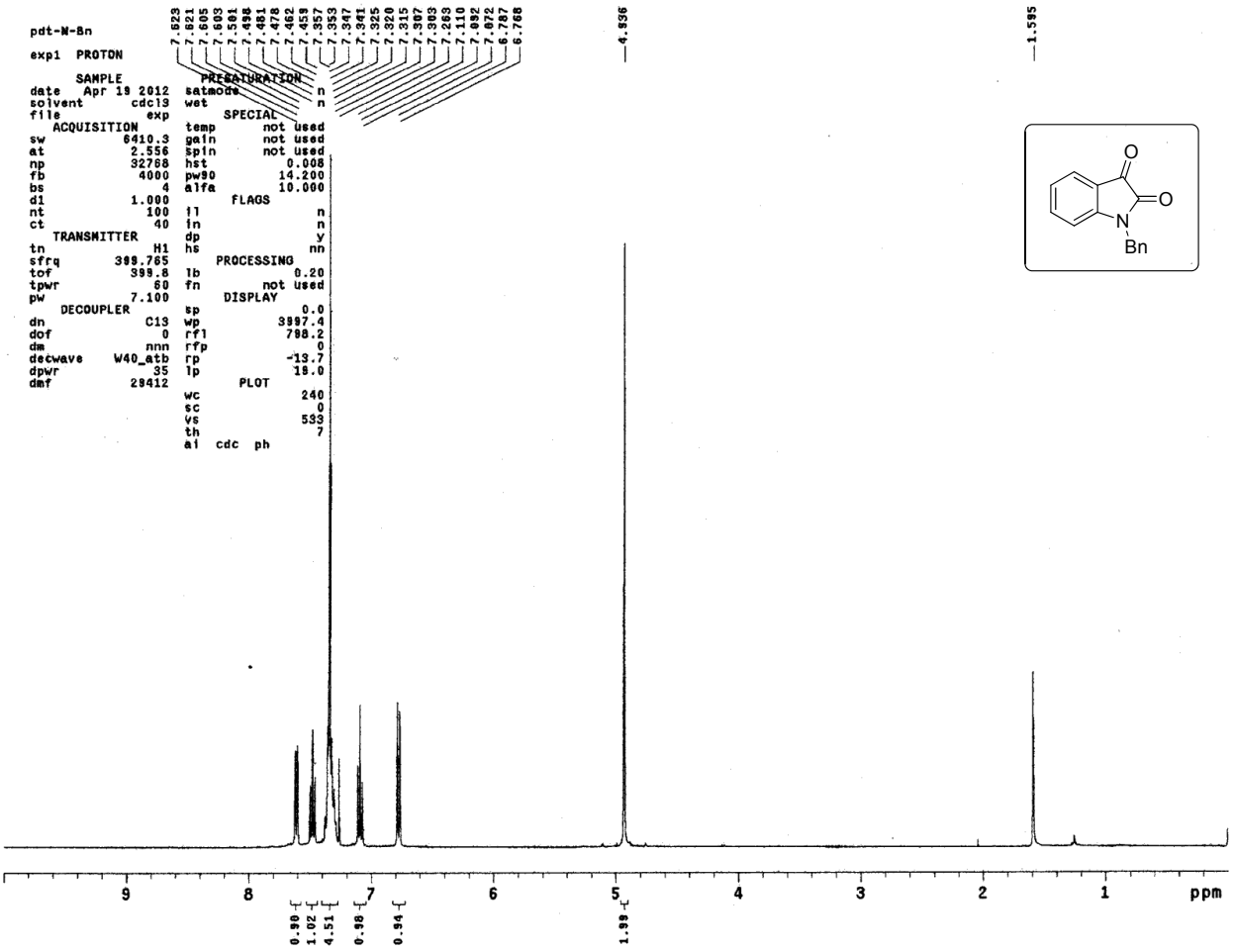


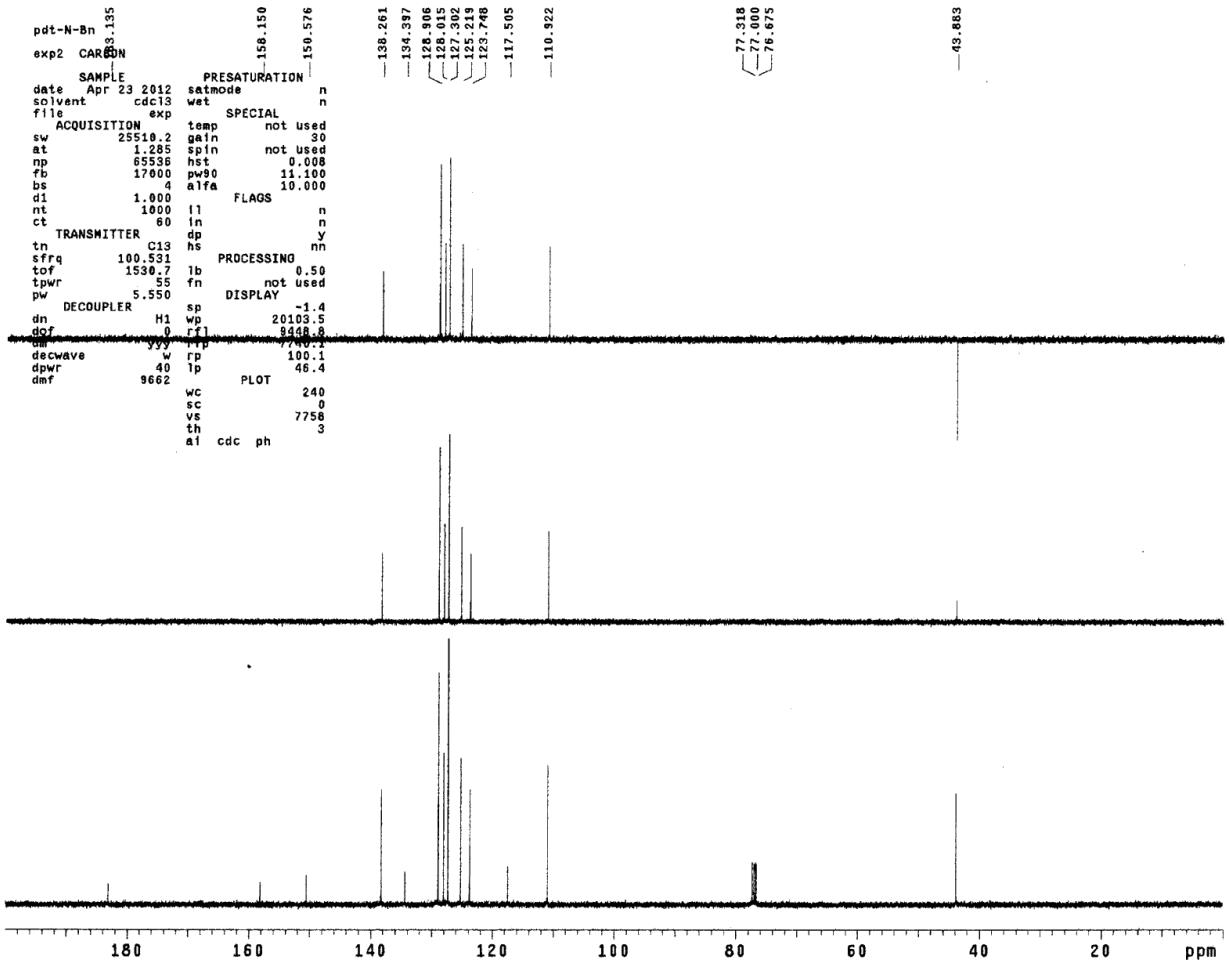
^{1}H and ^{13}C NMR spectra of compound **2g**



