CHAPTER VI
SYNTHESIS OF POLYDIACETYLENE CONTAINING AZA-CROWN-ETHER BASED ON N,N-BIS(ALKYL-2-HYDROXYL)ALKYLAMINE DERIVATIVES AS A PENDANT MOIETY

6.1 Abstract

Although the preparation of polydiacetylenes (PDAs) monomers containing crown ethers have been reported, the complicated syntheses including low-yield of obtained products limit their uses in only basic-knowledge research. This present work shows a simple approach to synthesized PDAs monomers having an aza-crown ether as a pendant group through the chemistry of N,N-bis(alkyl-2-hydroxybenzyl)alkylamine (HBA). All synthesis steps show reasonable-high yield, more than 40% which only recrystallization is needed to obtain the high-purity products for further topochemical polymerization in the next step.

Keywords: benzoxazine, polydiacetylene, aza-crown ether, HBA derivatives

6.2 Introduction

Polydiacetylenes (PDAs) are known as conductive polymer under a highly ordered orientation of ene-yne conjugate backbone.[1, 2] In most cases, diacetylene monomers are preorganized as mono-layered thin film or crystal so that the topochemical reaction via UV- or γ- irradiation consequently initiates the formation of polydiacetylene chains.[3-6] Structurally, a favorable preorganization of diacetylene monomer is under the conditions of closed-packing structure, i.e., repeat distance ~5 Å, orientation angle ~45°.[7, 8] Alternatively, polymerization by thermal treatment in solid [9, 10] or melt [11] state was also reported.

The conjugated back bone of PDAs allows electron transfer and gives unique electrical and optical properties for promising applications, especially, sensors .[12] Ionic or molecular sensing is one of the most expected applications in the forms of hazardous-organic or toxic-metal sensor. However, to enhance the specific external stimuli, appropriate receptors to recognize the complexes are needed.[4, 13]

Crown ethers are ether-bonded cyclic molecules which are well known as host molecules for ions and molecular recognition.[14, 15] The guest-selectivity depends on the cavity size, the number of ether unit.[15, 16] To improve the molecular recognition of PDAs, modification of PDAs with crown ethers for analytical and pharmaceutical fields were reported.[17, 18] It should be noted that as preparation of crown ethers including the purification is multi-steps whereas the yields are not significant, other alternative receptors are still on the expectation.

In the past, Laobuthee et al. reported the synthesis of N,N-bis(alkyl-2-hydroxybenzyl)alkylamine (HBA) compounds, which are obtained from a single-ring opening of benzoxazine monomer with monophenols.[19] Due to an inter-and intra-molecular hydrogen bond of those compounds, the compounds terminate itself at the dimer level to terminate the reaction. This brings a high selectivity to yield a single type of macrocycle for about 80%.[20-22] Those macrocyclic compounds also show the molecular recognition as evidenced from the entrapments of alkaline and alkaline-earth cations, and perchlorate anions. [23, 24] However, the specificity for the guest recognition of those macrocycles is still studied in depth.

Based on this viewpoint, here, we propose a unique molecular design and synthesis of HBA based crown ether containing an alkyne functional group. The compound obtained is expected to perform as a PDA monomer for polymerization in further step. The fact that the monomers contain symmetrical aromatic ring and each monomer give rigid cavity (Scheme I), one expects for a promising self-organization under supramolecular stacking-conformation. In combination with a high-ordered orientation in solid state under the crystal forms, the polymerization of the crystals may give us a nano-channel formed by crown-ether

6.3 Experimental

6.3.1 Materials

Propargylamine (98%), 2,4-dimethylphenol, 1,4-butanediol, diethylene glycol, p-toluenesulfonyl chloride and N, N, N', N`-tetramethylethylaminediamine (TMEDA) were received from Sigma-Aldrich (Country). Acetonitrile, 1,4-dioxane, 2-propanol, pyridine, sodium hydroxide (NaOH) and 37% formaldehyde solution were obtained from Fisher (Country). Copper (I) chloride (CuCl) was purchased from Across, Belgium.

