การสังเคราะห์1,3-อัลเทอร์เนตคาลิกซ์[4]-ไซเคลน-เบนโซ คราวน์-6 และการเกิดสารประกอบเชิงซ้อนกับแคตไอออนของโลหะและโมเลกุลอินทรีย์

นางสาว เมธินี จามกระโทก

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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SYNTHESIS OF 1,3-ALTERNATE CALIX [4]-CYCLEN-BENZO CROWN-6 AND ITS COMPLEXATION WITH METAL CATIONS AND ORGANIC MOLECULES

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A Thesis Submitted in Partial Fullfillment of the Requirements
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การสังเคราะห์อนุพันธ์ชนิดใหม่ของ 1,3-อัลเทอร์เนตคาลิกซ์[4]เอรีน คือ 1,3-อัลเทอร์เนตคาลิกซ์[4]-ไซเคลน-เบนโซ-คราวน์-6 (**20**) ที่ประกอบด้วยหน่วยของไซเคลนและคราวน์อีเทอร์คนละด้านของระนาบของคาลิกซ์[4]เอรีนทำการสังเคราะห์ผ่านตัวกลางที่เป็นไดโบรไมด์ เมื่อทำการศึกษาคุณสมบัติการเกิดสารประกอบเชิงซ้อนกับเกลือปิเครตด้วยเทคนิคโปรตรอนเอ็นเอ็มอาร์สเปกโทรสโกปีพบว่าลิแกนด์ชนิดใหม่ที่สังเคราะห์ได้มีความสามารถในการเกิดสารประกอบเชิงซ้อนแบบ1:1กับไอออนของโลหะซีเซียมได้โดยที่ไอออนของโลหะซีเซียมจะอยู่ในโพรงของเบนโซ-คราวน์อีเทอร์ในขณะที่ไอออนของโลหะสังกะสีและโพแทสเซียมจะเกิดสารประกอบเชิงซ้อนแบบ1:1ได้โดยที่ไอออนของโลหะสังกะสีและโพแทสเซียมจะถูกจับอยู่ในโพรงของหน่วยไซเคลนเมื่อทำการศึกษาถึงผลกระทบของแอนไอออนที่มีต่อการเกิดสารประกอบเชิงซ้อนของลิแกนด์ที่สังเคราะห์ได้ด้วยเทคนิคโปรตอนเอ็นเอ็มอาร์สเปกโทรสโกปีพบว่าความสามารถในการระหว่างไอออนของโลหะสังกะสีกับลิแกนด์ขึ้นอยู่กับขนาด รูปร่างของและความสามารถในการจับของไอออนร่วมตามลำดับดังนี้ $SO_4^{2-} > AcO^- > NO_3^-$ และเมื่อทำการศึกษาถึงผลกระทบโดยเกลือเฮไลด์ของสังกะสี 3 ชนิดพบว่าแรงกระทำระหว่างไอออนของโลหะสังกะสีกับลิแกนด์ของการเกิดสารประกอบเชิงซ้อนเป็นดังนี้ **20**•$ZnCl_2$ < **20**•$ZnBr_2$ < **20**•ZnI_2 และเมื่อทำการศึกษาการเกิดสารประกอบเชิงซ้อนกับ $ZnSO_4$ โดยวิธีโปรตอนเอ็นเอ็มอาร์ไทเทรชั่นพบว่าลิแกนด์สามารถจับกับไอออนของสังกะสีทั้งแบบ 2:1 และ 1:1 (L:M) และเนื่องจากการลิแกนด์ที่สังเคราะห์ได้มี NH อะตอมที่มีความสามารถในการเกิดพันธะไฮโดรเจนกับโมเลกุลอินทรีย์เช่น ไดไฮดรอกซีเบนซีนพบว่า NH ของหน่วยไซเคลนมีความสามารถในการเกิดพันธะไฮโดรเจนกับซับสเตรตได้โดยพบการเคลื่อนที่ของสัญญาณโปรตอนของ C**H**$_2$N ของหน่วยไซเคลนและอะโรมาติกที่ติดกับหน่วยของไซเคลน

ภาควิชา เคมี ลายมือชื่อนิสิต.

สาขาวิชา เคมี ลายมือชื่ออาจารย์ที่ปรึกษา

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MATINEE JAMKRATOKE : SYNTHESIS OF 1,3–ALTERNATE CALIX[4]-CYCLEN-BENZO-CROWN-6 AND ITS COMPLEXATION WITH METAL CATIONS AND ORGANIC MOLECULES. THESIS ADVISOR : ASSIST. PROF. THAWATCHAI TUNTULANI, Ph.D.; THESIS CO-ADVISOR : BUNCHA PULPOKA, Ph.D. 82 pp. ISBN 974-13-1062-5.

A new derivative of 1,3-alternate calix[4]arene, 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**) containing a cyclen subunit on one site and benzo crown-6 on the other side has been synthesized. The complexation studies of the synthesized ligand were carried out by mean of ^{1}H-NMR spectroscopy. With picrate salts, ligand **20** formed 1:1 complex with Cs^{+} which resided in benzo crown ether loop. For a 1:1 complex of potassium and zinc picrates, ^{1}H-NMR spectra of these complexes shown that potassium and zinc ions were encapsulated in the cyclen unit of **20**. An influence of anions (as a counter ion) towards zinc complexes was studies. From ^{1}H-NMR spectra, it was found that interaction between zinc salts and ligand **20** depended on the shape, size and binding ability of counter ions and the interaction degrees were in order of $SO_4^{2-} > AcO^{-} > NO_3^{-}$. Moreover, two types of complexes, 2:1 and 1:1 complexes, were observed in the case of $ZnSO_4$. Its complexation behavior of **20**·$ZnSO_4$ was confirmed by ^{1}H-NMR titration. In zinc halides series, the interaction between zinc halides and ligand **20** were in the order of **20**·$ZnCl_2$ < **20**·$ZnBr_2$ < **20**·ZnI_2. Due to the synthesized compound possesses NH groups at the cyclen unit, the complexation studies of this ligand with organic molecules were investigated. ^{1}H-NMR spectra, demonstrated the interaction between host **20** and guest molecules by means of hydrogen-bonding due to the migration of C**H**$_2$ signals of cyclen unit and the neighboring phenyl unit. It was also revealed that ligand **20** possessed a higher affinity towards disubstituted benzenes than monosubstituted ones.

Department Chemistry Student's signature .....

Field of study Chemistry Advisor's signature .....

Academic year 2000 Co-Advisor's signature .....

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Contents

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List of Abbreviations and Sings

Å	**Angstrom**
^{13}C-NMR	**Nuclear Magnetic Resonance Carbon**
° C	**Celsius**
DMAP	**4-Dimethylaminopyridine**
g	**Gram**
δ	**Chemical shift**
Hz	**Hertz**
^{1}H-NMR	**Proton Nuclear Magnetic Resonance**
J	**Coupling constant**
mp	**Melting point**
mL	**Milliliter**
mmol	**Millimol**
ppm	**Part per million**
M	**Molar**
M^{-1}	**Per molar**
RT	**Room Temperature**
TsCl	**Toluene-4-sulfonyl chloride**

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CHAPTER I

INTRODUCTION

1.1 Supramolecular chemistry

Molecular interactions from the basis of the highly specific recognition, reaction and translation processes occur in biological systems. Therefore, the chemists try to mimic that system in order to understand how the biological molecules work in biological processes. Since the discovery of crown ethers by Perderson, the beginning of the new branch of chemistry called *supramolecular chemistry* was marked. The area of supramolecular chemistry is still a young one; however, this field becomes more and more fascinating topic because it is not only closely related to bioorganic and bioinorganic chemistries but also to the basic knowledge for nanotechnology.[1,2]

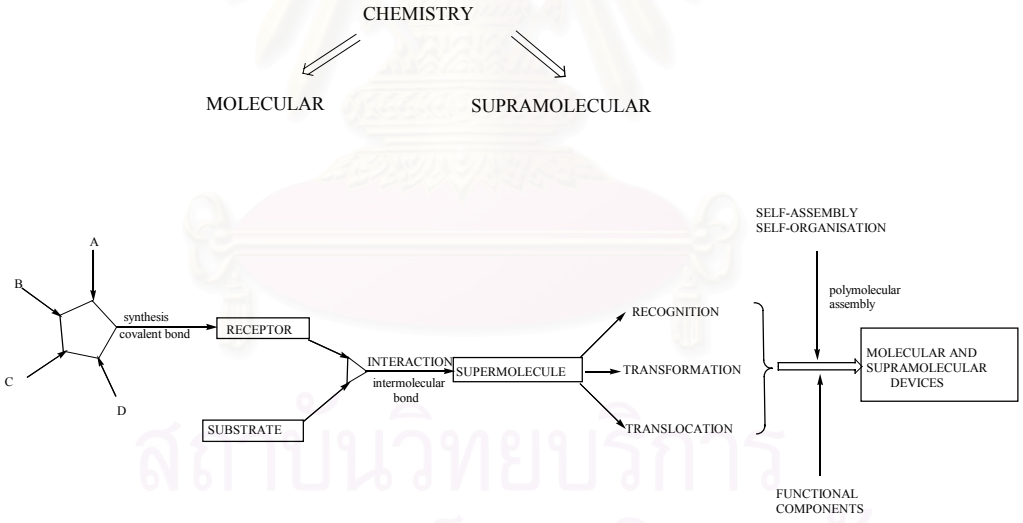


Figure 1.1 From molecular to supramolecular chemistry: molecules, supermolecules, molecular and supramolecular devices.

Supramolecular chemistry is a highly interdisciplinary field of science covering the chemical, physical, and biological features of greater complexity than molecules themselves. That are held together and organized by intermolecular (non-covalent) binding interactions.[1,2] Moreover, supramolecular chemistry is related with self-organization process (self-assembly) and self-recognition of molecules. This branch of chemistry was defined differently from coordination chemistry because of types of substrates. In supramolecular chemistry, substrate was not limited only to transition metals but also extended to cations, anions and neutral molecules. Almost of the beginning of supramocular chemistry has been associated with possible applications based on shape-selective interactions between molecules or between ions and molecules. These applications involve the translation of properties to a macroscopic level and will lead to new materials or devices.[1,2]

Molecular receptors and macrocyclic compounds

Molecular receptors are defined as organic structures held together by covalent bonds that are able to bind selectively ionic or molecular substrates (or both) by intermolecular interactions. The ideal receptor is designed for the high selectivity, stability, and flexibility for one substrate.[1]

Macrocyclic compounds are the large cyclic molecules, which have an affinity of including metal ions or organic molecules. Macrocyclic structures are more interested for designing artificial receptors because of large cavity structure and appropriated size and shape that allow the construction of given architecture endowed with specific dynamic structure for binding or including specific substrate. Affinities of complexing properties of macrocyclic ligands depend on several factors:

i) steric complementary: it depends on shape and size of both receptor and substrate;

ii) interaction complementary: electrostatic such as positive/negative, dipole/dipole, hydrogen bonding donor/acceptor and *van der Waals* interaction;

iii) large contact area between substrate and receptor;

iv) multiple non-covalent interactions;

v) strong overall binding.[1]

The stability of macrocyclic molecules depends on the size of macrocylic cavity, which the large cavity has higher flexibility than the small cavity. Therefore, the large cavity has an interaction with the substrate less than the small cavity.

In 1960s, Perderson[3] has found crown ethers, which are the two-dimension macrocyclic ligands. Until now, the macrocyclic ligand is a continuous interest in the synthesis and the complexation properties of the crown compounds. In order to enhancement of complexation abilities of macrocyclic compound, Lenh, Sauvge and Dietrich[4] have synthesized and studied the three-dimension macrocyclic ligands, called *cryptand*, the molecules containing heterodonor atoms such as nitrogen, sulfur or oxygen atom. These ligands form complexes with metal ion more stable than the two-dimension macrocyclic compounds due to the heteroatom presented in molecule and the three-dimension cavity of cryptand.

Cram and coworkers[5] have synthesized and studied a new group of macrocyclic compounds, *spherand*, on the basis of preorganization of ligand before complexation. The discovering of spherand led to the development of cyclic phenol compounds such as calixarenes.

1.1.1 Crown ethers

Crown ethers are two-dimensional macrocyclic molecules that can form complexes with metal ions and organic cations by oxygen atoms. The affinity of complexes depends on the fitting of cavity of crown ether and metal ion. Crown ethers can be designed to be a cation receptors and transporting agents, which can bind selectively toward particular cations.[3-6]

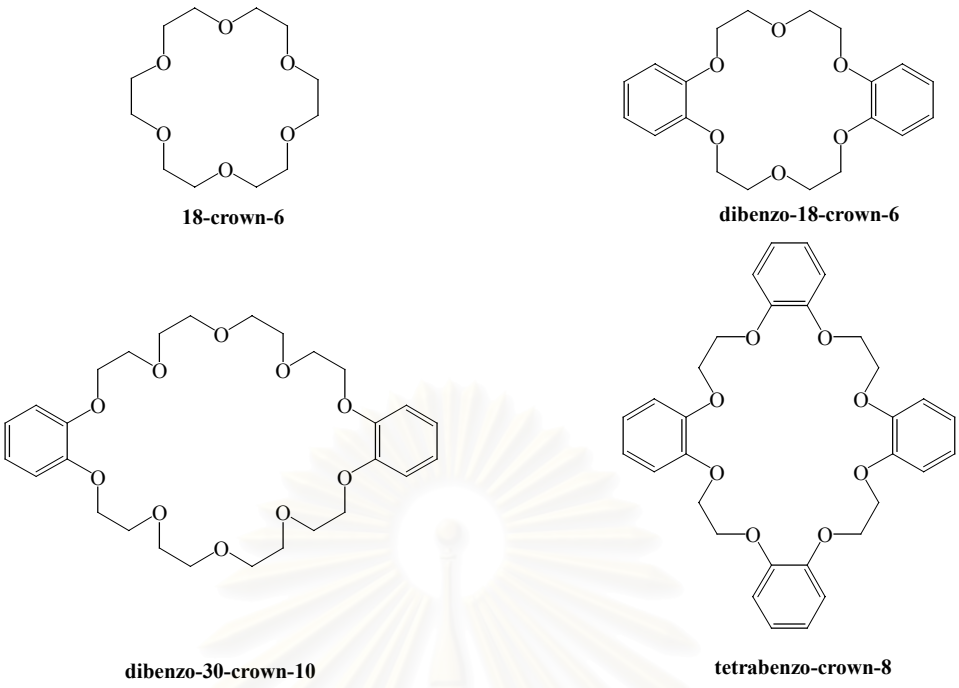


Figure 1.2 Some examples of crown ethers.

1.1.2 Macrocyclic polyaza compounds

The coordination chemistry of amines has undergone a considerable development since the first use of amines as a ligand. Tetraazacycloalkanes, especially *cyclen* and *cyclam* derivatives, have been the most extensively studied because of these tetraazamacrocycles are able to from highly stable complexes with transition metals cations, lanthanide and actinide cations including organic or inorganic anions, with the exact behavior depending on the cavity size and the nature of substituents. The presence of four secondary amine functions on molecules allows for unlimited derivatization of these compounds. This versatility makes possible for the use of azacrown such as purification of waste water, catalysis and medicinal purposes.[7,8]

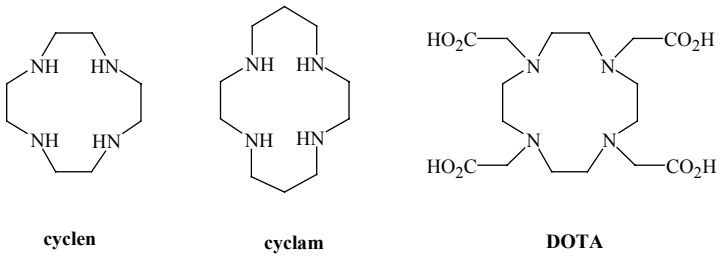


Figure 1.3 Most common tettrazacycloakanes.

1.1.3 Cryptands

Cryptands are the macrocyclic compounds that consisting of two or more crown rings, linking by C or N atom. The cage structure of cryptands has an affinity towards alkali ions much greater than two dimension crown ethers. The cyptands have the property of inducing alkali ion to solubilize in organic solvent. Because of their prominent characters, many research groups are studying on the chemistry and applications of cryptands.[6]

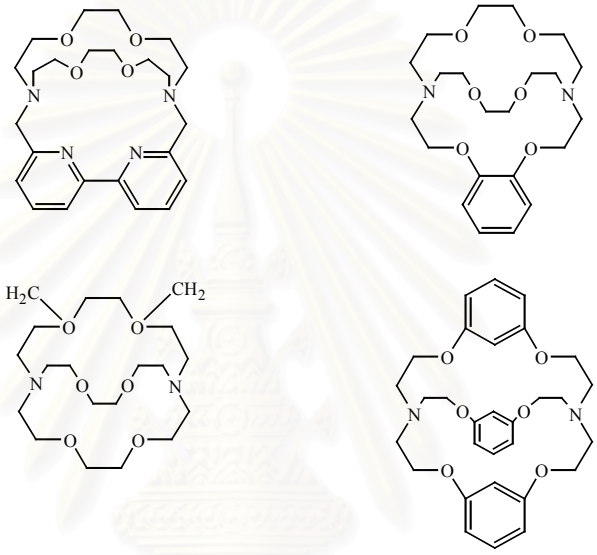


Figure 1.4 Some examples of cryptands.

1.2 Calixarenes

Calixarenes are cavity-shaped cyclic molecules obtained from the condensation of formaldehyde and *p*-alkyl phenol under alkaline condition. Among calixarenes, calix[4]arene is the most interesting plateform due to its ease of synthesis, functionalization and its conformations. The "beaker like shape" of calix[4]arene ("*calic"* means vase in Greek) can behave as versatile platform for inclusion of guest molecules due to their flexible cavities. [10-12]

In solution, calix[4]arene exists in 4 conformations calls cone, partial cone, 1,2-alternate, and 1,3-alternate (see Figure 1.5). Each of them has its own specific properties and characteristic utilization in host guest chemistry. Calix[4]arene is a very attractive compound that can be used as a platform for designing more sophisticated structure for binding ions and neutral molecules.[9-12]

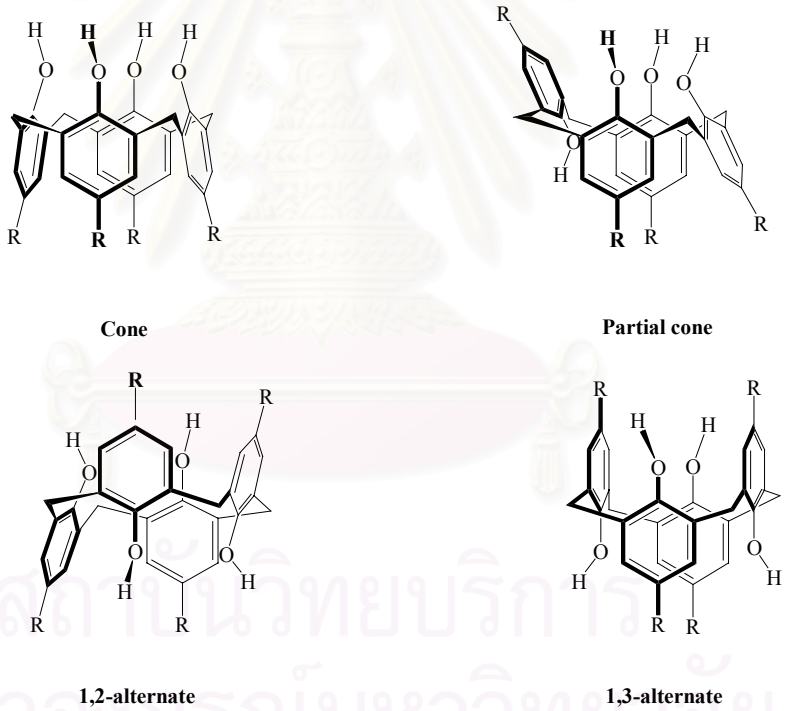


Figure 1.5 Calix[4]arene in 4 conformations.

Calix[4]arene can be fixed in one conformation when complexed with ions or neutral molecules and restricted the flipping motion of the benzene ring by fuctionalization with the groups bulkier than ethoxy groups at lower rim (at hydroxyl positions) or bridge each benzene ring intramolecularly or intermolecularly.[13]

1.2.1 Calix[4]arene in 1,3-alternate conformation

By both X-ray crystallographic and theoretical computational studies, 1,3-alternate calix[4]arene provides a D_{2h} symmetrical tube shaped π-basic cavity composed of four benzene rings.[14] Now, calix[4]arene derivatives in a 1,3-alternate conformation are interesting receptors because of its fantastic characters, for example:

i) 1,3-alternate calix[4]arene presents two binding sites on both sites of calix[4]arene framework which are linked to each other by a π-basic benzene tunnel.

ii) each metal binding sites composes of two '*hard*' (Oxygen donor) and two '*soft*' (π-basic benzene) donors.[15]

iii) π-basic tunnel which allows a cation, in a 1:1 complex of 1,3-alternate calix[4]arene, switches from one binding site to the other through the π-basic tunnel ("*tunneling effect*") which led chemists to connect several calix[4]arene in the 1,3-alternate conformation to synthesize "*nano tube*".[16,18]

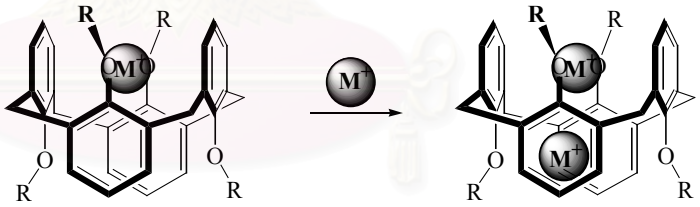
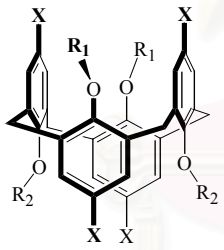


Figure1.6 Structure of 1,3-alternate calix[4]arene and its complexation behavior.

a) Syntheses and complexation studies of 1,3-alternate calix[4]arene podands

In early strategy, the synthesis of 1,3-alternate calix[4]arene was carried out by *tetra*-O-alkylation of calix[4]arene in presence of Cs_2CO_3 as a base in DMF.[14] The substitutents on these 1,3-alternate calix[4]arene podands are the groups bulkier than ethoxy group such as CH_2CONEt_2, CH_2COEt_2 and CH_2CONEt (Figure 1.7).[14-16] The conformation in which the calix[4]arene is fixed upon derivatization depends on temperature, the solvent, the base, the *para* substituents of calix[4]arene and the reactivity of electrophile.[14] Cone and 1,3-alternate derivative were prepared from substitution reaction of calix[4]arene with ethoxyethyl bromide by using NaH and Cs_2CO_3 as a base, respectively. Moreover, the 1,3-alternate derivative can be prepared by using K_2CO_3 as a base in dry acetone. From NMR spectroscopic and X-ray crytallographic studies, it was found that 1,3-alternate calix[4]arene has a structure as a open-end tube, with two binding sites linked by π-basic benzene tunnel.[14,15,19]



$R_1 = R_2$ = Pr, CH_2CONEt_2, CH_2CO_2Et		X = *t*-butyl[15,16,19]
$R_1 = R_2$ = Pr, $(CH_2)_2OEt$, CH_2CONEt_2		X = H[15,16]
$R_1 = CH_2CSN(CH_3)_2$	R_2 = Pr	X = H [17]
R_1 = Pr	$R_2 = CH_2OCH_3$	X = H [15]
R_1 = H	$R_2 = CH_2CONEt_2$	X = *t*-buty[16]

Figure1.7 Some 1,3-alternate calix[4]arene podands.

The complexation studies of 1,3-alternate calix[4]arene podand were carried out by studying with NMR spectroscopy and X-ray crystallography. It was shown that the metal affinity of 1,3-alternate calix[4]arene podand is much higher than other conformations because the metal contacts more closely with two oxygens and two phenyl rings.[15-19] This structure can form 1:1 as well as 1:2 complexes with certain metal cations; such as K^+, Na^+, and Ag^+. In 1:1 complex, the metal cation vibrates between the two metal binding sites through the π-basic tubular cavity by the aid of the phenyl rings.[14]

b) Syntheses and complexation studies of single bridge 1,3-alternate calix[4]arene.

Recently, the attempt to put together the special properties of crown ether and calix[4]arene in one molecule aimed to generate more elaborate structures was accomplished by single bridging of calix[4]arene with poly(oxyethylene) at 1,3 position. All these molecules were prepared by alkylation of calix[4]arene with activated bifunctional reagents (oligoethylene glycol ditosylates, diacid chlorides, *bis*-bromomethylated teranisyl system) by using Cs_2CO_3 as a base in acetonitrile or acetone.[20-23]

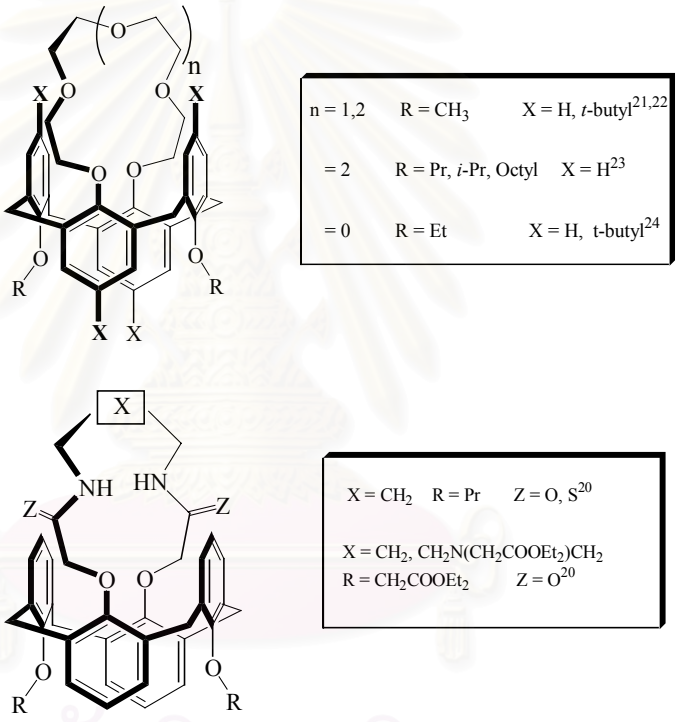


Figure1.8 Structures of 1,3-alternate calix[4]arene with single bridge.

