INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH & DEVELOPMENT

ISSN 2278 – 0211 (Online)

Synthesis and Characterization of N-Alkyl Substituted 2-Benzimidazolyl Pyridine

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Abstract:
benzimidazolyl pyridine and bis- benzimidazolyl methane were synthesized via condensation of O-phenylenediamine with 2-pyridine carboxylic acid (picolinic acid), and malonic acid respectively, upon N-alkylation of the above mentioned compounds a series of N-alkyl-substituted benzimidazoles were synthesized and characterized by NMR, mass spectroscopic techniques, and elemental analysis.

Keywords: *Bis- benzimidazolyl methane, 2-benzimidazolyl pyridine, dibromoalkane, N-alkylation*

1. Introduction

Imidazole is a potential heterocyclic ligand with nitrogen as the donor atom. It is also a component of biologically important molecules[1]. Because of this, the coordination chemistry of related ligands has been the subject of numerous investigations[1]. Amongst them, the coordination behaviour of chelating benzimidazole type ligands has been studied by several research groups, some of them with an interest in mimicking biological activities[2-6]. 1,2-Bis-benzimidazoles and 2,6-bis(benzimidazolyl)pyridine are well known compounds together with their late transition metal complexes [7-17].

Recently[18,19], we reported the synthesis of bis benzothiazolyls, bis-benzooxazolyls and bis(benzimidazolyl), 1,2-bis(benzimidazolyl)benzene, 1,2-bis(benzimidazolyl) ethane, 1,2-bis(benzimidazolyl)methane, and 1,2-bis(benzimidazolyl)-4-methylbenzene together with their transtion metal complexes and their activities toward ethylene polymerization.

Kikugawa[20] reported the use of powdered potassium hydroxide for N-alkylation of imidazoles and benzimidazoles. Xianjin[21] reported the synthesis of 2,6-bis(N-allylbenzimidazolyl)pyridine.

Wenjuan[22] reported the use of N-alkylated 2-(benzimidazolyl)pyridine and 2,6-bis(benzimidazolyl)pyridine. Herein we report the synthesis of N-N-alkyl-bis(benzimidazolyl) pyridine, N- di-(bromoalkyl)-bis-(benzimidazolyl)methane and N-bromoalkyl-benzimidazolyl)pyridine. The synthesized compounds were characterized by spectroscopic tchneques(NMR , Mass) and elemental analysis.

2. Experimental

All chemical used were of analytical grade and used without any further purifications. The spectrometers Varian Inova 300/400 M Hz and Bruker ARX 250 were used to record the NMR spectra. The samples routinely recorded at 25 °C. The chemical shifts in the ^{1}H NMR spectra are referred to the residual proton signal of the solvent ($\delta = 7.24$ ppm for $CDCl_3$, $\delta = 2.5$ ppm for DMSO) and in ^{13}C NMR spectra to the solvent signal $\delta = 77.0$ ppm for $CDCl_3$, $\delta = 39.5$ ppm for DMSO). Mass spectra were routinely recorded at the central laboratories of the University of Bayreuth with a VARIAN MAT CH-7 instrument (direct inlet, EI, E = 70 eV) and a VARIAN MAT 8500 spectrometer. Elemental analyses were performed with a VarioEl III CHN instrument.

2.1. Syntheses

2.1.1. Synthesis of the 1, 2-bis (benzoimidazoles)

- Method A: A diamine compound (0.05mol) was mixed with a dicarboxylic acid or an acid anhydride (0.025mol) and the mixture was poured in 50 ml of preheated (100°C) polyphosphoric acid. The mixture was stirred and heated at 175°C for 3-5 hours. The reaction mixture was then poured in ice cold water and allowed to stand overnight. The precipitate was removed

by filtration and washed several times with diluted sodium hydrogen carbonate solution and finally with water. The reaction product was then air dried and weighed.

- Method B: The diamine 0.05mol was added to 0.025 mol of di-carboxylic acid or acid anhydride in 100 ml of 5N hydrochloric acid. The reaction mixture was then refluxed for 10 hours, cooled and allowed to stand. The precipitate was filtered and extracted with hot diluted ammonium hydroxide solution and then washed with ethanol and air dried.

2.1.2. Synthesis of (2-benzimidazolyl) pyridine

Method A was used for the synthesis of the above mentioned compounds. Pyridine -2-carboxylic acid and the diamine were used in equimolar quantities.

