CHAPTER IV

MOLECULAR DESIGN AND SYNTHESIS OF BENZIMIDAZOLE HETEROCYCLE: A MODEL MOLECULE FOR A HYDROGEN BONDED PROTON TRANSFER NETWORK

4.1 Abstract

A series of difunctional benzimidazole-based compound, i.e., 1,4-di(1*H*-benzo[*d*]imidazol-2-yl)benzene, **1**, and 3,5-di(1*H*-benzo[*d*]imidazole-2-yl)benzenamine, **2** are designed as model compounds for the proton transferring pathway in water free system. The model compound **1** is developed by cyclizing terephthaloyl chloride and 1,2-phenylenediamine via amidation and ring closure reactions. In the same pathway, 5-aminoisophthalic acid and 1,2-phenylenediamine as the starting materials for **2** is also proposed. The work also shows how the reaction is effective if the amino group of 5-aminoisophthalic acid is protected during the reaction. The structures of the compounds are characterized by using FT-IR, ^{1}H-NMR, MALDI-TOF and EA techniques.

Keywords: Benzimidazole, Model compound, Proton transfer network, PEMFC, Hydrogen bond

4.2 Introduction

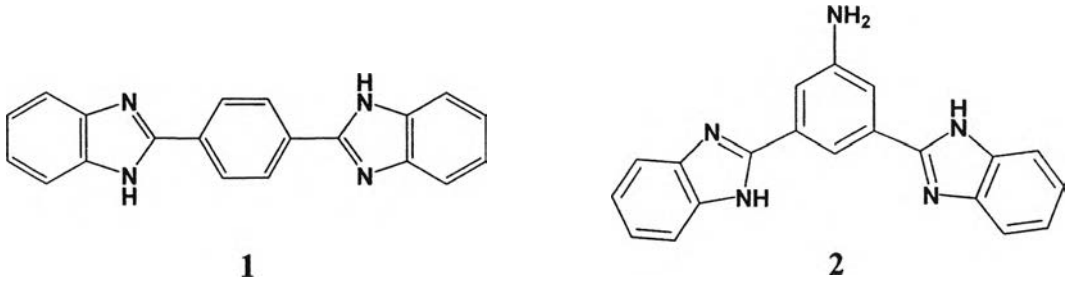
Nowadays, energy and environmental problems are critical concerns for human being and global issue. Fuel cells have received much attention as one of the green alternative power sources which convert the chemical reaction to electrical energy with water and heat as by- products. Polymer Electrolyte Membrane Fuel Cell (PEMFC) is accepted to be the most promising types of fuel cells for portable electrical devices and automotives due to its simplicity in compact size as well as high power density with fuel flexibility.[1]

One of the main components of PEMFC is the membrane which conducting proton from anode to cathode. Conventional membranes are perfluorosulfonic polymers which are commercially available under the commercial name of Nafion® (DuPont), Dow, Aciplex® and Flemion®. These membranes provide excellent chemical stability and high proton conductivity at low operating temperature, which is averagely below 80°C. However, the high operating temperature to overcome the Pt catalyst poisoning by a trace amount of CO impurity existed in hydrogen fuel is required. Moreover, an increase in proton conductivity can be expected at high operating temperature.[2] Based on these requirements, development of proton exchange membrane for working at elevated temperature is another challenge for research.

For the past several years, proton exchange system based on anhydrous membranes (water-free system) functioned via the resonance structure of heterocyclic molecule, have been recognized as an alternative way to overcome the limitation of water based system.[3] Many approaches have focused on the development of new materials either the incorporation of the heterocyclic molecule into the main chain [4,5] or side chain [6-8] or even blending with polymer [9-11]. Because the mechanism of proton exchange in anhydrous system is still unclarified, the development from fundamental viewpoint is indeed important. Therefore, it is an ideal if we can design some model compound to represent the proton exchange pathway and evaluate the most effective and efficient condition. Based on the information obtained from the model compound, we can design the most favorable

proton transfer pathway through heterocyclic system and achieve the high proton conductivity.

In water-free system, benzimidazole is one of ideal heterocyclic molecules which nitrogen atoms acts as the proton acceptors and proton donors by forming a regular hydrogen-bonded network to lead consequently proto transferring pathway.[12] Therefore, in our present work, we propose a series of model compounds, as shown in Figure 4.1, containing di-functional benzimidazoles to investigate the structure related to proton transfer mechanism.



1 2

Figure 4.1 Chemical structures of 1,4-di(1*H*-benzo[*d*]imidazol-2-yl)benzene, **1**, and 3,5-di(1*H*-benzo[*d*]imidazol-2-yl)benzenamine, **2**.

4.3 Experimental

Materials. 1,2-Phenylenediamine (99.5wt%) and 5-aminoisophthalic acid (94wt%) were purchased from Aldrich, Germany. Terephthaloyl chloride was purchased from Nacalai tesque, Kyoto, Japan. 1-Ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) was obtained from TCI, Japan. Triphenylphosphite, phthalic anhydride and 1-methyl-2-pyrrolidone were purchased from Fluka. Sodium hydrogen carbonate was the product of Riedel-de Haën. Hydrazine hydrate was purchased from Carlo Erba. Poly(ether ether ketone) (PEEK) was a gift from J.J.-Degusa company, Germany. All other chemicals and solvents were analytical grade and were used without further purification.

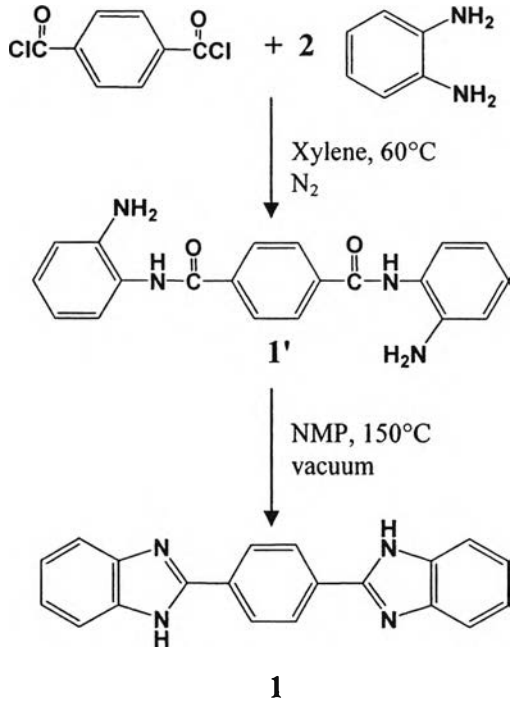
Instruments and Equipment. Fourier transform infrared (FTIR) spectra were recorded on KBr and ZnSe window by using a Thermo Nicolet/Nexus 670 with 32 scan at a resolution of 2 cm^{-1} in a frequency range of 4000-400 cm^{-1} equipped with deuterated triglycerinesulfate detector (DTGS) with specific detectivity of 1×

10^9 cm·$Hz^{1/2}$·w^{-1}. NMR spectra were obtained on a Varian Mercury 400 MHz spectrometer (USA). The deuterated solvent used was DMSO-d_6 and the internal reference for ^{1}H NMR was tetramethylsilane. Mass spectra were collected by using a microflex Bruker Daltomics MALDI-TOF mass spectrometer. The spectra were obtained based on doubly recrystallized α-cyano-4-hydroxy cinnamic acid (CCA) matrix. Elemental analyses were done by a PerkinElmer series II CHNS/O Analyzer 2400.

