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SUPPORTING INFORMATION

Selectivity control during the synthesis of 1,2-disubstituted benzimidazoles and mechanistic insight to rationalize selectivity

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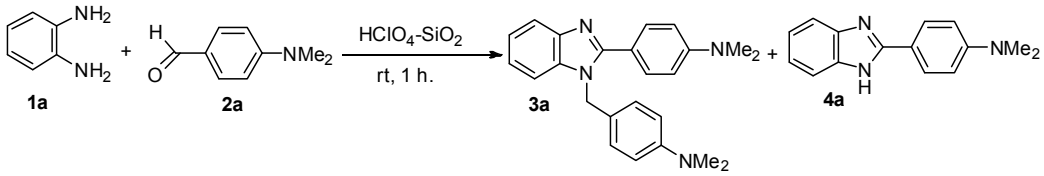
Effect of reaction medium on the selectivity control

Table 1. The selectivity in the formation of **3a** and **4a** during the $HClO_4$-SiO_2 catalysed reaction of **1a** with **2a** in various solvents.[a]

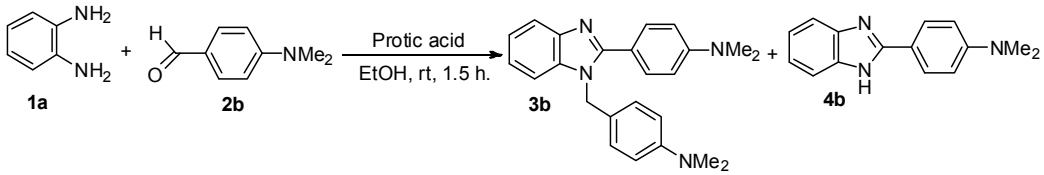


Entry	Solvent	Yield (%)[b],[c]	
		3a	**4a**
1	EtOH	90	00
2	MeOH	18	10
3	^{i}PrOH	20	08
4	^{t}BuOH	20	05
5	ethylene glycol	25	11
6	water	24	10
7	PEG-200	18	08
8	MeCN	32	12
9	DMF	12	traces
10	DCE	20	10
11	1,4-dioxane	16	20
12	THF	12	15
13	Et_2O	15	18
14	PhMe	traces	traces
15	neat	trace	traces

[a]**1a** (2.5 mmol) was treated with **2a** (5 mmol, 2 equiv) in various solvents (5 mL) in the presence of $HClO_4$-SiO_2 (0.5 mol%) at rt (~ 35-40 °C) for 1 h. [b]The isolated yield of **3a** and **4a** after column chromatographic purification. [c]The products were characterised by NMR (^{1}H & ^{13}C) and MS (APCI).

Selectivity control using protic acid alone

Table 2. Selectivity in the formation of **3b** and **4b** during the reaction of **1a** with **2b** under the catalytic influence of various protic acids without any solid support.[a]



Entry	Catalyst	Yield (%)[b]	
		3b	**4b**
1	$HClO_4$ (aq 70 %)	25	12
2	TfOH	22	12

3	TFA	trace	trace
4	*p*-TsOH	18	08
5	MSA	16	05
6	HCO_2H (aq 85%)	trace	trace
7	HOAc	trace	trace
8	HBr (aq 48 %)	trace	trace
9	H_2SO_4 (conc)	10	trace

[a]**1a** (1 mmol) was treated with **2b** (2 mmol, 2 equiv) in the presence of the catalyst (10 mol %) in EtOH (3 mL) at rt (~35 - 40 °C) for 1.5 h. [b]Isolated yield of **3b** and **4b** after column chromatographic purification.

Recovery and reuse of $HClO_4$-SiO_2

Table 3. The recyclability of $HClO_4$-SiO_2 during the reaction of **1a** with **2b**.[a]

Run/use	Scale (mmol)[b]	Amount of $HClO_4$-SiO_2 used (g)	recovered (g)	recovery(%)	Yield (%) [c],[d]
1	50	0.50	0.48	96	90
2	40	0.40	0.36	90	90
3	30	0.30	0.28	93	87
4	20	0.20	0.18	90	85
5	10	0.10	0.09	90	85

[a]**1a** was treated with **2a** (2 equiv) in EtOH in the presence of $HClO_4$-SiO_2 (0.5 mol%) at rt (~ 35-40 °C) for 1 h. [b]With respect to the amounts of **1a** used for the reaction. [c]The isolated yield of **3a**. [d]The product was characterised by NMR (^1H & ^{13}C) and MS (APCI).

Representative experimental procedure for recovery and reuse of $HClO_4$-SiO_2 during the synthesis of 1,2-disubstituted benzimidazole: The mixture of **1a** (5.4 g, 50 mmol), **2a** (14.91 g, 100 mmol, 2 equiv), and $HClO_4$-SiO_2 (0.5 g, 0.25 mmol, 0.5 mol %) in EtOH (100 mL) was stirred magnetically at rt (~25-30 ºC). After completion of the reaction (1 h, TLC, 3:1 n-hexane-EtOAc), the reaction mixture was diluted with EtOH (50 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOH (2 × 10 mL). The combined filtrates were evaporated and the crude product was purified by crystallization using 10 % aq EtOH to afford **3a** (16.67 g, 90 %) as white solid.[1] The cotton plug retaining the recovered catalyst was placed in a rb flask (50 mL) and dried by rotary vacuum evaporation when the catalyst separated out from the cotton (0.48 g, 96%). The catalyst was activated on heating under reduced pressure (10 mm Hg) at 80 °C for 24 h. The reaction was repeated with **1** and **2a** at 40 mmol, 30 mmol, 20 mmol and 10 mmol scales in the presence of the recovered $HClO_4$-SiO_2 (0.4 g, 0.3 g, 0.2 g and 0.1 g, respectively) to afforded **3a** in 13.34g (90 %), 9.67 g (87 %), 6.30 g (85 %) and 3.14 g (85 %) yields respectively.

[1] R. Varala, A. Nasreen, R. Enugala, S. R. T. Adapa, *Tetrahedron Lett*. **2007**, *48*, 69-72

Large scale synthesis (100 mmol) of 1,2-disubstituted benzimidazole

Representative experimental procedure for large scale synthesis (100 mmol) of 1,2-disubstituted benzimidazole using $HClO_4$-SiO_2: The mixture of **1a** (10.8 g, 100 mmol), **2a** (29.82 g, 200 mmol, 2 equiv), and $HClO_4$-SiO_2 (1 g, 0.50 mmol, 0.5 mol %) in EtOH (250 mL) was stirred magnetically at rt (~25-30 ºC). After completion of the reaction (1.5 h, TLC, 3:1 n-hexane-EtOAc), the reaction mixture was diluted with EtOH (100 mL), filtered through a plug of cotton (to separate the catalyst), and the cotton plug was washed with EtOH (2 × 20 mL). The combined filtrates were evaporated and the crude product was purified by crystallization (10% aq EtOH) to afford **3a** (34.83 g, 94%) as white solid.[2] The cotton plug retaining the recovered catalyst was placed in a rb flask (50 mL) and dried by rotary vacuum evaporation when the catalyst separated out from the cotton (0.95 g, 95%). The remaining reactions were carried out following these general procedures. The purification was carried out by crystallization in aq EtOH or passing through a column of silica-gel and eluting with 10% EtOAc in hexane, wherever required. In each occasion, the spectral data (IR, NMR, and MS) of known compounds were found to be identical with those reported in the literature.

Spectral data

1-Phenylmethyl-2-phenyl-1*H*-benzimidazole (Entry 1, Table 3): white solid; mp = 131-133 °C; IR (KBr) ν_{max} = 3392, 1602, 1508, 1460, 1388, 1264, 1161, 1129, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.1 Hz, 1H), 7.68 (m, 2H), 7.47 (m, 3H), 7.22-7.34 (m, 6H), 7.11 (d, *J* = 7.4 Hz, 2H), 5.46 (s, 2H); MS (APCI) m/z: 285 $(M+H)^+$.

1-(4-Methylphenylmethyl)-2-(4-methylphenyl)-1*H*-benzimidazole (Entry 2, Table 3): White Solid; mp = 128-130 °C; IR (KBr) ν_{max} =3545, 1683, 1610, 1441, 1248, 1183, 1119, 983 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 7.9 Hz, 1 H), 7.58 (d, *J* = 8.1 Hz, 2 H), 7.28-7.31 (m, 2 H),.20-7.24 (m, 3 H), 7.13 (d, *J* = 7.9 Hz, 2 H), 6.99 (d, *J* = 8.0 Hz, 2 H), 5.41 (s, 2 H), 2.40 (s, 3 H), 2.33 (s, 3 H); MS (APCI) m/z: 313 $(M+H)^+$.

1-(4-Methoxyphenylmethyl)-2-(4-methoxyphenyl)-1*H*-benzimidazole (Entry 3, Table 3): White Solid; mp = 129-130 °C; IR (KBr) ν_{max} = 3529, 1608, 1586, 1228, 1291, 1284, 1291, 1244, 1170, 1107, 1082, 1011, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.42 (d, *J* =

[2] R. Varala, A. Nasreen, R. Enugala, S. R. T. Adapa, *Tetrahedron Lett*. **2007**, *48*, 69-72

8.0 Hz , 1 H), 7.60 (t, *J* = 8.3 Hz, 3 H), 7.21-7.29 (m, 3 H), 6.84-7.04 (m, 6 H), 5.38 (s, 2 H), 3.83 (s, 3 H), 3.75 (s, 3 H); MS (APCI) m/z: 345 $(M+H)^+$.

1-(4-Chlorophenylmethyl)-2-(4-chlorophenyl)-1*H*-benzimidazole (Entry 5, Table 3): White Solid; mp =136 °C; IR (KBr) ν_{max} = 3447, 1601, 1493, , 1384, 1291, 1249, 1160, 765, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 6.6 Hz, 1 H), 7.59 (d, *J* = 6.7 Hz, 2 H), 7.43 (d, *J* = 6.8 Hz, 2 H), 7.30-7.36 (m, 3 H), 7.19 (t, *J* = 7.8 Hz, 2 H), 7.02 (d, *J* = 7.0 Hz, 2 H), 5.36 (s, 2 H); MS (APCI) m/z: 354 $(M+H)^+$.

1-(4-Bromophenylmethyl)-2-(4-bromophenyl)-1*H*-benzimidazole (Entry 6, Table 3): White Solid; mp =140-141 °C; IR (KBr) ν_{max} = 3035, 2890, 1618, 1592, 1052 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.92 Hz, 1 H), 7.60 (d, *J* = 7.52 Hz, 2 H), 7.53 (d, *J* = 8.36 Hz, 2 H), 7.48-7.46 (m, 2 H), 7.34 (t, *J* = 7.24 Hz, 1 H), 7.27 (t, *J* = 8.36 Hz, 1 H), 7.20 (d, *J* = 7.96 Hz, 2 H), 6.96 (d, *J* = 7.88 Hz, 2 H), 5.38 (s, 2 H); MS (APCI) m/z: 440 $(M+H)^+$.

1-(4-Trifluoromethylphenylmethyl)-2-(4-(trifluoromethyl)phenyl)-1*H*-benzimidazole (Entry 7, Table 3): White Solid; mp = 145-147 °C; IR (KBr) ν_{max} = 3025, 1609, 1589, 1108, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.96 Hz, 1 H), 7.61 (d, *J* = 8.48 Hz, 2 H), 7.54-7.46 (m, 4 H), 7.36-7.33 (m, 2 H), 7.29-7.26 (m, 1 H), 7.20 (d, *J* = 7.96 Hz, 2 H), 6.97 (d, *J* = 8.32 Hz, 2 H), 5.38 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): 152.4, 143.1, 140.0, 135.9, 131.9, 130.5, 129.5, 127.8, 126.2, 126.1, 125.9, 125.1, 125.0, 123.9, 123.3, 122.4, 119.7, 119.6, 110.3, 48.0; MS (APCI) m/z: 421.2 $(M+H)^+$; Anal. Calcd. For $C_{22}H_{14}F_6N_2$: C, 62.86; H, 3.36; N, 6.66 % Found: C, 62.88; H, 3.38; N, 6.67 %.

1-(4-Phenylmethyloxyphenylmethyl)-2-(4-benzyloxy-phenyl)-1*H*-benzimidazole (Entry 8, Table 3): White Solid; mp =127 °C; IR (KBr) ν_{max} = 3434, 1610, 1511, 1455, 1384, 1246, 1175, 1024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.5 Hz, 2 H), 7.63 (d, *J* = 8.3 Hz, 2 H), 7.29-7,42 (m, 9 H), 7.21 (d, *J* = 2.8 Hz, 4 H), 7.06 (dd, *J* = 2.9 Hz & 3.3Hz, 4 H), 6.92 (d, *J* = 8.2 Hz, 2 H), 5.38 (s, 2 H), 5.11 (s, 2 H), 5.03 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): 160.64, 158.90, 137.04, 136.59, 131.28, 129.20, 128.68, 128.61, 128.04, 127.80, 123.32, 123.11, 120.26, 115.90, 115.66, 110.98, 70.63, 48.44; MS (APCI) m/z: 497.5 $(M+H)^+$; Anal. Calcd. For $C_{34}H_{28}N_2O_2$: C, 82.23; H, 5.68; N, 5.64 % Found: C, 82.25; H, 5.67; N, 5.66 %.

(4-Nitro-phenyl)-1*H*-benzimidazole (Entry 10, Table 3): Yellow Solid; mp =327 °C; IR (KBr) ν_{max} = 3442, 1612, 1525, 1460, 1385, 1232, 1140, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.54 (s, 1 H), 8.30 (d, *J* = 6.4 Hz, 2 H), 8.06 (m, 3 H), 7.26 (m, 1 H), 7.13 (m, 1 H); MS (APCI) m/z: 240.3 $(M+H)^+$.

2-Benzo[1,3]dioxol-5-yl-1-benzo[1,3]dioxol-5-ylmethyl-1*H*-benzimidazole (Entry 11, Table 3): White solid; mp = 162 °C; IR (KBr) ν_{max} = 3344, 1608, 1501, 1487, 1388, 1325, 1243, 1190, 1115, 1076, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.0 Hz, 1 H); 7.53 (s, 2 H), 7.17 (m, 2 H), 6.88 (t, *J* = 8.7 Hz, 1 H), 6.75 (d, *J* = 8.3 Hz, 1 H), 6.56 (s, 2 H), 6.04 (s, 2 H), 5.95 (s, 2 H), 5.35 (s, 2 H); MS (APCI) m/z: 373 $(M+H)^+$.

2-Naphthalen-2-yl-1-naphthalen-2-ylmethyl-1*H*-benzimidazole (Entry 12, Table 3): White Solid; mp = 125-126 °C; IR (KBr) ν_{max} = 3056, 1600, 1439, 1378, 1325, 1253, 1143 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 7.85-7.95 (m, 6 H), 7.74 (t, *J* = 7.3 Hz, 2 H), 7.48-7.57 (m, 5 H), 7.28-7.35 (m, 4 H), 5.36 (s, 2 H); MS (APCI) m/z: 385 $(M+H)^+$.

2-Furan-2-yl-1-furan-2-ylmethyl-1*H*-benzimidazole (Entry 13, Table 3): White solid; mp = 94°C ; IR (KBr) ν_{max} = 3393, 1608, 1511, 1456, 1378, 1108, 921 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.79 (s, 1 H), 7.50 (s, 2 H), 7.22 (m, 4 H), 6.62 (s, 1 H), 6.27 (d, *J* = 12.39 Hz, 2 H), 5.65 (s, 2 H); MS (APCI) m/z: 265.2 $(M+H)^+$.

2-Thiophen-2-yl-1-thiophen-2-ylmethyl-1*H*-benzimidazole (Entry 14, Table 3): White solid; mp =145-147 °C; IR (KBr) ν_{max} = 3064, 1610, 1556, 1443, 1422, 1369, 1283, 1160, 1087, 1004 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.9 Hz, 1 H), 7.50 (d, *J* = 13 Hz, 1 H), 7.37 (d, *J* = 6.3 Hz, 2 H), 7.23-7.49 (m, 4 H), 7.14 (t, *J* = 4.9 Hz, 1 H), 6.90 (t, *J* = 4.8 Hz, 2 H), 5.70 (s, 2 H); MS (APCI) m/z: 297.5 $(M+H)^+$.

2-Pyridin-2-yl-1-pyridin-2-ylmethyl-1*H*-benzimidazole (Entry 15, Table 3): White Solid; mp =128-130 °C; IR (KBr) ν_{max} = 3401, 1633, 1592, 1462, 1444, 1388, 1331, 1046 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 8.47 (d, *J* = 7.7 Hz, 1 H), 7.49 (t, *J* = 16.4 Hz 1 H), 7.29-7.38 (m, 4 H), 7.14 (s, 1 H), 6.90 (d, *J* =7.5 Hz, 1 H), 6.29 (s, 2 H); MS (APCI) m/z: 287.2 $(M+H)^+$.

1-((1*H*-Indol-3-yl)methyl)-2-(1*H*-indol-3-yl)-1*H*-benzimidazole (Entry 16, Table 3): Brown Solid; mp = 253-255 °C; IR (KBr) ν_{max} = 3035, 1615, 1598, 1258, 1108, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 7.76 Hz, 1 H), 7.86 (d, *J* = 2.56 Hz, 1 H), 7.67 (d, *J* = 7.48 Hz, 1 H), 7.55 (d, *J* = 7.4 Hz, 1 H), 7.49 (d, *J* = 7.92 Hz, 1 H), 7.31 (d, *J* = 8.16 Hz, 1 H), 7.25-7.23 (m, 2 H), 7.20-7.12 (m, 3 H), 7.04-7.01 (m, 2 H), 6.83 (t, *J* =7.56 Hz, 1 H), 5.82 (s, 2 H); MS (APCI) m/z: 363 $(M+H)^+$.

2-Cyclohexyl-1-cyclohexylmethyl-1*H*-benzimidazole (Entry 17, Table 3): White Solid; mp = 90-91 °C IR (KBr) ν_{max} = 3369, 1613, 1457, 1347, 1273 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.74 (m, *J* = 2.7 Hz, 1 H), 7.28 (t, *J* = 3.4 Hz, 1 H), 7.17-7.21 (m, 2 H), 3.93 (t, *J* = 5.7 Hz, 2 H), 2.82 (d, *J* = 2.8 Hz, 1 H), 1.60-1.90 (m, 14 H), 1.40 (m, 2 H), 1.01-1.17 (m, 3 H), 0.87-0.94 (m, 2 H), MS (APCI) m/z: 297 $(M+H)^+$.

1-Isobutyl-2-isopropyl-1*H*-benzimidazole (Entry 18, Table 3): Viscous liquid; IR (neat) ν_{max} = 3400, 1614, 1508, 1461, 1416, 1282, 1086 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.72-7.78 (m, 1 H), 7.18-7.30 (m, 3 H), 3.92 (d, *J* = 7.5 Hz, 1 H), 3.14-324 (m, 1 H), 2.17-2.27 (m, 1 H), 1.44 (d, *J* = 6.73 Hz, 6 H), 0.95 (d, *J* = 6.73 Hz, 6 H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 160.71, 143.07, 135.64, 122.34, 122.20, 119.77, 110.21, 51.35, 29.81, 26.91, 20.76, 19.65; MS (APCI) m/z: 217.4 $(M+H)^+$; Anal. Calcd. For $C_{14}H_{20}N_2$: C, 77.73; H, 9.32; N, 12.95 %. Found: C, 77.74; H, 9.30; N, 12.94 %.

1-(3,3-Dimethylbutyl)-2-neopentyl-1*H*-benzimidazole (Entry 19, Table 3): Viscous liquid; IR (neat) ν_{max} = 3343, 1605, 1444, 1378, 1354, 139, 1074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.73-7.76 (m, 1 H), 7.21-7.27 (m, 3 H), 4.13-4.19 (m, 2 H), 2.77 (s, 2 H), 1.60-1.66 (m, 2 H), 1.09 (s, 9 H), 1.06 (s, 9 H); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 151.94, 141.87, 133.48, 127.76, 120.67, 118.40, 108.00, 46.00, 41.52, 39.46, 33.62, 30.30, 28.95; MS (APCI) m/z: 273.4 $(M+H)^+$; Anal. Calcd. For $C_{18}H_{28}N_2$: C, 79.36; H, 10.36; N, 10.28 %. Found: C, 79.34; H, 10.34; N, 10.30 %.

2-*tert*-Butyl-1*H*-benzimidazole (Entry 20, Table 3): White solid; mp = 321-323 °C; IR (KBr) ν_{max} = 3342, 1610, 1440, 1375, 1355, 1392, 1081 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 12.07 (bd, *J* = 6.64 Hz, 1 H), 7.52 (d, *J* = 6.64 Hz, 1 H), 7.40 (d, *J* = 7.2 Hz, 1 H), 7.06-7.14 (m, 2 H), 1.39 (s, 9 H); MS (APCI) m/z: 175.2 $(M+H)^+$.

