การสังเคราะห์อนุพันธ์ของคาลิกซ์[4]เอรีนที่มีอินโดอนิลีนเพื่อเป็นเซ็นเซอร์สำหรับแอลคาไลแคตไอออน

นาย สุเทียม เครือวัลย์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต

สาขาวิชาเคมี ภาควิชาเคมี

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ปีการศึกษา 2549

ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

SYNTHESIS OF INDOANILINE-DERIVED CALIX [4]ARENES AS ALKALI CATION SENSORS

Mr. Sutiam Kruawan

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

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By	Mr. Sutiam Kruawan
Field of Study	Chemistry
Thesis Advisor	Associate Professor Thawatchai Tuntulani, Ph.D.
Thesis Co-Advisor	Assistant Professor Boosayarat Tomapatanaget, Ph.D.

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

.....Dean of the Faculty of Science
(Professor Piamsak Menasveta, Ph.D.)

Thesis Committee

.....Chairman
(Associate Professor Sirirat Kokpol, Ph.D.)

.....Thesis Advisor
(Associate Professor Thawatchai Tuntulani, Ph.D.)

.....Thesis Co-Advisor
(Assistant Professor Boosayarat Tomapatanaget, Ph.D.)

.....Member
(Associate Professor Orawon Chailapakul, Ph.D.)

.....Member
(Associate Professor Nongnuj Muangsin, Ph.D.)

สุเทียม เครือวัลย์ : การสังเคราะห์อนุพันธ์ของคาลิกซ์[4]เอรีนที่มีอินโดอนิลินเพื่อเป็นเซ็นเซอร์สำหรับแอลคาไลแคตไอออน (SYNTHESIS OF INDOANILINE-DERIVED CALIX[4]ARENES AS ALKALI CATION SENSORS) อาจารย์ที่ปรึกษา: รศ.ดร. ธวัชชัย ตันฑุลานิ; อาจารย์ที่ปรึกษาร่วม: ผศ. ดร. บุษยรัตน์ ธรรมพัฒนกิจ; 52 หน้า

ได้สังเคราะห์อนุพันธ์ของคาลิกซ์[4]เอรีนที่มีอินโดอนิลีนชนิดใหม่ **L1** **L2** และ **L3** ซึ่งสามารถสังเคราะห์ได้จากการทำปฏิกิริยาระหว่างคาลิกซ์[4]เอรีน (**1a**) และ ดับเบิลคาลิกซ์[4]เอรีน (**3a**) ตามลำดับกับเอ็น,เอ็น′-ไดเมทิล-2-เมทิล-1,4-ฟีนิลลีนไดเอมีนโมโนไฮโดรคลอไรด์เมื่อมีโซเดียมไฮดรอกไซด์และโพแทสเซียมเฮกซาไซยาโนเฟอร์เรท(III)อยู่ การศึกษาการเกิดสารประกอบเชิงซ้อนของสารประกอบ **L1** **L2** และ **L3** กับแอลคาไลแคตไอออน ลิเธียม โซเดียม โพแทสเซียม รูบีเดียม และซีเซียม กระทำโดยการไทเทรตด้วยเทคนิคยูวีวิสสิเบิลสเปกโทรสโกปี พบว่าสารประกอบ **L1** และ **L2** ไม่แสดงการเปลี่ยนแปลงที่ชัดเจน ในขณะที่สารประกอบ **L3** เกิดการเปลี่ยนแปลงอย่างชัดเจน ดังนั้นจึงศึกษาการเกิดสารประกอบเชิงซ้อนเฉพาะสารประกอบ **L3** เท่านั้น โดยความสามารถในการเกิดสารประกอบเชิงซ้อนของสารประกอบ **L3** กับแอลคาไลแคตไอออนเป็นดังนี้ โพแทสเซียม > ลิเทียม > รูบีเดียม > โซเดียม > ซีเซียม ดังนั้นแสดงว่าสารประกอบ **L3** มีความจำเพาะต่อไอออนโพแทสเซียม

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ภาควิชา.....เคมี..... ลายมือชื่อนิสิต.....สุเทียม.....เครือวัลย์.....