As previously mentioned, 1,3 alternate calix[4]arene based receptors represents the most potent complexing agents for alkali metal ions, with high efficiency and selectivity. Calix[4]-crowns with different cavity sizes (Figure 1.8) show the high complexation abilities toward different alkali ions, calix[4]-crown-6, calix[4]-crown-5 and calix[4]-crown-4 show selectivities to cesium[24,25], potassium[20,21] and sodium ions,[15,19] respectively. Calix[4]-aza-crowns were observed to complex preferentially with soft cations.[24]

c) Syntheses and complexation studies of double bridges 1,3-alternate calix[4]arene

1,3-Alternate calix[4]arene with double bridges possesses two binding sites on both sides of calixarne plane linked each other by a π-basic tunnel. *O*-tetraalkylation of calix[4]arene can design various ionophoric cavities. Calix[4]-*bis*-crowns (Figure 1.9) were synthesized by one step 1+3 and 2+4 condensations with polyethylene glycol ditosylate.[24-28] These calix[4]arene receptors bear symmetrical metal binding sites, which well adapted for the formation of 1:1 and 1:2 complexes (Figure 1.10). In 1:1 complexes, the cation (alkali, silver or ammonium ions) switches from one cavity to the other throught π-basic tunnel (Figure 1.11).[25,26] Capped calix[4]-*bis*-aza-crowns (Figure 1.12) bind preferently soft cations probably due to the presence of nitrogen atoms in binding sites.[24,25,29,30]

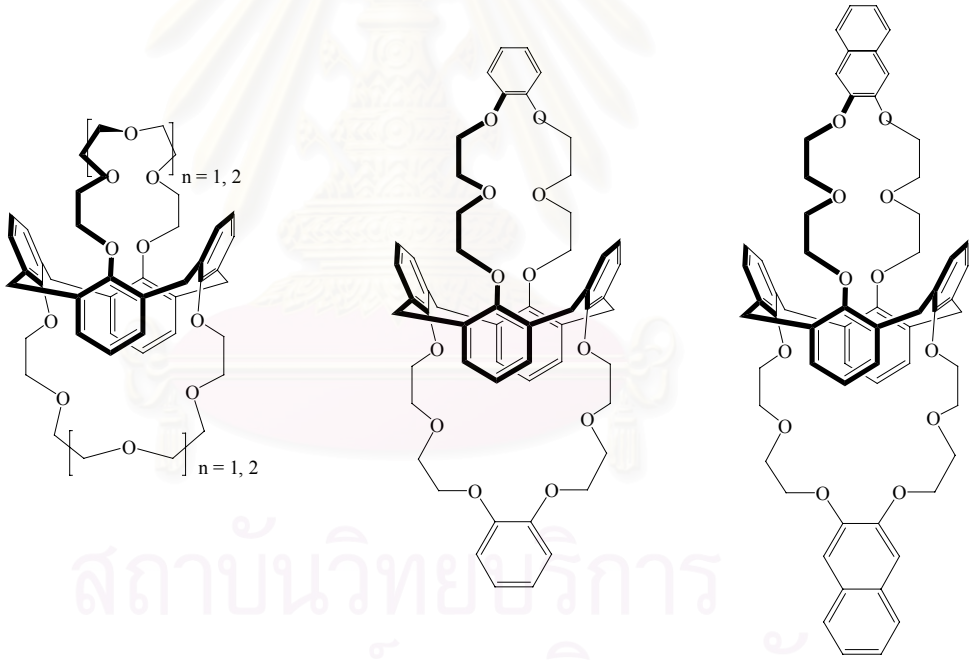
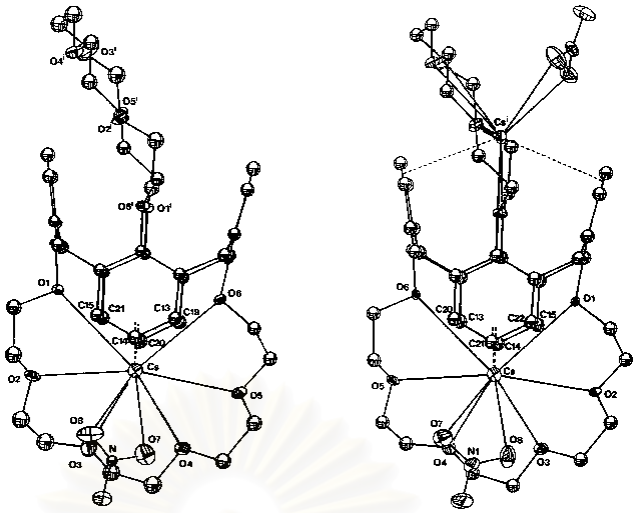


Figure1.9 Structures of 1,3-alternate calix[4]-*bis*-crown.



a **b**

Figure1.10 Crystal structures of 1,3-alternate calix[4]-*bis*-crown-6 complexed with Cs^+ a) mononuclear complex b) dinuclear complex

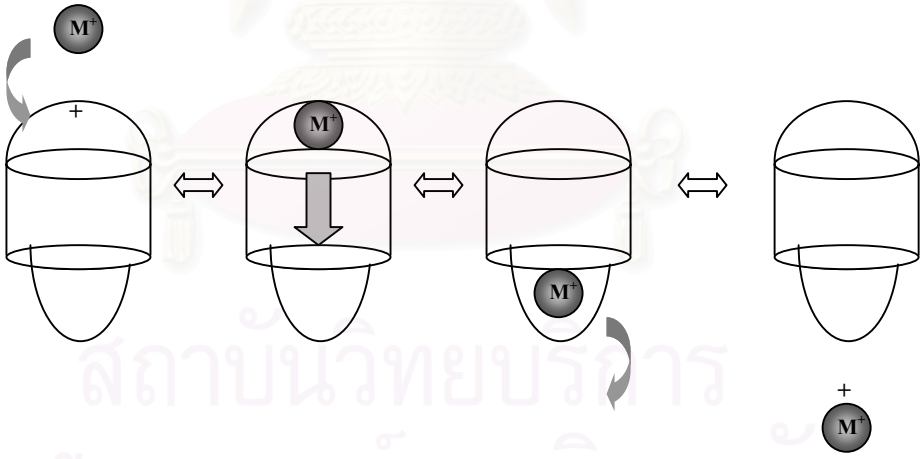


Figure1.11 Intermolecular and intramolecular cation exchange process in calix[4]-*bis*-crown.[31]

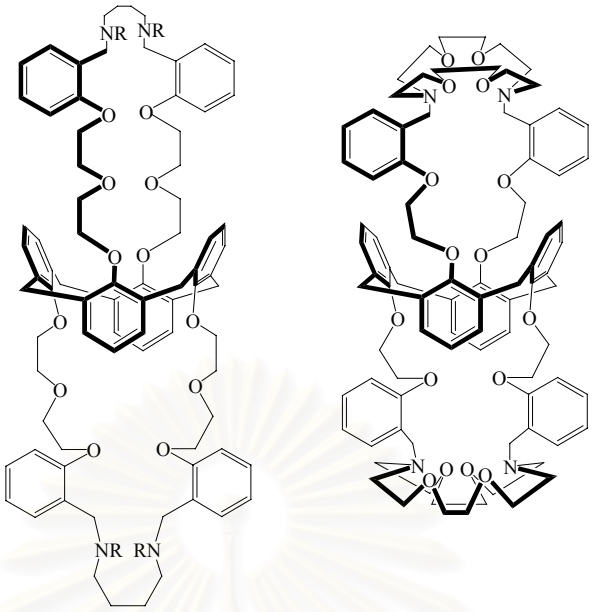


Figure1.12 Structures of 1,3-alternate calix[4]-*bis*-aza-crown.

1,3-Alternate calix[4]arenes with asymmetrical cavities (Figure 1.13) have been synthesized to afford bifunctional receptors which can bind different ions.[32-34] Furthermore, the asymmetrical calix[4]-crowns have an ability to control a translation of ion through a π-basic tunnel.[32-35]

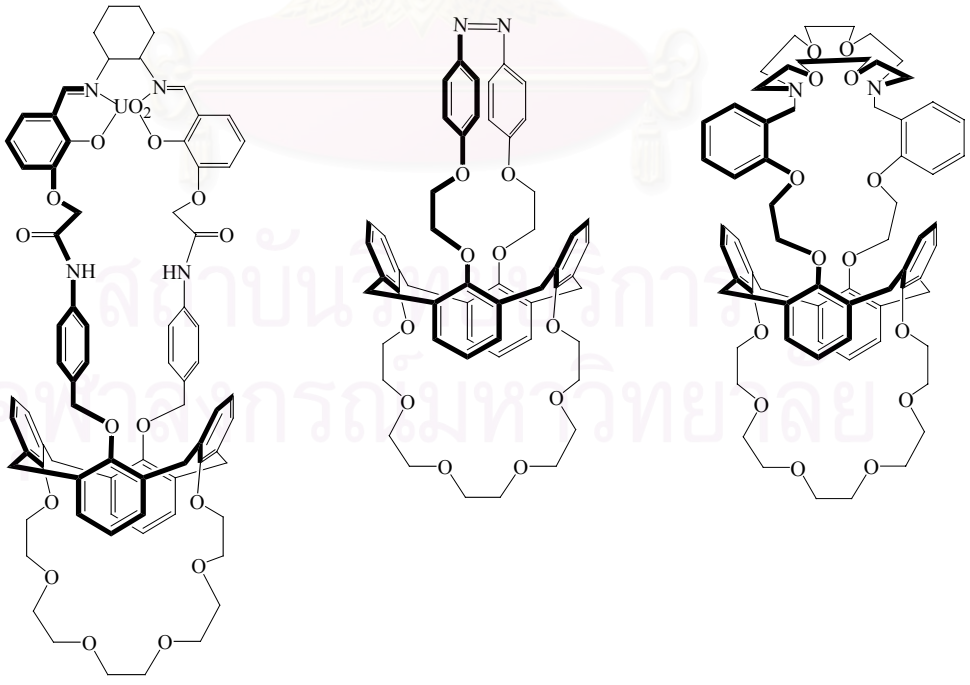


Figure1.13 Structures of asymmetric 1,3-alternate calix[4]arene.

1.2.2 Applications of 1,3-alternate calix[4]arene derivatives

1,3-Alternate calix[4]arene derivatives have been introduced in supramolecular chemistry to produce transport ionophores and selective sensing agents in the microconstruction of ion sensory devices.[36-39]

Calix[4]-crowns were used as the active components in supported liquid membrane[21,22,36]and the cation ion detection by chemically modified field effect transistors[21,22,38,39,44] because of their high selectivity and efficiency. Calix[4]-crown-6 and calix[4]-crown-5 were bound to silica gel to perform a chromatographic separation for some alkali ions such as K^+ and Cs^+.[42] Due to their selectivity, efficiency and stability in acidic medium, the 1,3-alternate calix[4]-crowns were applied for the removal of $^{137}Cs^+$ from radio active waste.[23]

A serie of *N*-chromogenic calix[4]-crown was synthesized to serve as chromogenic receptors for potassium ion. The chromogenic group was attached to calix[4]-crown to permit a the determination of metal ions by UV spectrophotometry.[42-45]

In order to imitate the cation transportation in living system, the chemist attempts to connect 1,3-alternate calix[4]arene which have a π-basic system with several spacers. The 1,3-alternate calix[4]arene nano tube (Figure 1.14) allows cation to pass through the π-basic tunnel by the aid of cation π-interaction. The metal-oscillations depends mainly on size of cations which should be smaller than the inner diameter of *nano-tube*.[15,26]

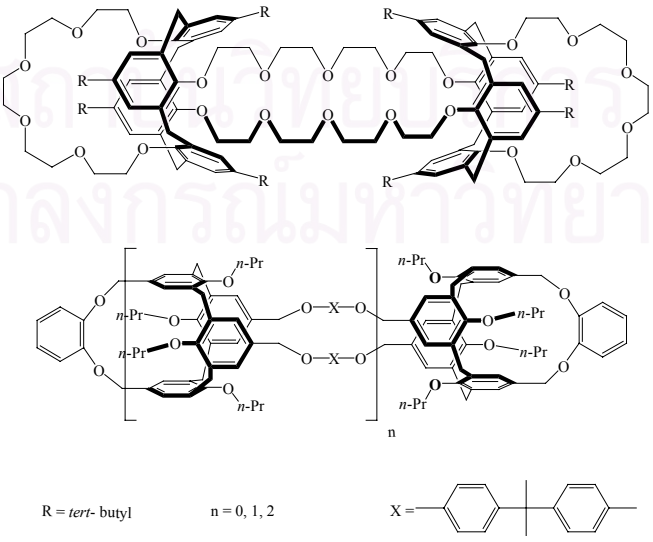


Figure1.14 Different *nano*-tubes designed from 1,3-alternate calix[4]arene.

In order to incorporate the mechanical property onto 1,3-alternate calix[4]arene, the “mappe-monde” calix[4]arene was designed and synthesized. With the absence of cation in solution, the rotation around axis of calix[4]-*bis*-crown was observed but when the cation was added this mapped monde was in stop-rotation mode.[44]

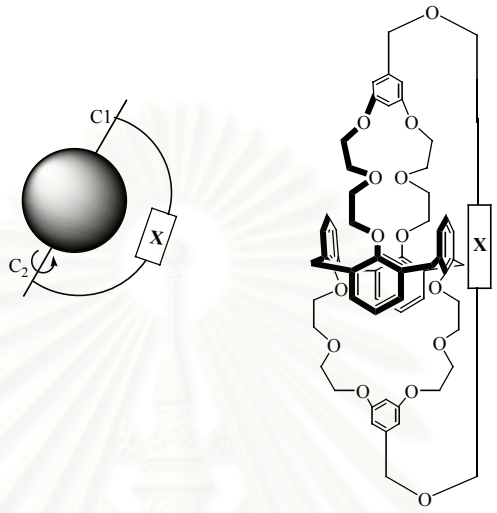


Figure1.15 Calix[4]-*bis*-crown moiety represents the earth ball which pole (C1 and C2) are linked by a polyether loop X serving as an arm.

Recently, a molecular syringe was designed and synthesized based on the tunnelling effect property of 1,3-alternate calix[4]arene. When the nitrogen atom in crown ether ring was protonated, the metal cation can pass through the π- basic cavity to the *bis*(ethoxyethoxy) side because of the electrostatic repulsions.[45]

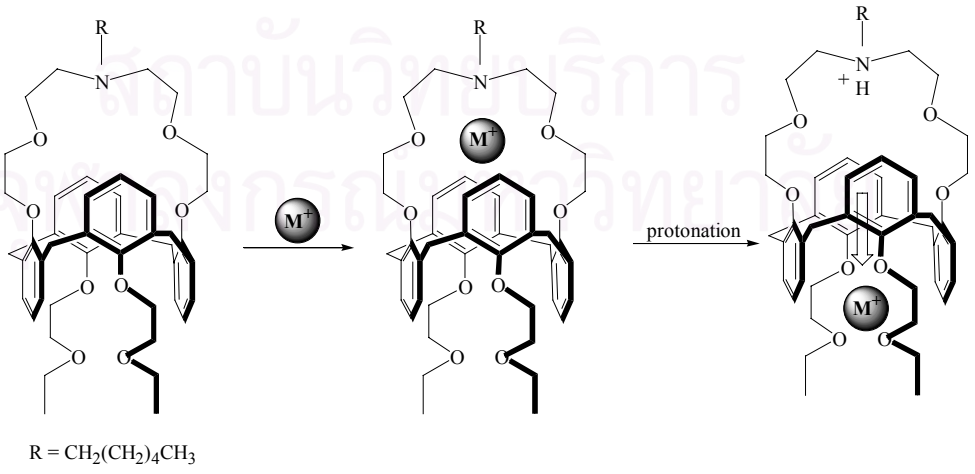
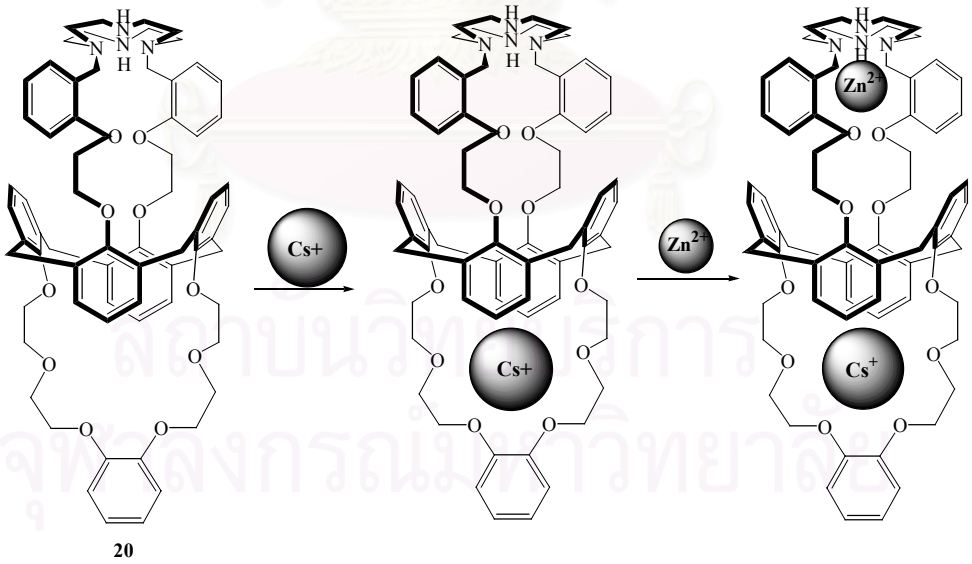


Figure1.16 Schematic representation of a reversible metal pumping in “molecular syringe” designed from 1,3-alternate calix[4]arene.

1.3 Objectives and scope of this research

Calix[4]arene in 1,3-alternate conformation is the most interesting conformation among calix[4]arene because that 1,3-alternate calix[4]arene provided two binding site on each sides of calix[4]arene platform, which can be functionalized to obtain two cavities symmetrically or asymmetrically. Many 1,3-alternate calix[4]arene building-blocks incorporating different cavities have also been synthesized by combination of two different moieties onto a calix[4]arene platform.

The aims of this work are to develop a new class of "*hard-soft"* receptor based on 1,3-calix[4]arene, 1,3-alternate calix[4]-cyclen-benzo-crown-6, and to study its complexation properties. This ligand consists of 1,4,7,10-tetraazacyclododecane or '*cyclen'* unit, which can form high stable transition metal and lanthanide complexes[7,8] and a benzo-crown ether subunit which can form the stable cesium complexes[17,28,29] on each binding sites of calix[4]arene platform. The heteroditopic ligand is also aimed to approach to a *'hard-soft'* receptor, which could bind hard and soft ions strongly and selectively. This ligand can act as molecular sensor and/or catalysts capable of detecting or catalyzing redox reaction on guest species.



20

Figure1.17 Schematic representation of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**) as a *'hard-soft'* receptor.

CHAPTER II

EXPERIMENTAL SECTION

2.1 General Procedures

2.1.1 Analytical Instruments

Elemental analyses were carried on a Perkin Elmer CHON/S analyzer (PE2400 series II). Mass Spectra were recorded on a Fishion mass spectrometer modelTrio 2000. Melting points were obtained on an Electrothermal 9100 apparatus. Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker ACF 200 MHz nuclear magnetic resonance spectrometer. In all cases, samples were dissolved in deuterated cholorofrom and chemical shifts were recorded using a residual chloroform signal as internal reference except indication of other dueterated solvents.

2.1.2 Materials

All reagents in standard analytical grade were purchased from Fluka, J.T. Baker and Merck and used without further purification. Commercial grade solvents such as dichloromethane, acetone, hexane, and methanol were disstillated before used. Acetonitrile and toluene were dried over CaH_2 and distrillated under N_2 atmosphere for 24 hours before use.

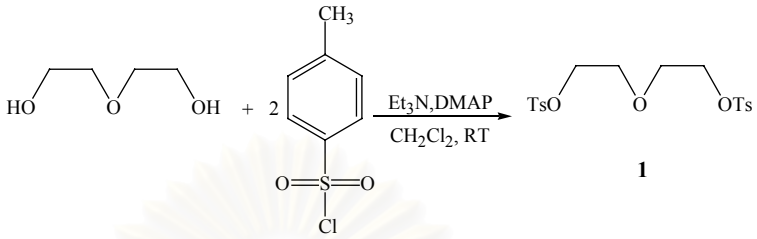
Chromatography separations were performed on either silica (silica gel 60 Merck 7734) or aluminium oxide (aluminium oxide 90 Merck 1097, standardised (activity II-III)). Thin layer chromatography (TLC) was carried out by using siliga or aluminium oxide plates (Kieseslgel 60 F_{254} for silica and Aluminiumoxide 60 F_{254} neutral (Type E) for alumina).

Calix[4]arene[46] and cyclen·$2H_2SO_4$[7,8] were prepared following literature procedures.

2.2 Synthesis of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (20)

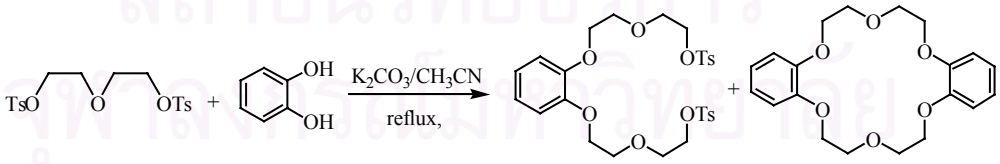
2.2.1 Preparation of 1,2-*bis*(diethyleneglycol tosyl)benzene (2)

Pathway I



Step I**:** Into a 1000 mL 2 necked round bottom flask containing diethylene glycol (10.62 g, 100 mmol), triethylamine (14.5 mL, 200 mmol), a catalytic amount of DMAP in dichloromethane (400 mL) chilled to 0 °C with ice bath, the solution of TsCl (38.10 g, 200.0 mmol) in dichloromethane (100 mL) was slowly added. The reaction mixture was stirred at room temperature for 4 hours and extracted with water (2 × 100 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, a white solid of diethylene glycol ditosylate (**1**) was separated from the yellow oil residue by an addition of with diethyl ether (25.7 g, 62 %, mp 84 - 85 °C).

Characteristic data for diethylene glycol ditosylate (1): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.76 (d, 4H, $J_{H\text{-}H}$ = 8.3 Hz, Ar**H**), 7.33 (d, 4H, $J_{H\text{-}H}$ = 8.3 Hz, Ar**H**), 4.07 (t, 4H, $J_{H\text{-}H}$ = 4.6 Hz, TsOC**H$_2$**CH_2), 3.59 (t, 4H, $J_{H\text{-}H}$ = 4.8 Hz, C**H$_2$**O), 2.43 (s, 6H, ArC**H$_3$**)



1 **2** **3**

Step II**:** Into a 250 mL 2 necked round bottom flask containing catechol (1.10 g, 10.0 mmol), K_2CO_3 (13.82 g, 100 mmol) and acetonitrile (100 mL), a solution of diethylene glycol ditosylate (**1**) (20.72 g, 50.0 mmol) in acetonitrile (50 mL) was added dropwise. The reaction mixture was refluxed with stirring at under

nitrogen atmosphere for 5 days. After cooling to room temperature, the solvent was evaporated off. The obtained residue was dissolved in dichloromethane (100 mL) and extracted with 3 M HCl (1 × 100 mL) and water (2 × 100 mL), respectively. The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off to give the yellow oil residue. Compound **2** was separated by column chromatography (silica gel, CH_2Cl_2 : Acetone; 96 : 4) as a yellow oil (0.15 g, 9 %) and a white solid of dibenzo-18-crown-6 (**3**) (0.55 g, 31 %).

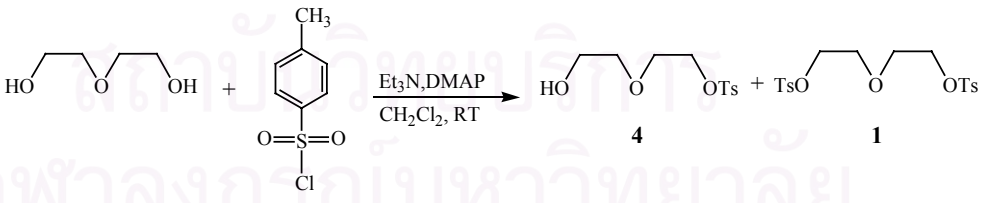
Characteristic data for (2): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.77 (d, 4H, $J_{H\text{-}H}$ = 6.73 Hz, Ar**H**), 7.26 (d, 4H, $J_{H\text{-}H}$ = 7.9 Hz, Ar**H**), 6.86 (s, 4H, Ar**H**), 4.14 (t, 4H, $J_{H\text{-}H}$ = 4.7 Hz, TsOC**H$_2$**), 4.02 (t, 4H, $J_{H\text{-}H}$ = 4.7 Hz, OC**H$_2$**), 3.74-3.70 (m, 8H, C**H$_2$**OC**H$_2$**), 2.37 (s, 6H, C**H$_3$**); **IR spectrum (KBr (cm^{-1}))**: 3067 (CH, st (aromatic)), 2809 (CH_2, st), 1589, 1494, 1465 (C=C, st), 1367, 1186 (S=O, st), 1128 (O-C-C, st)

Elemental analysis: *Anal calcd* for $C_{28}H_{34}O_{10}S_2$: C, 56.55%; H; 5.77%, S; 10.76%

Found: C, 56.25%; H, 5.79%; S, 10.65%

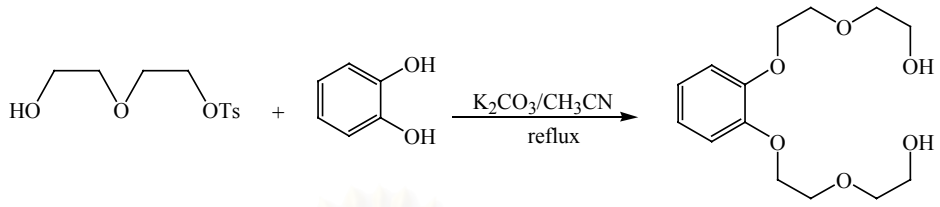
Characteristic data for dibenzo-18-crown-6 (3): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 6.91 (m, 8H, Ar**H**), 4.17-4.11 (m, 8H, ArOC**H$_2$**), 4.05- 3.99 (m, 8H, OC**H$_2$**)

Pathway II



Step I: Into a 1000 mL 2 necked round bottom flask containing a solution of diethylene glycol (10.62 g, 100 mmol), triethylamine (14.5 mL, 200 mmol), a catalytic amount of DMAP in dichloromethane (400 mL) chilled at 0 °C, a solution of TsCl (19.05 g, 100 mmol) in dichloromethane (100 mL) was slowly added. The reaction mixture was stirred at room temperature for 4 hours and extracted with water (2 × 100 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and

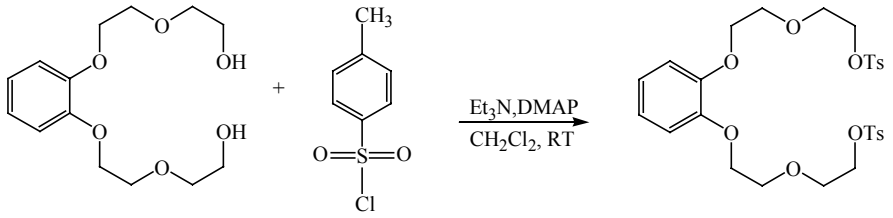
filtered off. After removal of solvent, a yellow oil of diethylene glycol monotosylate (**4**) (5.66 g, 22 %) was separated by column chromatrography (silica gel, CH_2Cl_2 : acetone; 96 : 4) and diethylene glycol ditosylate (**1**) was also obtained (14.9 g, 36%).