2.1.3. Synthesis of di-(bromo-alkyl) -N- bis-benzoimidazole and N,N-alkyl-bis-benzoimidazolyl pyridine and N-bromo-alkyl-benzoimidazolyl pyridine compounds

The general procedure for the reaction of N-alkylation was as follows: Benzimidazolyl pyridine (5g, 25.6 mmol) was dissolved in 10 ml anhydrous DMF. Then K_2CO_3 (1.4 equiv) was added to the solution at room temperature. Shortly afterwards (20 min),1,3-dibromopropane (25.6 mmol) was added in portions to the reaction mixture. The reaction was stirred at room temperature for two days. The inorganic salt was removed by filtration and rinsed twice with dichloromethane. The solution was poured into water and extracted with dichloromethane (2 x 50 ml). The combined organic layers were washed with brine, dried over anhydrous sodium sulphate, filtered, and concentrated in vacuo resulting in the formation of the product in 85% yield. Other N-alkyl substituted compounds were prepared similarly.

Compound No.	Calculated			Found		
	C	H	N	C	H	N
1	73.84	4.62	21.54	73.78	4.60	21.51
2	56.96	4.43	13.29	56.58	4.52	13.35
3	72.58	4.84	22.58	72.75	4.77	22.48
4	58.18	4.85	12.73	58.22	4.82	12.81
5	59.30	5.23	12.21	59.33	5.19	12.25
6	75.35	5.12	19.53	75.28	5.12	19.60
7	75.68	5.41	18.91	75.72	5.44	18.93
8	75.98	5.68	18.34	75.96	5.66	18.38
9	51.43	4.49	11.43	51.44	4.52	11.46
10	54.76	5.16	11.11	54.73	5.18	11.13
11	57.92	5.79	10.81	57.89	5.82	10.79

Table 1: Elemental analysis (CHN)

3. Results and Discussion

3.1. Synthesis of the bis (benzimidazoles) 3

The compound **3** was synthesized via condensation reactions of di-carboxylic acids or acid anhydrides and unsubstituted o-phenylenediamine, in a preheated polyphosphoric acid [23] or by refluxing the reactants in 4 N hydrochloric acid [24-26] (see Scheme 1. The bis(benzimidazole)s were insoluble in all organic solvents except DMSO. Both methods are suitable for bis(benzimidazole)s, but the first method gives better yields.

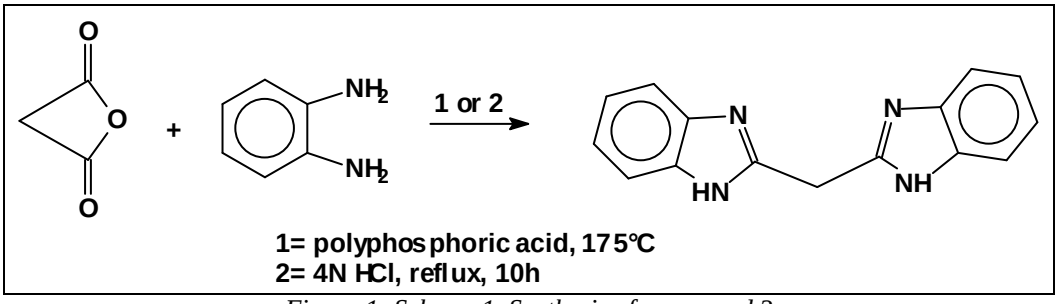


Figure 1: Scheme 1. Synthesis of compound 3

3.2. Synthesis of the Pyridine Derivative 1

The compound 1 was synthesized via the polyphosphoric acid method. Condensation reactions of 2-pyridine carboxylic acid, and o-phenylene diamine, was performed. The products were obtained in high yields (≥85%).

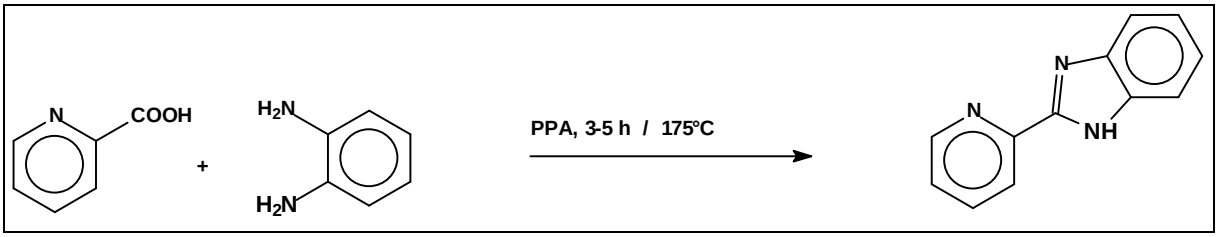


Figure 2: Scheme 2. Synthesis of compound 1

3.3. Synthesis of N-alkyl substituted benzimidazoles 2, 4-11.

N-alkyl substituted bis-benzimidazoles were prepared according to a published procedure[27]. In the presence of potassium carbonate, the N-alkylation proceeded readily to give the desired product in aprotic solvents, especially DMF under mild conditions. Generally, the introduction of one alkyl group is much easier compared with double alkylation.

