CHAPTER II
THEORETICAL BACKGROUP AND LITERATURE REVIEW

2.1 Supramolecular Chemistry

Supramolecular chemistry is related to the chemistry of the intermolecular non-covalent interactions (hydrogen bonding, metal coordination, hydrophobic force, van der Waals force, π-π interactions and electrostatic force), structures and functions of the supramolecules formed by the binding of substrate species to a molecular receptor (Lehn, 1995). Supramolecular system can exhibit molecular self-assembly, folding, molecular recognition, host-guest chemistry, mechanically-interlocked molecular architectures and dynamic covalent chemistry (Gennady *et al.*, 2007). Crown ether (Lindsten *et al.*, 1987), cyclodextrin (Tao, 1991) and calixarene (Bordunov *et al.*, 1995) are the good examples for macrocyclic structure in supramolecular system. Deoxycholic acid is a sample of self assembly compound (Audisio. 1984). In natural system, we can found the ideal cases of supramolecular structures such as protein structure, DNA, RNA, and enzymes (Ball, 1994).

2.1.1 Macrocyclic Chemistry

In supramolecular chemistry, macrocyclic compounds such as crown ethers, cryptans, cyclophanes, calixarenes, and cucurbiturils have received much attention for applying in catalysts, indicators and sensors due to their unique properties by employing the host-guest property (Ogoshi and Harada, 2008). One of the most important properties of macrocyclic compounds is inclusion phenomena of metal ions or guest molecules into its cavity that can completely surround guest molecules and may be chemically modified to fine-tune their properties (Ball, 1994). This leads to the development of synthetic supramolecules for using in many applications such as catalysts, indicators and sensors. Gianneschi *et al.* (2005) were developed functional macrocyclic supramolecular structures by weak-link approach (WLA) to supramolecular assemblies. This approach allows for the design of multi-metallic two- and three-dimensional arrays, host-guest architectures, sensors, catalysts, switches, and signal amplification devices. In some cases, supramolecules develop new functions such as magnetism, light, or pH responsive, etc. that do not appear in a single or

individual molecule. For example, Trippe *et al.* (2002) synthesized bis(pyrrolo)tetrathiafulvalene macrocycles which exhibited high binding affinities for Pb^{2+} and Ba^{2+} in order to induce optical or redox properties.

2.1.1.1 Macrocycle Synthesis

Normally, macrocyclic compound can be obtained via (i) simple cyclization, (ii) cyclization in conjugation with another molecule (capping) and (iii) condensation of two or four of bifunctional units as shown in Figure 2.1 (Dietrich, *et al.*, 1993).