สาขาวิชา.....เคมี..... ลายมือชื่ออาจารย์ที่ปรึกษา.....รศ.ธวัชชัย ตันฑุลานิ

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Derivatives of calix[4]arene containing indoaniline **L1**, **L2** and **L3** were obtained from reactions of calix[4]arene (**1a**) and double calix[4]arene (**3a**), respectively with *N,N'*-dimethyl-2-methyl-1,4-phenylenediamine monohydrochloride in the presence of sodium hydroxide and potassium hexacyanoferrate(III). Complexation of compounds **L1**, **L2** and **L3** with alkali metal ions such as Li^+, Na^+, K^+, Rb^+ and Cs^+ were carried out by UV-visible titration. The results showed that compounds **L1** and **L2** gave very small changes of spectra while compound **L3** showed significant changes of the spectra. Therefore, only compound **L3** was subjected to the recognition investigation. The binding abilities of compound **L3** with alkali metal ions were as follows; $K^+ > Li^+ > Rb^+ > Na^+ > Cs^+$. Compound **L3** thus bound selectively to K^+.

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Department……Chemistry……	student's signature……S. Kruawan……..
Field of study…Chemistry…….	Advisor's signature……T. Tuntulani…….
Academic year…2006……....	Co-advisor's signature…B. Tomapatanaget……

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LIST OF ABBREVIATIONS AND SYMBOLS

^{o}C	Degree Celsius
A	Absorbance
Ar	Aryl group
equiv.	Equivalent
DMAP	4-Dimethylaminopyridine
g	Gram
h	Hour
^{1}H NMR	Proton nuclear magnetic resonance
^{13}C NMR	Carbon 13 nuclear magnetic resonance
Hz	Hertz
mmol	Millimol
mL	Milliliter
min	Minute
M	Molar
M^{-1}	Per molar
ppm	Part per million
s, d, t, q, m	Splitting patterns of ^{1}H NMR (singlet, doublet, triplet, quartet, multiplet)
δ	Chemical shift
J	Coupling constant

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CHAPTER I

INTRODUCTION

1.1 Alkali metal ions

Many inorganic elements are now recognized as being important for the life of animals, plants and microbes; a number of metals are essential for all of life, these include the alkali metals sodium and potassium, the alkali earth calcium and magnesium and the transition metals manganese, iron, copper and zinc. The general roles of Na^+ and K^+ ions in biology; charge carries, osmotic and electrochemical gradients across cell membrane and nerve function. [1-2]

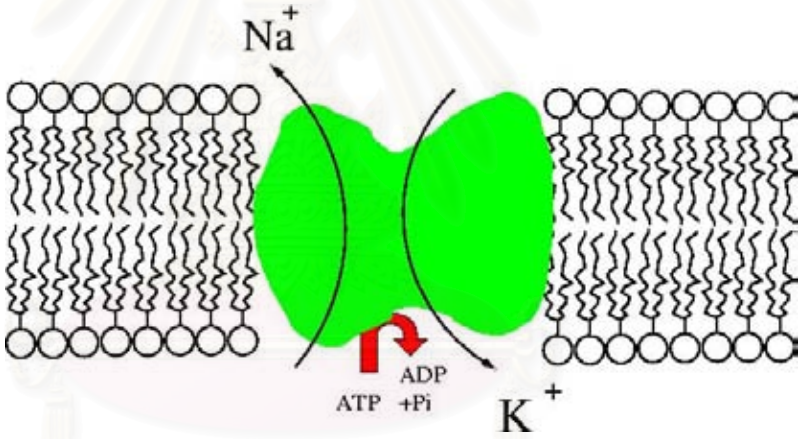

Figure 1.1 Na^+/K^+ pump located in a plasma membrane

In order to maintain the cell potential, cells must keep a low concentration of sodium ions and high levels of potassium ions within the cell (intracellular). Outside cells (extracellular), there are high concentrations of sodium and low concentrations of potassium, so diffusion occurs through ion channels in the plasma membrane. In order to keep the appropriate concentrations, the sodium-potassium pump transports sodium out and potassium in through the active transport as shown in **Figure 1.1**.[3]

