การสังเคราะห์คาลิกซ์[4]เอรีนควิโนนไดเมอร์

เพื่อใช้เป็นตัวตรวจวัดไอออนของโลหะแอลคาไล

นายเกรียงกมล ตันตระการย์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต

สาขาวิชา เคมี ภาควิชาเคมี

คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2545

ISBN 974-17-1454-8

SYNTHESIS OF CALIX[4]ARENEQUINONE DIMERS FOR ALKALI METAL ION SENSOR

Mr. Kriengkamol Tantrakarn

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Chemistry
Department of Chemistry
Faculty of Science
Chulalongkorn University
Academic Year 2002
ISBN 974-17-1454-8

Thesis Title	Synthesis of calix[4]arenequinone dimers for alkali metal ion sensor
By	Mr. Kriengkamol Tantrakarn
Field of Study	Chemistry
Thesis Advisor	Assistant Professor Thawatchai Tuntulani, Ph.D.

Accepted by the Faculty of Science, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

……Dean of Faculty of Science
(Associate Professor Wanchai Phothiphichitr, Ph.D.)

Thesis Committee

……Chairman
(Associate Professor Sophon Roengsumran, Ph.D.)

……Thesis Advisor
(Assistant Professor Thawatchai Tuntulani, Ph.D.)

……Member
(Assistant Professor Orawon Chailapakul, Ph.D.)

……Member
(Yongsak Sritana-Anant, Ph.D.)

……Member
(Nongnuj Muangsin, Ph.D.)

เกรียงกมล ตันตระการย์ : การสังเคราะห์คาลิกซ์[4]เอรีนควิโนนไดเมอร์เพื่อใช้เป็นตัวตรวจวัดไอออนของโลหะแอลคาไล (SYNTHESIS OF CALIX[4]ARENEQUINONE DIMERS FOR ALKALI METAL ION SENSOR) อาจารย์ที่ปรึกษา : ผศ.ดร.ธวัชชัย ตันฑุลานิ; 94 หน้า.
ISBN 974-17-1454-8

ทำการสังเคราะห์ลิแกนด์ 25,27-Di(ethyleneglycol)-bis-*p-tert*-butylcalix[4]arene **5** และ 25, 27-di(methoxy)-26, 28-di(ethylene glycol)-bis-*p-tert*-butylcalix[4]arene **11** โดยใช้วิธีการสังเคราะห์แบบขั้นตอนเดียว และแบบหลายขั้นตอน ตามลำดับ วิธีการสังเคราะห์แบบขั้นตอนเดียวภายใต้สภาวะความดันสูงสามารถทำการสังเคราะห์ลิแกนด์ที่มีความสมมาตร **5** ได้ปริมาณผลิตภัณฑ์ทั้งสิ้น 69% อนุพันธ์ของควิโนน 25,27-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] tetraquinone **12** และ 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] diquinone **13** สามารถสังเคราะห์ได้จากปฏิกิริยาระหว่าง **5** และ **11** ตามลำดับกับ $Tl(CO_2CF_3)_3$ ใน CF_3COOH การศึกษาแบบจำลองโมเลกุลแบบไดนามิคส์ของสารประกอบ **12** และ **13** ก่อนและหลังการเติม โซเดียมไอออนในสารละลายอะซิโตนไนไทรล์ แบบจำลองโมเลกุลแบบไดนามิคส์ที่อุณหภูมิ 300 เคลวินแสดงให้เห็นถึงการเปลี่ยนแปลงโครงรูป ได้แก่ โครงรูปแบบโคน แบบกึ่งโคน และแบบอัลเทอร์เนตโคน ของหน่วยคาลิกซ์เอรีน และทำการคำนวณค่าพลังงานต่ำสุดของแต่ละโครงรูปจากแบบจำลองโมเลกุลแบบไดนามิคส์ การศึกษาสมบัติพื้นฐานทางเคมีไฟฟ้าของ **12** และ **13** โดยอาศัยเทคนิคไซคลิกโวแทมเมทรีแสดงให้เห็นถึงการเปลี่ยนแปลงอย่างชัดเจนของสัญญาณรีดักชันของควิโนนเมื่อเติมโซเดียมไอออนลงในระบบ โวลแทมโมแกรม ของ **12** และ **13** แสดงถึงการถ่ายโอนอิเลคตรอนแบบซับซ้อนแล้วจึงตามด้วยการเปลี่ยนแปลงเนื่องจากปฏิกิริยาเคมี

ภาควิชา……...…….. ลายมือชื่อนิสิต……...……...……...
สาขาวิชา…….... ลายมือชื่ออาจารย์ที่ปรึกษา…...…….....
ปีการศึกษา...…….....

KEY WORDS: CALIXARENE/ BISCALIXARENE/ QUINONE/ CYCLIC VOLTAMMETRY/ MOLECULAR DYNAMIC SIMULATION

KRIENGKAMOL TANTRAKARN: SYNTHESIS OF CALIX[4]ARENE QUINONE DIMERS FOR ALKALI METAL ION SENSOR THESIS ADVISOR : ASSISTANT PROFESSOR THAWATCHAI TUNTULANI, Ph.D. 94 pp. ISBN 974-17-1454-8

25,27-Di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4]arene, **5**, and 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4]arene, **11**, have been synthesized by a one-pot method and a stepwise approach, respectively. The one pot reaction in a pressurized vessel resulted in the symmetrical biscalixarene **5** with high yield (69%). The quinone derivatives 25,27-di(ethylene glycol)-bis-*p*-*tert*-butylcalix[4]tetraquinone, **12**, and 25,27-di(methoxy)-26,28-di(ethylene glycol)-bis-*p*-*tert*-butylcalix[4]diquinone, **13**, were obtained from reactions of **5** and **11,** respectively with $Tl(CO_2CF_3)_3$ in CF_3COOH. Molecular dynamic simulations were performed for compounds **12** and **13** both before and after addition of Na^+ in acetonitrile solution. The MD calculation at 300 K showed the change of conformations among cone, partial cone and 1,3-alternate conformations of the calixarene unit. The lowest energy of each possible morphology has been determined. The preliminary investigation on electrochemical properties of **12** and **13** by cyclic voltammetry showed significant changes of the quinone reduction signals upon addition of Na^+ ion. Voltammograms of **12** and **13** exhibited complicated electrons transfer reduction processes following by chemical reactions.

Department……...…….. Student`s signature……...……...

Field of study…….... Advisor`s signature…….....

Academic year...…….....

Acknowledgement

No original research can be accomplished by one person, but by a collaborative effort. I have had the opportunity to work with a number of people while I was a student at the Department of Chemistry, Chulalongkorn University. Each has helped in theirown ways: sharing expertise, exchanging views or simply lending moral support. It gives me a great pleasure to acknowledge some of these people.

I would like to thank my supervisor, Assistant Professor Dr. Thawatchai Tuntulani, for his enthusiasm, vision and prudent advice, which proved crucial to this project. I also thank other members of my committee for their input and interest: Associate Professor Dr. Sophon Roengsumran, Assistant Professor Dr. Orawon Chailapakul, Dr. Yongsak Sritana-Anant and Dr. Nongnuj Muangsin. All of my committee members have made extensive and excellent comments on early works and drafts of the thesis, for which I am very grateful. I also appreciate discussions with Ms. Boosayarat Tomapatanaget and Mr. Nathavut Kerdpaiboon while we were working in the same area. I often came across new ideas to solve some problems arised from my experiments.

The Electroanalytical Chemistry Research Group at Chulalongkorn University has also been of help, offering excellent physical devices and ensuring that our synthesized compounds can find their practical use. Particular thanks, therefore, go to Assistant Professor Dr. Orawon Chailapakul, the leader of the group.

Current and former members of the Supramolecular Chemistry Research Group have greatly contributed to this thesis, made the work fun and stimulated my enthusiasm: Sirilux Poompradub, Praput Thavornyutikarn, Matinee Jamkratoke, Gamolwan Tuncharern, Chalita Ratanatewanate, Tipsukhon Pinsuk and everyone at the Department of Chemistry, Chulalongkorn University.

My love and thanks go to my parents and sister for their unwavering encouragements and supports.

Finally, I would like to thank the Thailand Research Fund, the Graduate School of Chulalongkorn University and the Department of Chemistry for financial support.

CONTENTS

Page

CONTENTS (continued)

LIST OF FIGURES

Page

LIST OF FIGURES (Continued)

LIST OF SCHEMES

Page

LIST OF TABLE

Page

LIST OF ABBREVIATIONS AND SYMBOLS

DMAP	4-(*N*,*N'*-dimethyl amino) pyridine
Å	Angstrőm
δ	Chemical shift
J	Coupling constant
CV	Cyclic voltammetry
^{o}C	Degree Celsius
K	Kelvin
Equiv.	Equivalent
FAB MS	Fast atom bombardment mass spectrometry
g	Gram
Hz	Hertz
mp	Melting point
Ms	Methane sulfonyl group
mmol	Millimol
mL	Milliliter
M	Molar
MD	Molecular dynamic
ppm	Part per million
psi	Pound per square inch
^{1}H-NMR	Proton nuclear magnetic resonance
RT	Room temperature
s, d, t, m	Splitting patterns of ^{1}H-NMR (singlet, doublet, triplet and multiplet)
THF	Tetrahydrofuran
Ts	Toluene sulfonyl group

CHAPTER 1

INTRODUCTION

Research over the past few decades has made apparent the role of electrochemical sensor, such as chemically modified field effect transistor (CHEMFETs)[1-3] and ion-selective electrodes (ISEs), in agrotechnical and environmental fields. As the selective detection elements, ion-selective sensors contain synthetic receptor molecules that selectively recognize a guest species. The properties of these molecules are essential for the overall performance of the chemical sensors as they determine the characteristics of the devices, which are selectivity, life time and response time.[4] A number of requirements have to be fulfilled to obtain ionophores that possess highly selective complexation properties and highly response time to become excellent chemical sensors. Firstly, the cavity size of the ionophore carrying coordinating atoms should be complementary with the size of the ion to be complexed. A better fit of the ion and the cavity higher selectivity of binding. Secondly, the selective receptor molecules should have the ionophores and the reporter groups in close proximity to enhance agility of signals.[5]

During 1970s and 1980s, synthetic ionophores, like crown ethers and cryptands, which are known for recognition of alkaline and alkaline earth metal ions, were applied in ISEs.[6] A more recently developed strategy for the synthesis of receptor molecules is the use of lipophilic molecules as platforms in which appropriate functionalities can be attached. One of the versatile classes of these building blocks is the calixarenes.

1.1 Calixarenes

Calixarenes are macrocyclic molecules having preorganized cavities, thet could recognize ions or organic molecules. The growing interest in these materials is due to the ease of their synthesis, thermal stability, particularly their recognition properties and their promises as selective complexation agents in sensors. Calixarenes can be functionalized with different functional groups leading to specific cavities for particular guest molecules.[7]

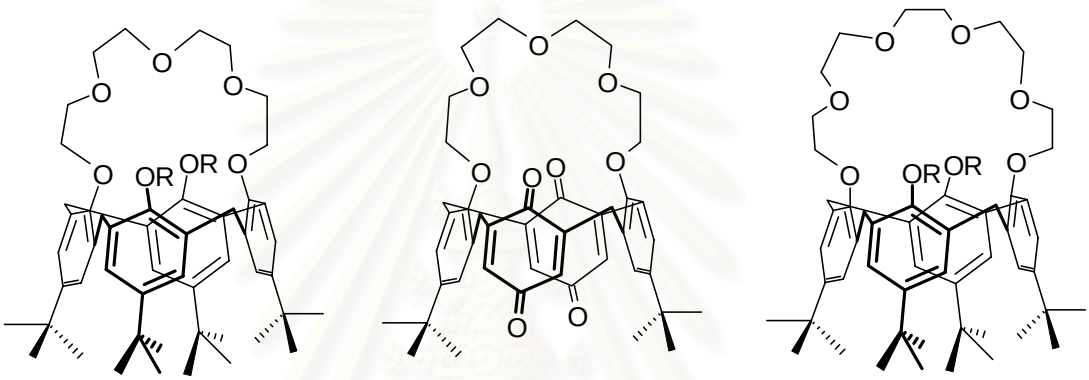
Calix[4]arenes are easily accessible from the base-catalyzed condensation of *p-tert*-butylphenol and formaldehyde. Selective de-butylation and reactions at one or more of the phenolic groups lead to rapidly increasing members of possible functionalized calix[4]arenes. A large variety of substituents, including alkyl, ester, ketone, amino and heterocyclic groups, can be prepared by selective *O*-alkylation or *O*-acylation at the lower rim.[8]

1.1.1 Receptor molecules based on calix[4]arene

Calix[4]arene derivatives with hard donating atoms, like oxygen, have a high affinity for hard alkali and alkaline earth ions.[9] The first successful ionophores based on calix[4]arenes were obtained from derivatives containing ether groups.[10-11] The hard donating oxygen atoms on carbonyl groups and four ethereal oxygen atoms were attractred by hard metal cations. Picrate extraction experiments showed that stable complexes were formed with different alkali metal ions (e.g. Li^+, K^+, Na^+, Rb^+ and Cs^+ with stability constants in the range of 10^2-10^6 M^{-1}).[12-13]

A further enhancement of the stability of the cation complexes was obtained by increasing the entropy of binding. With this in mind, conformational changes upon complexation must also be minimized, corresponding to a high degree of preorganization of the donating atoms. Preorganization of the receptor molecule can be optimized by introduction of a rigid bridge at the lower rim. In 1994, calix[4]arene

crown ethers have been used for the selective complexation of alkaline metal ions. Shinkai and coworkers reported calix[4]arene, **1**, as the selective receptor for complexation of Na^+ and applied it in ion-selective electrodes (ISEs).[14] The cone conformer exhibits a selectivity in an order of log $K_{Na/K}$ = -4.1. A calix[4]arene with quinone moieties, **2**, was also investigated as the receptor molecule in ISEs. Its Na^+/K^+ selectivity (log $K_{Na/K}$ = -3.4), was higher than obtained with **1**.[15]

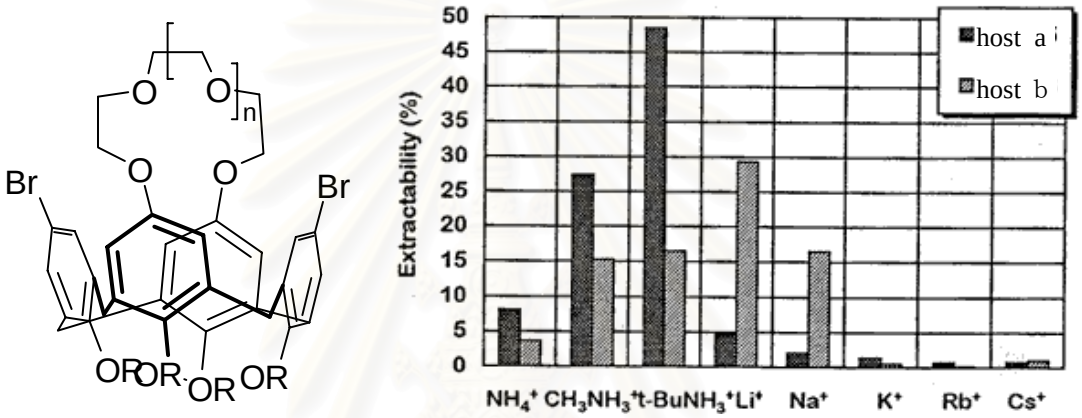


1 2 3

Figure 1.1 some structures of cryptand-liked calixarenes
1; calix[4]arene bridged with an ethyleneoxy units
2; calix[4]quinone bridged with an ethyleneoxy units
3; calix[4]arene bridged with a longer ethyleneoxy units

When the ring size of ethyleneoxy bridged calix[4]arene was extended by one and two ethyleneoxy units, the binding ability is changed in favor of larger ions, K^+ and Cs^+, respectively.[16-17] The Na^+/K^+ selectivity of CHEMFETs containing calixarene derivative, **3**, (log $K_{Na/K}$ = -4.2) is even better than that observed with CHEMFETs containing the natural ionophore valinomycin (log $K_{K/Na}$ = -3.9).

The preorganization of the receptor molecule by introduction of ethyleneoxy bridging unit at the upper rim was also described.[18] The cavities of these bridged calixarenes (Figure 1.2) were larger than the lower rim bridged calixarenes. The experiments showed that these calixarenes had a lower affinity for alkali metal ions than the lower rim bridged molecules.



host **a**: n = 3 ; host **b**: n = 4

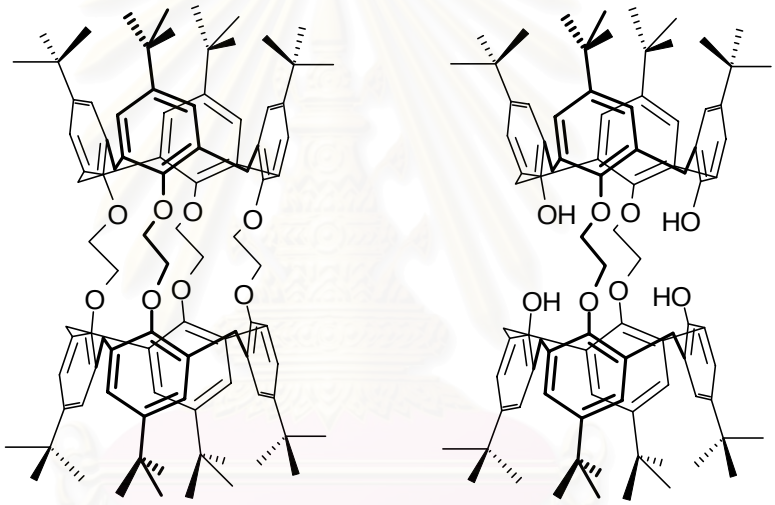
Figure 1.2 A series of upper rim bridged calix[4]arense and their cation extractability

However, simple calix[4]arene ethers with the cone geometry are cup-shaped molecules with a rather open and small cavity. The ability of which to bind guest molecules is limited. Much work has been done to modify both the lower rim with the phenolic hydroxyl groups,[19] and the upper rim positions[20-23] to create bridged calixarenes mainly for the extraction of simple cations, anions and small molecules.

Recently, the bridged calixarenes, such as bicyclocalixarenes,[24-25] calixcrowns,[17] calixspherands,[26] biscalixcrowns,[17,26] calixcryptands,[27] double and triple calixarenes, have received an increasing attention because of their well organized molecular structures. Some calixcrowns, which are poly(ethyleneoxy)

bridged calixarenes, present a new class of potassium-selective ionophore with $K_{K+/Na+}$ = 1.18x10^4. The more rigidly bridged calix-sphearands can form kinetically stable complexes with Na^+, K^+ and Rb^+.[28]

Doublecalixarenes are a kind of bridged calixarenes which also exhibit special molecular recognition abilities. They can be divided into three types according to their linking arrangements: lower-rim to lower-rim,[29-30] upper-rim to upper-rim[31] and lower-rim to upper-rim.[32]



4 5

Figure 1.3 some structures of cryptand-liked double calixarenes
4; calix[4]arene tube
5; 25, 27-di(ethylene glycol)-bis-*p*-tert-butyl-calix[4]arene

Doublecalixarenes and cryptand-liked calixarenes have been reported and attracted much attention due to their sophisticated molecular structures. For example, calix[4]arene tube,[33] **4**, was obtained by reacting *p-tert*-butylcalix[4]arene with the pertosylated derivative of calix[4]arene in a covalent self-assembly process, in which

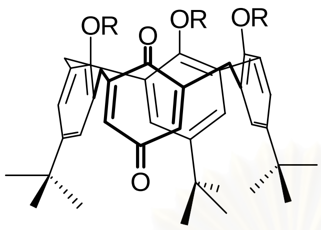
two calix[4]arene subunits were linked by four ethylene glycolic chains and the calix[4]arene moieties are in cone conformers. This calix[4]arene tube exhibits extraordinary complexation abilities toward alkali metal ions, especially K^+ with stability constant of $4x10^4$ $Lmol^{-1}$. Very recently, Tomapatanaget *et al.* has synthesized bis-*p*-tert-butylcalix[4]arene, **5**, by nucleophilic substitution reactions of *p*-tert-butylcalix[4]arene with bromoethyl tosylate using K_2CO_3 as base and yielded bis-*p*-tert-butylcalix[4]arene in 41%.[34] This reaction also produced bisbromoethoxy calix[4]arene which implied that the coupling process occurred in a stepwise manner whereas bisbromoethoxy calix[4]arene was the intermediate.

1.1.2 Calix[4]arenes based Electrochemical sensor

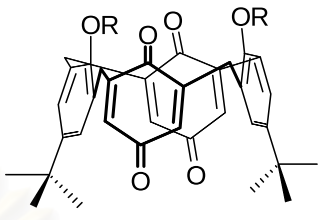
One of the most popular signaling units used by chemists are ferrocene and quinone.[35-38] An increasing interest in the synthesis of redox-active calixarenes has centered on the appropriate functionalization of phenol units after the possibility of calixarenes as enzyme mimics was suggested.[39] The conversion of phenolic rings to quinone and nitro aromatic moieties has been reported.[40-41] Calix[4]arenequinone compounds have especially attracted chemists` attention because of their selectivity toward certain cations and electrochemical properties.[42-44] The study on the effect of electron transfer processes in spatially constrained systems with multiple redox units of quinone made calix[4]arenequinone one of the molecular devices in redox switching studies.

In 1994, Gutsche and Echegoyen reported the redox and cation binding properties of a series of four quinone-functionalized calix[4]arenes in acetonitrile solution.[45] Mono-, di-, tri-, and terraquinone calixarenes **6**-**9** (Figure 1.4) exhibit successive first electron transfers for each of the quinone units. These calixarenes provide an opportunity for the elucidation of the effect on successive substitutions of redox units into the constrained calix[4]arene framework. When reduced to the mono anion state, compound **6**-**9** interacted with Na^+ and Ag^+ in various extent. Moreover,

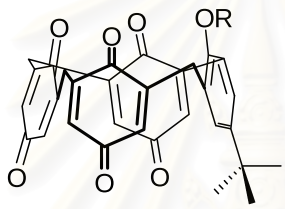
the neutral calix[4]arene monoquinone, **6** (Figure 1.4) binds Na^+ and shows a binding enhancement in the order of 10^6 when reduced to its monoanion state.



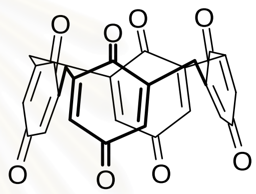
6



7



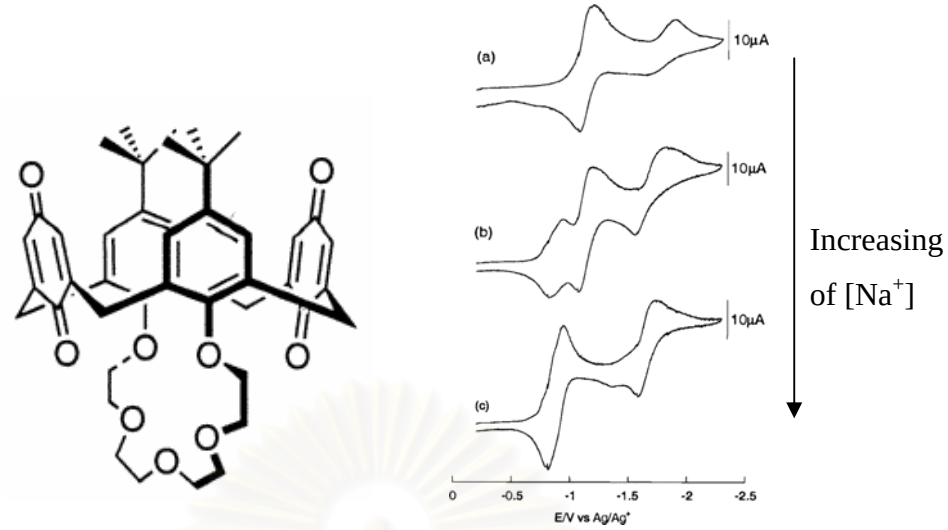
8



9

Figure 1.4 A series of calix[4]quinones

In 1997, a new series of ionophoric *p*-*tert*-butylcalix[4]diquinones containing ester and crown ether substituents has been synthesized by treatment of the respective 1, 3-disubstituted *p*-*tert*-butylcalix[4]arene with $Tl(OCOCF_3)_3$ in trifluoroacetic acid.[46] The electrochemical properties of the diquinone compounds (Figure 1.5) and their complexes have been studied using cyclic and square wave voltammetry. The reduction potentials of the alkali and alkaline earth metal ion complexes are significantly anodically shifted with respect to that of the free ligand.



10

Figure 1.5 Ionophore *p-tert*-butylcalix[4]diquinone, **10**, and its cyclic voltammograms in the presence of sodium cation

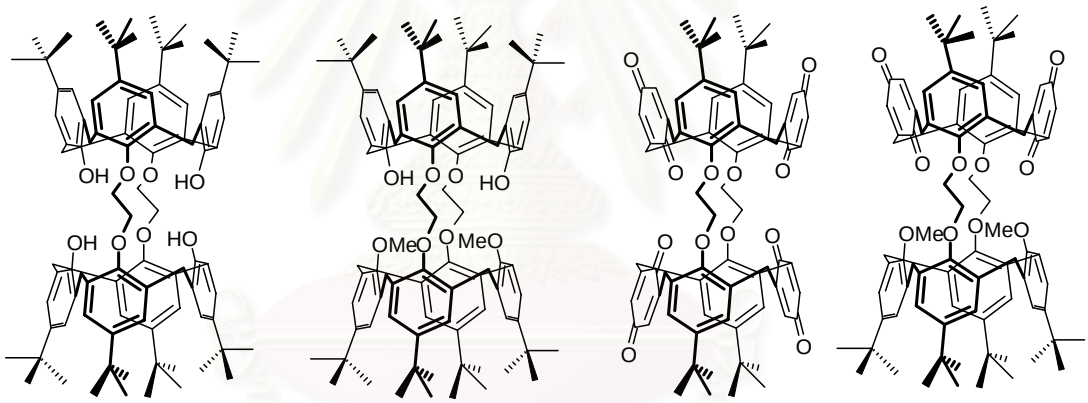
1.2 Objective of the Thesis

Several possibilities exist for preorganizing the cavity to enhance the binding of cationic guests. Calixarenes with ether functionalities or crown ether units are easily prepared and have the corresponding cavities. Unfortunately, they cannot be made conformationally rigid. Alternatively, one can extend the calix[4]arene at the upper rim positions by combining with another calix[4]arene unit. Examples of the latter strategy are the lower-rim-connection made by Reinhoudt and coworkers. Two calixarene units have also been elegantly joined by a self-assembled process and shown to include guest molecules.[47] The most difficult step in the connection of calixarenes via covalent links is the final coupling step, which is prone to side reactions. We have chosen the formation of ethylene glycolic chains from the nucleophilic substitution.