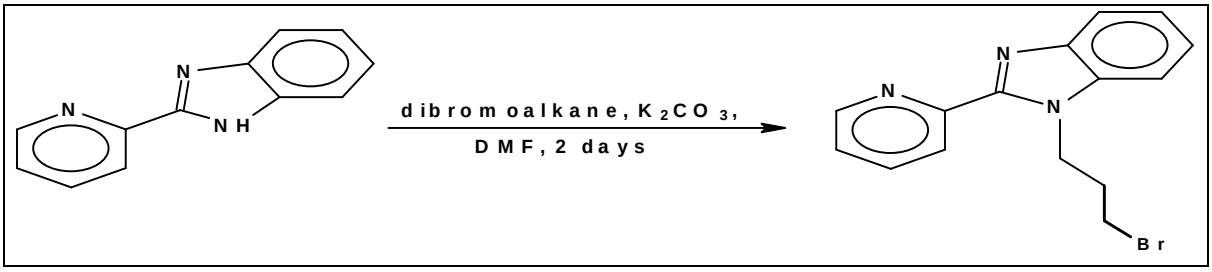


Figure 3: compounds 2, 4, 5

Figure 4: compounds 6-8

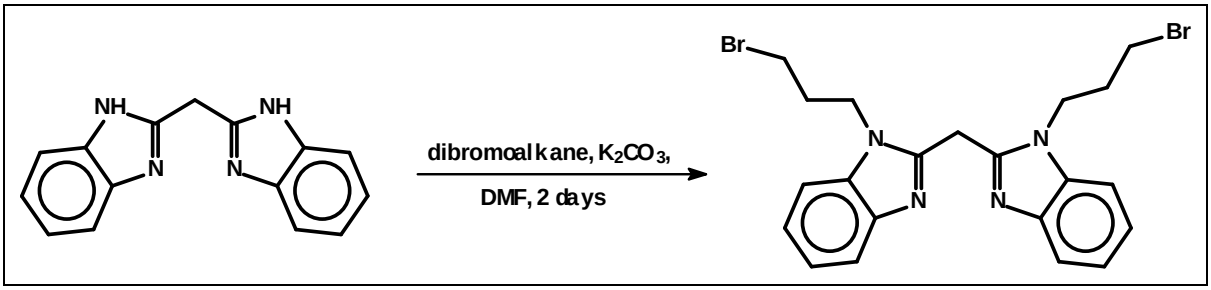


Figure 5: compounds 9-11

Scheme 3. synthesis of N-alkyl substituted imidazoles

3.4. Characterization

3.4.1. ^{1}H and ^{13}C NMR Spectroscopy

The compounds **1-11** were characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. The ^{1}H NMR spectrum of compound **3** (Scheme 4) shows four sets of resonance signals. The one downfield at δ =12.41 ppm is assigned to the NH protons, while the multiplet signal at δ = 7.49-7.46 ppm corresponds to four aromatic protons of the phenyl rings (H1,4). The signal at δ = 7.12- 7.10 ppm is assigned to 4 protons H2and H3. The methylene protons appear as a singlet at δ = 4.46 ppm. Scheme 6 shows the ^{1}H NMR spectrum of compound **6.**

The ^{13}C NMR spectrum of compound **3** (see Scheme 5) reveals five signals which can be assigned as follows: at δ = 150.8 ppm the amino carbon atoms appear (C7). The signal at δ = 138.4 ppm represents four carbon atoms of the aromatic rings (C1 and C6), the

signal at δ =122.9 ppm corresponds to four carbon atoms of the phenyl ring (C3 and C4). The signal at δ =115.2 ppm can be assigned to the four carbon atoms C2 and C5, while at δ = 29.8 ppm the methylene carbon atoms appear. (Scheme 7) shows the ^{13}C NMR spectrum of compound **6** The NMR data for the other compounds are given in Table 2.