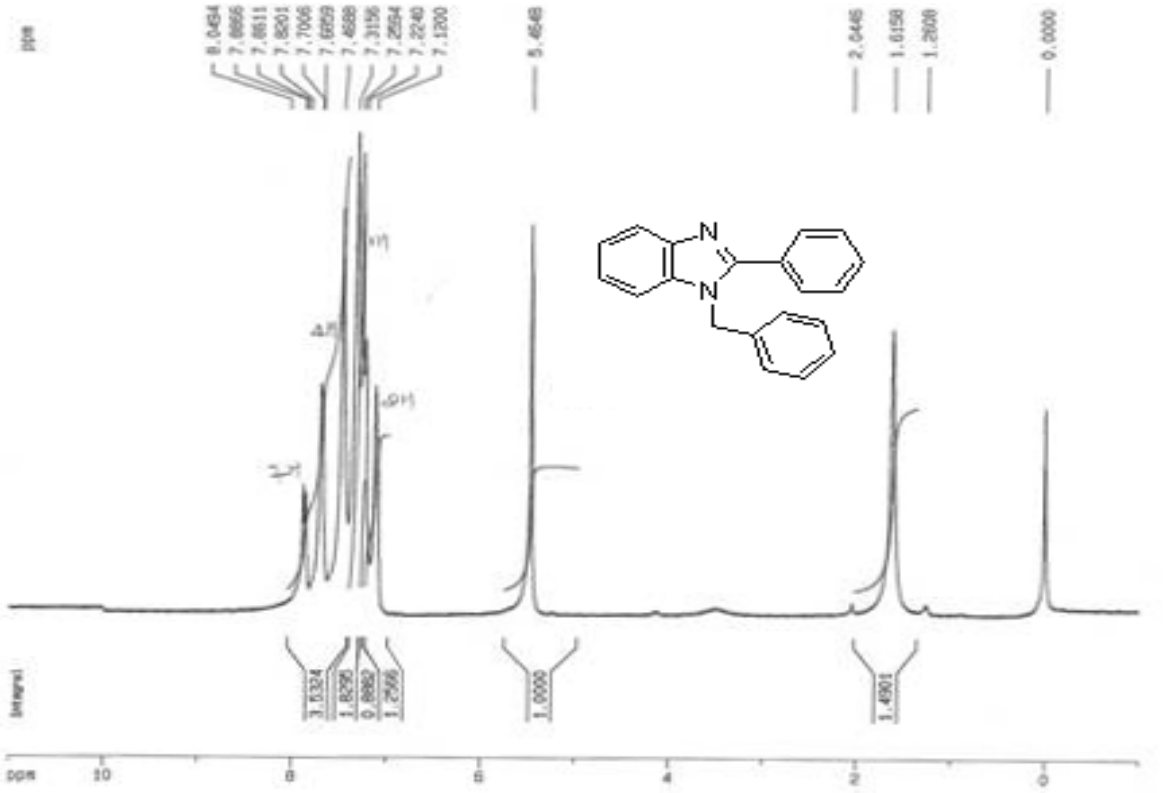
6-Nitro-2-phenyl-1*H*-benzimidazole 4c: Yellow solid; mp = 202-203 °C; IR (KBr) ν_{max} = 3245, 1470, 1630, 1621, 734 cm^{-1}; ^1H NMR (400 MHz, DMSO): δ = 8.49 (s, 1 H), 8.21 (d, *J* = 5.3 Hz, 2 H), 8.15 (d, *J* = 8.8 Hz, 1 H), 7.78 (d, *J* = 8.5 Hz, 1 H), 7.61(d, *J* = 6.4 Hz, 3 H); MS (APCI) m/z: 240.3 $(M+H)^+$.

6-Nitro-2-(4-nitrophenyl)-1*H*-benzimidazole 4e: Yellow solid; 270 °C (decomp); IR (KBr) ν_{max} = 3142, 1465, 1640, 1625, 730 cm^{-1}; ^1H NMR (400 MHz, DMSO): δ = 8.36 (m, 4 H), 8.15 (d, *J* = 2.8 Hz, 2 H), 7.95-7.98 (m, 2 H), 6.93 (bd, s, 1 H), 8.15 (d, *J* = 9.8 Hz, 1 H); MS (APCI) m/z: 285.2 $(M+H)^+$.

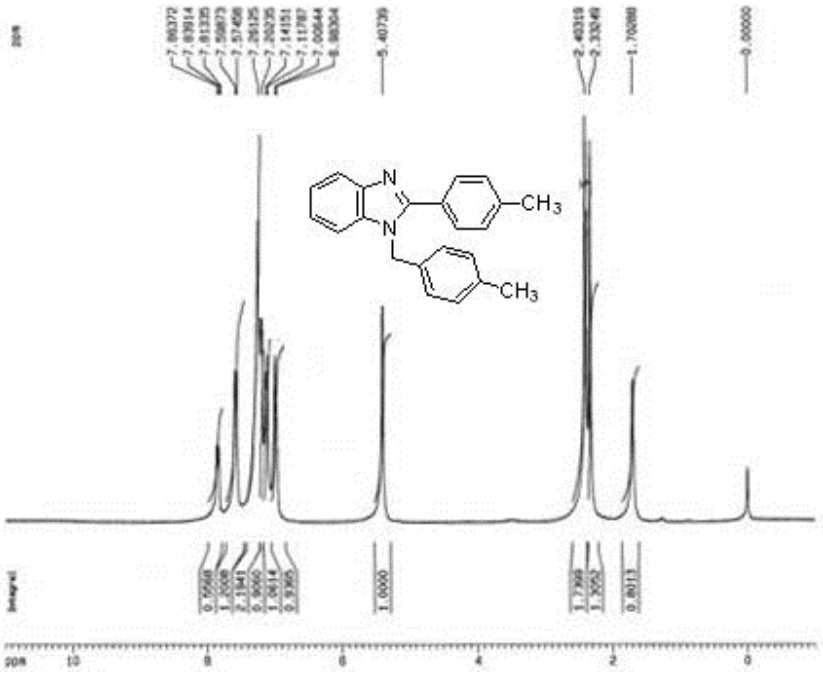
6-Nitro-2-(4-methoxyphenyl)-1*H*-benzimidazole 4f: White solid; mp = 235-236 °C; IR (KBr) ν_{max} = 3242, 1470, 1645, 11598, 825, 715 cm^{-1}; ^1H NMR (400 MHz, DMSO): δ = 8.10-8.12 (m, 2 H), 7.90 (s, 1 H), 7.89-7.91(m, 2 H), 7.08(m, 2 H); MS (APCI) m/z: 270.3 $(M+H)^+$.