In term of electrochemical properties, Cyclic Voltammetry (CV) technique has been chosen as a transduction method, allowing the conversion of a chemical

phenomenon such as ion binding into an electrical signal. This process is usually referred as electrochemical recognition. Reports on electrochemical recognitions have employed calixarene derivatives containing ferrocene,[48] quinone[49] or other electroactive groups.[50]

The aim of this work was to investigate the electroactivity of the synthesized biscalix[4]arene quinones **12** and **13** (Figure 1.6) in non-aqueous solution and their possible dependence upon complexation with suitable ions. We reported here the results of our preliminary studies of the electrochemical oxidative behaviors of biscalixarenes designed for ion binding with quinones as electrochemical signaling groups.



5 11 12 13

Figure 1.6 Structure of cryptand-like bis-*p*-tert-butyl-calix[4]arene derivative **5**, **11**, **12** and **13**

Our primary interest in this work was to probe the electroactivity of a biscalixarenes family with various number of quinone groups. Although development

of ion detection or biscalixarenes detection strategies wan not the goal of this work, clearly the data presented would support such eventual applications.

CHAPTER 2

EXPERIMENTAL SECTION

2.1 Instrument and materials

2.1.1 Analytical Instrument

Elemental analysis was carried out on a CHNS/O analyzer (Perkin Elmer PE2400 series II). Nuclear Magnetic Resonance (NMR) spectra were recorded on a Varian Gemini 200 or a Bruker ACF 200 MHz nuclear magnetic resonance spectrometer. In all cases, samples were dissolved in deuterated chloroform or deuterated acetonitrile and chemical shifts were recorded in part per million (ppm) using a residual proton signal as internal reference. Infrared spectra were obtained on a Nicolet Impact 410 with samples prepared in KBr pellet.

2.1.2 Materials

All materials were standard analytical or reagent grade, purchased from Fluka, Aldrich, Carlo Erba, Merck or J. T. Baker and used without further purification. Commercial grade solvents such as acetone, hexane, dichloromethane, methanol and ethyl acetate were distilled before use. Acetonitrile was dried over CaH_2 and freshly distilled under nitrogen prior to use. THF was dried by refluxing with Na and benzophenone under nitrogen atmosphere and distilled before used.

Column chromatography was carried out using silica gel (Kieselgel 60, 0.063-0.200 mm, Merck) or neutral aluminium oxide (aluminium oxide 90, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was performed on silica gel plates (Kieselgel 60 F_{254}, 1 mm, Merck) or aluminium oxide plates (aluminium oxide 60 F_{254}, neutral type E, Merck).

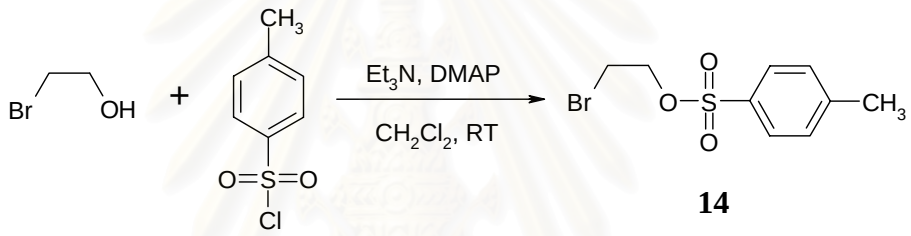
Starting materials such as *p-tert*-butylcalix[4]arene were prepared according to literature procedure.[51] All compounds were characterized by ^{1}H-NMR spectroscopy, mass spectrometry and elemental analysis.

2.2 Experimental Procedures

2.2.1 General procedure for the preparation of 25,27-di (ethyleneglycol)-bis-*p*-*tert*-butylcalix[4]arene (5)

Path way I: one-pot synthesis

Step I: Preparation of 2-bromoethyl toluene sulfonate (**14**)



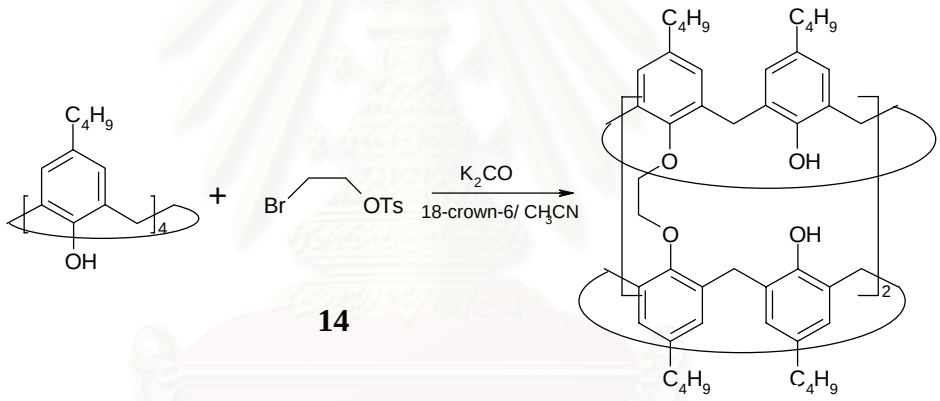
14

In a 500 mL two-necked round bottom flask equipped with a magnetic bar, dichloromethane solution (100 mL) of 2-bromoethanol (7.1 mL, 100 mmol), triethylamine (14.5 mL, 100 mmol) and a catalytic amount of DMAP was chilled to 0 ^{o}C with an ice bath and stirred under nitrogen for 30 minutes. The solution of TsCl (19.05 g, 100 mmol) in dichloromethane (100 mL) was then added dropwise to the mixture. The reaction mixture was stirred at room temperature under nitrogen atmosphere for 4 hours and extracted with water (2x100 mL). The combined organic layer was dried over Na_2SO_4 anhydrous and filtered. The combined filtrate was concentrated on a rotary evaporator to obtain yellowish brown oil. The residue was placed on a silica gel column and eluted with dichloromethane. The desired product, 2-bromoethyl toluene sulfonate, **14**, was obtained as light yellowish oil. (25.11 g, 90% yield) The product was dried in *vacuo* and kept in a desiccator before used.

Characterization data for 2-bromoethyl toluene sulfonate (14):

^{1}H-NMR spectrum ($CDCl_3$,δ (in ppm), 200 MHz): δ=7.73 (d, J = 8.0 Hz, 2H, ArH_a), 7.26 (d, J = 7.8 Hz, 2H, ArH_b), 4.20 (t, J = 6.1 Hz, 2H, -OCH_2) 3.39 (t, J = 6.2 Hz, 2H, BrCH_2), 2.36 (s, 3H, ArCH_3)

Step II: Preparation of 25,27-di (ethyleneglycol)-bis-*p-tert*-butylcalix[4]arene (**5**)



14 **2a**

In a 100 mL two-necked round bottom flask, *p-tert*-butylcalix[4]arene (3.0 g, 4.62 mmol), catalytic amount of 18-crown-6 and potassium carbonate (1.3 g, 9.24 mmol) were suspended in dried acetonitrile (20 mL). The mixture was stirred at room temperature for 30 minutes. Compound **1** (1.3 g, 4.62 mmol) was then added. The mixture was stirred and heated at 100 ^{o}C under nitrogen for 7 days. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a brown residue. The residue was dissolved in dichloromethane (100 mL) and the aqueous solution of 3 M hydrochloric acid was subsequently added until the pH of the solution reached 1. Water was added and the mixture was stirred for 30 minutes. The mixture was extracted with dichloromethane (3x50 mL) and washed

with water until the aqueous phase having pH 7. The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness to obtain a yellowish residue. The residue was dissolved in a minimum amount of dichloromethane and placed on a silica gel column using the ratio of the residue and silica gel of 1:30. Unreacted reactant *p-tert*-butylcalix[4]arene and desired product, 25,27-di (ethylene glycol)-bis-*p-tert*-butylcalix[4]arene, **5**, were separated by eluting with a mixture of hexane and dichloromethane (50:50). The collected fraction of bis-calix[4]arene solution was concentrated on a rotary evaporator to obtain a white solid compound. The product was recrystallized from the mixture of dichloromethane and methanol to afford a white crystalline solid (1.06 g, 34% yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] arene (5)

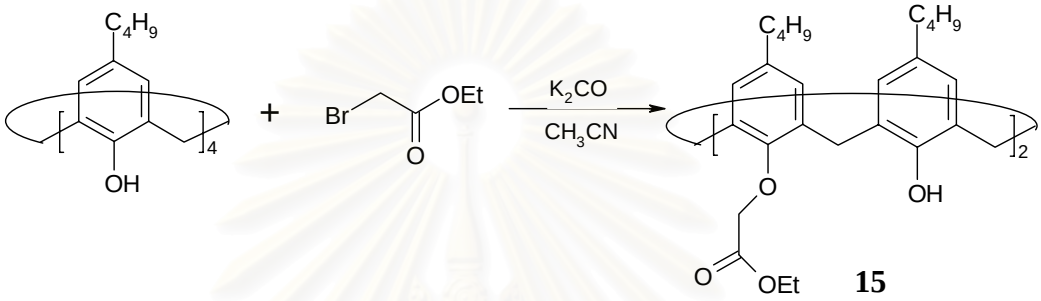
^{1}H-NMR spectrum ($CDCl_3$, δ (ppm), 200 MHz): δ = 7.65 (s, 4H, O*H*), 7.00 (s, 4H, m-*H*ArOH), 6.82 (s, 8H, m-*H*ArOCH$_2$CH$_2$OAr*H*). 4.55 (s, 8H, ArOC*H*$_2$C*H*$_2$OAr), 3.55, 4.50 (dd, J = 14.0 Hz, 16H, ArC*H*$_2$Ar), 1.25 (s, 36H, HOAr-*t*-C$_4$*H*$_9$), 0.99 (s, 36H, *t*-C$_4$*H*$_9$-ArOH)

FAB MS (m/z): 1367.8 [$M^+ + NH_4^+$]

Anal. Cald. for **5** ($C_{92}H_{116}O_8$): C, 81.86; H, 8.66 *Found*: C, 81.86; H, 8.86

Path way II: stepwise synthesis

Step I: Preparation of 25,27-di(carboethoxymethoxy)-*p-tert*-butylcalix[4]arene (**15**)



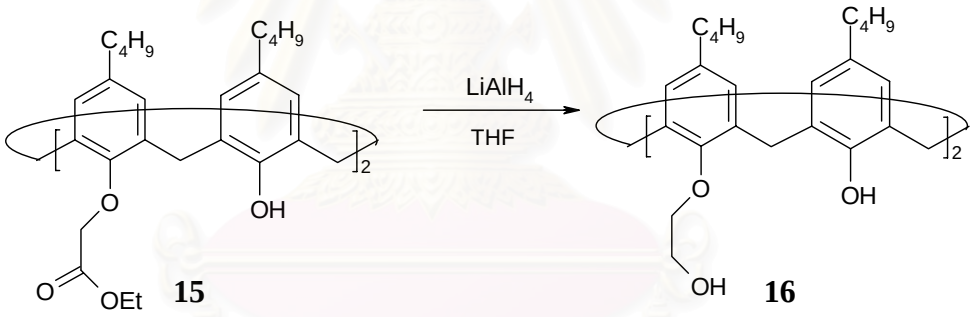
15

In a 500 mL two-necked round bottom flask, *p-tert*-butylcalix[4]arene (1.0 g, 1.5 mmol) and potassium carbonate (1.04 g, 7.5 mmol) were suspended in dried acetonitrile (75 mL). The mixture was stirred for 30 minutes. A solution of ethyl bromoacetate (0.5 mL, 4.5 mmol) in dried acetonitrile (25 mL) was then added dropwise. The mixture was stirred and heated at 70 ^{o}C under nitrogen atmosphere for 4 hours. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a brown residue. The residue was dissolved in dichloromethane (100 mL) and the saturated solution of ammonium chloride (100 mL) was subsequently added to destroy excess ethyl bromoacetate, followed by washing with saturated sodium chloride solutions (2x50 mL). Water (50 mL) was added and the mixture was stirred for 10 minutes and extracted with dichloromethane (3x50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness to obtain a white residue. The residue was dissolved in a minimum amount of dichloromethane and methanol was added to precipitate a white powder (1.02 g, 85 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(carboethoxymethoxy)-*p-tert*-butylcalix[4] arene (15):

^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): δ=7.09 (s, 2H, ArO*H*), 7.01 (s, 4H, *m*-HOAr*H*), 6.81 (s, 4H, *m*-ROAr*H*), 4.78 (s, 4H, OCH_2CO), 4.71 (s, 4H, ArOCH_2), 4.30 (q, J = 7.8 Hz, 4H, OCH_2CH$_3$), 3.34 and 4.40 (dd, J = 14.0 Hz, 8H, ArCH_2Ar), 1.30 (t, 6H, OCH$_2$CH_3), 1.24 (s, 18H, HOAr-t-C$_4H_9$), 0.97 (s, 18H, RO-t-C$_4H_9$)

Step II: Preparation of 25, 7-di(2-hydroxyethoxy)-*p-tert*-butylcalix[4]arene (**16**)



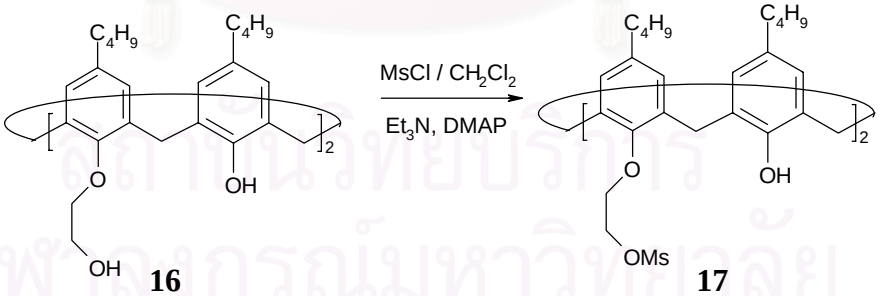
In a 100 mL two-necked round bottom flask, a solution of 25,27-di(carboethoxy methoxy)-*p-tert*-butylcalix[4]arene, **15**, (4.0 g, 5.02 mmol) in dried tetrahydrofuran (250 mL) was stirred for 30 minutes at 10 ^oC under nitrogen atmosphere. $LiAlH_4$ (0.76 g, 20.08 mmol) was then added gradually. The mixture was stirred at room temperature under nitrogen. After 4 hours, the aqueous solution of 3M hydrochloric acid was subsequently added until a precipitate had formed which was then filtered. The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness under reduced pressure to yield a brown residue. The residue was dissolved in dichloromethane (100 mL) and methanol was added to precipitate a

white powder (3.44 g, 97 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(2-hydroxyethoxy)-*p-tert*-butylcalix[4]arene (16)

^{1}H-NMR spectrum ($CDCl_3$, δ (ppm), 200 MHz): δ = 9.23 (s, 2H, ArO*H*), 7.07 (s, 4H, *m*-*H*OArH), 7.01 (s, 4H, *m*-ROAr*H*), 5.2 (s, 2H, CH_2OH), 4.29 (t, 8H, ArOCH_2CH_2OH), 4.30 and 3.43 (dd, J = 14.0 Hz, 8H, ArCH_2Ar), 1.20 (s, 18H, ROAr-t-C_4H_9), 1.19 (s, 18H, HOAr-t-C_4H_9)

<u>Step III</u>: Preparation of 25,27-di(methanesulfonyloxyethoxy)-*p-tert*-butyl calix[4]arene (**17**)



16 **17**

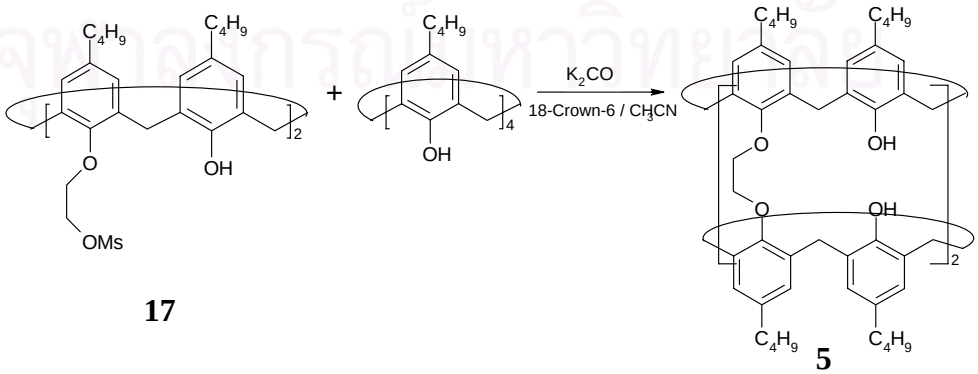
In a 100 mL two-necked round bottom flask equipped with a magnetic bar, dichloromethane solution (50 mL) of 25,27-di(hydroxylethoxy)-*p-tert*-butylcalix[4]arene, **16**, (2.2 g, 2.89 mmol), triethylamine (1.04 mL, 7.46 mmol) and a catalytic amount of DMAP was chilled to 0 ^oC with an ice bath and stirred under

nitrogen for 30 minutes. The solution of MsCl (0.46 mL, 5.96 mmol) in dichloromethane (10 mL) was then added dropwise. The reaction mixture was stirred at room temperature under nitrogen for 4 hours and extracted with water (2x50 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and filtered. The combined filtrate was concentrated on a rotary evaporator and methanol was added to precipitate a white powder (2.56 g, 96 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(methanesulfonyloxyethoxy)-*p*-*tert*-butylcalix[4]arene (17)

^{1}H-NMR spectrum ($CDCl_3$, δ (ppm), 200 MHz): δ=7.06 (s, 4H, RAr*H*), 6.74 (s, 4H, HOAr*H*), 6.67, (s, 2H, ArO*H*), 4.64 (m, 4H, MsCH_2CH_2O), 3.36 (m, 8H, ArCH_2Ar and MsCH_2CH_2O), 4.24 (d, J = 13 Hz, 4H, ArCH_2Ar), 3.23 (s, 6H, SO_2CH_3), 1.28 (s, 18H, HOAr-*t*-C_4H_9), 0.90 (s, 18H, ROAr-*t*-C_4H_9)

Step IV: Preparation of 25, 27-di(ethylene glycol)-bis-*p*-*tert*-butylcalix[4] arene (**5**)



17 **5**

In a 100 mL two-necked round bottom flask, *p-tert*-butylcalix[4]arene (0.38 g, 0.56 mmol), catalytic amount of 18-crown-6 and potassium carbonate (0.15 g, 1.12 mmol) were suspended in dried acetonitrile (20 mL). The mixture was stirred at room temperature for 30 minutes. 25, 27-Di(methanesulfonylethoxy)-*p-tert*-butylcalix[4] arene, **17**, (0.5 g, 0.56 mmol) was then added. The mixture was stirred and heated at 100 ^{o}C under nitrogen for 7 days. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a crude product. The residue was dissolved in dichloromethane (100 mL) and the aqueous solution of 3M hydrochloric acid was subsequently added until the pH of the solution reached 1. Water was added and the mixture was stirred 30 minutes at ambient atmosphere. The mixture was extracted with dichloromethane (3x50 mL) and washed with water until the aqueous phase having pH 7. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated on a rotary evaporator to obtain a white solid compound. The product was slowly recrystallized from the mixture of dichloromethane and methanol to afford a white crystalline solid (0.18 g, 24 % yield). The product was dried in *vacuo* and kept in a desiccator.

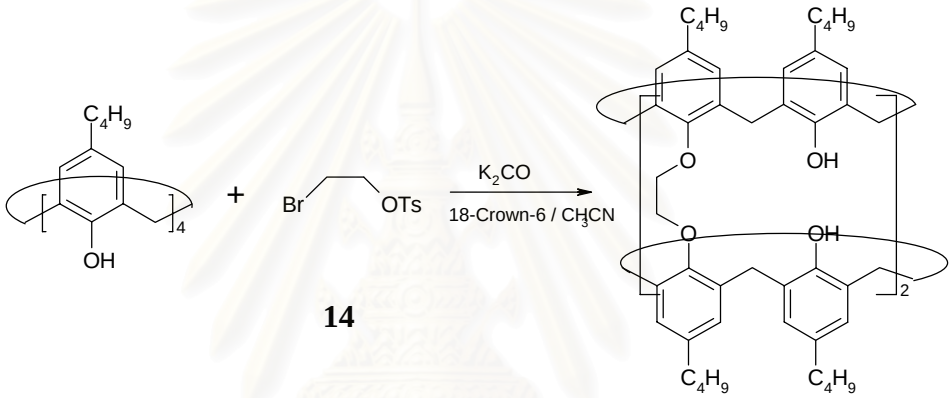
Characterization data for 25,27-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] arene (5)

(The characterization data are the same as in page 15.)

2.2.2 High pressure method for the preparation of 25,27-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4]arene (5)

Path way I: one-pot synthesis

Preparation of 25,27-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4]arene (**5**)



14 **5**

Into a high pressure tube (Ace Glass Co., Catalog No. 8648-29) equipped with valves and pressure gauge, *p*-*tert*-butylcalix[4]arene (3.0 g, 4.62 mmol), catalytic amount of 18-crown-6, compound **14** (1.3 g, 4.62 mmol) and potassium carbonate (1.3 g, 9.24 mmol) were suspended in anhydrous acetonitrile (10 mL). The tube was then pressurized with N_2 at 50 psi. The mixture was stirred and heated at 100 ^oC for 4 days. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a brown residue. The residue was dissolved in dichloromethane (100 mL) and 3 M hydrochloric acid was subsequently added until the pH of the solution reached pH 1. Water was added and the mixture was stirred for 30 minutes. The mixture was extracted with dichloromethane (3x50 mL) and washed with water until the aqueous phase having pH 7. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated on a rotary evaporator to obtain a white solid. The product was recrystallized by adding methanol to its

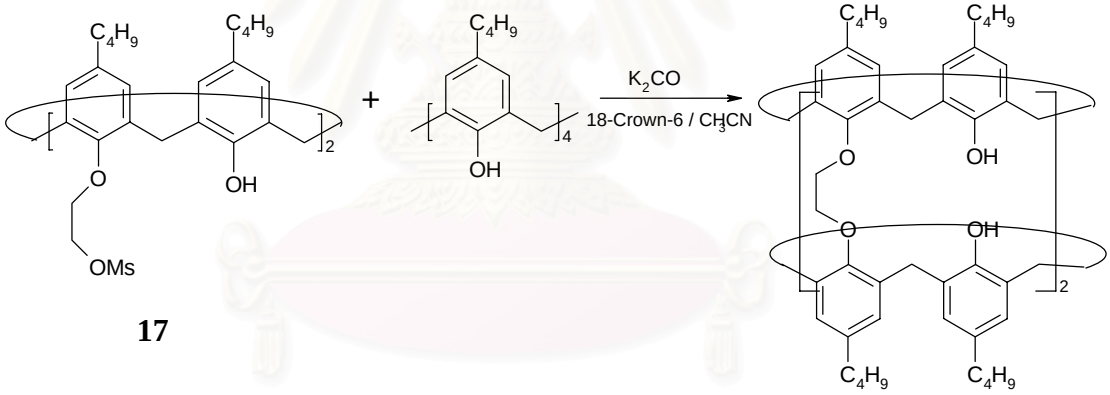
dichloromethane solution. White crystalline solid was obtained (2.16 g, 69 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4] arene (5)

(The characterization data are the same as in page 15.)

Path way II: stepwise synthesis

Preparation of 25,27-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4] arene (**5**)



17 **5**

Into a high pressure tube equipped with valves and pressure gauge, *p-tert*-butylcalix[4]arene (0.38 g, 0.56 mmol), 25,27-di(methanesulfonylethoxy)-*p-tert*-butylcalix[4]arene, **17**, (0.5 g, 0.56 mmol), catalytic amount of 18-crown-6 and potassium carbonate (0.15 g, 1.12 mmol) were suspended in dried acetonitrile (5 mL). The tube was pressurized with N_2 at 50 psi. The mixture was stirred and heated at 100 ^oC for 4 days. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a crude product. The residue was dissolved

in dichloromethane (100 mL) and the aqueous solution of 3M hydrochloric acid was subsequently added until the pH of the solution reached pH 1. Water was added and the mixture was stirred for 30 minutes. The mixture was extracted with dichloromethane (3x50 mL) and washed with water until the aqueous phase having pH 7. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated on a rotary evaporator to obtain a white solid. The product was recrystallized by adding methanol to afford a white crystalline solid (0.29 g, 38 % yield). The product was dried in *vacuo* and kept in a desiccator.

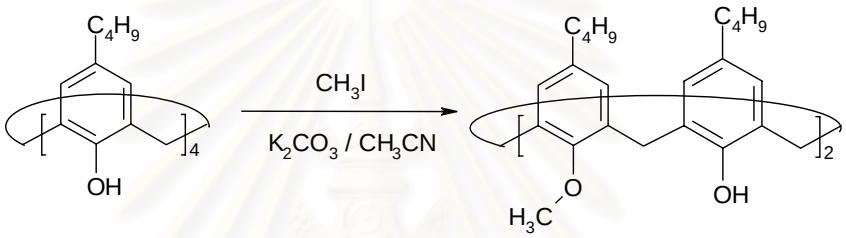
Characterization data for 25,27-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4] arene (2a)

(The characterization data are the same as in page 15.)