Synthesis of 1,4-di(1*H*-benzo[*d*]imidazol-2-yl)benzene, 1 (Scheme 4.1). Terephthaloyl chloride (6.6 mmole, 1.34 g) in xylene 150 ml was dropwisely added into a vigorously stirred solution of 1,2-phenylenediamine (2.88 g, 2.64×10^{-2} mol) in xylene (10 ml) at 60°C under nitrogen atmosphere. The reaction was proceeded for 12 hours obtaining the brown precipitate in yellow solution. The precipitate was collected and then dried at 60°C before washing by methanol. The precipitate obtained was dissolved in NMP (80 ml). After refluxing under vacuum at 150°C for 24 h, the white precipitate was obtained. The crude product was dried at 100°C under vacuum for 6 h.

Characterization: 65.8% yield; white powder; FT-IR (KBr, cm^{-1}): 3200-2500 (medium, hydrogen bonded N-H stretching); 1440 (strong, skeleton vibration of benzimidazole ring); 743 (strong, aromatic C-H bending). ^{1}H NMR (DMSO-d_6): δ 8.35 (4H, s, Ar-**H**); 7.40 (4H, d, Ar-**H**); 7.20 (4H, d, Ar-**H**). Mass spectrometry (m/z): 310.64. FW of $C_{20}H_{14}N_4$: 310. Elemental analysis (%) Found: C 77.74. H 4.26. N 17.90. Calcd. for $C_{20}H_{14}N_4$: C 77.42. H 4.52. N 18.06.

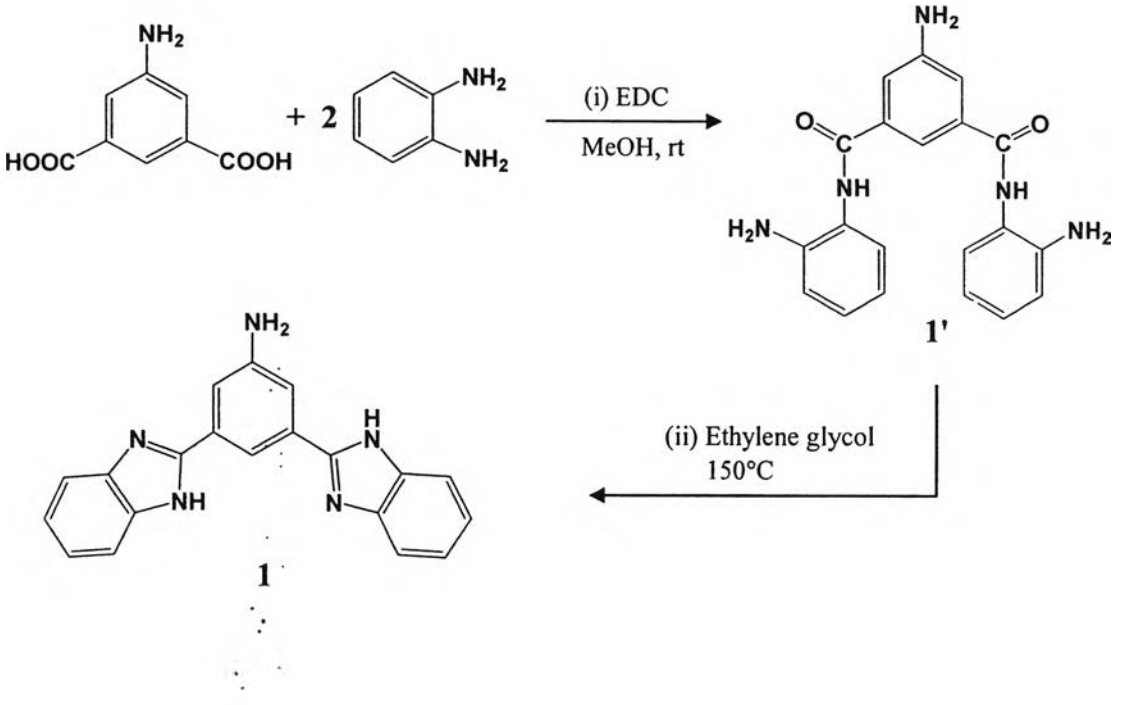
Scheme 4.1 Preparation of **1**.



Synthesis of 3,5-di(1*H*-benzo[*d*]imidazol-2-yl)benzenamine, 2 via pathway A (Scheme 4.2). Methanol (100 ml) solution containing 5-aminoisophthalic acid (5 mmole, 0.9649 g) was dropped wisely into the methanol solution (10 ml) containing 1.20 g (11 mmole) of 1,2-phenylenediamine and 2.15 g (11 mmole) of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) in methanol. The mixture was stirred overnight at room temperature. The white powder obtained was filtered and washed several times by methanol. The white powder was dried in vacuum at 80°C for 6 h, dissolved in ethylene glycol (100 ml) and refluxed under vacuum at 150°C for 24 h. The solvent was removed and the crude product was dried in vacuum at 80°C for 6 h.

Characterization: 58.5% yield; brown powder; FT-IR (KBr, cm^{-1}): 3200-2500 (medium, hydrogen bonded N-H stretching); 1628 (strong, C=N stretching); 1450 (strong, skeleton vibration of benzimidazole ring); 745 (strong, aromatic C-H bending). Mass spectrometry (m/z): 325.70. FW of $C_{20}H_{15}N_5$: 325.

Scheme 4.2 Preparation of **2** via pathway A.