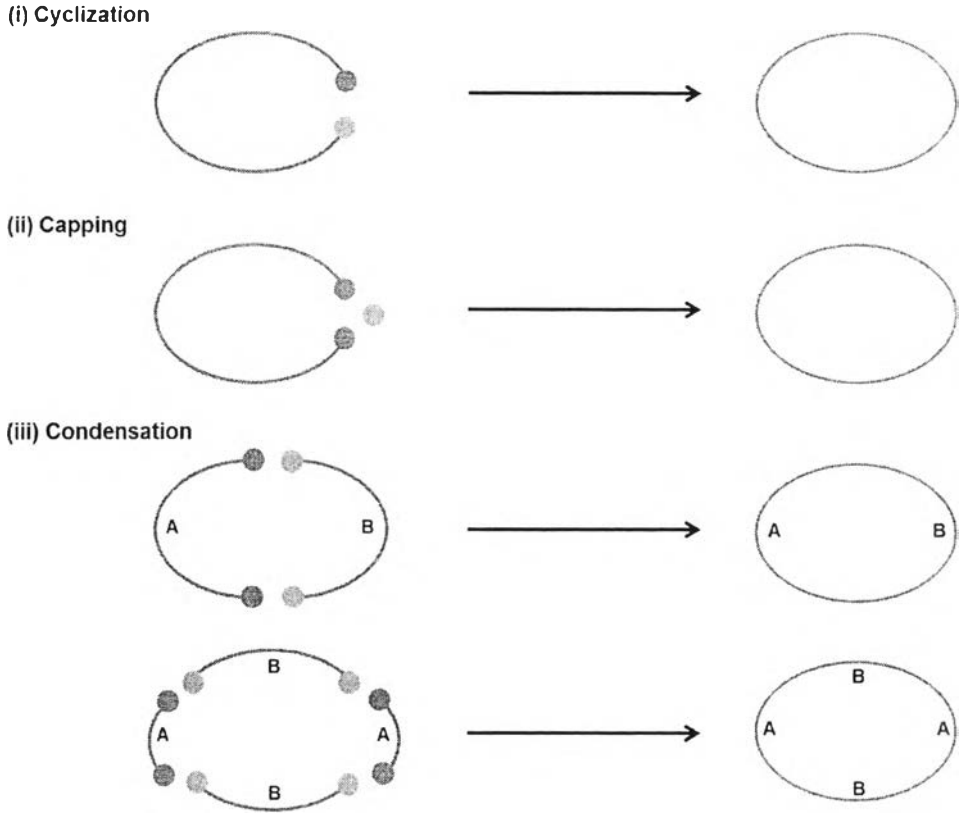


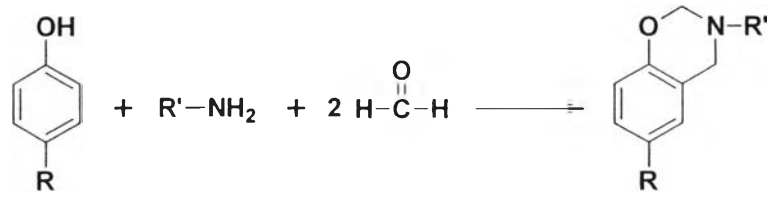
Figure 2.1 Methods of cyclization.

In general, macrocyclization was carried out in high dilution condition in order to favor intramolecular reaction over intermolecular reaction (Durola *et al.*, 2007). Moreover, the preparation of those macrocyclic compounds deals with complicated syntheses especially purification processes, and giving a low-yield product. For example, Mahbubul (2011) reported the template synthesis of macrocy-

clic compound derived from pyridine-2,6-dicarboxaldehyde and 1,2-bis(2-aminoethoxy)ethane with 30% yield.

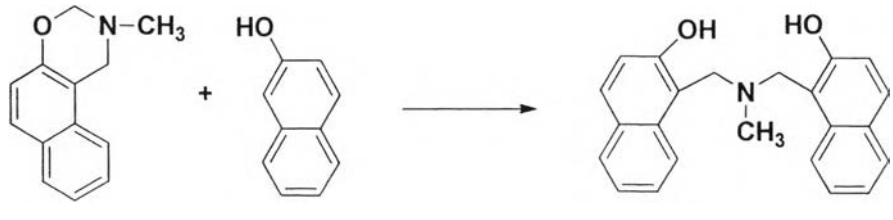
2.2 Development of Benzoxazines

Benzoxazines are heterocyclic compounds obtained from Mannich reaction between phenol, formaldehyde and amine derivatives (Scheme 2.1 (Burke, 1949)).



Scheme 2.1

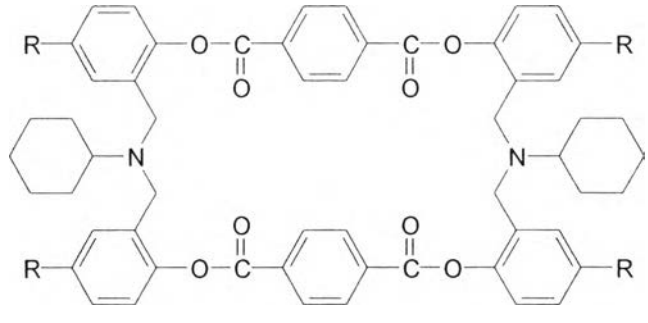
Burke *et al.* (1965) reported that the two unit of phenol linked with aza-methylene compound can be obtained by ring-opening reaction. This report is very useful since it is proven that the ring-opening reaction occurred preferentially at ortho position of phenols, which can be a guideline to design the many opened ring benzoxazines. For example, 2,3-dihydro-2-methyl-*1H*-naphth[1,2-e][1,3]oxazine reacted readily with 2-naphthol to give *N,N*-bis(2-hydroxy-l-naphthylmethyl)methylamine (Scheme 2.2).