Scanned NMR spectra

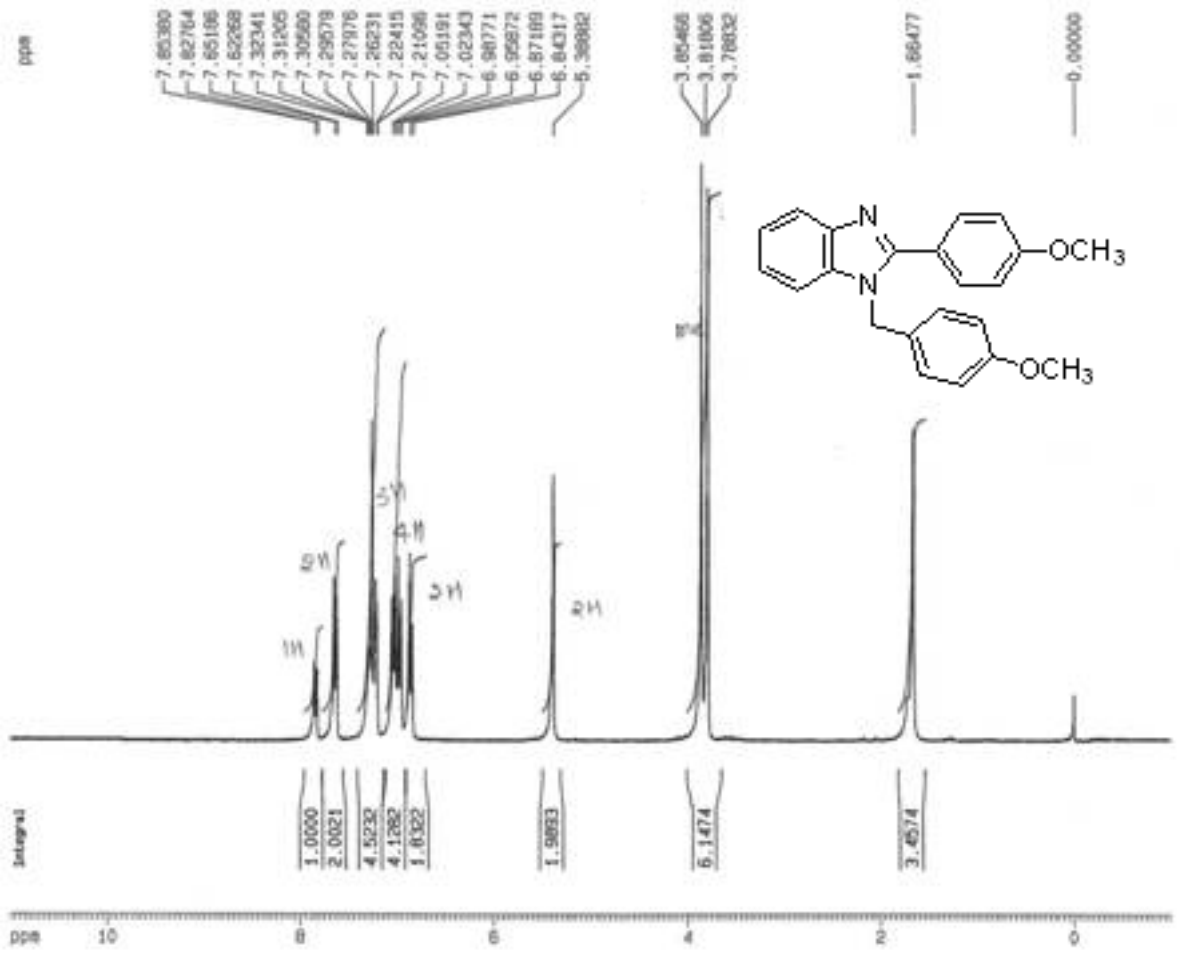
Entry 1, Table 3, ^{1}H NMR



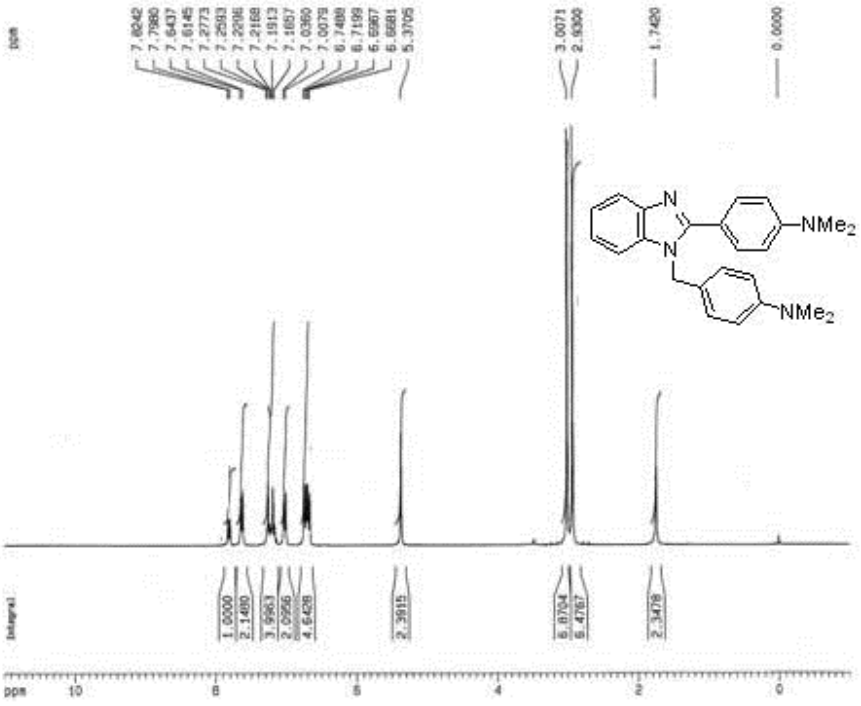
Entry 2, Table 3, ^{1}H NMR



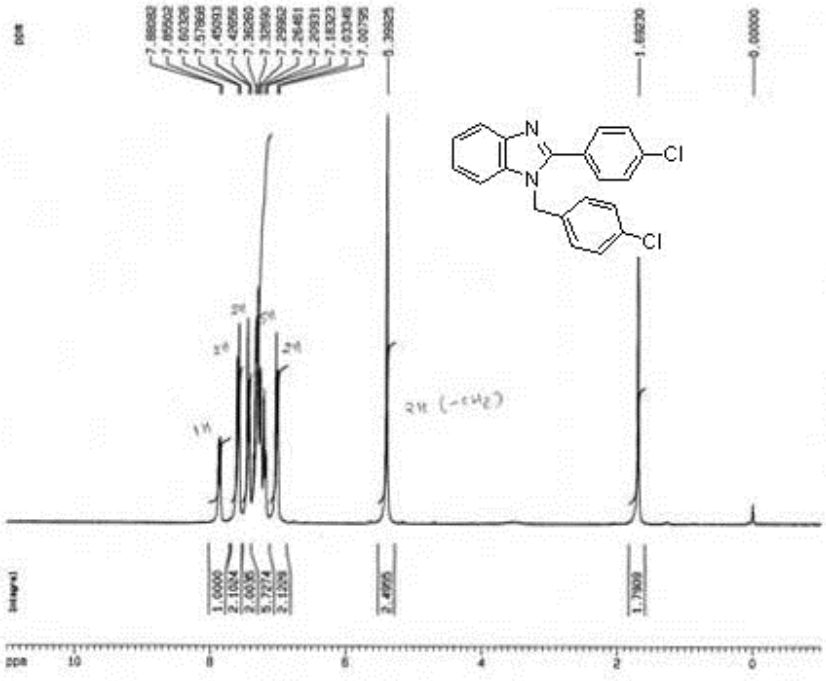
Entry 3, Table 3, ^{1}H NMR



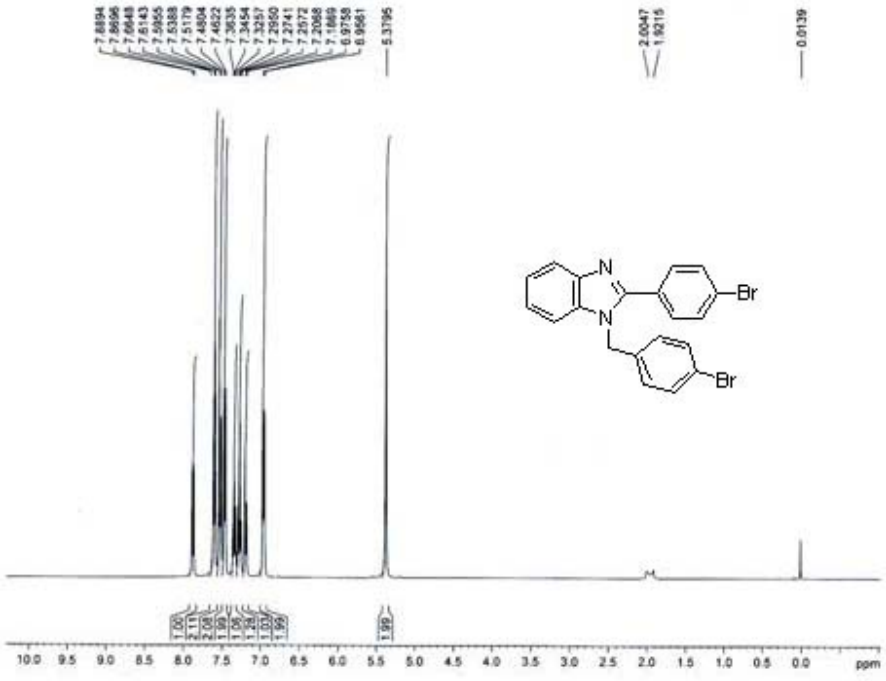
Entry 4, Table 4, ^{1}H NMR



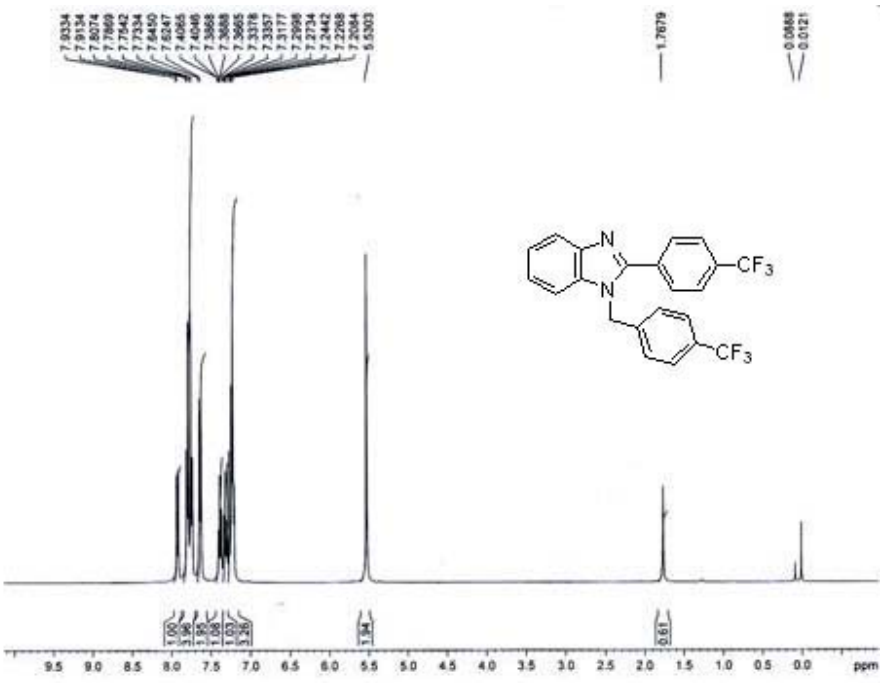
Entry 5, Table 3, ^{1}H NMR



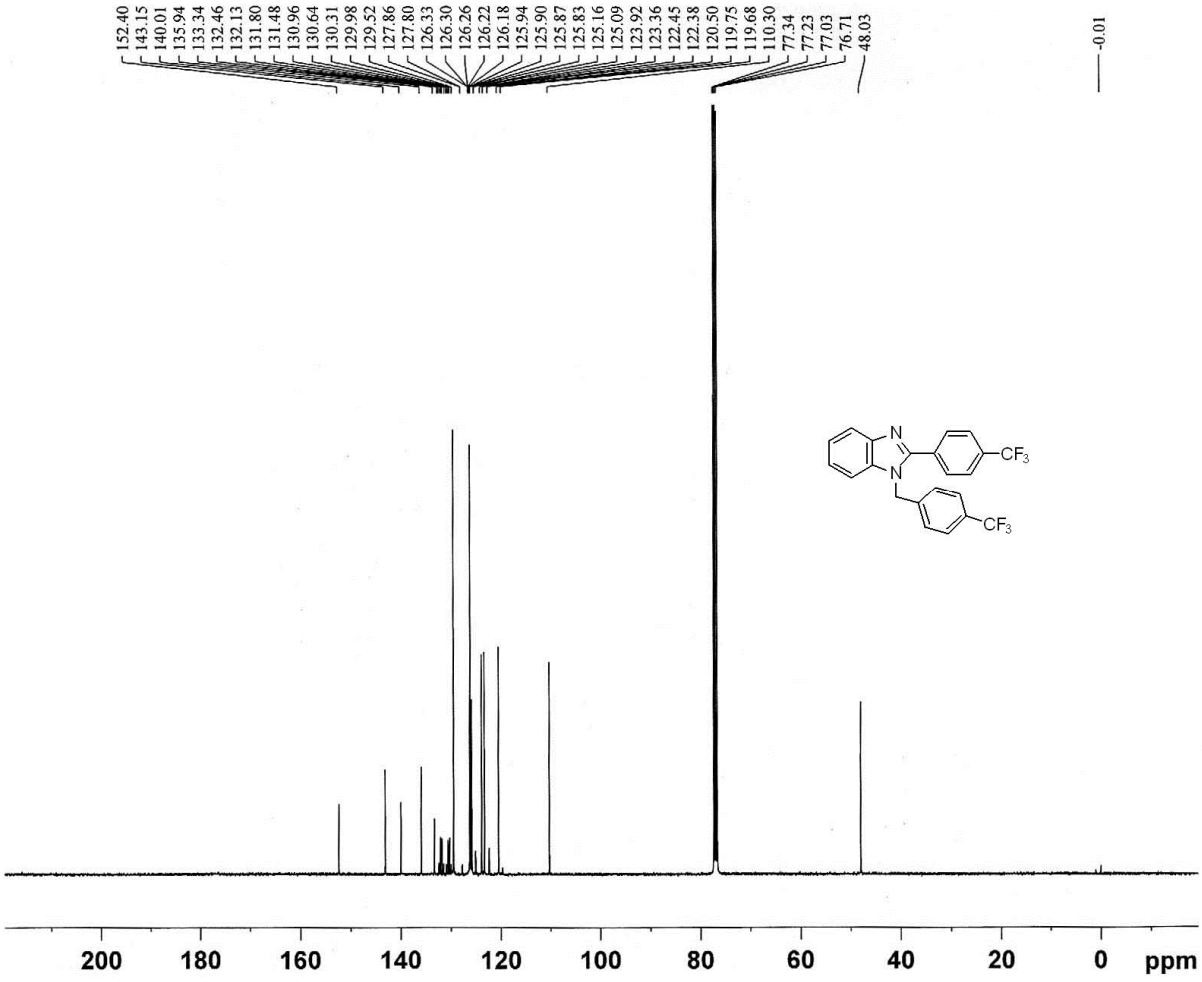
Entry 6, Table 3, ^{1}H NMR



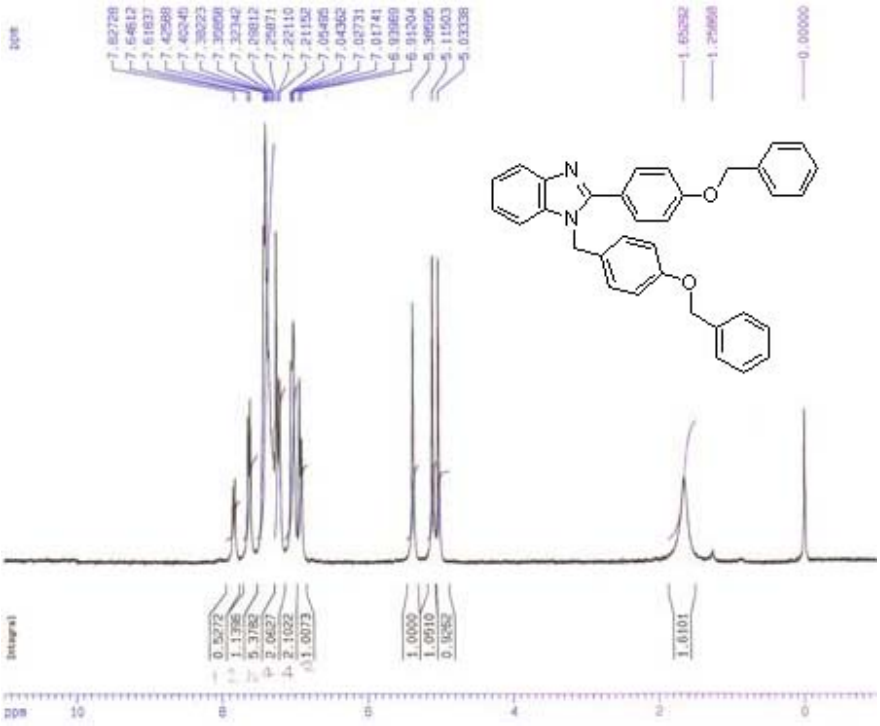
Entry 7, Table 3, ^{1}H NMR



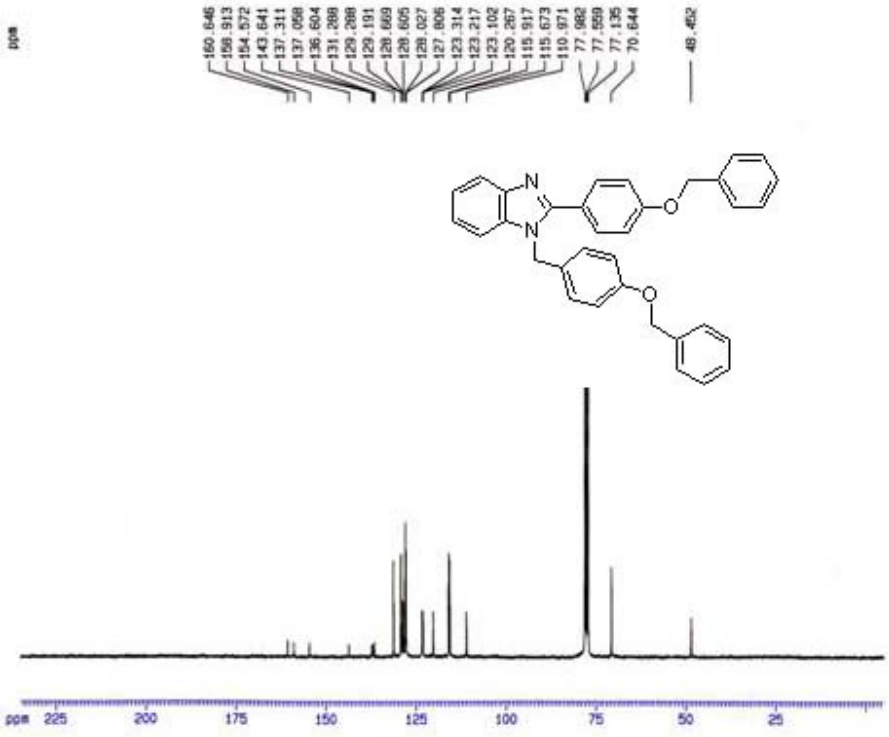
Entry 7, Table 3, ^{13}C NMR



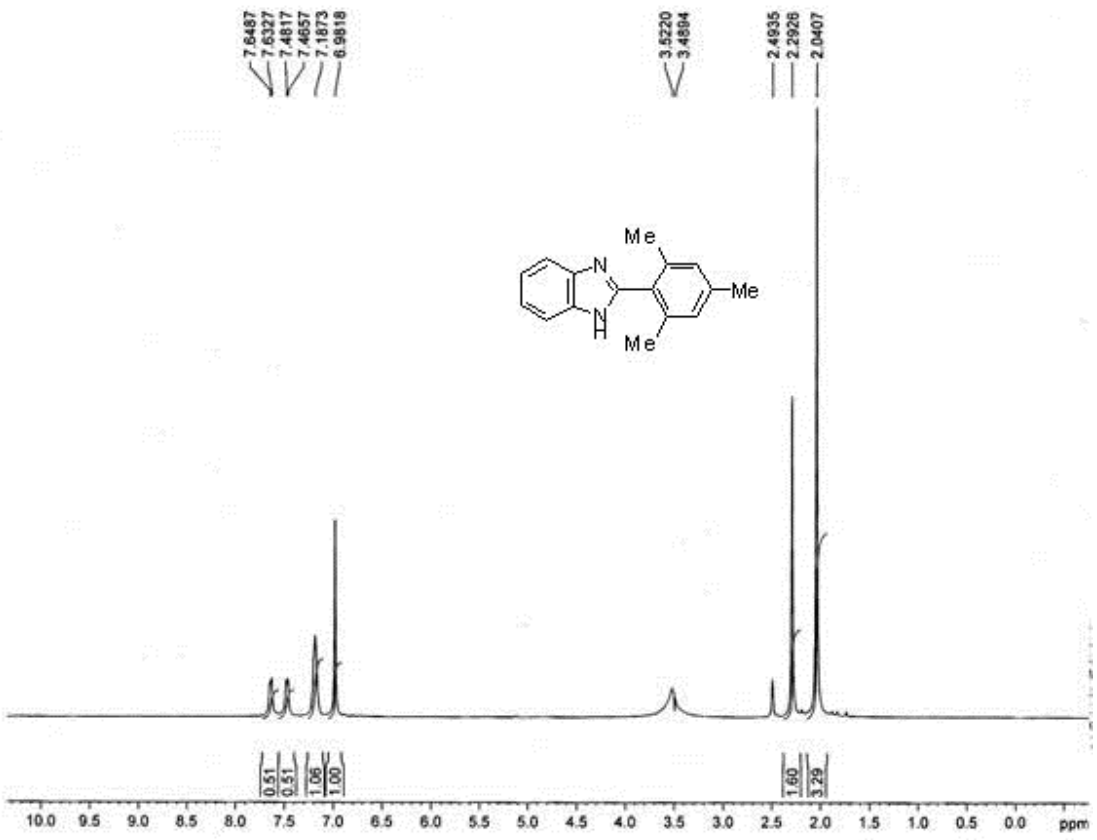
Entry 8, Table 3, ^{1}H NMR



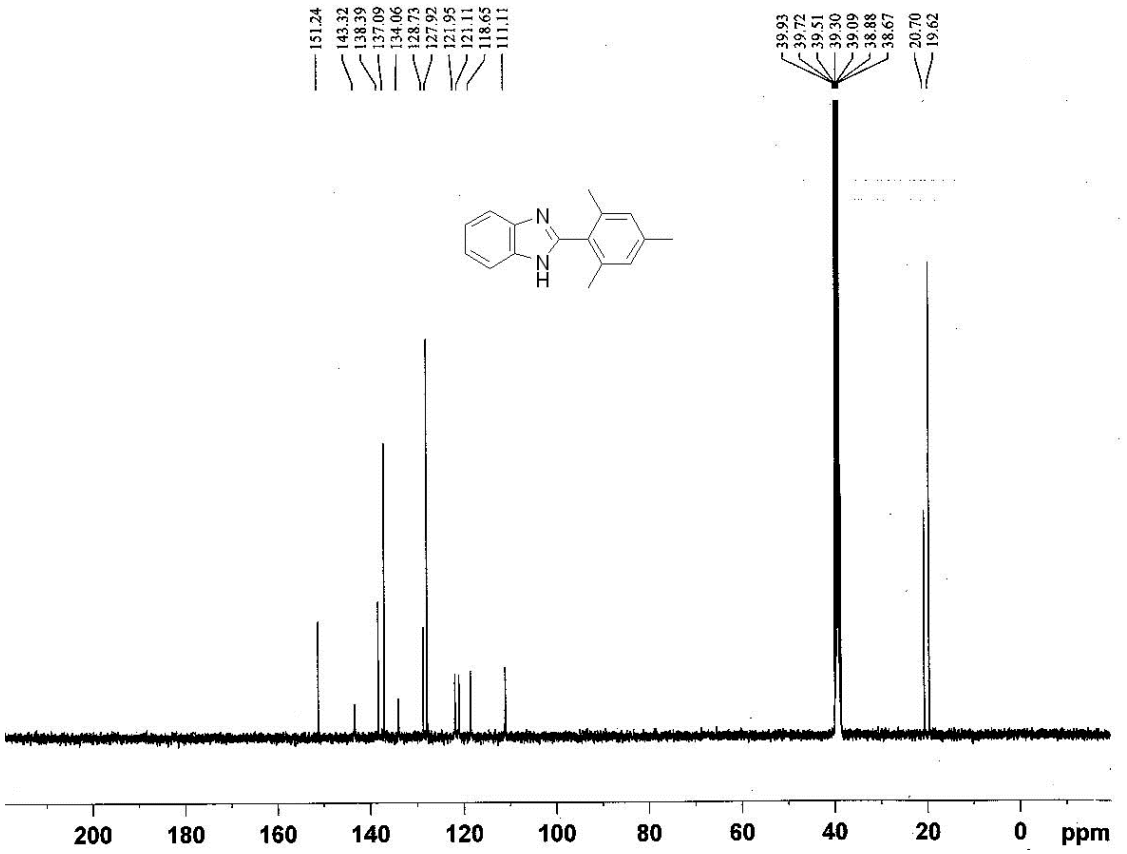
Entry 8, Table 3, ^{13}C NMR



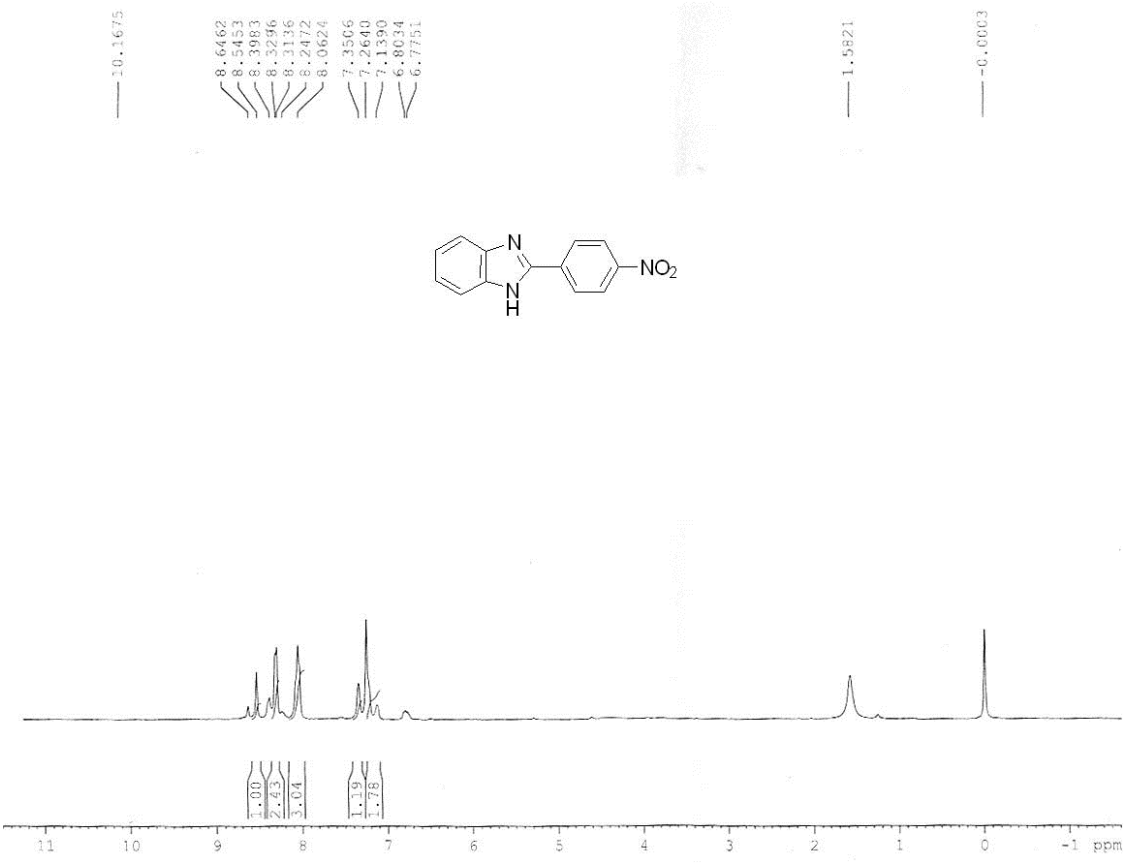
Entry 9, Table 3, ^{1}H NMR



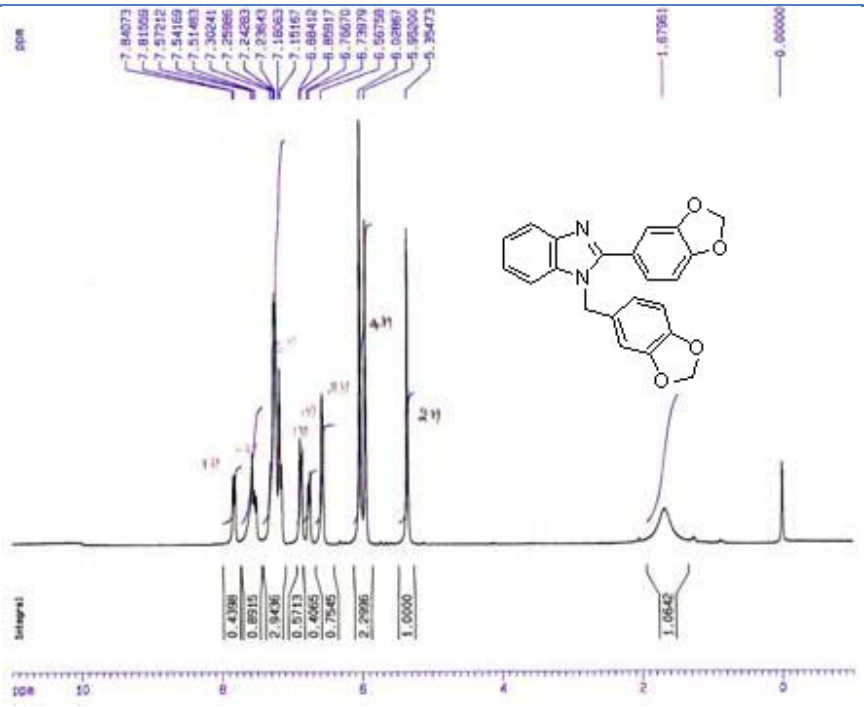
Entry 9, Table 3, ^{13}C NMR



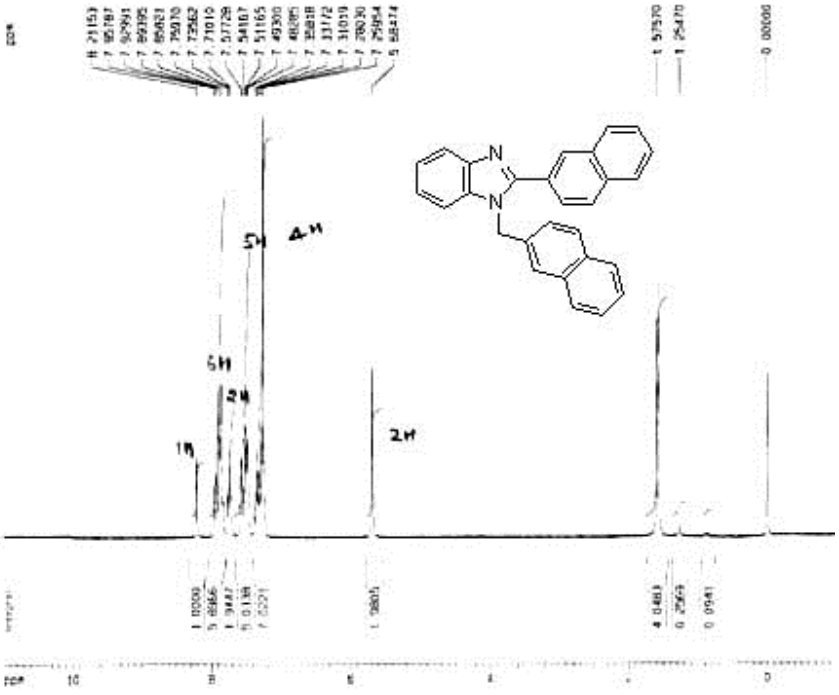
