



CHAPTER I INTRODUCTION

Supramolecular chemistry has received much attention due to the unique molecular recognition under inclusion phenomena between host and guest species with non-covalent interactions or secondary bonds (Pedersen, 1967; Cram *et al.*, 1985; Arduini *et al.*, 1986; Vögtle, 1991; Lehn, 1995). Up to now, various host molecules such as crown ethers (Pedersen, 1967), cyclodextrins (Bender *et al.*, 1978), calixarenes (Vicens *et al.*, 1991), and their derivatives have been developed and used for many applications.

Crown ethers are macrocyclic compounds obtained by the cyclization of two or more different molecules under the dilute system (Dietrich, 2004). There are many reports on the preparation of crown ethers and their inclusion properties. For example, monoazathiacycrown ethers, which showed the Ag^+ and Hg^{2+} extraction abilities, were obtained by the reaction of bis(2-chloroethyl)amine with dithiol derivatives (Tanaka *et al.*, 2001). The cyclization of ditosylated compounds with the substituted diols gave diaza-18-crown-6 and diaza-12-crown-4 performing as ligands for acceptance barium ions (Zhang *et al.*, 1995). In all cases, the purification at final step involved with column chromatography, extraction, and recrystallization providing the low yield products (11-39%).

For the past few years, our group has focused on *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine since its advantages of simple preparation and purification as well as giving high yield (80%-90%) (Laobuthee *et al.*, 2001, 2003; Phongtamrug *et al.*, 2004, 2005, 2006). These derivatives were obtained by the single ring opening reaction of benzoxazine derivatives with phenol compounds. Considering the structure of these derivatives, the single crystallography analysis pointed out the unique structures with inter- and intramolecular hydrogen bonds network to provide asymmetric compounds (Laobuthee *et al.*, 2001). We also extended to the supramolecular chemistry of *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine to declare that these derivatives performed as the host molecule to accept various guest species such as alkali, alkaline earth, and transition ions (Laobuthee *et*

al., 2003; Phongtamrug *et al.*, 2004). The information obtained from crystal structure analysis revealed that the host-guest interaction was stable under charge-transfer coordination (Phongtamrug *et al.*, 2006).

Our challenge in development the good cyclic structure based on *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine is started when we succeeded in preparing a series of macrocyclic esters (Laobuthee *et al.*, 2002) and macrocyclic ethers (Chirachanchai *et al.*, 2003) via simple, effective, and selective conditions. In all cases, [2+2] macrocycles were carried out via the cyclization of para-substituted *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine with ditosylated compounds. These macrocycles performed inclusion phenomena with alkali ions at different the host-guest stoichiometric ratios depending on the type of metal ion (Chirachanchai *et al.*, 2003). It is important to note that the ortho-substituted group in phenol group of these derivatives might play an important role on the macrocyclization. The present work (Chapter III), therefore, focuses on an investigation of the ortho-substituted group in phenol group of *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine in the selective crown ethers based macrocyclization. We also extend the works to the inclusion phenomena of these macrocycles with alkali ions.

Charbonnière *et al.* (2000) proposed the synthesis of novel crown ethers, i.e., cyclic di[(*o*-polyethyleneglycoxy)phenyl]amine by treating diarylamine with ditosylated tri-, tetra-, or pentaethyleneglycol using Cs₂CO₃ as the base. Ágai *et al.* (1996) reported on the preparation of dibenzo-monoaza crown ethers from cyclization phenol-aza-phenol derivatives with the appropriate ditosylated under the presence of K₂CO₃. In both cases, the cyclization of crown ring with various chain lengths of ditosylated compound gave only a single type of macrocycle, i.e., [1+1] macrocycle, with the modest yields (22-68%). Currently, we found that the reaction of a derivative of *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine with various chain lengths of ditosylated compound not only gives [1+1] macrocycle but also [2+2] one. The present work (Chapter IV) involves with the structure of *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine itself inducing the selective macrocyclization to provide both [1+1] and [2+2] macrocycles.

According to many reports on the macrocyclization of crown ethers, a good approach for providing the well-defined macrocyclic structure is using a metal

template (Dietrich, 2004; Reinhoudt *et al.*, 1976; Busch, 1992). However, in most cases, the yield is limited to about 30-40%. When the backbone molecules are in a H-bond network, the non-template macrocyclic synthesis via condensation, conjugation, or coupling reactions is also an effective pathway (Xing *et al.*, 2005). This leads us to the idea about the synergistic function of both a metal template and H-bonds in macrocyclization. The present work (Chapter V) also aims to demonstrate a model in which the macrocyclization can be initiated by not only the effects of a specific metal template but also a H-bond network.

In previous, [1+1] and [2+2] macrocycles based *N,N*-bis(2-hydroxyalkylbenzyl)alkylamine performed the inclusion properties with alkali ions (Chirachanchai *et al.*, 2003; Rungsimanon *et al.*, 2006). Although we have reported the inclusion properties of those macrocycles, comparative studies on the structural factors related to the ion acceptance abilities have not yet been carried out. The present work (Chapter VI), therefore, focuses on dibenzo-monoaza-crowns and how their structures are involved with the metal ion selectivity.