Scheme 2.2

Benzoxazine monomers provide linear or cross-linked polymers depending on the reaction occurring at ortho and additional para positions. Ishida *et al.*(1994)

showed a successful polymerization of bisphenol-based benzoxazines to obtain a novel thermosetting polymer by ring-opening reaction. However, our group found that polymerization of benzoxazine tends to self-terminate at dimer level since the inter- and intramolecular hydrogen bonds of dimer (*N,N*-bis(2-hydroxybenzyl)alkylamine derivatives) are very strong to obstruct the continuous polymerization. *N,N*-bis(2-hydroxybenzyl)alkylamine derivatives show inclusion phenomena with transition metals. Moreover, we also succeeded in preparing the macrocyclic compounds based on benzoxazine chemistry without using template. The reaction of *p*-substituted phenol-based benzoxazine dimers with diacid chloride or ditosylated glycol is simple, selective and effective reaction without specific catalyst and further complicated purification to produce a series of macrocyclic ester and macrocyclic ether (**1** and **2**). Supramolecular chemistry of benzoxazine based macrocyclic compounds shows stoichiometric ratio of host-guest interaction with metal ions that related to structure and cavity sizes of the macrocycles.



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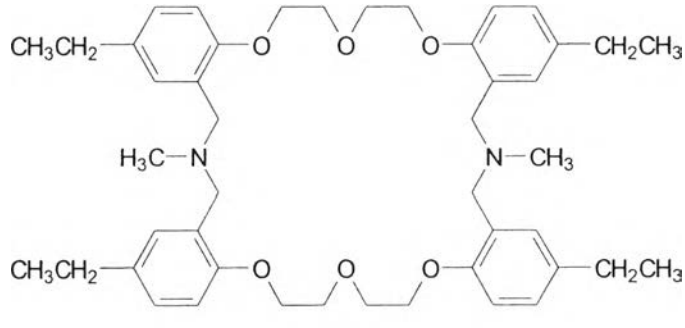

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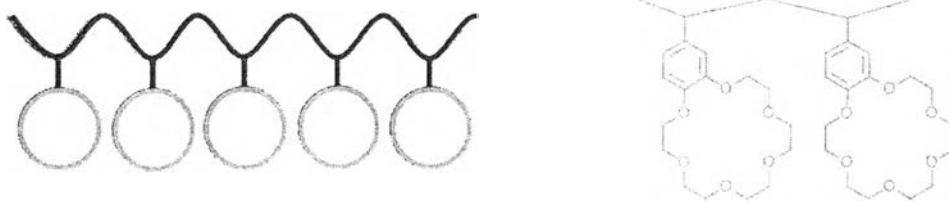
Scheme 2.3

2.3 Macrocyclic Polymer

Macrocyclic polymers are the polymers containing macrocycles such as crown ether, and calixarene in side chain or main chain. The macrocyclic polymers have received much more attention due to their supramolecular properties including host-guest chemistry, metal and molecular recognition. Moreover, in most cases, the macrocyclic polymers were found that metal ion binding properties of those macrocyclic polymers are more efficient than macrocyclic monomer. From those reasons, in the recent years, many researchers have developed a novel macrocyclic polymer due to its unique properties as seen from a significant increase of articles. Normally, the macrocyclic polymers can be divided in to 2 types.

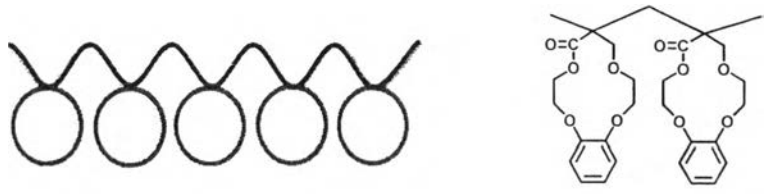
2.3.1 Polymer Containing Macrocycles as a Side Chain

In general, the polymers containing macrocycles as a side chain can be synthesized via polymerization of monomers which have a large ring as a substituent. For example, Kopolow *et al.* (1973) synthesized poly (vinylbenzo-18-crown-6) (Scheme 2.4) and found that poly (vinylbenzo-18-crown-6) showed the inclusion phenomena of metal ions more efficient than its monomer.