2.2.3 General procedure for the preparation of 25,27-di(methoxy)-26,28-di(ethylene glycol)-bis-*p*-*tert*-butylcalix[4]arene (11)

Path way I

Step I: Preparation of 25,27-di(methoxy)-*p*-*tert*-butylcalix[4]arene (**18**)



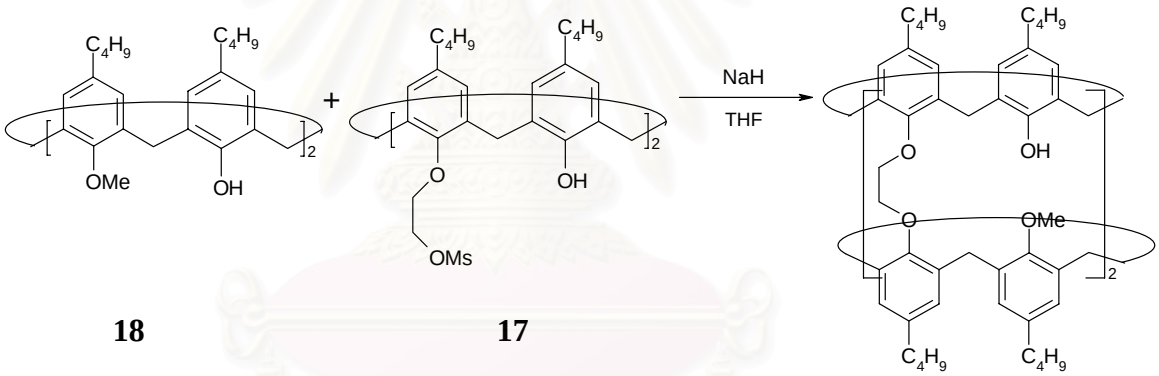
18

In a 500 mL two-necked round bottom flask, *p*-*tert*-butylcalix[4]arene (5.0 g, 7.70 mmol) and potassium carbonate (2.13 g, 15.41 mmol) were suspended in dried acetonitrile (250 mL). The mixture was stirred at room temperature for 30 minutes. Methyl iodide (0.97 mL, 15.41 mmol) was then added. The mixture was stirred and heated at 70^{o}C under nitrogen for 4 hours. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a yellow residue. The residue was dissolved in dichloromethane (100 mL) and washed with amount of water (3x50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness to obtain a white residue. The residue was dissolved in a minimum amount of dichloromethane and methanol was added to precipitate a white powder (4.02 g, 77 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(methoxy)-*p-tert*-butylcalix[4]arene (18):

^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): δ=7.25 (s, 2H, ArO*H*), 7.13 (s, 4H, *m*-ROAr*H*), 6.77 (s, 4H, *m*-HOAr*H*), 3.94 (s, 6H, ArOCH_3), 4.25 and 3.29 (dd, J = 13 Hz, 4H, ArCH_2Ar), 1.30 (s, 18H, ROAr-*t*-C$_4H_9$), 0.94 (s, 18H, HOAr-*t*-C$_4H_9$)

Step II: Preparation of 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4]arene (**11**)

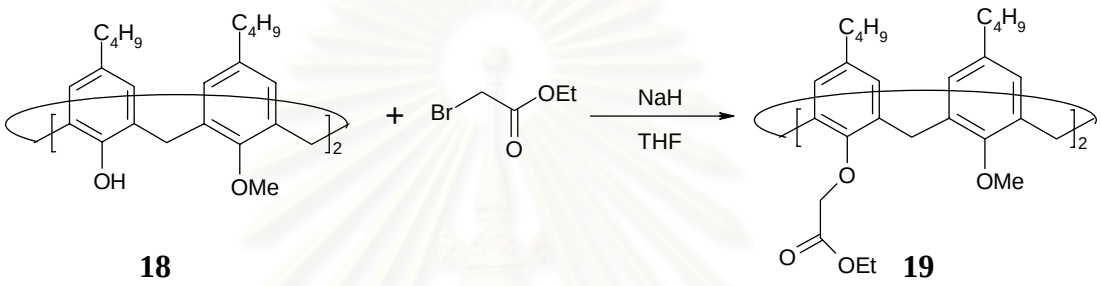


18 **17** **11**

Into a 100 mL two-necked round bottom flask, 25,27-di(methoxy)-*p-tert*-butylcalix[4]arene, **18**, (0.38 g,0.56 mmol) and sodium hydride (0.06 g, 2.5 mmol) were suspended in tetrahydrofuran (20 mL). The mixture was stirred at room temperature for 30 minutes. A THF solution of 25, 27-Dimethanesulfonyl ethoxy-*p-tert*-butylcalix[4]arene, **17**, (0.5g, 0.56 mmol) was then added. The mixture was stirred and heated at 100 ^{o}C under nitrogen. After 7 days, no desired product was obtained.

Path way II

Step I: Preparation of 25,27-di(methoxy)-26,28-di(carboethoxymethoxy)-*p-tert*-butylcalix[4] arene (**19**)



18 **19**

In a 100 mL two-necked round bottom flask, 25,27-di(methoxy)-*p-tert*-butylcalix[4]arene, **18**, (3.0 g, 4.43 mmol) and sodium hydride (0.32 g, 13.29 mmol)were suspended in dried tetrahydrofuran (50 mL). The mixture was stirred at room temperature for 30 minutes. Ethyl bromoacetate (1.00 mL, 8.86 mmol) was then added. The mixture was stirred and heated at reflux under nitrogen for 4 hours. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a yellow residue. The residue was dissolved in dichloromethane (100 mL) and the saturated solution of ammonium chloride (50 mL) was subsequently added to destroy excess ethyl bromoacetate, followed by washing with saturated sodium chloride solution (2x50 mL). Water (50 mL) was added and the mixture was stirred for 10 minutes and extracted with dichloromethane (3x50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness to obtain a yellowish residue. The residue was dissolved in a minimum amount of dichloromethane and methanol was added to precipitate a white powder (3.63 g, 64 % yield). The product was dried in *vacuo* and kept in a desiccator.

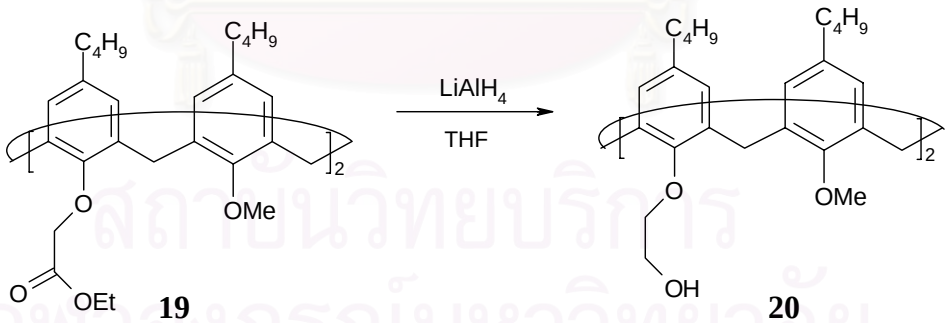
Characterization data for 25,27-di(methoxy)-26,28-di(carboethoxymethoxy)-*p-tert*-butylcalix[4]arene (19):

^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 400 MHz): δ= 7.13 (s, 4H, *m*-HOAr*H*), 6.9-6.42 (m, 4H, *m*-ROAr*H*), 4.60 (s, 2H, OC*H*$_2$CO), 4.25 (s, 2H, OC*H*$_2$CO), 4.03 (m, 4H, ArOC*H*$_3$), 3.8 (d, 4H, OC*H*$_2$CH$_3$), 3.34 and 4.40 (dd, J = 14.0 Hz, 8H, ArC*H*$_2$Ar), 1.4 (s, 36H, HOAr-t-C$_4$*H*$_9$), 1.10 (t, 3H, OCH$_2$C*H*$_3$), 0.9 (t, 3H, OCH$_2$C*H*$_3$)

FAB MS (m/z): 281 [$M^+ + NH_4^+$]

Anal. Cald. for **19** ($C_{52}H_{68}O_8$): C, 75.998; H, 8.176 *Found*: C, 76.280; H, 8.176

Step II: Preparation of 25,27-di(methoxy)-26,28-di(2-hydroxyethoxy)-*p-tert*-butylcalix[4]arene (**20**)



19 **20**

Into a 100 mL two-necked round bottom flask, a solution of 25,27-di (methoxy)-26,28-di(carbomethoxyethoxy)-*p-tert*-butylcalix[4]arene, **19**, (3.0 g, 3.53 mmol) in dried tetrahydrofuran (50 mL) was stirred for 30 minutes at 10^{o}C under nitrogen. $LiAlH_4$ (0.56 g, 14.13 mmol) was then added gradually. The mixture was stirred at room temperature under nitrogen atmosphere. After 4 hours, the aqueous

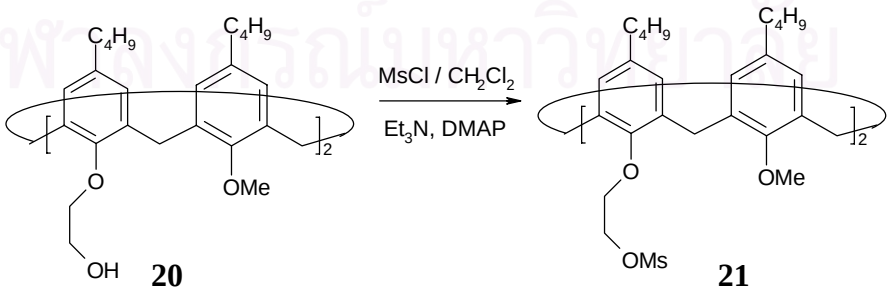
solution of 3 M hydrochloric acid was added gradually until a precipitate had formed and then was filtered. The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to dryness under reduced pressure to yield a crude product. The residue was dissolved in dichloromethane (100 mL) and methanol was added to precipitate a white powder (2.50 g, 93 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(methoxy)-26,28-di(ethoxyl)-*p*-*tert*-butyl calix[4]arene (20)

^{1}H-NMR spectrum ($CDCl_3$, δ (ppm), 200 MHz): δ =7.12-7.0 (m, 4H, *m*-ROAr*H*), 6.5 (s, 4H, C*H*$_3$OAr*H*), 5.15 (t, 2H, ArOCH$_2$CH$_2$O*H*), 4.1 (m, 8H, ArOC*H*$_2$C*H*$_2$OH), 3.80 (s, 3H, ArC*H*$_3$), 4.30 and 3.2 (dd, J = 14.0 Hz, 8H, ArC*H*$_2$Ar), 1.30 (s, 18H, ROAr-t-C$_4$*H*$_9$), 1.19 (m, 18H, HOAr-t-C$_4$*H*$_9$)

FAB MS (m/z): 765 [$M^+ + NH_4^+$]

<u>Step III</u>: Preparation of 25,27-di(methoxy)26,28-di(methanesulfonyloxyethoxy)-*p*-*tert*-butylcalix[4]arene (**21**)



20 **21**

In a 100 mL two-necked round bottom flask equipped with a magnetic bar, dichloromethane solution (50 mL) of 25,27-di(methoxy)-26,28-di(2-hydroxyethoxy)-*p-tert*-butylcalix[4]arene, **20**, (2.4 g, 3.13 mmol), triethylamine (1.0 mL, 7.73 mmol) and a catalytic amount of DMAP was chilled to 0 ^{o}C with an ice bath and stirred under nitrogen for 30 minutes. The solution of MsCl (0.5 mL, 6.26 mmol) was then added dropwise into the mixture. The reaction mixture was stirred at room temperature under nitrogen for 4 hours and extracted with water (2x50mL). The combined organic layer was dried over anhydrous sodium sulfate and filtered. The combined filtrate was concentrated on a rotary evaporator and methanol was added to precipitate a white powder (0.68 g, 23% yield). The product was dried in *vacuo* and kept in a desiccator.

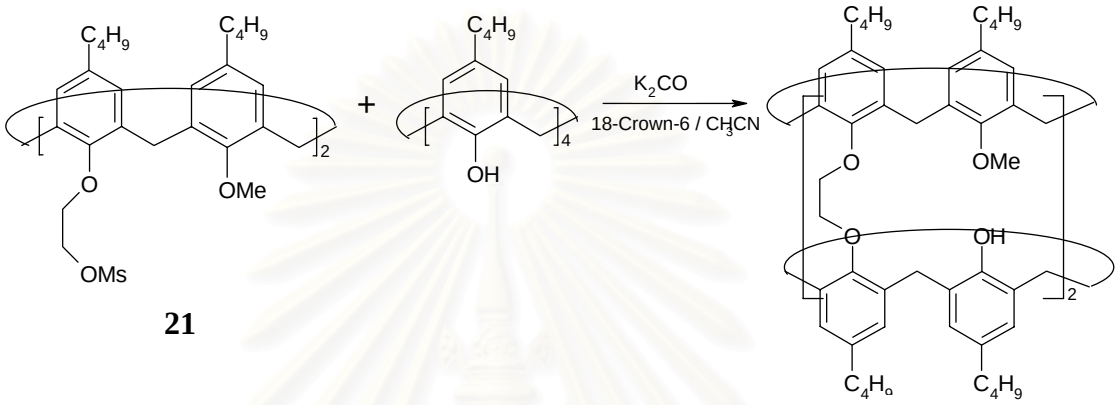
Characterization data for 25,27-di(methoxy)26,28-di(methanesulfonyl)ethoxy-*p-tert*-butylcalix[4]arene (21)

^{1}H-NMR spectrum ($CDCl_3$, δ (ppm), 200 MHz): δ=7.06 (s, 4H, RAr*H*), 6.56 (s, 4H, HOAr*H*), 4.64 (s, 2H, $MsCH_2CH_2O$), 4.3 (s, 2H, $MsCH_2CH_2O$), 3.74 (s, 3H, $ArOCH_3$), 4.04 and 3.10 (dd, J = 13 Hz, 8H, $ArCH_2Ar$), 3.35 (s, 6H, SO_2CH_3), 1.28 (s, 18H, HOAr-*t*-C_4H_9), 0.90 (d, 18H, ROAr-*t*-C_4H_9)

FAB MS (m/z): 921 [$M^+ + NH_4^+$]

Anal. Cald. for **21** ($C_{52}H_{72}O_{10}S_2$): C, 67.758; H, 7.684 *Found*: C, 67.906; H, 7.993

Step IV: Preparation of 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4]arene (**11**)



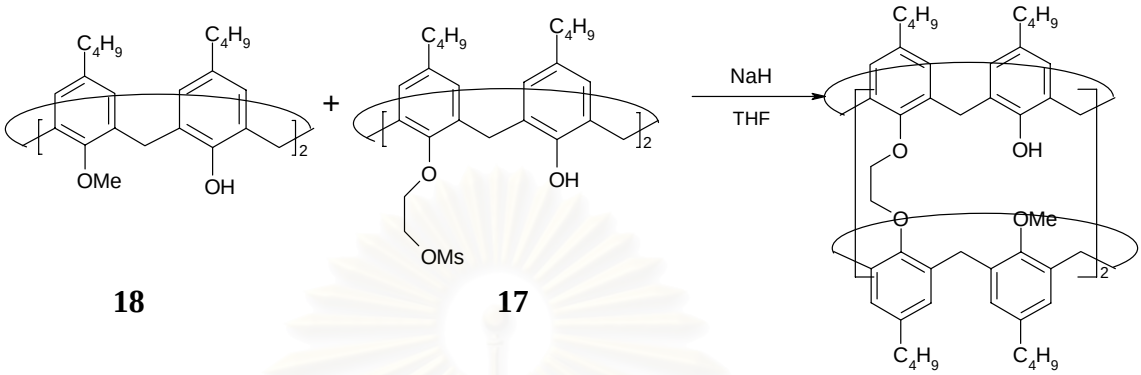
21 **11**

In a 100 mL two-necked round bottom flask, *p-tert*-butylcalix[4]arene (0.70 g, 1.08 mmol), catalytic amount of 18-crown-6 and potassium carbonate (0.19 g, 1.36 mmol) were suspended in dried acetonitrile (5 mL). The mixture was stirred at room temperature for 30 minutes. 25, 27-di(methoxy)26, 28-di(methanesulfonyloxy ethoxy)-*p-tert*-butylcalix[4]arene (**21**), (0.5g, 0.54 mmol) was then added. The mixture was stirred and heated at 100 ^{o}C under nitrogen atmosphere. After 4 days, no desired product was obtained.

2.2.4 High pressure method for the Preparation of 25,27-di(methoxy)-26,28-di(ethylene glycol)-bis-*p-tert*-butylcalix[4]arene (11)

Path way I

Preparation of 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] arene (**2b**)

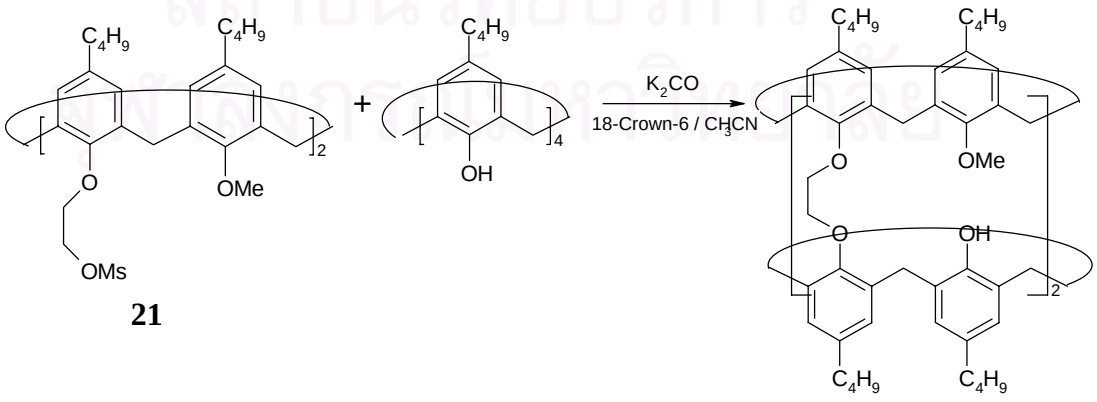


18 **17** **11**

In a high pressure tube equipped with valves and a pressure gauge, 25,27-di(methoxy)-*p-tert*-butylcalix[4]arene, **18**, (0.38 g,0.56 mmol) and 25,27-di(methanesulfonyl)-*p-tert*-butylcalix[4]arene, **17**, (0.5g, 0.56 mmol) and sodium hydride (0.06 g, 2.5 mmol) were suspended in dried tetrahydrofuran (20 mL). The tube was pressurized with N_2 at 50 psi. The mixture was stirred and heated at 100 ^oC for 4 days. No desired product was obtained.

Path way II

Preparation of 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butyl calix[4]arene (11)



21 **11**

In a high pressure tube equipped with valves and a pressure gauge, *p-tert*-butylcalix[4]arene (0.70 g, 1.08 mmol), 25,27-di(methoxy)26,28-di(methanesulfonyl) ethoxy-*p-tert*-butylcalix[4]arene, **21**, (0.5g, 0.54 mmol), catalytic amount of 18-crown-6 and potassium carbonate (0.19 g, 1.36 mmol) were suspended in dried acetonitrile (5 mL). The tube was then pressurized with N_2 at 50 psi. The mixture was stirred and heated at 70 ^oC for 4 days. The solution was allowed to cool to room temperature and evaporated to dryness under reduced pressure to yield a crude product. The residue was dissolved in dichloromethane (100 mL) and the aqueous solution of 3M hydrochloric acid was subsequently added until the pH of the solution reached pH 1. Water was added and the mixture was stirred for 30 minutes. The mixture was extracted with dichloromethane (3x50 mL) and washed with water until the aqueous phase having pH 7. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated on a rotary evaporator to obtain a white solid compound. The product was recrystallized by adding methanol to its dichloromethane solution to afford a white crystalline solid (0.082 g, 11 % yield). The product was dried in *vacuo* and kept in a desiccator.

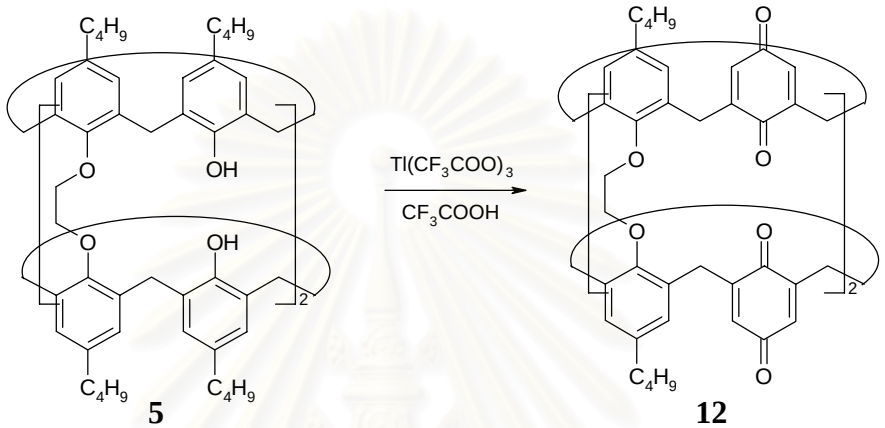
Characterization data for 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] arene (11)

^{1}H-NMR spectrum ($CDCl_3$, δ (ppm), 200 MHz): δ = 10.27 (s, 2H, ArO*H*), 7.09 – 6.70 (m, 16H, *H*Ar), 4.78-4.12 (m, 22H, OCH_2CH_2O, ArCH_2Ar and –OCH_3), 3.40-3.15 (m, 8H, ArCH_2Ar), 1.30 (s, 18H, Ar-*t*-C_4H_9), 1.25 (s, 18H, Ar-*t*-C_4H_9), 0.92 (s, 36H, Ar-*t*-C_4H_9).

ESI MS (m/z): 1395.2 ($M^+ + NH_4^+$).

Anal. Cald. for **11** ($C_{94}H_{120}O_8$): C, 80.014; H, 8.433 *Found*: C, 80.405; H, 80.433

2.2.5 Synthesis of 25,27-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4]tetraquinone (12)



5 **12**

In a 50 mL two-necked round bottom flask, a suspension of thallium trifluoroacetate (1.6 g, 3.7 mmol) in trifluoroacetic acid (10 mL) was stirred in the dark under nitrogen for 1 hour. 25,27-Di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4] arene, **5**, (0.5 g, 0.37 mmol) was then added. The mixture was stirred in the dark for another 2 hours. The solution was then poured into ice. Chloroform (50 mL) was added and extracted with 3 M hydrochloric acid. The mixture was washed with water until the aqueous phase having pH 7. The organic phase was separated and dried over anhydrous sodium sulfate. The solvent was then removed under reduced pressure to obtain a brown residue. The residue was dissolved in a small amount of dichloromethane and methanol was added to precipitate a brownish powder. The recrystallizaton was repeated 3 times to afford a crystalline yellow solid (0.09 g, 21 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4] tetraquinone (12)

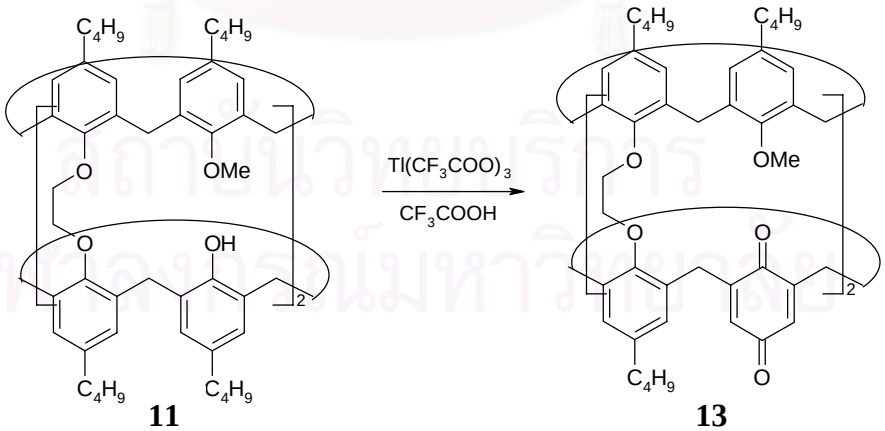
^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): δ = 7.10 (s, 8H, ROAr*H*), 5.86 (s, 8H, H of quinone), 4.39 (s, 8H, OCH_2CH_2O), 4.52 and 3.00 (dd J = 13.9 Hz, ArCH_2Ar), 1.33 (s, 36H, Ar-t-C_4H_9)

ESI MS (m/z): 1203.4 ($M^+ + 4H + NH_4^+$)

IR (ν_{CO}): 1664.86 cm^{-1}

Anal. Cald. for 3a ($C_{76}H_{76}O_{12}\cdot 2H_2O$): C, 74.98; H, 6.62 *Found*: C, 74.99; H, 6.20

2.2.6 Synthesis of 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butyl calix[4]diquinone (13)



11 **13**

In a 50 mL two-necked round bottom flask, a suspension of thallium trifluoroacetate (0.38 g, 0.7 mmol) in trifluoroacetic acid (3 mL) was stirred in the

dark under nitrogen for 1 hour. 25,27-Di(methoxy)-26,28-di(ethyleneglycol)-bis-*p*-*tert*-butylcalix[4] arene, **11**, (0.09 g, 0.07 mmol) was then added. The mixture was continued stirring in the dark under nitrogen for 2 hours. The solution was poured into ice. Chloroform (50 mL) was added and extracted with 3M hydrochloric acid. The mixture was washed with water until the pH of the aqueous phase became pH 7. The organic phase was separated and dried over anhydrous sodium sulfate. The solvent was then removed under reduced pressure to obtain a brown residue. The residue was dissolved in a small amount of dichloromethane and methanol was added to precipitate a brownish powder. Recrystallizaton was repeated 3 times to afford a crystalline yellowish solid (0.05 g, 56 % yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p*-*tert*-butyl calix[4]diquinone (13)

^{1}H-NMR spectrum ($CDCl_3$, δ(ppm), 200 MHz): δ = 7.15 (br s, 12H, *H*ArOR), 6.50 (s, 4H, $H_{quinone}$), 4.70 – 4.40 (m, 16H, OCH_2CH_2O, $ArCH_2Ar$), 4.15 (s, 6H, $-OCH_3$), 3.38-3.12 (m, 8H, $ArCH_2Ar$), 1.30 (s, 36H, Ar-*t*-C_4H_9), 0.80 (s, 18H, Ar-*t*-C_4H_9)

ESI MS (m/z): 1315.8 ($M^+ + 4H + NH_4^+$)

IR (ν_{CO}): 1657.14 cm^{-1}

Anal. Cald. for 3b ($C_{86}H_{100}O_{10}\cdot 3H_2O$): C, 76.64; H, 7.93 *Found*: C, 77.20; H, 8.52

2.3 Molecular dynamic studies

The essential aspect of molecular recognition is to understand the nature of the interaction of one molecule with another. There should be a specific arrangement of the two molecules in which the energy after the recognition at one orientation is lower than the energy of other possible orientations. It is important to identify the exact arrangement of the two molecules in solution. The result will lead to the understanding of the factors affecting the way molecules behave in solution.

Molecular dynamic (MD) simulation is a particularly suitable approach to examine the conformational change[52] and to predict the trend in binding selectivity.[53] We decided to perform a molecular dynamics study on the conformational properties of bis-*p*-tert-butylcalix[4]quinones **12** and **13** and their complexation with alkali metal cations (Li, Na and K), particularly emphasizing free energy calculation.

2.3.1 General setting

All calculations in this work were performed with the HyperChem package (HyperChem release 7, Hypercube, Inc., USA). The primitive starting confirmation of **12** and **13** for the simulation of L in acetonitrile were generated with general geometry optimization in gas phase using molecular mechanics force field BIO+(CHARMM)[54], Chemistry at Harvard Macromolecular Mechanics) which is primarily designed to explore macromolecules.