6.3.2 Preparation of 6,8-dimethyl-3-(prop-2-ynyl)-3,4-dihydro-2H-benzo[e][1,3]oxazine (2,4DM-pa)

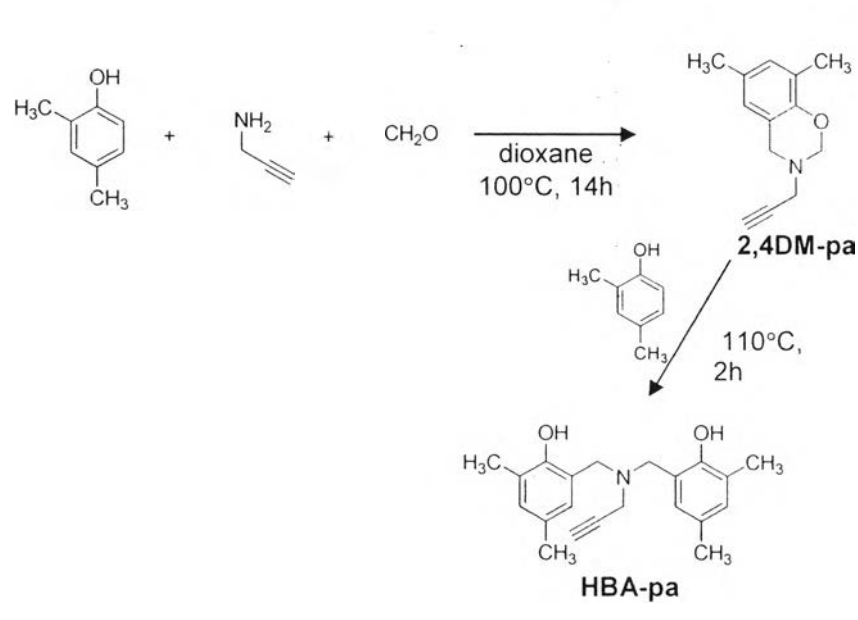
Propargylamine (1.65 g, 30 mmol) and formaldehyde (37% w/w in water) (5.12 g, 60 mmol) were added in dioxane (20 ml), and stirred at room temperature for 30 min. 2,4-Dimethylphenol (3.66 g, 30 mmol) in dioxane (10 ml) was further added and stirred at 100°C for 14 hours. After removal of solvent, the crude product was dissolved in ethyl acetate (100 ml), and then washed with 0.1 N NaOH (100 ml) and water (100 ml) for three times each. The solution obtained was dried over sodium sulfate anhydrous. The solvent was removed to obtain the yellowish viscous product of **2,4DM-pa**, and it was used for next-step synthesis without any further purification. ^{1}H NMR ($CDCl_3$), ppm: δ = 2.32 (s, C≡CH), 3.51 (s, CH_2), 3.83 (s, CH_2, oxazine), 4.92 (s, CH_2, oxazine), 6.65 (s, H Ar) and 6.83 (s, H

Ar). FT-IR ν (cm-1) (KBr) = 3290 and 2120 (C≡C), 1490 (tetrasubstitued benzene ring), 1216 (C-O-C asymmetric stretching) and 936 (out-of-plane C-H).

6.3.3 Preparation of 6,6'-(prop-2-ynylazanediyl)bis(methylene)bis(2,4-dimethylphenol) (HBA-pa)

2,4DM-pa (0.33 g, 1.6 mmol) and 2,4-dimethylphenol (0.20, 1.6 mmol) were mixed and stirred in melting state at 110°C for 2 hours (Scheme 6.1). The crude product obtained was recrystalized in 2-propanol to obtain needle-like crystal of **HBA-pa** (yield ca. 44.0%). ^{1}H NMR ($CDCl_3$), ppm: δ = 2.38 (s, C≡CH), 3.30 (s, CH_2), 3.29 (s, N-CH_2-C≡C), 3.81 (s, N-CH_2-Ar), 6.80 (s, H Ar), 6.88 (s, H Ar) and 7.60 (br, -OH). ^{13}C NMR (DMSO-d6) ppm: δ = 40.19 (N-C-C≡C), 54.58 (N-C-Ar) and 77.80 (C≡C). FT-IR ν (cm^{-1}) (KBr) = 3400 (-OH), 3290 (C≡C), 2120 (C≡C), 1490 (tetrasubstitued benzene ring) and 1200 (C-N-C). ESI MS (m/z): 378.26 ($M+H^+$).

Scheme 6.1 Synthesis of **2,4DM-pa** and **HBA-pa**



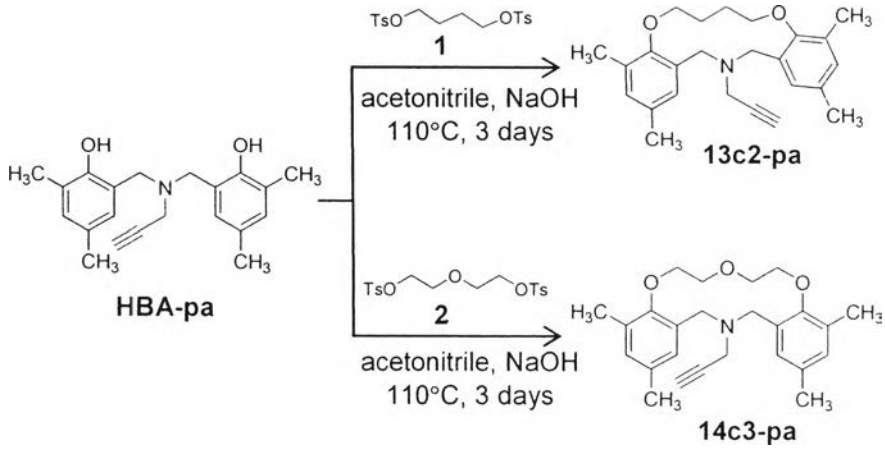
6.3.4 Preparation Dibenzo-monoaza-13-crown-2 propargyl (13c2-pa)

HBA-Pa (0.323 g,1.0 mmol) was dissolved in acetonitrile (100 ml) with NaOH (0.084 g,2.1 mmol) . The solution was stirred for 30 min, followed by adding butane-1,4-diyl bis(4-methylbenzenesulfonate),**1,** (0.399 g, 1.0 mmol) in acetonitrile (50 ml) solution dropwisely. The mixture was stirred at 110°C for 72 h (Scheme 6.2). The mixture was filtrated and the solvent was removed followed by recrystallizing in 2-propanol to obtain needle-like clear crystal (yield ca. 43.7%). ^{1}H NMR ($CDCl_3$), ppm: δ = 2.02 (t, C-CH_2-C), 2.46 (s, C≡CH), 3.14 (s, N-CH_2-C≡C), 3.76 (s, N-CH_2-Ar), 3.98 (t, Ar-O-CH_2-C), 6.92 (s, H Ar) and 7.09 (s, H Ar). FT-IR ν (cm^{-1}) (KBr) = 3290 (C≡C), 2120 (C≡C), 1080 (Ar-O-CH_2) and 1200 (C-N-C). ESI MS (m/z): 378.26 ($M+H^+$).