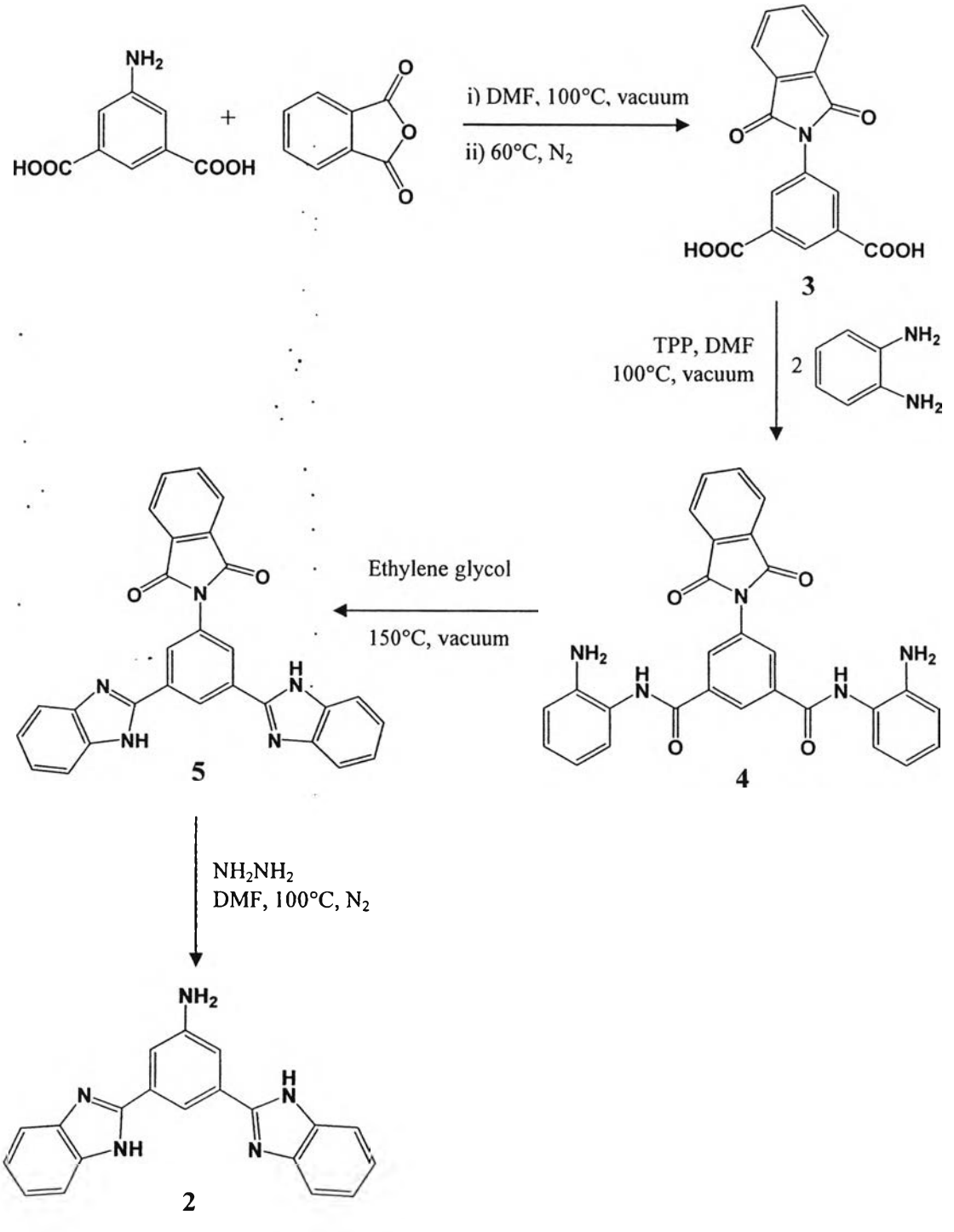


Synthesis of 2 via pathway B (Scheme 4.3). Phthalic anhydride (4 mmole, 0.62 g) and 5-aminoisophthalic acid were dissolved in dimethylformamide (20 ml) and stirred at 100°C under vacuum for 8 h. The crude product, **3**, was obtained by removing the solvent followed by washing with methanol. The solution of **3** in dimethylformamide was dropped wisely into the mixture of 1,2-phenylenediamine (4 mmole, 0.44 g) and triphenyl phosphite (4 mmole, 2 ml) in dimethylformamide (50 ml) and stirred at 100°C for 6 h. The solvent was removed and the product was dried in vacuum at 80°C for 6 h. The product obtained was dissolved in dichloromethane before extracting with saturated $NaHCO_3$ aqueous solution. The organic layer was treated with Na_2SO_4. The solvent was removed to obtain **4**. Compound **4** was dissolved in ethylene glycol (50 ml) and refluxed at 150°C under vacuum for 24 h to obtain **5** after removing solvent and washing with methanol. Compound **5** was stirred in dimethylformamide and heated to 100°C under nitrogen. Hydrazine monohydrate was added and stirred for 1 h. After solvent removing, light pink solid was obtained and recrystalized by ethyl acetate to give the colorless crystal.

Characterization: 27.5% yield; colorless crystal; FT-IR (KBr, cm^{-1}): 3429 (medium, N-H stretching); 3150-2500 (medium, hydrogen bonded N-H stretching); 1620

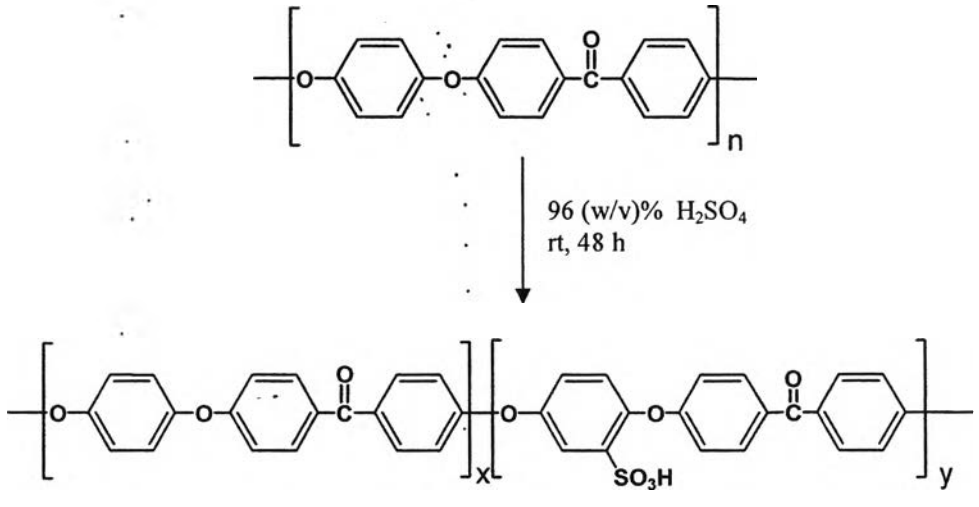
(strong, C=N stretching); 1481 (medium, skeleton vibration of benzimidazole ring); 770, 741 (medium, aromatic C-H bending). ^{1}H NMR (DMSO-d_6): δ 8.13 (7H, s, Ar-**H**); 7.94 (4H, d, Ar-**H**). Mass spectrometry (m/z): 319.68. FW of $C_{20}H_{15}N_5$: 325.