Entry 10, Table 3, ^{1}H NMR



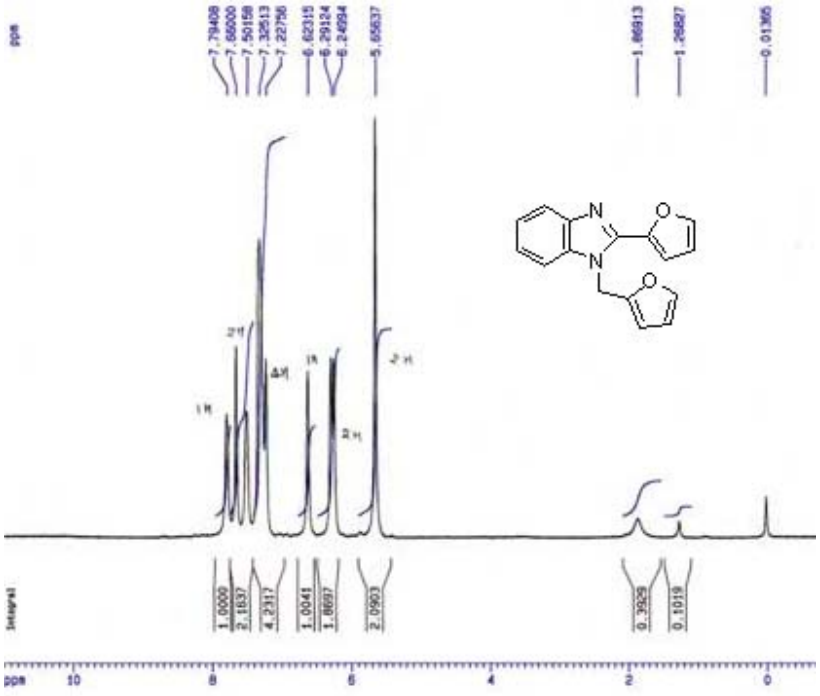
Entry 11, Table 3, ^{1}H NMR



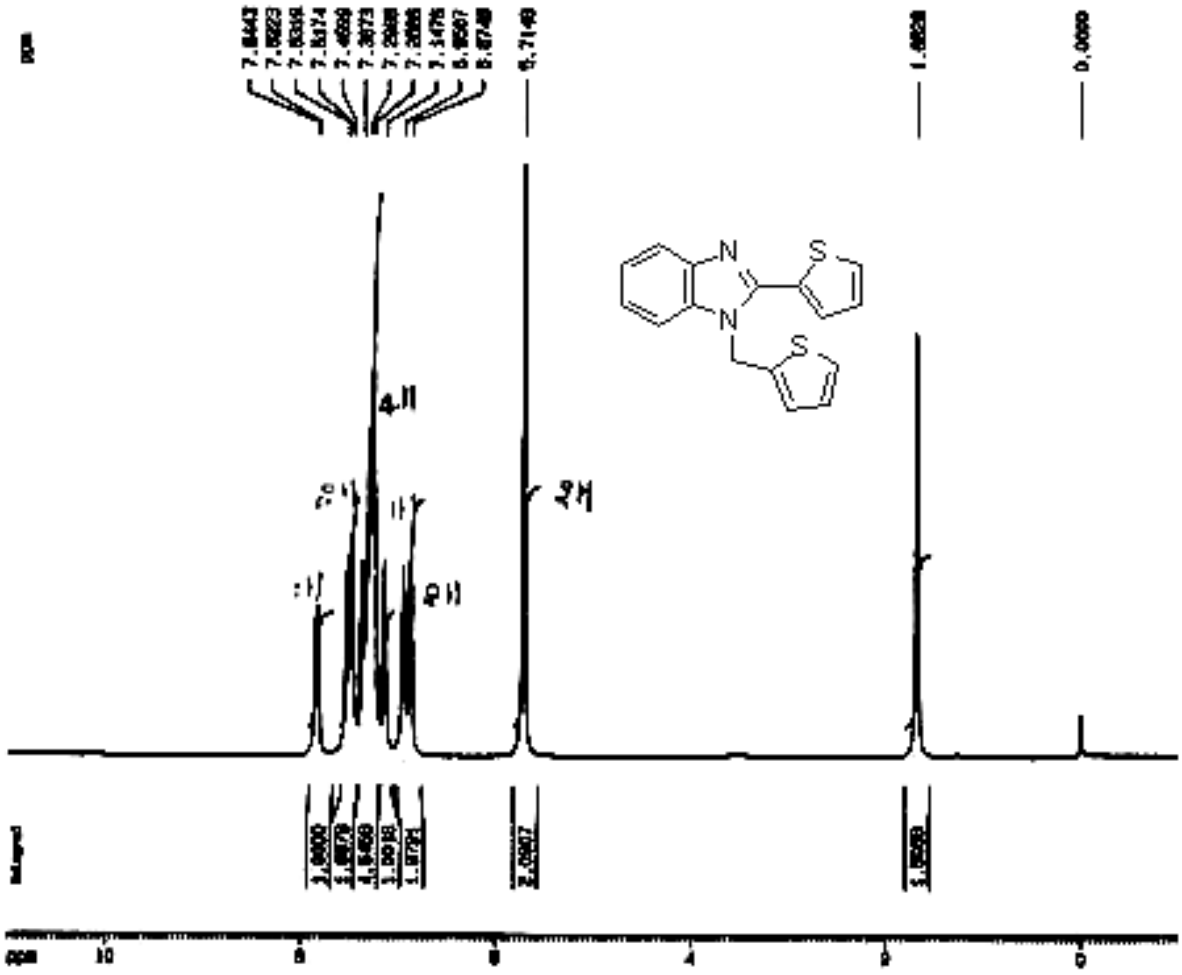
Entry 12, Table 3, ^{1}H NMR



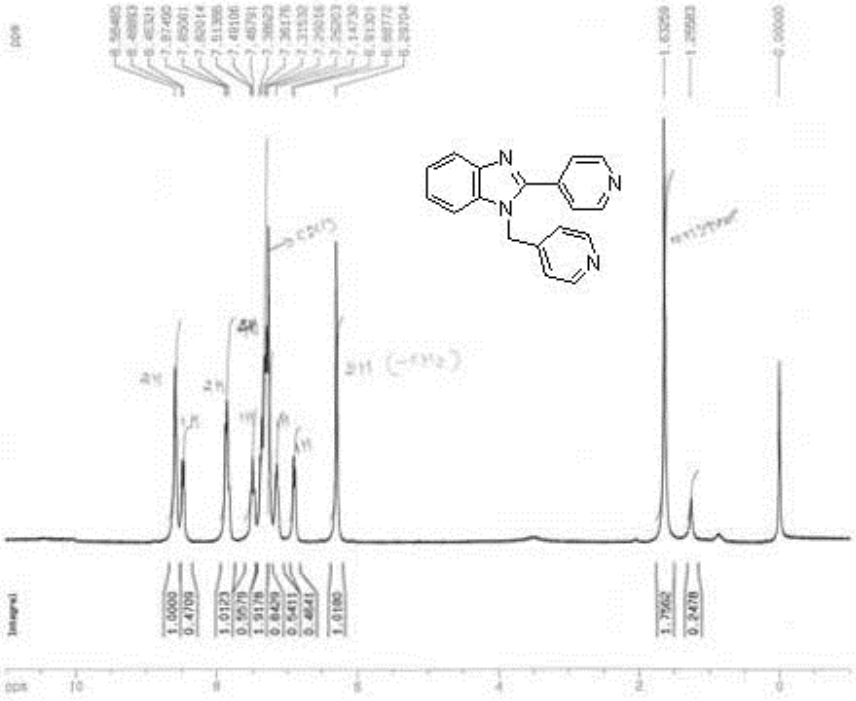
Entry 13, Table 3, ^{1}H NMR



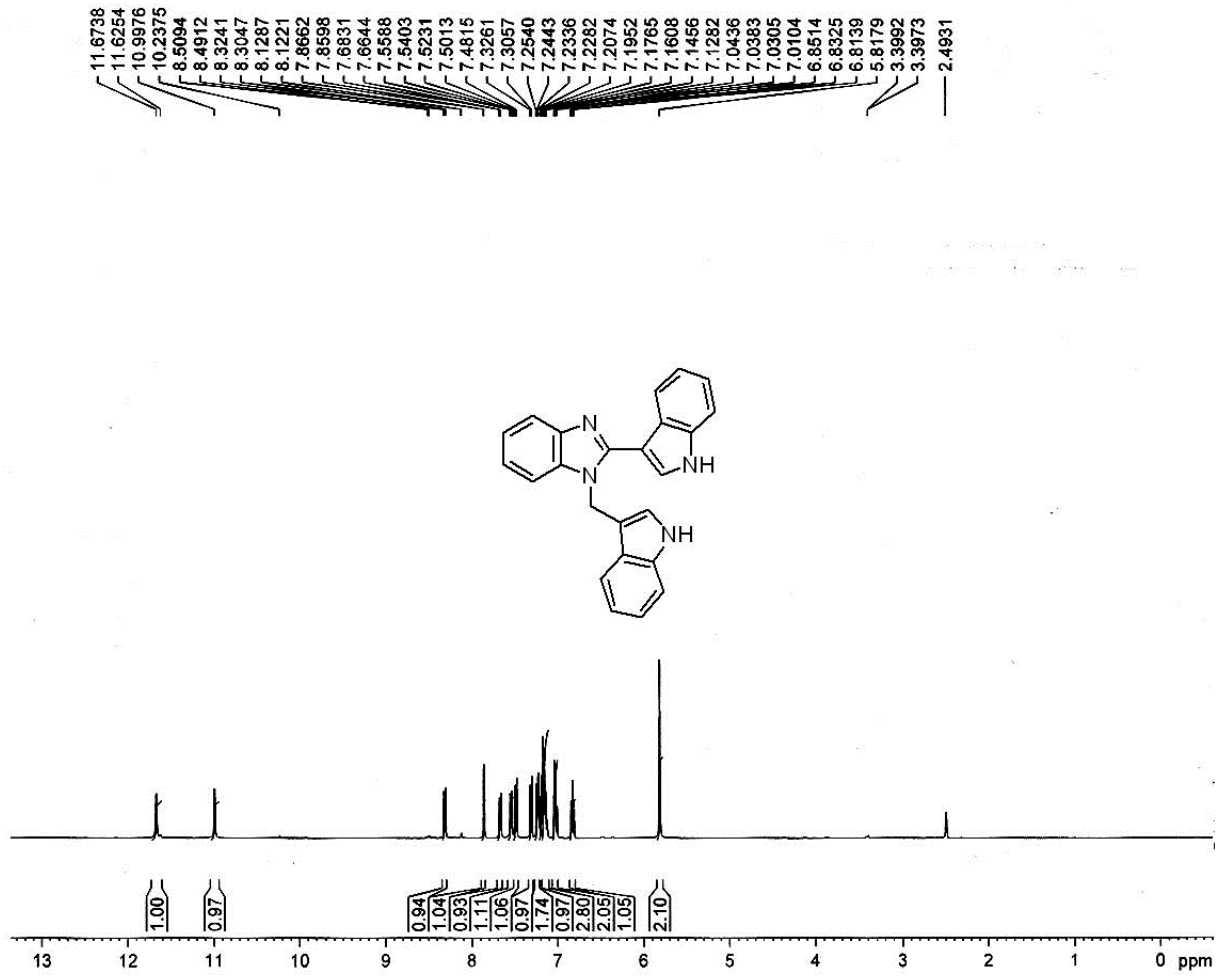
Entry 14, Table 3, ^{1}H NMR



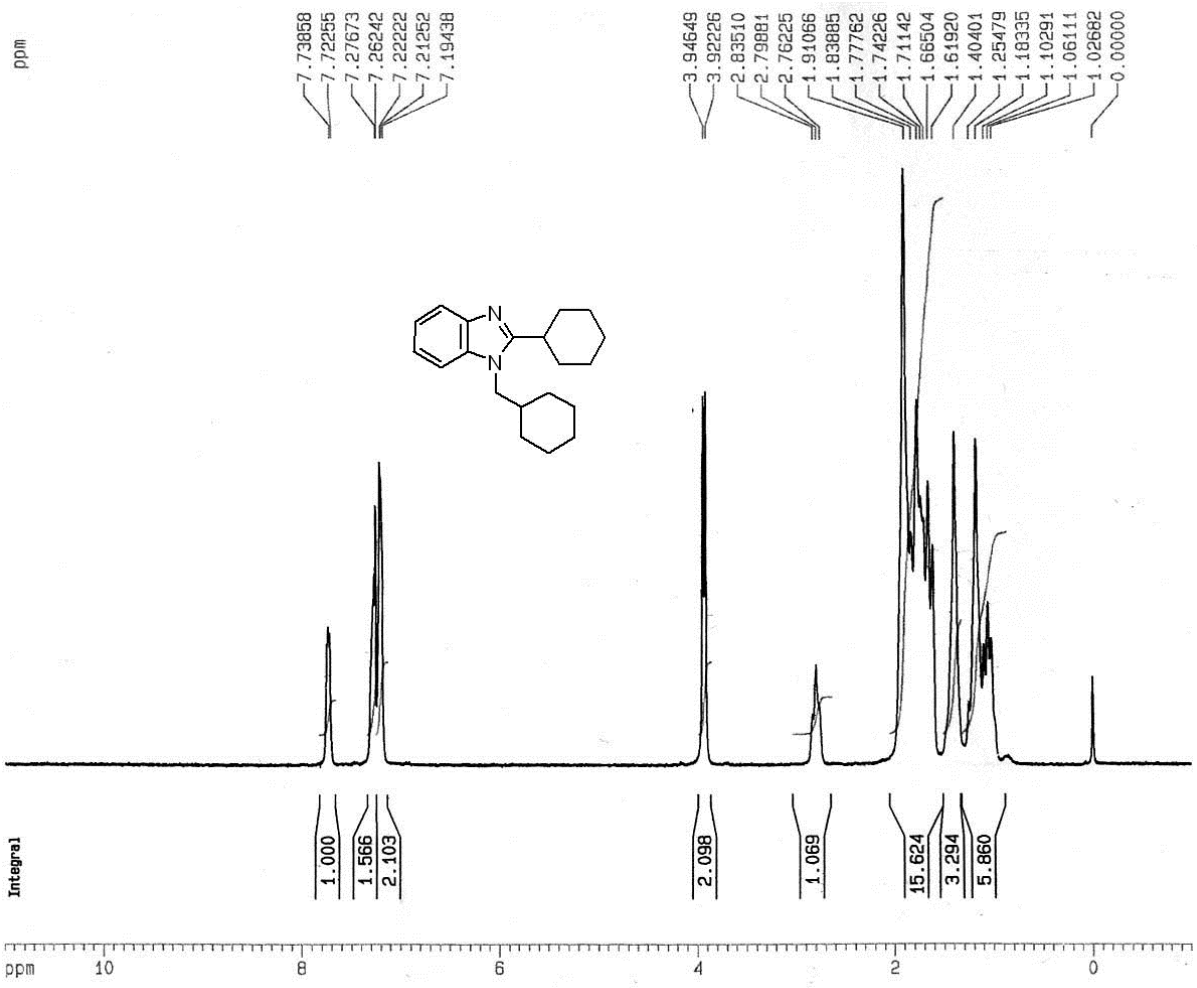
Entry 15, Table 3, ^{1}H NMR



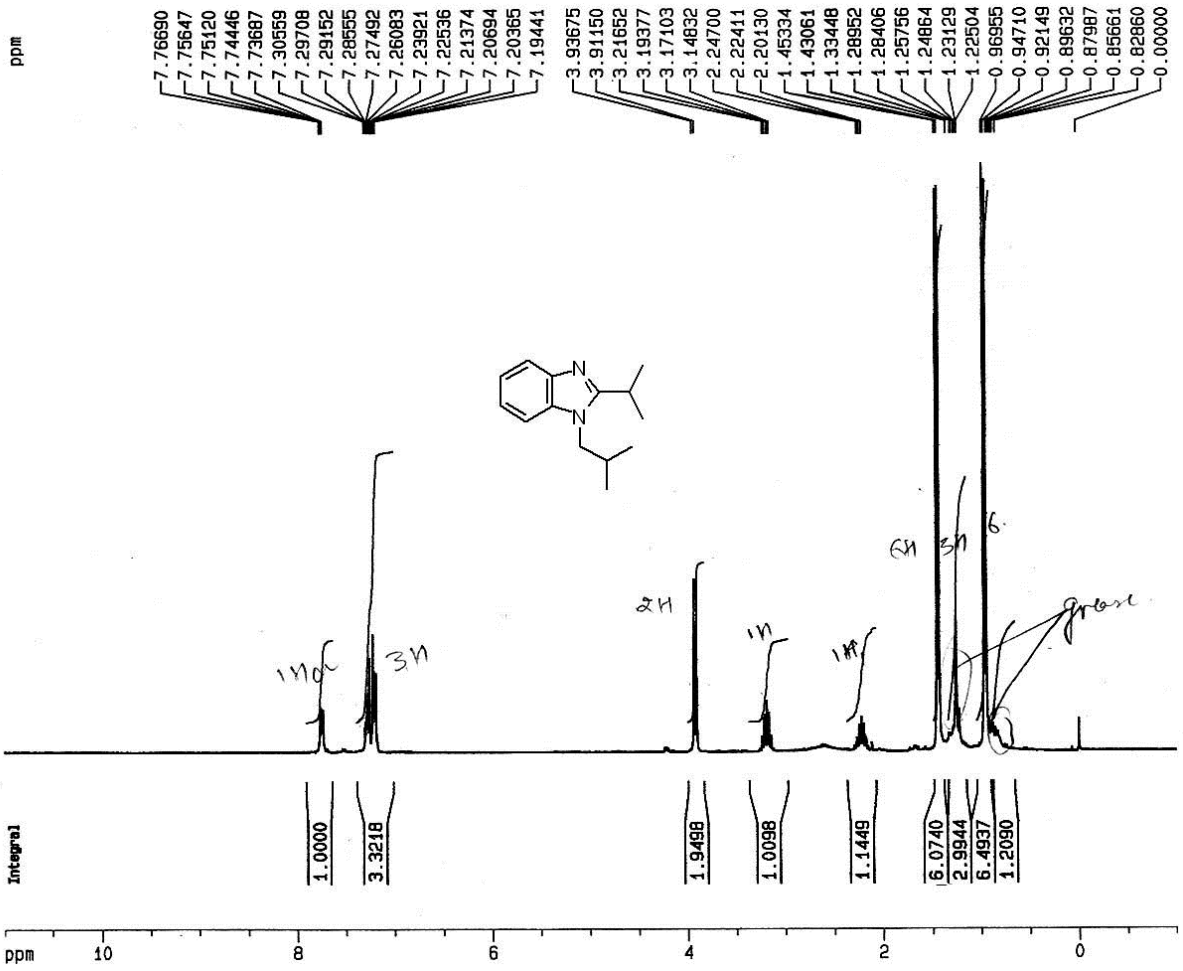
Entry 16, Table 3, ^{1}H NMR



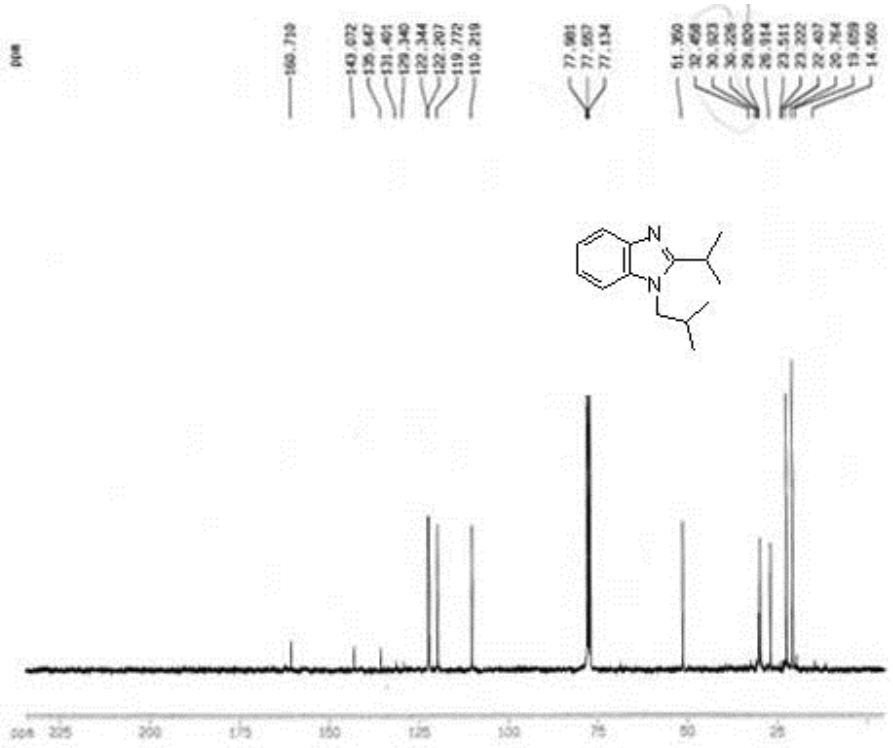
Entry 17, Table 3, ^{1}H NMR



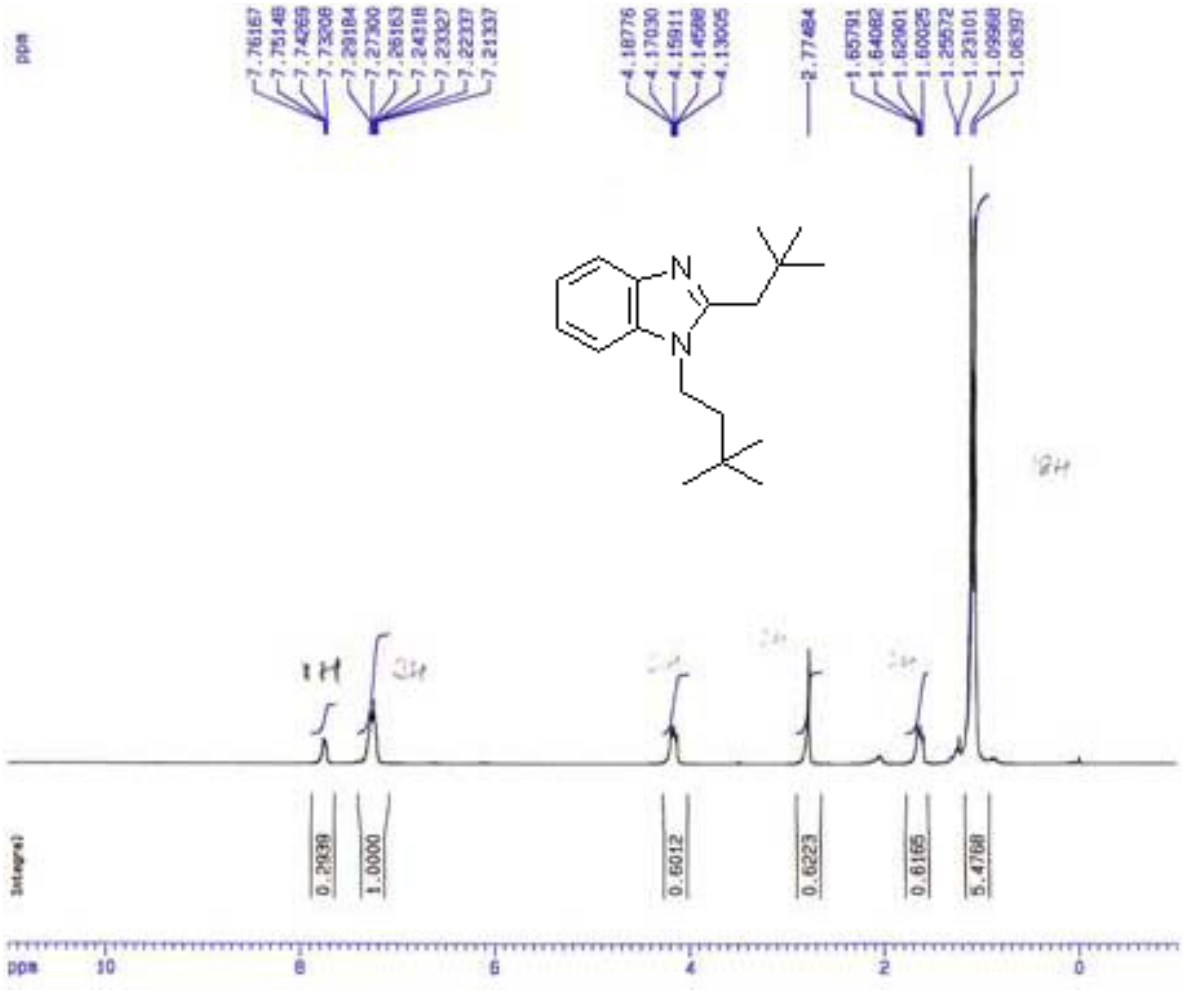
Entry 18, Table 3, ^{1}H NMR



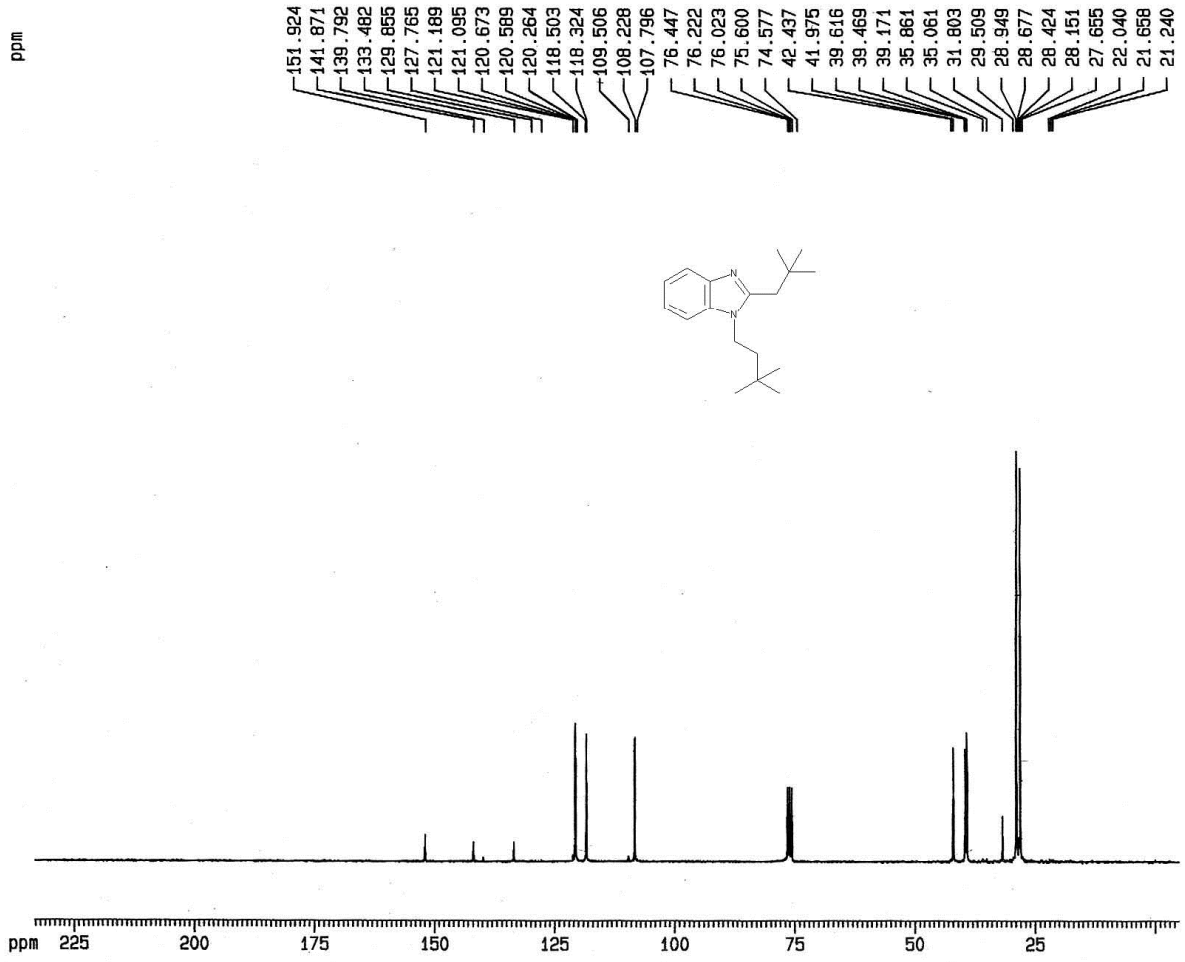
Entry 18, Table 3, ^{13}C NMR



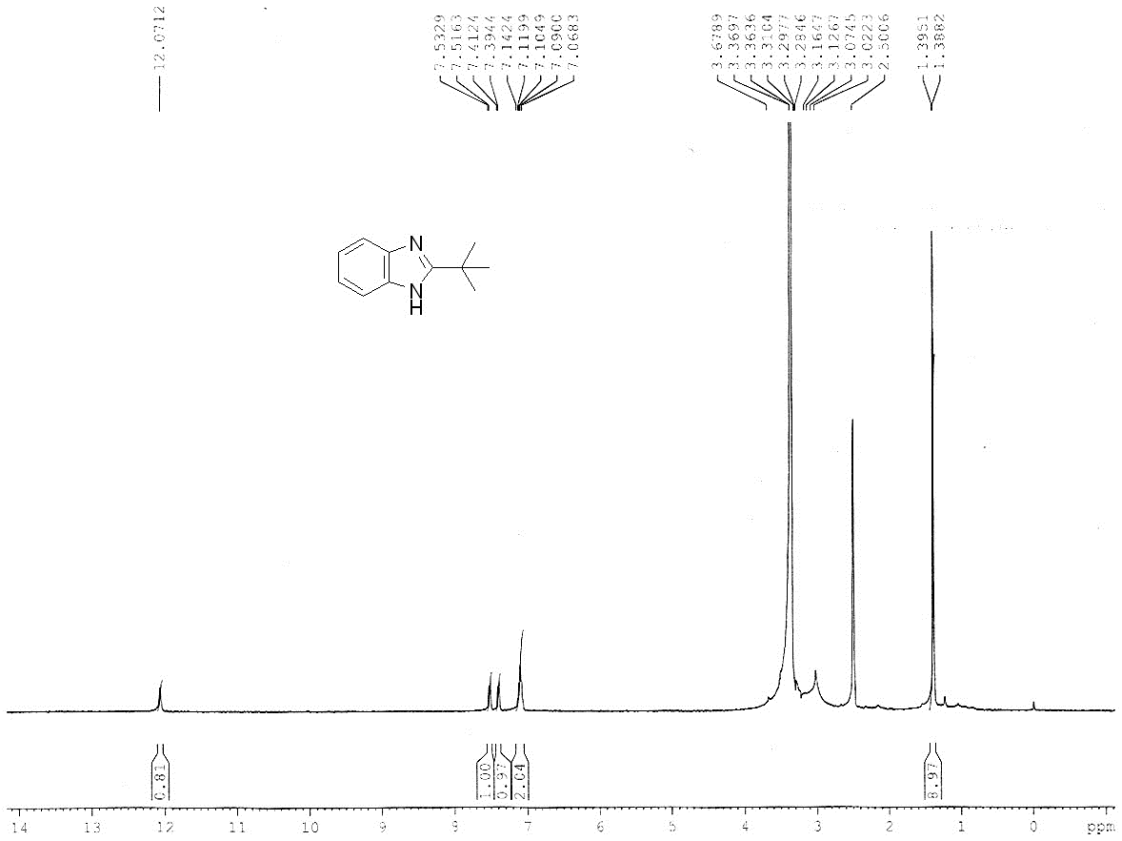
Entry 19, Table 3, ^{1}H NMR



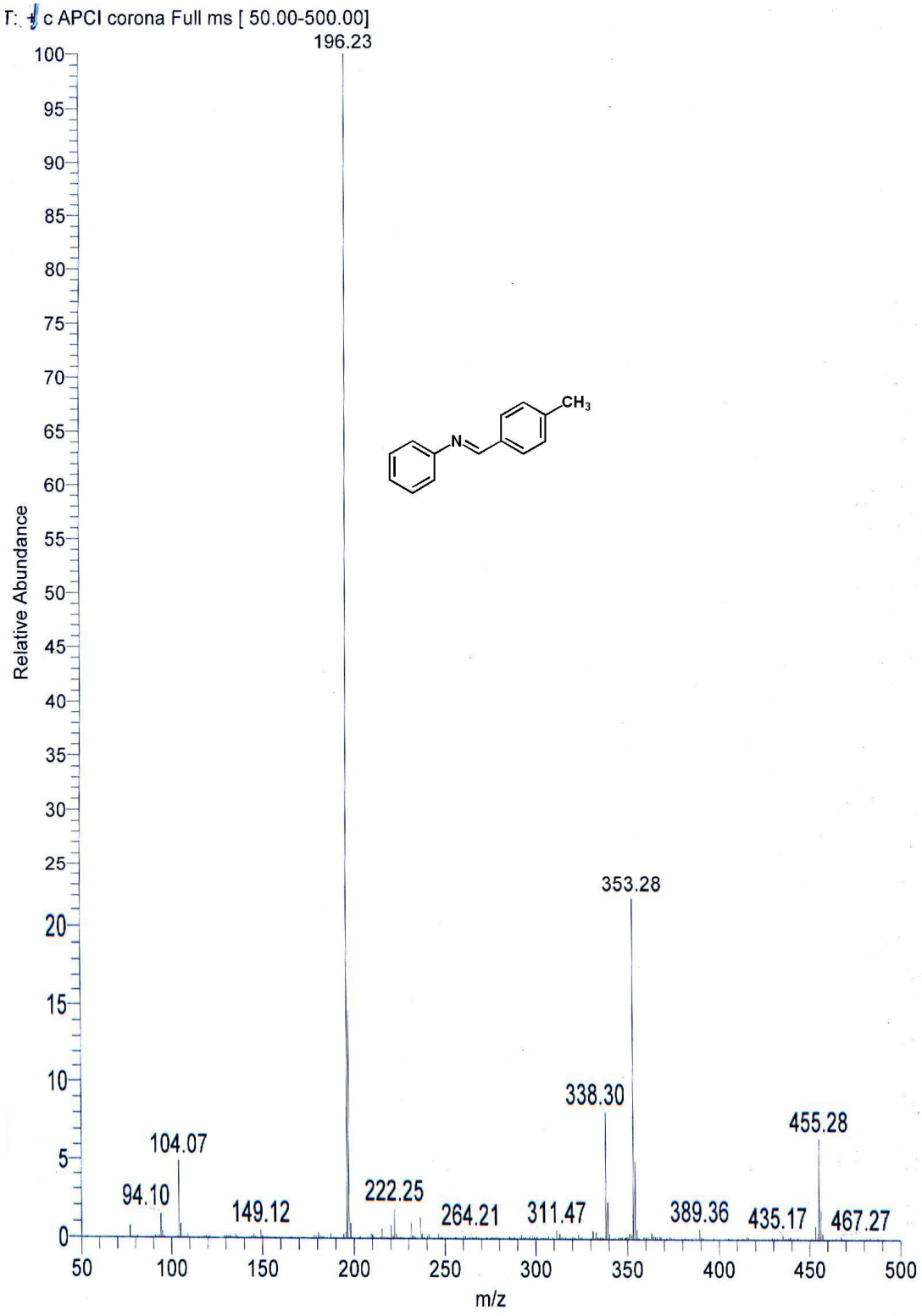
Entry 19, Table 3, ^{13}C NMR



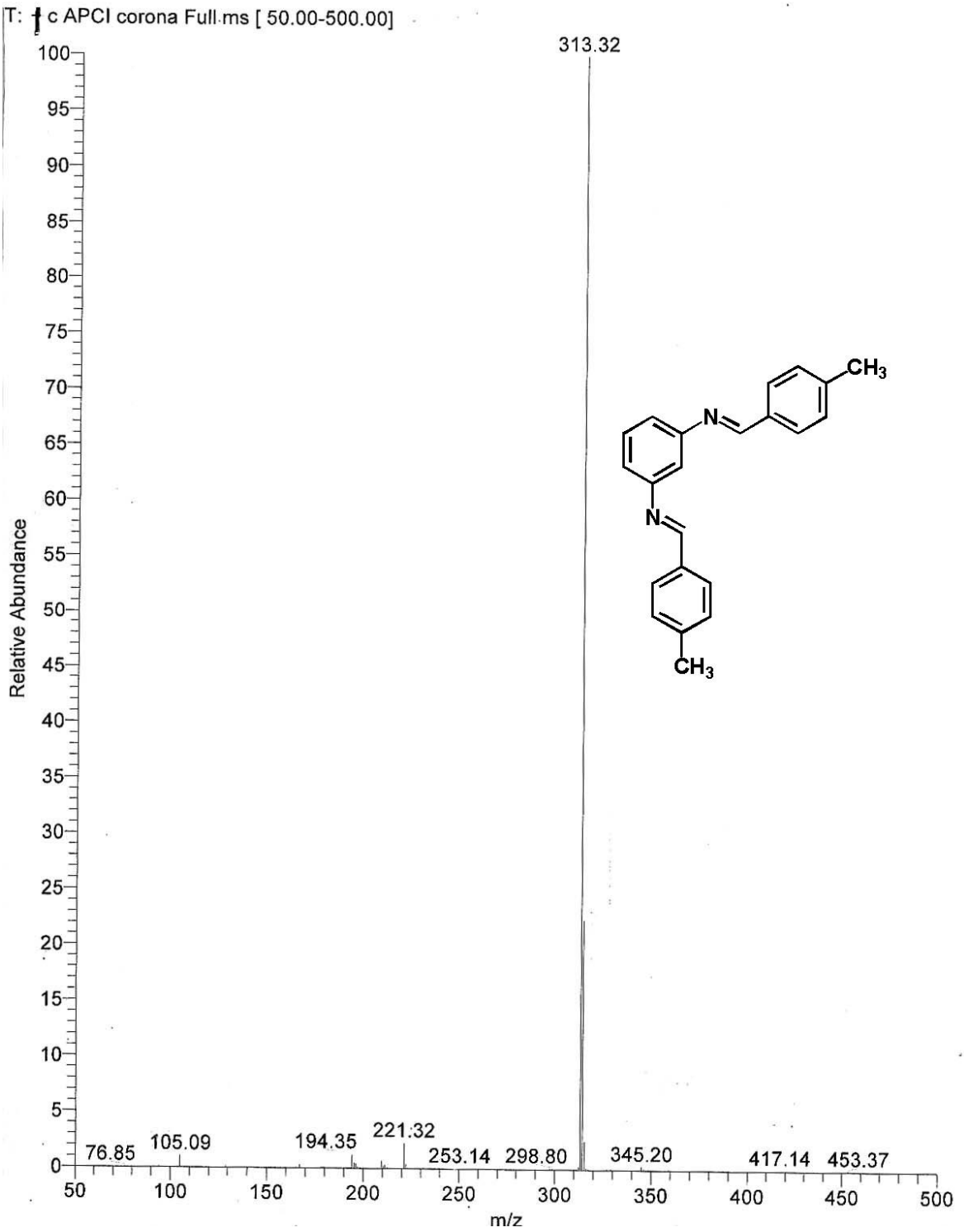
Entry 20, Table 3, ^{1}H NMR