Moreover, other functions include its role in the maintenance of acid-base balance and the excitation of nerve and muscle. Potassium is a major intracellular metal ion of the body. Intracellular K^+ concentration is 150 mM compared to a

plasma K^+ concentration of 3.5 to 5.0 mM. Potassium has two major physiological functions. It has an important role in cell metabolism and neuromuscular excitation.[4] Lithium is used for the treatment of manic/depressive (bipolar) and depressive disorders. In addition, lithium increases the charged atoms such as sodium, potassium, calcium, and magnesium, which are in production of white blood cells in the bone marrow. It is therefore important to maintain the blood concentration in the 0.5-1.5 mM range. Lithium is ineffective for treatment if it is too low.[5]

1.2 Chemical sensors (Chemosensors)

As mentioned above, alkali cations play a fundamental role in a wide range of chemical and biological processes, and numerous efforts have been devoted to the development of abiotic receptors for cationic species.[6] There have been a number of reviews describing the chemistry of host molecules for cations.[7-11] In a related advanced supramolecular concept, recognition sites can be coupled to certain groups that are capable of "reporting" the cation coordination process. In this case, the binding process is transduced into a signaling event. Receptors specifically designed for sensing purposes are generally called chemosensors.[12] One basic design principle in these new multi component systems is that the sensing event has to be related with an easy to measure signal. In fact, many chemosensors display in the presence of a certain guest.

Typically, chemosensors are molecules of abiotic origin that are able to bind selectively and reversibly the analyte of interest with a concomitant change in one or more properties of the system, such as redox potentials, absorption or fluorescence spectra. Because of the two different processes occur during analyte detection, i.e., molecular recognition and signal transduction, chemosensors can usually be schematized as made of three possible different components (**Figure 1.2**): a receptor unit (responsible for the selective analyte binding), a signaling unit (whose properties should change upon complexation) and, eventually, a spacer that can change the geometry of the system and tune the electronic interaction between the two former moieties.[13-14]

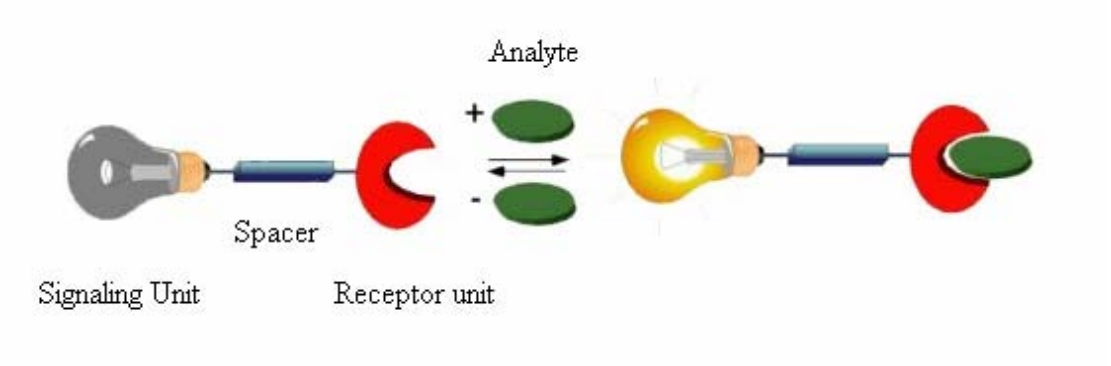

Figure 1.2 Cation chemosensors based on the binding site-signaling subunit approach

As we will see in **Figure 1.2**, many chemical sensors follow the approach of the covalent attachment of signaling subunits and binding sites as schematically shown. The coordination site binds the cation in such a way that the properties of the signaling subunit are changed in the color (chromogenic chemosensor). This has been the most widely used approach in the development of cation chemosensors and will surely be a fundamental approach in the future developments.[15-16]

The role of the signaling subunits is to act as a signal transducer. That is, it translates chemical information at the molecular level (the cation binding process) into a signal. Here, we will consider the use of spectroscopic signaling subunits able to transduce the coordination event into changes in color behavior.