Scheme 4.3 Preparation of **2** via pathway B.



Sulfonation of poly(ether-ether-ketone) (PEEK) (Scheme 4.4). The sulfonation was carried out as follows. An amount of PEEK (6g) was gradually added into 96% sulphuric acid (300 ml) and vigorously stirred for 48 h at room temperature. The solution was precipitated in ice water and washed with deionized water until neutral. The precipitates were dried in a vacuum at 70°C for 24 h. Characterization: 80% yield; FT-IR (KBr, cm^{-1}): 3500-2500 (broad, O-H stretching); 1078, 1021 (medium, sym, asym O=S=O stretching). ^1H NMR (DMSO-d_6): δ 7.74 (4H, m, C**H**-C-C=O); 7.48 (1H, s, C**H**-C-SO_3H); 7.22 (2H, s, Ar-**H**); 7.10 (4H, m, Ar-**H**); 7.00 (4H, d, Ar-**H**).

Scheme 4.4 Sulfonation of poly(ether ether ketone).



4.4 Results and Discussion

Synthesis of 1. Compound **1** was prepared from two steps; amidation of terephthaloyl chloride and 1,2-phenylendiamine and benzimidazole cyclization. In amidation, the dilute concentration of terephthaloyl chloride in xylene was added dropwisely into an excess amount of 1,2- phenylendiamine for suppressing the polymerization between both starting materials. The brown precipitate was collected after the reaction was proceeded for 12 hours. The characterization confirms the formation of 1' (Figure 4.2(a)), for example, the appearance of peaks at 1648 and 1534 cm^{-1} referring to C=O stretching vibration of amide I and N-H bending

vibration of amide II, respectively. This implied that an intermediate was easily occurred without the addition the catalyst. This might be due to the strong reactivity of terephthaloyl chloride and the acidity of the by-product (HCl). For the benzimidazole ring closure, the precipitate was refluxed in NMP at 150°C under vacuum to form benzimidazole rings by dehydration. FT-IR spectrum (Figure 4.2(b)) shows the important peaks of the intermediate obtained which are hydrogen bonded N-H stretching of benzimidazole unit at 3200-2500 cm^{-1}, skeleton vibration of benzimidazole ring at 1440 cm^{-1} and C-H bending of aromatic at 743 cm^{-1}.

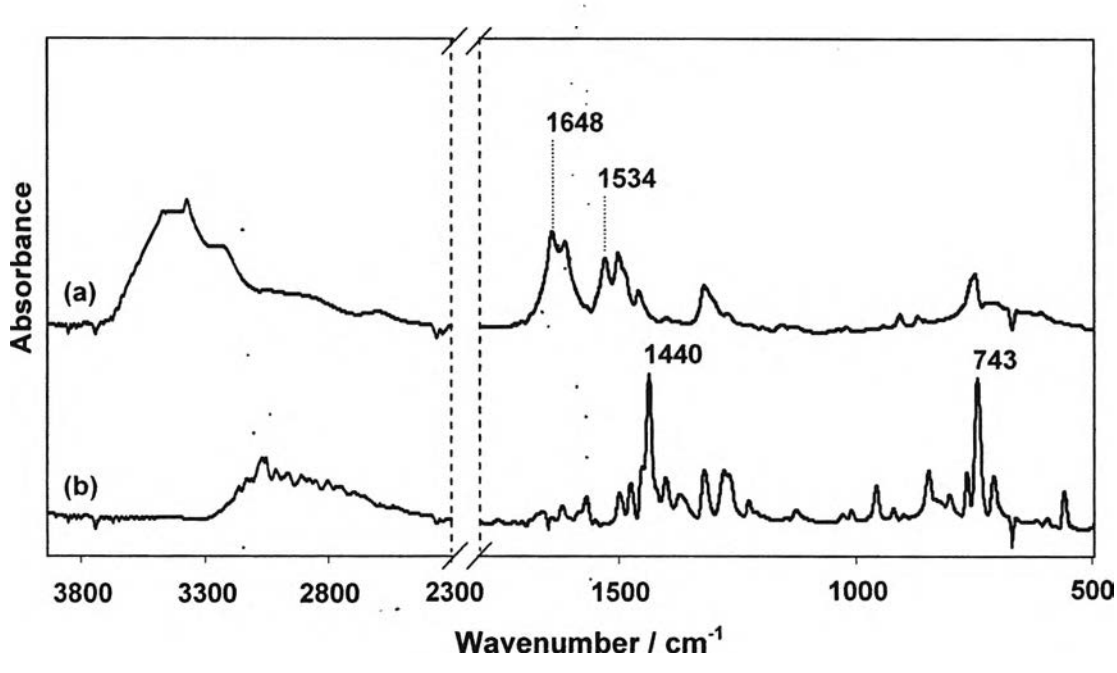


Figure 4.2 FT-IR spectra of **1'** (a) and **1** (b).

^{1}H-NMR spectrum (Figure 4.3) indicates the peaks related to the structure of **1**. The singlet signal at 8.35 ppm corresponds to 4 protons of Ar-**H** position of aromatic ring at the center. The doublet peaks at 7.40 and 7.20 ppm refer to Ar-**H** position of benzimidazole ring. In addition, MALDI-TOF mass spectrum (Figure 4.4) confirms the successful preparation of **1**. The parent peak at m/z = 310.64 which confirms the molecular weight of 1 (formular weight of 1 = 310).