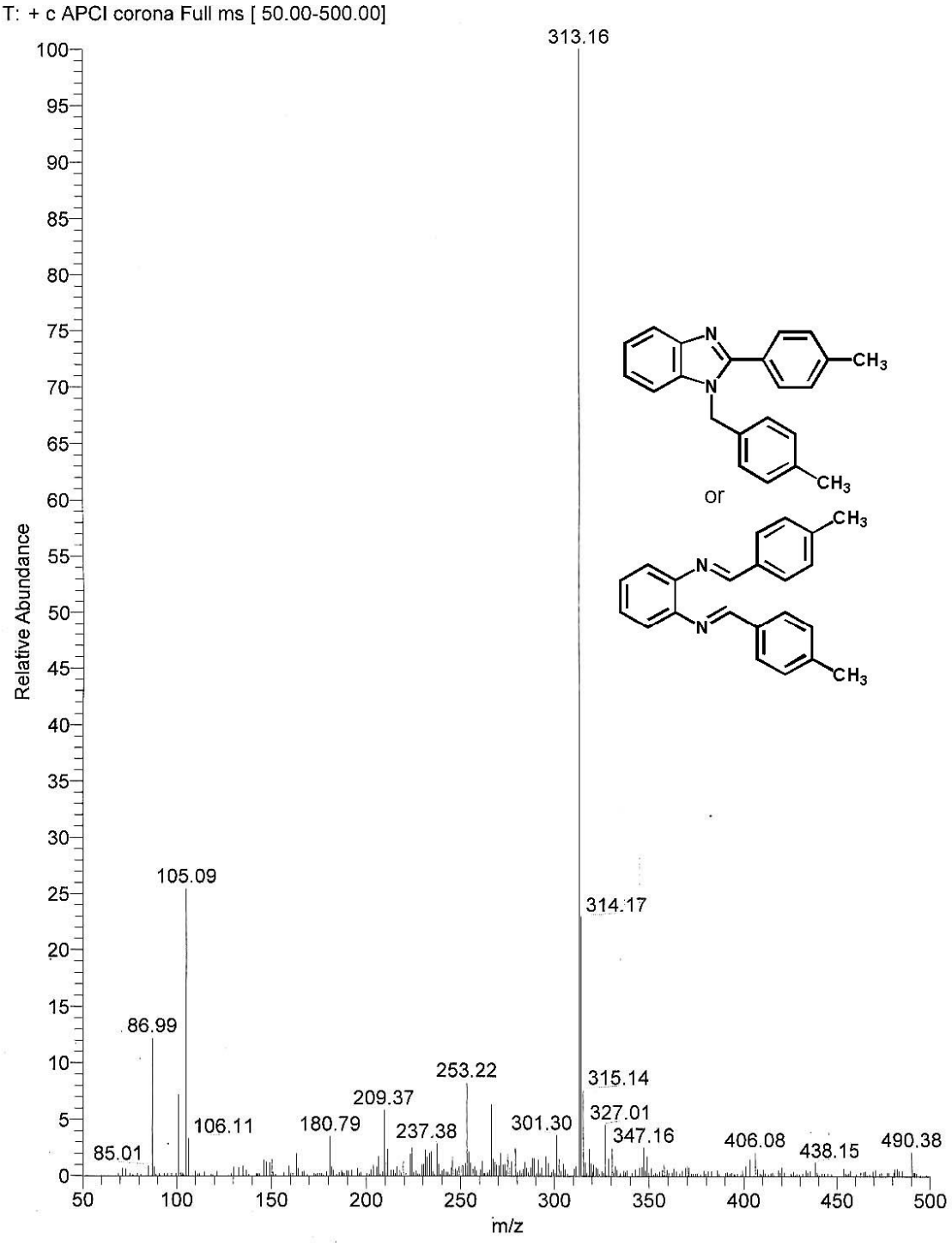
Mass spectra (APCI) of *N*-(4-methylbenzylidene) aniline (Reaction b/w aniline & 4-methylbenzaldehyde; 1:1)



Mass spectra (APCI) of bis(4-methylbenzylidene)benzene-1,3-diamine (Reaction b/w *m*-phenylelediamine & 4-methylbenzaldehyde; 1:2)



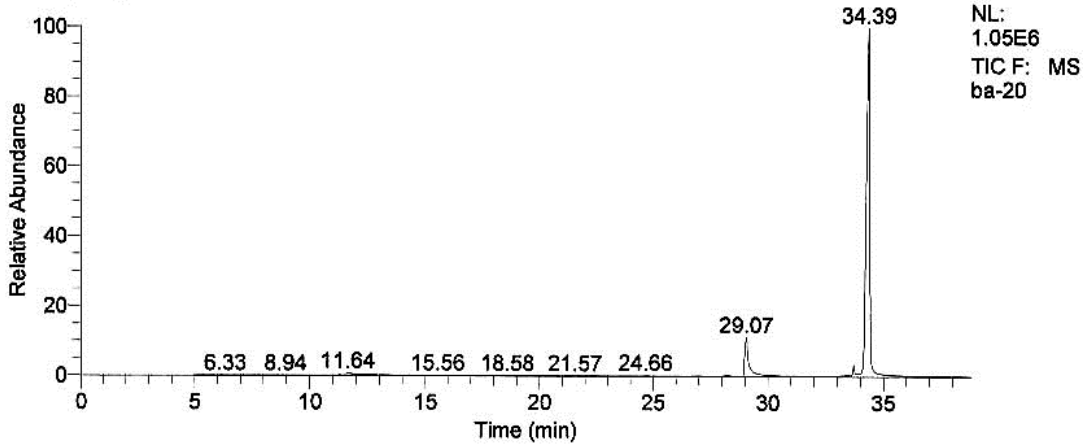
Mass spectra (APCI) of aliquot sample of reaction mixture (b/w *o*-phenylelediamine & 4-methylbenzaldehyde; 1:2 in EtOH)



GCMS spectra at different time interval for the reaction b/w *o*-phenylelediamine and 4-methylbenzalsehyde (1:2) in EtOH

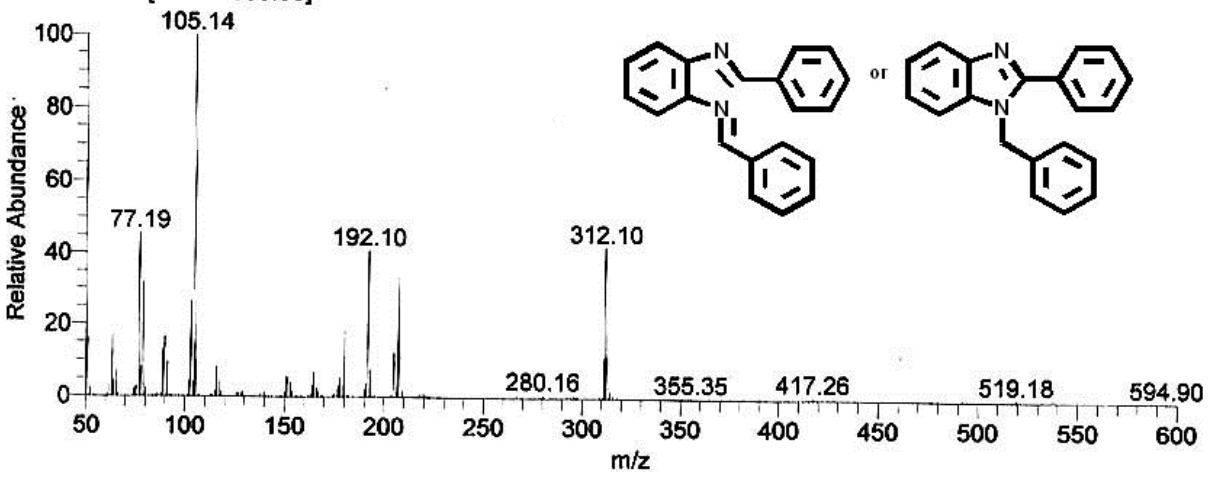
@ 10 min

Low Mass (m/z): 50.00
High Mass (m/z): 600.00
RT: 0.00 - 38.78 SM: 7G



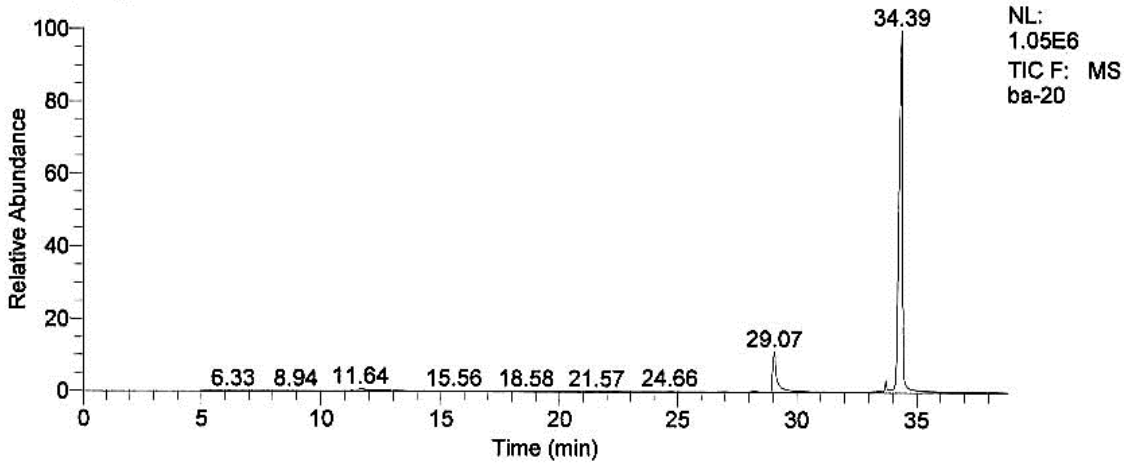
RT	Area %	Peak Area	Peak Height
29.06	9.00	726716	89972
33.72	1.40	112734	19834
34.38	89.60	7231889	837018

RT: 34.32 AV: 1 NL: 1.19E5
T: + c Full ms [50.00-600.00]