If the spectroscopic characteristics of the signaling subunit in the molecular ensemble are different from those in its non-coordinated state, then the cation binding process is coupled to a signaling event. As can be inferred, the stability constant for the formation of the complex between the binding sites can be known. Only in this way will the displacement reaction take place; hence, the signaling event indicating the presence of the target cation will be observed. Additionally, selectivity can be achieved by a formation stability constant that occurs between the signaling unit and the potentially interfering cations. [17]

In this contest we have developed the series of chemosensors for alkali metal ions, with a particular attention for those having a relevant importance in biological and environmental systems. The selective detection of these ions in the presence of others in mixed solutions remains a challenging task.

1.3 Chromoionophores

Chromophores discovered independently by Kaneda et al. and by Dix and Vogle are reagents undergoing color changes upon interaction with ions.[18] A variety of method for the detection of cations in the solution are well established and have been extensively described by using chemosensor molecules whose optical properties change upon direct binding of the cations (*chromoionophores*).[19-20]

Molecular design of dyes exhibiting selective complex formation with ions is in the centre of current research interesting since such dyes can be used in optical sensors for the quantitative determination of particular ions in multi-ionic systems. In order to simplify the optimization of optically-based systems, in some cases, the ionophore and chromophore have been linked covalently.[21]

In the alkali metal salt complexes of ionophores, the positive cation charge influences the donor heteroatom (O, N, and S) and their electronic surrounding by ion-dipole forces. If one of the heteroatom is a constituent of chromoionophores, the electronic disturbance propagates the whole (n+π) system. Due to different influences on the ground and photo excited states by cations, changes occur in the absorption spectra. Basically, the change of color of chromoionophores occurs through two mechanisms. [22-23]

1.3.1 Cation-induced hypsochromic band shifts (blue shift)

When a chromoionophore contains an electron donor group conjugated to an aromatic ring (electron acceptor), it can complex a cation as well as being a chromophore. The amine nitrogen atoms of the chromoionophore are positively polarized, the excited states being more strongly destabilized by cations than the ground state, therefore, results in hypsochromic shifts (**Figure 1.3**).

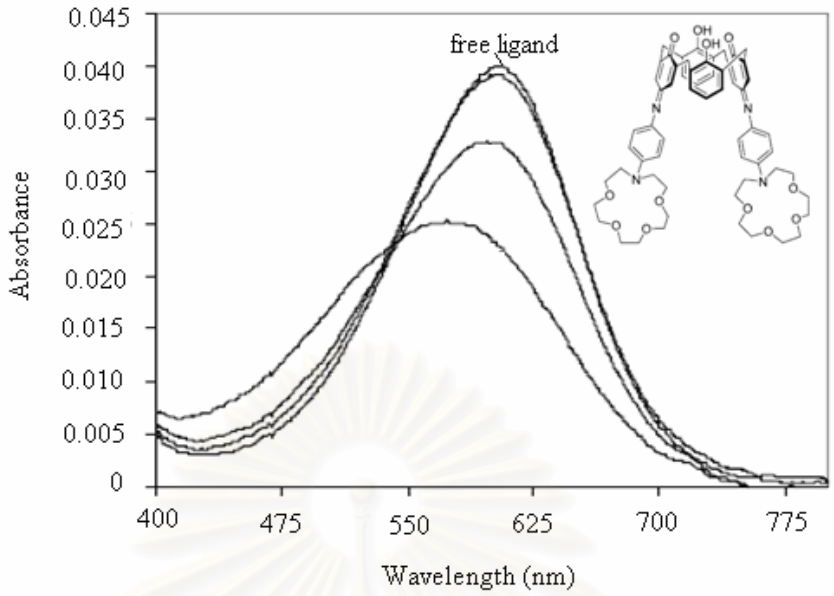

Figure 1.3 A chromoionophore which induces blue shift upon binding with guests [24]