2.3.2 Setting for molecular dynamic simulation

Molecular dynamic simulations were performed with a time step of 0.001 ps. The solute centre of mass and solvent were coupled to thermal baths at 300 K. Relaxation times 0.2 ps were used. For the alkali metal complexes (LM^+), the ion was considered a sub-molecule. Simulations in solution were performed using periodic boundary conditions. The solute, the free ligand L as well as its LM^+ complex were placed in the centre of a cubic box, dimension 28Å x 28Å x 28Å, and surrounded by 300 randomly distributed solvent molecules, with a minimum solute-solvent distance of 0.3 nm. Every simulation takes 300-600 ps and cut at the time the molecule reaches its stability, normally 30 or 60 ps. After finish the simulation, snap shots can be taken. At each snap shot, we then calculate the minimum energy, (didn't change the conformation). Minimization runs were performed to remove any possible strain in the initial configurations. The calculated enthalpy changes of each stable forms were performed using single point calculation with BIO+(CHARMM) force fields

2.3.3 Setting for determining conformational change

To determine the comformation of L, The carbon of the four phenyl moieties of each calix[4]arene unit are in the apex of a square. We examine the shape and mobility of the different part of calix[4]arene and calix[4]quinone building block using pairs of crossed distances C_1Q_1-C_1Q_3 and C_1P_2-C_1P_4 as well as C_2Q_1-C_2Q_3 and C_2P_2-C_2P_4 which are of time dependence. Pairs of crossed distances of phenyl rings are shown in Figure 2.1.

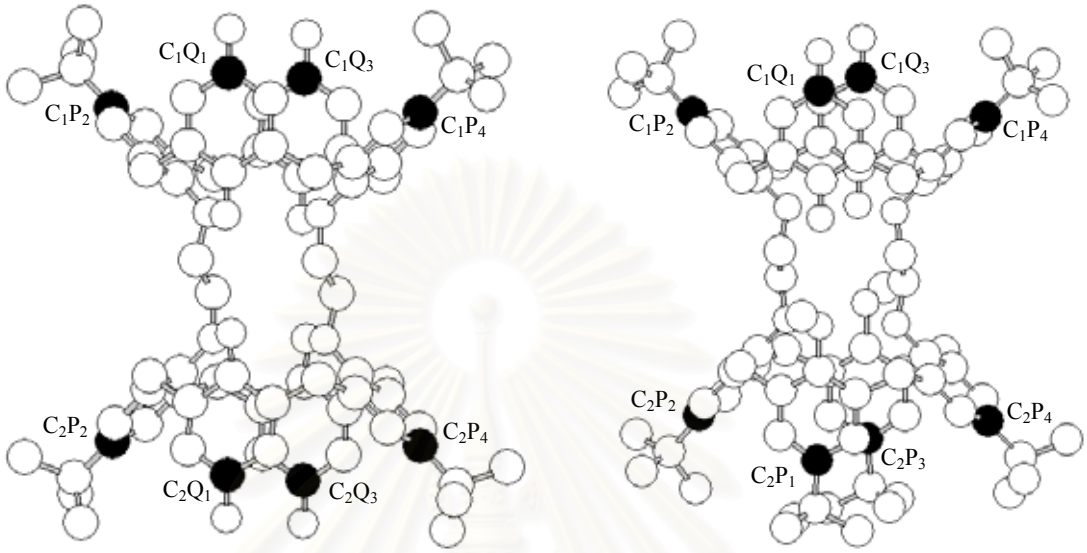


Figure 2.1 Schematic representation of crossed distances of bis-*p*-tert-butylcalix[4]arene tetraquinone, **12**, and dimethoxy bis-*p*-tert-butylcalix[4]arene diquinone, **13**

From MD calculations, the changing of conformations can be observed directly from model. The molecule move like an animation depended on time. We used crossed distances as an evidence for indicating the conformational change. This is a common method for observe changing of cavity size of calixarene. Distances between the opposite *para*-carbon should be varied as follows: cone ≈ alternate > partial cone.

2.4 Electrochemical Studies

2.4.1 Apparatus

Cyclic voltammetry was performed using an AUTOLAB PGSTAT 100 (Eco-chemie, Netherlands) with a three-electrode system. It is consisted of a glassy carbon electrode with a conducting area of 3mm diameter, a platinum wire counter electrode and an Ag/AgCl reference electrode. All CV measurements were digitized using the GPES software (Version 4.7). All scans were done at room temperature and scan rates were varied.

Cleaning of the glassy carbon electrode was done using a BAS polishing kit with stepwise finer abrasives down to 0.05 μm alumina powder slurry. The electrode was then sonicated in 0.005 M H_2SO_4 for 20 minutes and extensively rinsed with distilled water. Dried electrode surface was then soaked with acetonitrile and dichloromethane. This cleaning procedure was repeated in each measurement. The platinum wire counter electrode was cleaned by scrubbing with sand paper No.1000 and by immerged in 3M HNO_3 for 5 min, rinsed with distilled water and wiped to dryness before use. The reference electrode was cleaned by immerged in 3M HCl solution for 5 min followed by rinsing with distilled water.

2.4.2 Preparation of solution

Unless otherwise indicated, all experiments were carried out in an electrolyte solution of 0.1 M tetrabutyl ammonium tetrafluoroborate ($TBABF_4$) in 20% of dichloromethane in acetonitrile. For electrochemical investigation of biscalix[4] quinones and sodium ion complexes, stock solutions of biscalix[4]quinones were

prepared by adding dry powder of biscalix[4]quinones to $TBABF_4$ electrolyte solution and sonicated for at least 1 hour at room temperature. The result solutions were stored at low temperature. For preparation of the 25,27-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4]tetraquinone (**12**) + Na complexes, $NaClO_4$ was added into a stock solution of **12** and the solution was gently stirred for 15 min. Stocks of 0.2 M $NaClO_4$ solution were prepared by adding the dry crystal of $NaClO_4$ to electrolyte solution and stirring until the crystal was completely dissolved. The clear solution was stored at 5 °C during the experiment. For determining the standard half-wave potential $E^o_{1/2}$ a free biscalix[4]quinones solution was prepared without $NaClO_4$.

2.4.3 CV measurement of biscalix[4]quinones solution

All CV measurements were done in a cell compartment enclosed with a build-in Teflon cap. All solutions were deaerated by bubbling with nitrogen for at least 20 min prior to each experiment and were kept under nitrogen atmosphere during measurements.

Cyclic voltammograms were recorded over a range of scan rate from 0.020 to 0.200V/s. The values of E_p and i_p were determined graphically from the CV by plotting a tangent to the leading baseline of the peak to correct for the background current. At a scan rate of 0.100V/s the half-wave potential $E_{1/2}$ was determined as $(E_{pa}+E_{pc})/2$.

2.4.4 CV measurement of biscalix[4]quinones + Na complexes

Solutions containing 1 mM of biscalix[4]quinones and various $NaClO_4$ concentration were deaerated and the cyclic voltammograms were measured as mentioned above. In each experiment, a stock solution of 0.2M $NaClO_4$ were added to the ligand solution containing $TBABF_4$ to obtain a desired mole ratio. Prior to

measurement of the redox current, the Na complex solutions were kept statically (without stirring) for 5 min. Redox currents were determined from CV scans of the complex solutions at scan rate 100 mV s^{-1} using the same methods as described previously.

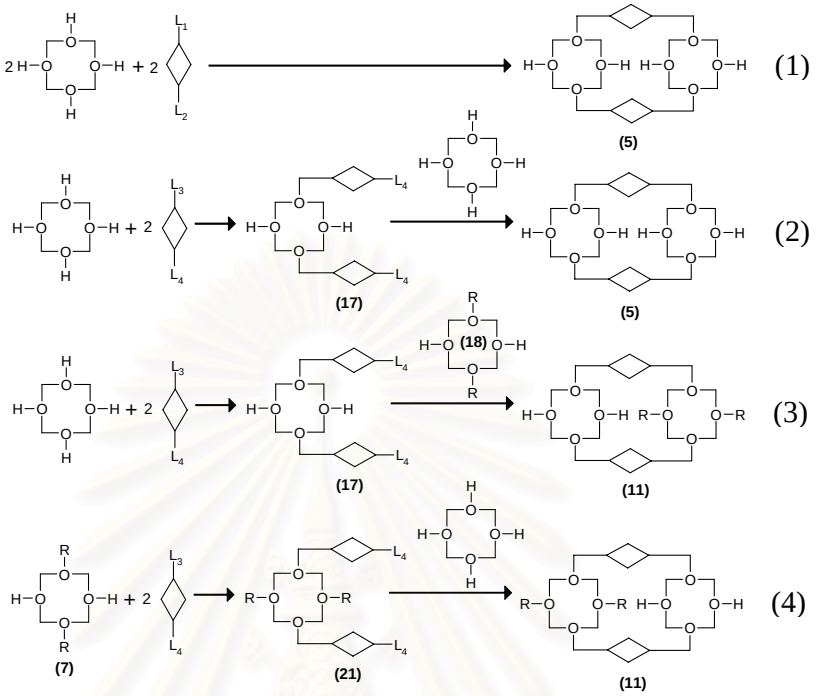
CHAPTER 3

RESULTS AND DISCUSSION

3.1 Design, synthesis and characterization

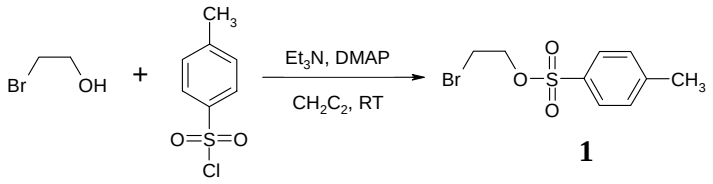
Calix[4]arene is one of the most versatile molecular building blocks suitable for attaching both receptor and sensory units on the same molecules. Many calix[4]arene derivatives containing ferrocene and *p*-quinone have been synthesized and their binding and sensing properties towards metal ions and anions have been studied.[35-38] However, calix[4]quinones in particular have a superior property over ferrocene for the direct connection to the calixarene framework. Therefore, one can design and construct a molecular sensor from a calix[4]quinone using its available oxygen atoms as donors for binding alkali cations. This should enhance both the selectivity and sensitivity of the sensors. A number of biscalixarenes have been synthesized and their binding studies with metal ions have been reported.[55] It is of interest to synthesize different biscalix[4]arenes using ethylene bridges connecting lower rim phenoxy groups. The substituents at the other *o*-phenoxy groups can also be varied. Upon oxidation, we expect to obtain various kinds of biscalix[4]quinones possessing a different number and various positions for the quinone moieties. This should lead to new selectivity and sensitivity for the compounds.

The syntheses of the symmetric (**5**) and a nonsymmetric (**11**) bis-*p*-*tert*-butyl calix[4]arene are outlined in Scheme 3.1. There are 2 strategic pathways to synthesize the compounds: a one-pot synthesis and a stepwise synthesis. Equations 1 and 2, respectively, show the one-pot and stepwise synthetic procedure for the symmetric bis-*p*-*tert*-butyl calix[4]arene. The nonsymmetric bis-*p*-*tert*-butyl calix[4]arene can be synthesized by stepwise procedures shown in equations 3 and 4**.**



Scheme 3.1 Synthetic strategies for bis-*p*-*tert*-butylcalix[4]arene (**5** and **11**)

In the one-pot pathway, 2-bromoethyl toluene sulfonate (**14**) was synthesized by the reaction between 2-bromoethanol and tosylchloride (TsCl) in the presence of triethylamine as base in dichloromethane with a small amount of DMAP as catalyst according to equation 5. After 4 hours, compound **14** was collected and purified by silica gel column chromatography using dichloromethane as eluent. Compound **14** was obtained in 90% yield. The ^{1}H-NMR spectrum of **14** showed the doublet of signals of aromatic proton (Ar*H*) at 7.73 and 7.26 ppm and singlet signal of methyl proton (ArCH_3) at 2.36 ppm instead of the broad signal of hydroxyl protons at 4.39 ppm (*H*OCH_2CH_2Br).



(5)

1

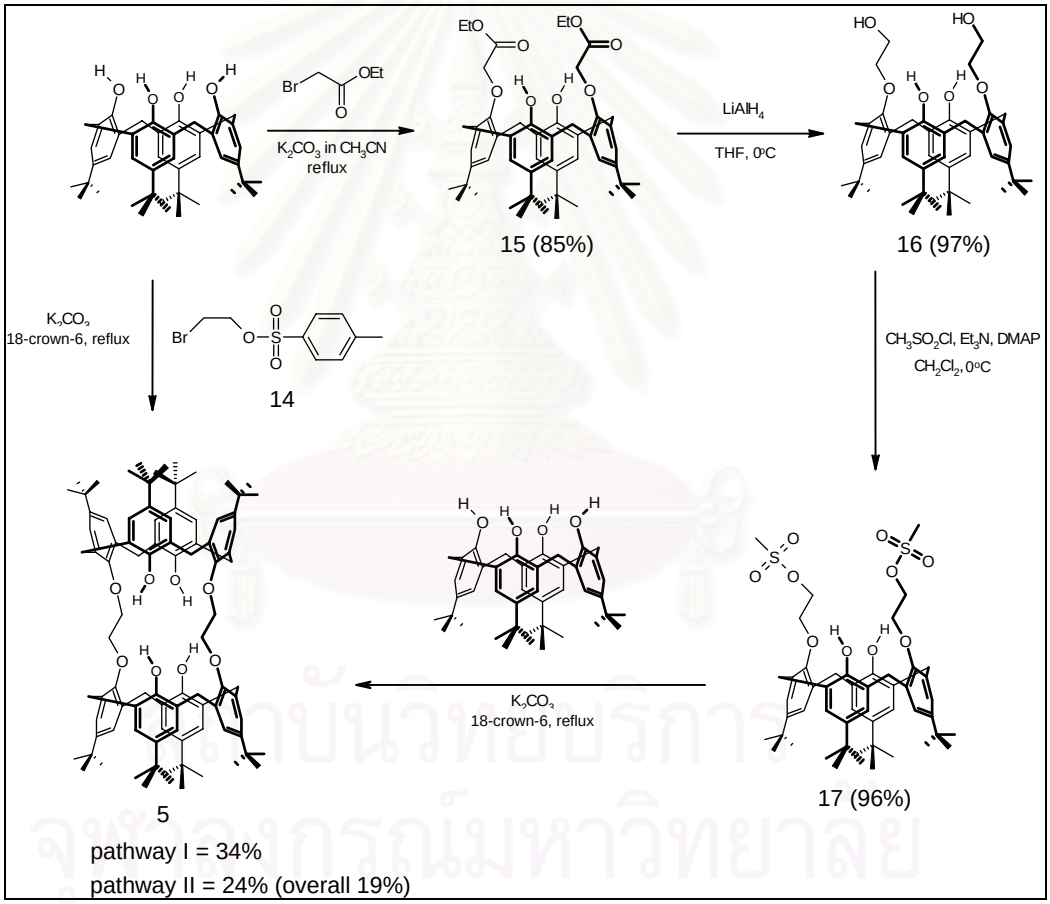
The coupling reaction of *p-tert*-butylcalix[4]arene in acetonitrile with 1.0 equivalent of compound **1 4** in the presence of 18-crown-6 as phase transfer catalyst yielded a crude product of bis-*p-tert*-butyl calix[4]arene (**5**). The yellow product was purified by silica gel column chromatography using dichloromethane and the mixture of dichloromethane and hexane (80:20) as eluents, yielding 34% of **5**. The bridging glycolic protons (OCH_2CH_2O) appeared at 4.55 ppm and AB-system protons (ArCH_2Ar) appeared at 3.55 and 4.50 ppm. The hydroxy protons (ArO*H*) showed up at 7.67 ppm. Mass spectrum and microanalysis results agree well with the proposed structure.

In the case of the stepwise method, the procedure is shown in Scheme 3.2. In first step, nucleophilic substitution reaction of *p-tert*-butylcalix[4]arene with ethyl bromoacetate (2.5 equivalents) employing potassium carbonate as base in dried acatonitrile yielded diester product **15** in 85% yield. The ^{1}H-NMR spectrum of **15** showed the quartet and triplet peaks of the ethylester protons at 4.30 and 1.30 ppm respectively, indicating the incorporation of the ethyl ester units in compound **15**.

Reduction of **15** was carried out by addition of 4 equivalents of $LiAlH_4$ into the solution of **15** in dried THF and subsequently acidified with dilute HCl to afford an alcohol derivative **15** in 97% yield. This compound exhibited two broader peaks due to phenolic hydroxy and alkyl hydroxy protons at 9.23 and 5.2 ppm, respectively with integral ratio of 1:1 on the ^{1}H-NMR spectrum. The hydroxyl product **16** underwent nucleophilic substitution of the hydroxy protons with methanesulfonate groups (mesyl) and gave the compound **17**. Typically, 2.5 equivalents of tristhylamine were used with catalytic amount of DMAP. The reaction was chilled to 0 ^{o}C. After adding MsCl, the desired product (**17**) was obtained in 96% yield. The ^{1}H-NMR

spectrum of **17** showed methyl proton signals of methane sulfonyl groups at 3.23 ppm.

Finally, the methane sulfonyl derivative **17** was coupled with *p-tert*-butylcalix[4]arene in the presence of 2.0 equivalents of potassium carbonate as base and catalytic amount of 18-crown-6 as phase transfer catalyst. After purification by crystallization, the bis-*p-tert*-butylcalix[4]arene product (**5**) was obtained in 24% yield.



Scheme 3.2 A stepwise synthetic pathway of bis *p-tert*-butylcalix[4]arene (**5**)

It is clearly seen that in the case of the symmetric biscalix[4]arene, the one-pot synthesis approach gives much higher yields than that of the stepwise approach. Nevertheless, to synthesize a nonsymmetric biscalix[4]arene having different number of phenolic hydroxyl groups, the stepwise synthetic pathway should be employed.

The stepwise pathway required a modified *p-tert*-butylcalix[4]arene containing methoxy groups as starting material. The dimethoxy calix[4]arene (**18**) was synthesized by a substitution of *p-tert*-butylcalix[4]arene with methyl iodide. The dimethoxy product (**18**) was obtained in 77%. The ^{1}H-NMR spectrum of **18** showed the doublet of signals of aromatic protons (Ar*H*) at 7.13 and 6.77 ppm and a singlet signal of the methyl protons (ArOCH_3) at 3.94 ppm.

The coupling between dimethoxy *p-tert*-butylcalix[4]arene (**18**) in acetonitrile with 1.0 equivalent of dimethane sulfonyl *p-tert*-butylcalix[4]arene (**17**) in the presence of 18-crown-6 as phase transfer catalyst did not afford the desired product after long period of the reaction time. The reactants, **17** and **18**, were recovered from the reaction flask. The steric hindrance of methoxy groups may be a main obstacle for a substitution reaction. We, therefore, tried to synthesize an unsymmetric bis-*p-tert*-butyl calix[4]arene again with an alternative stepwise route.

Nucleophilic substitution reaction of dimethoxy *p-tert*-butylcalix[4]arene (**18**) with 2.5 equivalents of ethyl bromoacetate in the presence of 3 equivalents of sodium hydride as base in dried tetrahydrofuran yielded 25,27-di(methoxy)-26,28-di(carboethoxymethoxy)-*p-tert*-butylcalix[4]arene (**19**) in 64% yield. The ^{1}H-NMR spectrum of **19** is broad due to the phenyl ring inversion stemming from the lack of intramolecular hydrogen bonding.

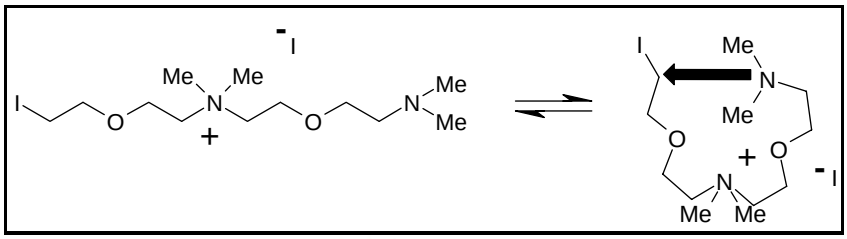
Reduction of **19** was carried out by addition of 4 equivalents of $LiAlH_4$ into the solution of **19** in dried THF and subsequently acidified with dilute HCl resulting

in an alcohol derivative, 25,27-di(methoxy)-26,28-di(2-hydroxyethoxy)-*p-tert*-butylcalix[4] arene (**20**), in 93% yield. This compound also exhibited broad signals due to the lack of intramolecular hydrogen bonding. Compound **20** underwent a nucleophilic substitution reaction with methane sulfonyl chloride and gave 25,27-di(methoxy)-26,28-di(methanesulfonyloxyethoxy)-*p-tert*-butylcalix[4]arene (**21**) in 23% yield. ^{1}H-NMR spectrum of **21** is not resolved due to the ring inversion from lacking intramolecular hydrogen bonding.

Coupling between *p-tert*-butylcalix[4]arene and **21** were perform in acetonitrile in the presence of of 18-crown-6 as phase transfer catalyst yielded a yellow crude compound which could not identify as desired product. (Scheme 3.4)

The one-pot synthesis route not only produces bis-*p-tert*-butylcalix[4]arene (**5**) but also give a small amount of bisbromoethoxy-*p-tert*-butylcix[4]arene. The result implies that the coupling process occurred in a stepwise manner in which bisbromoethoxy-*p-tert*-butylcalix[4]arene was produced in the first step. Subsequent nucleophilic substitution with another unit of calix[4]arene resulted in bis-p-*tert*-butylcalix[4]arene (**5**). The second step is in competition with the possible chain polymerization which is accounted for the low yield of the desired product.

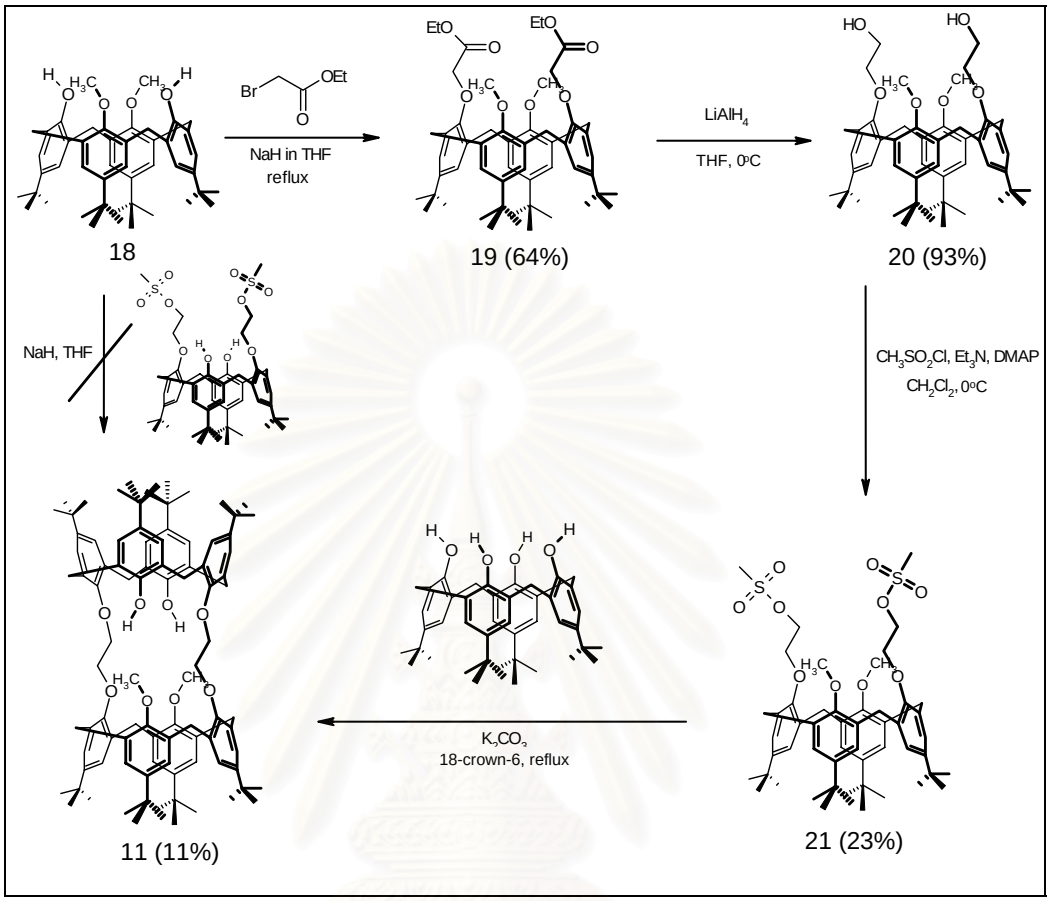
There are several reports on high-pressure demethylation procedures by Ostaszewski and Jurczak. The high-pressure method was successfully used for the synthesis of simple and chiral bicyclic cryptands and diazocoronands.[56] They found that the linear intermediate compound obtained in the reaction mechanism is in equilibrium with the quasi-cyclic form which seems to be favored under high pressure (Scheme 3.3). Janssen et al. also found that use of pressure for selective alkylation of calix[6]arene resulted in high yield of the alkylated products.[57]



Scheme 3.3 Quasi-cyclic equilibrium of diazocoronands

It was expected that under high pressure the reaction leading to linear polymers in disfavored because of the increase in solvent viscosity that prevents inter molecular collisions. From their postulation, the high pressure approach is thus introduced to the synthesis of **5** and **11** aiming to increase the cyclization rate.

The reaction between *p-tert*-butylcalix[4]arene and 1 equivalent of bromoethyl tosylate (**14**) in acetonotrile using potassium carbonate as base with a catalytic amount of 18-crown-6 as phase transfer catalyst was pressurized with N_2 at 50 psi a high concentration technique with heat at 100^{o}C yielded a white precipitate of bis-*p-tert*-butylcalix[4]arene (**5**) in 69%. In the same manner, symmetrical and nonsymmetrical biscalix[4]arene, (**5** and **11**) were successfully obtained using stepwise approach under high pressure in 38% and 11% yields, respectively.

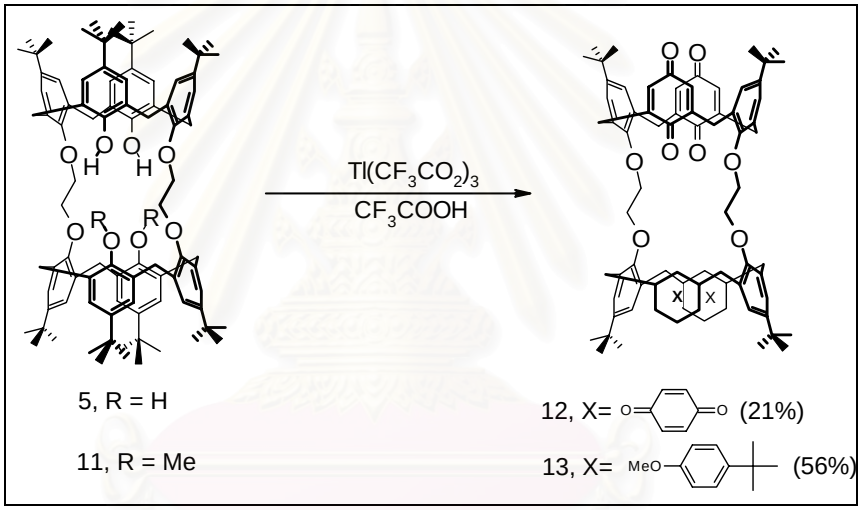


Scheme 3.4 Synthetic pathway of dimethoxy biscalix[4]arene (**11**)

3.2 Synthesis and characterization of bis *p-tert*-butylcalix[4]quinines derivative (12 and 13)

Bis-*p*-*tert*-butylcalix[4]arenes (**5** and **11**) were then transformed to their quinone derivatives (**12** and **13**). Oxidation of compounds **5** and **11** were carried out using $Tl(CF_3CO_2)_3$ in CF_3COOH in darkness under N_2 atmosphere as illustrated in Scheme 3.5. After extracted with water and chloroform, compounds **12** and **13** were obtain in 21% and 56%, respectively, as yellow powder after crystallized from a mixture of dichloromethane and methanol. ^{1}H-NMR spectrum of **12** exhibited a singlet signal due to the aromatic proton at 7.10 ppm. Moreover, the appearance of a

singlet signal of quinone protons at 5.86 ppm and the vanishing of phenolic hydroxyl protons at 7.65 ppm indicating that the molecules are in the form of 1,4 benzoquinone. Infrared spectrum showed the appearance of CO stretching at 1,664 cm^{-1}. ^{1}H-NMR spectrum of **13** exhibited a singlet signal due to the OH proton at 10.27 ppm. Moreover, the appearance of several singlet signals of conjugate and non-conjugated protons around 7.20-6.75 ppm was observed in the spectrum. Infrared spectrum showed the appearance of CO stretching at 1,657 cm^{-1}.