4 **5**

Step II: Into a 250 mL 2 necked round bottom flask containing catechol (0.89 g, 8 mmol), K_2CO_3 (11.07 g, 80 mmol) and acetonitrile (100 mL), a solution of diethylene glycol monotosylate (**4**) (5.65 g, 20 mmol) in acetonitrile (50 mL) was added dropwised. The reaction mixture was stirred and refluxed under nitrogen atmosphere for 5 days. After cooling to room temperature, the solvent was removed off. The obtained residue was dissolved in dichloromethane (100 mL) and extracted with 3 M HCl (1 × 100 mL) and water (2 × 100 mL), respectively. The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off to give a yellow oil residue. Compound **5** was purified by column chromatography (silica gel, CH_2Cl_2 : Acetone; 96 : 4) as a yellow oil (2.19 g, 95%).

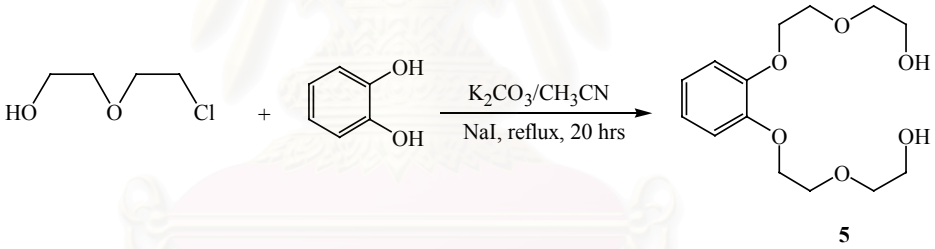
Characteristic data for 1,2-*bis*(diethylene glycol)benzene (5): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 6.87 (s, 4H, Ar**H**), 4.13 (t, 4H, $J_{H\text{-}H}$ = 4.1 Hz, ArOC**H$_2$**), 3.89 (t, 4H, $J_{H\text{-}H}$ = 4.3 Hz, ArOCH$_2$C**H$_2$**OH), 3.74 (t, 4H, $J_{H\text{-}H}$ = 4.3 Hz, OC**H$_2$**CH$_2$OH), 3.64 (t, 4H, $J_{H\text{-}H}$ = 4.1 Hz, ArOCH$_2$C**H$_2$**), 3.13 (s, 2H, O**H**); **IR spectrum (KBr (cm^{-1}))**, 3381 (OH, st), 3067 (CH, st (aromatic)), 2809 (CH_2, st), 1589, 1494,1465, (C=C, st), 1128 (C-O-C, st), 1054 (C-OH, st)



5 **2**

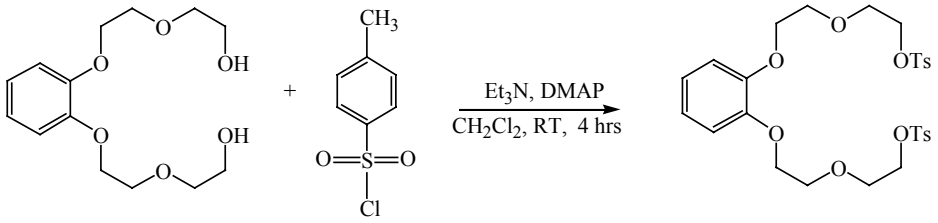
Step III: Into a 500 mL 2 necked round bottom flask containing compound **5** (2.19 g, 7.7 mmol), triethylamine (1.7 mL, 23 mmol), a catalytic amount of DMAP in dichloromethane (200 mL) cooled to 0 °C, a solution of TsCl (2.90 g 15.2 mmol) in dichloromethane (60 mL) was slowly added. After stirring at room temperature for 4 hours, the reaction mixture was extracted with water (2 × 100 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, a white solid of compound **2** was separated by column chromatrography (silica gel, CH_2Cl_2 : Acetone; 96 : 4) as a yellow oil (2.27 g, 56 %).

Pathway III



5

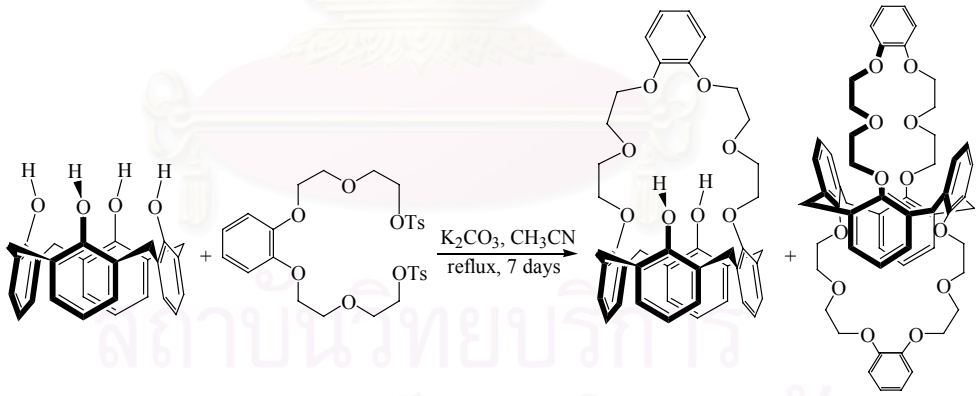
Step I: Into a 250 mL 2-necked round bottom flask containing diethylene glycol monochlorohydrin (10.60 mL, 100 mmol), K_2CO_3 (27.65 g, 200 mmol), NaI (catalytic amount) and acetonitrile (100 mL) were added dropwise with a solution of catechol (2.21 g, 20 mmol) in acetonitrile (50 mL). The reaction mixture was stirred at reflux under nitrogen atmosphere for 24 hours. After the reaction mixture was allowed to cool to room temperature, K_2CO_3 was filtered off. The solvent was removed to dryness under reduced pressure. The obtained residue was dissolved in dichloromethane (100 mL). The solution was extracted with 3 M HCl (2 × 50 mL) and washed with water (2 × 50 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. The solvent was removed to afford compound **5** as a yellow oil (7.54 g), which was used for next step without further purification.



5 **2**

Step II: Into a 500 mL 2-necked round bottom flask, containing compound **5** from the step I, triethylamine (10.94 mL, 79.0 mmol) and catalytic amount of DMAP dissolved in dichloromethane (100 mL) and chilled to 0 °C with ice bath, a solution of TsCl (15.07 g, 79.0 mmol) in dichloromethane (200 mL) was added dropwise. The reaction mixture was stirred at room temperature for 4 hours. The reaction mixture was extracted with water (2 × 100 mL) and dried over Na_2SO_4 anhydrous. After filtered off, the solvent was removed off to give a yellow viscous residue. The compound **5** was purified by silica gel column chromatography (EtOAc : CH_2Cl_2; 5 : 95) as a yellow oil (5.00 g, 42 %).

2.2.2 Preparation of calix[4]-benzo-crown-6 (6)



2 **6** **7**

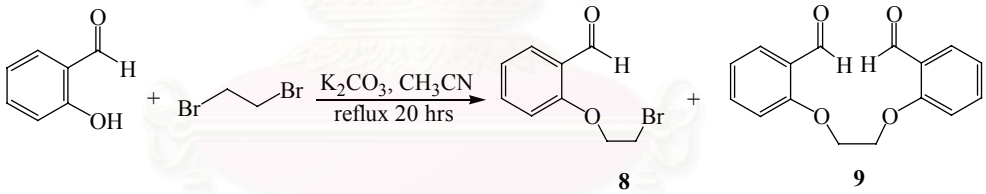
Into a 250 mL 2-necked round bottom flask containing calix[4]-arene (4.9 g, 1.2 mmol), K_2CO_3 (0.17 g, 1.2 mmol) and acetonitrile (100 mL) was added dropwise a solution of 1,2-*bis*(diethyleneglycol tosyl)benzene (**2**) (0.69 g, 1.2 mmol) dissolved in acetonitrile (50 mL). The reaction mixture was stirred and refluxed under nitrogen atmosphere for 7 days. After cooling to room temperature, the solvent was removed to give a yellow viscous oil. The obtained residue was dissolved in dichloromethane (100 mL), extracted with 3M HCl (1 × 50 mL) and washed with water (2 × 50 mL).

The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, the obtained residued was purified by column chromatography (silica gel, CH_2Cl_2 : Acetone; 95 : 5), a white solids of calix[4]-benzo-crown-6 (**6**) (0.073 g, 9 %) and 1,3-alternate calix[4]-*bis*(benzo-crown-6) (**7**) (0.14 g, 26 %) were obtained.

Characteristic data for (6): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.73 (s, 2H, ArO**H**), 7. 06 (d, 4H, $J_{H\text{-}H}$ = 7.4 Hz, Ar**H**), 6.95 (s, 4H, Ar**H**), 6.89 (d, 4H, $J_{H\text{-}H}$ = 9.7 Hz, Ar**H**), 6.74 - 6.65 (m, 4H, Ar**H**), 4.32 - 4.16 (m, 16H, OC**H** $_2$), 4.13, 3.35 (dd (AB system), 8H, $J_{H\text{-}H}$ = 13.0 Hz, ArC**H$_2$**Ar)

Characteristic data for (7): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.06 (d, 8H, $J_{H\text{-}H}$ = 7.5 Hz, Ar**H**), 6.98 (s, 8H, Ar**H**), 6.68 (t, 8H, $J_{H\text{-}H}$ = 7.3 Hz, Ar**H**), 4.13 (t, 8H, $J_{H\text{-}H}$ = 4.3 Hz, ArOC**H**$_2$), 3.77 (s, 8H, ArC**H$_2$**Ar), 3.69 (t, 8H, $J_{H\text{-}H}$ = 4.4 Hz, ArOCH$_2$C**H**$_2$), 3.60 - 3.53 (m, 16H, C**H**$_2$OC**H**$_2$)

2.2.3 Preparation of 2-(2′-bromoethoxy)benzaldehyde (8)



8 **9**

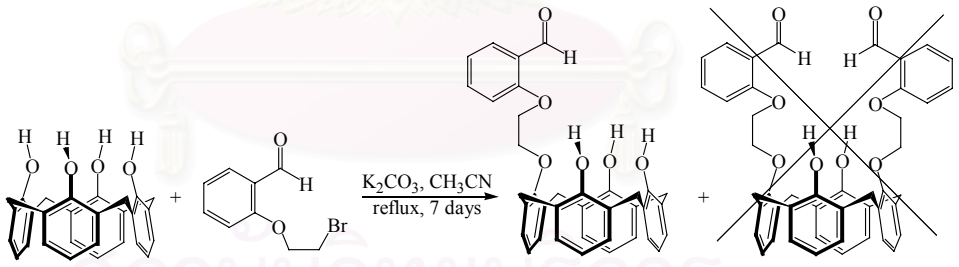
Into a 1000 mL 2-necked round bottom flask containing salicylaldehyde (12.42 g, 100.0 mmol), K_2CO_3 (26.10 g, 200.0 mmol) and acetonitrile (250 mL) was added dropwise a solution of 1,2-dibromoethane (86.6 mL, 1000 mmol). The reaction mixture was stirred and refluxed under nitrogen atmosphere. After 8 hours of reaction, the reaction mixture was allowed to cool to room temperature. K_2CO_3 was filtered off and washed with dichloromethane. The filtrate was evaporated to dryness and dissolved in dicloromethane (200 mL). The solution was extracted with 10% W/V NaOH (100 × 2 mL) and water (2 × 100 mL), respectively. The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, a yellow oil residue was afforded. The obtained residue was purified by column chromatography (silica gel, 100% CH_2Cl_2) to give the white solids of compound **8**

(5.27 g, 23%, mp 57-58°C) and 1,2-*bis*(2-carboxaldehydephenoxy)ethane (**9**) (3.99 g, 22%, mp 128-129 °C).

Characteristic data for (8): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 10.55 (s, 1H, ArC**H**O), 7.87 (dd, 1H, J_{H-H} = 1.8, 7.7 Hz, Ar**H**), 7.56 (dt, 1H, J_{H-H} = 0.9, 6.4 Hz, Ar**H**), 7.08 (t, 1H, J_{H-H} = 7.4 Hz, Ar**H**), 6.96 (d, 1H, J_{H-H} = 8.4 Hz, Ar**H**), 4.43 (t, 2H, J_{H-H} = 6.0 Hz, ArOC**H$_2$**), 3.72 (t, 2H, J_{H-H} = 6.1 Hz, C**H$_2$**Br); **IR spectrum (KBr (cm^{-1}))**: 3034 (CH, st (aromatic), 2865 (CH_2, st), 2762 (CHO, st), 1677 (C=O, st), 1484, 1451 (C=C, st), 1228 (O-C-C, st), 1183 (CH-Br, st)

Characteristic data for (9): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 10.42 (s, 2H, ArC**H**O), 7.83 (dd, 2H, J_{H-H} = 2.0, 8.1 Hz, Ar**H**), 7.56 (dt, 2H, J_{H-H} = 1.9, 7.6 Hz, Ar**H**), 7.24-7.02 (m, 4H, Ar**H**), 4.51 (s, 4H, ArOC**H$_2$**); **IR spectrum (KBr (cm^{-1}))**: 3071 (CH, st (aromatic), 2950 (CH_2, st), 2771 (CHO, st), 1691 (C=O, st), 1484, 1451 (C=C, st), 1240 (O-C-C, st)

2.2.4 Preparation of calix[4]-dibenzaldehyde (11) by using K_2CO_3 as base



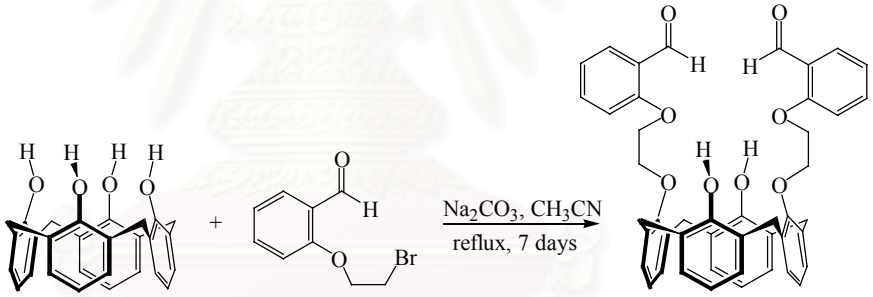
8 **10** **11**

Into a 250 mL 2-necked round bottom flask containing calix[4]arene (2.12 g, 5 mmol), K_2CO_3 (5.30 g, 50 mmol) and acetonitrile (150 mL) was added dropwise a solution of 2-(2′-bromoethoxy)benzaldehyde (**8**) (2.51 g, 11 mmol) in acetonitrile (50 mL). The reaction mixture was stirred at reflux under nitrogen atmosphere for 7 days. After cooling to room temperature, the solvent was removed under reduced pressure to give a colorless viscous oil. The obtained residue was dissolved in dichloromethane (100 mL) and extracted with 3 M HCl (1 × 50 mL) and water (2 × 50 mL), respectively. The combined organic layer was dried over Na_2SO_4 anhydrous and

filtered off. After the removal of the solvent, the obtained residue was purified by column chromatography (silica gel, hexane : CH_2Cl_2; 30 : 70) and compound **10** was obtained as a white solid (2.33 g, 35%) without calix[4]-dibenzaldehyde (**11**) desired.

Characteristic data for (10): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 10.61 (s, 1H, ArC**H**O), 9.53 (s, 1H, ArO**H**), 9.23 (s, 2H, ArO**H**), 7.92 (dd, 2H, $J_{H\text{-}H}$ = 1.8, 7.7 Hz, Ar**H**), 7.64 (t, 2H, $J_{H\text{-}H}$ = 8.1 Hz, Ar**H**), 7.24 (m, 10H, Ar**H**), 7.15 (t, 4H, $J_{H\text{-}H}$ = 8.8 Hz, Ar**H**), 4.77 (t, 2H, $J_{H\text{-}H}$ = 4.26 Hz, ArOC**H$_2$**), 4.62 (t, 2H, $J_{H\text{-}H}$ = 4.28 Hz, $ArOCH_2C$**H$_2$**) 4.43 (dd (AB system), 2H, $J_{H\text{-}H}$ = 13.0 Hz, ArC**H$_2$**Ar), 4.15 (dd (AB system), 2H, $J_{H\text{-}H}$ = 13.0 Hz, ArC**H$_2$**Ar), 3.51, 3.42 (dd (AB system), 4H, $J_{H\text{-}H}$ = 13.0 Hz, ArC**H$_2$**Ar); **IR spectrum (KBr (cm^{-1}))**: 3278(OH, st), 3070 (CH, st (aromatic)), 2931(CH_2, st), 2865(CHO, st), 1682, (C=O, st), 1597,1510, 1461 (C=C, st), 1214 (O-C-C, st)

2.2.5 Preparation of calix [4]-dibenzaldehyde (11) by using Na_2CO_3 as base



8 **11**

Into a 250 mL 2-necked round bottom flask containing calix[4]arene (2.12 g, 5 mmol), Na_2CO_3 (5.30 g, 50 mmol) and acetonitrile (150 mL) was added dropwise a solution of 2-(2′-bromoethoxy)benzaldehyde (**8**) (2.51 g, 11 mmol) in acetonitrile (50 mL). The reaction mixture was stirred at reflux under nitrogen atmosphere for 7 days. After cooling to room temperature, the solvent was removed under reduced pressure to give a colorless viscous oil. The residue was dissolved in dichloromethane (100 mL) and extracted with 3 M HCl (1 × 50 mL) and water (2× 50 mL), respectively. The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After the removal of about two third of the solvent, hexane was added to

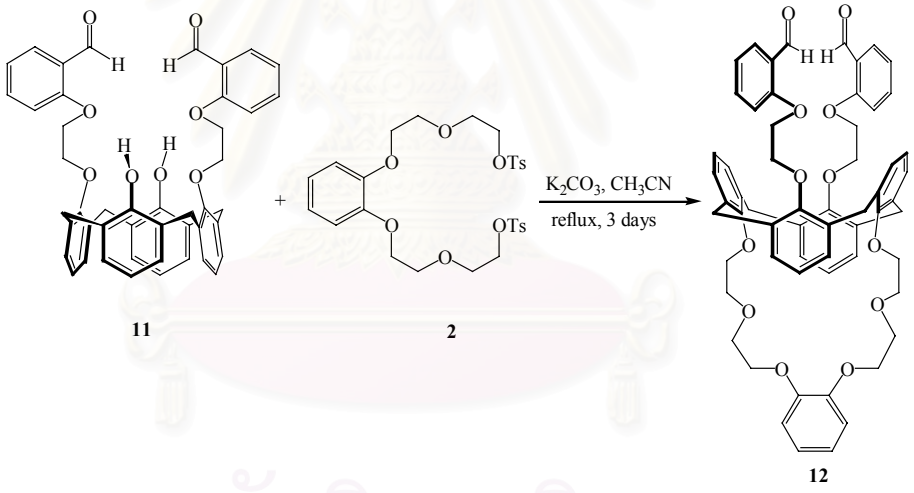
precipitate, compound **11** was obtained as a white solid (2.33 g, 65 %, mp 209 - 210 °C).

Characteristic data for (11): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 10.31(s, 2H, ArC**H**O), 7.89 (s, 2H, ArO**H)** 7.86 (d, 2H, J_{H-H} = 7.6 Hz, Ar**H**), 7.52 (dt, 2H, J_{H-H} = 1.2 Hz, 8.7 Hz, Ar**H**), 7.04 - 6.99 (m, 6H, Ar**H**)**,** 6.95 - 6.91 (m, 6H, Ar**H**)**,** 6.77 (dt, 2H, J_{H-H} = 7.5 Hz, 1.9 Hz, Ar**H**), 6.64 (t, 2H, J_{H-H} = 7.5 Hz, Ar**H**), 4.39, 3.45 (dd (AB system), 8H, J_{H-H} = 13.0 Hz, ArC**H$_2$**Ar), 4.33 (s, 8H, ArOC**H$_2$**); **IR spectrum (KBr (cm^{-1}))**: 3034 (CH, st (aromatic)), 2921 (CH_2, st), 2865 (CHO, st), 1682 (C=O, st), 1597, 1507, 1456 (C=C, st), 1240 (O-C-C, st)

Elemental analysis: *Anal calcd* for $C_{46}H_{40}O_8$: C, 76.69%; H, 5.70%

Found: C, 75.90%, H; 5.70%

2.2.6 Preparation of 1,3-alternate calix[4]-dibenzaldehyde-benzo-crown-6 (12)



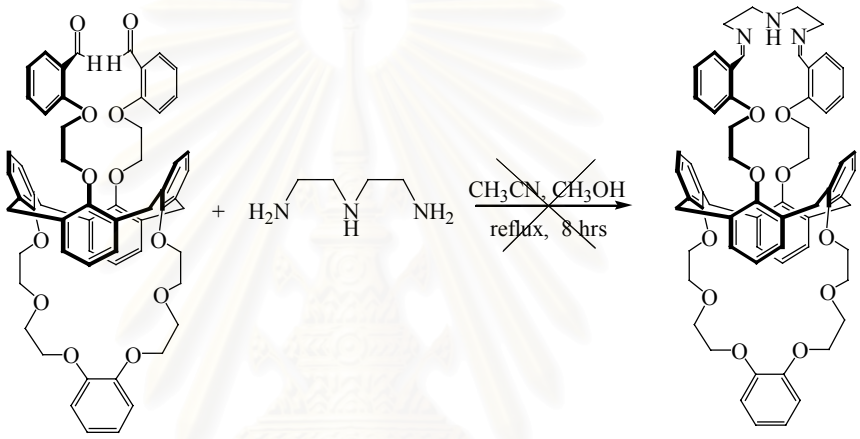
11 **2** **12**

Into a 100 mL 2-necked round bottom flask containing calix[4]-dibenzaldehyde (**11**) (1.0 g, 1.39 mmol), K_2CO_3 (1.92 g, 13.87 mmol) and acetonitrile (70 mL) was added dropwise a solution of 1,2-*bis*(diethyleneglycol tosyl)benzene (**2**) (0.73 g, 1.39 mmol) in acetonitrile (30 mL). The reaction mixture was stirred and refluxed under nitrogen atmosphere. After 3 days, the reaction mixture was allowed to cool to room temperature. The solvent was removed to give a yellow viscous oil. The obtained residue was dissolved in dichloromethane (50 mL) and slowly added 3M HCl until the *pH* reached to 1. After 30 minutes of stirring, the organic layer was separated and washed with water (2 × 20 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, compound **12** was

eluted from column chromatography (silica gel, EtOAc : CH_2Cl_2; 5 : 95) as a white solid (1.28 g, 95 %).

Characteristic data for (12): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 10.31(s, 2H, ArC**H**O), 7.83 (d, 2H, $J_{H\text{-}H}$ = 7.5 Hz, Ar**H**), 7.48 (t, 2H, $J_{H\text{-}H}$ = 7.6 Hz, Ar**H**), 7.10 - 6.98 (m, 12H, Ar**H**), 6.97 (s, 4H, Ar**H**), 6.74 - 6.59 (m, 4H, Ar**H**), 4.13 (t, 4H, $J_{H\text{-}H}$ = 4.6 Hz, ArOC**H$_2$**), 3.89 (s, 8H, ArC**H$_2$**Ar), 3.78 (s, 8H, ArOC**H$_2$**), 3.73 (t, 4H, $J_{H\text{-}H}$ = 4.6 Hz, OC**H$_2$**C**H$_2$O**), 3.56 (m, 8H, C**H$_2$**O)

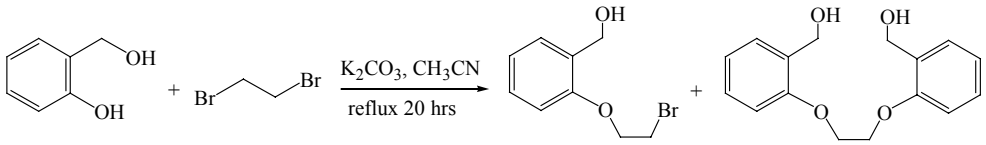
2.2.7 Synthesis of calix[4]-diimine–benzo-crown-6 (13)



12 **13**

Into a 250 mL 2-necked round bottom flask containing a solution of calix[4]-dibenzaldehyde-benzo crown-6 (**12**) (1.22 g, 1.32 mmol) in acetonitrile (100 mL) was added dropwise a solution of diethylene triamine (0.14 mL, 1.32 mmol) in methanol (30 mL). After 12 hours of reflux, the reaction mixture was allowed to cool to room temperature to afford a yellow solution. The solvents were evaporated to dryness. The obtained residue was characterized by ^{1}H-NMR spectroscopy but signal of imine proton (-C**H**=N-) at about 8.6 ppm was not observed on the ^{1}H-NMR spectrum indicated that the desired product was not obtained.

2.2.8 Preparation of 2-(2′-bromoethoxy)benzyl alcohol (14)



14 **15**

Into a 250 mL 2-necked round bottom flask containing 2-hydroxybenzyl alcohol (6.20 g, 50 mmol), K_2CO_3 (34.55 g, 250 mmol) and acetonitrile (250 mL) was added dropwise with a solution of 1,2-dibromoethane (43.09 mL, 500 mmol). The reaction mixture was stirred and refluxed under nitrogen atmosphere. After 8 hours of reaction, the solution mixture was allowed to cool to room temperature. K_2CO_3 was filtered off and washed with dichloromethane (50 mL). The filtrate was evaporated to dryness and dissolved in dicloromethane (200 mL). The solution was extracted with 3 M HCl (1 × 50 mL) and water (2 × 50 mL), respectively. The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, a yellow oil residue was afforded (12.06 g). The obtained residue was dissolved in diethyl ether and chilled with ice bath to afford a white solid of compound **15** (4.35 g, 32 %, mp 139-140°C). After filtered compound **15**, the filtrate was evaporated to dryness to give a compound **14** as a yellow oil (7.71 g, 66 %).