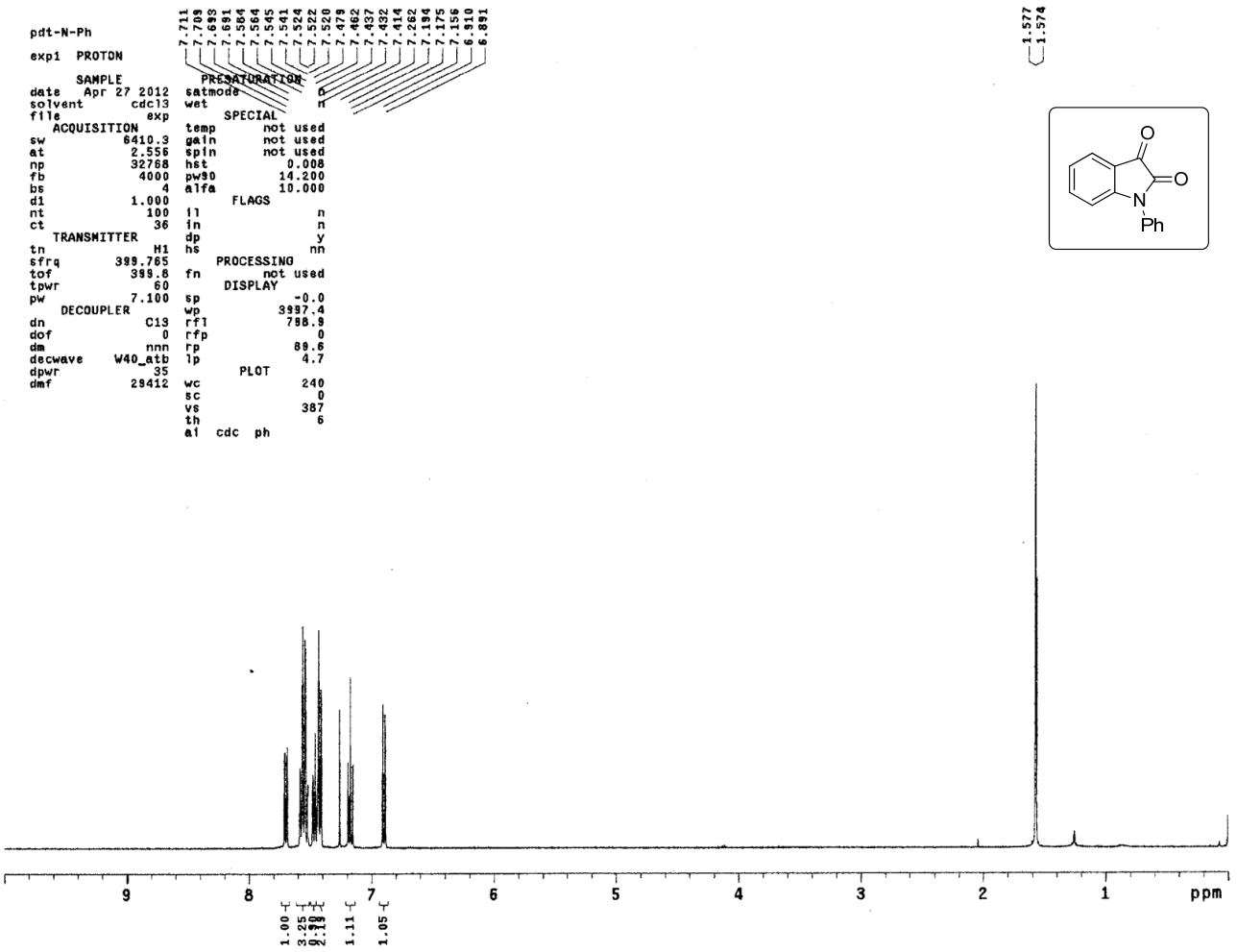


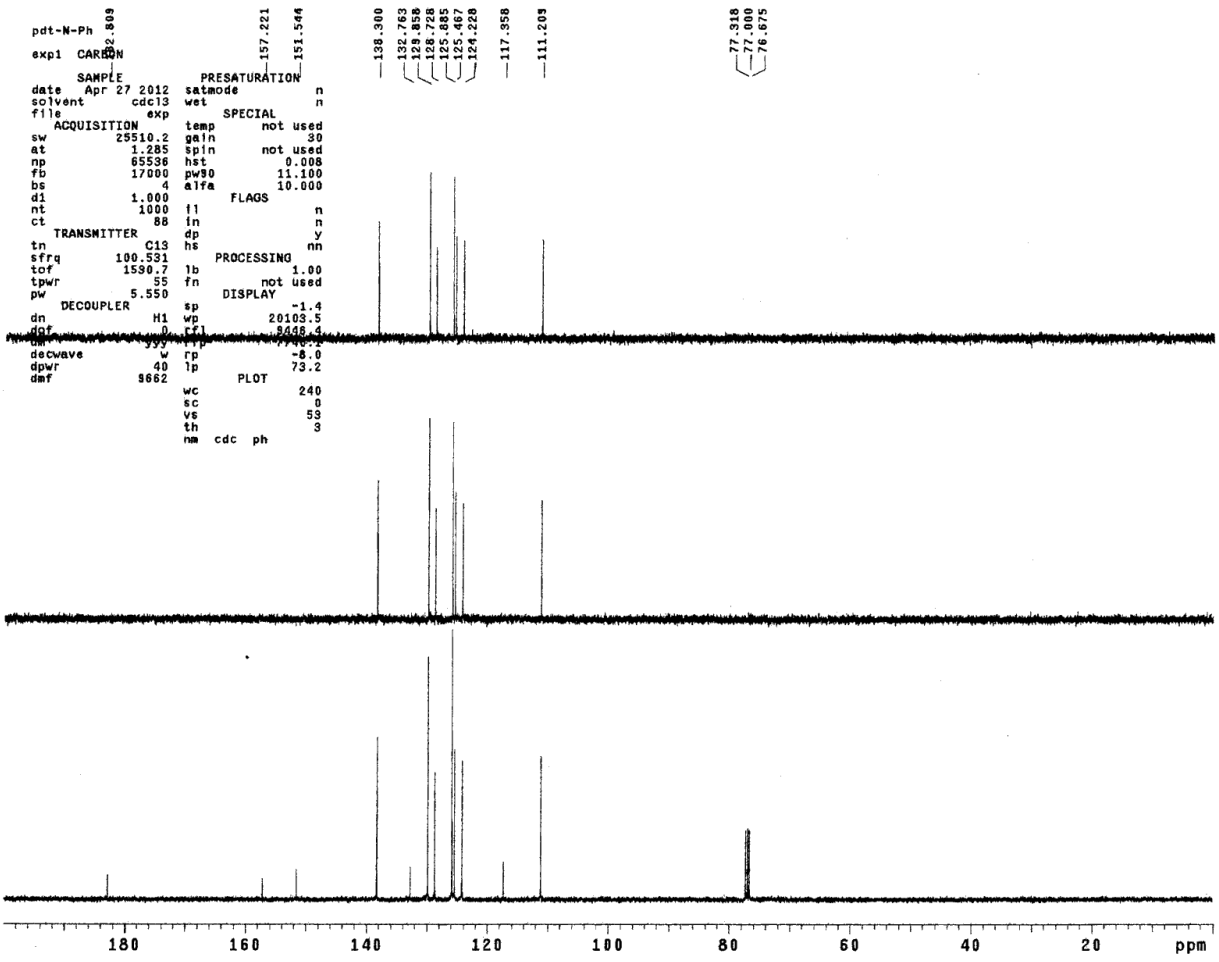
^{1}H and ^{13}C NMR spectra of compound **2h**