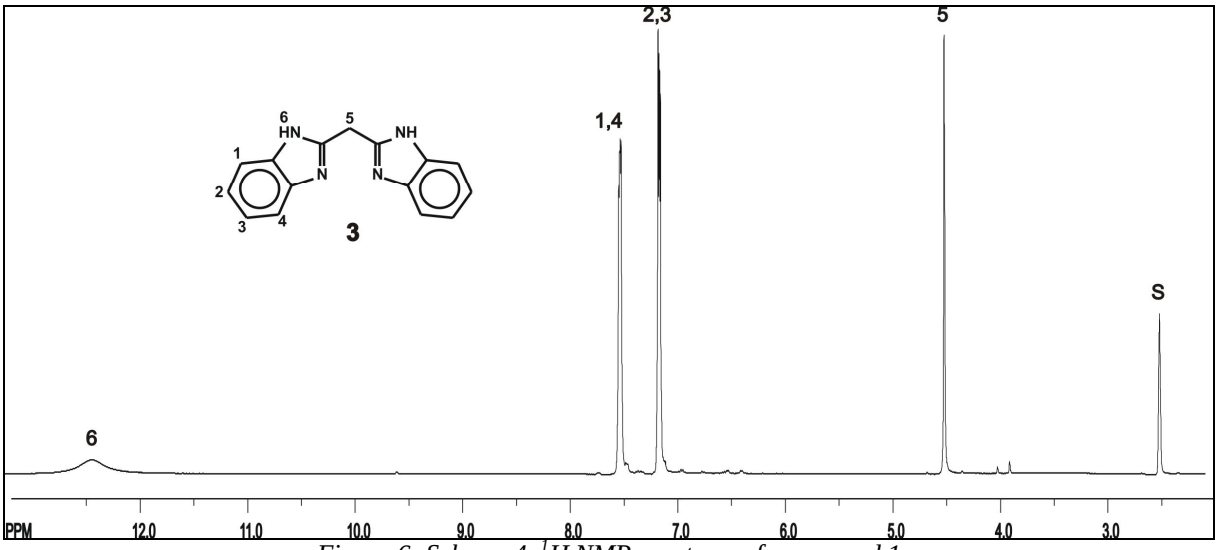


Figure 6: Scheme 4. ^{1}H NMR spectrum of compound 1

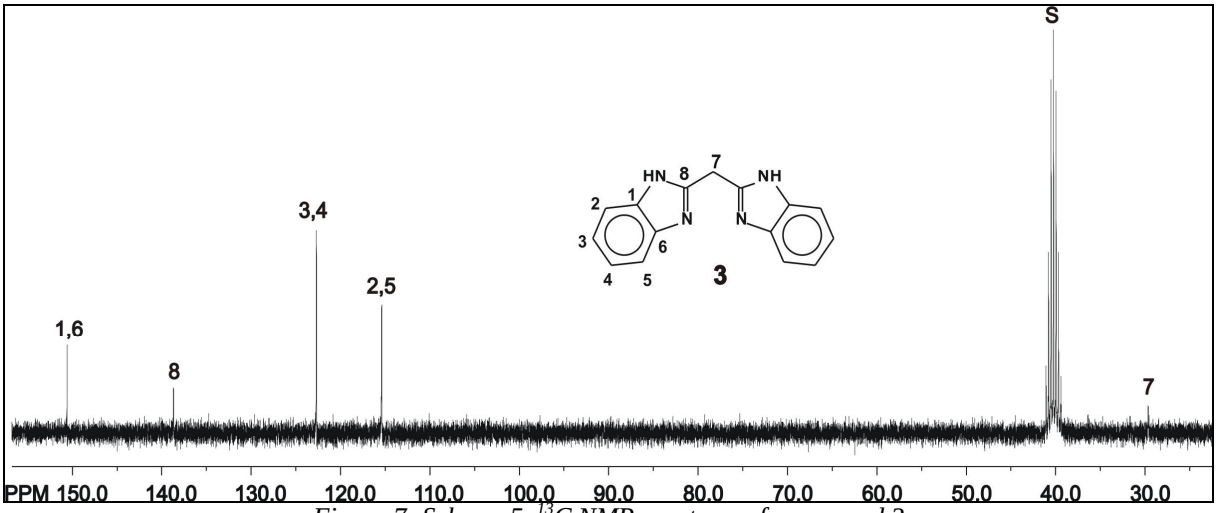


Figure 7: Scheme 5. ^{13}C NMR spectrum of compound 3

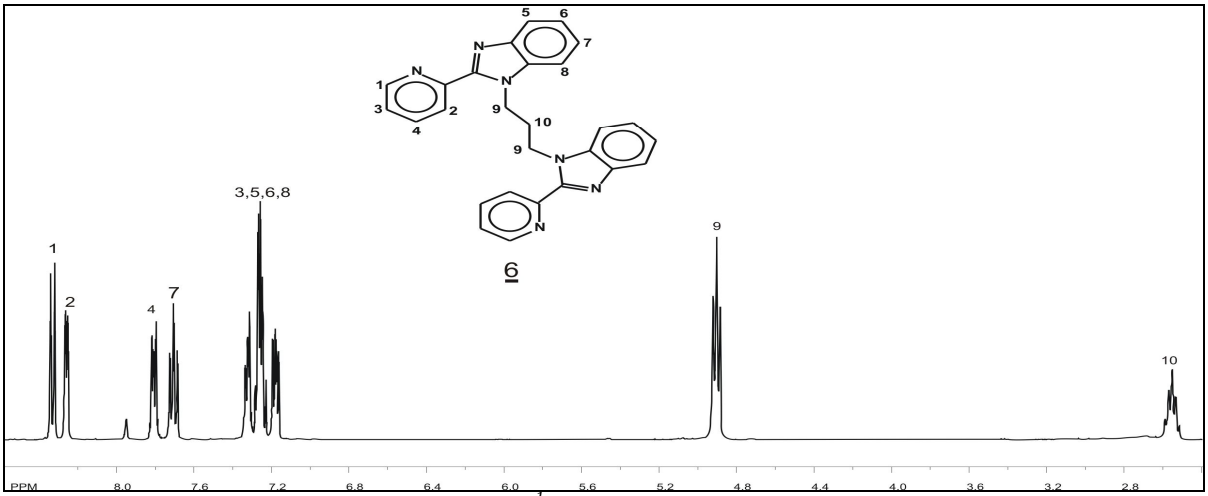


Figure 8: Scheme 6. ^{1}H NMR spectrum of compound 6

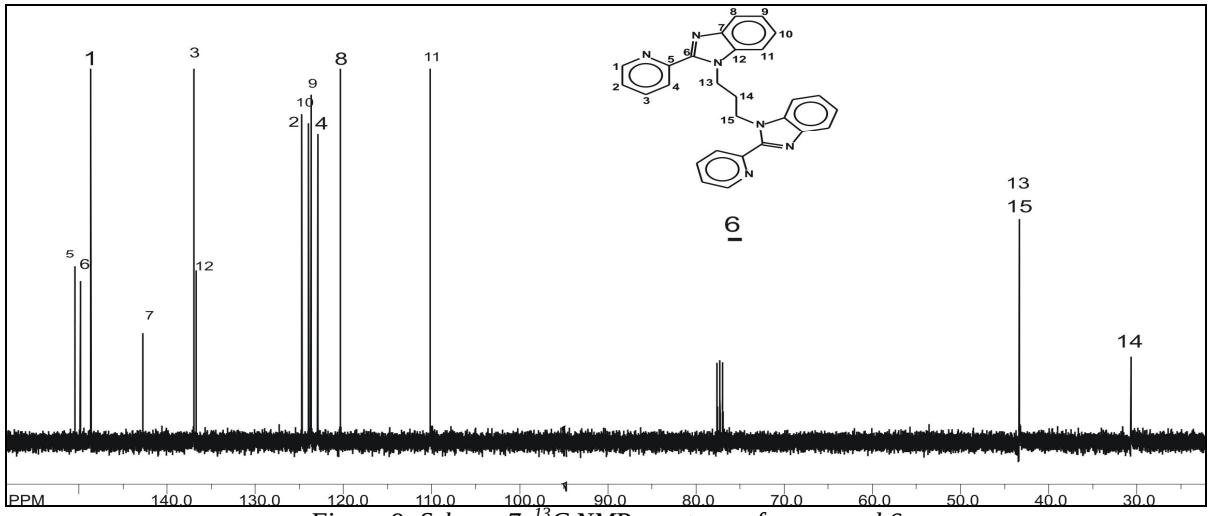


Figure 9: Scheme 7. ^{13}C NMR spectrum of compound 6

3.4.2. Mass Spectroscopy

Scheme **8** shows the mass spectrum of compound **3**. The peak with m/z = 248 represents the molecular ion peak. Scheme 9 and 10 show the mass spectra of compound 1 (m/z = 195) and compound 5 (m/z = 344) respectively. The data for the other compounds are given in Table.2.