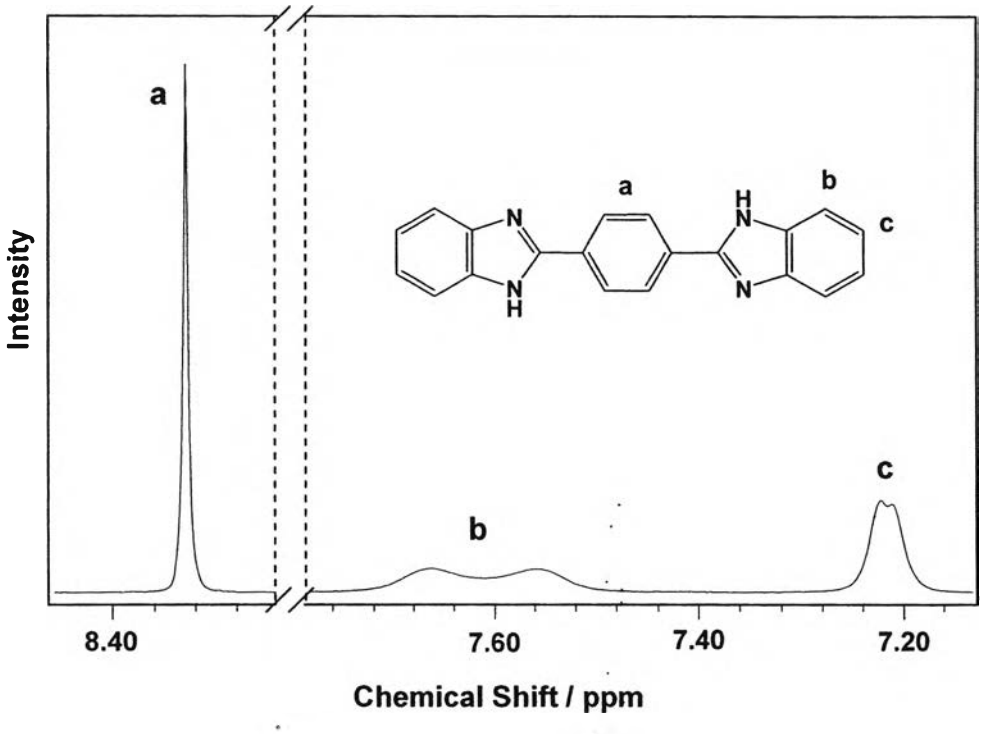


Figure 4.3 ^{1}H-NMR spectrum of **1**.

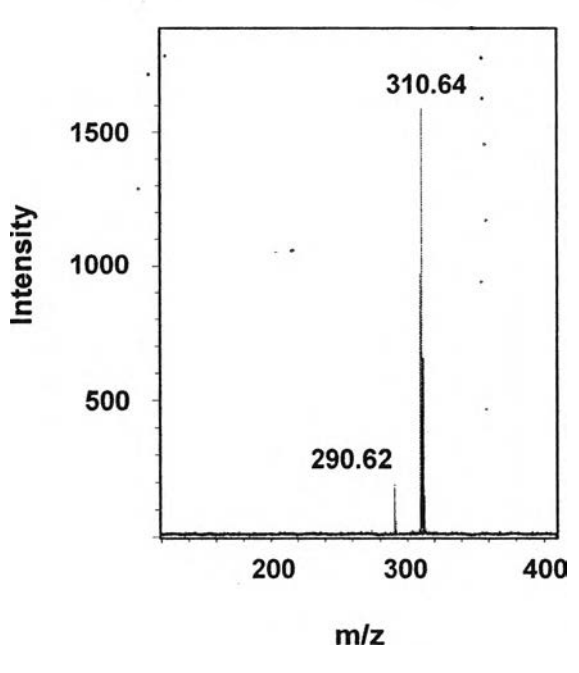


Figure 4.4 MALDI-TOF mass spectrum of **1.**

Synthesis of 2 following pathway A. Compound **2** was synthesized by a direct condensation (amidation) between 5-aminophthalic acid and 1,2-phenylendiamine using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide

hydrochloride (EDC) as a coupling agent and a ring closure reaction under vacuum at high temperature (Scheme 4.2). In the direct condensation, EDC reacts with two carboxyl groups on 5-aminoisophthalic acid to form amine reactive *O*-acylisourea intermediate. The conjugation with an amino group of 1,2-phenylenediamine gives a stable amide linkage molecule. Compound **2'** shows the characteristic peaks at 1633 cm^{-1} (amide I), 1517 cm^{-1} (amide II) implying the amide bond on the molecule (Figure 4.5(a)). The ring closure is confirmed from the two absorption peak at 1450, 1628 cm^{-1} corresponding to the skeleton vibration of benzimidazole ring and C=N stretching vibration of benzimidazole ring are observed, respectively (Figure 4.5(b)).

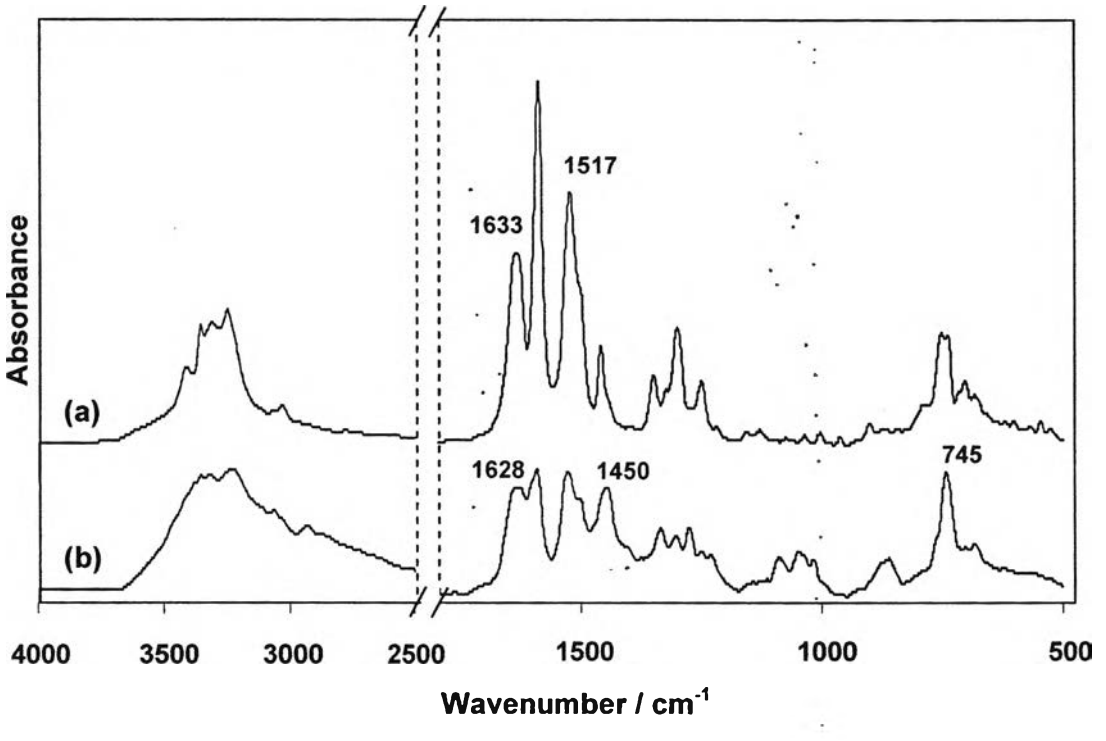


Figure 4.5 FT-IR spectra of **2'** (a) and **2** (b).

MALDI-TOF mass spectrum (Figure 4.6) shows a peak at m/z = 325.70 corresponding to the molecular weight of **2**. The other peaks at m/z = 343.72 and 526.16 might represent mono-substituted benzimidazole and oligomer species formed in the reaction (Scheme 4.5). As there were by-products in the system which might be due to the incompleted ring closure and self condensation. The purification was further considered.