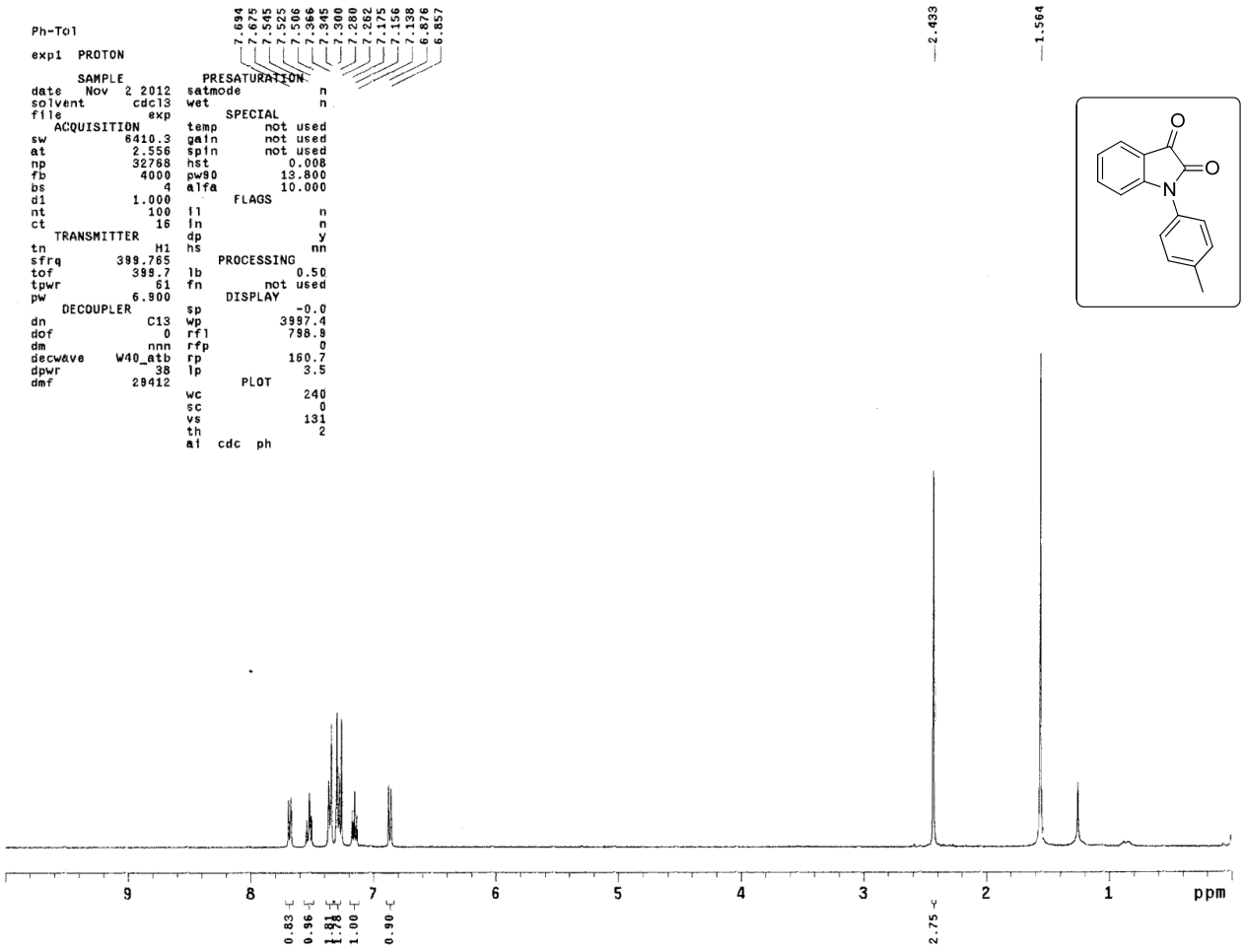


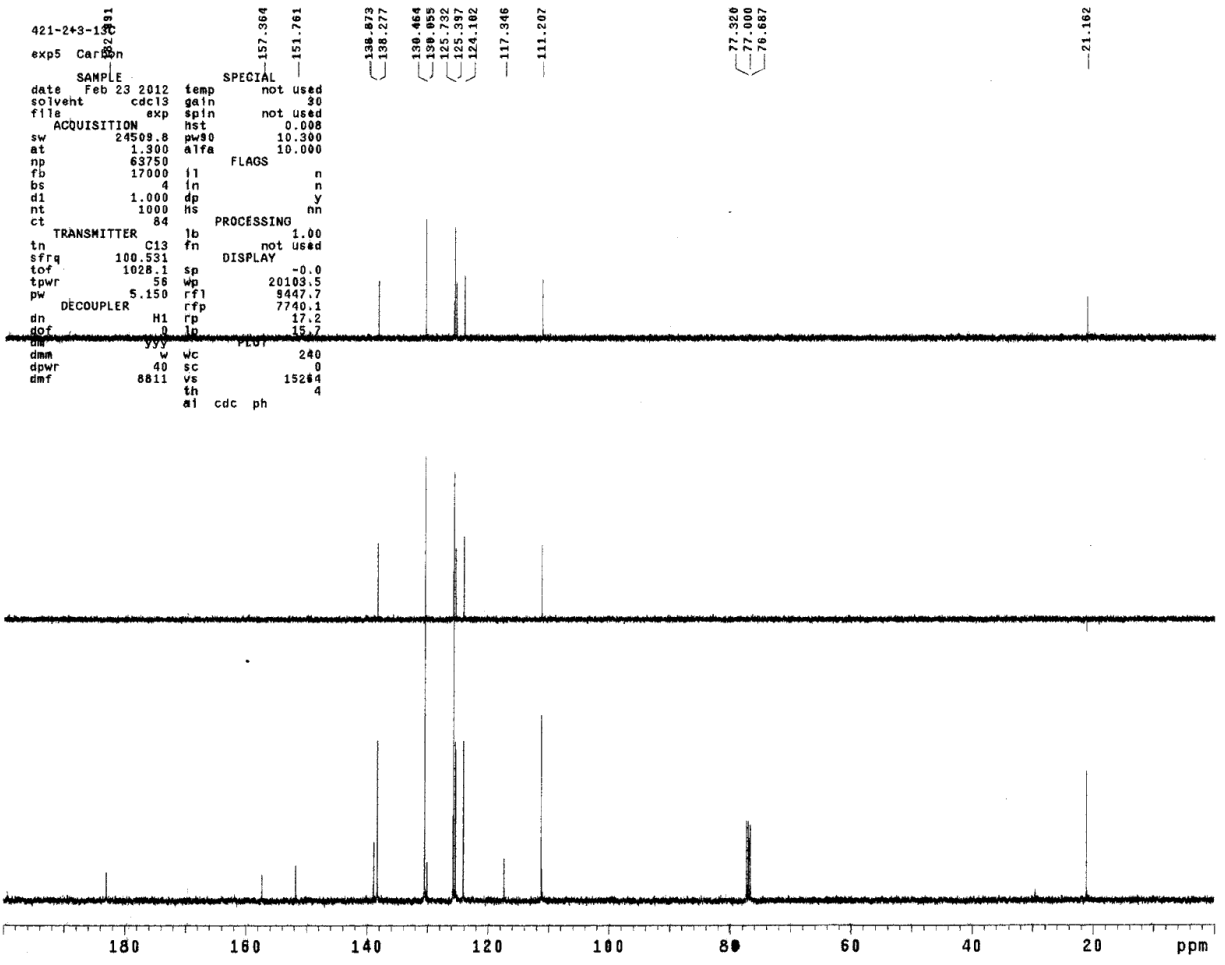
^{1}H and ^{13}C NMR spectra of compound **2l**