6.3.5 Preparation Dibenzo-monoaza-14-crown-3 propargyl (14c3-pa)

14c3-pa was prepared from **HBA-Pa** and 2,2'-oxybis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate), **2,** by using the same procedure as that of **13c2-Pg** to obtain needle-like clear crystal (yield ca. 27.0%). ^{1}H NMR ($CDCl_3$), ppm: δ = 2.40 (s, C≡CH), 3.10 (s, N-CH_2-C≡C), 3.78 (s, N-CH_2-Ar), 3.96 (t, C-O-CH_2-C-O), 4.04 (t, Ar-CH_2-C-O), 6.91 (s, H Ar) and 7.03 (s, H Ar). ^{13}C NMR ($CDCl_3$) ppm: δ = 38.29 (N-C*-C≡C), 54.22 (N-C-Ar),74.54 (-C*≡CH) and 78.93 (-C≡C*H). FT-IR ν (cm^{-1}) (KBr) = 3290 (C≡C), 2120 (C≡C), 1051 (Ar-O-CH2), 1100 (CH_2-O-CH_2) and 1200 (C-N-C). ESI MS (m/z): 394.26 ($M+H^+$).

Scheme 6.2 Synthesis of dibenzo-monoaza-based **HBA-pa** derivatives



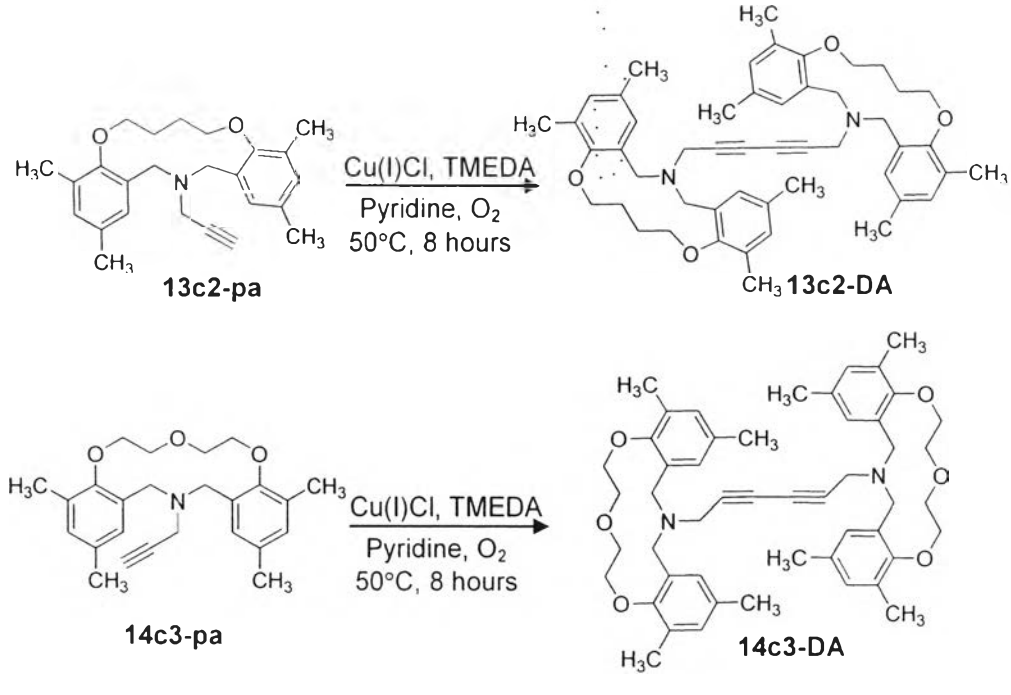
6.3.6 Preparation of dibenzo-monoaza-13-crown-2 diacetylene dimer (13c2-Da)

TMEDA (0.0147 g, 0.126 mmol) and CuCl (0.0125 g, 0.126 mmol) were dissolved in 1 ml pyridine with O_2 bubling. After stirring for 15 min, **13c2-pa** (0.0959 g,0.254 mmol) in pyridine (2 ml) was added dropwisely, and stirred at 50°C for 8 h , Scheme 6.3. The product was reprecipitated in water to obtain white powder, followed by recrystallization in mixed solvent (chloroform: 2-propanol, 4: 1 v/v) to obtain needle-like crystal.