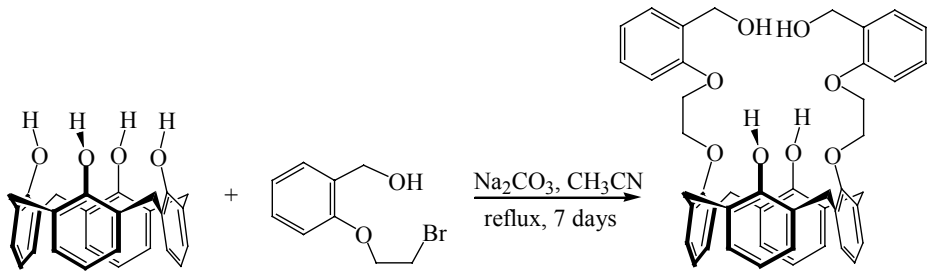
Characteristic data for (14): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.30-7.20 (m, 2H, Ar**H**), 6.95 (t, 1H, $J_{H\text{-}H}$ = 7.4 Hz, Ar**H**), 6.80 (d, 1H, $J_{H\text{-}H}$ = 8.0 Hz, Ar**H**), 4.68 (s, 2H, ArC**H**$_2$), 4.28 (t, 2H, $J_{H\text{-}H}$ = 5.7 Hz, ArOC**H**$_2$), 3.66 (t, 2H, $J_{H\text{-}H}$ = 5.7 Hz, ArCH$_2$C**H**$_2$Br), 2.95 (s, 1H, ArCH$_2$O**H**); **IR spectrum (KBr (cm^{-1}))**: 3562 (OH, st), 3075(CH, st(aromatic)), 2869 (CH, st), 1602,1491 (C=C, st), 1224(C-O, st)

Elemental analysis: *Anal calcd* for $C_9H_{11}Br\ O_2$: C, 46.96%; H, 4.82%

Found: C, 46.97%; H, 4.77%

Characteristic data for (15): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.30-7.23 (m, 4H, Ar**H**), 7.01-6.89 (m, 4H, Ar**H**), 4.36 (s, 4H, ArC**H**$_2$OH), 4.40 (s, 4H, OC**H**$_2$C**H**$_2$O), 3.07 (s, 2H, ArCH$_2$O**H**); **IR spectrum (KBr (cm^{-1})):** 3315 (OH, st), 3075(CH, st(aromatic)), 2869 (CH$_2$, st), 1598, 1586 (C=C, st), 1235 (C-O, st)

2.2.9 Preparation of 1,3-calix[4]-dibenzyl alcohol (16)



14 **16**

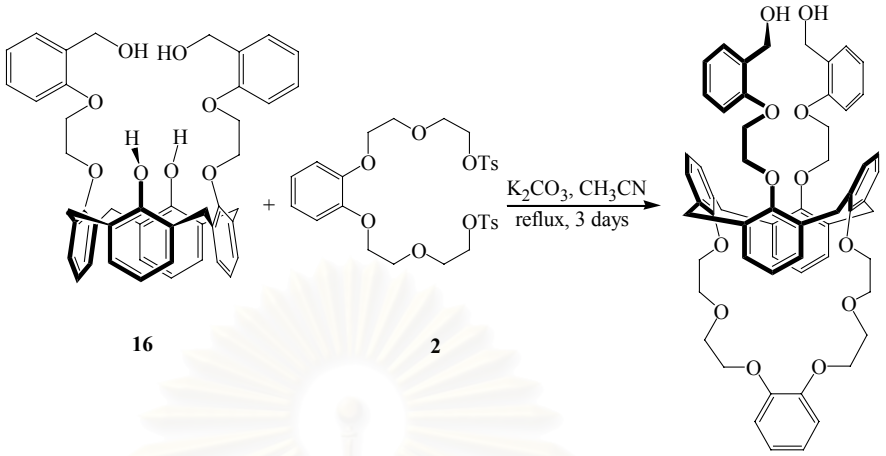
Into a 250 mL 2-necked round bottom flask containing calix[4]arene (4.24 g, 10 mmol), Na_2CO_3 (10.60 g, 100 mmol) and acetonitrile (150 mL) was added dropwise with a solution of 2-(2′-bromoethoxy)benzyl alcohol (**14**) (6.93 g, 30 mmol) in acetonitrile (50 mL). After the reaction was stirred and refluxed under nitrogen atmosphere for 7 days. The reaction mixture was allowed to cool to room temperature, the solvent was removed under reduced pressure to give a colorless viscous oil. The obtained residue was dissolved in dichloromethane (100 mL) and slowly added 3M HCl until *pH* of the solution reached 1. After 30 minutes of stirring, the organic layer was washed with water (2 × 50 mL). The combined organic layers were dried over Na_2SO_4 anhydrous and filtered off. After the removal of the solvent, hexane was added to afford a white solid of compound **16** (3.86 g, 53 %, mp 213 - 214 °C).

Characteristic data for (16): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 8.85 (s, 2H, ArO**H)** 7.31-7.23 (dd, 2H, J_{H-H} = 1.7, 7.3 Hz, Ar**H**), 7.16 (dt, 2H, J_{H-H} = 1.2, 7.8 Hz, Ar**H**), 7.07- 6.90 (t, 4H, J_{H-H} = 8 Hz, Ar**H**)**,** 6.98 (d, 4H, J_{H-H} = 8.7 Hz, Ar**H**), 6.94 (dt, 2H, J_{H-H} = 1.9, 7.9 Hz, Ar**H**), 6.85 (t, 2H, J_{H-H} = 7.5 Hz, Ar**H**), 6.77 - 6.60 (m, 4H, Ar**H**), 4.62 (d, 4H, J_{H-H} = 6.8 Hz, ArC**H$_2$**), 4.39, 3.45 (dd (AB system), 8H, J_{H-H} = 13.0 Hz, ArC**H$_2$**Ar), 4.33 (s, 8H, ArOC**H$_2$**); **IR spectrum (KBr, (cm^{-1}))**: 3449 (OH, st), 3075(CH, st (aromatic)), 3017 (CH_2, st), 1589, 1494,1465, (C=C, st), 1081 (C-O, st)

Elemental analysis: *Anal calcd* for $C_{46}H_{44}O_8$: C, 76.22%; H, 6.12%

Found: C, 76.19%, H; 6.08%

2.2.10 Preparation of 1,3-alternate calix[4]-dibenzyl alcohol-benzo-crown-6 (17)



16 **2** **17**

Into a 100 mL 2-necked round bottom flask containing calix[4]-dibenzylalcohol (**16**) (0.725 g, 1 mmol), K_2CO_3 (1.38 g, 10 mmol) and acetonitrile (50 mL), was added dropwise a solution of 1,2-*bis*(diethyleneglycol tosyl)benzene (**2**) (0.56 g, 1 mmol) dissolved in acetonitrile (20 mL). The reaction mixture was stirred and refluxed under nitrogen atmosphere for 3 days. The reaction mixture was allowed to cool to room temperature. The solvent was removed off to give a yellow viscous oil. The obtained residue was dissolved in dichloromethane (50 mL) and slowly added 3M HCl until the *pH* reached 1. After stirring the mixture for 30 minutes, the organic layer was washed with water (2 × 20 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of solvent, the residue was purified by column chromatography (silica gel, EtOAc : CH_2Cl_2; 5 : 95) to give compound **17** as a white solid (0.93 g, 98 %, mp 72 - 73 °C).

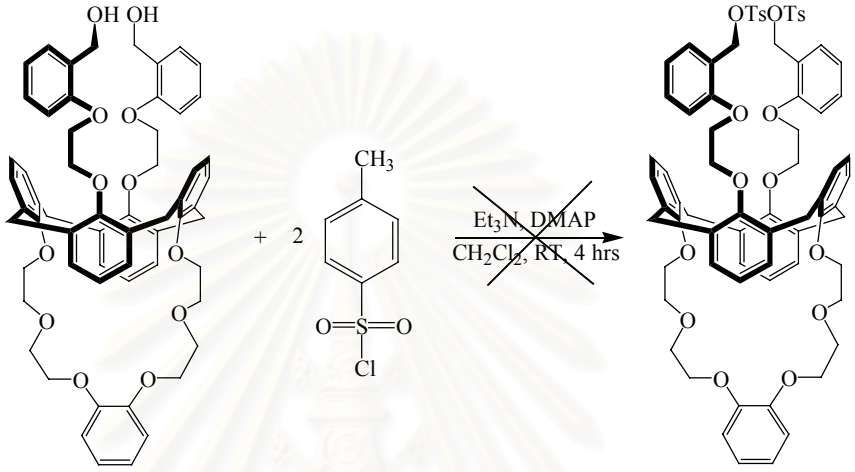
Characteristic data for (17): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.33 (dd, 2H, $J_{H\text{-}H}$ = 7.3 Hz, 1.4 Hz, Ar**H**), 7.21 (d, 2H, $J_{H\text{-}H}$ = 7.3 Hz, Ar**H**), 7.07 (d, 4H, $J_{H\text{-}H}$ = 7.6 Hz, Ar**H**), 7.03 (d, 4H, $J_{H\text{-}H}$ = 7.6 Hz, Ar**H**), 6.99 (d, 4H, $J_{H\text{-}H}$ = 7.6 Hz, Ar**H**), 6.95 (s, 4H, Ar**H**), 6.76 - 6.68 (m, 4H, Ar**H**), 4.65 (s, 4H, ArC**H$_2$**OH), 4.17-4.10 (m, 4H, ArOC**H$_2$**), 3.81 (s, 8H, ArC**H$_2$**Ar), 3.77 - 3.72 (m, 12H, OC**H$_2$**), 3.61 (dd, 4H, $J_{H\text{-}H}$ = 6.7, 4.6 Hz, OC**H$_2$**), 3.55 (d, 4H, $J_{H\text{-}H}$ = 4.4 Hz, OC**H$_2$**), 2.65 (s (broad), 2H, ArCH$_2$O**H**); **IR spectrum (KBr/(cm^{-1}))**: 3442 (OH, st), 3065 (CH, st

(aromatic)), 2918 (CH, st), 1589, 1494,1465 (C=C, st), 1124 (C-O-C, st), 1054 (C-OH, st)

Elemental analysis: *Anal calcd* for $C_{60}H_{62}O_{12}$: C, 75.90%, H, 6.41%

Found: C, 75.65%, H, 6.53%

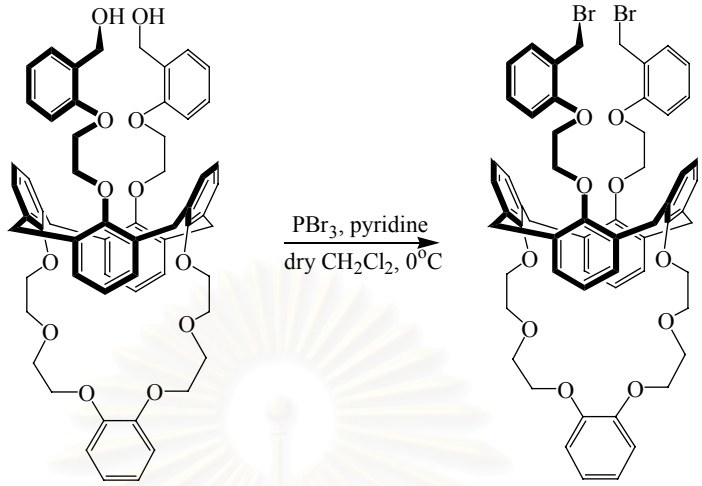
2.2.11 Synthesis of calix[4]-dibenzyl tosylate-benzo-crown-6 (18)



17 **18**

Into a 250 ml 2-necked round bottom flask containing a solution of calix[4]-dibenzyl alcohol benzo-crown-6 (**17**) (1.63 g, 1.72 mmol) and triethylamine (0.52 mL, 3.61 mmol) in dichloromethane (100 mL) and catalytic amount of DMAP was added dropwise a solution TsCl in dichloromethane (50 mL) at 0°C. After 4 hours of stirring under nitrogen atmosphere at room temperature, the reaction mixture was extracted with water (2 × 50 ml). The combined organic layer was dried over Na_2SO_4 and solvent was removed to dryness. The obtained crude product was separated by column chromatography (silica gel, MeOH : CH_2Cl_2; 40 : 60). The compound in each fraction was characterized by ^{1}H-NMR spectroscopy. The desired product (**18**) was not observed.

2.2.12 Preparation of 1,3-alternate calix[4]-dibenzyl bromide-benzo-crown-6 (19)



17 **19**

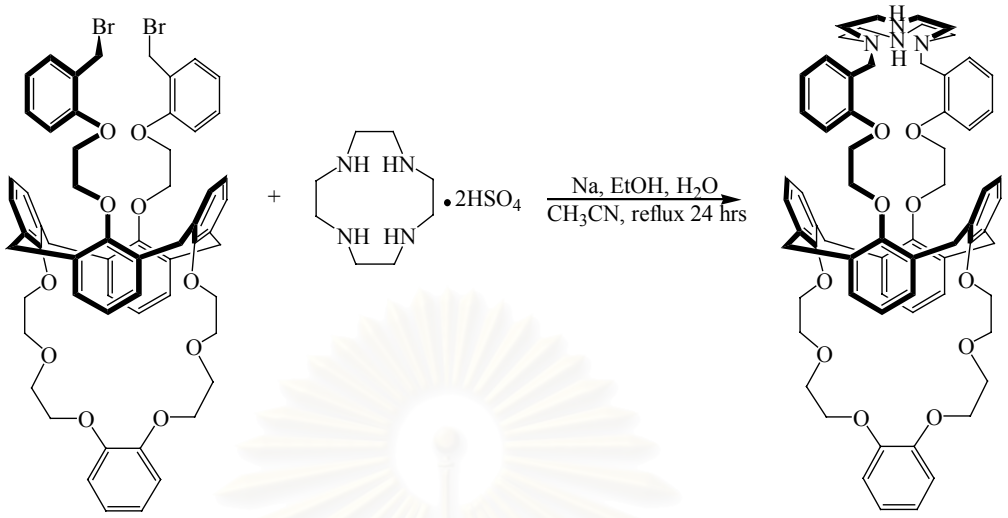
Into a 100 mL 2-necked round bottom flask equipped with a magnetic bar and a drying tube, was charged with calix[4]-dibenzyl alcohol-benzo crown-6 (**17**) (1.95 g, 2 mmol), pyridine (0.16 mL, 2 mmol) and dry dichloromethane (50 mL). The reaction mixture was stirred and cooled to 0 °C. PBr_3 (0.19 mL, 2 mmol) was slowly added into the solution. After the disapperance of compound **17** (the completion of the reaction) as monitored by TLC, the unreacted PBr_3 was quenched with water. The reaction mixture was washed with water (2 × 50 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (silica gel, hexane : EtOAc; 20 : 80) to give compound **19** as a white solid (2.15 g, 98 %, mp 66 - 67°C).

Characteristic data for (19): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.33 (dd, 2H, $J_{H\text{-}H}$ = 1.3, 7.4 Hz, Ar**H**), 7.18 (dt, 2H, $J_{H\text{-}H}$ = 1.3, 7.8 Hz, Ar**H**), 7.08 (d, 8H, $J_{H\text{-}H}$ = 7.5 Hz, Ar**H**), 6.98 (s, 4H, Ar**H**), 6.89 (t, 2H, $J_{H\text{-}H}$ = 7.4 Hz, Ar**H**), 6.74-6.68 (m, 6H, Ar**H**), 4.54 (s, 4H, ArC**H**$_2$Br), 4.13 (t, 4H, $J_{H\text{-}H}$ = 5.0 Hz, ArOC**H**$_2$), 3.89 – 3.83 (m, 8H, ArOC**H**$_2$), 3.82 (s, 8H, ArC**H**$_2$Ar), 3.71 (t, 4H, $J_{H\text{-}H}$ = 4.9 Hz, OC**H**$_2$), 3.64 – 3.54 (m, 8H, OC**H**$_2$); **IR spectrum (KBr (cm^{-1}))**: 3059 (CH, st(aromatic)), 2910 (CH, st), 1589, 1494, 1465 (C=C, st), 1252 (C-O, st), 606 (CH-Br, st)

Elemental analysis: *Anal calcd* for $C_{60}H_{60}O_{12}Br$: C, 65.46 %; H, 5.49 %

Found: C, 65.89 %; H, 6.06 %

2.2.14 Preparation of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (20)



19 **20**

Into a 250 mL 2-necked round bottom flask containing absolute ethanol (10 mL) was placed with Na (0.46 g, 20 mmol) which was cut into small pieces. The solution mixture was stirred until sodium reacted completely. Then a solution of cyclen·$2H_2SO_4$[7] (0.37 g, 1 mmol) in water (5 mL) was slowly added to the mixture. After stirring the reaction mixture for 30 minutes, the 1,3-alternate calix[4]-dibenzyl bromide-benzo-crown-6 (**19**) (1.10 g, 1 mmol) in acetonitrile (200 mL) was added dropwise. The reaction mixture was stirred and refluxed under nitrogen atmosphere for 24 hours. The reaction mixture was allowed to cool to room temperature then the solvent was removed to give a yellow viscous oil. The obtained residue was dissolved in dichloromethane (100 mL) and extracted with water (3 × 50 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered off. After removal of the solvent under reduced pressure, the obtained crude was purified by column chromatography (aluminium oxide, acetone : CH_2Cl_2; 25 : 75). The compound **20** was obtained as a white solid (0.05 g, 10 %, mp 190 - 200 °C (dec)).

Characteristic data for (20): ^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): 7.49 (d, 2H, $J_{H\text{-}H}$ = 6.2 Hz, Ar**H**), 7.15 (t, 2H, $J_{H\text{-}H}$ = 7.2 Hz, Ar**H**), 7.08 (t, 4H, $J_{H\text{-}H}$ = 7.8 Hz, Ar**H**), 7.03 (d, 4H, $J_{H\text{-}H}$ = 8.4 Hz, Ar**H**), 6.97 (s, 4H, Ar**H**), 6.92 (t, 2H, $J_{H\text{-}H}$ =6.9 Hz, Ar**H**), 6.82 - 6.70 (m, 6H, Ar**H**), 4.13 (t, 4H, $J_{H\text{-}H}$ = 4.8 Hz, ArOC$\mathbf{H}_2$), 3.79 (s, 8H, ArC$\mathbf{H}_2$Ar), 3.77 - 3.72 (m, 20H, NC$\mathbf{H}_2$ and OC$\mathbf{H}_2$), 3.63 - 3.53 (m, 8H, ArC$\mathbf{H}_2$N

and OC**H**$_2$), 3.54 (t, 4H, $J_{H\text{-}H}$ = 5.5 Hz, OC**H**$_2$), 2.82 (d, 8H, $J_{H\text{-}H}$ = 9.1 Hz, **H**NCH$_2$);

IR spectrum (KBr (cm^{-1})): 3058 (CH, st(aromatic)), 2918 (CH, st), 1635 (C-N, st), 1589, 1494, 1465 (C=C, st), 1362 (C-N, st), 1243, 1049 (C-O, st)

ES –TOF MS (m/z): 1110.3 (100 %), 1111.3 (59.3 %)

Elemental analysis: *Anal calcd* for $C_{68}H_{78}O_{10}N_4$. 0.5 CH_2Cl_2: C, 71.32 %; H, 6.55 %; N, 4.84%

Found: C, 70.81%; H, 6.55%; N, 2.48%

2.3 Complexation studies

2.3.1 Complexation studies of ligand 20 with Cs^+, K^+ and Zn^{2+} picrates

A solution of 0.01 M of ligand **20** (0.005 mmol) in $CDCl_3$ (0.5 mL) was prepared in NMR tubes. An excess of metal picrates were added directly to the solution. The ^{1}H-NMR spectra were recorded after addition and every 24 hours.

2.3.2 Complexation studies of ligand 20 with zinc salts

A 0.025 M solution of ligand **20** (0.025 mmol) in $CDCl_3$ (2 mL) was prepared. The excess amount of $ZnX{\cdot}nH_2O$ (X = SO_4^{2-}, $(AcO^-)_2$, $(NO_3^-)_2$, CO_3^{2-}, $(Cl^-)_2$,$(Br^-)_2$, $(I^-)_2$) were dissolved with methanol-d_4 (0.1 mL) in NMR tubes. The 0.2 mL of ligand solution was added into the solutions of ZnX prepared. The ^{1}H-NMR spectra were recorded after addition and every 24 hours.

2.3.3 Tritration of ligand 20 with $ZnSO_4$

A 0.025 M solution of ligand **20** (0.025 mmol) in $CDCl_3$ (2 mL) was prepared. 0.2 mL of ligand solution was added into the solutions of 0-2 equivalents of $ZnSO_4{\cdot}7H_2O$ in 0.1 mL of methanol-d_4 in NMR tubes. The ^{1}H-NMR spectra were recorded after addition and every 24 hours.

Table 2.1 Mole ratio of ligand **20** and $ZnSO_4$ in CD_3OD /$CDCl_3$

Mole ratio Zn^{2+}: **20**	$ZnSO_4{\cdot}7H_2O$ (mg)	Volume of (mL)		
		0.025 M of **20**	$CDCl_3$	CD_3OD
0.0 : 1.0	0	0.2	0.2	0.1
0.2 : 1.0	0.3	0.2	0.2	0.1
0.4 : 1.0	0.6	0.2	0.2	0.1
0.6 : 1.0	0.9	0.2	0.2	0.1
0.8 : 1.0	1.2	0.2	0.2	0.1
1.0 : 1.0	1.4	0.2	0.2	0.1
1.4 : 1.0	2.0	0.2	0.2	0.1
2.0 : 1.0	2.9	0.2	0.2	0.1

2.3.4 Complexation studies of ligand 20 with organic molecules

A solution of 0.025 M of ligand **20** (0.025 mmol in $CDCl_3$ 2 mL) was prepared and 0.2 mL (0.005 mmol) of the prepared solution was put into each NMR tubes. 1 equiv. (0.005 mmol) of neutral molecules (phenol, aniline, catechol, resorcinol, dihydroxyquinone and phthalic acid**)** were added directly into each NMR tubes. The ^{1}H-NMR spectra were recorded after addition and every 24 hours.

CHAPTER III

RESULTS AND DISCUSSION

3.1 Synthesis and characterization of 1,2-*bis*(diethyleneglycol tosyl) benzene (2)

Vicens and coworkers have reported that the presence of a phenyl ring in crown ether can increase the complexation ability toward cesium ion. This is because sp^2 carbon in the benzene unit can cause a flatting of the polyether ring and participate in complexation by a cation-π interaction.[47, 48] Therefore, the benzo crown-6 subunit is chosen to attach onto the calix[4]arene framework.

The synthesis of 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) was carried out in three pathways as shown in Figure 3.1.

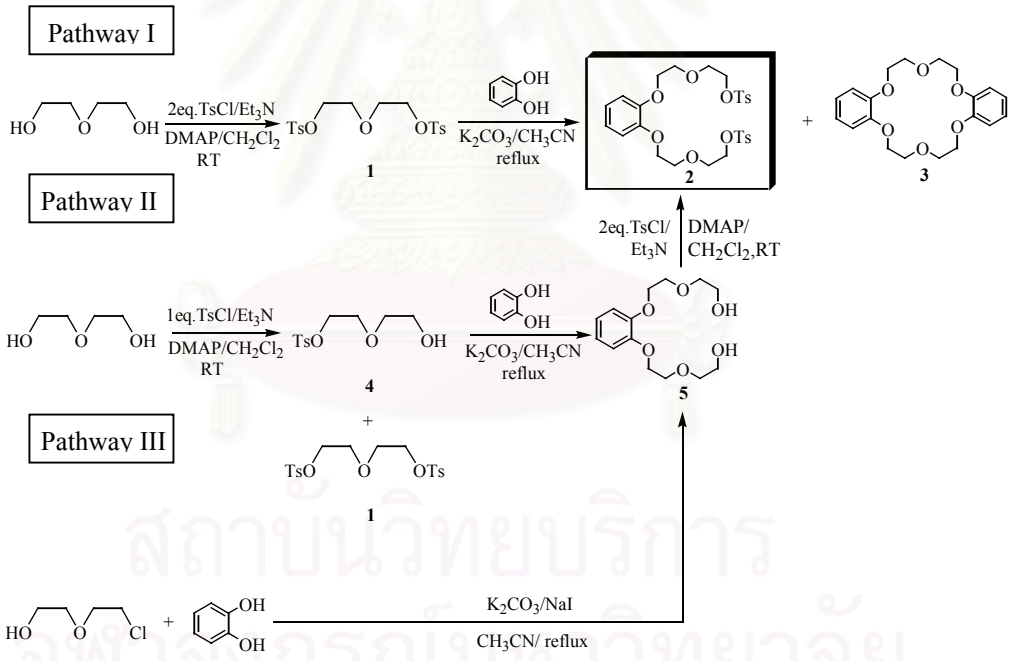


Figure 3.1 Synthetic pathways of 1,2-*bis*(diethylene glycol tosyl)benzene (**2**).

Pathway I

In the beginning, we planed to synthesized 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) by condensation of diethylene glycol ditosylate (**1**) with catechol. This synthetic pathway started with a preparation of diethylene glycol ditosylate (**1**) by tosylation of diethylene glycol in presence of 3 equiv. of triethylamine and a catalytic amount of DMAP in dichoromethane at room temperature for 4 hours. A white solid of compound **1** was obtained in 45% yield by precipitating with diethylether. The ^{1}H-NMR spectrum of compound **1** showed the characteristic peaks of tosyl groups, singlet of C**H**$_3$ at 2.42 ppm and two doublets of Ar**H** at 7.72 and 7.34 ppm ($J_{H\text{-}H}$ = 8.3 Hz). They are accordance with the structure of diethyleneglycol ditosylate (**1**). The substitution reaction of catechol with compound **1** was carried out in the presence of excess K_2CO_3 as a base in acetonitrile for 7 days. After chromatography, a white solid and a yellow oil were obtained. The ^{1} H-NMR spectrum indicates that the yellow oil is the desired product, compound **2** (9% yield). This is due to the presence of characteristic peaks of tosyl groups, a singlet of C**H**$_3$ at 2.37 ppm and two doublet of Ar**H** at 7.77 and 7.26 ppm ($J_{H\text{-}H}$ = 7.7 Hz) of tosyl groups, and singlet of benzene unit of benzo-crown-ether at 6.86 ppm. On the other hand, the ^{1} H-NMR spectrum of compound **3** does not show a characteristic peak of tosyl groups and suggested that the obtained solid has a symmetric structure. The structure of the product was thus deduced to be dibenzocrown-6 (**3**) (31% yeld). The overall yield of this pathway was 5%.

Pathway II

Due to the formation of dibenzo-crown-6 was higher than the desired product, we replaced the ditosylate derivative (**1**) with a monotosylate derivative (**4**) as shown in pathway II.

The monotosylate derivative (**4**) was synthesized by tosylation of diethylene glycol by using 1 equiv. of TsCl, 2 equiv. of triethylamine and catalytic amount of DMAP in dichoromethane at room temperature for 4 hours. After purification on a silica gel column, a clear oil and a white solid were obtained. The ^{1}H-NMR spectrum of the clear oil shows the characteristic peaks of tosyl groups, one siglet at 2.43 ppm and two doublet at 7.77 and 7.33 ppm (J_{H-H}= 7.76 Hz), and a broad signal of hydroxyl group at 3.77 ppm. The ^{1}H-NMR spectrum also indicates that the obtained white solid was the diethyleneglycol ditosylate (**1**). The lower yield of monotosylate derivative (**4**) than ditosylate derivative (**1**), 22% and 36% respectively, may due to the greater solubility of the monotosyl derivative in dichloromethane than that of diethylene glycol.