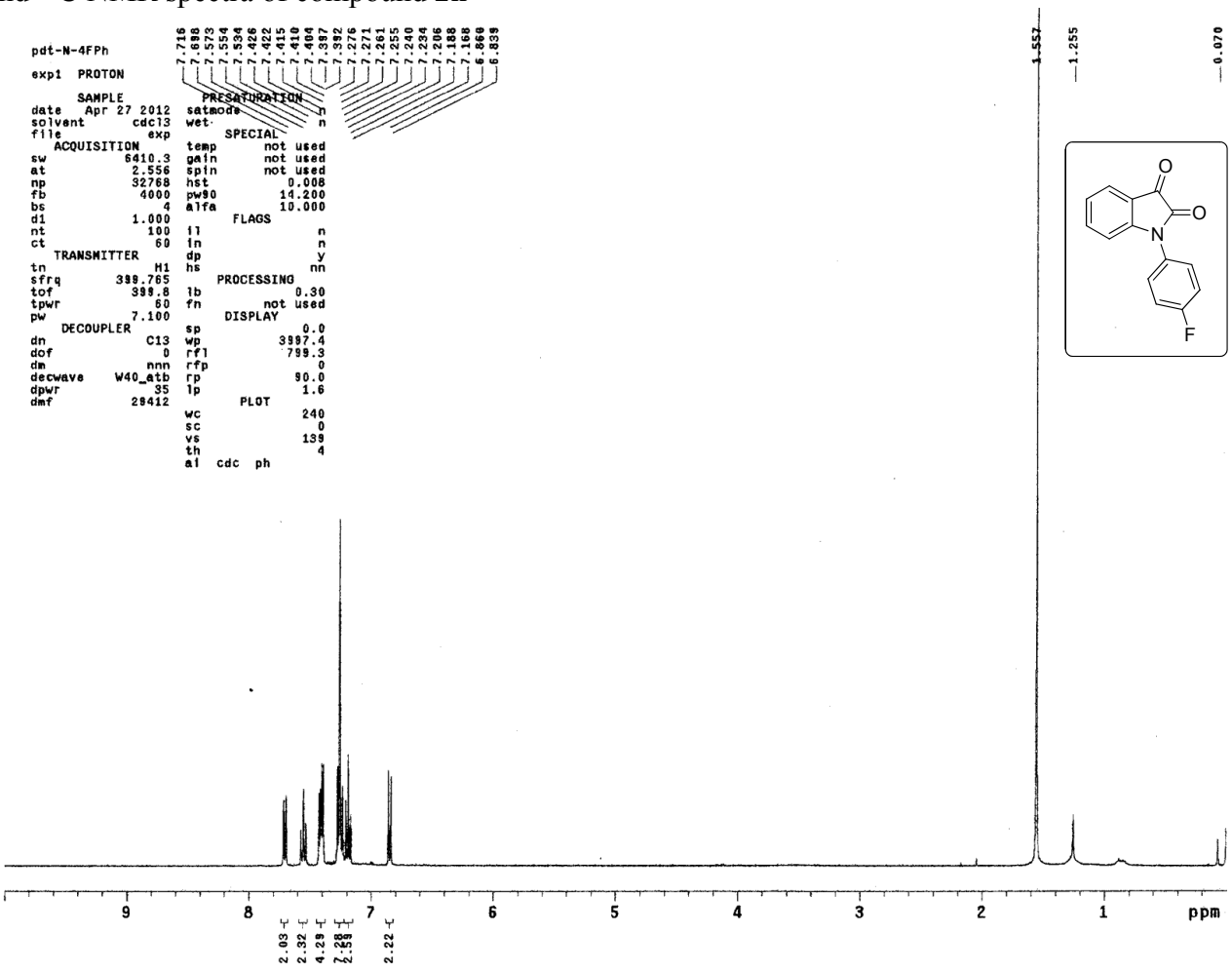


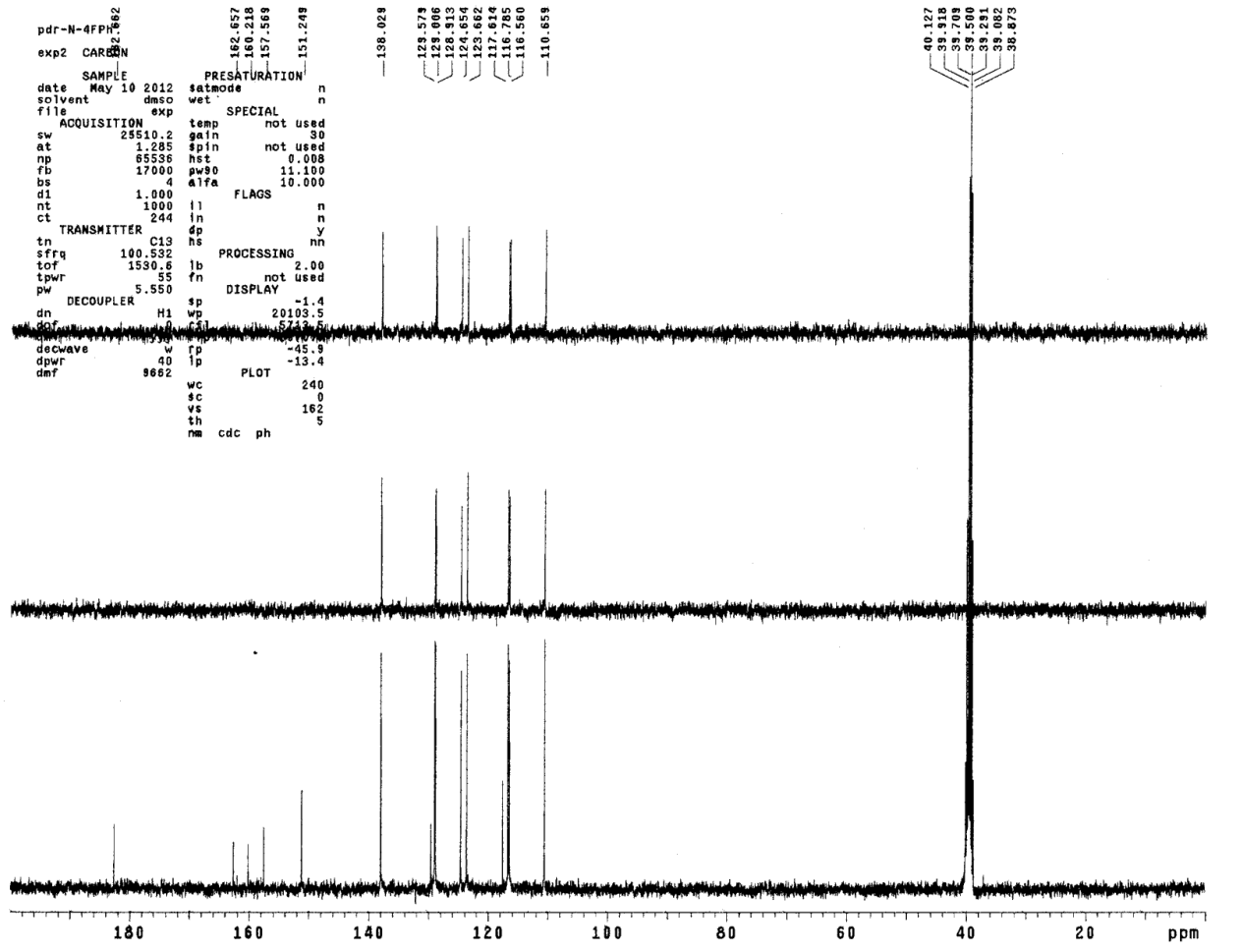
^{1}H and ^{13}C NMR spectra of compound **2m**