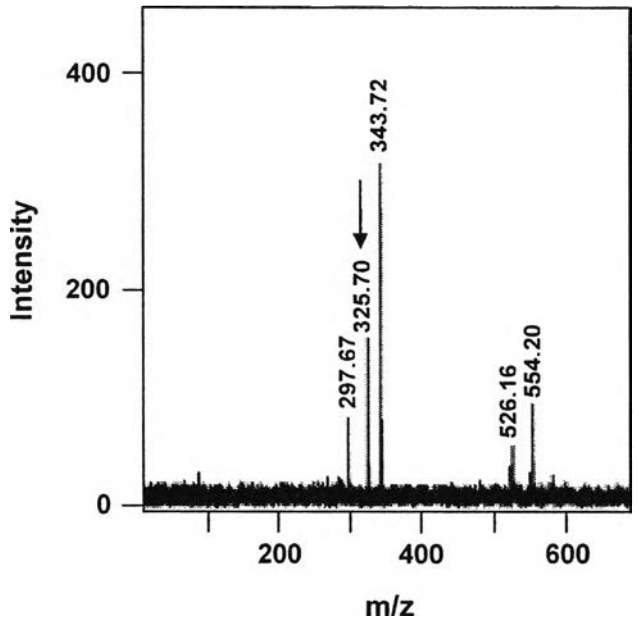
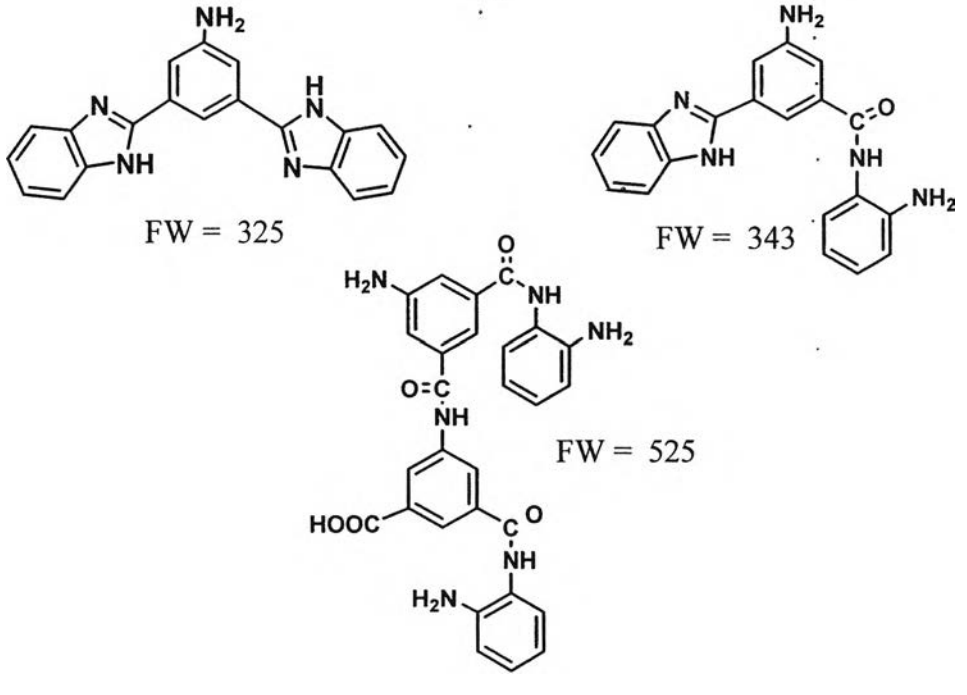


Figure 4.6 MALDI-TOF mass spectrum of crude product from the pathway A.

Scheme 4.5 Probable structures of by-products.



In order to purify the mixture of **2**, the column chromatography technique was applied. However, the structures of the by-products are so similar and this obstructs the efficient separation.

To achieve **2** without or small amount of impurities, we consider how to avoid the self condensation reaction when EDC is incorporated to the reaction. The amino group of acid molecule needs to be protected before reacting with 1,2-phenylenediamine and EDC to reduce the possibility of side reactions.

Synthesis of 2 following pathway B. In this procedure, we focused on amidation reaction between two carboxylic groups on 5-aminoisophthalic acid and a single amino group of 1,2-phenylendiamine. To achieve this goal, the protection of the amino group with phthalic anhydride was carried out in the first step. Figure 4.7(a) shows the phthalimido characteristic peaks at 1776 and 1714 cm^{-1} referring to carbonyl anhydride[13] and 1730 cm^{-1} belonging to carbonyl group of dicarboxylic acid containing on 5-aminoisophthalic acid. The amidation was further carried out by using triphenylphosphite (TPP) as dehydrating agent to form amide linkage. Figure 4.7(b) shows two peaks at 1660, 1596 cm^{-1} referring to amide I and amide II. In this step, small molecules, i.e. water, was generated as a by- product and the product obtained was purified by $NaHCO_3$ and water, respectively. For benzimidazole ring closure, the solution was refluxed at 150°C for 24 h. Figure 4.7(c) shows the absorption band at 1639 cm^{-1} corresponding to C=N stretching vibration of benzimidazole ring[8]. Hydrazine monohydrate was added to deprotect the amino group. The pink solid was obtained and was recrystallized in ethyl acetate to obtain the colorless needle-liked crystal. Figure 4.7(d) shows the characteristic peak corresponding to benzimidazole ring at 3429 cm^{-1} (intramolecular N-H stretching vibration), a broad band at 2500-3200 cm^{-1} (intermolecular N-H stretching vibration), a strong absorption peak at 1620 cm^{-1} (C=N stretching vibration), a medium peak at 1481 cm^{-1} (skeleton vibration of benzimidazole ring) and a peak at 741 cm^{-1}(C-H bending of benzene ring).

Figure 4.8 shows ^{1}H-NMR spectrum of **2**. The singlet signal at 8.14 ppm represents 7 protons of -C=C**H**-C= of benzimidazole and benzene groups. The doublet signal at 7.94 ppm is referred to 4 protons of -C=C**H**-C= of benzimidazole group.