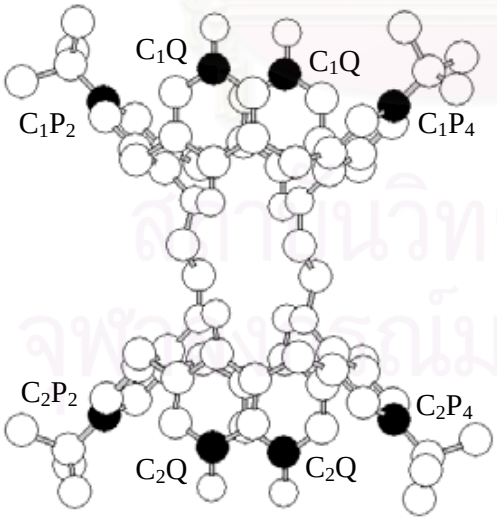
Scheme 3.5 Synthetic pathway of bis *p-tert*-butylcalix[4]quinone (**12** and **13**)

3.3 Molecular dynamic simulation of metal ions complexation

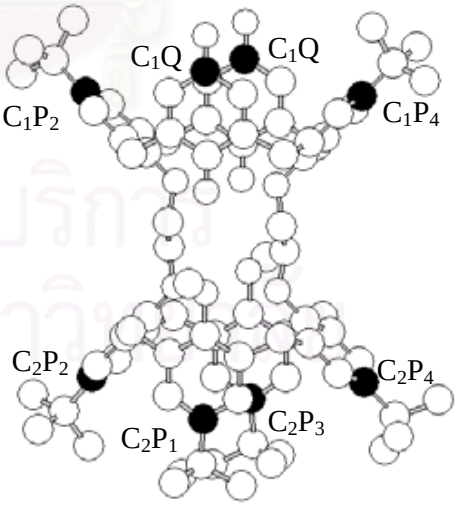
Molecular dynamics can provide information about the conformational properties of molecular systems, and the way in which the conformation changes with time. Molecular graphic programs such as HYPERCHEM can facilitate the analysis of such simulations by displaying the structural parameters of interest in a manner that enables the time dimension to be taken into account.

3.3.1 Conformation of free ligands

p-tert-Butylcalix[4]arene can possibly have 4 conformations: cone, partial cone, 1,2-alternate and 1,3-alternated conformations. Biscalix[4]quinones, however, possess two glycol units linking between the two calixarene units. They can, therefore, have only three possible conformations, namely, cone, partial cone and 1,3-alternate. The variation of corresponding C-C crossed distances of the opposite phenyl ring (shown below) upon time indicates the conformational change of each calix[4]quinone building block. This agrees with snap shots from molecular dynamic simulations of **12** and **13**. Parallelograms of the different crossed distances characteristic of **12** and **13** as a function of time, are plotted in Figure 3.1 and Figure 3.2.



12



13

Normally, the crossed distance criteria for cone, partial cone and 1,3-alternate cone conformation 10.0902 , 9.10586 and 6.05079 Å. However, in biscalix quinone, it has a steric effect of the other calixarene unit. Therefore, the distances for alternate conformation cannot reach 6.05079 Å, but approach a closer value to the distance in cone conformation.

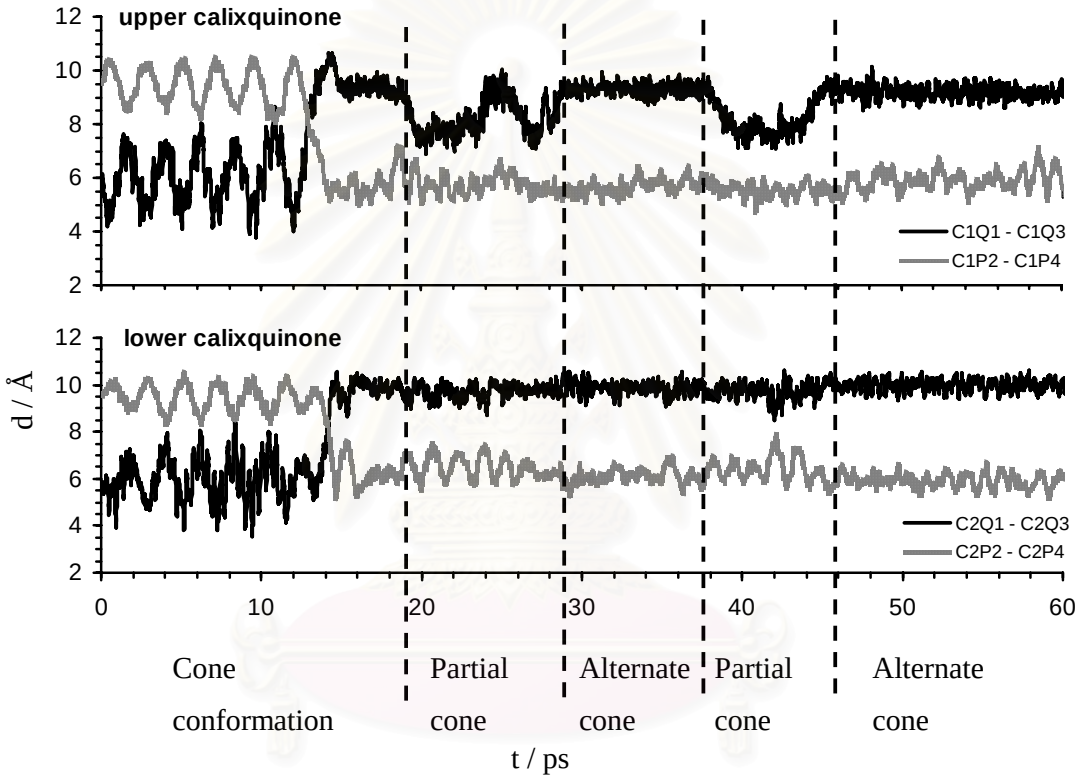


Figure 3.1 Time evolution of crossed distances characterizing the conformation of ligand **12**

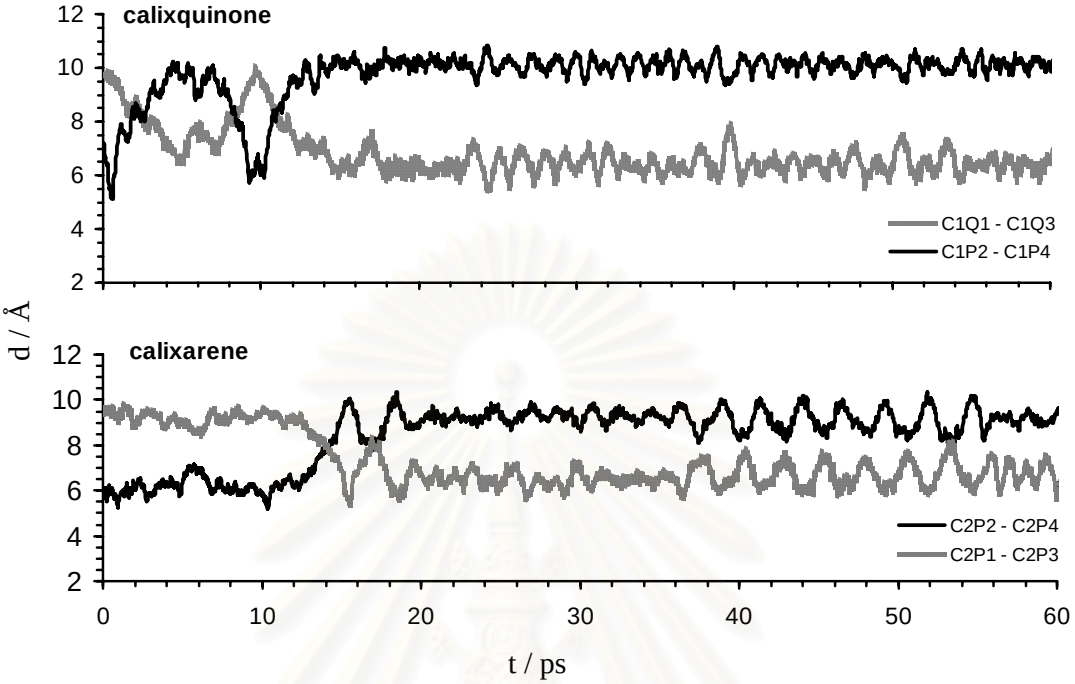
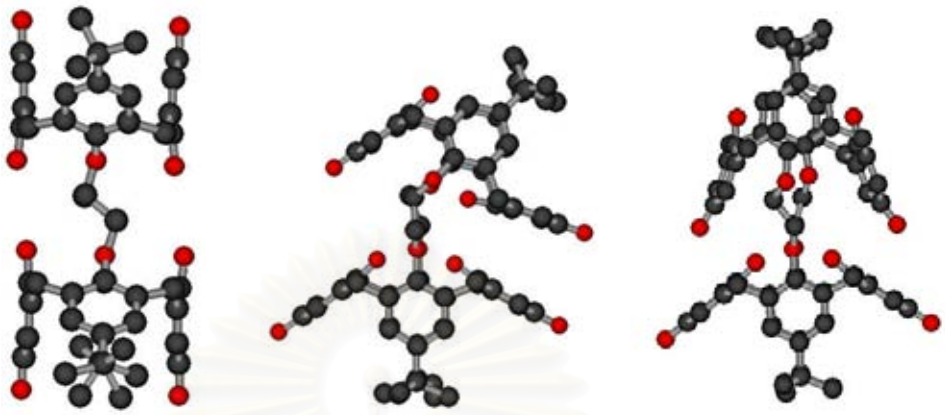


Figure 3.2 Time evolution of crossed distances (see Figure 2.1) characterizing the conformation of ligand **13**

Starting with the optimized geometry of **12** in gas phase, the structure presents in the form of two coupled cone-conformation. After temperature of the whole system reached 300K in the MD simulation, the oscillation of each phenyl ring observed with average crossed distance of 6.121Å and 9.339Å. The inter-conversion behavior is observed at t = 14.16 ps, causes changing of conformation to the lower energy forms (equilibrium between partial and alternate cone confirmation). The partial cone conformation presents with C_1Q_1-C_1Q_3 average to 8.833Å, while alternate cone conformation presents in 9.556Å. The conversion of three conformations are well agreeable with total energy calculated by the single point simulation of each snap shot as shown in Figure 3.3.



Cone | Partial cone | Alternat

E_{tot} = 127.922 kCal mol^{-1} | E_{tot} = 121.448 kCal mol^{-1} | E_{tot} = 121.436 kCal mol^{-1}

Figure 3.3 Snap shots from molecular dynamic simulation at 300K, characterizing the conformation of ligand **12**

The parallelograms of crossed distance of **13** are observed with the oscillation behavior. However, after the inversion of each phenyl ring, the conformation still stable in the cone conformer with average C_1Q_1-C_1Q_3 crossed distances constantly at 10.112 Å, as shown in Figure 3.2.

Cone conformation

E_{tot} = 196.116 kCal mol^{-1}

Figure 3.4 Snap shots from molecular dynamic simulation at 300K, characterizing the conformation of ligand **13**

3.3.2 Complexation with Alkali cations

In order to analyze the dynamic motion of complex, MD simulation study on the complex was carried out with a constant temperature at 300K and simulation time 30ps. The structure and the movement of the inclusion complexes can be monitored by the interatomic distance as a function of time in MD calculation same as above method. The guest moves rapidly within the host cavity as is clearly seen in MD simulation.

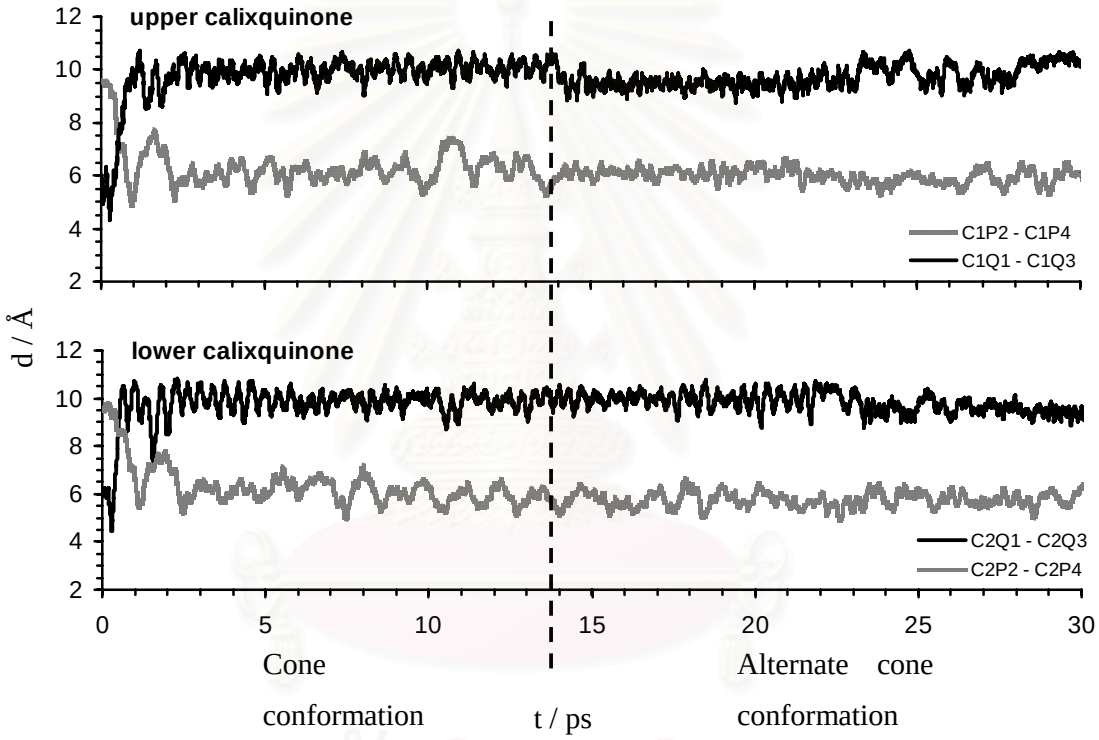
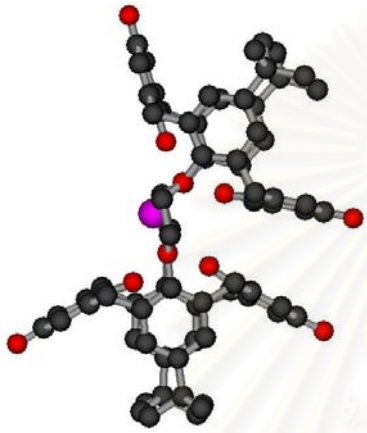


Figure 3.5 Time evolution of crossed distances in the simulation of LNa^+ of **12**

The changing conformation behavior of **12** also found in the MD simulation with all of alkali cations, Li^+, Na^+ and K^+. Plots in Figure 3.5 shows a 30 ps simulation of LNa^+. The average cross distances of each pair of quinone and phenolic carbons are 9.794Å and 6.124Å, respectively. The snap shots of MD simulation indicate that the alternate cone conformation is not observed in LM^+ complexation. The single point calculations of each conformation of free L with inclusion of alkali cations and the total enthalpy change are shown in Table 3.1. The

single point energy calculation results are consistent with conformations found in MD simulation. Only cone and partial cone conformations are stable. In addition, the non-stability of alternate cone conformation can be explained with the lowest total energy of an intermedaite



12 + Na^+ (cone)

E_{tot} = 100.381 kCal mol^{-1}

12 + Na^+ (partial cone)

E_{tot} = 97.034 kCal mol^{-1}

12 + Na^+

E_{tot} = 107.587 kCal mol^{-1}

13 + Na^+ (cone)

E_{tot} = 156.283 kCal mol^{-1}

Figure 3.6 Snap shots from molecular dynamic simulation in the simulation of LNa^+ of **12** and **13** at 300K

partial cone conformation. The snap shots of each complex are shown in Figure 3.6. The results of complexation simulation between ligand **13** and alkali cations (Table 3.1) indicate that the most suitable complexes of ligand **13** are sodium and potassium complexes.

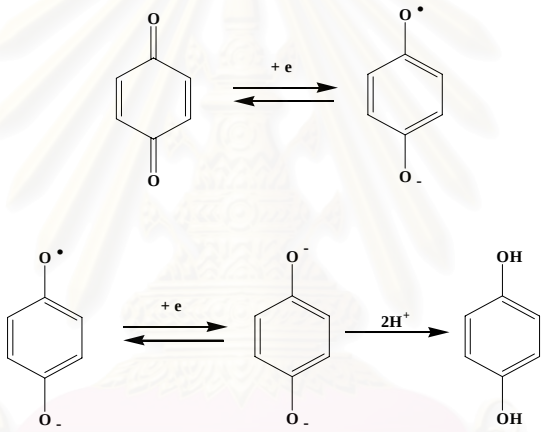
Table 3.1 Calculated enthalpy changes (kcal mol^{-1}) of complexes

		Li^+	Na^+	K^+
12	Cone	-22.913	-27.514	-26.626
	Partial cone	-18.906	-24.414	-13.861
	Alternate cone	-6.485	-13.047	-12.916
13	cone	-32.793	-39.833	-40.692

(see appendix)

3.4 Cyclic voltammetric studies

Quinones are commonly used as a reflection of its importance in natural electron transfer systems. In nonaqueous, aprotic solvents, quinones undergo two consecutive one-electron transfer processses. In addition, the reduced form of quinone can undergo a chemical reaction to produce hydroquinone according to the following equations.



Voltammograms of bis-*p*-tert-butylcalix[4]arene tetraquinone (**12**) and dimethoxy bis-*p*-tert-butylcalix[4]arene diquinone (**13**) in 20% dichloromethane/acetonitrile using $TBABF_4$ as supporting electrolyte and glassy carbon electrode as working electrode are shown in Figure 3.7 and Figure 3.8, respectively. In the case of **12**, one would expect to see 8 one-electron transfer signals in the voltammogram. However, only two quasireversible signals were observed. This suggests that quinone moieties in **12** have interactions with each other and thus cause a complicated electron transfer proceses. The first anodic signal designated as IIa, with a related cathodic peak (IIc) indicating a couple of multi-electron transfer. The second wave, IIIa (anodic) is broad with the quasi-reversible natures of complicated electron transfer related to IIIc, probably signifying the formation of CH_2Cl_2-insoluble hydroquinone, suggested by Casnati and co-workers.

These behavior are totally agree with a complicate electron transfer mechanism that is quite similar to calix[4]arene tetraquinones reported by Beer and co-workers.[58]

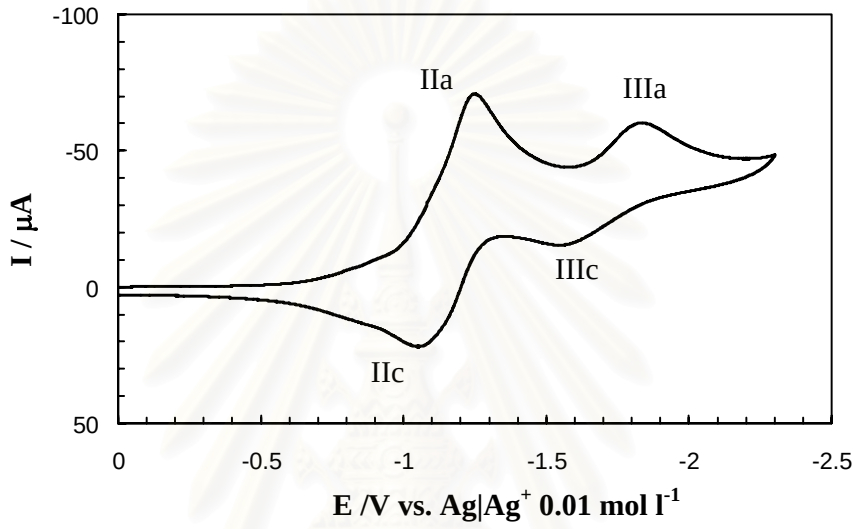


Figure 3.7 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.100Vs^{-1}

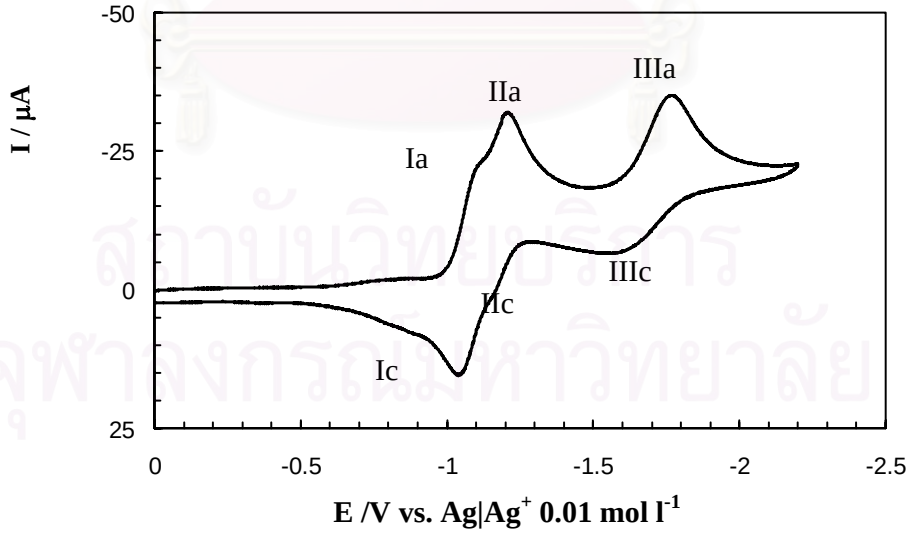
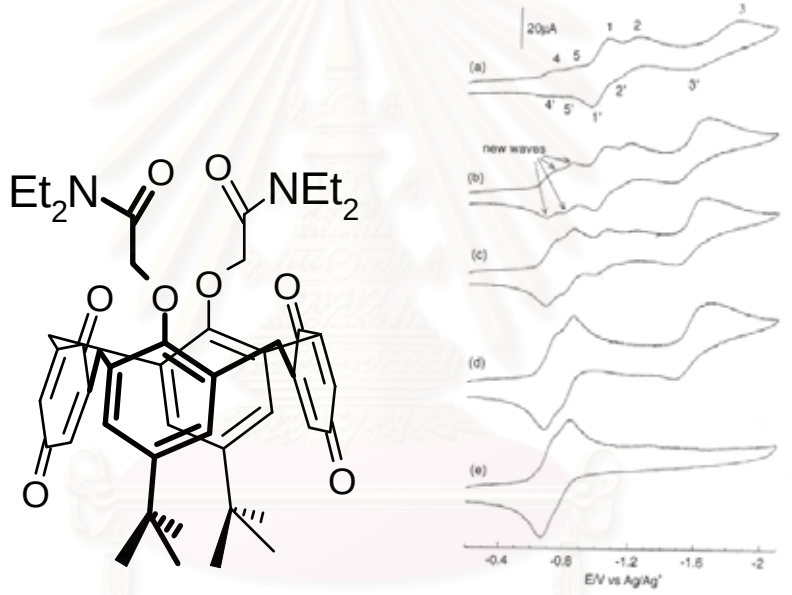


Figure 3.8 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.100Vs^{-1}

The cyclic voltammogram of compound **13** exhibit 3 waves I, II and III at -1092, -1201 and –1754 mV, respectively. This voltammogram is similar to the calixdiquinone esters and amides, **22**, reported by Beer and colleagues (figure 3.9).[46] The first two couples indicate two one-electron transfer processes. Wave 3 is an irreversible wave probably involving a reduction of the quinone to its radical form and subsequent protonation to the hydroquinone.



22

Figure 3.9 Cyclic voltammorams of **22** in the present of different concentration of sodium cations (a) 0; (b) 0.21; (c) 0.42; (d) 0.63; (e) 2.7, Scan rate: 0.100Vs^{-1}

Several intermediate peaks (IVc and Vc) are also presented after variation of scan rate. Table 3.2 reports the main electrochemical parameters measured with scan rate of 20, 50, 100 and 200 mVs^{-1}.

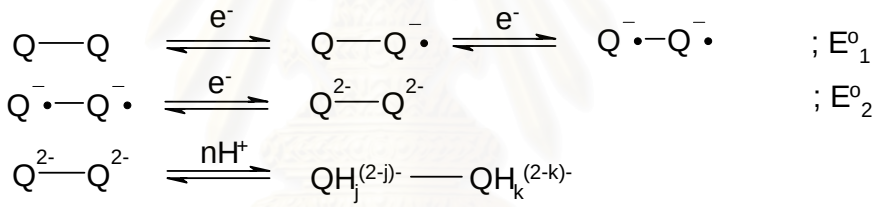
Table 3.2 Main electrochemical parameter for **12** and **13**

	Scan	$-E_{pIa}$ mV	$-E_{pIc}$ mV	$-E_{pIIa}$ mV	$-E_{pIIc}$ mV	$-E_{pIIIa}$ mV	$-E_{pIIIc}$ mV	$-E_{pIVc}$ mV	$-E_{pVc}$ mV
12	20	-	-	1234	1100	1815	1637	-	-
	50	-	-	1235	1074	1790	1578	-	-
	100	-	-	1243	1069	1834	1580	-	-
	200	-	-	1251	1053	1851	1566	-	-
13	20	1094	1064	1220	1160	1758	1592	-	-
	50	1092	1050	1201	1164	1754	1609	-	-
	100	1090	1040	1198	1162	1764	1604	392	776
	200	1094	1043	1232	1162	1805	1605	345	795

3.4.1 Effect of scan rate

The CV of compounds **12** and **13** showed strong dependence on the scan rate. At slow scan rate, the voltammogram of **12** (Figure 3.10) is composed of two anodic regions. The first wave, II_a, is well defined. The second wave, III_a is broad. In cathodic region, the first one (II_c) with variable currents, represent the region wave IIc according to the changing scan rate. The second wave, IIIa, is related to wave IIIc as shown by the reversal of potential. The signals of IIa and IIIa correspond to quasi-reversible reduction process by considering the increasing of separation between anodic and cathodic waves, not the significant shifts of E_p and $\Delta E_{(p-p/2)}$, and remaining the diffusion control ($I_{pc} \propto v^{1/2}$). As scan rate increases, wave IIIa disappears while IIa become increasing in the current as decreasing ration of IIIa and negative shifts for all the anodic waves and positive shifts for the cathodic ones are observed.