6.3.7 Preparation of dibenzo-monoaza-14-crown-3 diacetylene dimer (14c3-Da)

14c3-Da was prepared by oxidative coupling reaction of **14c3-pa** in the same procedure as preparing **13c2-Da** to obtain needle-like clear crystal. (yield ca. 60.3%) ^{1}H NMR ($CDCl_3$), ppm: δ = 3.22 (s, N-CH_2-C≡C), 3.87 (s, N-CH_2-Ar), 3.95 (t, C-O-CH_2-C-O), 4.04 (t, Ar-CH_2-C-O), 6.92 (s, H Ar) and 7.01 (s, H Ar). ^{13}C NMR ($CDCl_3$) ppm: δ = 38.29 (N-C*-C≡C), 54.22 (N-C-Ar), 71.45 (-C≡C*-C*≡C-) and 74.12 (-C*≡CH).

Scheme 6.3 Synthesis of dibenzo-monoaza-crown diacetylene monomers



6.3.8 Structural Characterization

FT-IR spectra were collected with a resolution of 32 cm^{-1}on a Bomem Michaleson MB100 equipped with deuterated triglycine sulfide (DTGS) detector using KBr plate. ^{1}H and ^{13}C NMR spectra were acquired in deuterated chloroform (CDCl3) on a Varian NMR at a proton frequency of 200 MHz and a Varian Oxford AS600 at a carbon frequency of 150.9 MHz.

6.4 Results and Discussion

6.4.1 Synthesis of HBA-pa

HBA-pa obtained from oxazine-ring-opening reaction of 2,4 dimethyphenol and **2,4DM-pa** which was prepared from propargylamine, formaldehyde and 2,4 dimethylphenol as shown in Scheme 7.1. As shown in Figure 6.1, the spectrum (b) shows an appearance of OH functional group at 3400 cm^{-1} and the disappearance of C-O-C of oxazine ring at 1216 cm^{-1} and 936 cm^{-1}. The spectrum implies the ring-opening reaction of **2,4DM-pa** to be di-phenolic **HBA-pa**. . In addition, the strong peak at 3290 cm^{-1} corresponding to absorption of C≡C is observed, indicating an availability of propargyl moiety in **HBA-Pa**. ^{13}C NMR spectrum shows the characteristic peaks at 77.82 ppm (f) and 77.67 ppm (e), and the unique mannich-bridge carbon appears at 54.58 ppm (c) (Figure 6.2(A)). Also, ESI-mass spectrum shows the parent peak ($M+H^{+}$) at m/z = 324.22 (Cal.324.20) which confirms the structure of **HBA-pa** (Figure 6.2(B)).

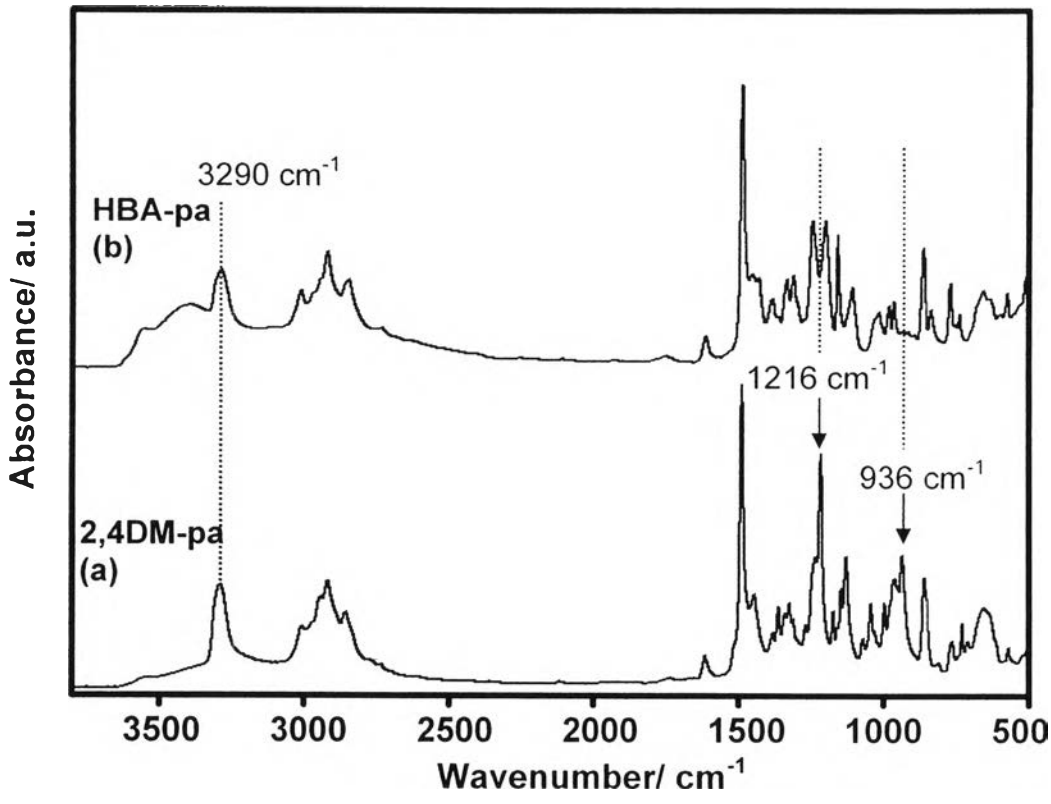


Figure 6.1 FT-IR spectra of **(a) 2,4DM-pa,** and **(b) HBA-pa**.