The influence of the ligand ring size on the selectivity is obvious by the rule that the strongest maximum wavelength is always affected by the cation which best fits into the ligand cavity. The observable changes of the absorption spectra can be described satisfactorily by the electronic states. The chromophores are influenced by these ion-dipole forces, depending upon the size and direction of the dipole moment. The more the dipole moment alters during the excitation, the more the absorption band shifts.

1.3.2 Cation-induced bathochromic shifts (red shift)

When a chromoionophore contains an electron acceptor, it can give color change upon complexation. Because the donor atom will surely be polarized positively in the ground state, the excited states are more strongly stabilization by the binding of a cation at the acceptor site, causing bathochromic band shifts (**Figure 1.4**).

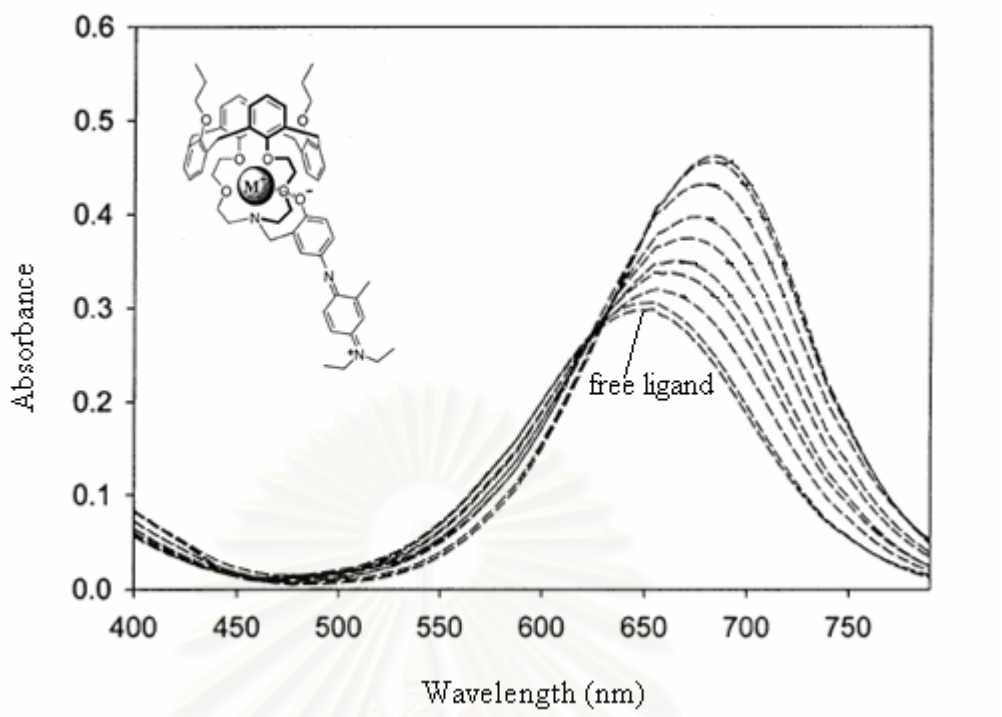

Figure 1.4 A chromoionophore which induces red-shift upon binding with guests [25]

1.4 Calix[4]arenes

In supramolecular chemistry, a wide variety of macrocyclic receptors are able to form host-guest complexes with neutral, anionic, and cationic species.[26-28] In particular, calix[4]arenes have received much attention as a result of their role as biological and synthetic receptor models and their easy single-step preparation.[29-31]

The flexible calixarene framework requires small energy changes to accommodate guests, which make them exceptionally resourceful host molecules [32]. Calix[4]arene compounds have been widely regarded as an important class of macrocyclic host molecules for a couple of decades, since they have selective and efficient binding properties for specific metal ions.[33-34] It is known that the calix[4]arenes are able to exist in the following four different conformations: cone, partial cone, 1,2-alternate, and 1,3-alternate (**Figure 1.5**).