@ 20 min

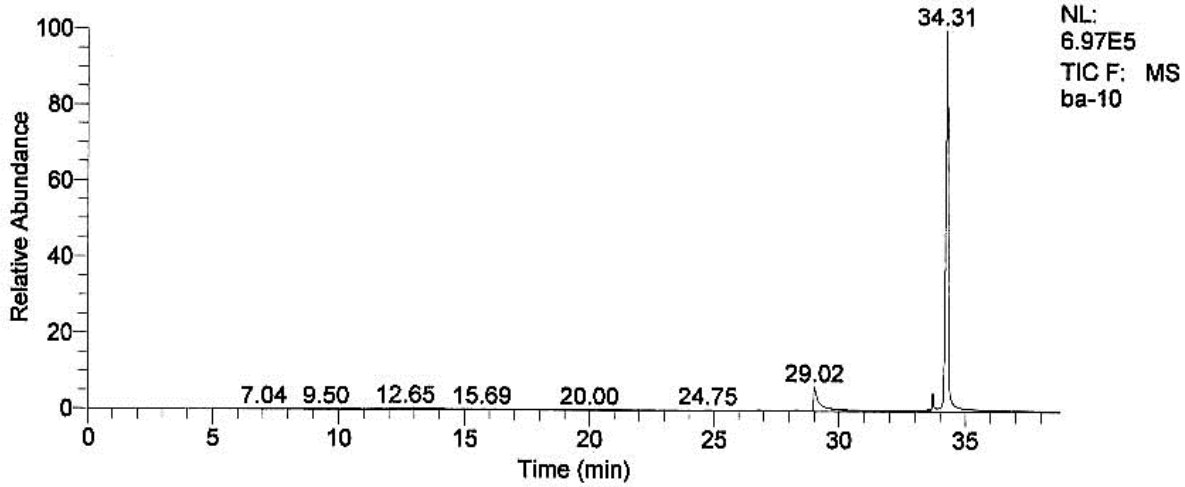
Low Mass (m/z): 50.00
High Mass (m/z): 600.00
RT: 0.00 - 38.78 SM: 7G



RT	Area %	Peak Area	Peak Height
29.06	9.00	726716	89972
33.72	1.40	112734	19834
34.38	89.60	7231889	837018

@ 30 min

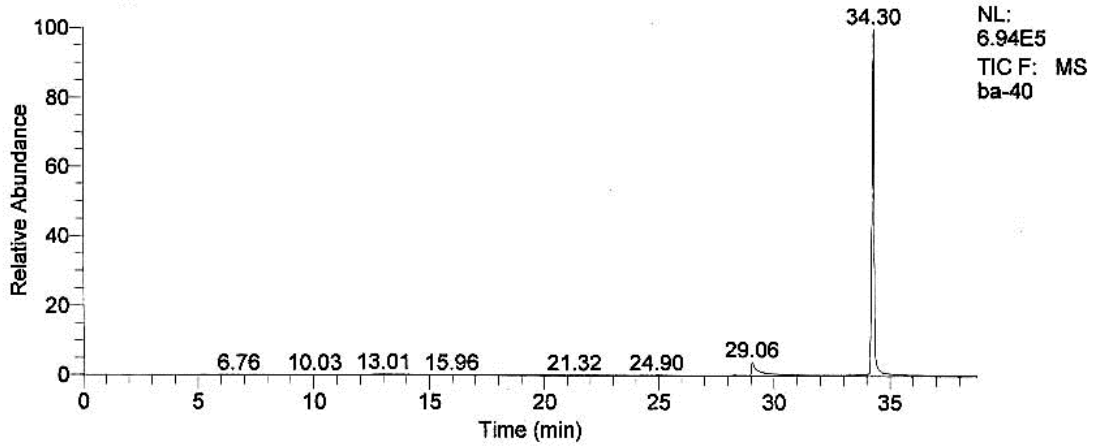
Low Mass (m/z): 50.00
High Mass (m/z): 600.00
RT: 0.00 - 38.77 SM: 7G



RT	Area %	Peak Area	Peak Height
12.25	0.96	40959	975
29.03	5.77	245528	31711
33.71	2.56	108953	19761
34.29	90.71	3860772	545683

@ 40 min

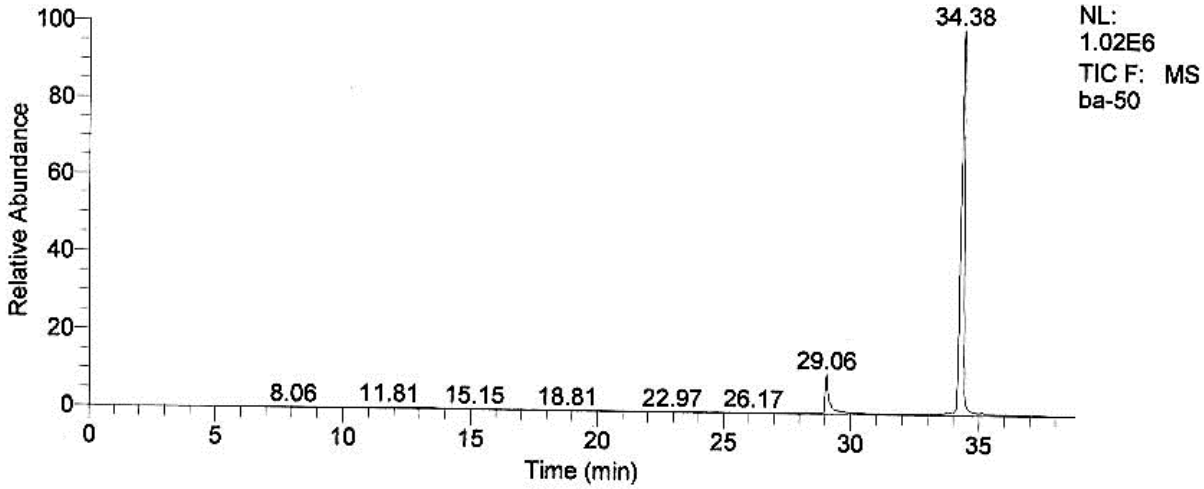
Low Mass (m/z): 50.00
High Mass (m/z): 600.00
RT: 0.00 - 38.76 SM: 7G



RT	Area %	Peak Area	Peak Height
12.85	0.28	11070	700
29.07	3.92	155226	19394
34.29	95.81	3798553	553140

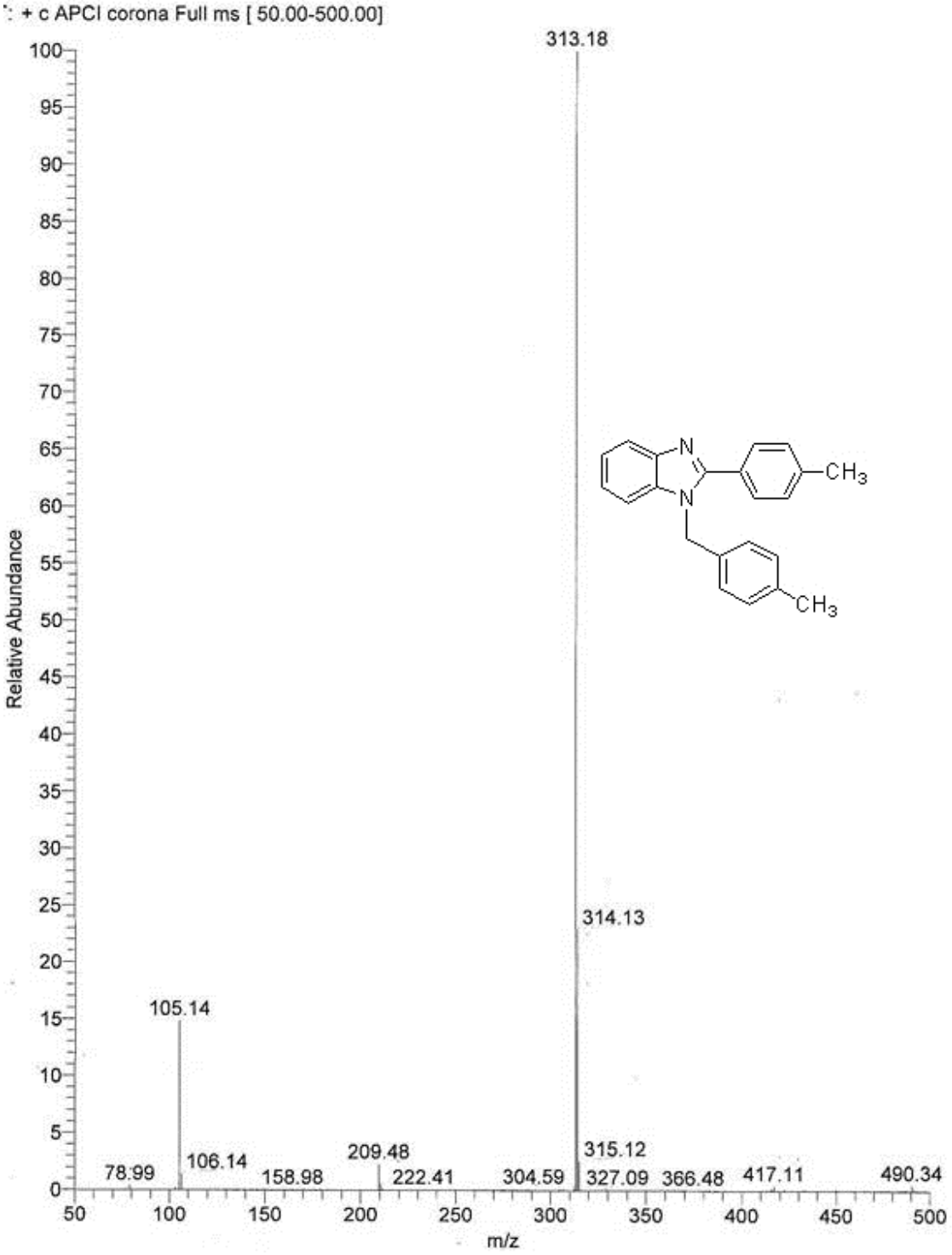
@ 50 min

Low Mass (m/z): 50.00
High Mass (m/z): 600.00
RT: 0.00 - 38.78 SM: 7G

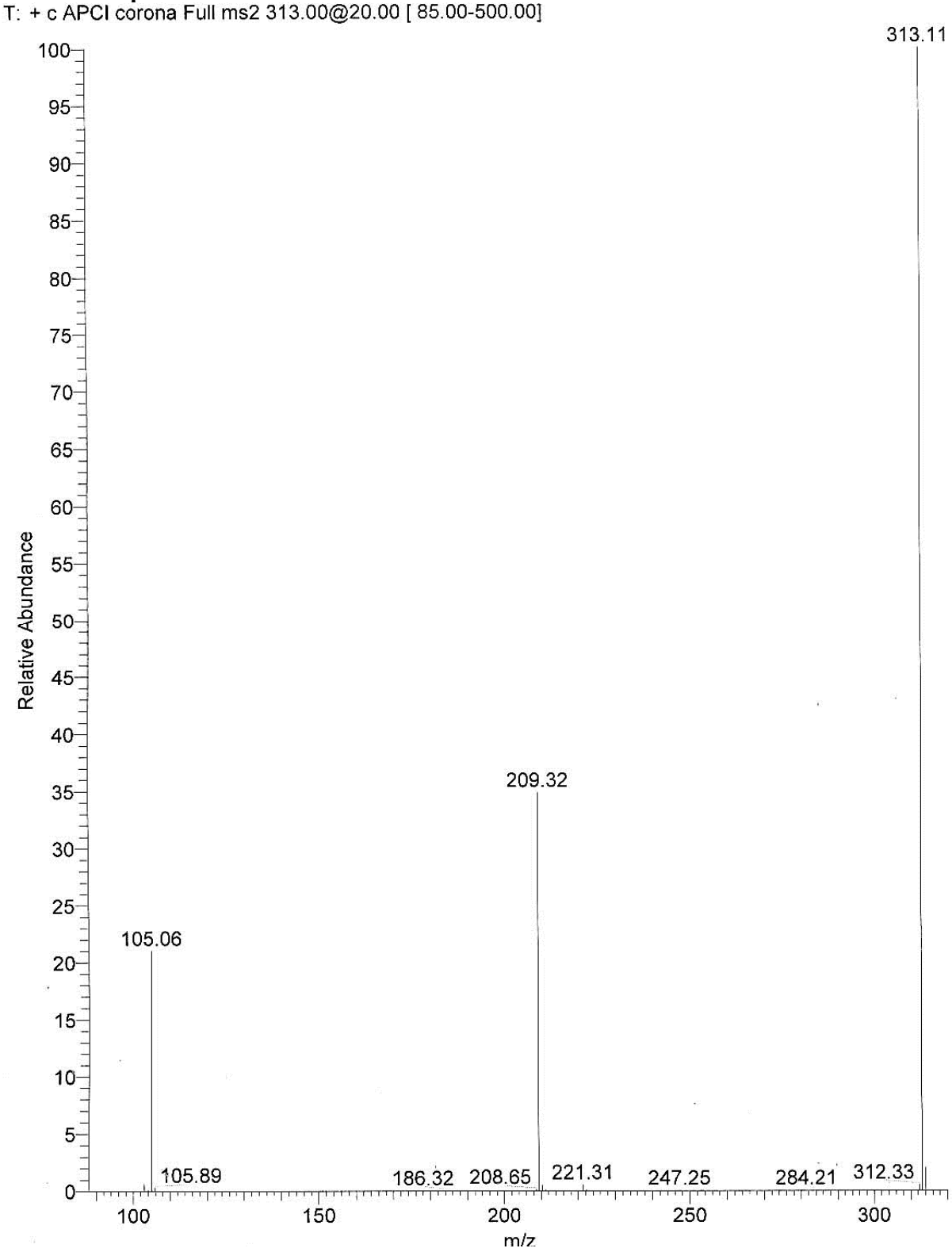


RT	Area %	Peak Area	Peak Height
11.79	0.37	26807	2005
29.05	7.86	573734	79080
34.36	91.77	6697956	812136

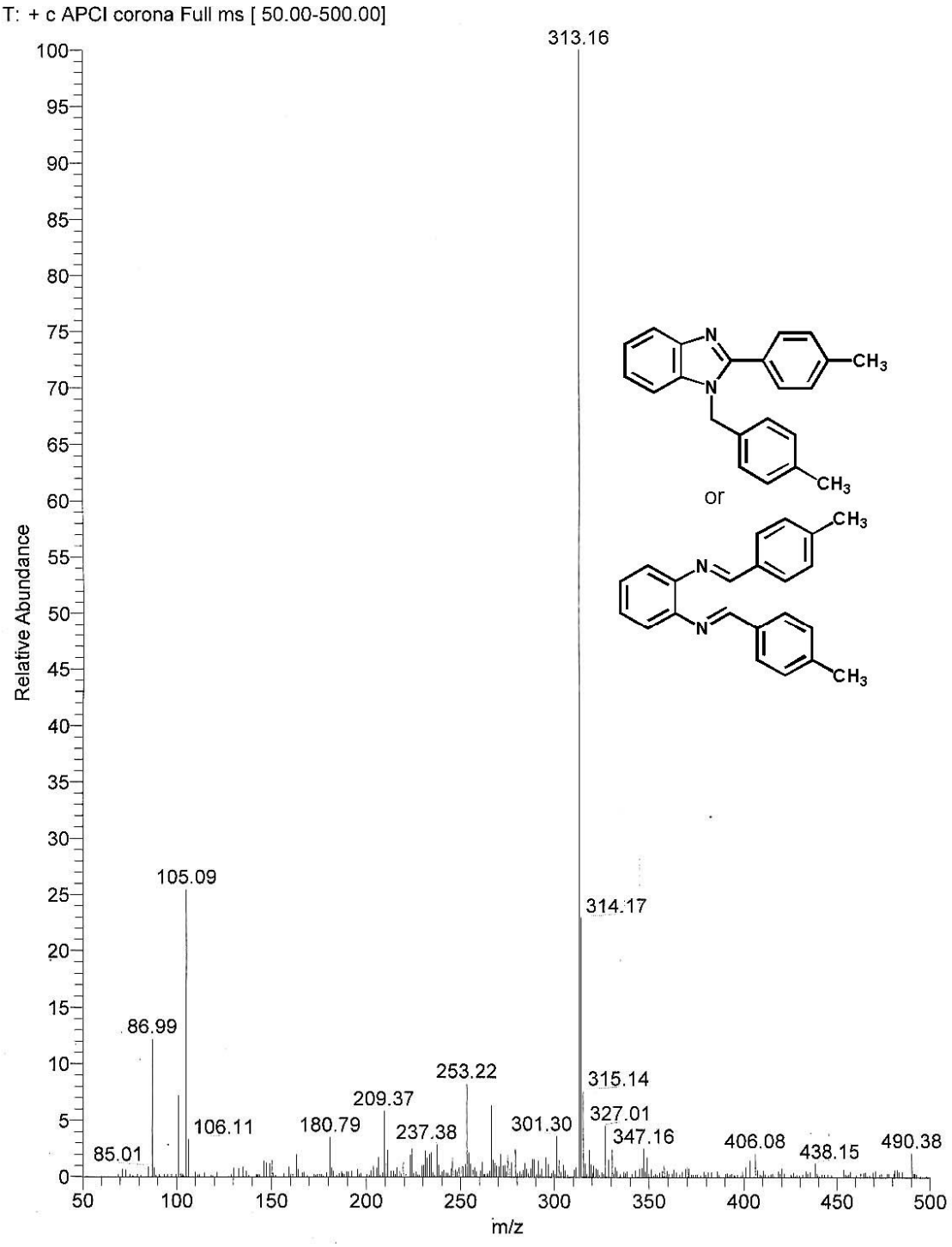
Mass spectra (APCI) of 1-(4-Methylphenylmethyl)-2-(4-methylphenyl)-1*H*-benzimidazole



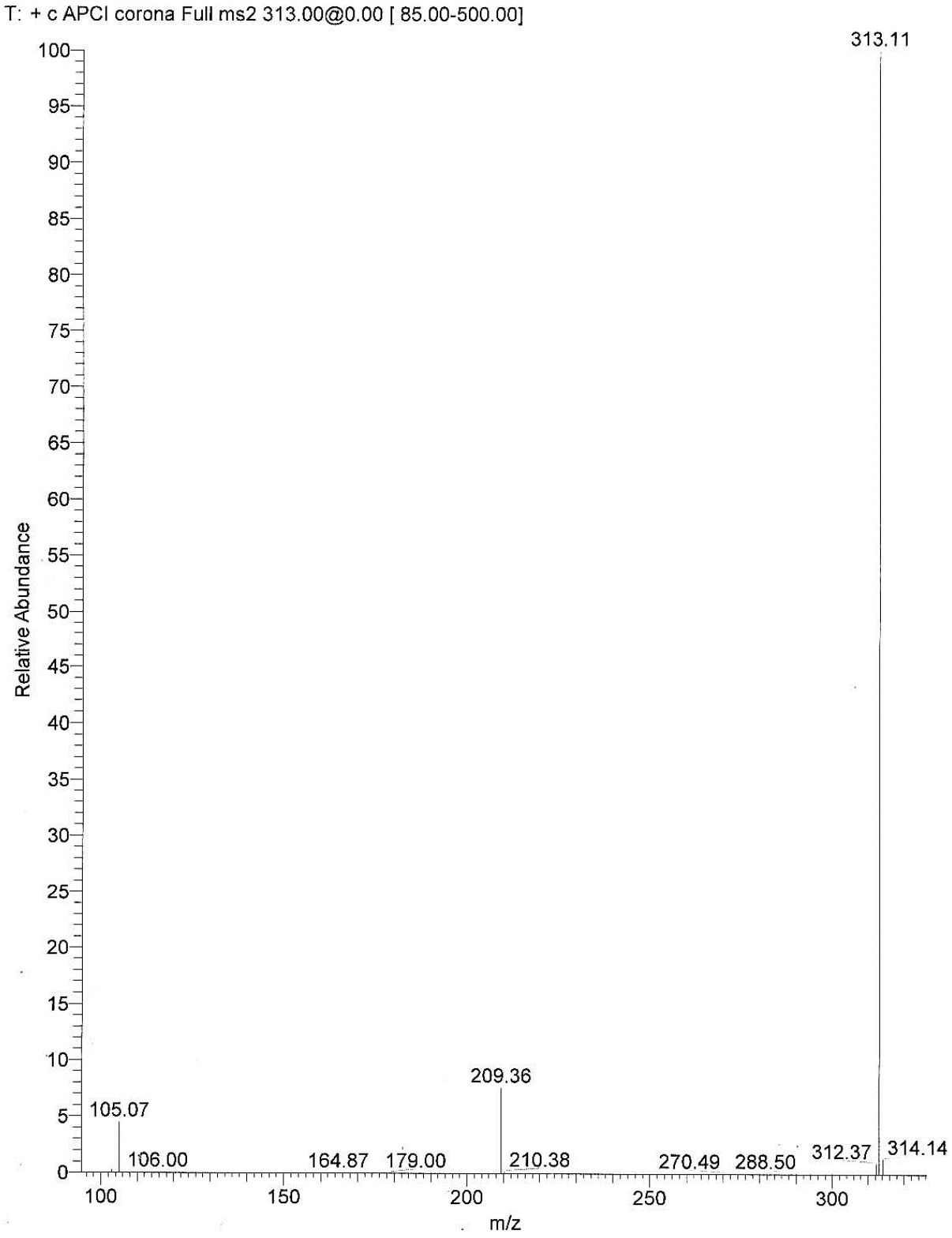
MS^2 of mass peak 313



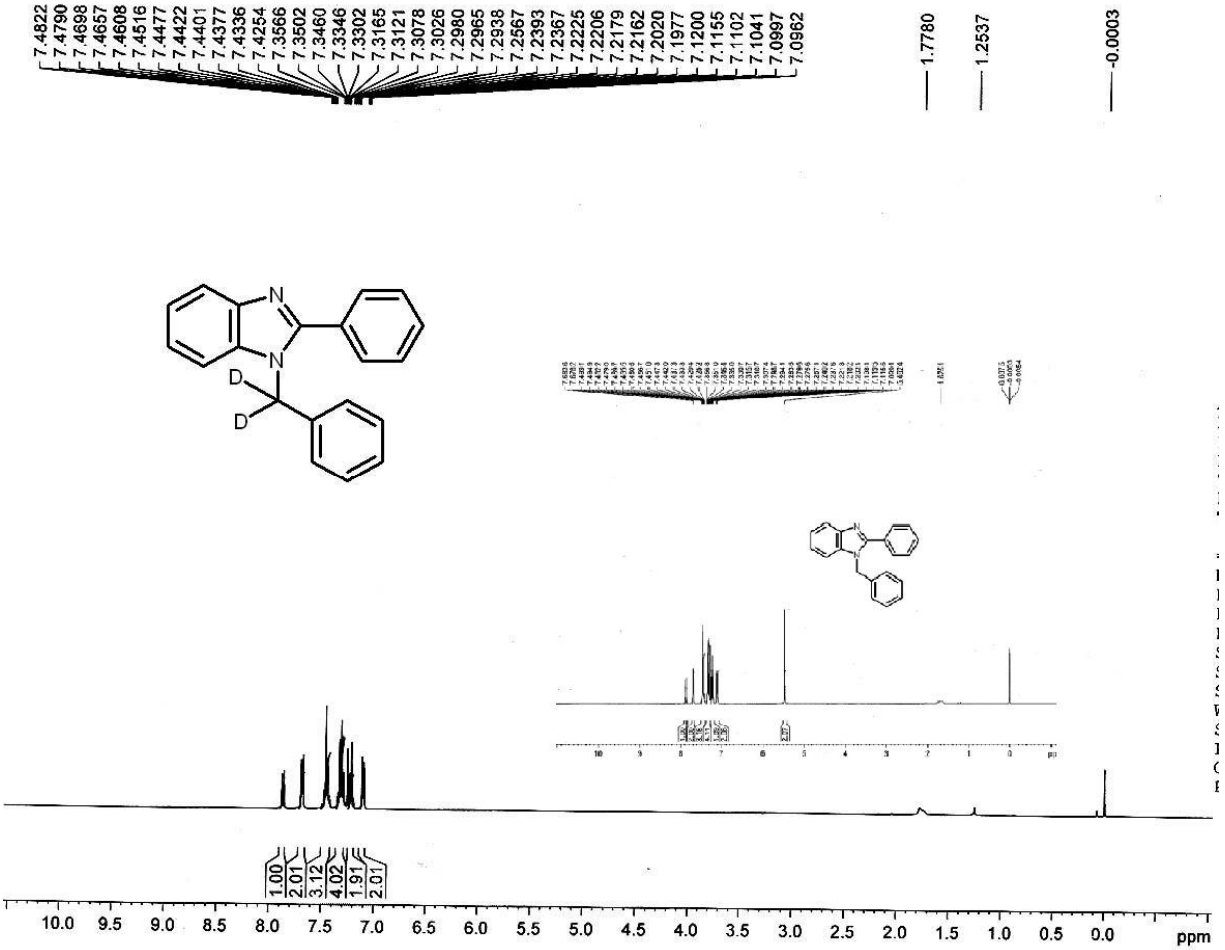
Mass spectra (APCI) of aliquot sample of reaction mixture (*o*-phenylelediamine & 4-methylbenzaldehyde; 1:2) subjected after 10 min