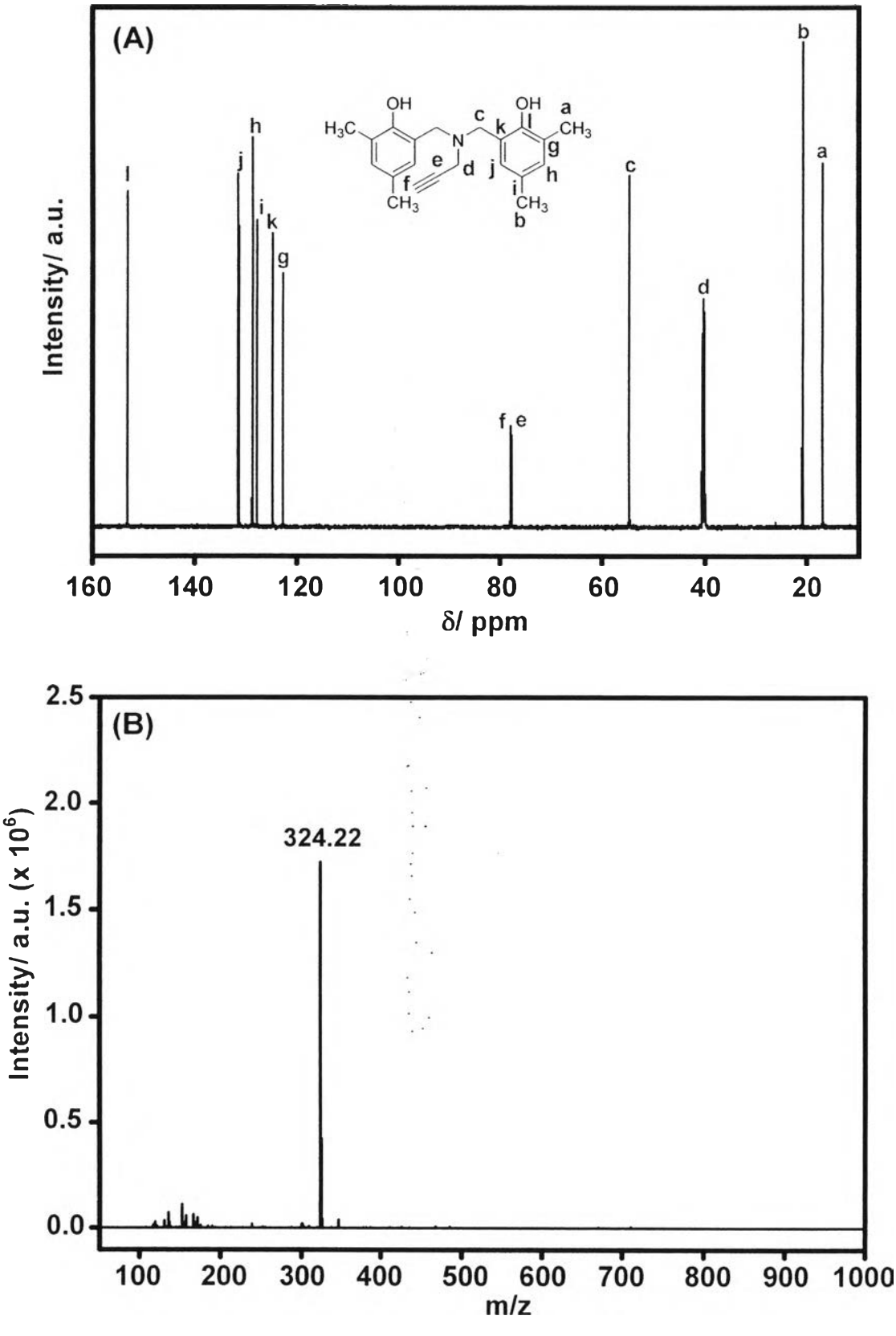


Figure 6.2 ^{13}C NMR (A) and ESI-mass (B) spectra of **HBA-pa**.

6.4.2 Synthesis of dibenzo-monoaza-crown based HBA-pa derivatives

The dibenzo-monoaza-crown compounds were synthesized from **HBA-pa** and ditosylated compounds as reported elsewhere. After the reaction for three days, the crude products were recrystallized to obtain needle-like crystal without any complicated purification. As compared to the FT-IR spectra of **1,** and **HBA-pa**, the spectrum of **13c12-pa** shows the characteristic peak of C≡C at 3290 cm^{-1} as observed in and the peak of Ar-O-C, ether bonds in aza-ether crown at 1080 cm^{-1} . Furthermore, it also shows the disappearances of the peaks at 1356 cm^{-1} and 1178 cm^{-1} which are typical characteristic peaks of -SO_2- as a result of nucleophilic substitution of di-phenol moieties in **HBA-pa** with tosylate-leaving groups in **1** (Figure 6.3).