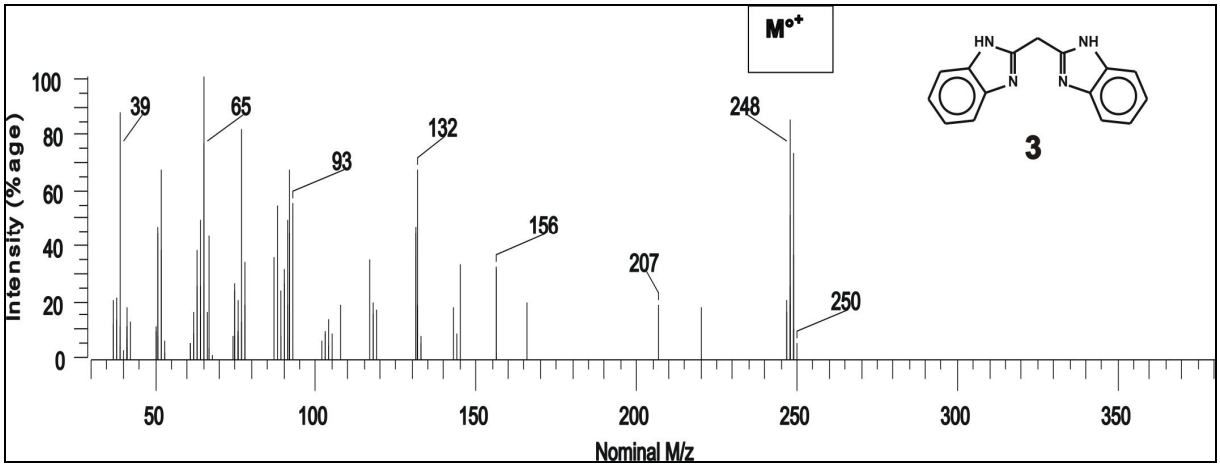


Figure 10: Scheme 8. Mass spectrum of compound 3

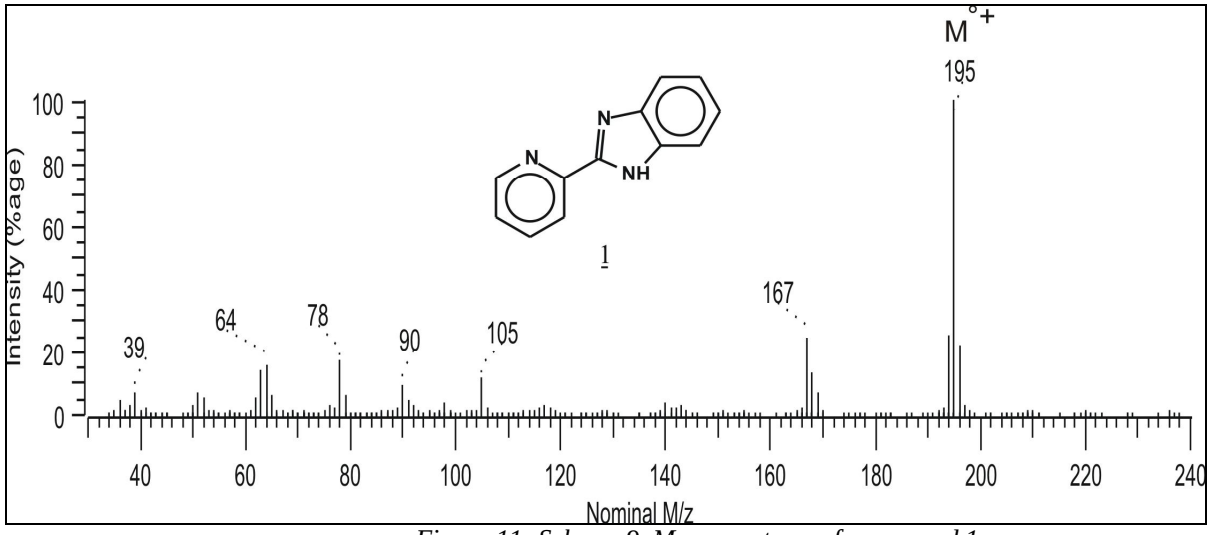


Figure 11: Scheme 9. Mass spectrum of compound 1

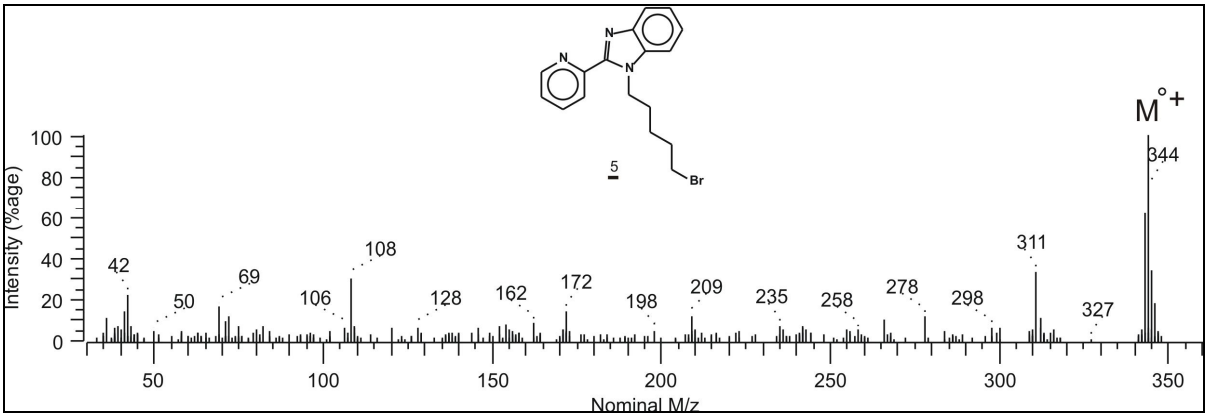
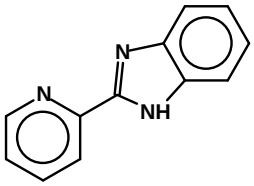
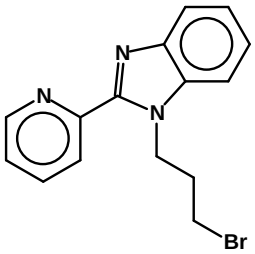