Scheme 2.4

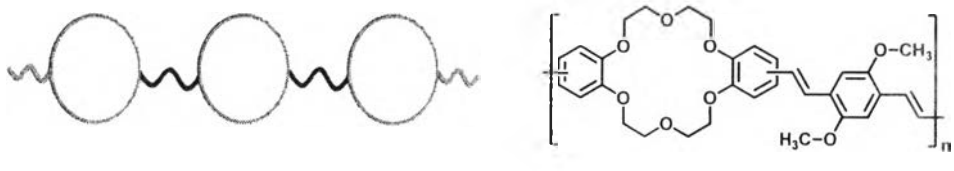
The other approach to obtain the macrocyclic polymer is the polymerization of macrocyclic vinyl monomers which have macrocyclics perpendicularly arranged on the main chain (Scheme 2.5). For instance, Habaue *et al.* (2002) succeeded in preparing a novel vinyl polymer with crown ether as a side chain via anionic polymerization.



Scheme 2.5

2.3.2 Polymer Containing Macrocycles as a Main Chain

The polymers containing macrocycles which are linked and fixed through the main chain have been normally synthesized by copolymerization. The novel copolymers containing 1,4-bis(phenylethenyl)-2,5-dimethoxybenzene chromophores alternated with crown ether which exhibit good thermal stability were synthesized by the Wittig polycondensation reaction as shown in Scheme 2.6 (Sun *et al.*, 2003).

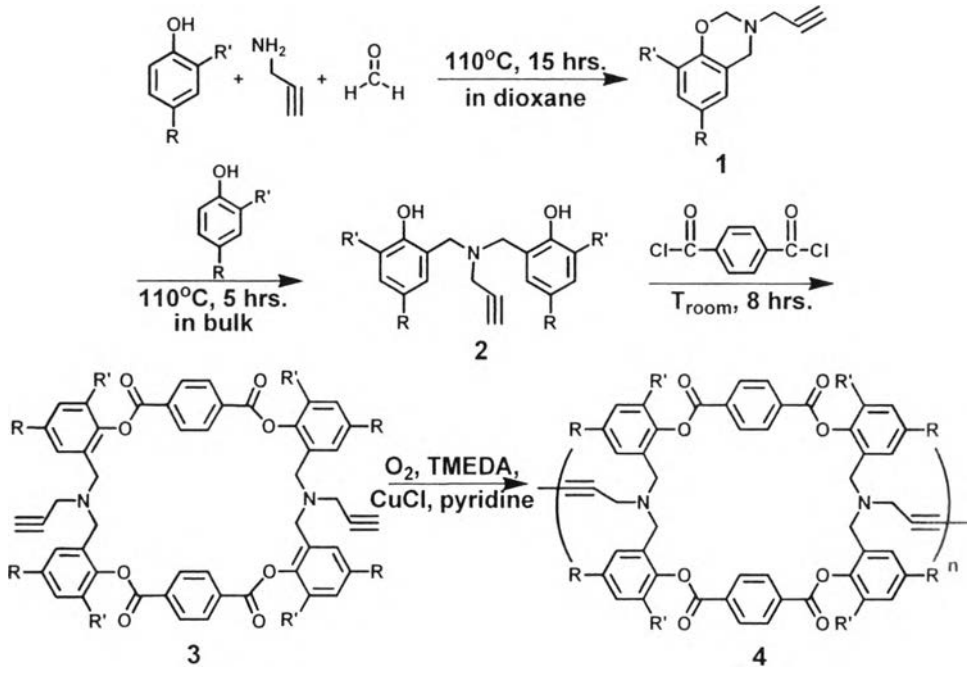


Scheme 2.6

2.4 Points of the Present Work

As the preparation of those polymers containing macrocycles deals with complicated synthesis and purification processes including problem of the low-yield product, the simple synthesis together with unique molecular design is still on expectation. Previously, our group succeeded in preparation of [2+2] macrocyclic ester in high yield (85%) via esterification of *N*,*N*-bis(2-hydroxy-5-ethylbenzyl)cyclohexylamine with terephthaloyl dichloride. It comes to our question that how to synthesize the benzoxazine-based macrocyclic containing propargyl moieties by further applying simple and effective reaction of benzoxazine dimer for further modification as a macrocyclic polymer.

In this work, as shown in Scheme 2.7, we propose a novel benzoxazine macrocyclic compound including the molecular design and macrocycle synthesis. Furthermore, we also extend the work to show macrocyclization condition to obtain the benzoxazine-based macrocyclic.



Scheme 2.7