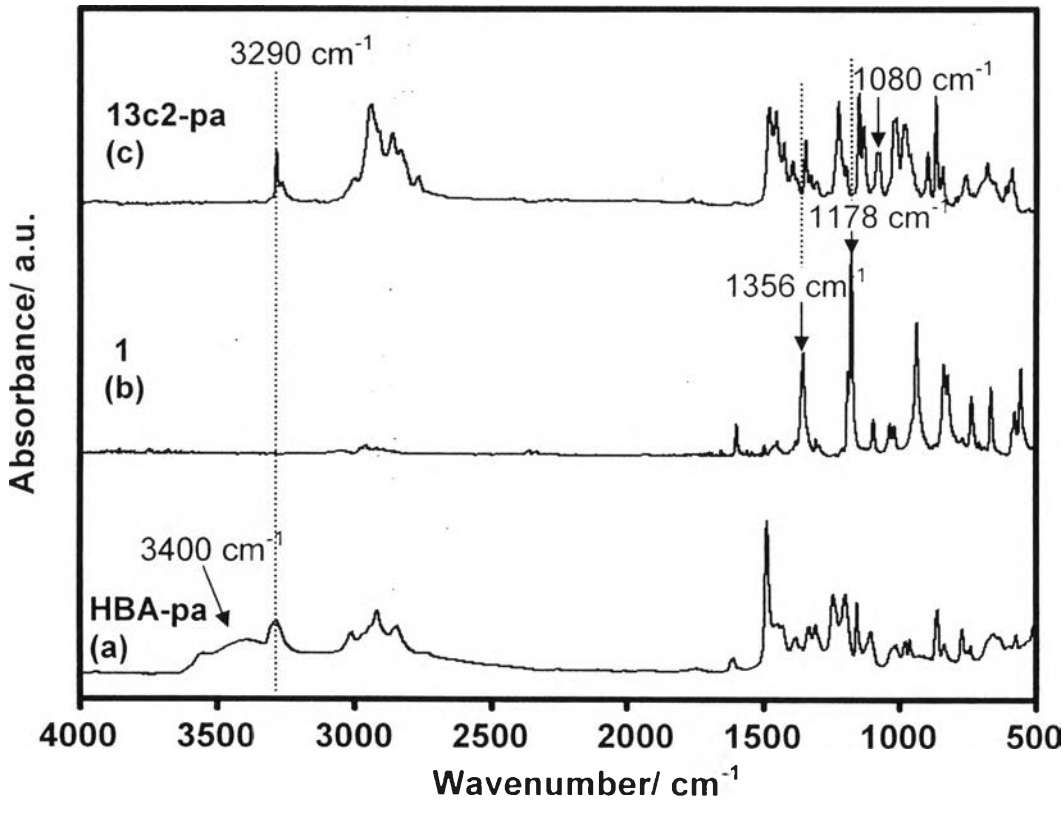


Figure 6.3 FT-IR spectra of (a) **HBA-pa**, (b) **1** and, (c) **13c2-pa**.

However, there are two possible structures which are [1+1] and [2+2] from this coupling cyclization. To verify the structure of the cyclic compounds, ESI-mass spectroscopy was used. The results clearly show the parent peak ($M+H^+$) at m/z = 378.26 (Cal.378.25) and m/z = 394.26 (Cal.393.23) indicating a [1+1] cyclic structure for both **13c12-pa** and **14c3-pa**, respectively. It is important to note that a specific macrocyclization might be based on the synergistic effect of metal template, i.e. Na^+ ion from NaOH, and H-bonds of HBA derivative compounds as seen in the case of HBA derivatives and ditosylated-propane which was reported previously.[22] Furthermore, the chemical structure of the macrocyclic products were confirmed by ^1H NMR as shown in Figure 6.5 for **13c12-pa** which is almost similar to **14c3-pa**. As shown in the spectrum (a), (b), and (c), the singlet proton at Manich bridge resonance at 3.81 ppm (e in (a)) and the doublet protons N-CH2-C≡C resonance at 3.31 ppm (f in (a),) of **HBA-pa**, slightly shifted to 3.98 ppm (e in (c)) and 3.16 ppm (f in (c)), respectively, are observed. The resonance protons of **1** (3.77 ppm (h in (c)) and 2.02 ppm (i in (c)) are also clearly seen. These confirm the successful preparation of **13c12pa**.