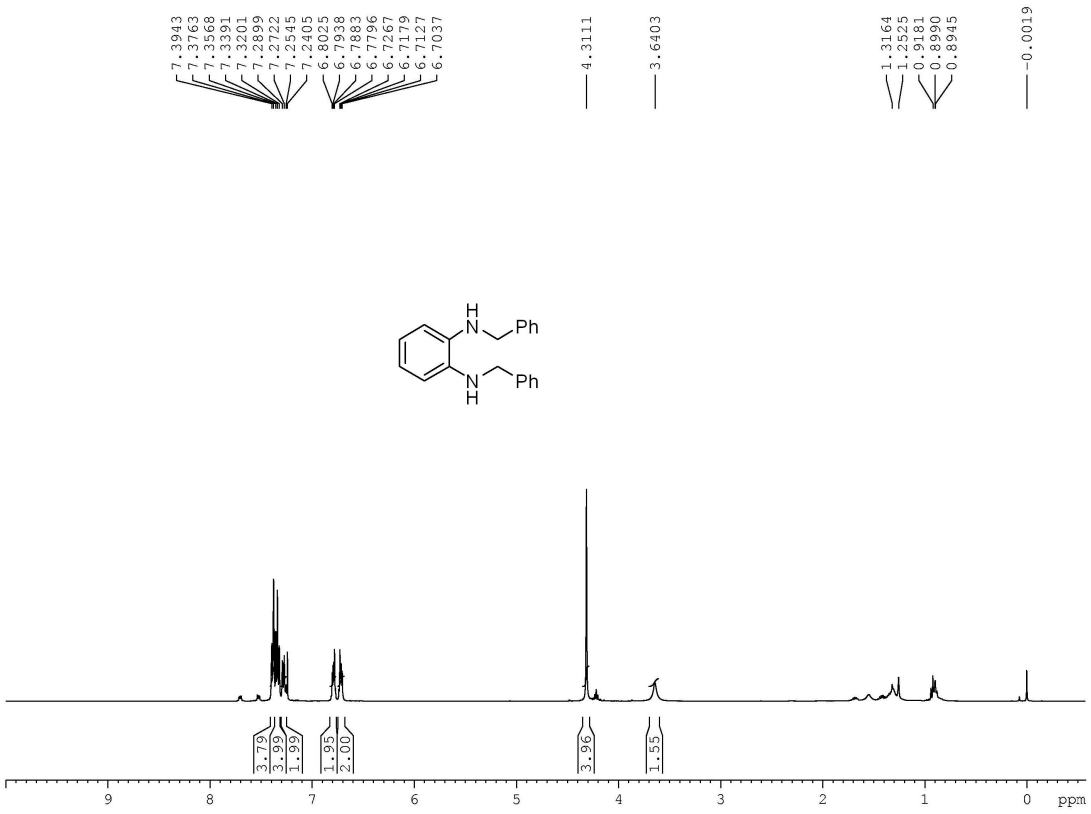
MS^2 of mass peak 313



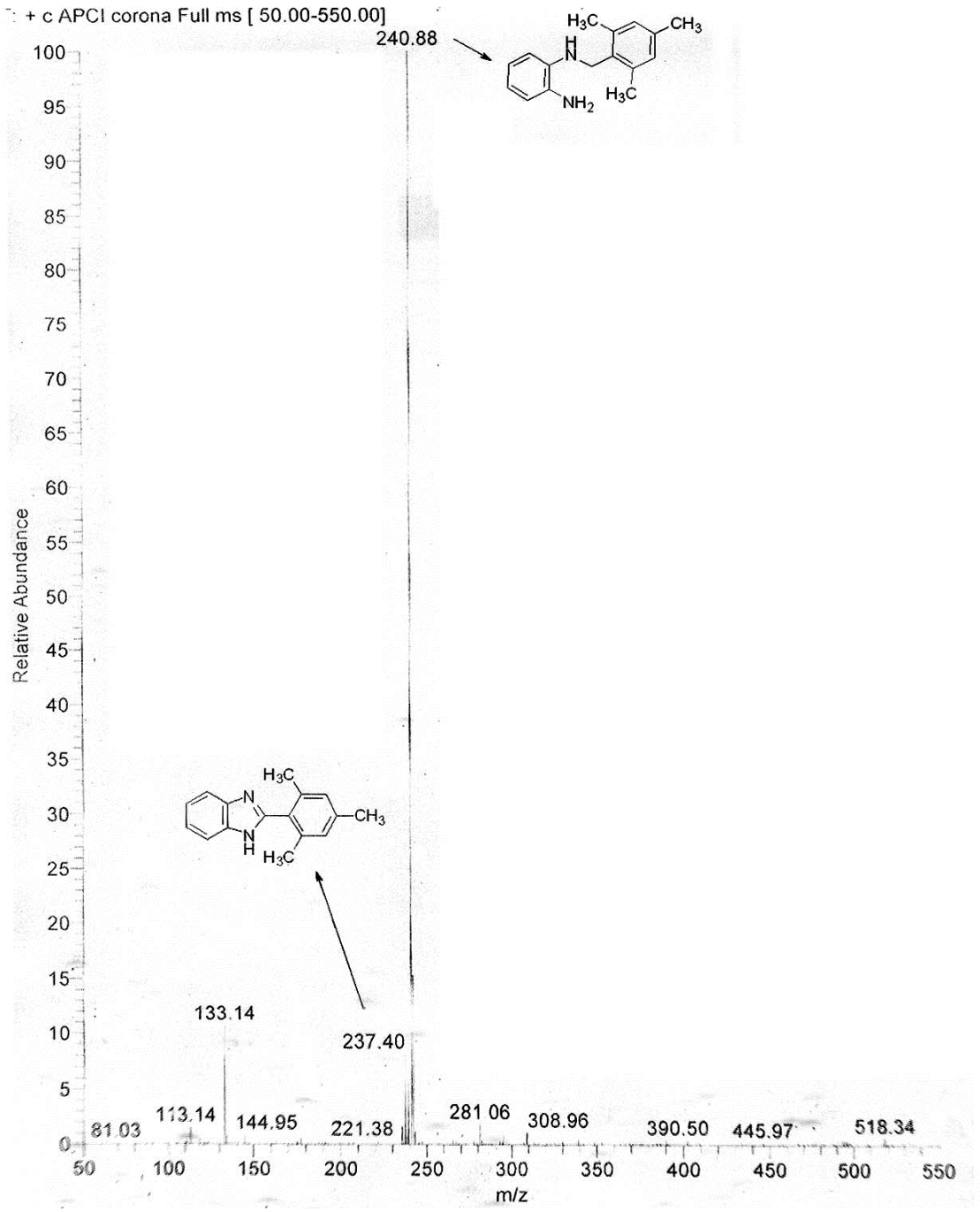
^{1}H NMR spectra of 2-Phenyl-1-α-d_2-phenylmethyl-1*H*-benzimidazole (Scheme 5)



^{1}H NMR spectra of N^1, N^2-dibenzylbenzene-1,2-diamine (Scheme 4)

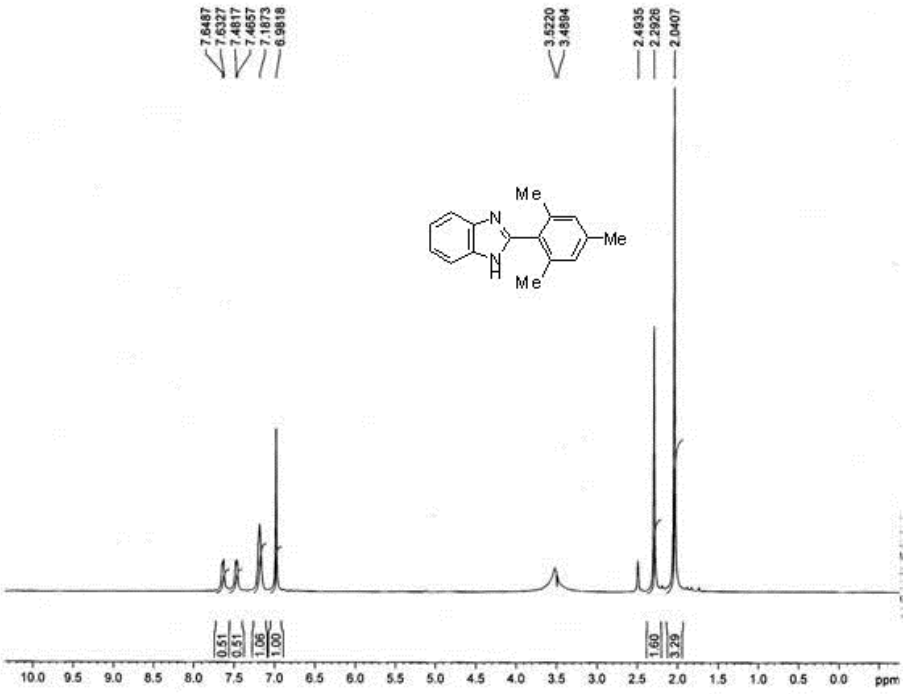


Mass spectra (APCI) of $NaBH_4$ treated aliquot sample of reaction mixture involving *o*-phenylelediamine & 2,4,6-trimethylbenzaldehyde (1:2) in $HClO_4$-SiO_2/EtOH (Scheme 6)

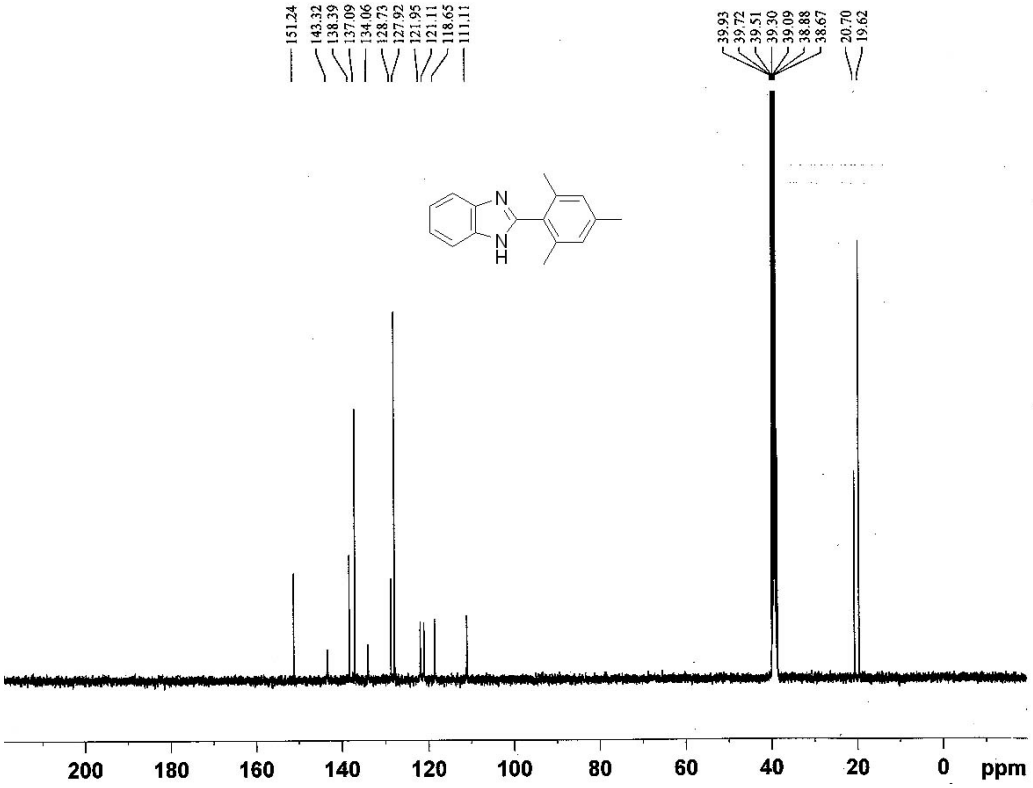


NMR spectra of 2-(2,4,6-trimethylphenyl)-1*H*-benzimidazole (Scheme 6)

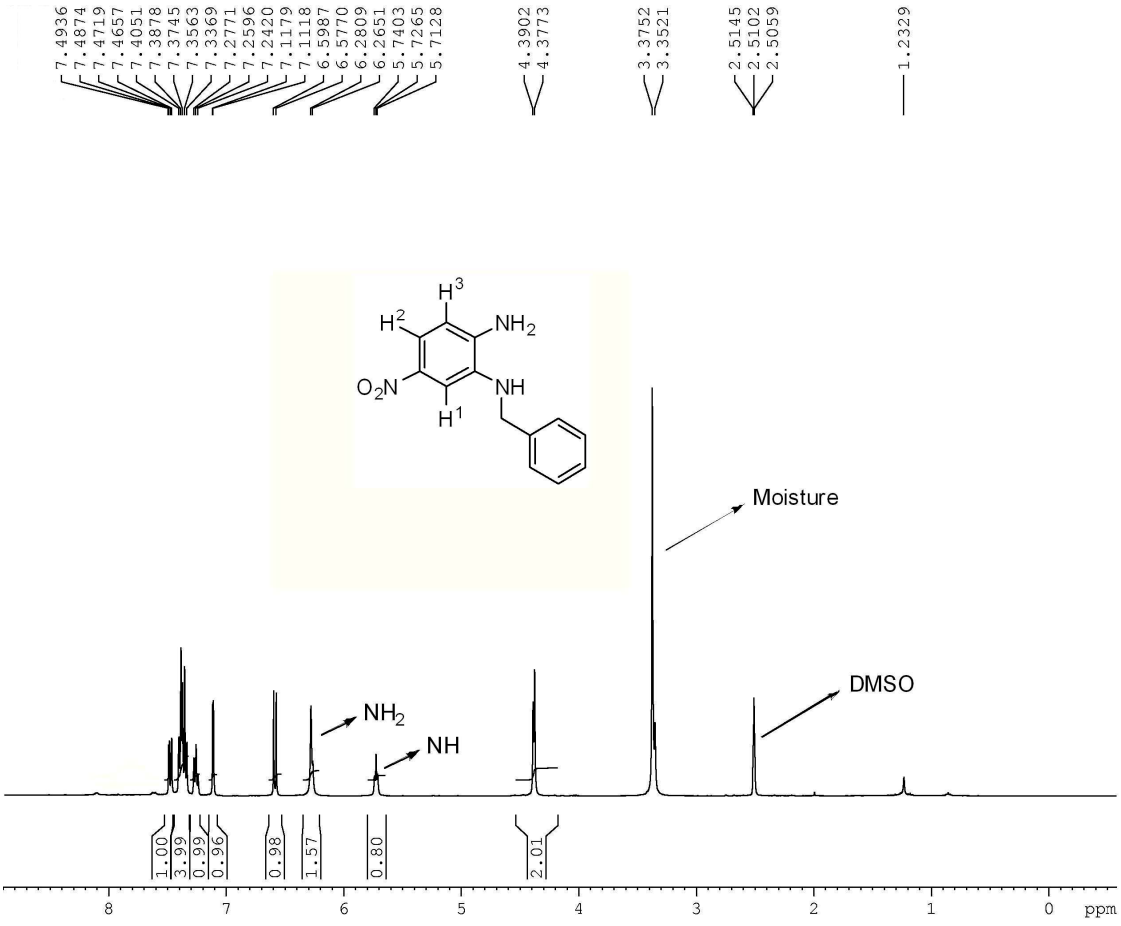
^{1}H NMR spectra



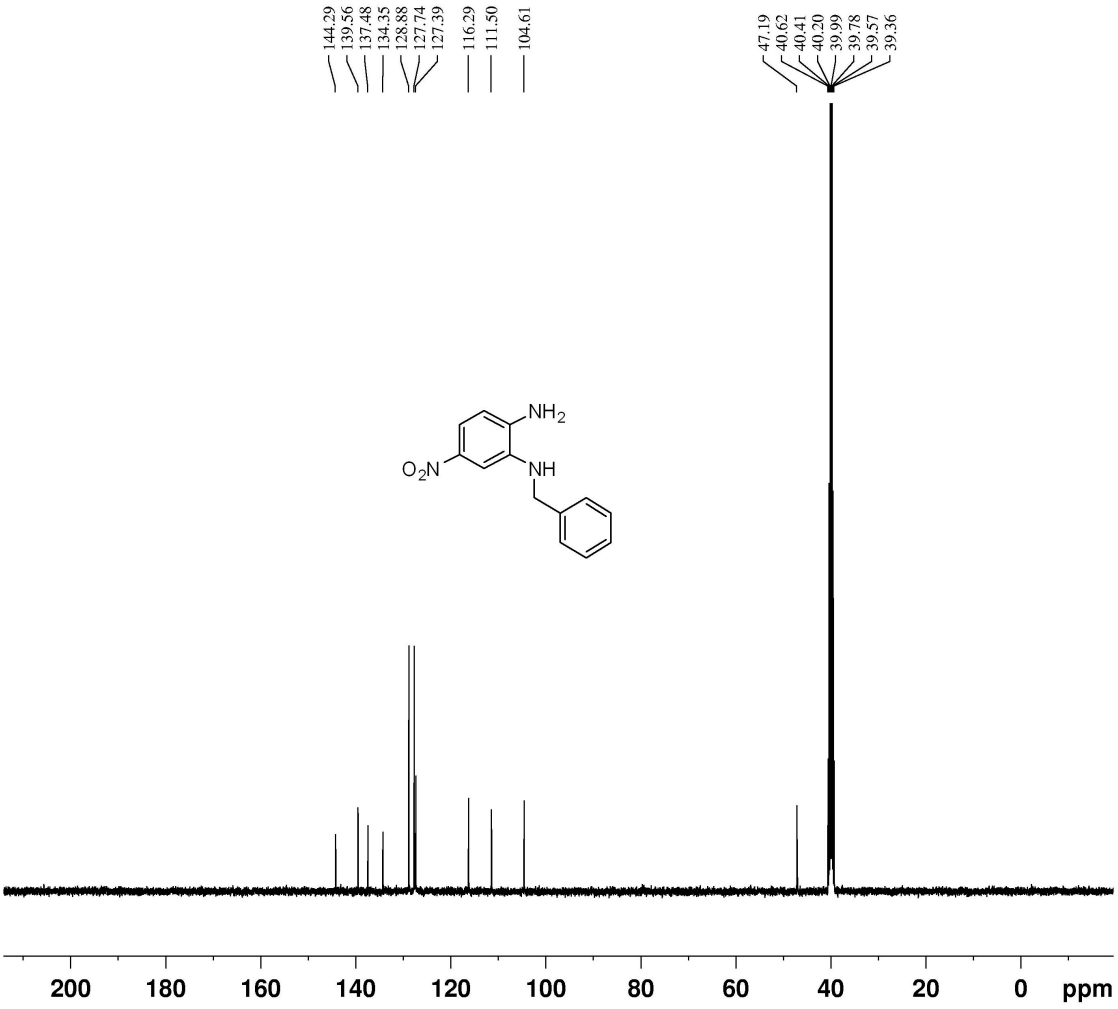
^{13}C NMR spectra



^{1}H NMR spectra of N^1-benzyl-5-nitrobenzene-1,2-diamine (Scheme 7)