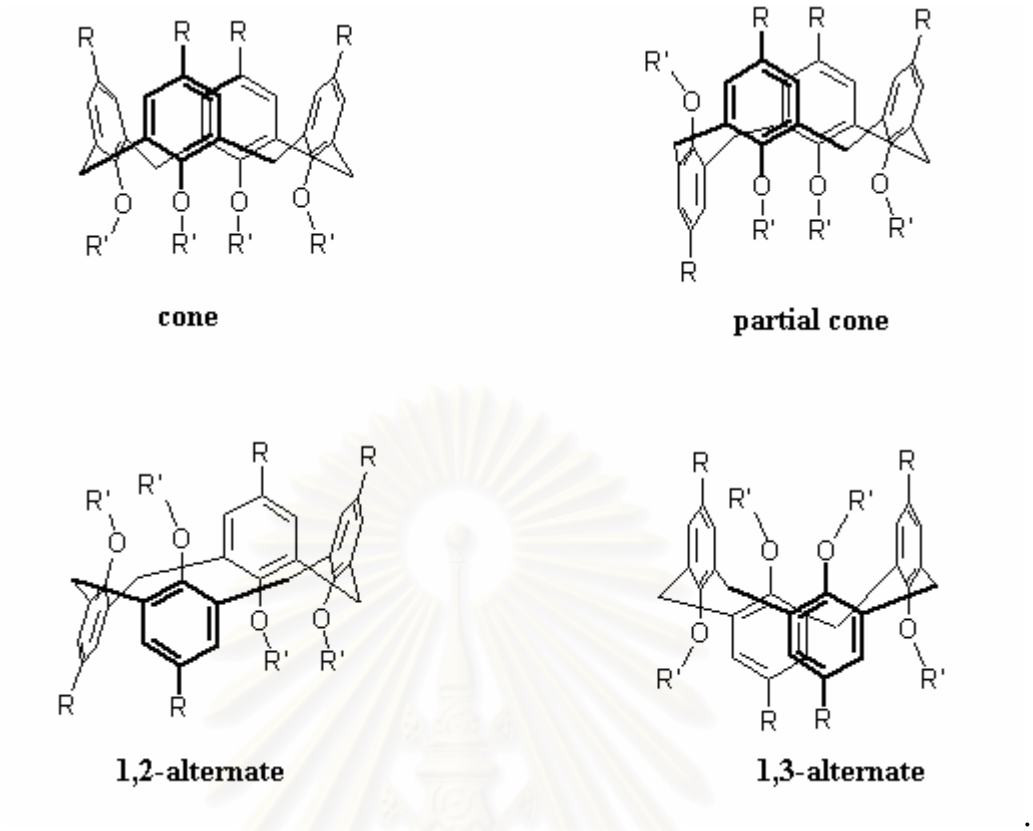

Figure 1.5 Four possible conformations of calix[4]arene

Wide and narrow rim functionalization of calix[4]arenes led to higher substrate specificity. Many artificial ionophores of calix[4]arene derivatives have known to exhibit interaction with the alkali metal ions which are very important cations in biological systems.[35-38] Kubo et al. found that the quinone carbonyl group of indoaniline-type ligands interacts with divalent metal ions to cause a pronounced color change.[39] Thus, the combined of the chromophore constrained within a calixarene receptor framework would be of great interest in the design of chromoionophore receptors. Among them, **1** containing two indoaniline chromophores designed to combine the specific complexation of the two ethyl acetate groups in a 1,3-fashion to oxygens on the narrow rim, shows a large bathochromic shift induced by the complexation of Ca^{2+}.