The monotosyl diethylene glycol (**4**) was attached to catechol by using K_2CO_3 as a base in refluxing acetonitrile for 5 days. After purification by column chromatography, compound **5** was obtained as a clear oil with 95% yield. The ^{1}H-NMR spectrum of compound **5** shows a singlet peak of benzene unit at 6.87 ppm and a broad signal of hydroxyl group at 3.77 ppm which agreed with the structure of 1,2-*bis*(diethylene glycol)benzene (**5**). A tosylation of compound **5** was carried out by using 2 equiv. of TsCl, 2 equiv. of triethylamine and a catalytic amount of DMAP in dichoromethane at room temperature for 4 hours. The 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) was eluted from column chromatography in 56% yield. The overall yield of this pathway was 12%.

Pathway III

Because the preparation the monotosyl diethylene glycol and the synthetic pathway II required of too many steps, we tried to improve the synthesis of desired product (**2**) by using other starting products in pathway III.

The compound **5** was synthesized by a condensation reaction of catechol with diethylene glycol monochlorohydrin by using an excess amount of K_2CO_3 as base in refluxing acetonitrile for 24 hours. The crude product of compound **5** was used without further purification in the tosylation step using the same method mentioned in pathway II. After purification by column chromatography, the compound **2** was obtained in 45% yield and its structure was confirmed by ^{1}H-NMR spectroscopy.

Therefore, we chose the pathway III to synthesized of 1,2-*bis*(diethylene glycol tosyl)benzene (**2**).

3.2 Synthesis and characterization of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (20)

In early attempt, we tried to synthesize compound **20** by the synthetic pathway shown in Figure 3.2.

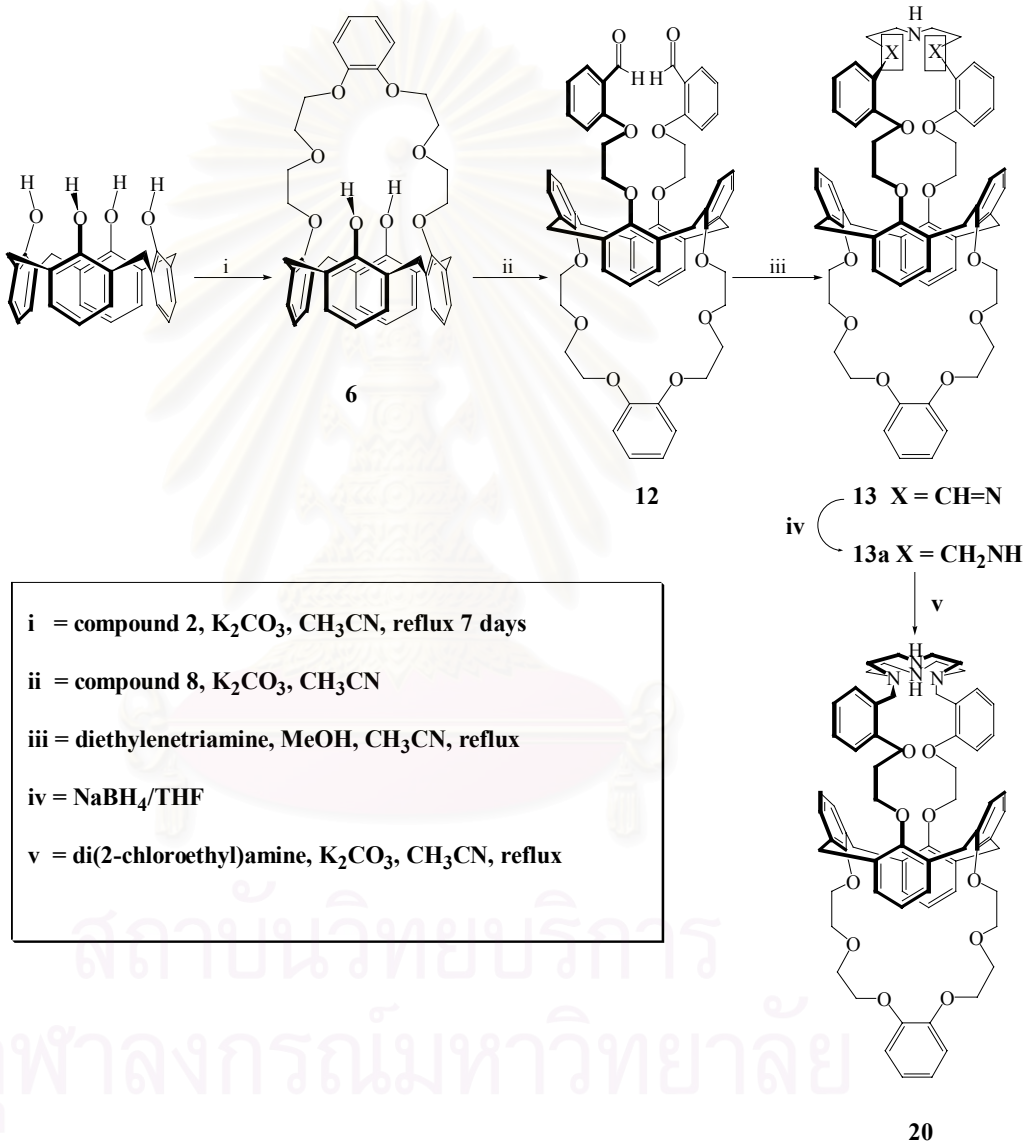


Figure 3.2 Synthetic pathway I of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**)

A condensation of 1 equiv. of 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) with calix[4]arene was carried out by using K_2CO_3 as a base in acetonitrile for 7 days. After purification by column chromatography, two white solids were obtained. From ^{1}H-NMR spectra, the first one is a single bridge derivative, compound **6**. This derivative exists in cone conformation due to a presence of AB-system of Ar$C\mathbf{H}_2$Ar with $J_{H\text{-}H}$ = 13 Hz. On the other hand, the second white solid was deduced to be calix[4]-*bis*(benzo crown-6), compound **7.** This derivative exists in a 1,3-alternate conformation due to a singlet of Ar$C\mathbf{H}_2$Ar at 3.77 ppm. The higher yield of 1,3-alternate calix[4]-*bis*(benzo crown-6) (**7**) (26%) compared to that of desired product (9%). This may come from that calix[4]-benzo crown-6 (**6**) was preorganized to be bridged with 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) easier than calix[4]arene itself and the greater solubility in acetonitrile of compound **6** than calix[4]arene itself.

By the synthetic pathway I, we revealed that the bridging of calix[4]arene with 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) should be done after the disubstitution of 2-(2′bromoethoxy)benzaldehyde (**8**) onto calix[4]arene. This led us change the synthetic pathway as depicted in Figure 3.3.

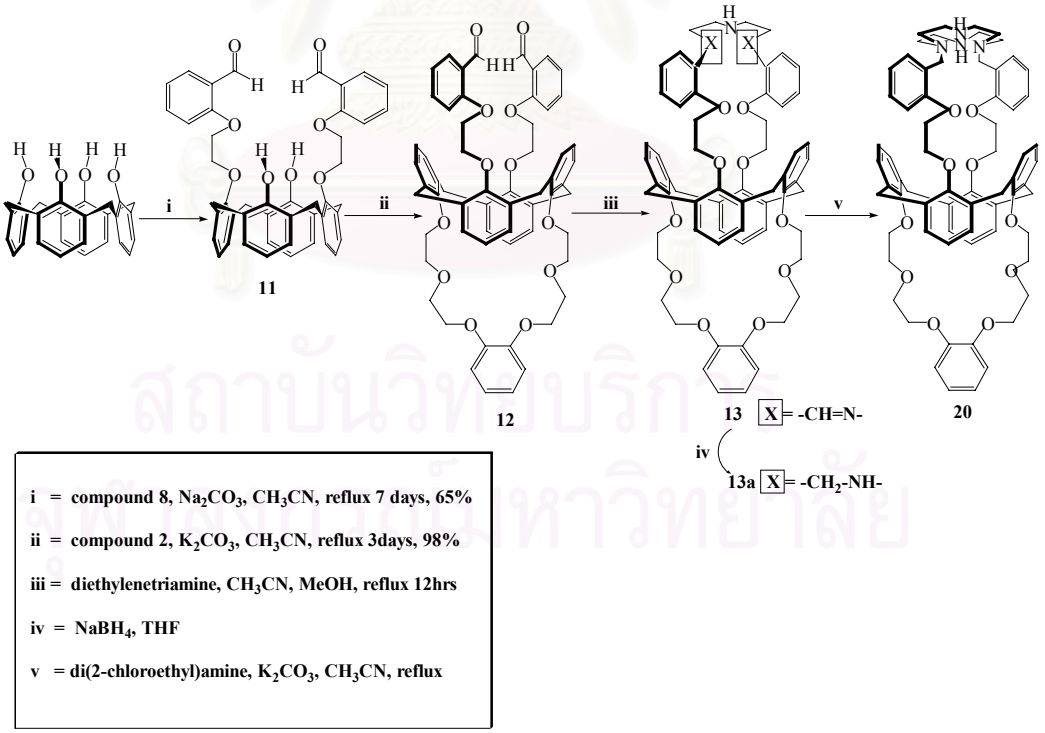


Figure 3.3 Synthetic pathway II of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**)

This synthetic pathway begins with a substitution of calix[4]arene with 2-(2′bromoethoxy)benzaldehyde (**8**). In first attempt, K_2CO_3 was used as base as described elsewhere[13-16, 24] but the desired product, compound (**11**), was not afforded. The main product obtained was calix[4]-monobenzaldehyde (**10**) which indicated by ^{1}H-NMR spectrum. The singlet peak of aldehyde presents at 10.61 ppm and two AB-systems of methylene protons, ArC**H**$_2$Ar are observed at 4.43 and 4.15 ppm ($J_{H\text{-}H}$ = 13 Hz) and 3.51 and 3.42 ppm ($J_{H\text{-}H}$ = 13 Hz). Besides these two singlets of hydroxyl protons at 9.53 ppm and 9.23 ppm with integration ratio of 2:1 are also observed. By analogue reaction,[49] it was found that substitution of calix[4]arene with 2-(2′bromoethoxy)nitrobenzene by using an excess of Na_2CO_3 as a base gave calix[4]-dinitrobenzene in cone comformation. We, then, tried to carry out the reaction between calix[4]arene and **8** in the presence of Na_2CO_3, the disubstituted product was obtained with 65% yield after precipitation with hexane. The ^{1}H-NMR spectrum shows a singlet of aldehyde protons at 10.35 ppm and an AB system of ArC**H**$_2$Ar at 4.39 and 3.45 ppm ($J_{H\text{-}H}$ = 13 Hz). This indicates that compound **11** presents in cone conformation.

Bridging of compound **11** was accomplished by the reaction with 1,2-*bis*(diethyleneglycol tosyl)benzene (**2**) in an excess of K_2CO_3 in refluxing acetonitrile for 3 days. The compound **12** was separated by column chromatography as a white solid (98%). It exists in 1,3-alternate conformation due to a singlet signal of ArC**H**$_2$Ar of calix[4]arene at 3.87 ppm on ^{1}H-NMR spectrum. The Shciff's base reaction of compound **12** with diethylene triamine was processed in a refluxing mixture of acetonitrile and methanol. The reaction mixture turned yellow when started refluxing. After 8 hours, the solvent was removed. The obtained residue was monitored by using ^{1}H-NMR spectroscopy. The obtained spectrum does not contain any immine peak around 8.6 ppm. This indicates that the desired product did not form.

Because that Shciff's base formation step in synthetic pathway II (Figure 3.3) could not afford the desired product, we decided to change the aldehyde moiety to an alcohol one. A new synthetic pathway of **20** was designed as shown in Figure 3.4. This synthetic pathway begins with 1,3-*distal* disubstitution of calix[4]arene with 2-(2′bromoethoxy)benzylalcohol. The ditosylate derivative of glycolic chain was

bridged at 1,3-position of calix[4]-dibenzyl alcohol (**16**) to provide crown ether loop. In the last step, a condensation of cyclen·$2H_2SO_4$ was processed after the conversion of hydroxy groups of calix[4]-dibenzylalcohol-benzo-crown-6 (**20**) to bromide groups.

Firstly, 2-(2′-bromoethoxy) benzylalcohol (**14**) was prepared by an alkylation reaction of 2-hydroxybenzyl alcohol with 1,2-dibromoethane in a presence of excess K_2CO_3 in acetonitrile with reflux for 8 hours. A yellow oil of the compound **14** (66%) and a white solid of minor product, compound **15** (32%), were afforded. The ^{1}H-NMR spectrum of compound **14** shows a triplet of C**H**$_2$Br at 3.66 ppm (J_{H_H} = 5.7 Hz) and a broad signal of hydroxyl group at 2.95. Whereas, the ^{1}H-NMR spectrum of compound **15** shows a singlet of OC**H**$_2$C**H**$_2$O at 4.40 ppm and a singlet of hydroxyl group at 3.07 ppm due to its symmetrical structure.

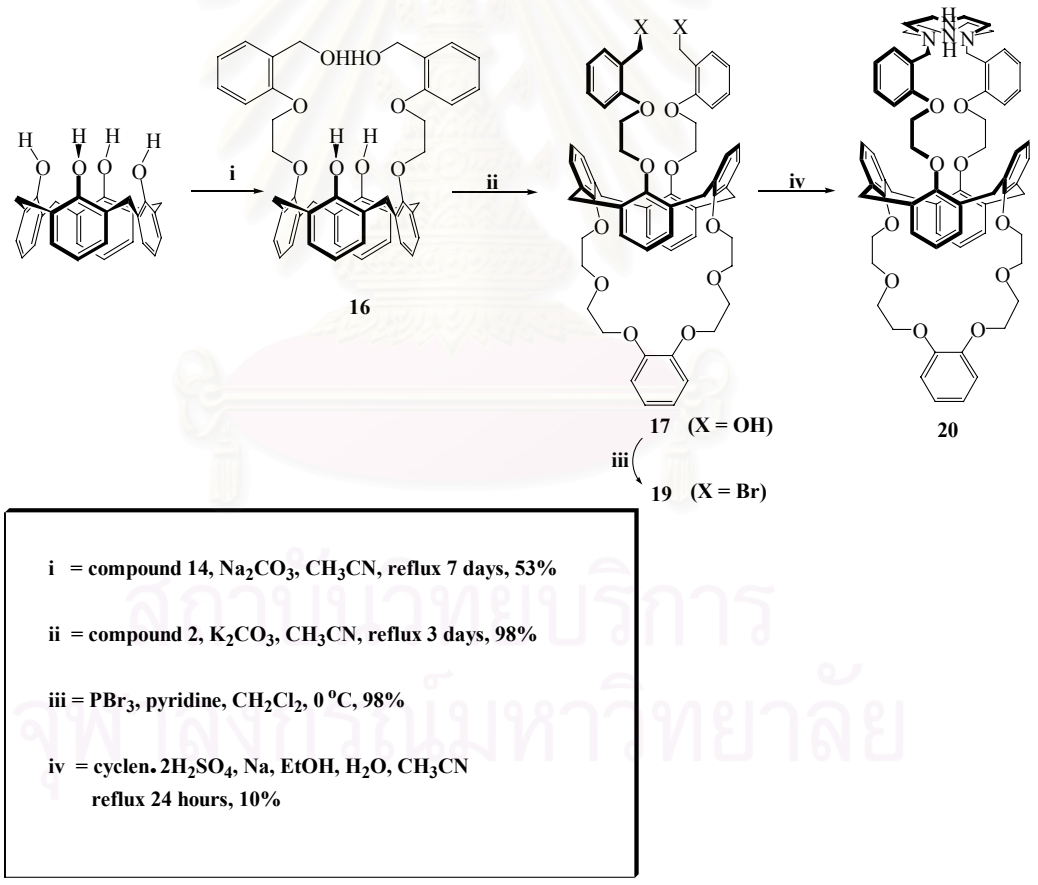


Figure 3.4 Synthetic pathway III of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**)

A benzyl alcohol derivative of calix[4]arene (**16**) was prepared by a substitution reaction of calix[4]arene with 3 equiv. of 2-(2′-bromoethoxy)benzyl alcohol (**14**) in presence of an excess of Na_2CO_3 in acetonitrile. After refluxing for 7 days, compound **16** was separated by precipitation with hexane as a white solid (53%). Compound **16** exists in cone conformation due to the presence of AB-system at 4.39 and 3.45 ppm with a coupling constant of 13 Hz on ^{1}H-NMR spectrum.

Bridging of compound **16** was accomplished by the reaction of 1 equiv. of 1,2-*bis*(diethylene glycol tosyl)benzene (**2**) in presence of an excess K_2CO_3 in acetonitrile for 3 days of reflux. The compound **17** was purified by column chromatography and obtained as a white solid in 98%. This derivative presents in 1,3-alternate conformation due to a presence of a singlet of ArC**H**$_2$Ar of calix[4]arene at 3.82 ppm on ^{1}H-NMR spectrum. Besides this, the benzo protons of crown cavity represent as a singlet at 6.95 ppm.

Conversions of hydroxyl groups of compound **17** to more leaving groups should be carried out in the next step. In an early attempt, we tried to changed to a tosyl groups by a direct tosylation onto hydroxyl groups. The obtained residue was characterized by ^{1}H-NMR spectroscopy, which shows that the desired product was not obtained. This may stem from the steric effect of the tosyl groups. The conversion of hydroxyl groups of compound **17** to bromide groups was accomplished by treating with PBr_3 in a presence of pyridine in dry CH_2Cl_2 at 0 °C. The reaction was quenched with water after the TLC plate shows the disappearance of compound **17**. The ^{1}H-NMR spectrum of compound **19** shows upfield shifts of C**H**$_2$Br protons (from 4.66 to 4.53 ppm) and disappearance of a singlet of CH_2O**H** protons at 2.65 ppm. This derivative preserves 1,3-alternate conformation due to the presence of a singlet at of ArC**H**$_2$Ar 3.85 ppm on the ^{1}H-NMR spectrum.

The cyclen·2H_2SO_4 was prepared following the literature.[7,8] This synthesis was begun with condensation of a disodium salt of N,N′,N′′-*tris*(*p*-toluenesulfonyl) diethylenetriamine with N,O,O′-*tris*(*p*-toluenesulfonyl)diethanolamine deriving from tosyltion of diethylenetriamine and diethanolamine. The deprotection of tetratosyl derivative was carried out by treating with 98% H_2SO_4 at 100 °C for 48 hours to afford the brown solid of cyclen·2H_2SO_4. The structure was confirmed by ^{13}C-NMR and IR spectroscopy, which are in accordance with the literatures.[7,8,50]

This cyclen was extracted difficultly from its basic solution of cyclen·$2H_2SO_4$ salt because of a great solubility of cyclen in water. The condensation of compound **19** with cyclen was begun with the generation of free cyclen in *situ* by using a mininum quantity of water with ethanolic NaOEt. Then, 1 equiv. of compound **19** in acetonitrile was slowly added to the cyclen solution, and reaction was refluxed for 24 hours. After purification by column chromatography, a white solid of the desired product (**20**) was obtained (10%). The disappearance of a singlets of C**H**$_2$Br at 4.53 ppm and an appearance of a singlet of CH_2N at 2.82 ppm of cyclen moiety in ^{1}H-NMR spectrum and a mass spectroscopy result (m/z =1110.3 (100%), 1111.3 (59.3%)) confirmed the identity of compound **20**.

3.3 Complexation studies of compound 20 with picrate salts

Interactions between cations and the ligand were studied employing picrate salts because these salts are not soluble in $CDCl_3$ without complexation. The picarte salts were used as a solid and added directly into the solution of the investigated ligand in $CDCl_3$ in NMR tubes. The inclusion of cation into the ligand can be monitored by a singlet of picrate aromatic protons around 8.7-8.9 ppm. The integration ratio of picrate protons and ligand protons indicates the stoichiometry of complexes.

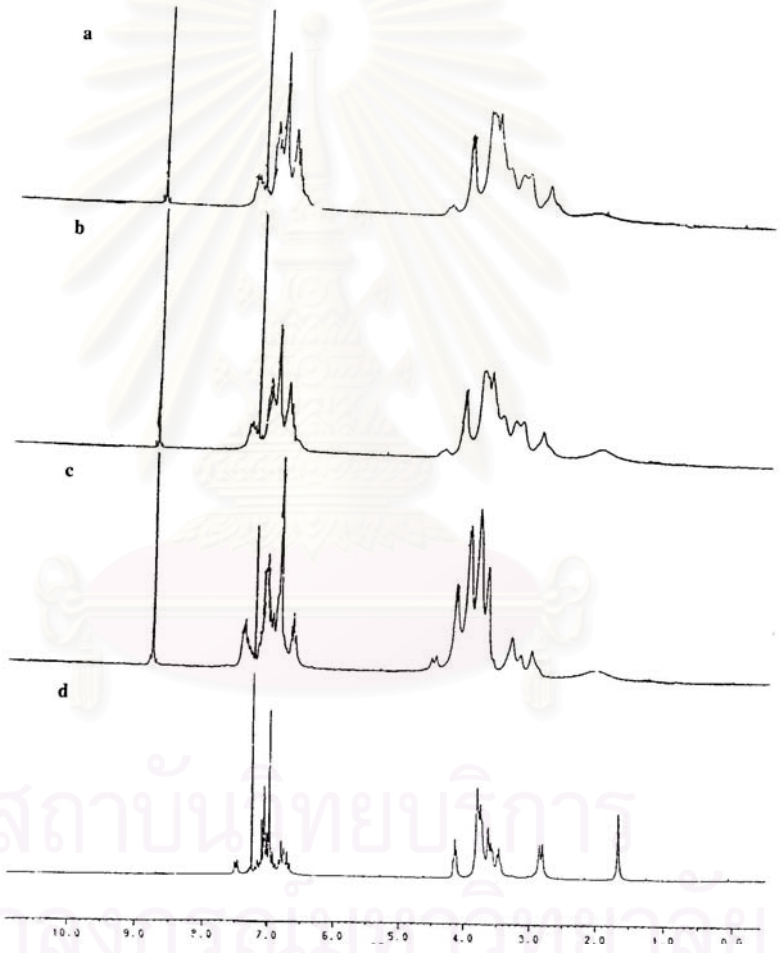


Figure 3.5 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of a) **20** with zinc picrate**,** b) **20** with potassium picrate c) **20** with cesium picrate, and d) **20**.

When a cesium picrate was added to the $CDCl_3$ solution of **20**, the solution turned yellow immediately. This indicates that inclusion of cesium ion into ligand occured. From ^{1}H-NMR spectra (Figure 3.5 (c) and (d)), the singnals of **20** in the presence of cesium picrate are different from those of pure ligand. The complexation of cesium picrates with **20** lead to the appearance of a singlet of picrate protons at 8.80 ppm and an upfield shift of aromatic protons of benzo-crown unit from 7.02 to 6.86 ppm. Moreover, the glycolic ethylene protons of benzo-crown unit dislocated from a multiplet at 3.79-3.72 ppm to a singlet at 3.99 ppm. The integration ratio between picrate protons and aromatic protons of ligand indicates the formation of a 1:1 complex after 7 days. From these results, the cesium ion probably resides in the crown ether loop and the cation-π interaction of phenylene unit may also stabilize the complex as observed elsewhere.[48]

With potassium picrate, the solution of **20** also turned to yellow immediately. This indication implies an inclusion of potassium ion with ligand **20**. From ^{1}H-NMR spectra (Figure 3.5 (b) and (d)), the singlet of picrate protons is observed at 8.76 ppm. The signals of **20** in the presence of potassium picrate are different form those of pure **20**. The doublet of aromatic protons at 7.48 ppm became a broad signal at 7.38 ppm. Beside these, the triplet of glycolic protons at 3.46 ppm became a multiplet at 3.76-3.61 ppm. The doublet of NHC$\mathbf{H}_2$C$\mathbf{H}_2$NH of the cyclen unit at 2.84 ppm ($J_{H\text{-}H}$ = 9.0 Hz) became a broad signal at 3.20 ppm. The upfield shift of phenylene unit of benzo-crown ether was not observed due to the K^+ ion was not located in crown ether loop. These results suggest that K^+ was complexed by the cyclen loop. By comparing the integration ratio of the pirate protons and aromatic protons of the ligand, the 1:1 complex was obtained after 2 weeks.

In case of zinc picrate, an addition of zinc picrate into the $CDCl_3$ solution of the ligand led to a changing color of the solution to yellow and the presence of the singlet of picrate protons at 8.78 ppm. The signals of **20** in the presence of zinc picrate are different form those of the pure ligand but similar to those of **20** in the presence of potassium picrate. It is observed that a doublet and a triplet of aromatic protons at 7.48 ($J_{H\text{-}H}$ = 9.0 Hz) and 7.19 pmm ($J_{H\text{-}H}$ = 8.7 Hz) respectively, became to a multiplet at 7.38-7.29 ppm. The doublet of NHC$\mathbf{H}_2$C$\mathbf{H}_2$NH of the cyclen unit at 2.82 ($J_{H\text{-}H}$ = 9.0 Hz) became to a broad signal at 3.20 ppm. These results suggest that Zn^{2+} ion was coordinated to the cyclen crown cavity.

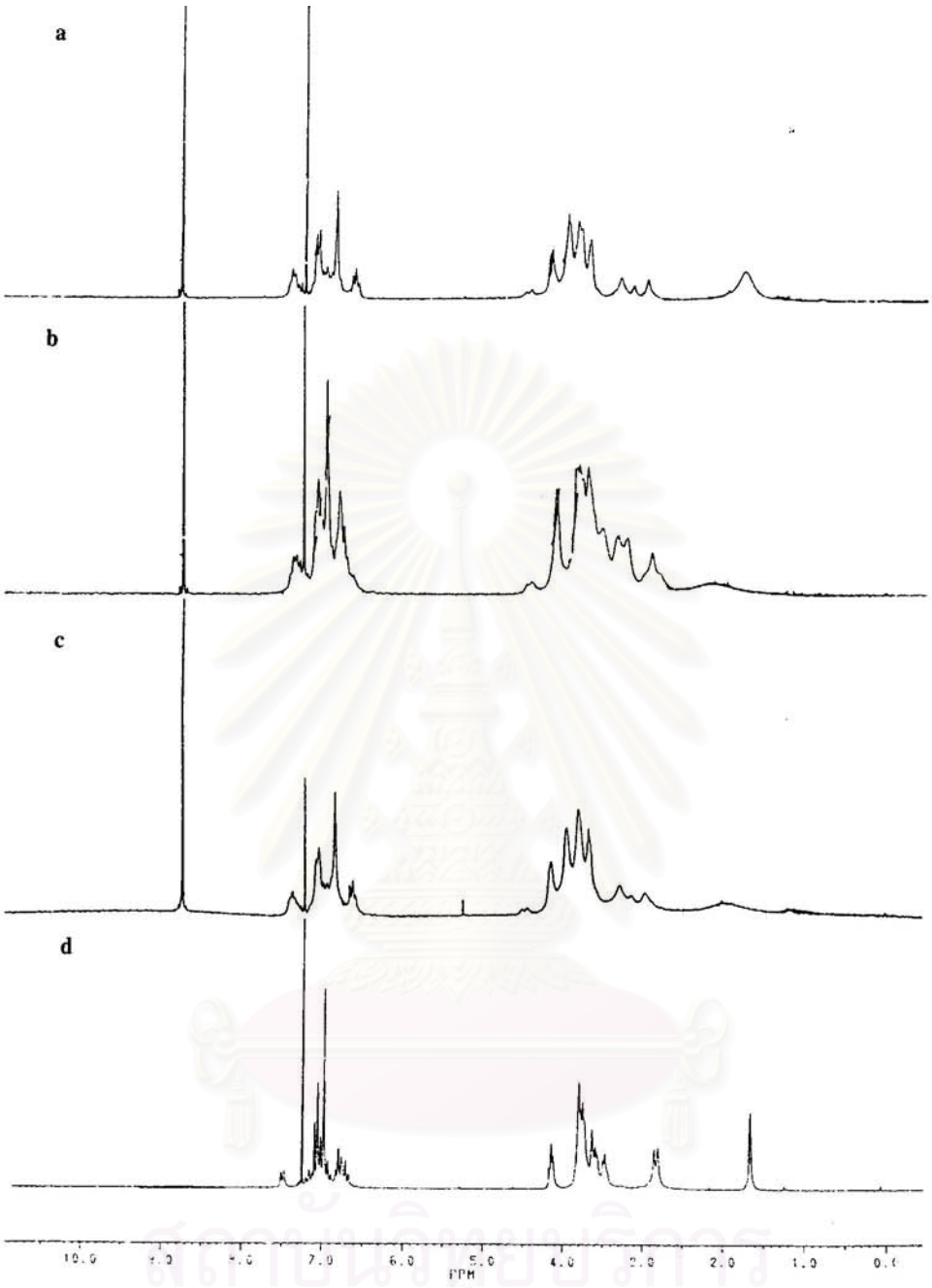


Figure 3.6 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) **20** with cesium and zinc picrate**, (** b) **20** with zinc picrate, (c) **20** with cesium picrate and (d) **20**.