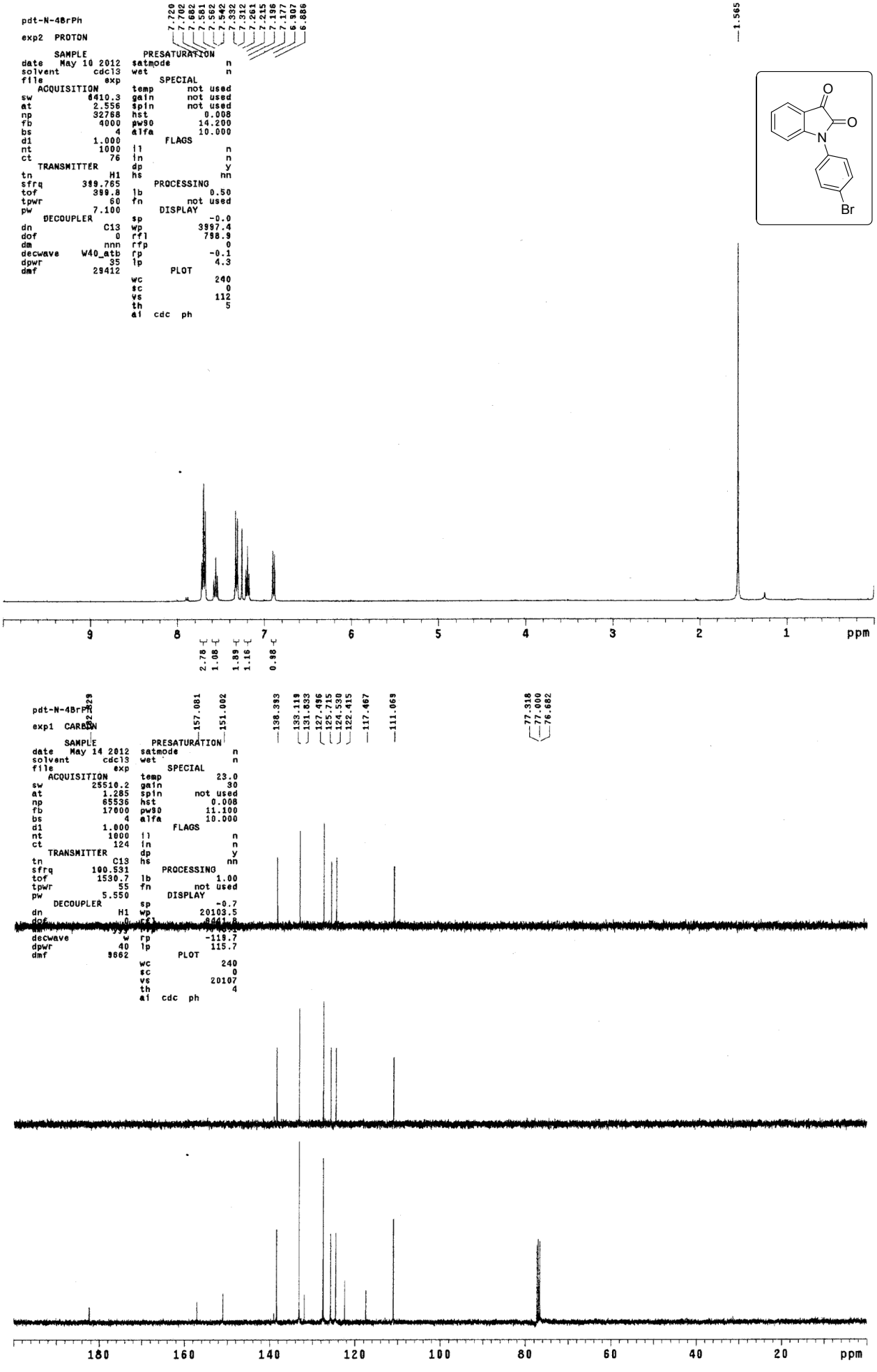


^{1}H and ^{13}C NMR spectra of compound **2n**

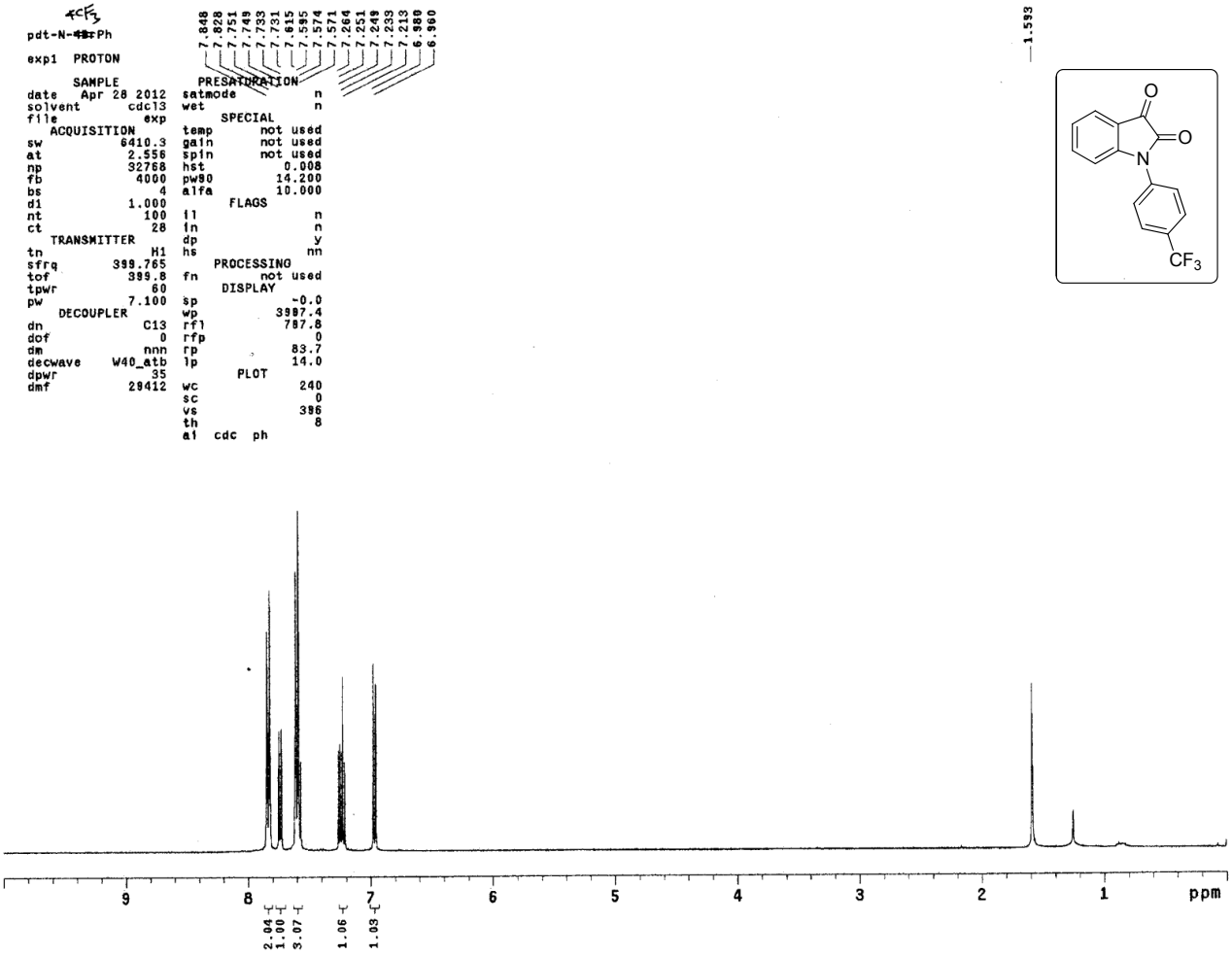


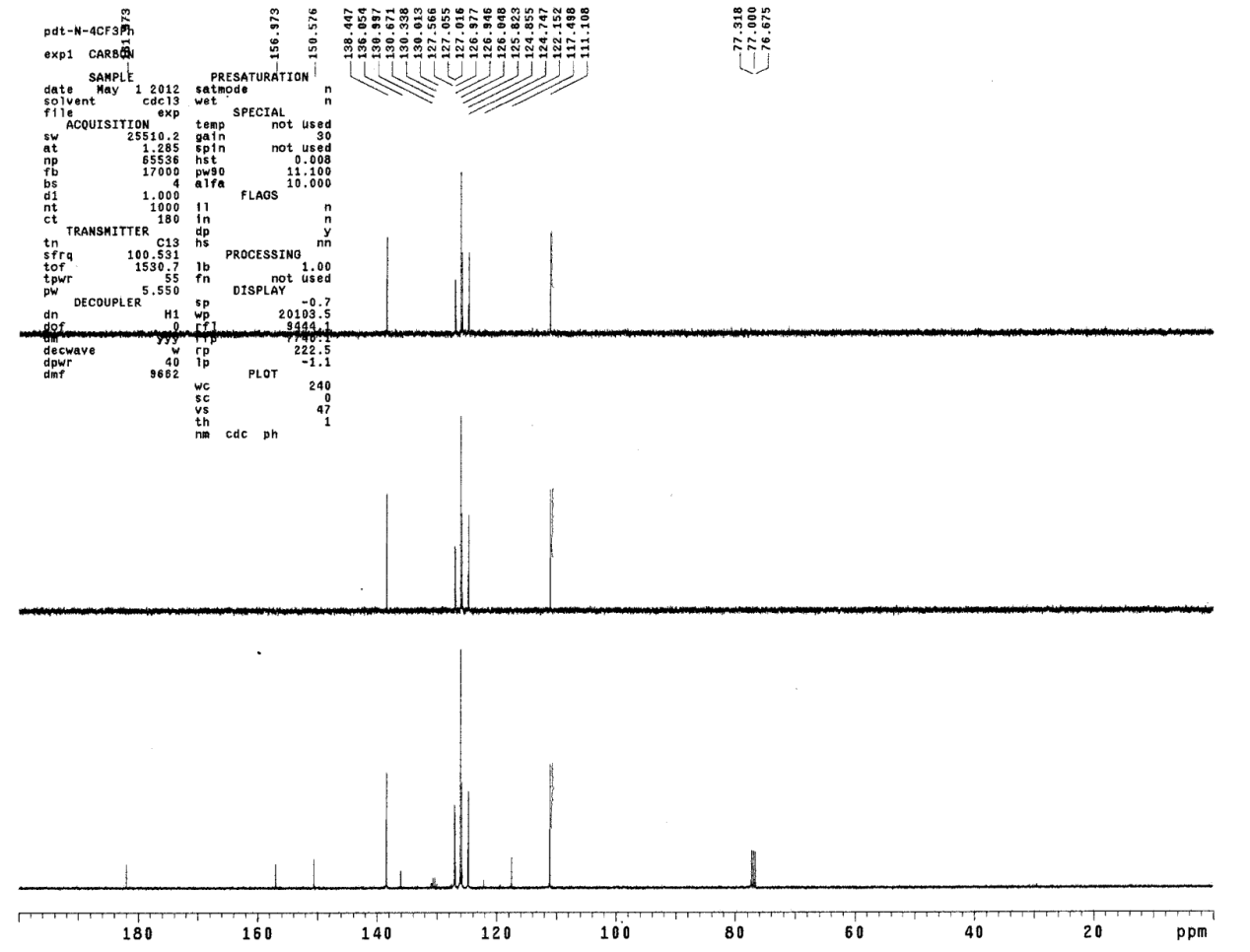