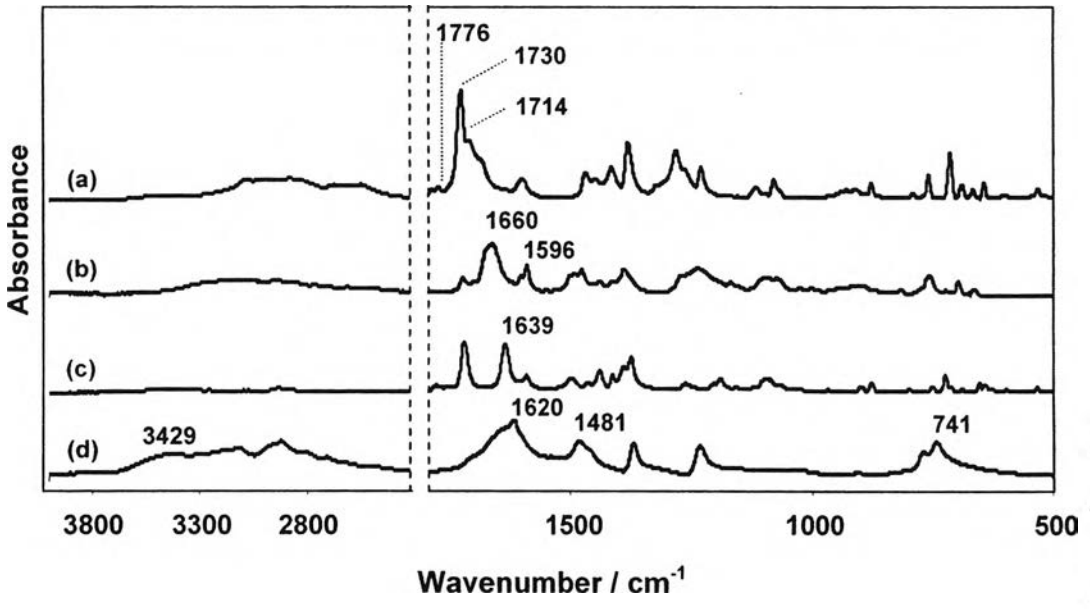


Figure 4.7 FT-IR spectrum of **2** from the pathway B.

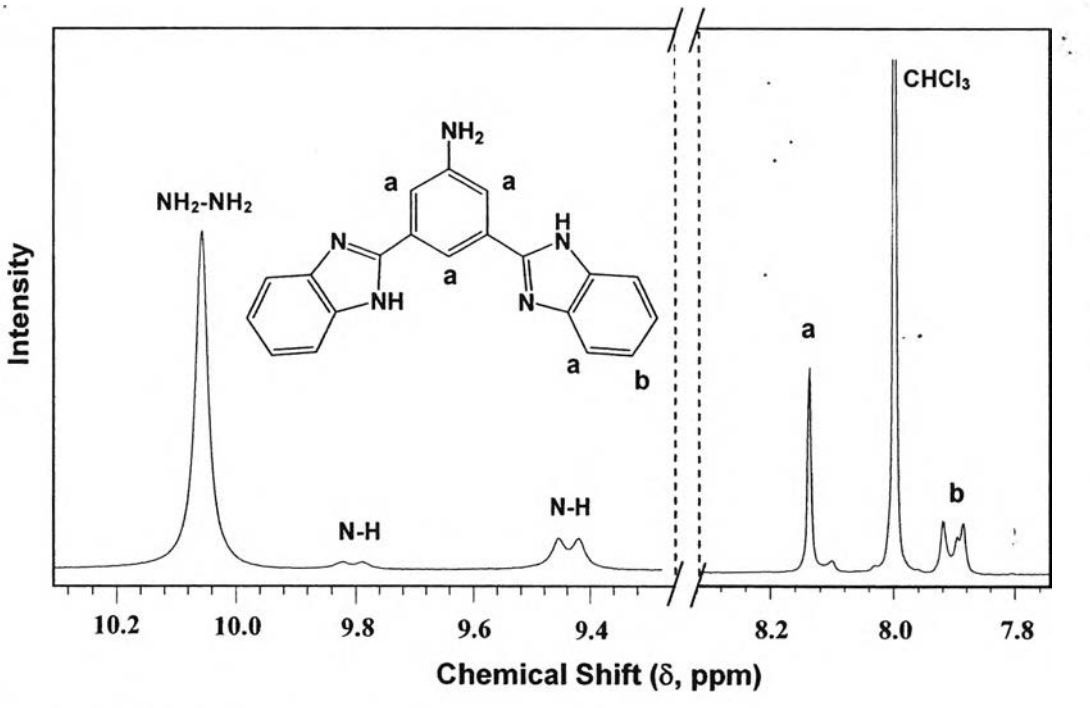


Figure 4.8 ^{1}H-NMR spectrum of **2** from pathway B.

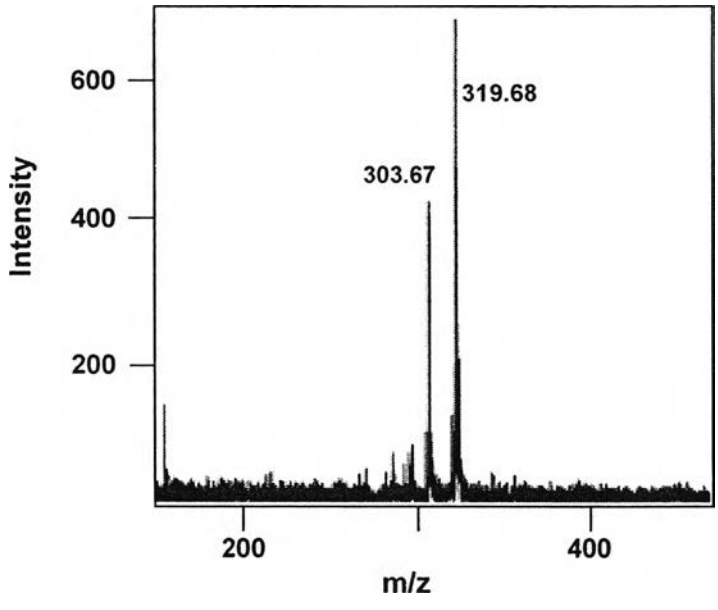


Figure 4.9 MALDI-TOF mass spectrum of **2** from pathway B.

MALDI-TOF mass spectrum is expected to represent the strongest intensity at m/z = 325 referring to molecular weight of **2**. However, Figure 4.9 shows two peaks at m/z = 319.68 and 303.67 which is a little lower than an ideal value. They might be due to the fragmentation of the molecule during measurement.

Sulfonation of PEEK. Figure 4.10(b) confirms the successful preparation of SPEEK. As compared to Figure 4.10(a), the broad band at 2500-3500 cm^{-1} is due to the O-H stretching of sulfonic acid group (SO_3H) where as the new absorptions at 1021 and 1078 cm^{-1} are assigned to symmetric and asymmetric stretching vibration of O=S=O belonging to sulfonic acid group[14].