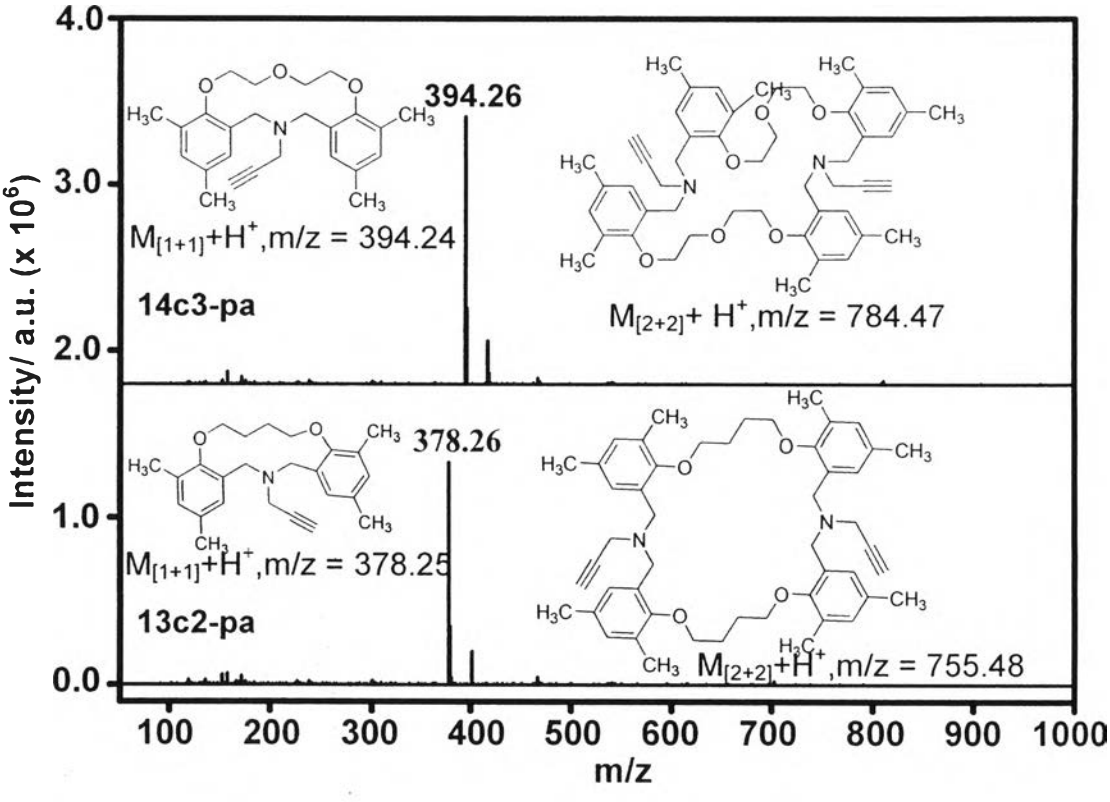


Figure 6.4 ESI-mass spectra of **13c2-pa** and **14c3-pa**.

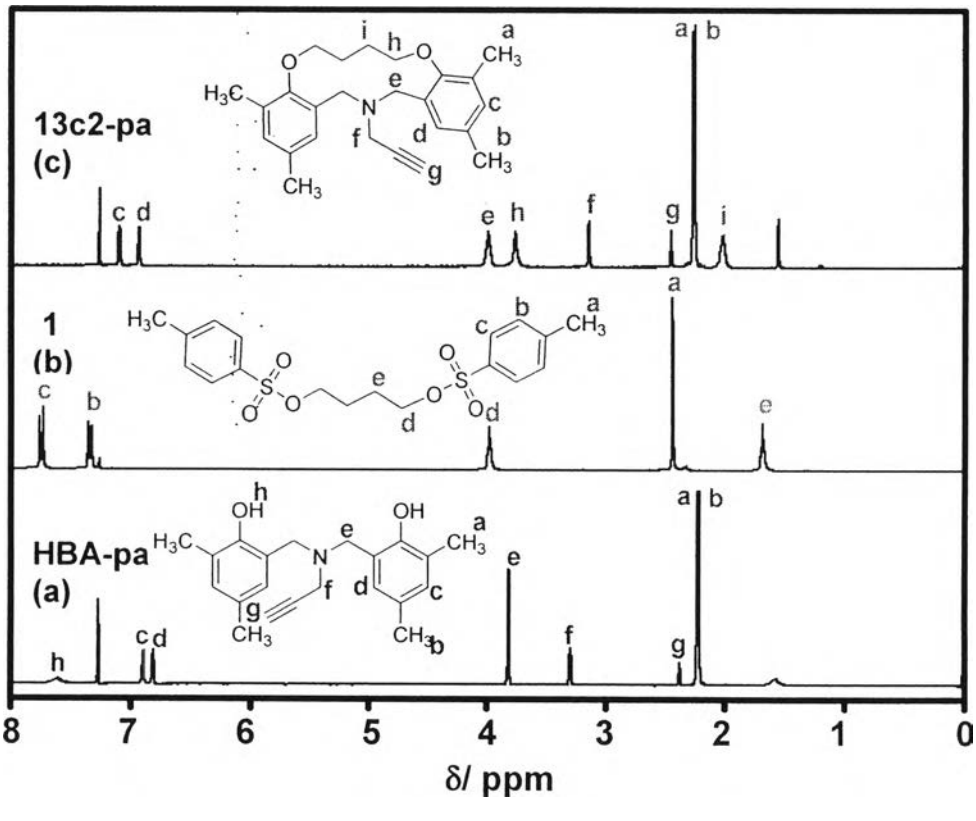


Figure 6.5 ^{1}H NMR spectra of (a) **HBA-pa**, compound (b)**1** and (c) **13c2-pa**

6.4.3 Synthesis of dibenzo-monoaza-crown diacetylene dimer

The dimerization of aza-crown-based **HBA-pa** compounds were firstly synthesized by oxidative coupling via Hay condition[25] (O_2, CuCl and pyridine) at room temperature. Due to insolubility of the intermediate compounds, the progress of the reaction was rather slow and it was not completed even for 72 h. Then, TMEDA was used as chelating agent for copper-catalyst complex which is soluble in various organic solvents.[26] The coupling reaction under the standard Hay condition (O_2, CuCl and TMEDA) shows faster reaction rate which it can be completed in 48 h. at room temperature. However, the coupling reaction can be accelerated under an elevated temperature of 50°C which the reaction can be accomplished within 8 h. The success of the reaction can be confirmed by the disappearance of C≡CH resonance at 2.40 ppm (b in A(a)) and shifting of the protons N-CH_2-C≡C resonance at 3.10 ppm (a in A(a)) to the higher field in ^{1}H NMR spectra (Figure 6.6A). The chemical structure of **14c3-DA** was further confirmed by ^{13}C NMR (Figure 6.6B) to find the disappearance of the carbon resonance of propargyl at 86.8 ppm (b in B (a)) and a new peak at 71.5 ppm (b in B(b)) assigning to the carbon of C≡C*- was observed. The results clearly clarify the structure of the dibenzo-monoaza-crown diacetylene dimers which successfully synthesized in high yield, ~65%.