^{1}H and ^{13}C NMR spectra of compound **2o**

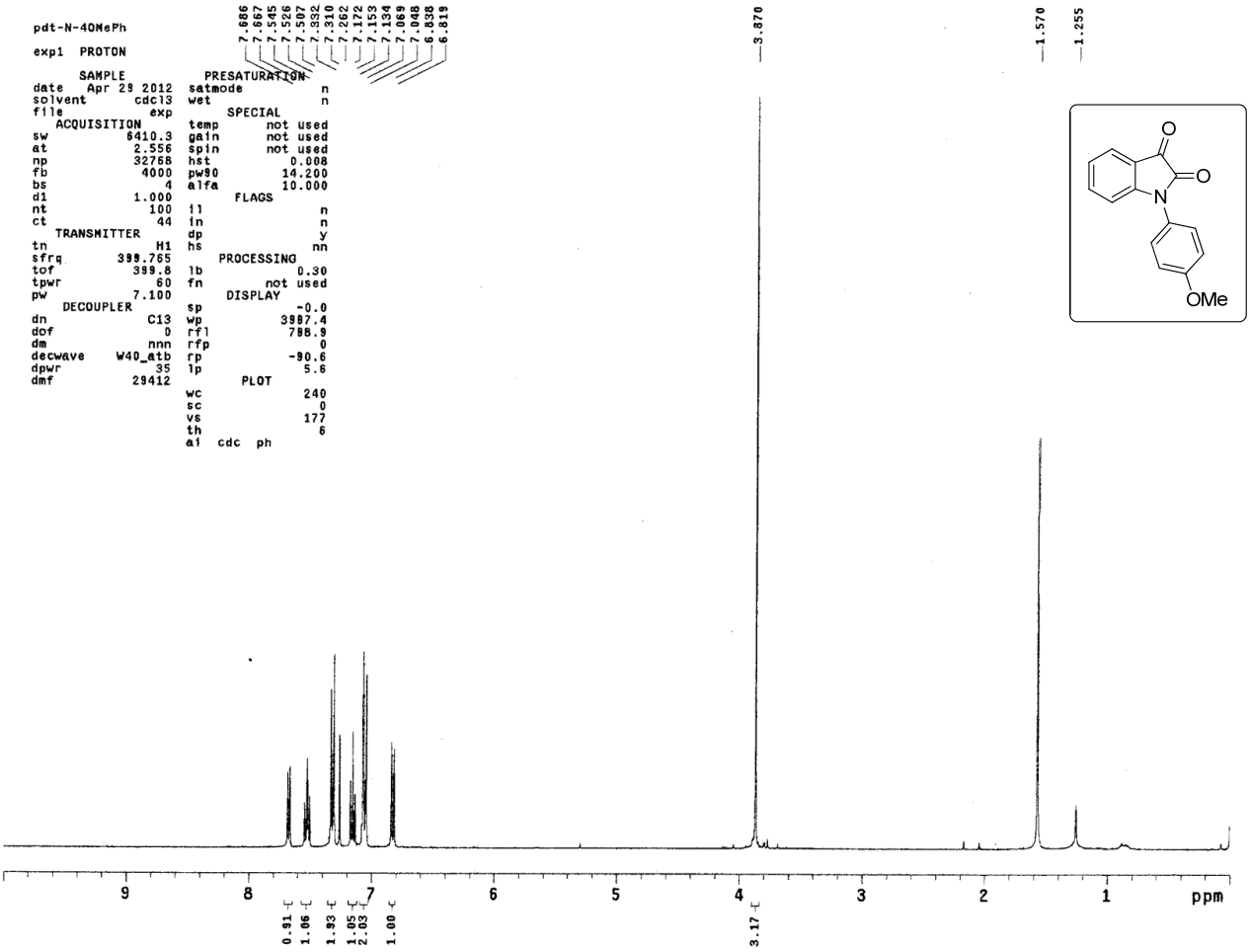


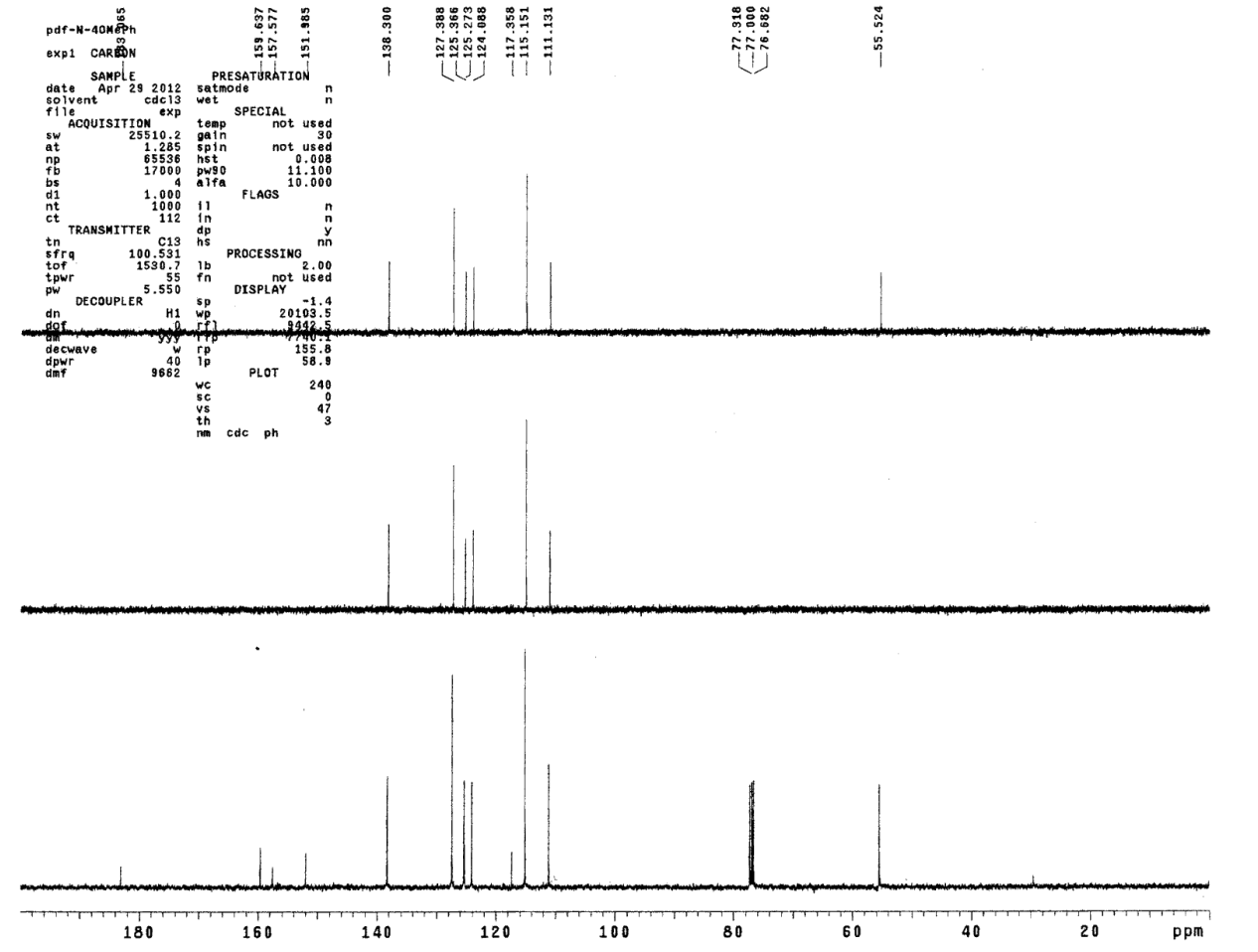
^{1}H and ^{13}C NMR spectra of compound **2p**