The voltammogram of **13** (Figure 3.11) is also defined in the same way. The wave couple I and II is implied to the first and second electron transfer for each quinone moiety, respectively. The third and fourth electron transfer are presented using higher energy, well agree with the redox characteristic of benzoquinone, referred to the defined wave IIIa and IIIc. However, upon increasing the scan rate, two new irreversible oxidation waves, IV and V, appear at 750 and 337 V. This may signify that wave IIIa represents a two-electron transfer reduction process. The result suggests that **13** undergo an electron transfer, electron transfer and chemical reaction (EEC) mechanism as shown below.



While Q, $Q^{\cdot-}$, Q^{2-}, $QH_j^{(2-j)-}$ and $QH_k^{(2-k)-}$ (n=j+k; j=0, 1, 2; k= 0, 1, 2; k and j may be a different or equal) represent the neutral, radical anion, dianion and the protonated froms of the quinone moiety in the molecule. E^o_i (i=1, 2) is the formal redox potential of the corresponding electron transfer reactions.

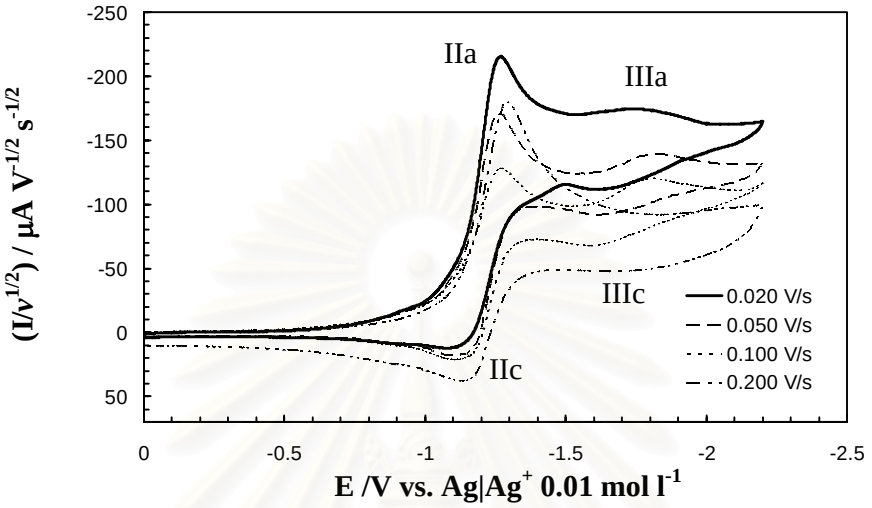


Figure 3.10 Normalized cyclic voltammograms of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, and Effect of scan rate.

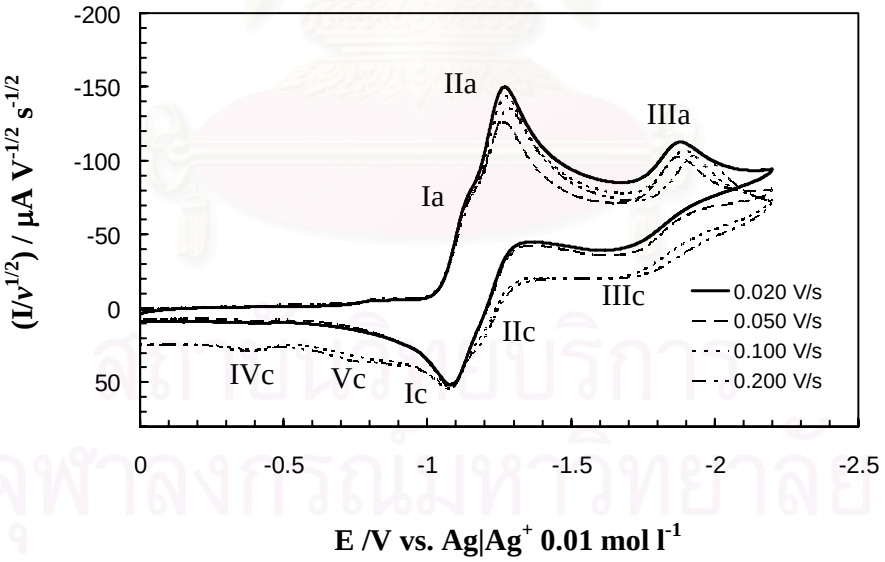


Figure 3.11 Normalized cyclic voltammograms of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, and Effect of scan rate.

3.4.2 Effect of added metal ion (Na^+)

In the present of a Na^+ source, $NaClO_4$, the electron transfer mechanism is affected according to the concentration of sodium. In case of **12** (figure 3.12) with 0.2 equivalent of Na^+, new reversible wave, VIa, at lower potential begin to appear related to VIc (E_p = -885 mV) and the quasi-reversible reduction wave IIIa shift more anodic while wave IIa shifts insignificantly. Figure 3.11 shows the cyclic voltammograms of **12** upon addition of sodium source. As concentration of Na^+ increases, reduction wave VIa growth continually but E_p still unchanged. The waves II and III remain opposite shift until disappear at two times higher in concentration of Na^+ resulted in new irreversible wave VIIa at –1466 mV.

Addition of Na^+ to the solution of **13** (Figure 3.13) a reversible wave VIa also appears, related to a redox couple wave VIc at Ep = -880 mV, correspondent to the disappearance of Ia. It is evident that the added sodium ion affected the quinone reduction considerably. As increasing in concentration of Na^+, the well-defined waves IIa and IIIa shift insignificantly dependent to Na^+ concentration.

In both cases, the evolution of a new reversible peak VIa and VIc which constant E_p while increasing of metal ion concentration evident in the changing of the first electron transfer affected by complexation of **12** and **13** with Na^+. The conclusions of changing of each redox couple are summarized in Table 3.3.

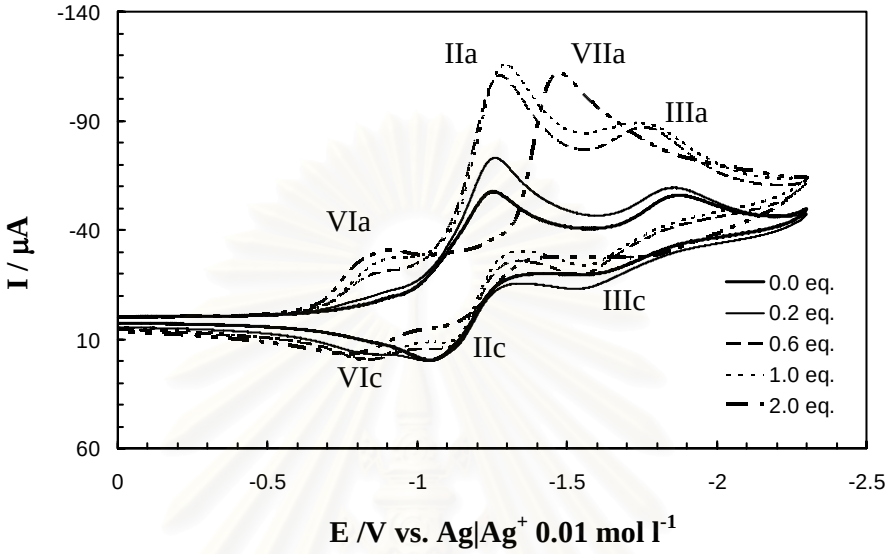


Figure 3.12 Cyclic voltammograms of 0.1mM **12** with various concentration of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, and Effect of added Na^+.

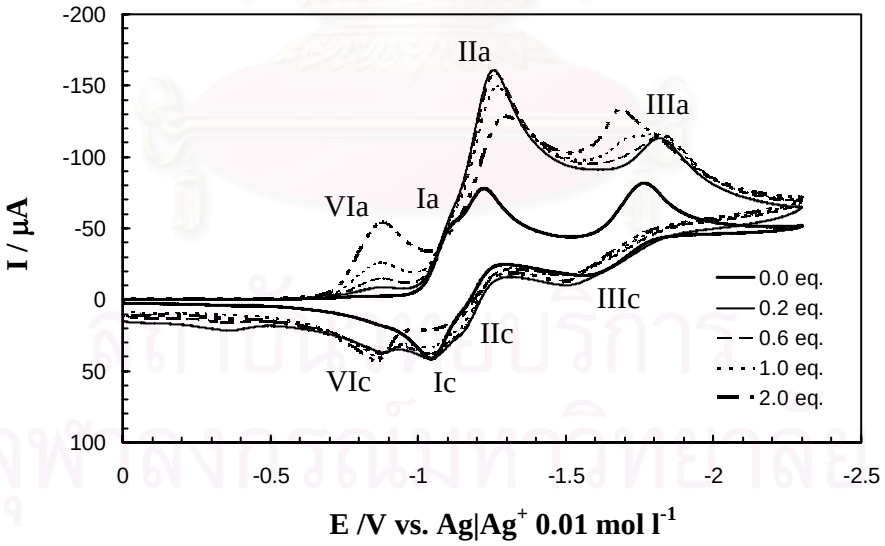


Figure 3.13 Cyclic voltammograms of 0.1mM **13** with various concentration of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, and Effect of added Na^+.

Table 3.3 Changing of electrochemical parameter for 12 and 13. Effect of added Na^+

	Na^+(eq)	E_{pVIa}/mV	E_{pVIc}/mV	$-E_{pIa}$/mV	$-E_{pIc}$/mV	E_{pIIa}/mV	$-E_{pIIc}$/mV	E_{pIIIa}/mV	E_{pIIIc}/mV	E_{pVIIa}/mV
12	0.0	-	-	-	-	1242	1056	1865	1652	-
	0.2	786	849	-	-	1254	1058	1857	1566	-
	0.6	833	832	-	-	1266	1136	1774	1564	-
	1.0	870	827	-	-	1280	1137	1774	1578	-
	2.0	859	767	-	-	-	1157	-	-	1470
13	0.0	-	-	1101	1048	1217	1164	1761	1590	-
	0.2	862	867	1100	1047	1252	1163	1824	1533	-
	0.6	861	861	1091	1047	1255	1169	1833	1534	-
	1.0	868	859	-	1046	1262	1140	1816	1528	-
	2.0	875	857	-	-	1285	1127	1693	1522	-

CHAPTER 4

CONCLUSION

Two bis-calix[4]arene compounds, 25,27-di(ethyleneglycol)-bis-*p-tert*-butyl calix[4]arene, **5**, and 25,27-di(methoxy)-26,28-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4]arene, **11**, have been synthesized by a one-pot coupling method and a stepwise approach, respectively. The one pot coupling reaction between *p*-tert-butyl-calix[4]arene and 2-bromoethyl toluene sulfonate in the present of 18-crown-6 as phase transfer catalyst and K_2CO_3 as base in a pressurized vessel resulted in the symmetrical biscalixarene **5** in 69% yield. Both symmetric bis-calixarene, **5**, and unsymmetric product, **11**, were able to be obtained by stepwise approaches in 24% and 11% yields, respectively. The quinone derivatives, 25,27-di(ethyleneglycol)-bis-*p-tert*-butylcalix[4]tetraquinone (**12**) and 25,27-di(methoxy)-26,28-di(ethylene glycol)-bis-*p-tert*-butylcalix[4]diquinone (**13**) were synthesized by oxidizing **5** and **11** with $Tl(CO_2CF_3)_3$ in CF_3COOH and were obtained in 21% and 56% yields, respectively.

The morphology of free ligands and their complexes with alkali metal ions was carried out by mean of molecular dynamic simulations at 300K. Molecular dynamic calculations showed that both free ligands and complexes changed the conformations upon time. The most stable conformations for the free ligands **12** and **13** are partial cone conformation and cone conformation, respectively. The results of molecular dynamic simulations indicated that stabilities of the 1:1 inclusion complexes of ligands **12** and **13** with alkali cations were in the order of $Na^+ \approx K^+ > Li^+$.

The preliminary investigation of electrochemical properties of **12** and **13** by cyclic voltammetry showed significant changing of their voltammograms upon

addition of Na^+. Voltammograms of **13** exhibited one and two electrons transfer reduction processes that revealed to an electron transfer, electron transfer and chemical reaction (EEC) mechanism while those of **12** showed a more complicated electron transfer mechanism. The changing of voltammograms in the presence of Na^+ suggested the possibility to use both **12** and **13** as alkali metal ion sensor.

Suggestion for future works

From all obtained results and discussion, future works should be focused on;

1. X-ray crystal structures of both ligand **12** and **13** as well as their alkali metal cation complexes should be obtained in order to understand the structure of the synthetic receptors and their coordination chemistry with alkali metal ions.

2. ^{1}H-NMR and UV-Visible titrations with alkali metal ions should be investigated to obtain their complexation constants and structural behaviors upon complexation.

3. Cyclic voltammetry study of compound **12** and **13** with other alkali metal ions should be studied to afford the detail of electron transfer mechanism that will give valuable informations for using bis-calix[4]quinones as alkali metal ion sensor.

4. The kinetic studies of both quinone based receptors by cyclic voltammetry technique should be carried out to identify the complexation and the electron transfer mechanism.

REFERENCES

1. Domansky, K.; Janata, J.; Josowicz, M.; Petelenz, D. Present state of fabrication of chemical sensitive field-effect transistors *Analyst* **1993**, *118*, 335-340.

2. Bergveld, P. Future applications of ISFETs *Sens. Actuators B* **1991**, *4*, 125-133.

3. Cattral, R. W. *Chemical Sensor* Oxford Chemistry Primers: Oxford Science Publisher: Oxford, U.K., 1997.

4. Beer, P. D. Transition-metal receptor systems for the selective recognition and sensing of anionic guest species *Acc. Chem. Res.* **1998**, *31*, 71-80.

5. Beer, P. D.; Gale, P. A.; Chen, G. Z. Electroochemical molecular recognition; parthways between complexation and signaling *J. Chem. Soc., Dalton Trans.* **1999**, 1897-1909.

6. Lehn, J. M. Supermolecular chemistry-scope and perspectives molecules, supramolecules, and molecular devices *Angew. Chem.Int. Ed. Engl.* **1988**, *27*, 89-112.

7. Gutche, D. *Calixarenes* Royal Society of Chemistry: Cambridge, 1989.

8. Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J. *Calixarenes 2001* Kluwer Academic Publishers: Dordrecht, 2001.

9. Pearson, R. G. Hard and soft acids and bases *J. Am. Chem. Soc.* **1963,** *85,* 3533.

10. Arduini, A.; Pochini, A.; Reverbi, S.; Ungaro, R. Para-tetra-butyl-calix[4]arene tetracarbonylic acid-A water-soluble calixarene in a cone structure *J. Chem. Soc., Chem. Commun.* **1984**, 981-982.

11. Arduini, A.; Pochini, A.; Reverbi, S.; Ungaro, R.; Andrectti, G. D.; Ugozzoli, F. The preparation and properties of a new lipophilic sodium selective ether ester ligand derived from para-tert-butylcalix[4]arene *Tetrahedron* **1986**, *7,* 2089-2100.

12. Mckervey, M. A.; Seward, E. M.; Ferguson,G.; Ruhl, B.; Harris, S. J. Synthesis, X-ray crystal-structure and cation transfer properties of alkyl calixaryl acetates, a new series of molecular receptors *J. Chem. Soc., Chem. Commun.* **1985**, 388-390.

13. Chang, S. K.; Cho, I. New metal cation-selective ionophores derived from calixarenes-their synthesis and ion-binding properties *J. Chem. Soc., Perkin Trans. I* **1986**, *2,* 211-214.

14. Yamamoto, H.; Shinkai, S. Molecular design of calix[4]arene-based sodium-selective electrodes which show remarkable high 10(5.0)-10(5.3) sodium/potassium selective *Chem. Lett.* **1994**, 1115-1118.

15. Yamamoto, H.; Ueda, K., Suenga, H.; Sakaki, T.; Shinkai, S. Exploitation of Na^+-selective electrodes for protein solutions from crown-bridged calix[4]quinones *Chem. Lett.* **1996**, 39-40.

16. Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harlema, S.; Abu El-Fadl, A.; Reinhoudt, D. N. Complexation of alkali-metal cation by conformationally rigid, stereoisomeric calix[4]arene crown ethers-a quantitative-evalution of preorganization *J. Am. Chem. Soc.* **1990,** *112*, 6979-6985.

17. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M. J.; Egberink, R. J. M.; Jong, F.; Reinhoudt, D. N. Synthesis, complexation, and membrane-transport studies of 1,3-alternate calix[4]arene-crown-6 conformers-a new class of cesium selective ionophores *J. Am. Chem. Soc.* **1995**, *117*, 2767-2777.

18. Peak, K. S.; Ihm, H. J. Synthesis and binding property of tunable upper-rim calix[4]crowns *Chem. Lett.* **1996**, 311-312.

19. Iwamoto, K.; Fujimoto, K.; Matsuda, T.; Shinkai, S. Remarkable metal template effects on selective synthesis of para-tert-butylcalix[4]arene conformers *Tetrahedron Lett.* **1990**, *31*, 7169-7172.

20. Almi, M.; Arduini, A.; Casnati, A.; Pochini, R.; Ungaro, R. Chloromethylation of calixarenes and synthesis of new water-soluble macrocyclic hosts *Tetrahedron* **1989**, *45*, 2177-2182.

21. Gutsche, C. D.; Nam, K. C. Calixarenes 22 Synthesis, properties and metal complexation of aminocalixarenes *J. Am. Chem. Soc.* **1988**, *110*, 6153-6162.

22. Gutsche, C. D.; Pagoria, P. E. Calixarene 16 Functionalized calixarenes-the direct substitution route *J. Org. Chem.* **1985**, *50*, 5795-5802.

23. Verboom, W.; Durie, A.; Egberink, R. J. M.; Asfari, Z.; Reinhoudt, D. N. Ipso nitration of para-tert-butylcalix[4]arenes *J. Org. Chem.* **1992**, *57*, 1313-1316.

24. Böhmer, V.; Vogt, W. Calix[4]arene, bridged at the upper rim *Pure & App. Chem.* **1993**, *65*, 403-408.

25. Berger, B.; Böhmer, V.; Pawlus, E.; Rodriguez, A.; Vogt, W. Bicyclocalix[4]arenes *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 96-99.

26. Arduini, A.; Casnati, A.; Dodi, L.; Pochini, A.; Ungaro, R. Selective 1,2-functionalization of calix[4]arenes at the lower rim-synthesis of a new type of bis calixcrown ether *J. Chem. Soc., Chem. Commun.* **1990**, 1597-1958.

27. Beer, P. D.; Martin, J. P.; Drew, M. G. B. Calix[4]arene cryptand and new 1,3-bis-pyridyl and 1,3-bis-alkylthioether calix[4]arenes designed to coordinated transition-metal cations *Tetrahedron* **1992**, *48*, 9913-9928.

28. Kraft, D.; Loon, J. D.; Owens, M.; Verboom,W.; Vogt, W.; McKervey, M. A.; Böhmer, V.; Reinhoudt, D. N. Selective functionalization of calix[4]arenes at the upper rim *Tetrahedron Lett.* **1989**, *20*, 2681-2684.

29. Struck, O.; Chrisstoffels, L. A. J.; Lugtenberg, R. J. W.; Verboom, V.; Hummel, G. T.; Harkema, S.; Reinhoudt, D. N. Head-to-head linked double calix[4]arenes: Convenient synthesis and complexation properties *J. Org. Chem.* **1997**, *62*, 2487-2493.

30. Kanamathareddy, S.; Böhmer, V. Calixarene-selective functionalization and bridge building *J. Org. Chem.* **1995**, *60*, 6070-6075.

31. Wasikiewicz, W.; Rokicki, G.; Kielkiewiez, J.; Böhmer, V. Head-to-tail linkage in double calix[4]arenes *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 214-216.

32. Ohseto, F.; Shinkai, S. Synthesis of and metal cation oscillation in ionophoric biscalix[4]arenes *J. Chem. Soc., Perkin Trans. II* **1995**, 1103-1109.

33. Schmitt, P.; Beer, P. D.; Drew, M. G. B.; Sheen, P. D. Calix[4]tube: A tubular receptor with remarkable potassium ion selective *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1840-1842.

34. Tomapatanaget, B.; Pulpoka, B.; Tuntulani, T. Preparation of diaza dioxa dithia crown p-tert-butylcalix[4]arene by S-alkylation reactions: Use of metallo-calix[4]arene complexes as reaction templates *Chem. Lett.* **1998**, 1037-1038.

35. Cooper, J. B.; Drew, M. G. B.; Beer, P. D.; Alkali metal cation cooperative anion recognition by heteroditopic bis(calix[4]arene) rhenium(I) bipyridyl and ferrocene receptor molecules *J. Chem. Soc., Dalton Trans.* **2000**, 2721-2728.

36. Beer, P. D.; Hesek, D.; Nam, K.; Drew, M. G. B. Anion recognition properties of new upper-rim cobaltocenium calix[4]arene receptors *Organometallics* **1999**, *18*, 3933-3943.

37. Chung, T. D.; Kang, S. K.; Kim, H.; Kim, J. R.; Oh, W. S.; Chang, S. K. Synthesis and electrochemical behavior of a new water soluble Ca^{2+}-selective ionophore based on calix[4]arene-triacid-monoquinone *Chem. Lett.* **1998**, 1225-1226.

38. Nam, K. C.; Kang, S. O.; Jeong, H. S.; Jeon, S.; Urea derivative of calix[4]diquinone: HSO_4^- ion selective receptor *Tetrahedron Lett.* **1999**, *40*, 7343-7346.

39. Gutsche, C. D. Calixarene *Acc. Chem. Res.* **1983**, *16*, 161-170.

40. Reddy, P. A.; Gutsche, C. D. Calixarenes 32 Reactions of calix[4]quinones *J. Org. Chem.* **1993**, *58*, 3245-3251.

41. Kelderman, E.; Derhaeg, L.; Hecsink, G. J. T.; Verboom, W.; Engbersen, J. F. J.; Van Hulst, N. F.; Persoons, A.; Reinhoudt, D. N. Nitrocalix[4]arenes as molecules for 2nd-order nonlinear optics *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1075-1077.

42. Suga, K.; Fugihara, M.; Monta, T.; Agawa, T. Electrochemical study on calix[4]quinone and calix[4]hydroquinone in N,N-dimethylformamide *J. Chem. Soc., Faraday Trans.* **1991**, *87*, 1575-1578.

43. Beer, P. D.; Chen, Z.; Gale, P. A. Diester-calix[4]arenediquinone complexation and electrochemical recognition of group-1 and group-2, ammonium and alkyl ammonium guest cations *Tetrahedron* **1994**, *50*, 931-940.

44. Gomez-Kaifer, M.; Reddy, P. A.; Gutsche, C. D.; Echegoyen, L. Electroactive calixarenes 1 Properties of calixquinones redox and cation-binding *J. Am. Chem. Soc.* **1994**, *116*, 3580-3587.

45. Wang, Y.; Alvarez, J.; Kaifer A. E. Redox control of host-guest recognition: a case of host selection determined by the oxidation state of the guest *Chem. Commun.* **1998**, *14*, 1457-1458.

46. Beer, P. D.; Gale, P. A.; Chen, Z.; Drew, M. G. B.; Heath, J. A.; Ogden, M. I.; Powell, H. R. New ionophoric calix[4]diquinones: Coordination chemistry, electrochemistry, and X-ray crystal structures *Inorg. Chem.* **1997**, *36*, 5880-5893.

47. Wolber, M. P. O.; van Veggel, F. C. M. J.; Heeringa, R. H. M.; Hofstraat J. W.; Geurts, F. A. J.; van Hummel, G. J.; Harkema, S.; Reinhoudt D. N. Biscalix[4]arene ligands for dinuclear lanthanide ion complex *Liebigs Ann-Recl* **1997**, *12*, 2587-2600.

48. Beer, P. B.; Keefe, A. D.; Drew, M. G. B. Electrochemical molecular recognition: pathways between complexation and signaling *J. Chem. Soc. Dalton Trans.* **1999**, 1897-1909.

49. Bethell, D.; Dougherty, G.; Cupertino, D. C. Dynamic factors in the design of redox-switched calix[4]arene cationophores *Acta. Chem. Scand.* **1998**, *52*, 407-416.

50. Chung, T. D.; Kim, H. Electrochemistry of calixarene and its analytical applications *J. Inclusion Phenom. Mol.* **1998**, *32*, 179-193.

51. Gutsche, C. D.; Iqbal, M. *p-tert*-Butylcalixarene *Org. Synth.* **1990**, *68*, 234-237.

52. Fantoni, A. C.; Maranon, J.; Conformational behaviour and alkali metal cation binding selectivity of 5,11,17,23-tetra-tert-butyl[25,26,27,28-tetrakis(2-pyridylmethyl)oxy]-calix[4]arene: a molecular dynamics study *J. Chem. Phy.* **2000**, *262*, 359-368.

53. Iwamoto, H.; Hirakata, M.; Usui, S.; Haino, T.; Fukazawa, Y. Dynamic structure of inclusion complexes of monodeoxycalix[4]arene with small organic guests in solution *Tetrahedron lett.* **2002**, *43*, 85-87.

54. Brooks, B. R.; Bruccoleri, R. E.; Olafson, B. D. CHARMM-a program for macromolecular energy, minimization, and dynamics calculations *J. Comp. Chem.* **1983**, *4*, 187-217.

55. Asfari, Z.; Weiss, J.; Vicens, J. Double-calixarene design, synthesis, and properties *Synlett.* **1993**, 719-725.

56. Janssen, R. G.; Verboom, W.; Reinhoudt, D. N.; Casnati, A.; Freriks, M.; Pochini, A.; Ugozzoli, F.; Ungaro, R.; Nieto, P. M.; Carramolino, M.; Cuevas, F.; Prados, P.; de Mendoza, J. *Synthesis* **1993**, 380.

57. Jurczak, J.; Ostaszewski, R. High-pressure approach to the synthesis of diazacoronands and cryptands *J. Coord. Chem. Part B* **1992**, *27*, 201-214.

58. Webber, P. R. A.; Chen, G. Z.; Drew, M. G. B.; Beer, P. D. Cesium- and rubidium-selective redox-active Bis(calix[4]diquinone) ionophores *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 2265.