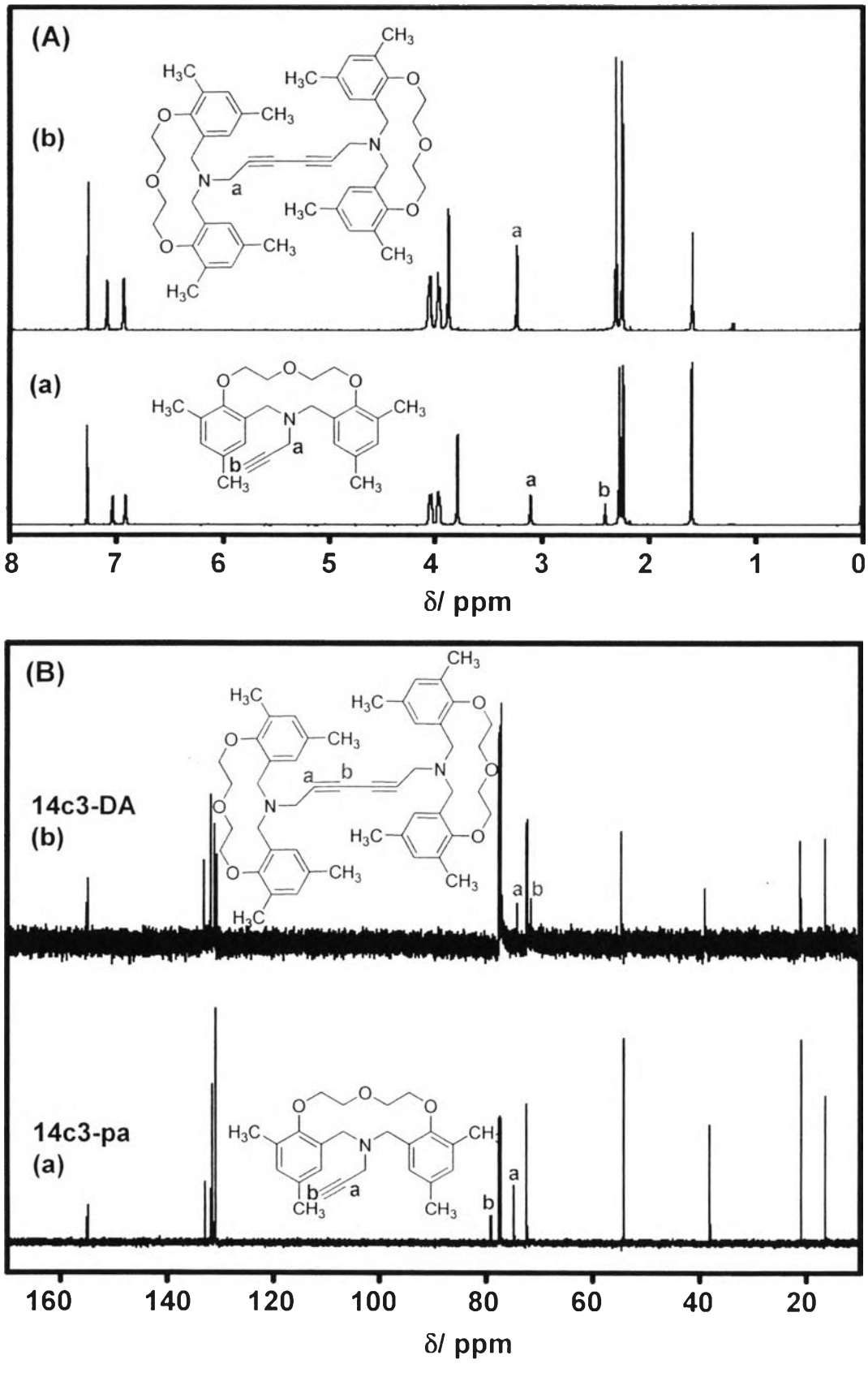


Figure 6.6 ^{1}H (A) and ^{13}C (B) NMR spectra of (a) **14c3-pa**, and (b) **14c3-DA**

6.5 Conclusions

Up to present, only a few successes to synthesize PDAs containing crown ethers have been reported. However, the synthesis of PDAs monomer deals with complicated synthesis and purification. This present work demonstrates the synthesis of PDAs monomers containing aza-crown ethers in a simple approach. All synthesis steps give the reasonable yield of high-purity products, more than 40%, which only recrystallization of crude products is needed.

6.6 Acknowledgements

S. C. and W. R. would like to express their gratitude to the Royal Golden Jubilee Program (the Thailand Research Fund (PHD/0058/2550)) for financial support for Ph.D program and short-term research of W. R. at Case Western Reserve University.

6.7 References

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