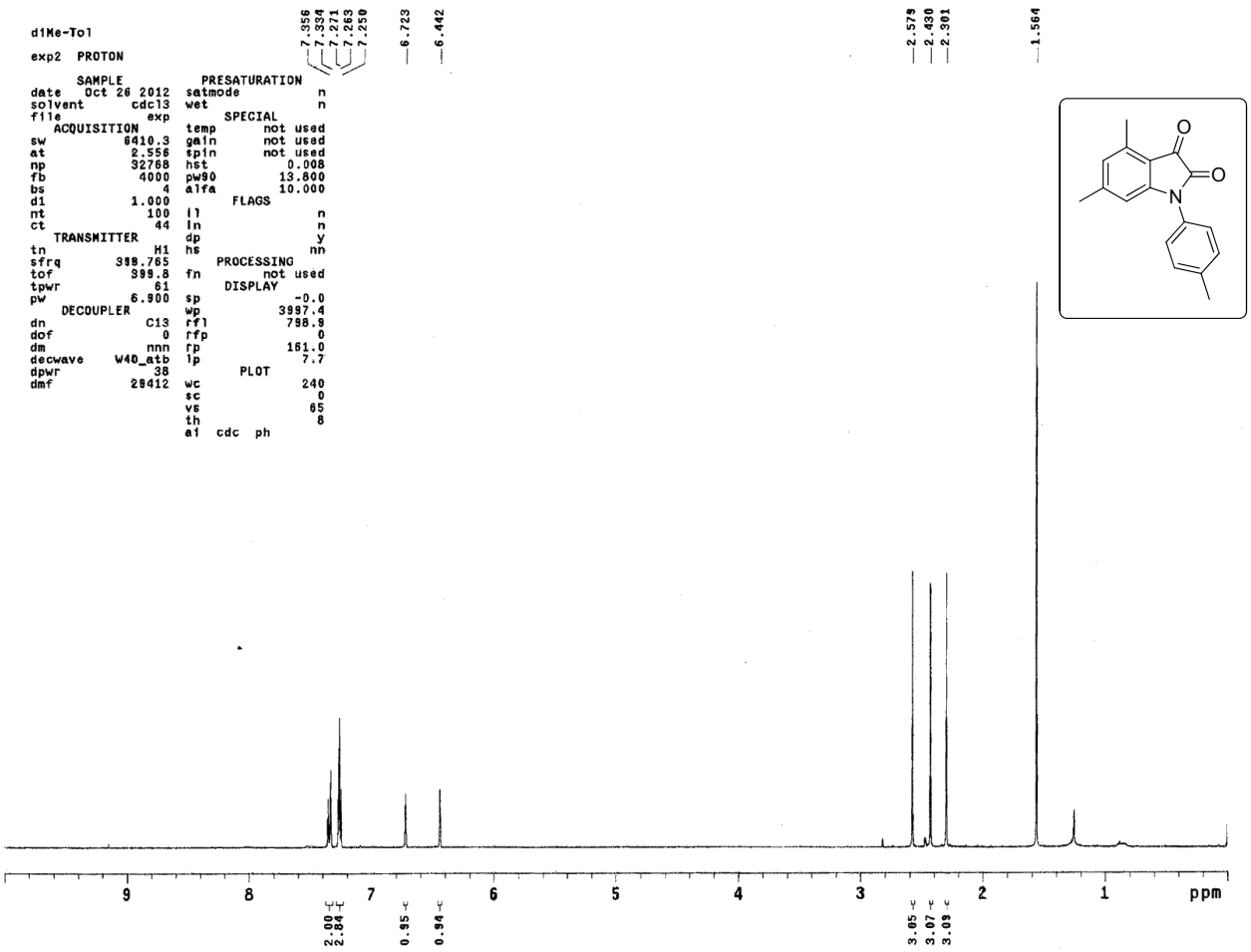


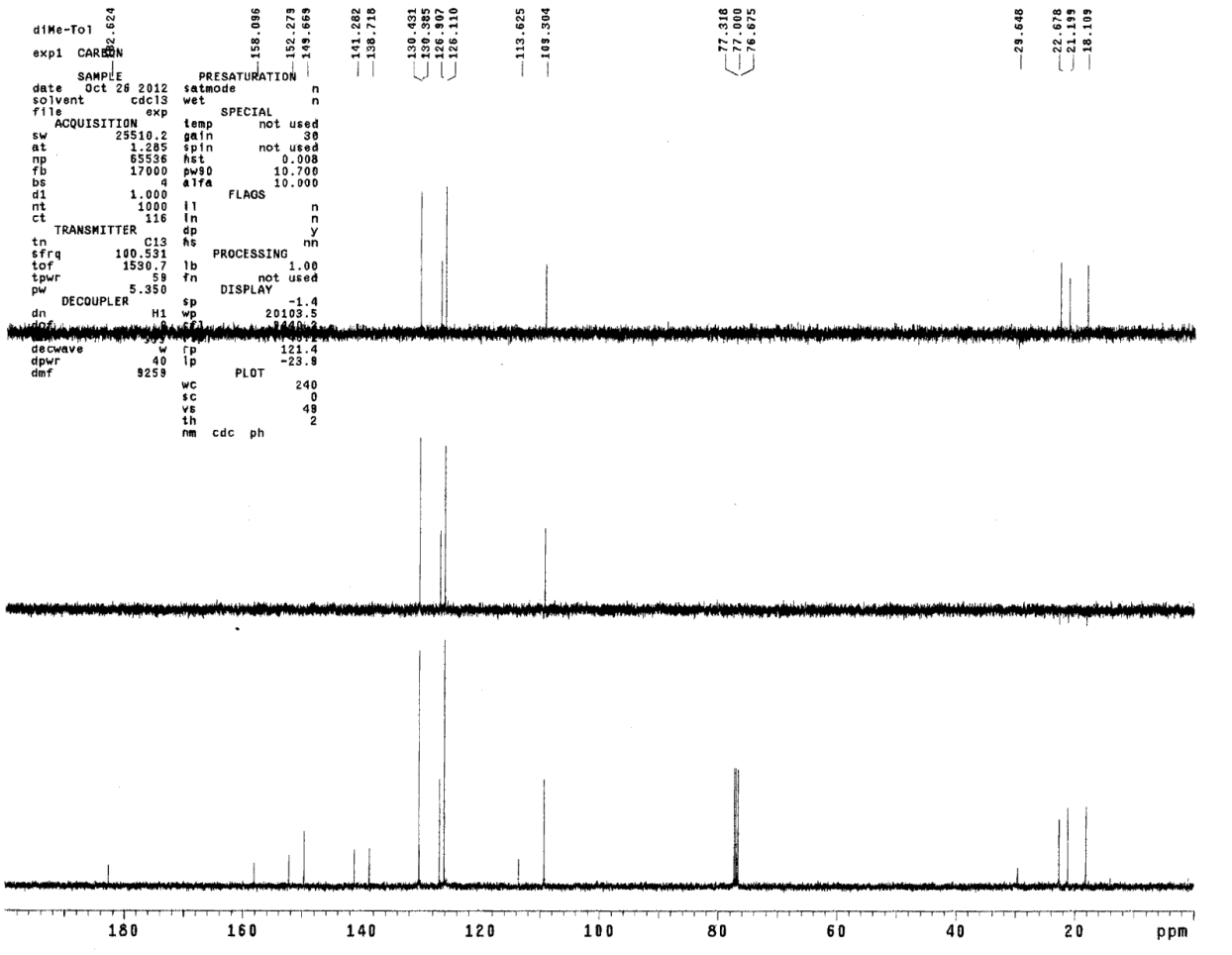
^{1}H and ^{13}C NMR spectra of compound **2q**