In order to prepare a heterobinuclear complex of **20**, the zinc picrate was added into the $CDCl_3$ solution of 1:1 cesium complex in NMR tube. From ^{1}H-NMR spectra (Figure 3.6), the signals of **20** in the presence of both cesium and zinc picrates are different form those of **20** in the presence of only zinc picrate or cesium picrate. The migration of signals of phenylene protons of the crown ether loop from 6.95 ppm to 6.75 ppm and NHC**H**$_2$C**H**$_2$NH of the cyclen unit from 2.82 ppm to broad signal at 3.10 ppm ($J_{H\text{-}H}$ = 9.0 Hz) is observed. Moreover, the integration ratio between picrate protons and aromatic protons increased and finally reached to a 1:1:1 complex. These results imply that Cs^+ and Zn^{2+} ions were included into **20**.

In conclusion, the synthesized calix[4]-cyclen-benzo crown-6 (**20**) can act as a *hard-soft* receptor. This ligand can accommodate Zn^{2+} ion in cyclen unit and Cs^+ ion in benzo-crown ether cavity. These results lead us to propose the structure of a *hetero-binuclear* complex of ligand **20** as shown in Figure 3.7.

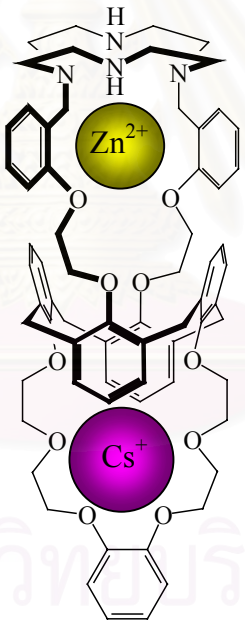


Figure 3.7 A proposed structure of *hetero-binuclear* complex of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**) with Cs^+ and Zn^{2+} ions.

3.4 Complexations of ligand 20 with Zinc salts (ZnX_2)

From complexation studies with picrate salts, ligand **20** showed an affinity towards Cs^+ ion and Zn^{2+} ion. In these studies, we were interesting in the influence of anions towards the complexation of ligand with Zn^{2+}. In this investigation, the zinc salts used were $Zn(NO_3)_2$, $ZnCO_3$, $ZnSO_4$, $Zn(AcO)_2$, $ZnCl_2$, $ZnBr_2$ and ZnI_2 which are different in both shape, size and binding ability of anions.

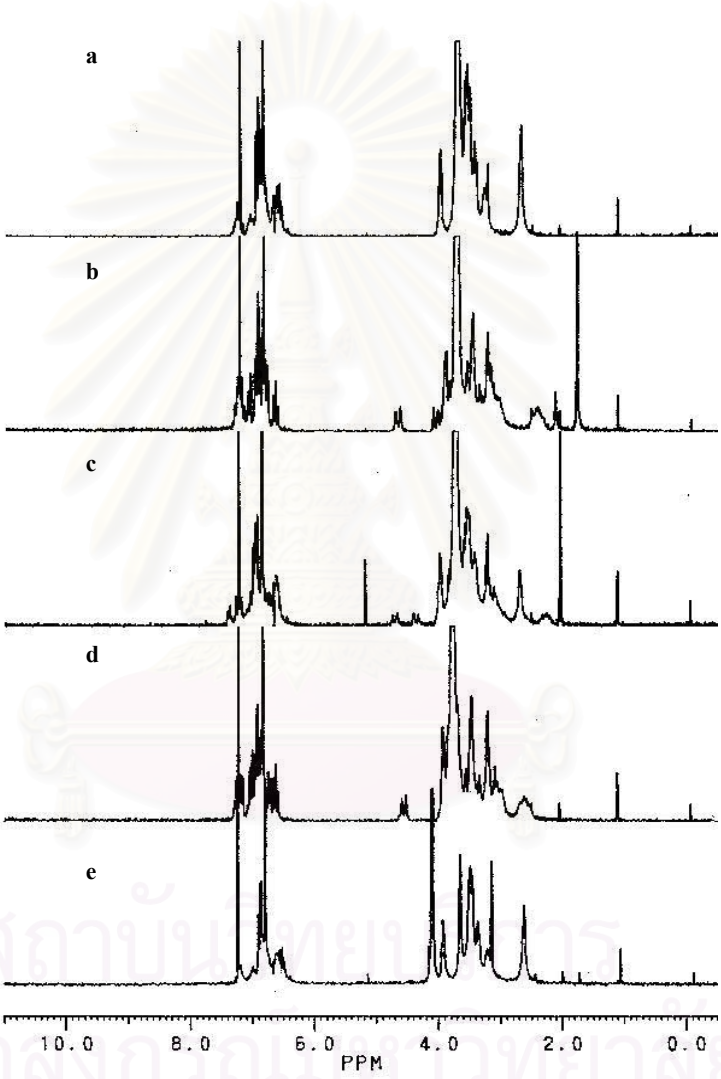


Figure 3.8 The ^{1}H-NMR ($CDCl_3/CD_3OD$, 200 Hz) spectra of (a) **20·** $ZnCO_3$, (b) **20·** $Zn(AcO)_2$, (c) **20·** $ZnSO_4$, (d) **20·** $Zn(NO_3)_2$, and (e) **20**.

From ^{1}H-NMR spectra (Figure 3.8), the spectra of **20** in presence of zinc salts are different from that of the pure ligand, except in the $ZnCO_3$ case(Figure 3.8(a)). The spectrum of **20** with $ZnCO_3$ resembles the spectrum of pure ligand in $CDCl_3$. This may stem that $ZnCO_3$ draws methanol-d_4 to solvate itself. By addition of $Zn(NO_3)_2$, the ^{1}H-NMR spectrum (Figure 3.78 (d)) shows the displacement of signals. This implies that the complex of $Zn(NO_3)_2$ with **20** occurred. It is also observed that the multiplet of NC**H**$_2$Ar at 3.26-3.49 ppm became a doublet at 4.65 ppm ($J_{H\text{-}H}$ = 14 Hz). Moreover, a doublet and a triplet of Ar**H** nearby the cyclen unit also dislocated from 7.19 and 6.96 ppm to 7.34 ppm ($J_{H\text{-}H}$ = 7.4 Hz) and 7.26 ppm ($J_{H\text{-}H}$ = 3.0 Hz), respectively. The signal of methylene protons of the cyclen unit shifts downfield from 2.87 ppm to 3.16 ppm. These results indicate that Zn^{2+} ion located in the cyclen cavity of the investigated ligand.

The ^{1}H-NMR spectrum of the complexation of $ZnSO_4$ with **20** (Figure 3.7 (c)) is different from pure ligand. This indicates the formation of a complex. In this case, two doublets of NC**H**$_2$Ar are observed at 4.80 and 4.51 ppm with $J_{H\text{-}H}$ = 15.3 Hz in a different integration ratio. Moreover, a singlet of methylene protons of cyclen unit at 2.60 ppm became two broad signals at 3.02 and 2.33 ppm. These results implie that two types of complexes, were formed. The ^{1}H-NMR spectrum of $Zn(AcO)_2$ (Figure 3.8 (b)) complex is similar to that of **20** in the presence of the $ZnSO_4$ but in this case a signal of NC**H**$_2$Ar migrates from a multiplet at 3.23-3.56 ppm to two doublets at 4.74 and 4.13 ppm with $J_{H\text{-}H}$ = 14.8 Hz. Moreover, the change of signals of methylene protons of the cyclen unit from 2.80 ppm to two broad signals at 3.09 and 2.59 ppm is observed. Again, the reaction of $Zn(AcO)_2$ with ligand **20** gave two types of complexes as previously observed in case of $ZnSO_4$. The different extent the displacment of signals and coupling constants between ligand **20** with $ZnSO_4$ and ligand **20** with $Zn(AcO)_2$ implies that the interaction between **20** and $Zn(AcO)_2$ is weaker than **20** and $ZnSO_4$. This can be explained that, when **20** bind with Zn^{2+} ion SO_4^{2-} ion liberated. This anion is stabilized by hydrogen-bonding with NH groups on ligand, Due to the hydrogen bonds between NH and SO_4^{2-} are stronger than those of NH and AcO^-, the ineraction between ligand **20** and $ZnSO_4$ is stronger than **20** and $Zn(AcO)_2$. The proposed structures of 2:1 (L:M) complex and 1:1 (L:M) complexes of ligand **20** with $ZnSO_4$ and $Zn(AcO)_2$ are presented in Figure 3.9.

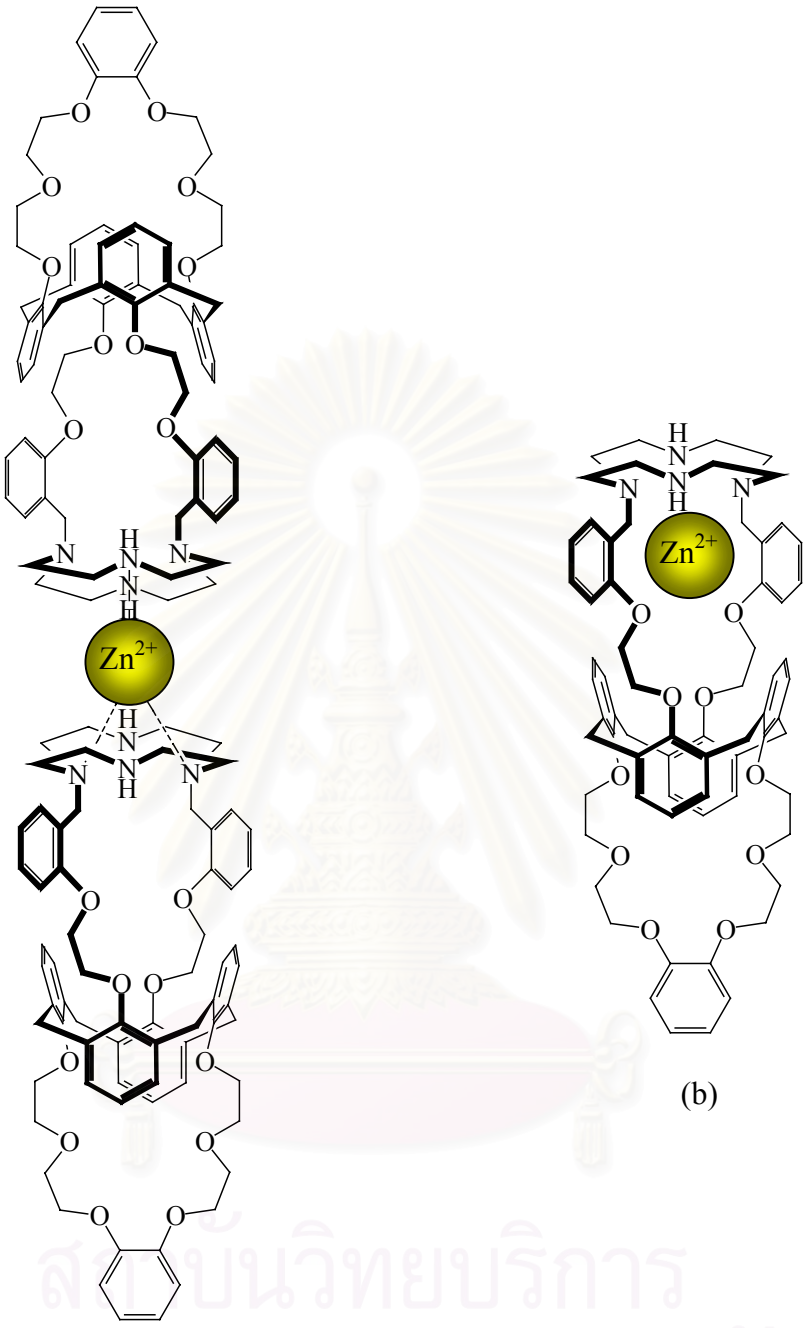


Figure 3.9 The proposed structures of complexes of **20** with $ZnSO_4$ and $Zn(AcO)_2$ a) 2 : 1 complex and b) 1:1 complex

In zinc halide series, the complex formations are shown change of by a multiplet of NC**H**$_2$Ar at 3.29-3.49 ppm to a doublet at 4.63 ppm ($J_{H\text{-}H}$ = 13 Hz), 4.72 ppm ($J_{H\text{-}H}$ = 13 Hz) and 4.73 ppm ($J_{H\text{-}H}$ = 13 Hz) in the case of $ZnCl_2$, $ZnBr_2$ and ZnI_2, respectively. The change of methylene protons signals of the cyclen unit from 2.61 ppm to two sets of broad signals at 2.70, 2.99 ppm ($ZnCl_2$), 2.75, 2.99 ppm ($ZnBr_2$) and 2.88, 3.01 ppm (ZnI_2) are observed. The ^{1}H-NMR spectra of these complexes also show the up-field shift of the signals of neighboring cyclen aromatic protons. The degree of displacement of a doublet and a triplet at 7.28 ppm increases in the order of $ZnCl_2$ (7.28 ppm and 7.10 ppm) < $ZnBr_2$ (7.29 ppm and 7.12 ppm) < ZnI_2 (7.38 ppm and 7.17 ppm). This implies that the interaction between **20** and zinc salts varied as **20.**ZnI_2 > **20.**$ZnBr_2$ > **20.**$ZnCl_2$.

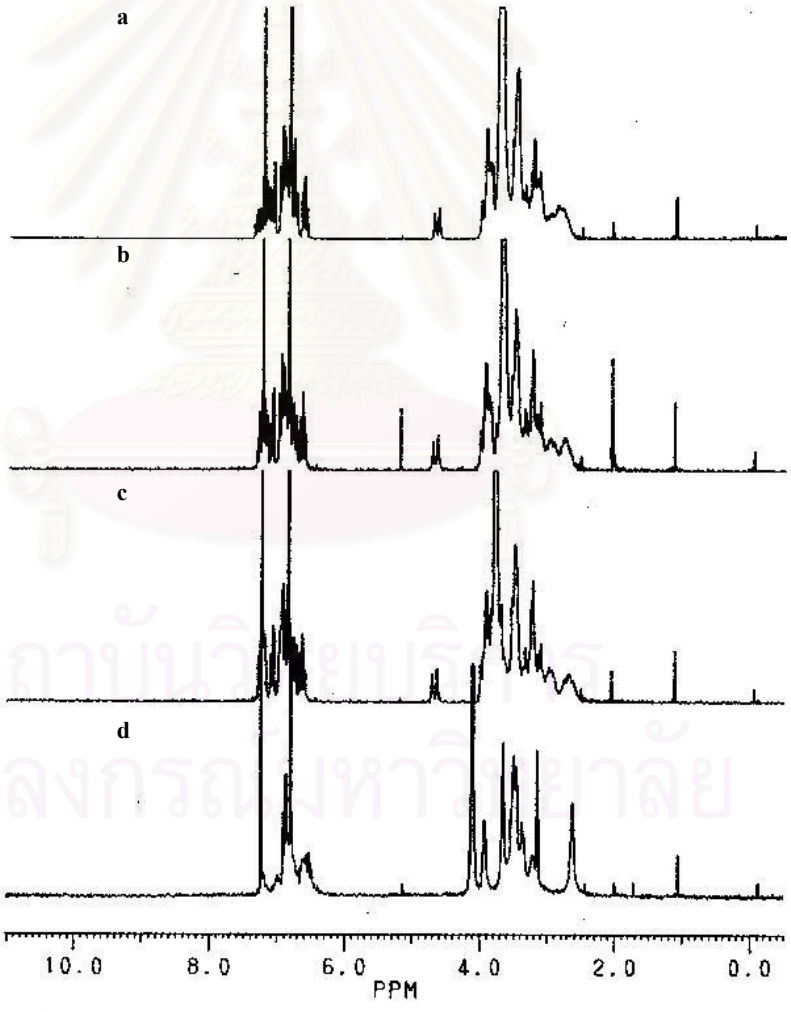


Figure 3.10 The ^{1}H-NMR ($CDCl_3$/CD_3OD, 200 Hz) spectra of (a) **20**·ZnI_2, (b) **20**·$ZnBr_2$, (c) **20**·$ZnCl_2$ and (d) **20**.

In conclusion, ligand **20** has an affinity towards Zn^{2+} ion which shows by the migration of proton signals of the ligand on the ^{1}H-NMR spectra upon the addition of zinc salts ($Zn(NO_3)_2$, $ZnSO_4$, $Zn(AcO)_2$, $ZnCl_2$, $ZnBr_2$ and ZnI_2). The complexation properties of **20** with Zn^{2+} ion were also depended on the shapes, sizes and binding ability of the counter ions, which induced the organization of the benzene and methylene groups of cyclen.

3.5 Titration of ligand 20 with $ZnSO_4$

From aforementioned study of $ZnSO_4$ with synthesized ligand (**20**), we believed that two types of complex were formed. To confirm the complexation behavior, we therefore conducted titration experiments between ligand **20** with $ZnSO_4$. The ^{1}H-NMR spectra of ligand **20** and the different concentrations of $ZnSO_4$ are shown in Figure 3.10.

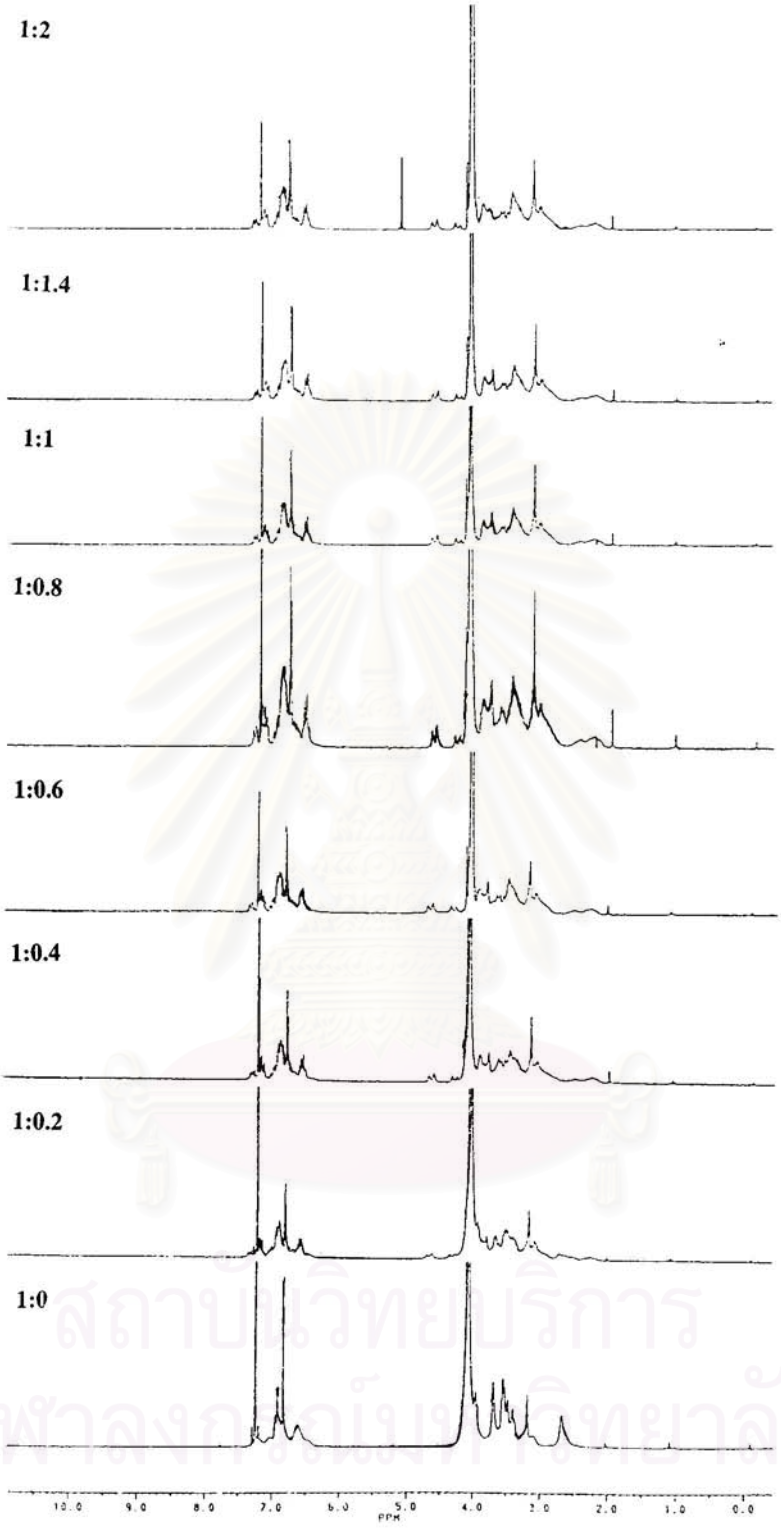


Figure 3.11 The ^{1}H-NMR ($CDCl_3/CD_3OD$, 200 Hz) spectra of ligand **20** with 0-2 equivalents of $ZnSO_4$.

From ^{1}H-NMR spectra (Figure 3.11) it is found that, at low concentrations of $ZnSO_4$, the integration of the doublet at 4.69 ppm are at the same magnitude to those of the doublet at 4.36 ppm. When the concentrations of $ZnSO_4$ increase, the integrations of the doublet at 4.69 ppm increase while those of the doublet at 4.36 ppm decrease. This implies that a 2:1 (L:M) complex formes at a lower mole ratio of $ZnSO_4$ and **20** and decreases at a higher mole ratio. On the other hand, the 1:1 (L:M) complex formation increase at the higher mole ratio.

3.6 Complexations of ligand 20 with organic molecules

Becasuse ligand **20** possesses NH groups at the cyclen unit, these groups can act as hydrogen-bond donor/acceptor. So we were interested in studing its complexing ability towards organic molecules (phenol, aniline, catechol, resorcinol, dihydroquinone and phthalic acid). The ^{1} H-NMR spectra of **20** with phenol and **20** with aniline are shown in Figure 3.12.

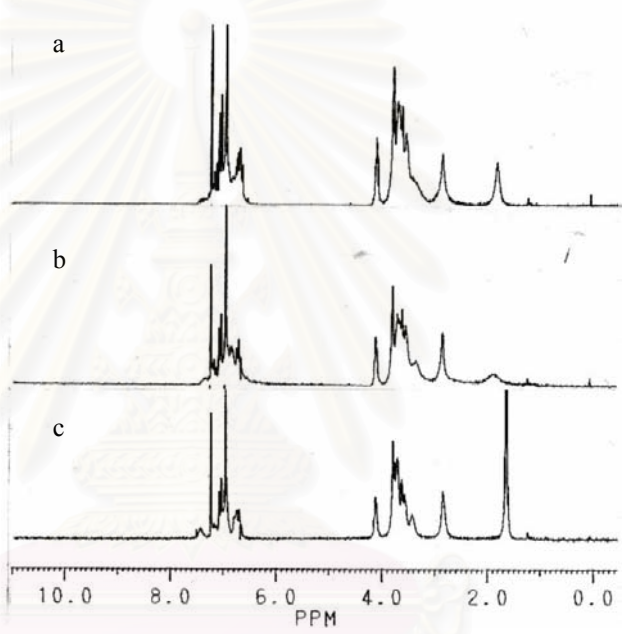


Figure 3.12 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) **20**·aniline, (b) **20**·phenol and (c) **20**.

By comparison between the spectra of ligand **20** in the presence of phenol (Figure 3.12 (b)) or aniline (Figure 3.12 (c)) and the spectrum of the pure ligand (**20**), they indicate that ligand **20** can bind aromatic molecules containing hydrogen-bond donor/acceptor group.

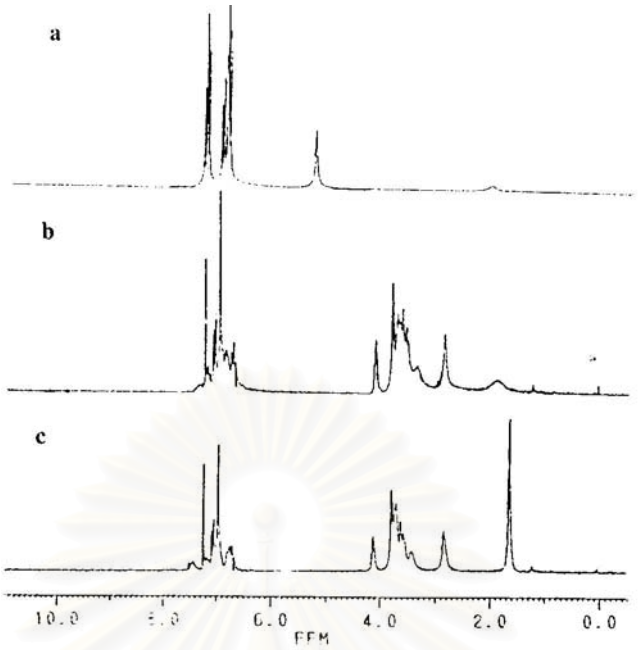


Figure 3.13 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) phenol, (b) **20**·phenol and (c) **20**.

In the case of phenol, the ^{1}H-NMR spectra (Figure 3.13) show that the signals of ligand **20** in the presence of phenol are different from those of the pure ligand. The migration of C**H**$_2$C**H**$_2$NH of the cyclen unit from 2.79 ppm to 2.85 ppm is observed. This may cause by to the hydrogen-bonding of OH of phenol and NH at cyclen unit of ligand. Moreover, a displacement of a triplet of neighboring aromatic protons of the cyclen unit at 7.50 ppm to a board signal at 7.28 ppm. However the migration of the signals of phenol is not clearly observed.