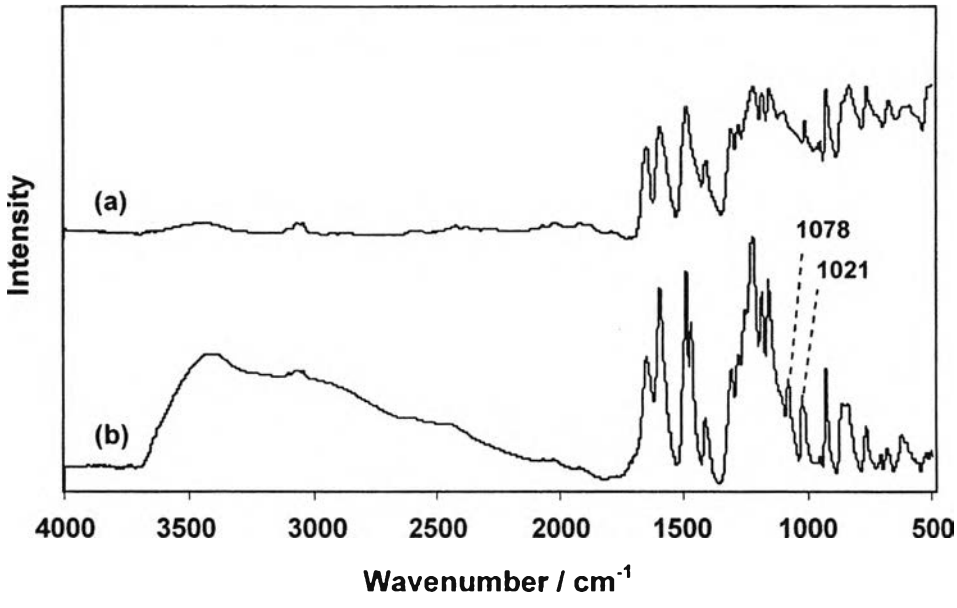


Figure 4.10 FT-IR spectra of PEEK (a) and SPEEK (b).

^{1}H-NMR was applied to quantity of the degree of sulfonation. The degree of sulfonation (DS), expressed as the number of $-SO_3Na$ groups per average repeat unit of the SPEEK. The DS can be calculated from the following equation:

$$\frac{n}{12\text{-}2n} = \frac{A_{H_{13}}}{\sum A_{H_{1\text{-}15}}} \qquad 0 \le n \le 1 \qquad (1)$$

Based on the structure in Figure 4.11, H_1, H_2, H_3, and H_4 of non-sulfonated repeat units show their characteristic singlet peak at ~7.02 ppm. When the sulfonic functional group is introduced to the aromatic ring, the signal of H_{13} protons (the singlet at ~7.5 ppm) is also appeared. According to the equation 1, the degree of sulfonation is 0.63. The DS is known to reflect the solubility of SPEEK in solvents. If the DS is approximately less than 0.4, SPEEK is insoluble in a conventional solvent such as DMF, DMAc, DMSO and NMP. When the DS of SPEEK exceeds 0.7, it is soluble in methanol but still exhibits poor chemical stability in hot water. Therefore, the SPEEK obtained with DS = 0.63 is suitable for membrane preparation in common solvent such as DMF, DMSO and NMP in further step.

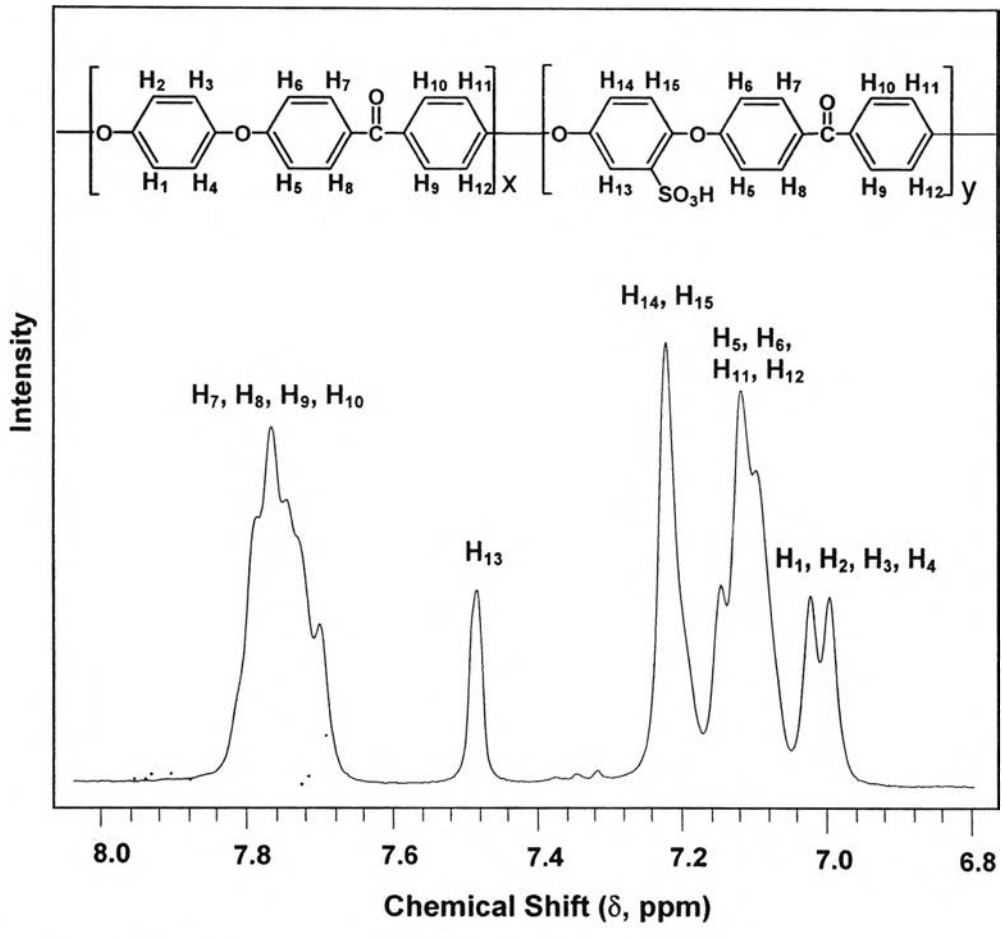


Figure 4.11 ^{1}H-NMR spectrum of SPEEK.

4.5 Conclusions

1,4-Di(1H-benzo[d]imidazol-2-yl)benzene, **1** was successful prepared by the amidation and cyclization reactions between terephthaloyl chloride and 1,2-phenylenediamine as confirmed by FT-IR, ^{1}H-NMR, MALDI-TOF MS and EA characterization techniques. 3,5-Di(1*H*-benzo[*d*]imidazol-2-yl)benzenamine, **2** was successfully obtained from the pathway with amino group protection. The compound obtained showed colorless crystal. The work also extended to develop the condition for sulfonation of SPEEK. The proton conductivity of **1** and **2** and the single crystal analysis including the blend with SPEEK were studied and achieved the information for future work.

4.5 Acknowledgements

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