APPENDIX

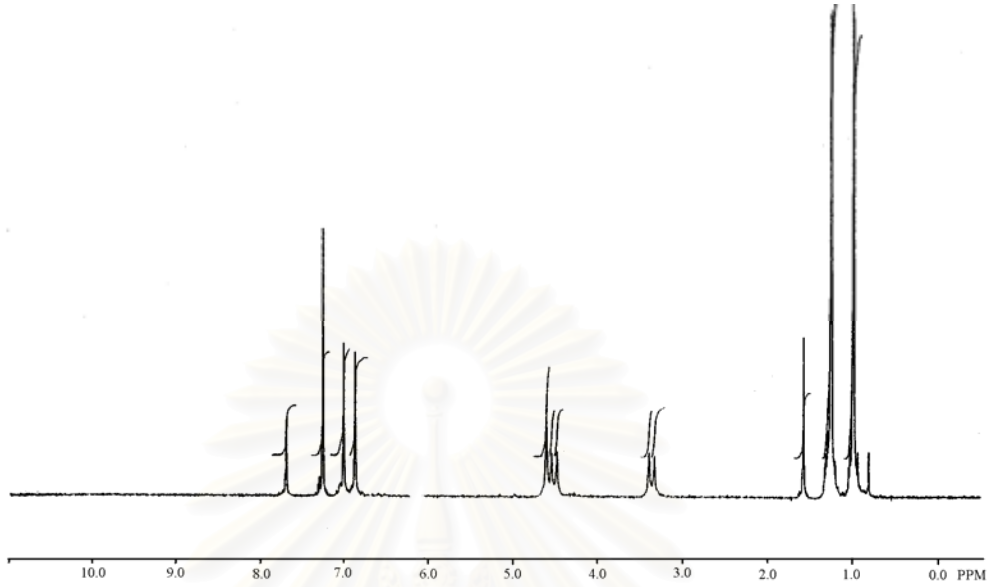


Figure A.1 ^{1}H-NMR (200 MHz, $CDCl_3$) spectrum of 25, 27-di (ethylene glycol)-bis-*p-tert*-butylcalix[4]arene (5)

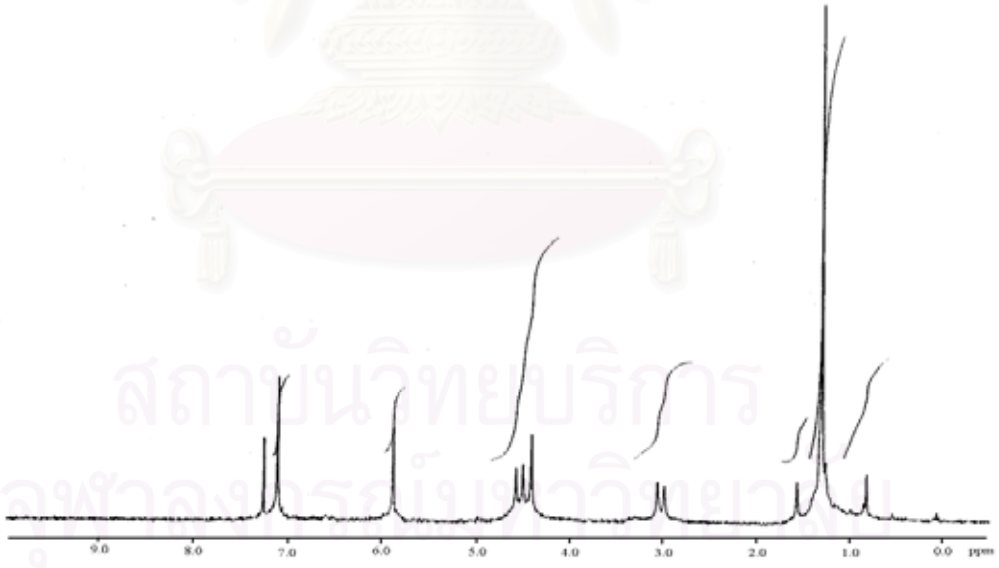


Figure A.2 ^{1}H-NMR (200 MHz, $CDCl_3$) spectrum of 25, 27-di(methoxy)-26, 28-di(ethylene glycol)-bis-*p-tert*-butylcalix[4]arene (**11**)

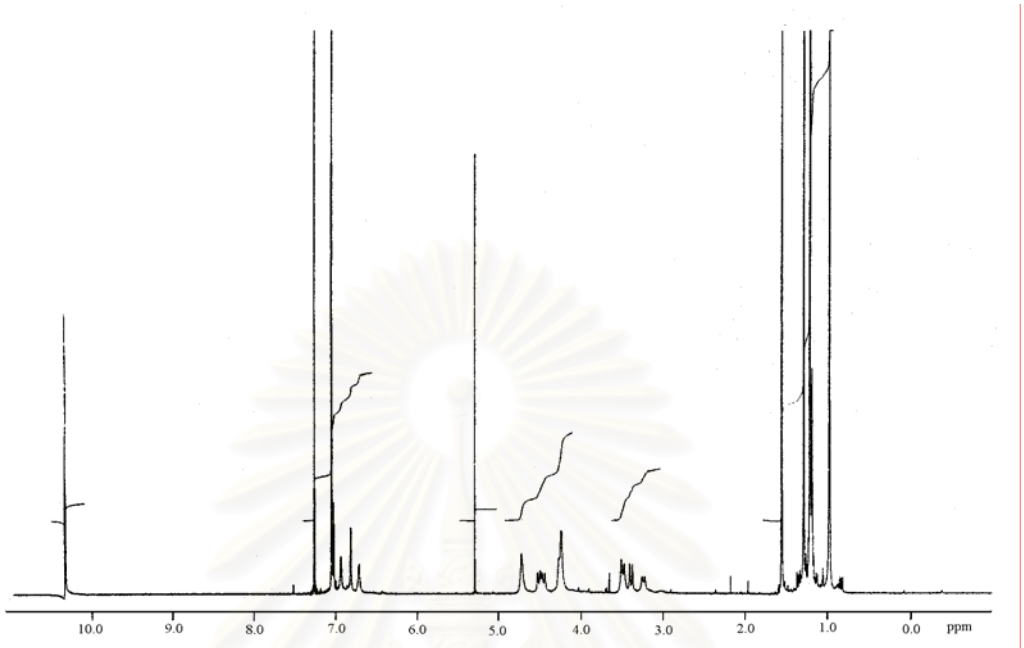


Figure A.3 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of 25, 27-di(ethylene glycol)-bis-*p-tert*-butylcalix[4]tetraquinone (**12**)

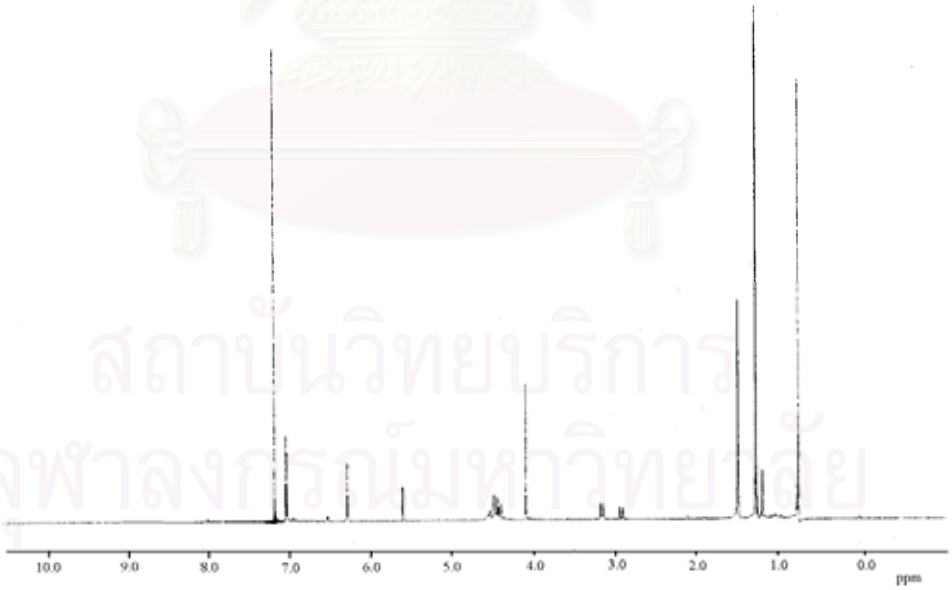


Figure A.4 ^{1}H-NMR (400 MHz, $CDCl_3$) spectrum of 25, 27-di(methoxy)-26, 28-di(ethylene glycol)-bis-*p-tert*-butyl calix[4]diquinone (**13**)

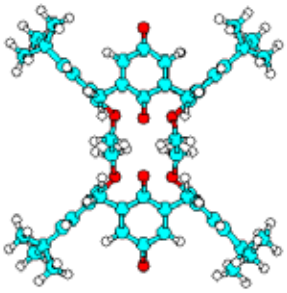


Figure B.1 Snap shots from molecular dynamic simulation at 300K of **1 2**

Cone conformation
E_{tot} = 127.9226 kCal mol^{-1}
Gradient = 0.000398

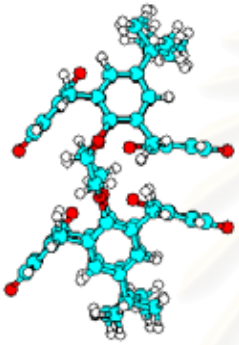


Figure B.2 Snap shots from molecular dynamic simulation at 300K of **12**

Partial cone conformation
E_{tot} = 121.4477 kCal mol^{-1}
Gradient = 0.000329

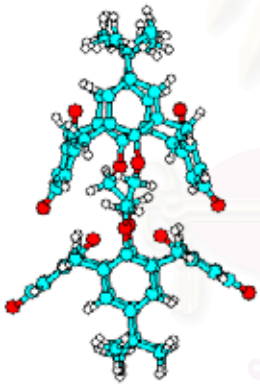


Figure B.3 Snap shots from molecular dynamic simulation at 300K of **12**

Altenate cone conformation
E_{tot} = 121.4360 kCal mol^{-1}
Gradient = 0.000356

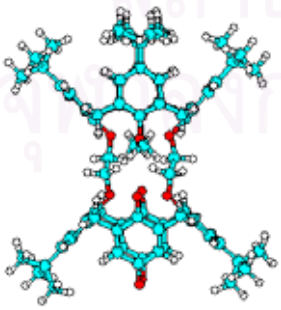


Figure B.4 Snap shots from molecular dynamic simulation at 300K of **13**

Cone conformation
E_{tot} = 196.1157 kCal mol^{-1}
Gradient = 0.125430

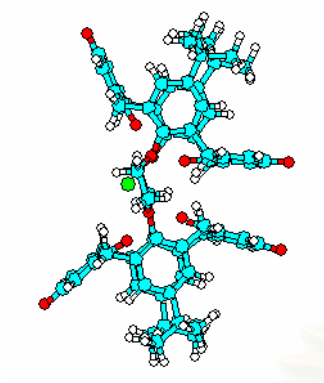


Figure B.5 Snap shots from molecular dynamic simulation at 300K of **12**

Cone conformation + Li ion
E_{tot} = 105.0092 kCal mol^{-1}
Gradient = 0.000353

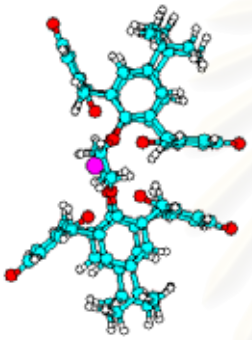


Figure B.6 Snap shots from molecular dynamic simulation at 300K of **12**

Cone conformation + Na ion
E_{tot} = 100.3814 kCal mol^{-1}
Gradient = 0.000334

Figure B.7 Snap shots from molecular dynamic simulation at 300K of **12**

Cone conformation + K ion
E_{tot} = 101.2960 kCal mol^{-1}
Gradient = 0.000334

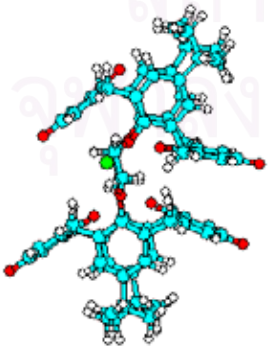


Figure B.8 Snap shots from molecular dynamic simulation at 300K of **12**

Partial cone conformation + Li ion
E_{tot} = 102.5417 kCal mol^{-1}
Gradient = 0.000392

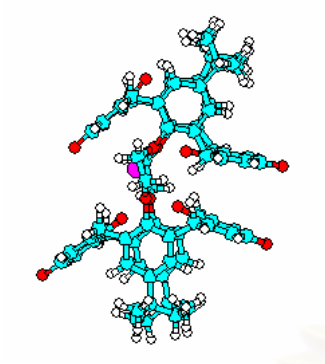


Figure B.9 Snap shots from molecular dynamic simulation at 300K of **12**

Partial cone conformation + Na ion
E_{tot} = 97.0338 kCal mol^{-1}
Gradient = 0.000378

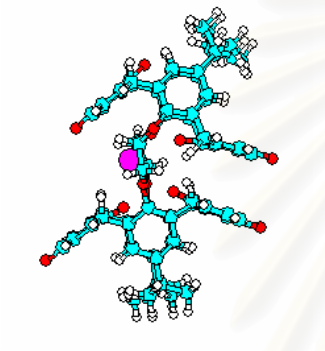


Figure B.10 Snap shots from molecular dynamic simulation at 300K of **12**

Partial cone conformation + K ion
E_{tot} = 107.5874 kCal mol^{-1}
Gradient = 0.000364

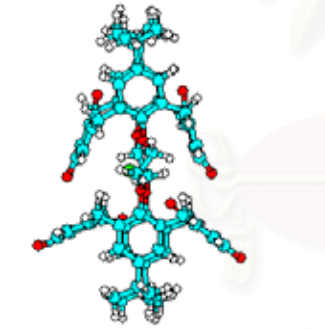


Figure B.11 Snap shots from molecular dynamic simulation at 300K of **12**

Alternate cone conformation + Li ion
E_{tot} = 114.9516 kCal mol^{-1}
Gradient = 0.000354

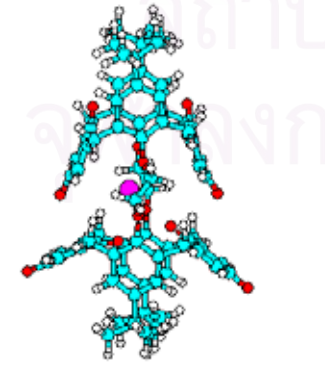


Figure B.12 Snap shots from molecular dynamic simulation at 300K of **12**

Alternate cone conformation + Na ion
E_{tot} = 108.3893 kCal mol^{-1}
Gradient = 0.000366

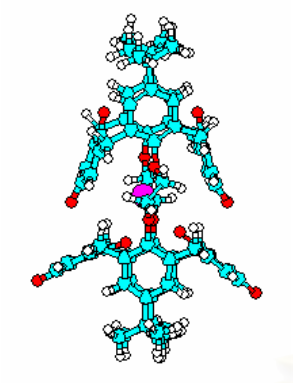


Figure B.13 Snap shots from molecular dynamic simulation at 300K of **12**

Alternate cone conformation + K ion
E_{tot} = 108.5201 kCal mol^{-1}
Gradient = 0.000341

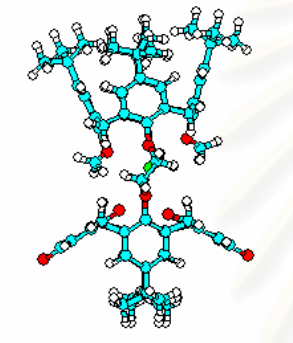


Figure B.14 Snap shots from molecular dynamic simulation at 300K of **13**

Cone conformation + Li ion
E_{tot} = 163.1226 kCal mol^{-1}
Gradient = 0.000690

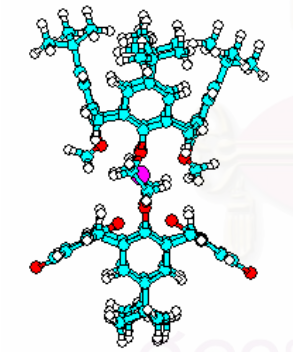


Figure B.15 Snap shots from molecular dynamic simulation at 300K of **13**

Cone conformation + Na ion
E_{tot} = 156.2826 kCal mol^{-1}
Gradient = 0.000587

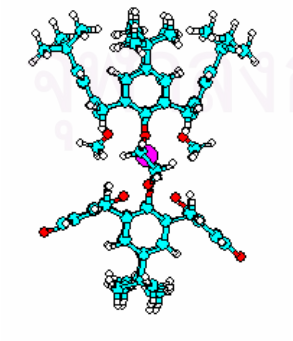


Figure B.16 Snap shots from molecular dynamic simulation at 300K of **13**

Cone conformation + K ion
E_{tot} = 155.4214 kCal mol^{-1}
Gradient = 0.000504

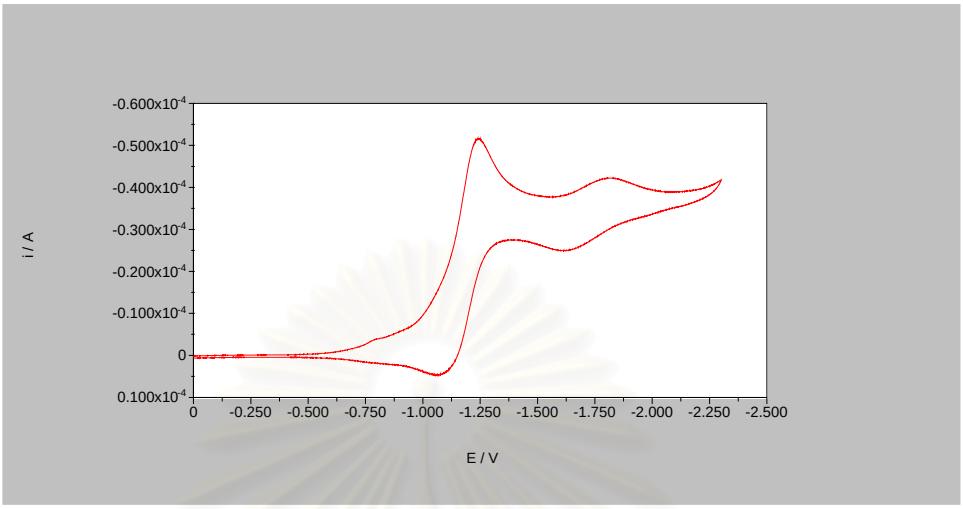


Figure C.1 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.020Vs^{-1}

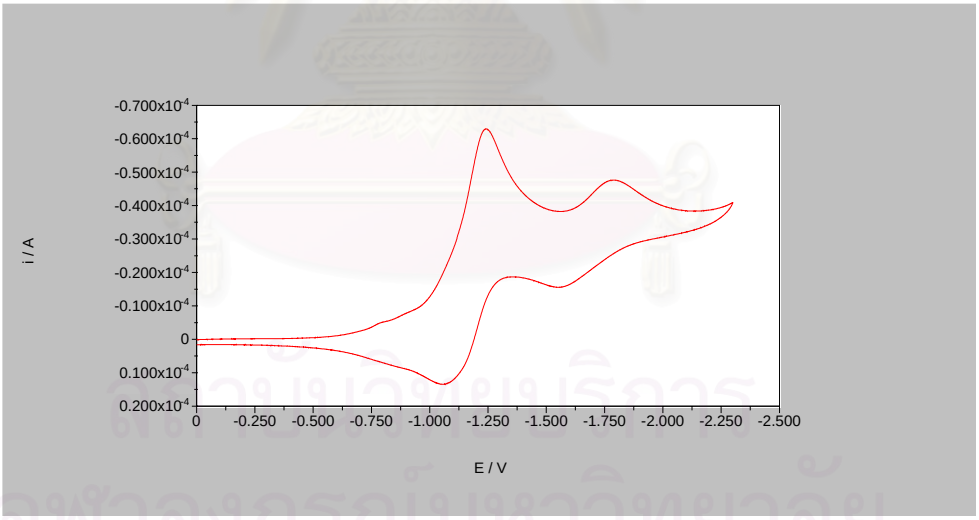


Figure C.2 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.050Vs^{-1}

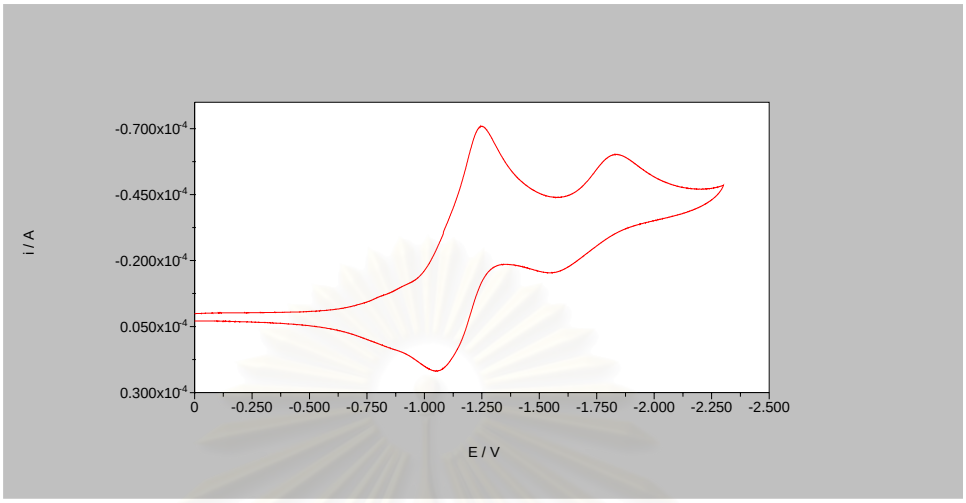


Figure C.3 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.100Vs^{-1}

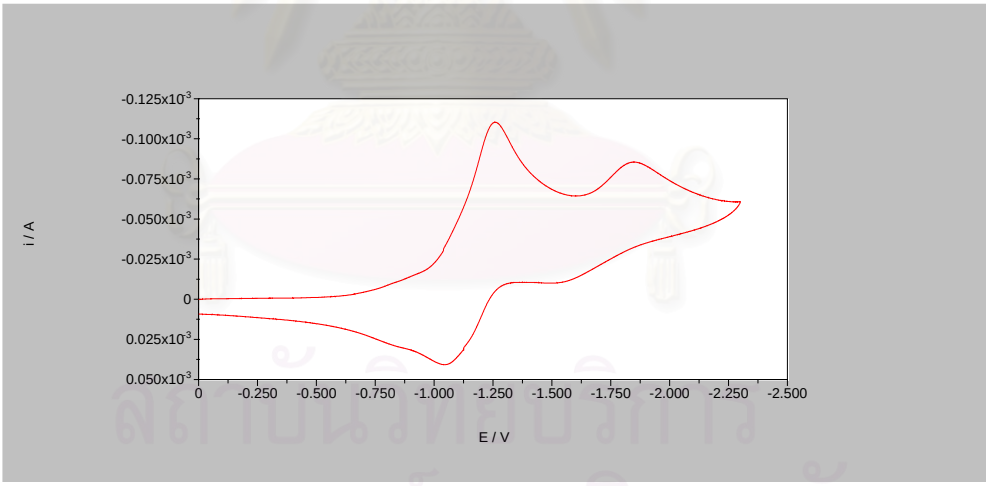


Figure C.4 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.200Vs^{-1}

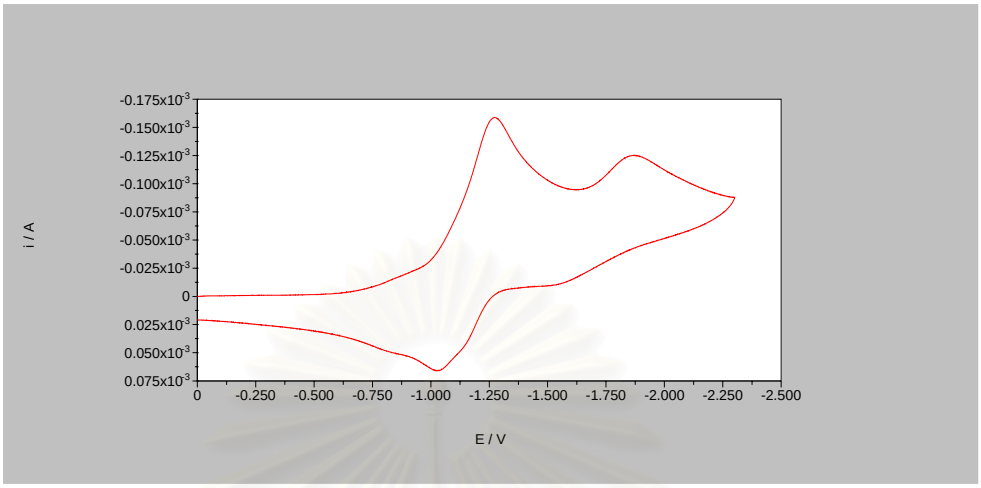


Figure C.5 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.400Vs^{-1}

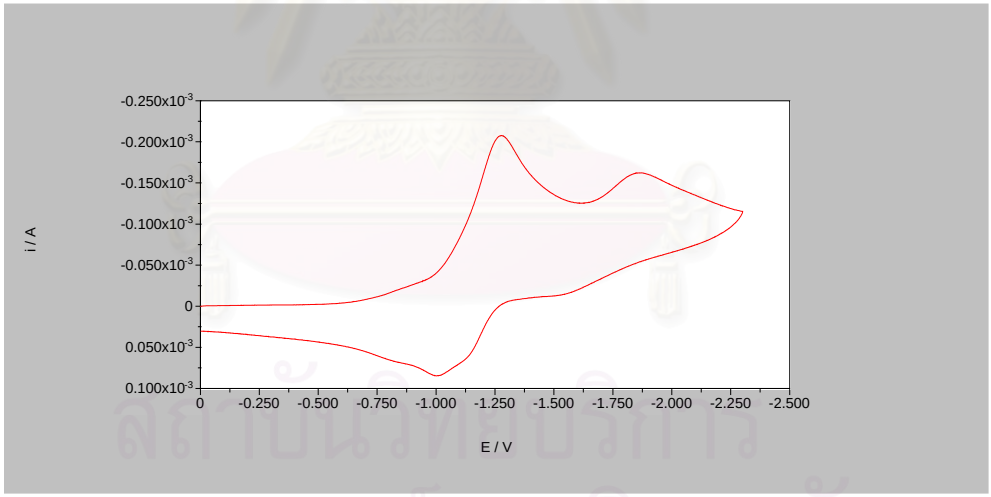


Figure C.6 Cyclic voltammogram of 0.1mM **12** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.600Vs^{-1}