In case of aniline, the migrations of signal of ligand protons in presence of aniline are observed on the ^{1}H-NMR spectrum of ligand **20** (Figure 3.14) as found in the case of phenol. Comparing the spectra of the free ligand **20** and ligand **20** with aniline, it is remarked that the signal of C**H**$_2$C**H**$_2$N protons of cyclen unit shifts from 2.79 ppm to a broad signal at 2.85 ppm. It is also observed the displacement of neighboring aromatic protons of the cyclen unit from 7.50 to be a board signal at 7.48 ppm. For the signals of aniline, a singlet signal of N**H** shifts from 3.48 ppm to 3.56 ppm. These results indicate that ligand **20** could bind with aniline by nydrogen-bonding between NH of aniline and the cyclen unit of ligand.

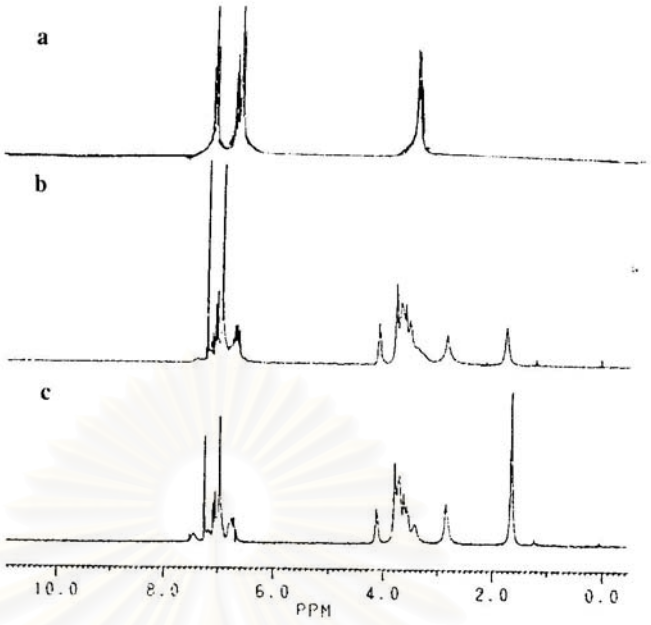


Figure 3.14 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) aniline, (b) **20**·aniline and (c) **20**.

By these complexation studies with monosubstituted benzenes, we can conclude that ligand **20** could act as a host for organic molecules containing hydrogen bond donor/acceptor liked phenol and aniline. The complexation occurred *via* hydrogen-bonding.

From the complexation study of ligand **20** with monosubstituted benzene, we were interested in studing its complexation properties towards disubstituted benzenes. Three isomers of dihydroxybenzene, catechol (*o*-isomer), resorcinol (*m*-isomer) and dihydroquinone (*p*-isomer), and one dicarboxylic acid, phthalic acid, were subjected to study. ^{1}H-NMR spectra of ligand **20** in the presence of the mentioned guests are shown in Figure 3.15.

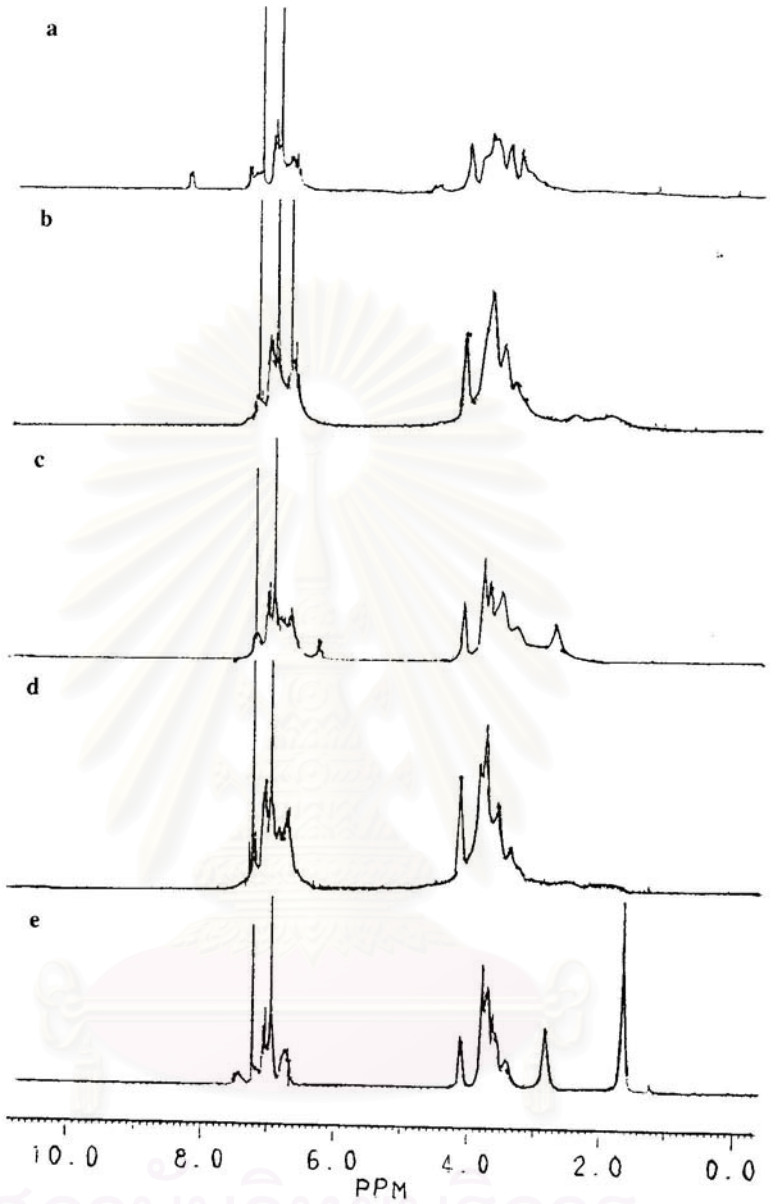


Figure 3.15 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) **20**·phthalic acid, (b) **20**·dihydroquinone, (c) **20**·resorcinol, (d) **20**·catecol and (e) **20**.

^{1}H-NMR spectra (Figure 3.16) show the migration of C**H**$_2$C**H**$_2$N of the cyclen unit from a doublet of 2.79 ppm to a broad signal at 3.34 ppm. The neighboring cyclen aromatic protons shift from 7.48 ppm to a broad signal at 7.33 ppm. These displacements of signals are due to hydrogen-bonding between NH of the cyclen unit and OH of the substrate.

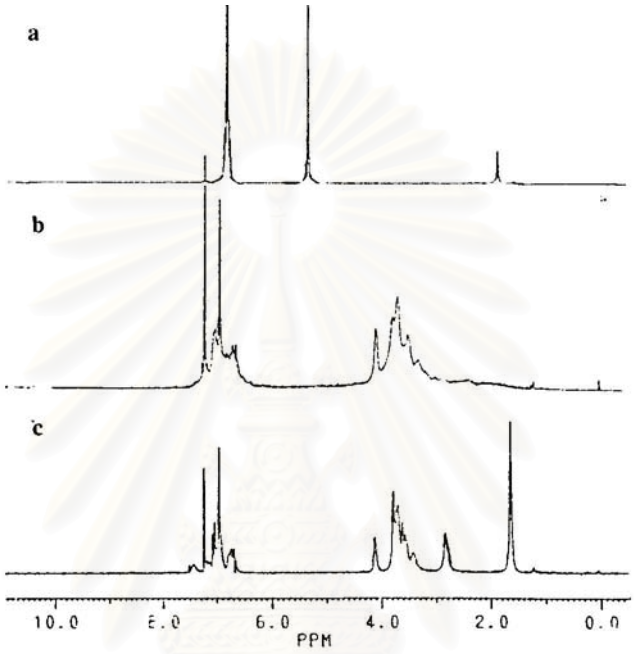


Figure 3.16 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) catechol, (b) **20**·catechol and (c) **20**.

For dihydroquinone, the obtained spectra are similar to that of ligand in the presence of *ortho* isomer. The migration of cyclen signal from 2.85 ppm to a broad signal at 3.34 ppm is revealed. The signal of neighboring aromatic protons of the cyclen unit displace from 7.50 ppm to a broad signal 7.33 ppm. The displacement of a signal of dihydroquinone from 6.70 ppm to 6.64 ppm is also observed. These results let us to conclude that the complexation with dihydroquinone took place by using hydrogen-bonding.

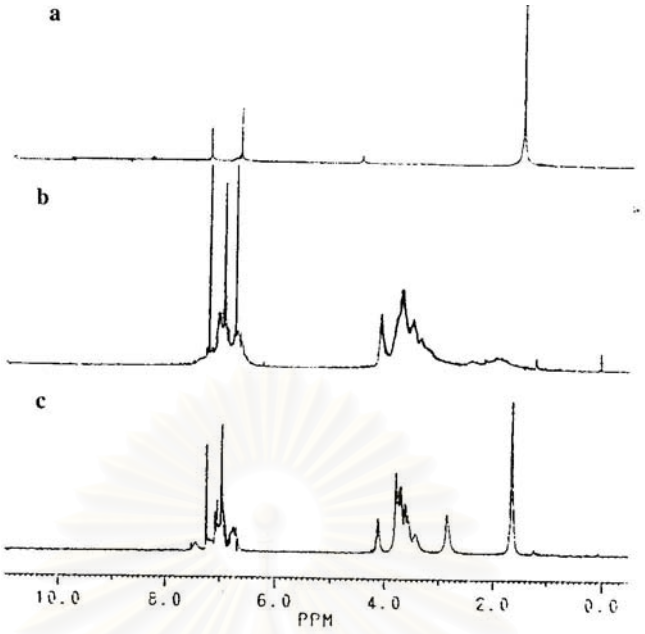


Figure 3.17 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) dihydroquinone, (b) **20**·dihydroquinone and (c) **20**.

In conclusion, the *ortho* and *para* isomers of dihydroxybenzene could bind the ligand by hydrogen-bonding between NH groups of the ligand and OH groups of substrates. The interactions between host and gust are somewhat in the same order.

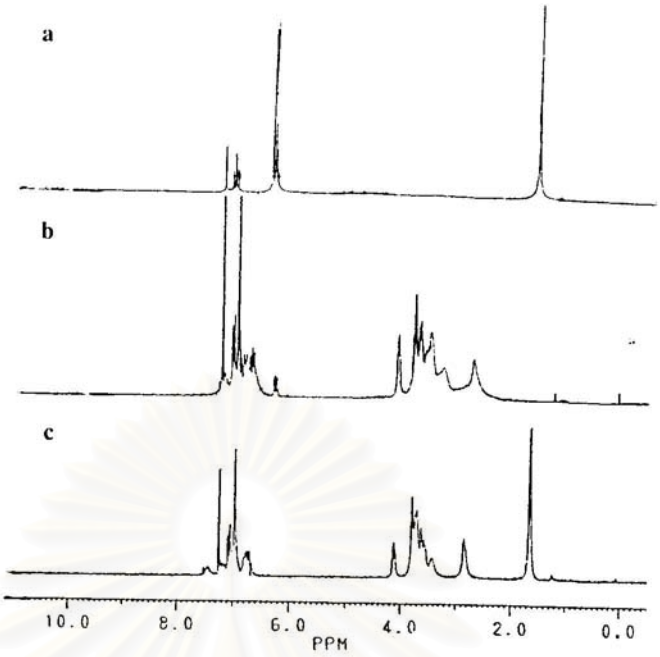


Figure 3.18 The ^{1}H-NMR ($CDCl_3$, 200 Hz) spectra of (a) resorcinol, (b) **20**·resorcinol and (c) **2**0.

In the presence of resorcinol, the signal of neighboring cyclen aromatic protons moves from 7.50 ppm to a multiplet at 7.28- 7.21 ppm. The signal of $C\mathbf{H}_2C\mathbf{H}_2N$ of the cyclen unit at 2.85 ppm shifts to broad signals at 2.71 ppm and 3.30 ppm is also observed. These results come from hydrogen-bonding between NH of the cyclen unit and OH of resorcinol. By comparison of the obtained spectra of complexes of *meta*-isomer with *para* and *ortho*-isomer, resorcinol complex shows less interaction towards the ligand than dihydroquinone and catechol. This implies that the position of hydrogen-bonding donor/acceptor groups of substrates has effect on the binding affinity towards the ligand.

These can be explained by the orientation of guest molecules. When catechol includes in **20**, two hydroxyl groups of catechol point to cyclen cavity of ligand **20** to from hydrogen bonds. In this isomer, the aromatic ring of catechol can form π-π interaction with aromatic units nearby cyclen unit to stabilize the complex. On the other hand, in the case of dihydroquinone, when one hydroxyl group point to form hydrogen bonds with the cyclen unit, the other one locates in crown ether loop to form

hydrogen bonds. But when resorcinol is complexed, one hydroxyl group forms hydrogen bond with the cyclen unit and the other one point outwards the cavity. The later can form hydrogen bond difficultly. From the result, the propose structure of complexes present in Figure 3.19.

ortho *meta* *para*

Figure 3.19 The proposed structures of complexes of **20** with dihydroxy benzenes.

From these results, it is implied that the interactions of the complexation of dihydroxy benzenes with ligand **20** are in the order of *ortho* ≈ *para* < *meta* isomers.

CHAPTER IV

CONCLUSION

The new derivative of 1,3-alternate calix[4]arene, 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**) was synthesized. The synthesis pathway was begun with a condensation of 2-(2′bromoethoxy)benzyl alcohol (**14**) with calix[4]arene by using Na_2CO_3 as a base in refluxing acetonitrile. A calix[4]-dibenzyl alcohol (**16**) was afforded with 53% yield. The second binding site of the ligand was constructed by the condensation of 1,2-*bis*-(diethyleneglycol tosyl)benzene (**2**) with compound **16** in presence of K_2CO_3 in refluxing acetonitrile. A 1,3-alternate calix[4]-dibenzyl alcohol-benzo crown-6 (**17**) was obtained with 98% yield. This derivative (**17**) exists in 1,3-alternate conformation. The conversion of hydroxyl groups to bromide groups were carried out by treating with PBr_3 in presence of pyridine in dry dichloromethane. Finally, the condensation of cyclen·$2H_2SO_4$ onto compound **19** was accomplished by using ethanolic NaOEt as base in refluxing acetonitrile. The desired product, 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**) was afforded in 10% yield.

The complexation of the synthesized ligand (**20**) was carried out by mean of ^{1}H-NMR spectroscopy. With picrate salts, the inclusion of cesium ion into ligand **20** occurred immediately and a 1:1 complex was achieved in 7 days. From ^{1}H-NMR spectra, it is revealed that cesium ion resides in the crown ether loop and is stabilized by a cation-π interaction of phenylene unit. For complexation investigation with potassium and zinc, a 1:1 complex with potassium ion was achieved after 7 days of the addition potassium picrate while a 1:1 complex with zinc ion was obtained after 2 weeks. From ^{1}H-NMR spectra of theses complex, it can be deduced that potassium and zinc ions were encapsulated in the cyclen unit of **20**. This ligand can act as a hetero-binuclear receptor in which zinc ion is bound by the cyclen unit and cesium ion was encapsulated in the benzo-crown ether cavity affording a 1:1:1 complex.

An influence of anions (as a counter ion) towards the stability of zinc complexes of ligand was studies using $ZnSO_4$, $Zn(AcO)_2$, $Zn(NO_3)_2$ and $ZnCO_3$ in $CDCl_3/CD_3OD$ as salts. It was found that ligand **20** can bind most of zinc salts except $ZnCO_3$. The interaction of complexation are in the order of $SO_4^{2-} > AcO^- > NO_3^-$.

Moreover, two types of complex, 2:1 and 1:1, were observed in the case of $ZnSO_4$. In zinc halides series, the interaction of complexation are in the order of **20**·$ZnCl_2$ < **20**·$ZnBr_2$ < **20**·ZnI_2.

In order to confirm the complexation behavior of ligand **20** with $ZnSO_4$, the titration was used to investigate. From ^{1}H-NMR spectra of **20** in the presence of 0-2 equivalents of $ZnSO_4$, it was found the relationship of the concentration of salts and integrations of two doublets of ArC**H**$_2$N at 4.69 and 4.36 ppm. It is demonstrated a 2:1 (L:M) complex was found in a lower concentration of $ZnSO_4$ and a 1:1 (L:M) complex increases at a higher concentration.

The complexation studies of ligand **20** with organic molecules, phenol, aniline, catechol, resorcinol, dihydroquinone, and phthalic acid, were also investigated. ^{1}H-NMR spectra revealed interactions between the host **20** and guest molecules. This can explain by the migration of C**H**$_2$ of the cyclen unit and the neighboring phenyl unit. It is revealed that ligand **20** has higher interactions toward dihydroxybenzenes (catechol, resorcinol and dihydroquinone) than monosubstituted ones (phenol and aniline). For the influence of position of the substituents, it is shown that the *ortho* and the *para* isomers of dihydroxybenzene, catechol and quinone, have higher interaction toward the ligand than *meta* isomer, resorcinol.

The suggestion for future work:

Future works should be focused on;

1. Complexation studies of the synthesized ligand with other transition metal ions using other techniques as potentiometric or UV-Visible titrations.
2. X-ray crystallographic studies of the synthesized ligand and its complexes, which will provide more precise informations.
3. Extraction studies of ligand **20** with mixed ions such as cesium and zinc ions.

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Appendix

Appendix

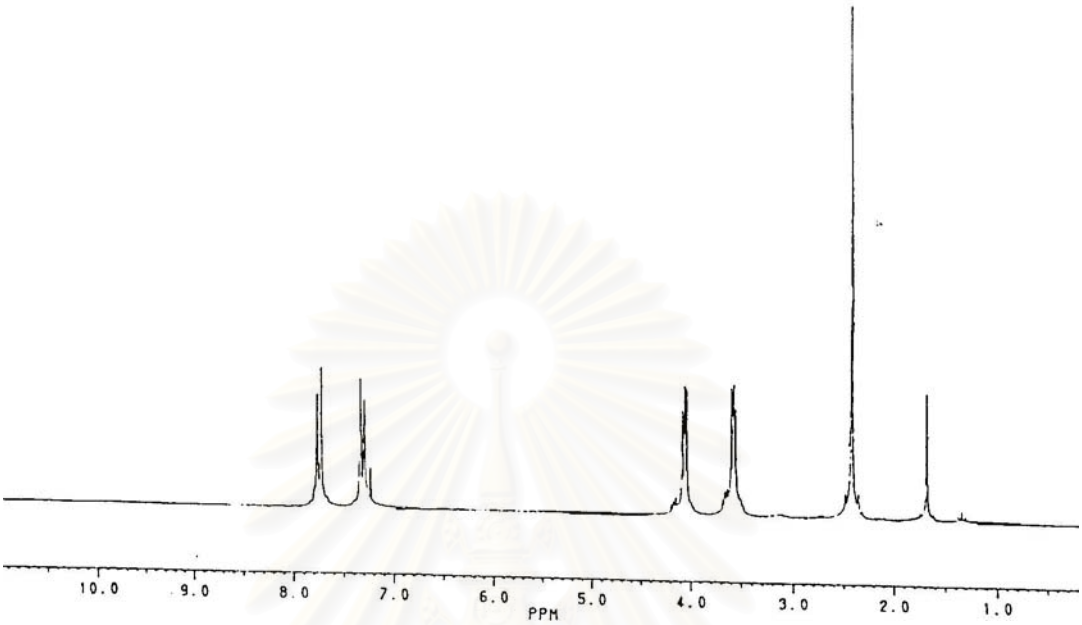

Figure A.1 ^{1}H-NMR ($CDCl_3$, 200 Hz) spectrum of diethylene glycol ditosylate (1).

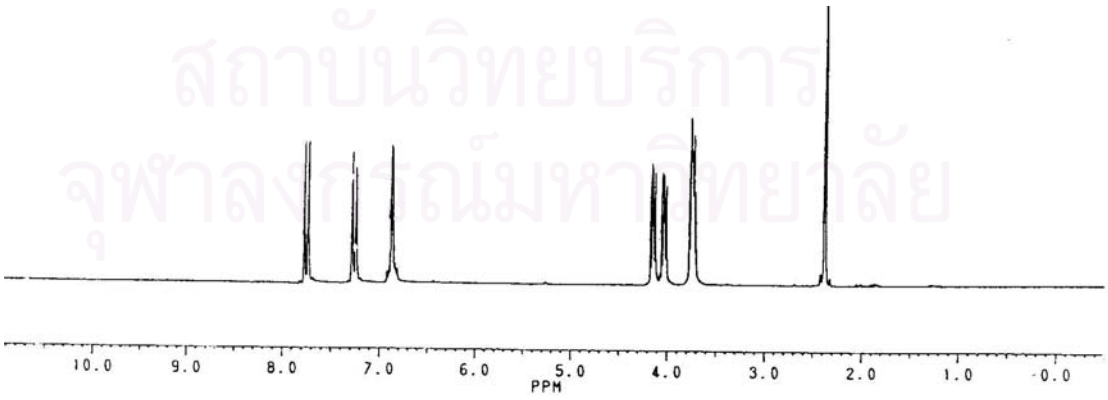

Figure A.2 ^{1}H-NMR ($CDCl_3$**,** 200 Hz) spectrum of 1,2-*bis*(diethyleneglycol tosyl) benzene (**2**).

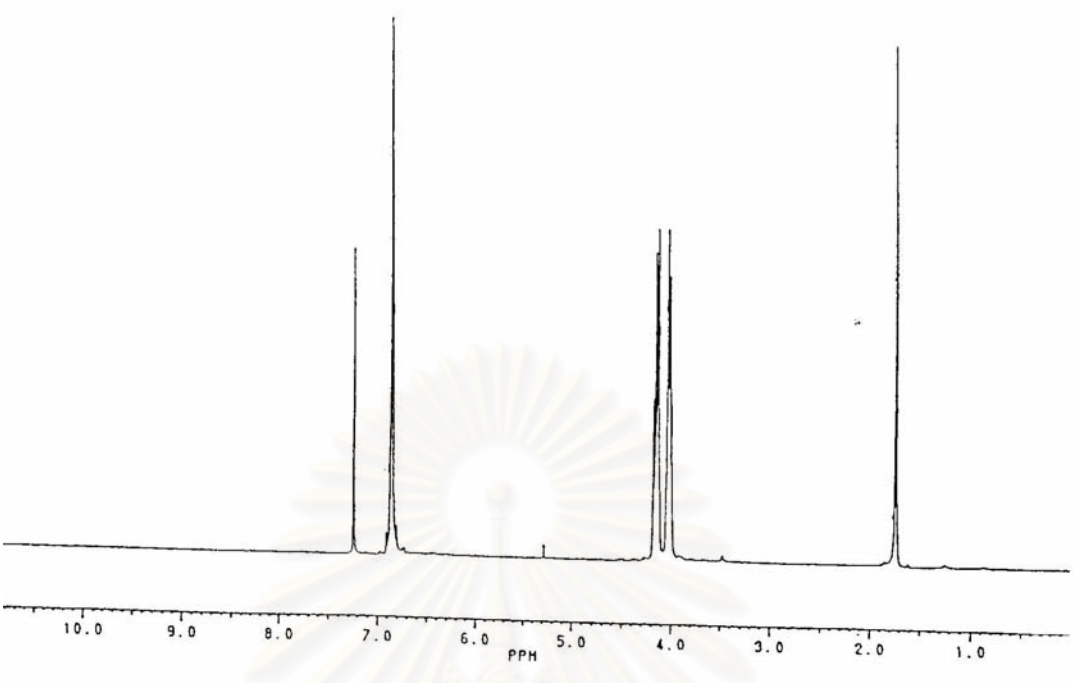

Figure A.3 ^{1}H-NMR ($CDCl_3$, 200 Hz) spectrum of dibenzo-18-crown-6 (**3**).

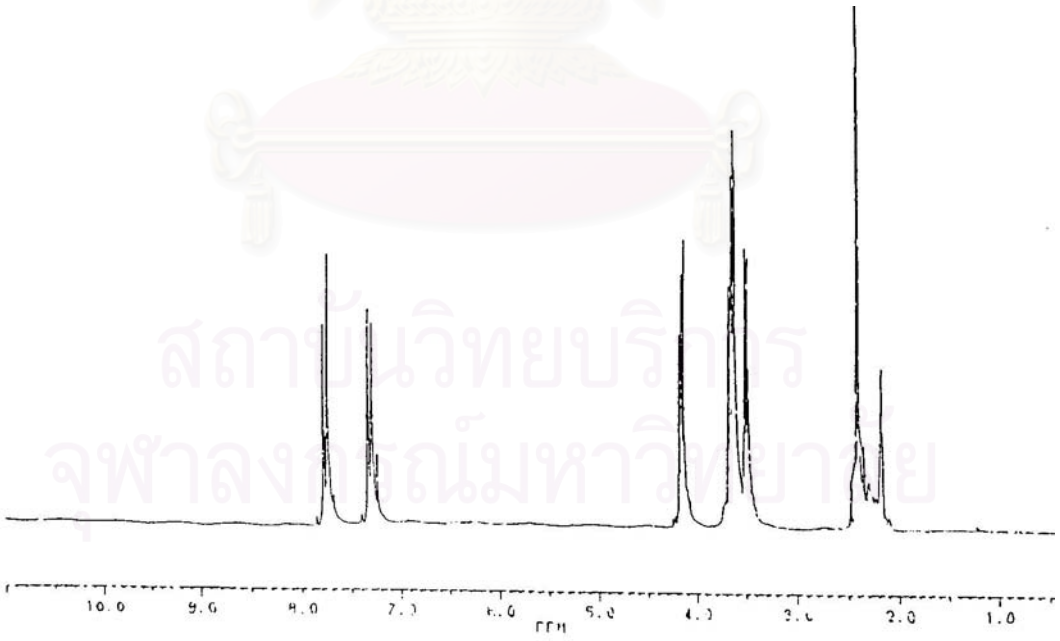

Figure A.4 ^{1}H-NMR ($CDCl_3$, 200 Hz) spectrum of diethyleneglycol monotosylate (**4**).