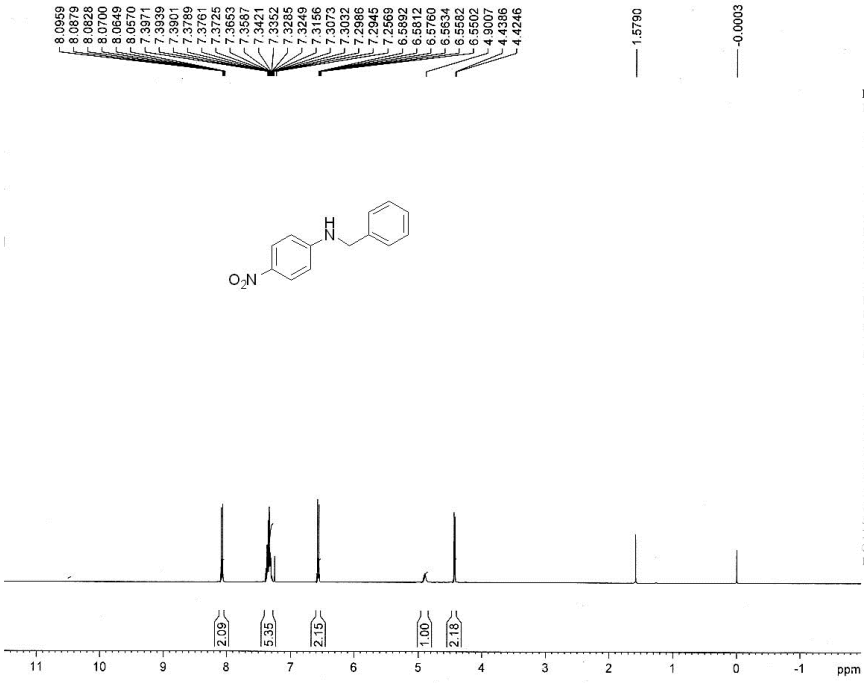


^{13}C NMR spectra of N^1-benzyl-5-nitrobenzene-1,2-diamine (Scheme 7)

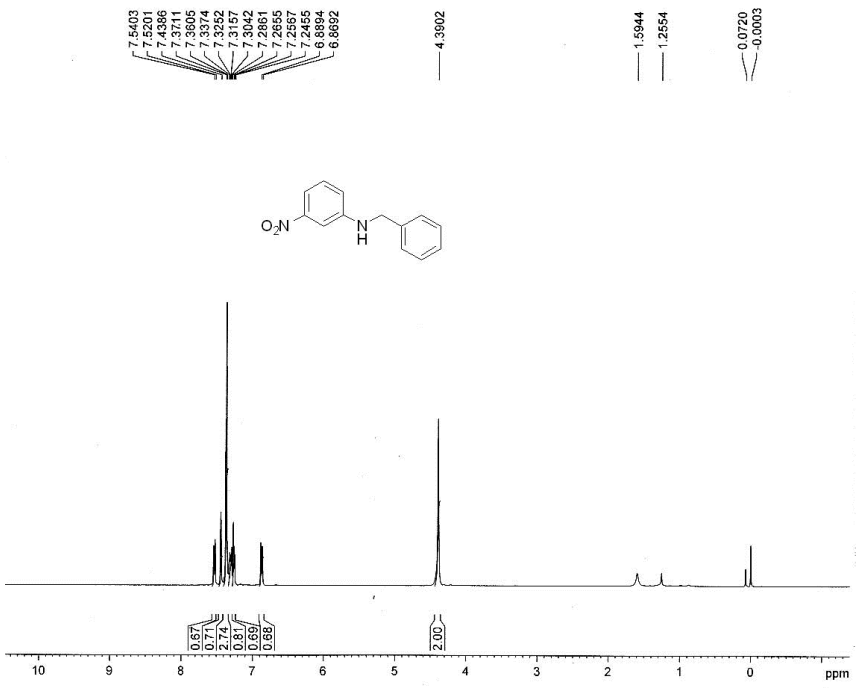


^{1}H NMR spectra of *N*-benzyl-4-nitroaniline & *N*-benzyl-3-nitroaniline (Scheme 7)

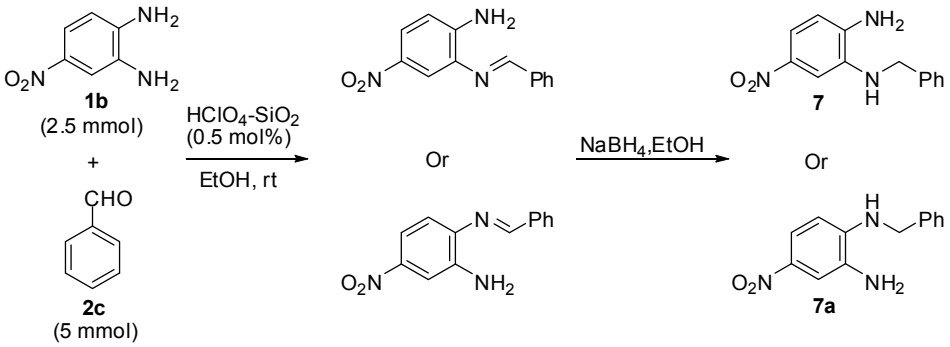
^{1}H NMR spectra of *N*-benzyl-4-nitroaniline



^{1}H NMR spectra of *N*-benzyl-3-nitroaniline

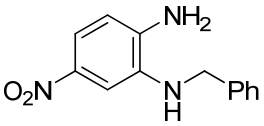


Structural elucidation of the reductive alkylation product for the reaction of 1b with 2c (following scheme).

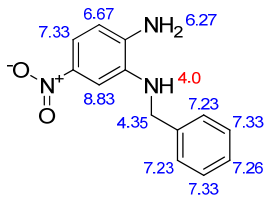


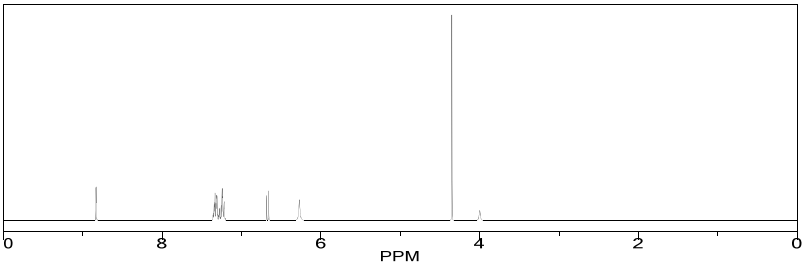
The reductive alkylation of **1b** with **2c** would form either **7** or **7a** due to the competitive imine formation by both anino groups. Due to the higher nucleophilicity of the amino group *meta* to nitro, it may be anticipated that the final (reductive amination) product would be **7**. In the absence of authentic sample of **7a**, the ChemNMR estimation (ChemBioDraw Ultra 11.0) was chosen as diagnostic tool to predict/assign the struture of the isolated product as **7** or **7a** on the basis of chemical shift of the benzylic proton/carbon. However, in both case (**7** and **7a**) the chemical shift of benzylic proton (δ = 4.35) and benzylic carbon (δ = 48) exhibit similar value making it as an inappropriate tool for determination/establishment of the structure of the final (reductive amination) product. Therefore, the 2D NMR analysis of **7** was carried out to determine the structure.

Chem NMR of 7

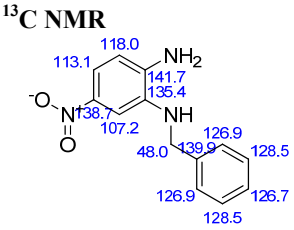


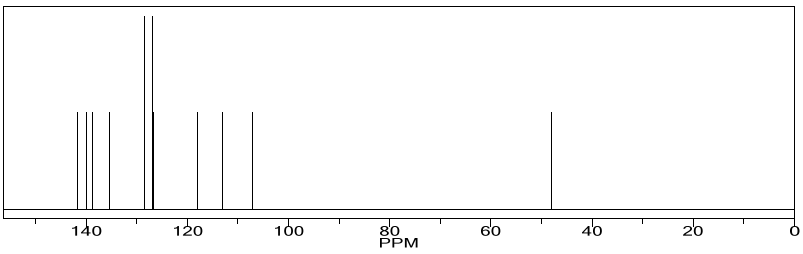
^{1}H NMR



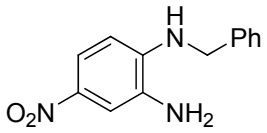


^{13}C NMR

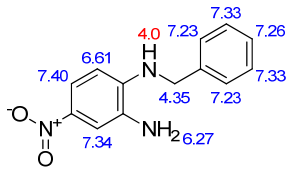


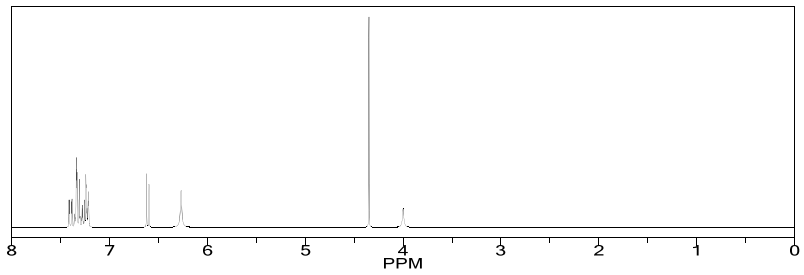


Chem NMR of 7a

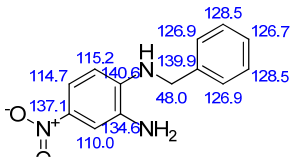


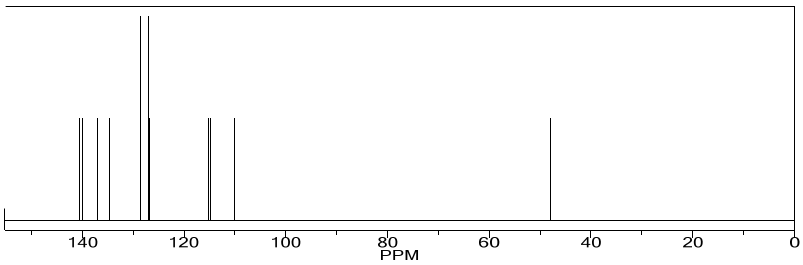
^{1}H NMR

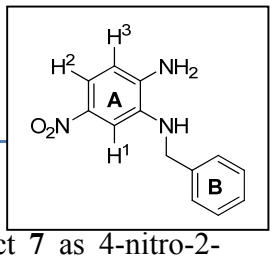




^{13}C NMR







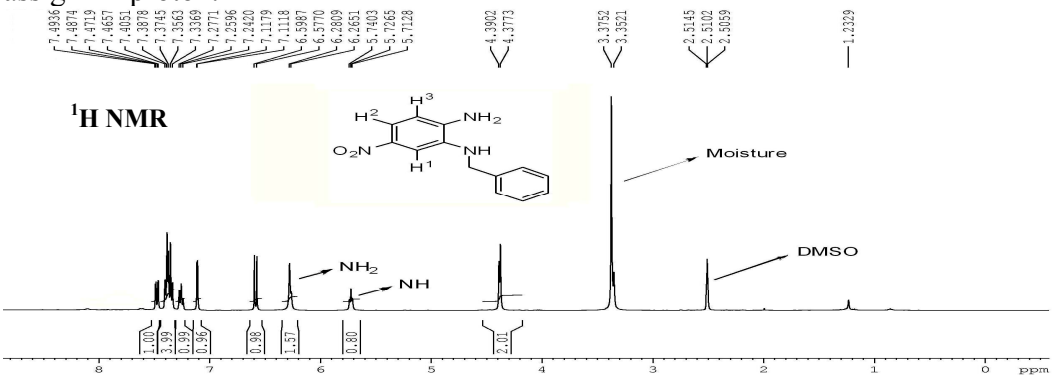
2D NMR Analysis

Work out Plan for 2D NMR analysis:

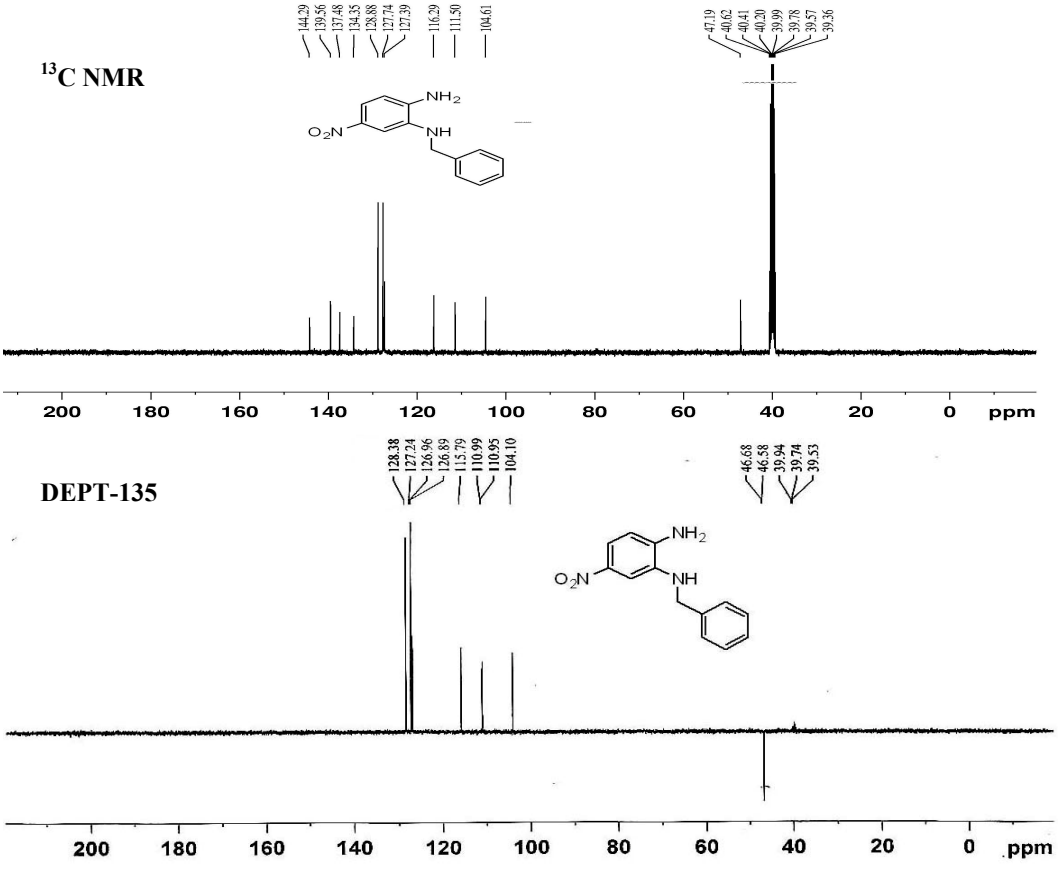
To establish the structure of the isolated reductive amination product **7** as 4-nitro-2-methylphenylamino aniline, the 2D NMR experiments of **7** were carried out and analyzed. The sequenec of analysis are given below:

Identification of H^{1} proton: Assignment of H^{1} proton was essential as it is required for NOESY experiment (correlation between H^{1} and benzylic protons). Out of eight aromatic protons, the five aromatic protons of ring B comes as complex multiplets with the chemical shift ranges from 7.24-7.40. The remaining three protons of ring A appear as dd (δ = 7.46-7.49) with coupling constant J = 8.7 Hz (*ortho* coupling) and J = 2.5 Hz (*meta* coupling), d (δ = 7.11) with coupling

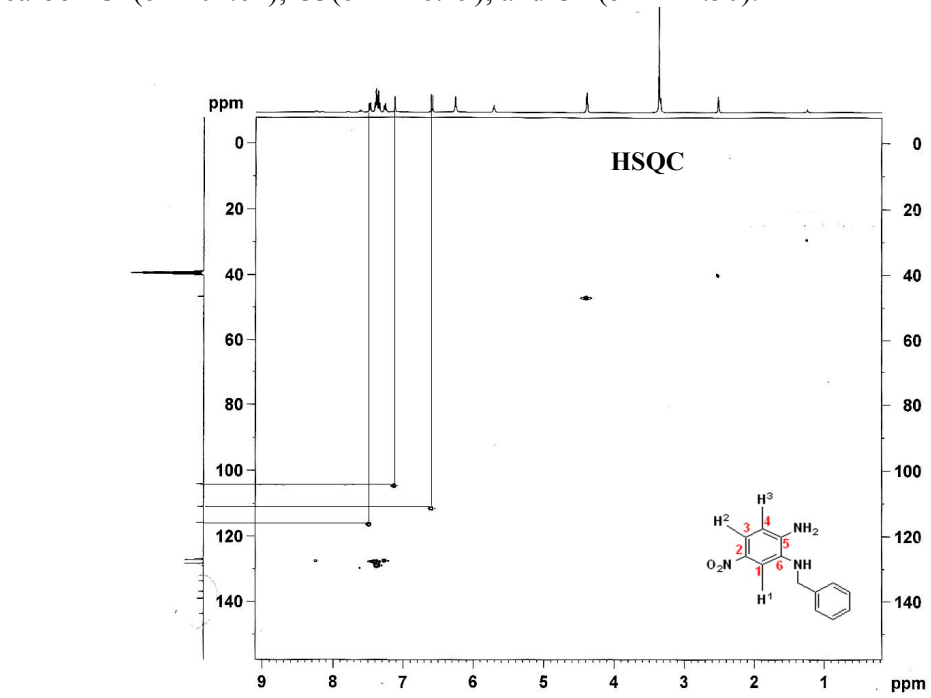
constant J = 8.7 Hz (*ortho* coupling), and d (δ = 6.58) with coupling constant J = 2.4 Hz (*meta* coupling). Out of these three protons, the *ortho* and *meta* coupling (J = 8.7, J = 2.4 Hz) is only possible with H^2 proton, the *ortho* coupling (J = 8.7 Hz) is only possible with H^3 proton and *meta* coupling (J = 2.4 Hz) is only possible with H^1 proton. Thus the splitting pattern and coupling constant were the key point to assign H^1 proton.

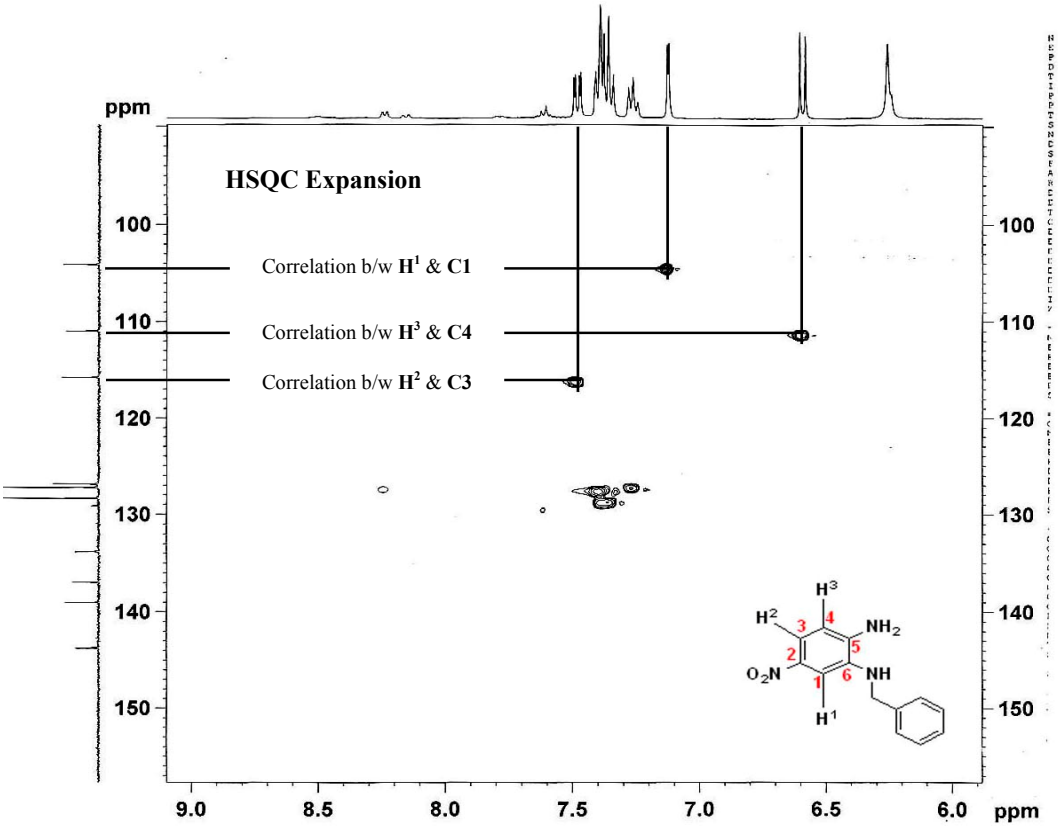


Next the DEPT-135 was carried out which eliminated the four quaternary aromatic carbons (δ = 144.29, 139.56, 137.48, and 134.35) and clearly differentiate the benzylic carbon (δ = 47.19). Further the three carbons of ring B were differentiated on the basis of peak intensity (δ = 128.88, 127.74, and 127.39). Now we left with three aromatic carbons (δ = 116.29, 111.50, and 104.61) belonging to the aromatic ring A and this could be any of H^1, H^2, and H^3.



Further validation of H^1 proton was carried out using HSQC experiment which clearly correlated the H^1 (δ = 7.11), H^2 (δ = 7.48), and H^3 (δ = 6.58) with respective carbon C1(δ =104.61), C3(δ = 116.29), and C4 (δ = 111.50).





NOESY Experiment: Finally NOESY experiment was carried out and correlation between H^1 proton and benzylic proton were established confirming the structure of **7** as **4-nitro-2-methylphenylamino aniline** and not as 2-methylphenylamino-5-nitro aniline.