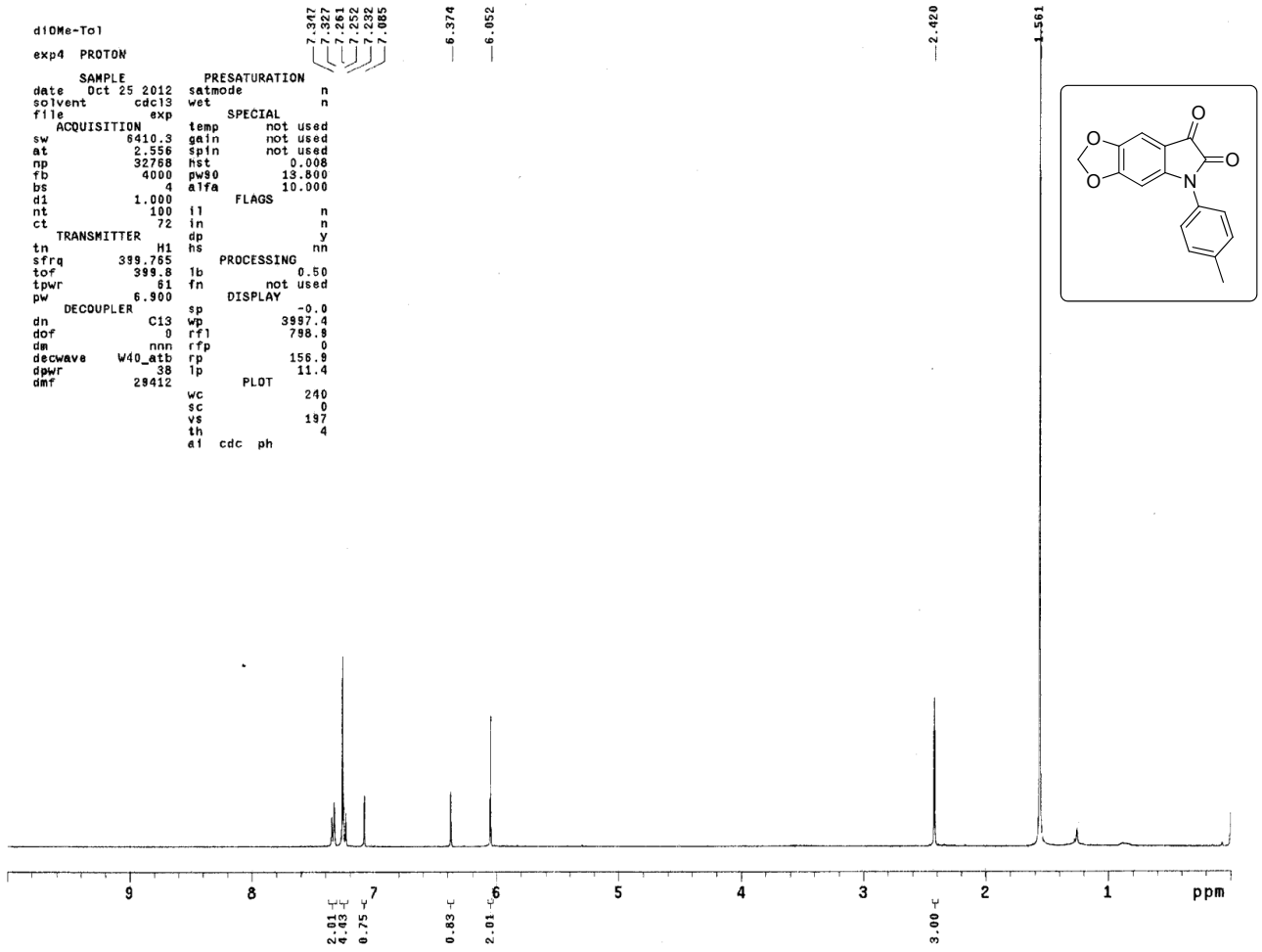


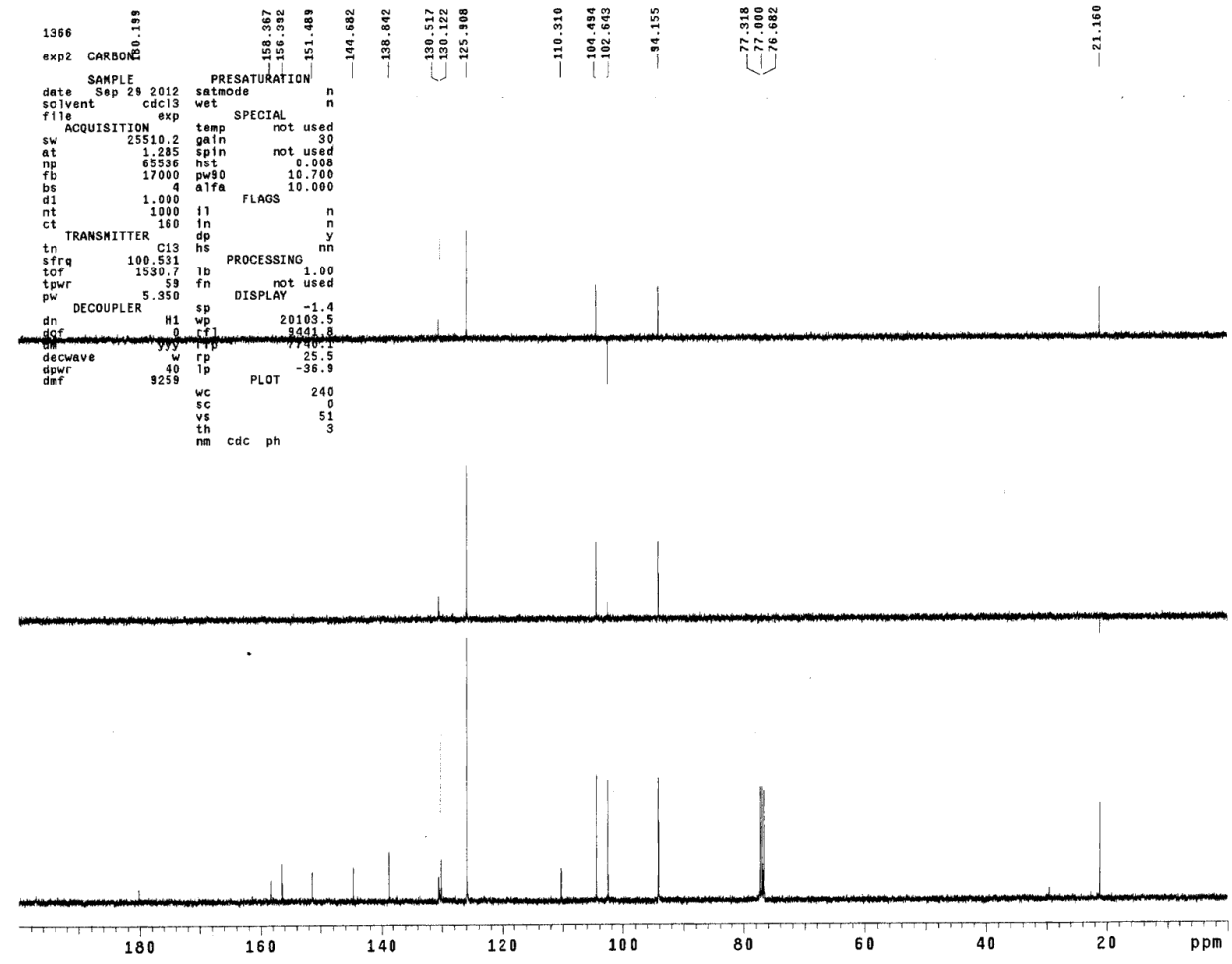
^{1}H and ^{13}C NMR spectra of compound **2r**





^{1}H and ^{13}C NMR spectra of compound **2s**





^{1}H and ^{13}C NMR spectra of compound **2t**