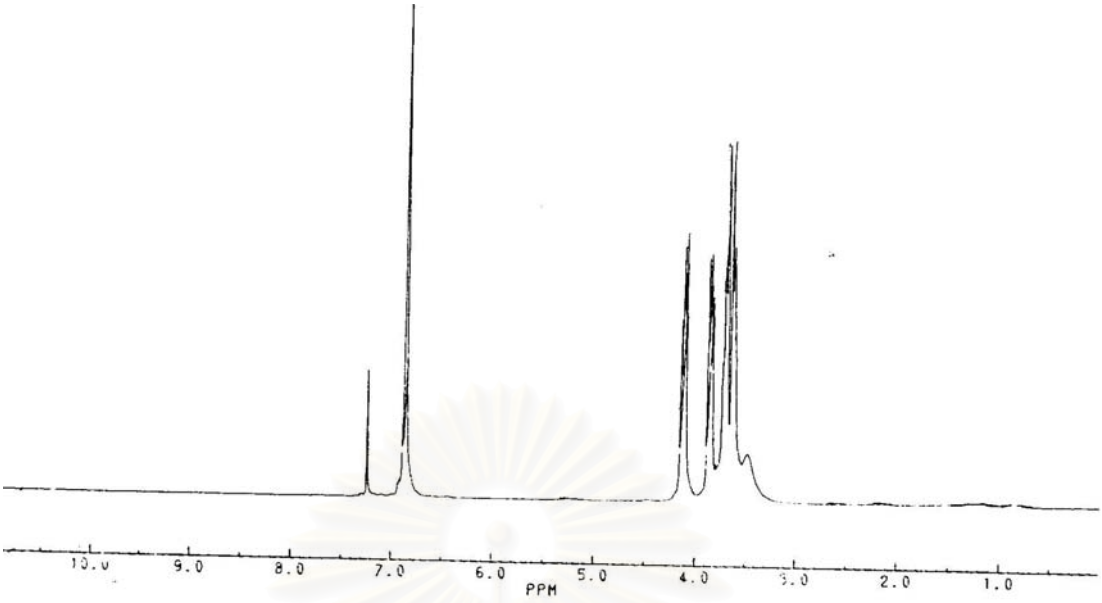

Figure A.5 ^{1}H-NMR ($CDCl_3$**,** 200 Hz) spectrum of 1,2-*bis*(diethylene glycol)benzene **(5)**.

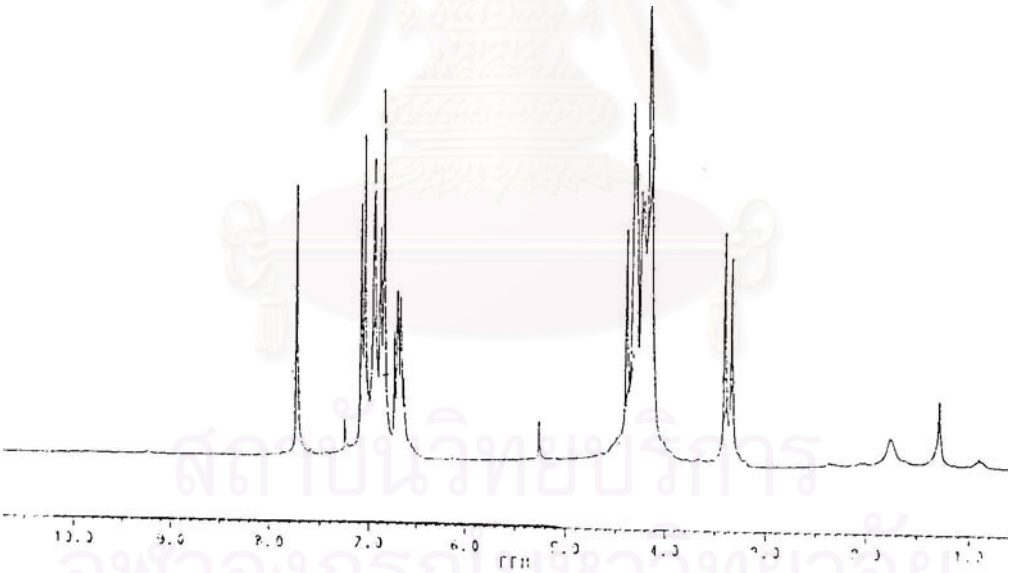

Figure A.6 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of calix[4]-benzo-crown-6 (**6**).

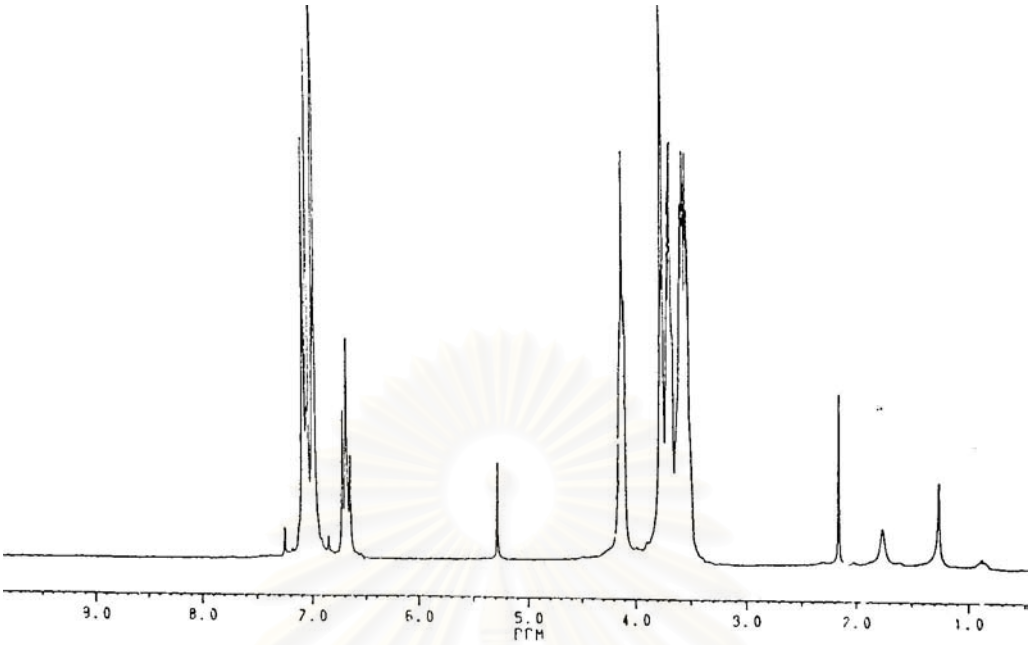

Figure A.7 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 1,3-alternate calix[4]-benzo-crown-6 (**7**)

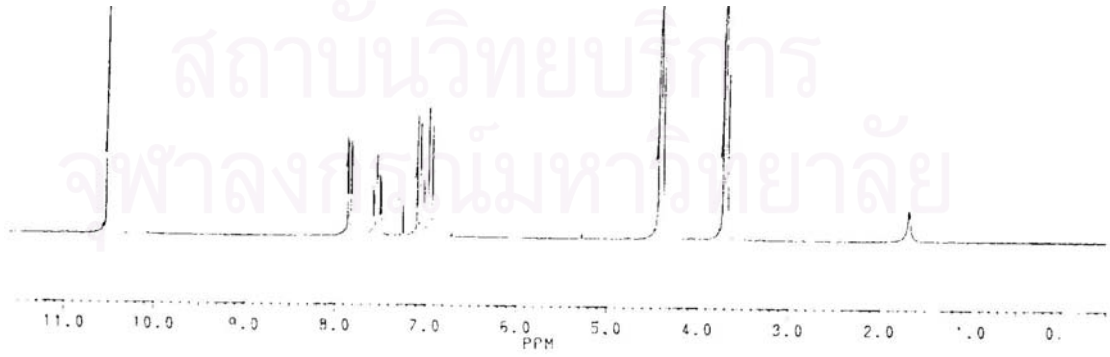

Figure A.8 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 2-(2′-bromoethoxy)benzyldehyde (**8**).

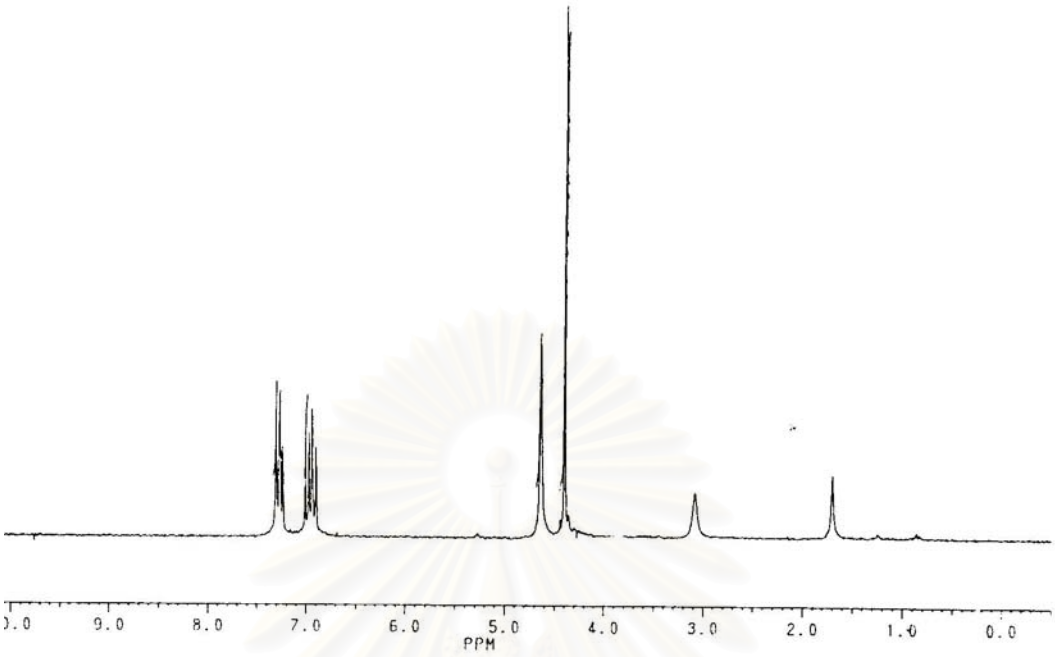

Figure A.9 ^{1}H-NMR ($CDCl_3$, 200 Hz) spectrum of 1,2-*bis*(2-carboxaldehyde phenoxy) ethylene (**9**).

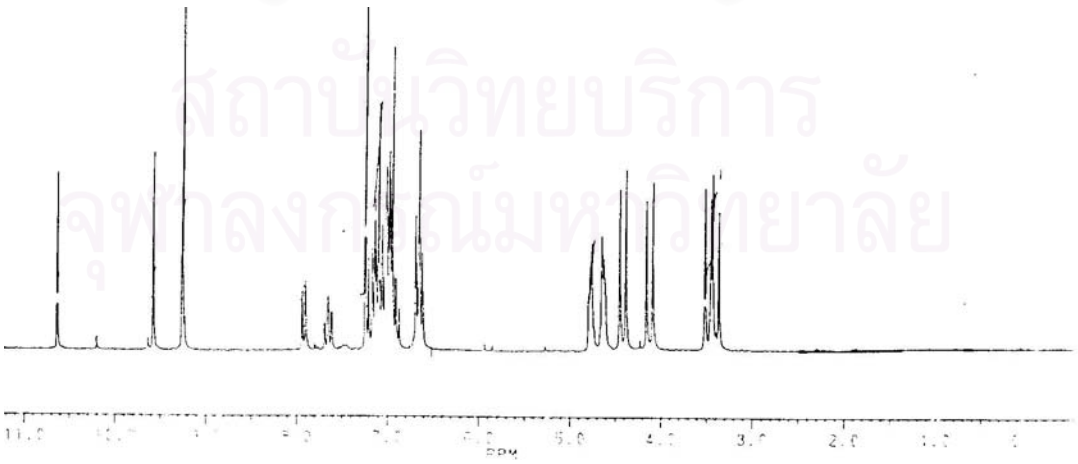

Figure A.10 ^{1}H-NMR ($CDCl_3$, 200 Hz) spectrum of calix[4]-monobenzaldehyde (**10**).

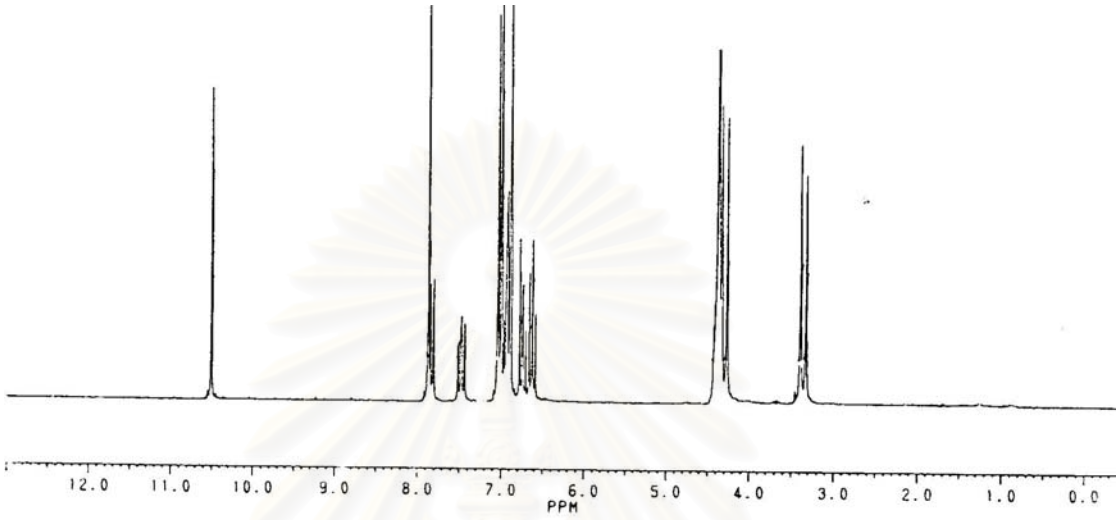

Figure A.11 ^{1}H-NMR ($CDCl_3$, 200 Hz) spectrum of calix[4]-dibenzaldehyde (**11**).

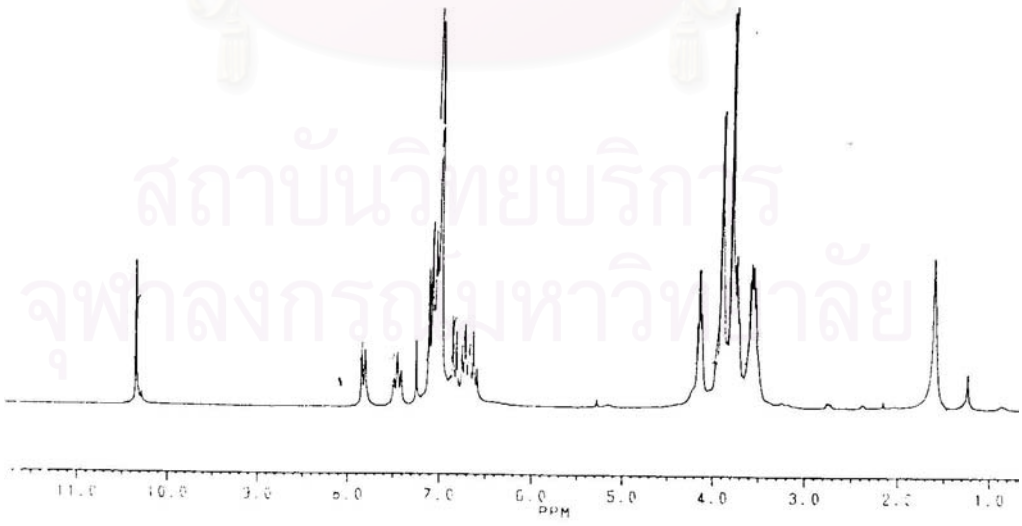

Figure A.12 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 1,3-alternate calix[4]-dibenzaldehyde-benzo-crown-6 (**12**).

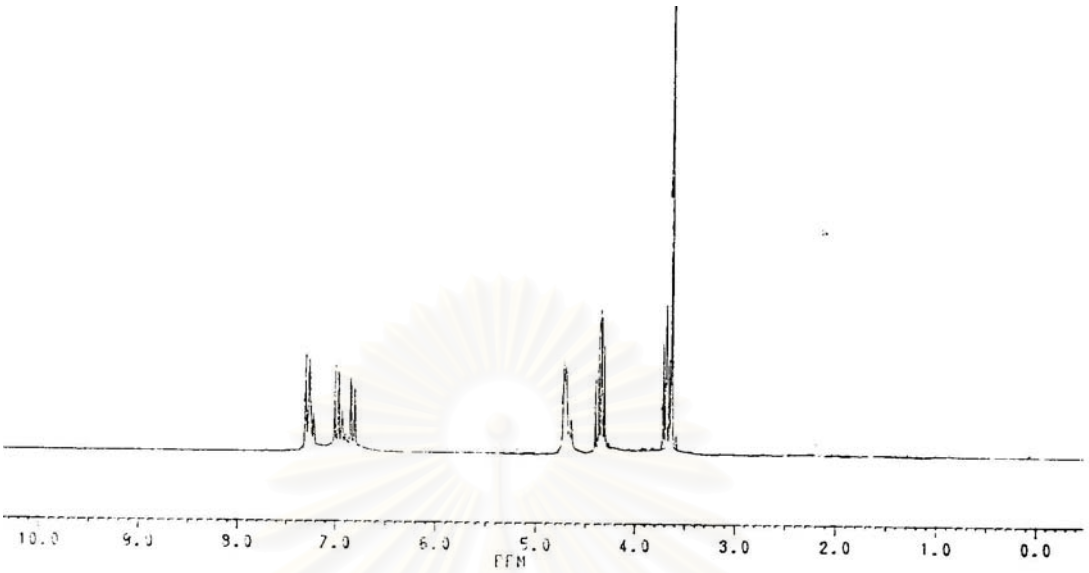

Figure A.13 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 2-(2′-bromoethoxy)benzyl alcohol (**14**).

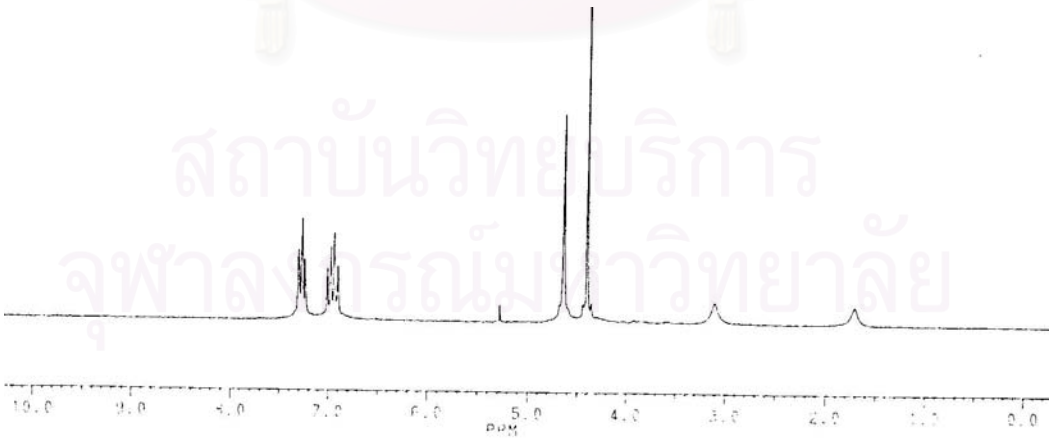

Figure A.14 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 1,2-dioxyethylene-*bis*-benzylalcohol (**15**).

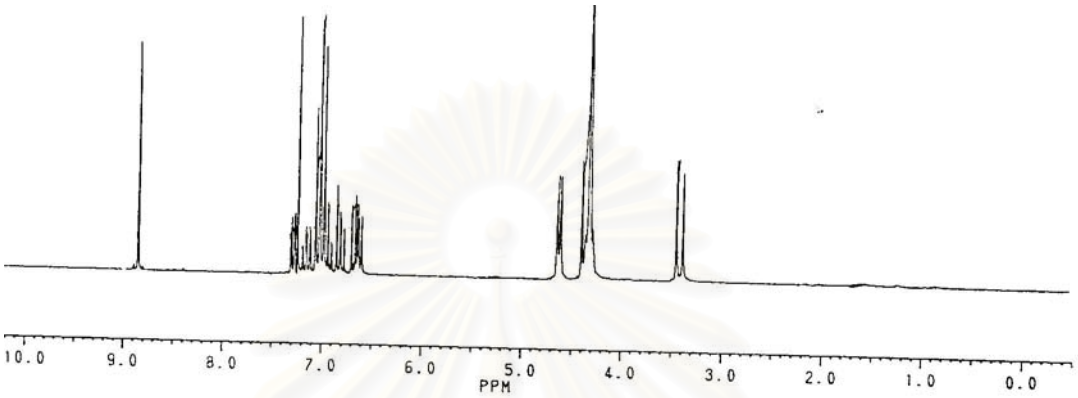

Figure A.15 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of calix[4]-dibenzyl alcohol (**16**).

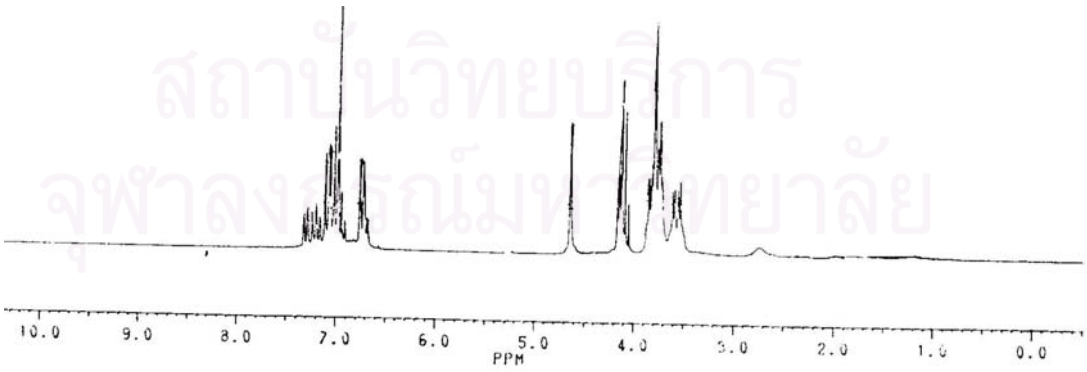

Figure A.16 ^{1}H-NMR ($CDCl_3$, 200Hz)) spectrum of 1,3-alternate calix[4]-dibenzyl alcohol-benzo-crown-6 (**17**).

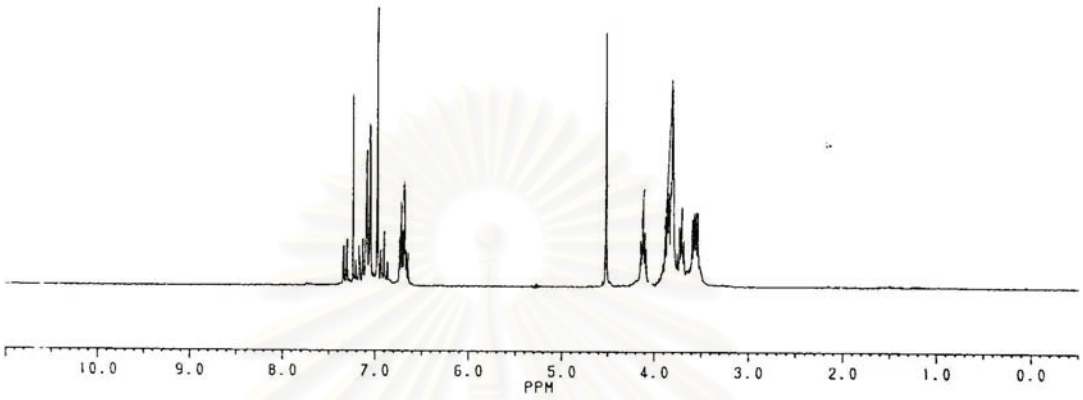

Figure A.17 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 1,3-alternate calix[4]-dibenzyl bromide-benzo-crown-6 (**19**).

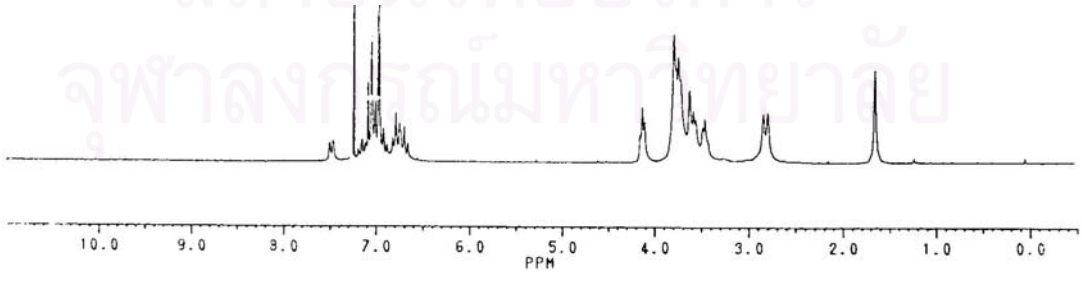

Figure A.18 ^{1}H-NMR ($CDCl_3$, 200Hz) spectrum of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**).

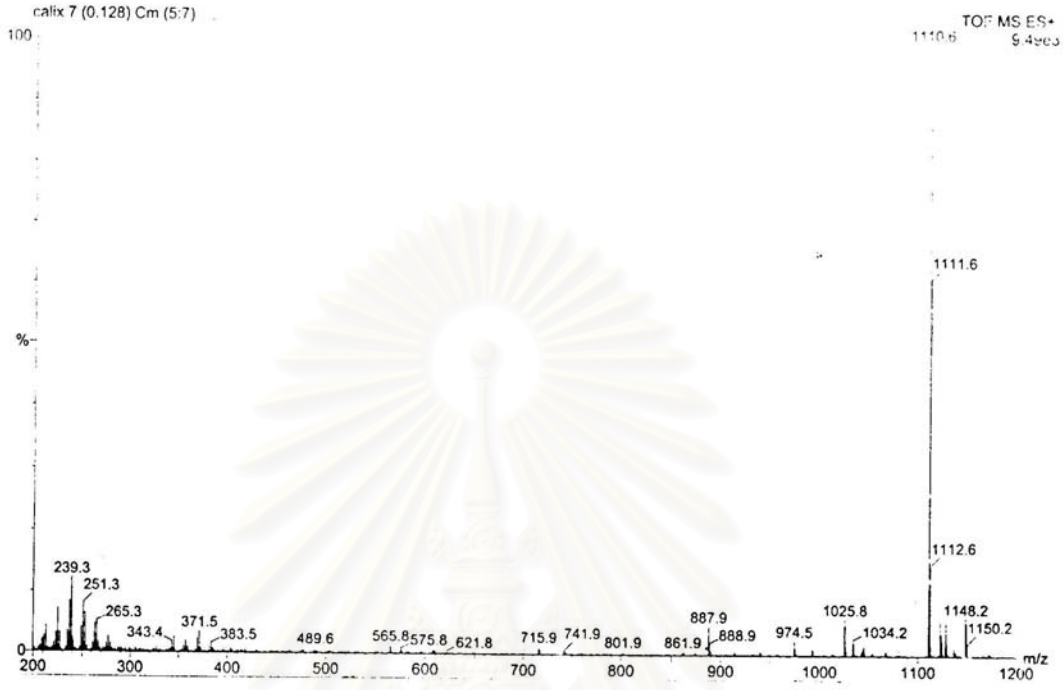

Figure A.19 ES –TOF MS spectrum of 1,3-alternate calix[4]-cyclen-benzo-crown-6 (**20**).

VITA

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