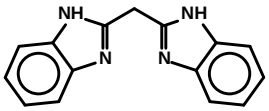
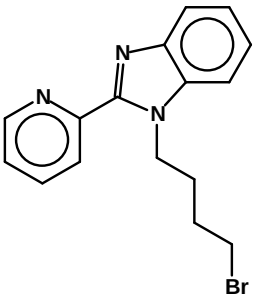
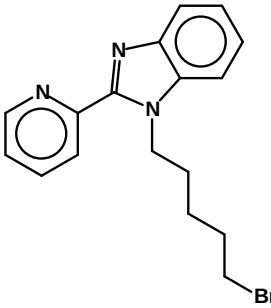
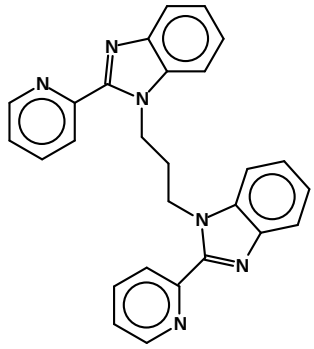
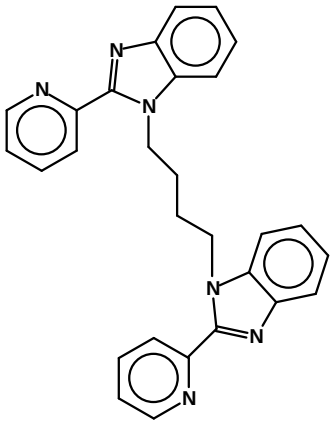
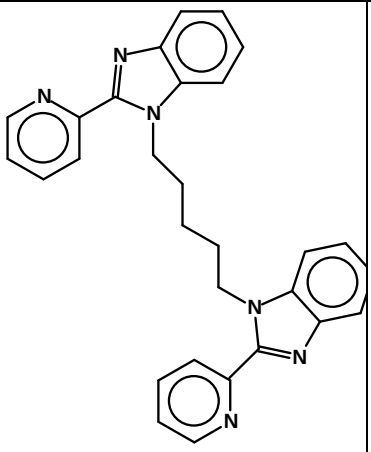
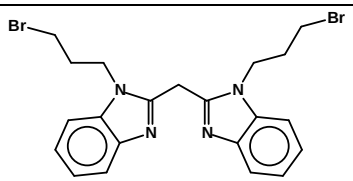
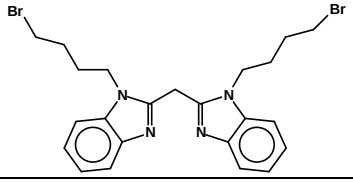