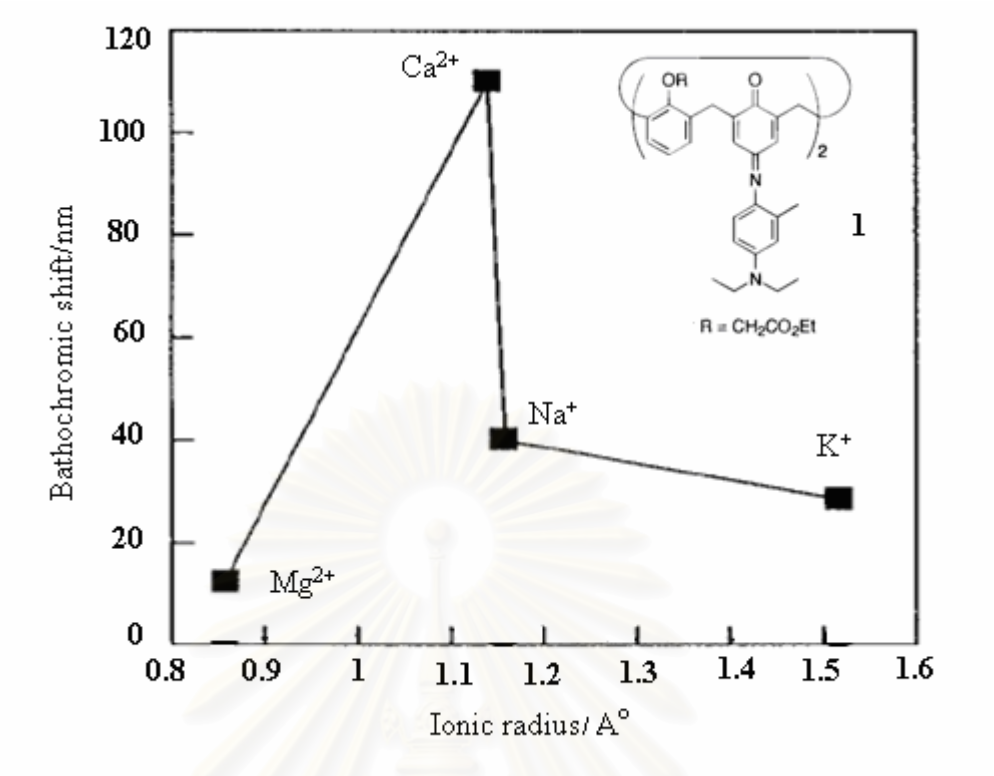

Figure 1.6 Influence of added cations on the absorption of **1** [39]

Liu et al. synthesized compound **2,** a calix[4]arene derivative containing two photochromic spirobenzopyran groups as chromophore, which can used to recognize lanthanide ions with naked eye sensor. When the colorless lanthanide solutions in acetonitrile were added to the purple solution of receptor **2** in acetonitrile, the color changed to yellow immediately and resulted in remarkable shifts of the UV-vis spectra. These spectroscopic properties might be applied to sense lanthanide ions by light (**Figure 1.7**).

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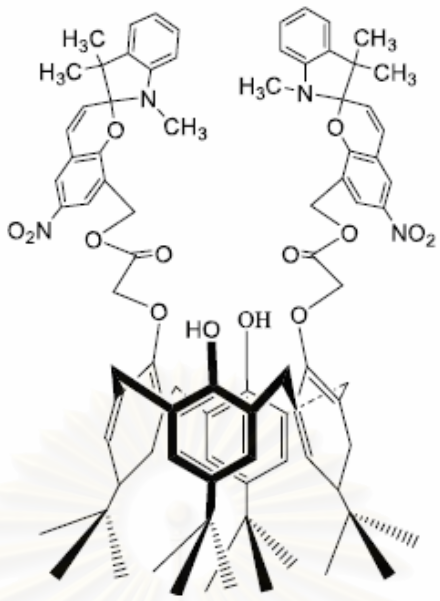