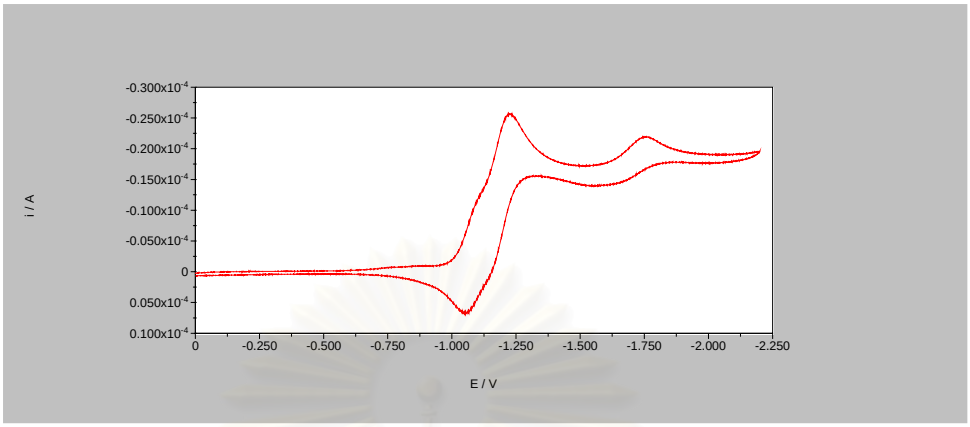


Figure C.7 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.020Vs^{-1}

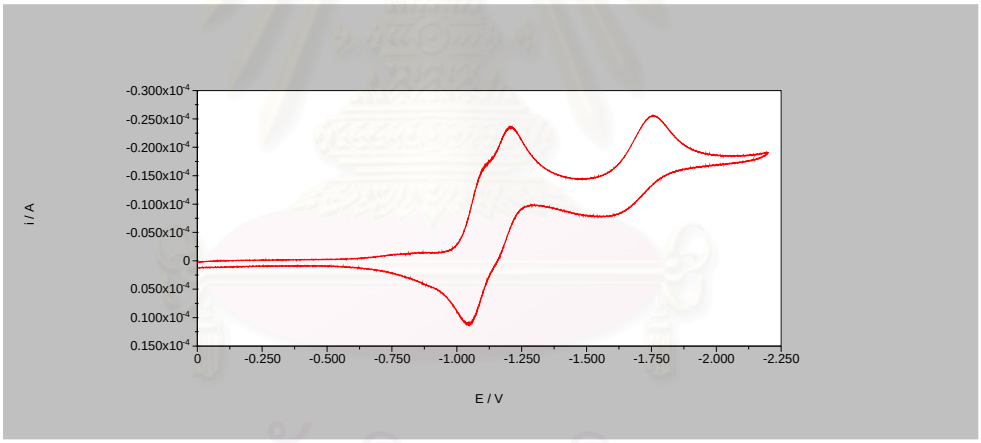


Figure C.8 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.050Vs^{-1}

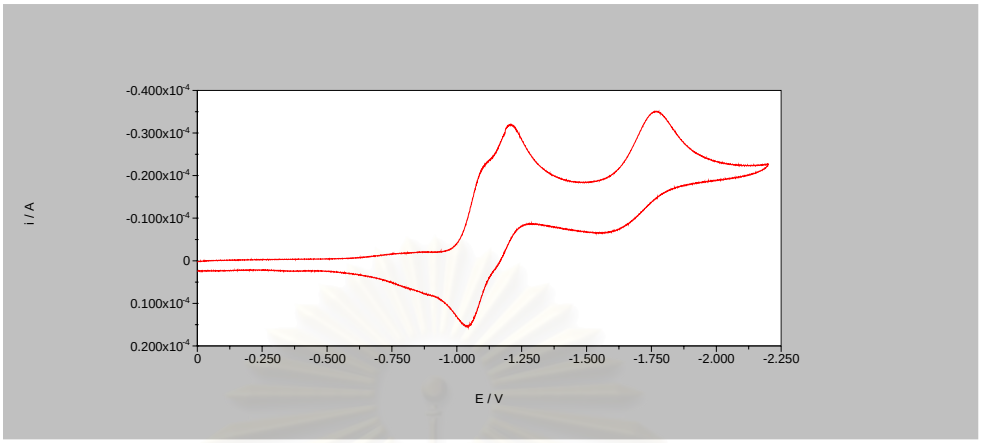


Figure C.9 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.100Vs^{-1}

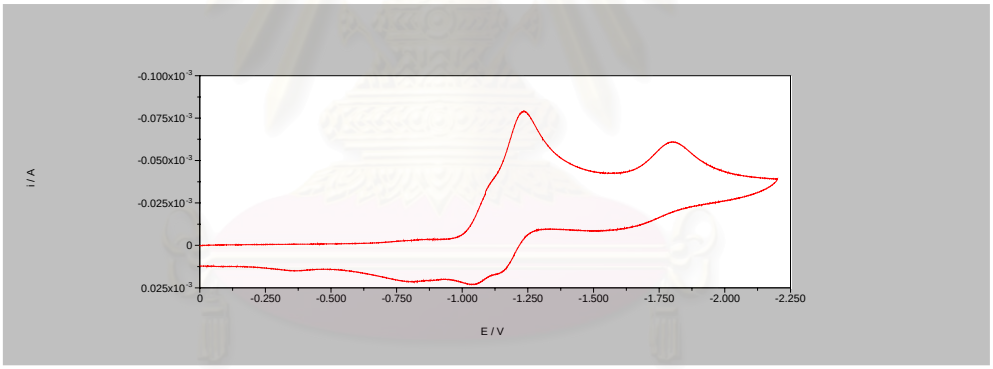


Figure C.10 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, v = 0.200Vs^{-1}

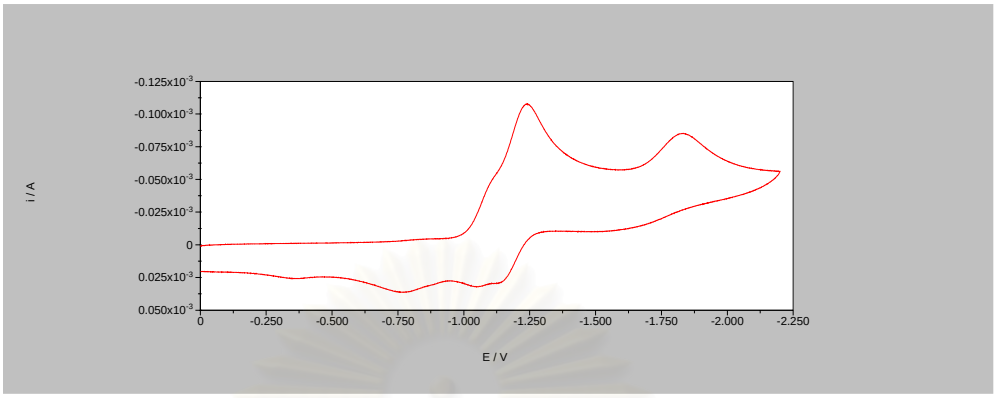


Figure C.11 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.400Vs^{-1}

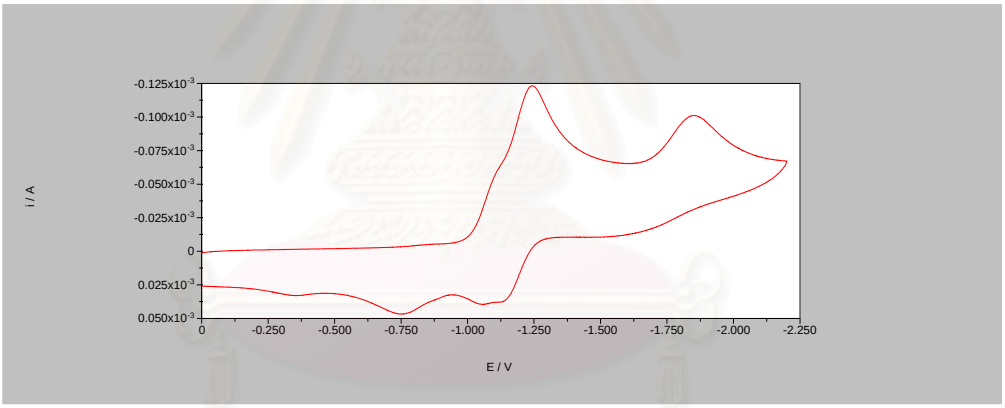


Figure C.12 Cyclic voltammogram of 0.1mM **13** in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.600Vs^{-1}

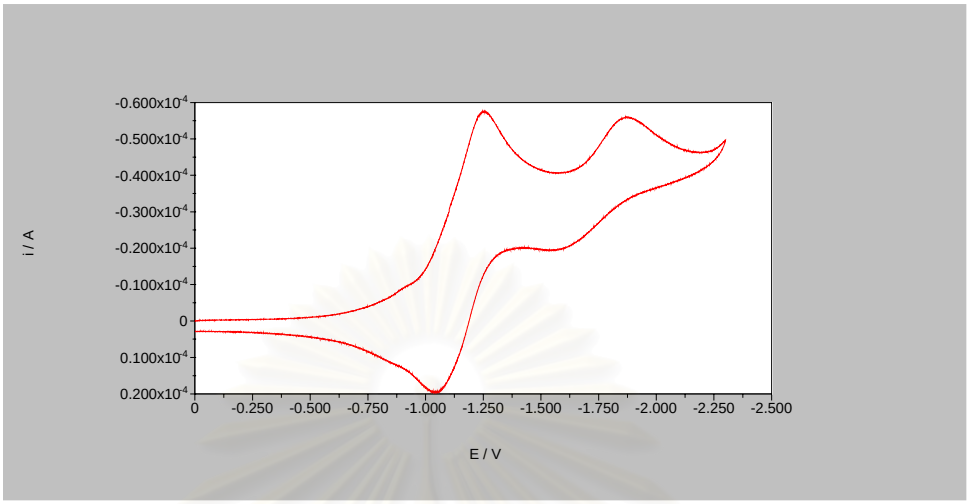


Figure C.13 Cyclic voltammograms of 0.1mM **12** with 0.0 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

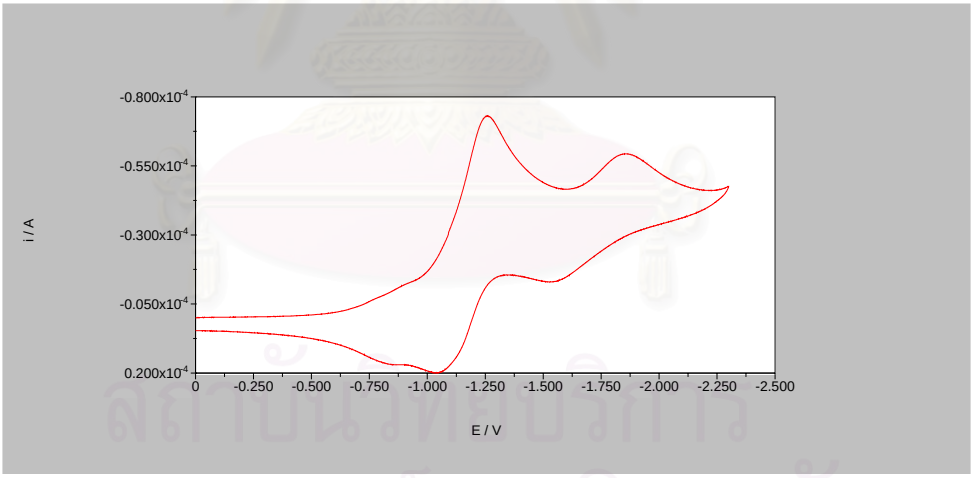


Figure C.14 Cyclic voltammograms of 0.1mM **12** with 0.2 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

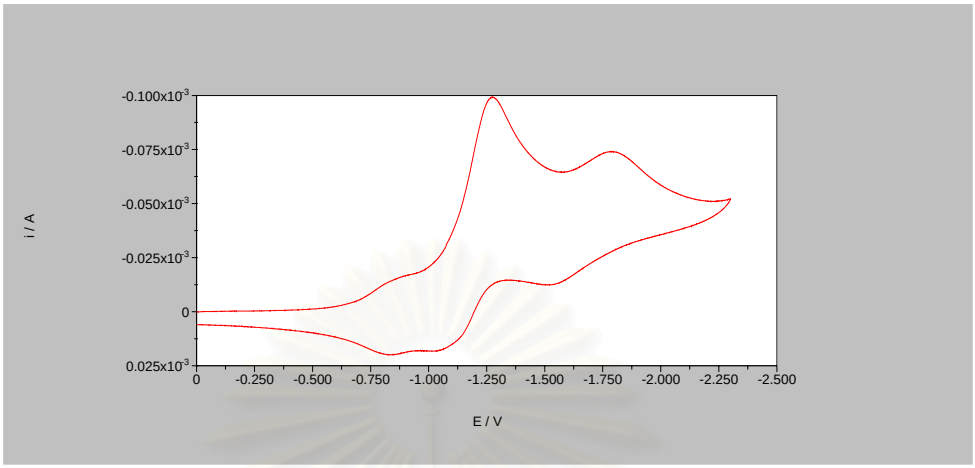


Figure C.15 Cyclic voltammograms of 0.1mM **12** with 0.4 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

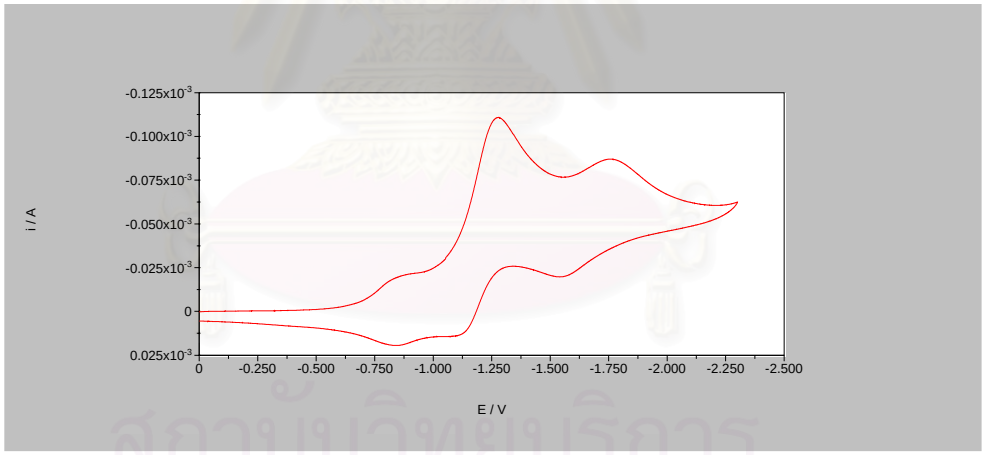


Figure C.16 Cyclic voltammograms of 0.1mM **12** with 0.6 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

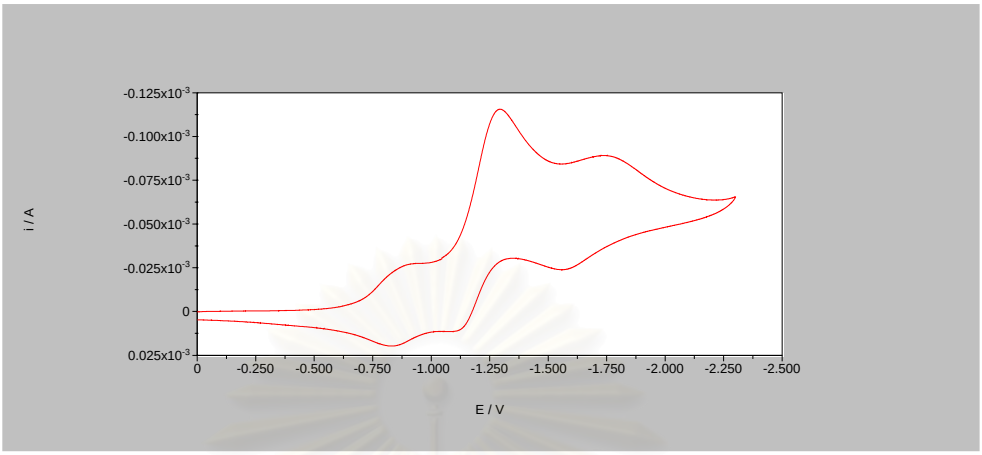


Figure C.17 Cyclic voltammograms of 0.1mM **12** with 1.0 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

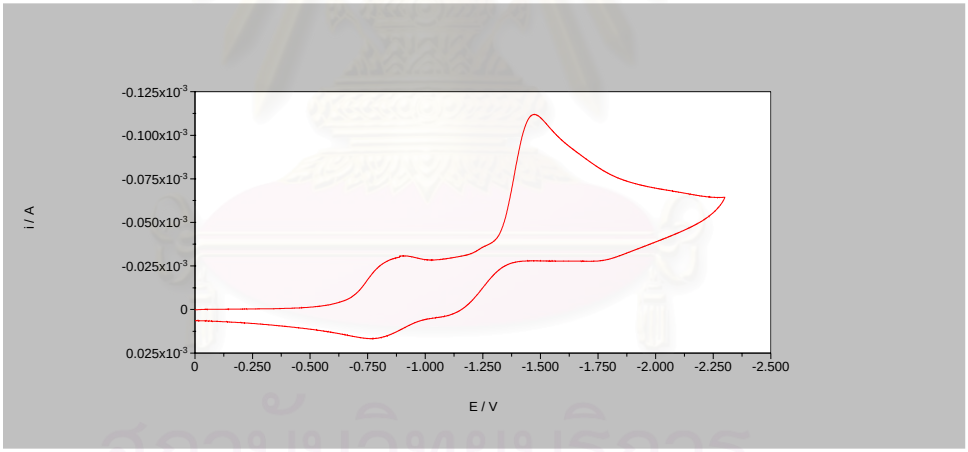


Figure C.18 Cyclic voltammograms of 0.1mM **12** with 2.0 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

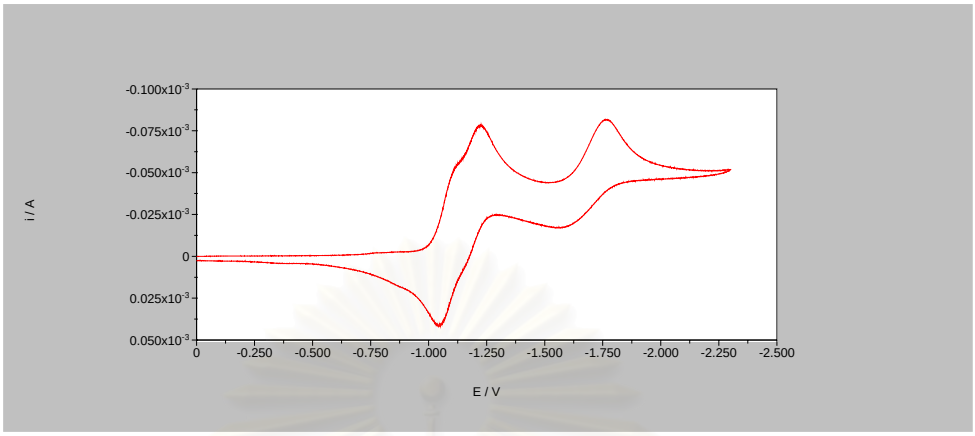


Figure C.19 Cyclic voltammograms of 0.1mM **13** with 0.0 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

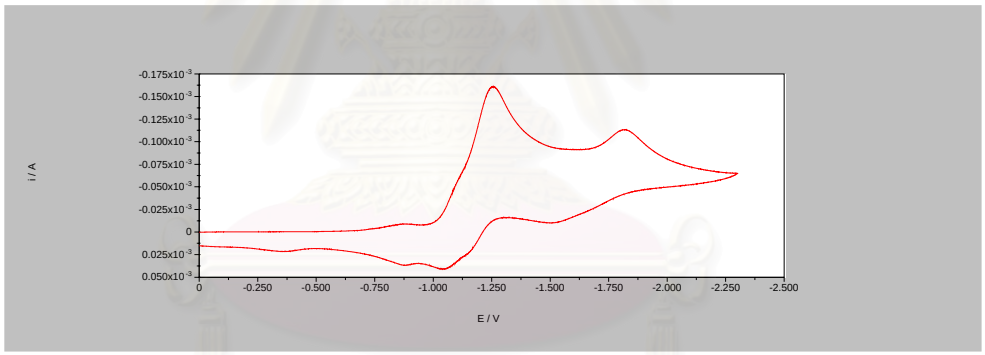


Figure C.20 Cyclic voltammograms of 0.1mM **13** with 0.2 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

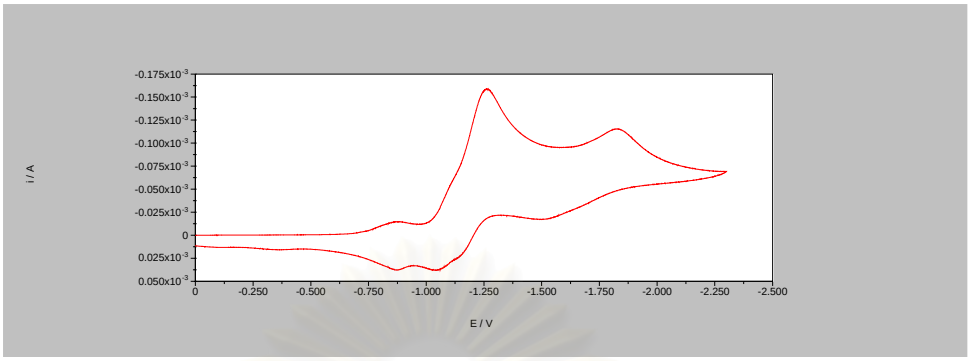


Figure C.21 Cyclic voltammograms of 0.1mM **13** with 0.6 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

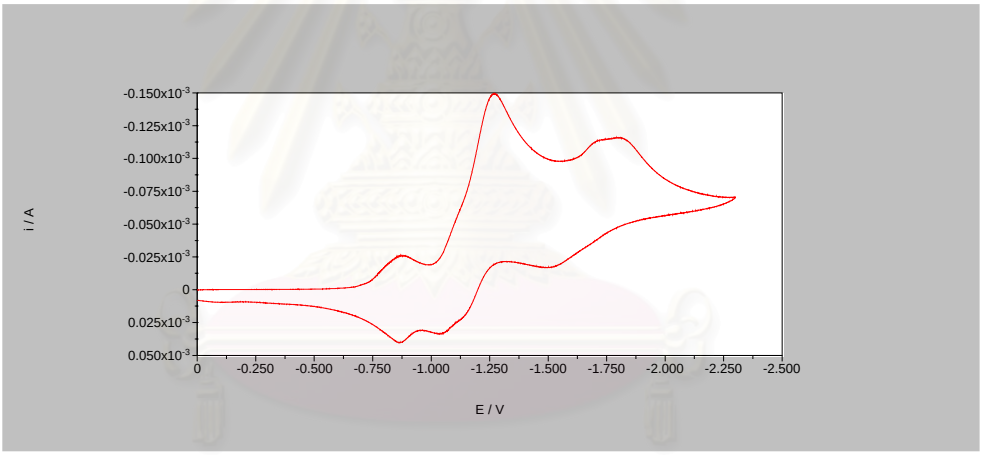


Figure C.22 Cyclic voltammograms of 0.1mM **13** with 1.0 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

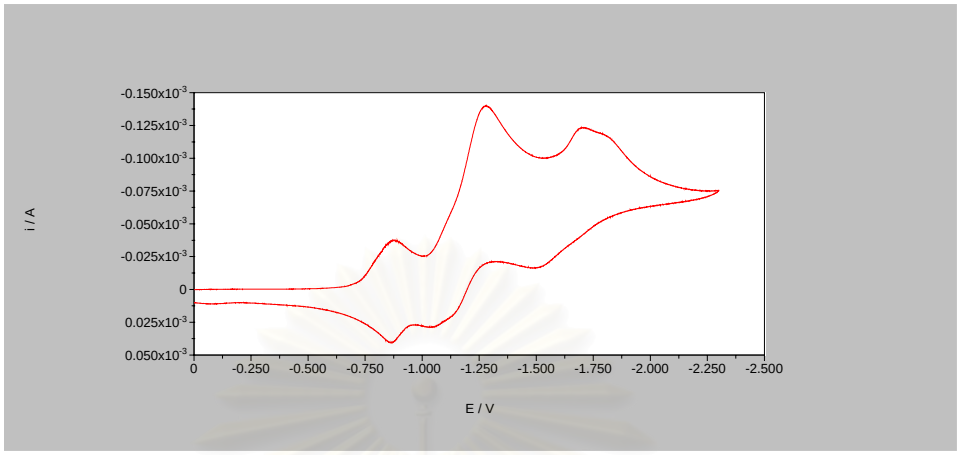


Figure C.23 Cyclic voltammograms of 0.1mM **13** with 1.4 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

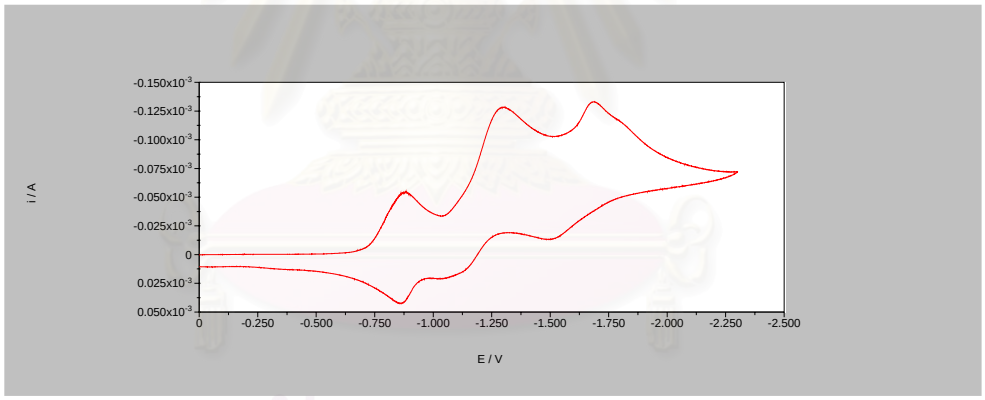


Figure C.24 Cyclic voltammograms of 0.1mM **13** with 2.0 equivalent of Na^+ in 20% DCM in CH_3CN, 0.1M $TBABF_4$, ν = 0.100Vs^{-1}

VITA

Mr. Kriengkamol Tantrakarn was born on December 23, 1977 in Bangkok, Thailand. He graduated with a high school diploma from Bodindecha (Sing Singhasene) School, Bangkok in 1994. He received his Bachelor's degree of Science in Chemistry from Chulalongkorn University in 1998. Since 1999, He has been a graduate student at the Department of Chemistry, Chulalongkorn University and become a member of the Supramolecular Chemistry Research Laboratory under the supervision of Assistant Professor Dr. Thawatchai Tuntulani.

Publication

1. Tantrakarn, K.; Ratanatawanate, C.; Pinsuk, T.; Chailapakul O.; Tuntulani, T. Synthesis of redox\active biscalix[4]quinines and their electrochemical properties *Tettrahedron Lett.* **2003**, *44*, 33-36.