Figure 12: Scheme 10. Mass spectrum of compound

NO	Compound	^{1}H NMR ∂ [ppm]	^{13}C NMR ∂ [ppm]	Mass m/z (%)
1		8.69(d,1H), 8.29(d,1H), 7.95(t,1H), 7.58(m,2H), 7.48(t,1H), 7.18 (m,2H)	151.3, 150.0, 149.1, 138.2, 125.4, 123.2, 122.1	195 $M^{\circ+}$ (100)
2		8.95(d,1H), 8.83(d,1H), 8.02(d,1H), 7.56(t,1H), 7.44(d,1H), 7.29(t,1H), 7.20(d,1H), 7.10(t,1H), 3.90(t,2H), 3.46(t,2H), 2.35(m,2H)	153.3, 152.8, 150.4, 150.0, 137.2, 135.8, 123.4, 121.9, 121.5, 121.2, 119.3, 110.1, 45.8, 29.9, 29.7	316$M^{\circ+}$ (100)
3		12.41(s,2H, NH) 7.46(m,4H), 7.11(m,4H), 4.43(s,2H,CH_2)	150.8, 138.4 122.9, 115.4, 29.8	248$M^{\circ+}$ (100)
4		8.79(m,2H), 8.03(t, 1H), 7.34(m,4H), 7.10(t,1H),3.90(t,2H), 3.35(t,2H),1.89(m,2H), 1.79(m,2H)	152.7, 152.5, 150.0, 149.6, 137.2, 135.6, 123.4, 121.9, 121.8, 121.6, 119.7, 109.0, 49.4, 29.1, 27.6, 25.6	330$M^{\circ+}$ (100)
5		8.83(m,2H), 8.02(t,1H), 7.28(m,5H), 3.88(t,2H), 3.31(t,2H),1.97(m,2H), 1.76(m,4H)	152.9,152.7,150.0, 149.9, 137.2, 134.7, 123.4, 121.9, 121.8, 121.6, 119.7, 109.6, 47.9, 32.2, 31.8, 30.9, 24.7	344$M^{\circ+}$ (100)

6		8.33(d,2H), 8.26(d,2H), 7.81(t,2H), 7.71(t,2H), 7.26(m,8H), 4.91(t,4H), 2.56(t,2H)	150.5, 149.9, 148.7, 142.8, 136.9, 136.7, 124.8, 124.0, 123.7, 122.9, 120.3, 110.2, 43.1, 30.9	$430M^{\bullet+}$ (100)
7		8.81(m,2H),8.02(t,1H), 7.43(t,1H), 7.29(t,1H), 7.24(d,1H), 7.17(d,1H), 7.10(t,1H), 3.91(d,4H), 1.93(t,4H)	153.3, 152.8, 150.4, 150.0, 137.2, 134.9, 123.4, 121.9, 121.8, 121.6, 119.7, 110.0, 48.7, 25.3	$444M^{\bullet+}$ (100)
8		8.82(m,4H), 8.13(t,2H), 7.41(t,2H), 7.30(d,2H), 7.25(d,2H), 7.20(d,2H), 7.13(t,2H), 3.79(d,4H), 2.09(m,4H), 1.67(m,2H)	152.9,152.8, 150.0, 149.9, 137.2, 135.6, 123.4, 121.9, 121.8, 121.6, 119.5, 109.6, 48.5(2C), 30.3(2C), 28.2	$458M^{\bullet+}$ (100)
9		7.58(t,2H), 7.50(d,2H), 7.32(d,2H), 7.25(t,2H), 4.19(s,2H), 3.63(t,4H), 3.46(t,4H), 2.35(m,4H)	155.1, 150.2, 135.6, 122.5, 122.2, 118.6, 109.3, 44.2, 29.8, 29.6, 16.8	$490M^{\bullet+}$ (100)
10		7.42(d,2H), 7.37(t,2H), 7.32(d,2H), 7.25(t,2H), 4.22(s,2H), 3.63(t,4H), 3.35(t,4H), 1.76(m,8H)	155.0, 149.3, 135.4, 122.6, 122.5, 119.0, 108.5, 47.7, 29.1, 27.7, 25.4, 16.7	$504M^{\bullet+}$ (100)

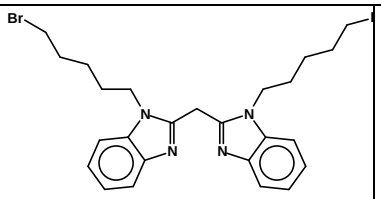
11		7.37(m, 8H), 4.19(s,2H), 3.61(t,4H), 3.30(t, 4H), 1.97(m,4H), 1.79(m,4H), 1.56(m,4H)	155.1, 149.7, 134.5, 122.6, 122,5, 119.1, 108.9, 46.1, 32.2, 31.8, 30.8, 24.7, 16.8	518M^{2+} (100)

Table 2: ^{1}H and ^{13}C NMR Spetra of the Synthesized compounds

4. Conclusions

A facile and efficient method for the synthesis of N-alkyl substituted benzimidazoles using aprotic solvents (DMF) and anhydrous potassium carbonate. The synthesized compound were further be used to form complexes with transition metals and study their catalytic behaviour towards olefin polymerization after activation with suitable co-catalyst.

5. Acknowledgement

Financial support for this work by Albaha university, Deanship for Scientific Research (project number 39/1434), is highly acknowledged, we also thankful to the Department of Inorganic Chemistry II ,University of Bayreuth, Germany for offering Lab Facilities (NMR, MASS) Spectrometers and elemental Analyzer.

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