2

Figure 1.7 Color changes of compound **2** induced by metal ions [40]

1.5 Double Calix[4]arenes

Calix[4]arenes are macrocyclic building blocks constructed from phenols and formaldehydes.[41] There have been many attempts to design and synthesize receptor molecules with enforced cavities by using calix[4]arenes as a key structural motif. A variety of sophisticated compounds have been prepared from these starting materials by carrying out the reactions at the phenolic hydroxyl groups or at the *p*-position after the removal of the *p-tert*-butyl groups. The representatives are double or multiple calix[4]arenes which may be constructed through wide rim-wide rim linkage (or head to head), narrow rim-narrow-rim linkage (or tail to tail), wide rim-narrow rim linkage (or head to tail) or non-covalently generated through hydrogen bonding interactions (**Figure 1.8**). A number of double calix[4]arenes have been synthesized and their binding studies with metal ions have been reported. [42-44]

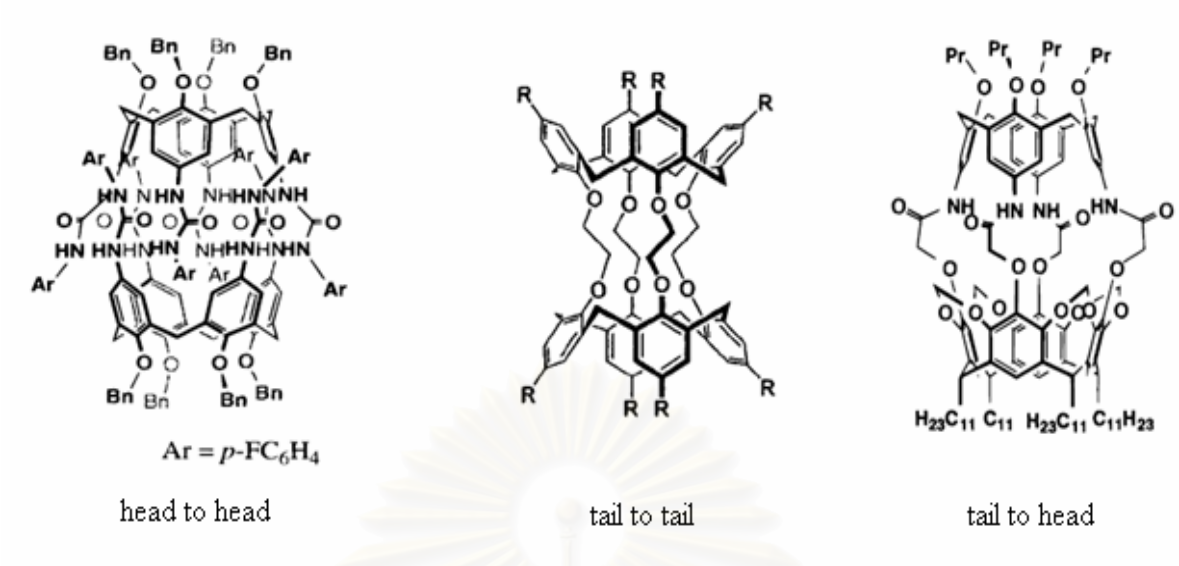

Figure 1.8 Example of double calix[4]arenes

The synthesis, structure and alkali metal ions extracting properties of double calix[4]arenes have been extensively investigated (**Figure 1.9**).[45] All of compounds **2-6** can be synthesized in just two steps from *p-tert*-calix[4]arene. It revealed that the length and nature of the bridging chain between the two calix[4]diquinone moieties crucially dictate the selectivity and strength of alkali metal ions.

Hence such molecules are extremely noteworthy for the development of optical sensors to measure the concentration of alkali metal species in clinical analysis. Therefore, if one could introduce an appropriated species it would cause a physical change in the opto-functional site which can be monitored by spectroscopy. As such, there has been emphasis on the double calix[4]arenes with the aim of developing new types of optical receptors.

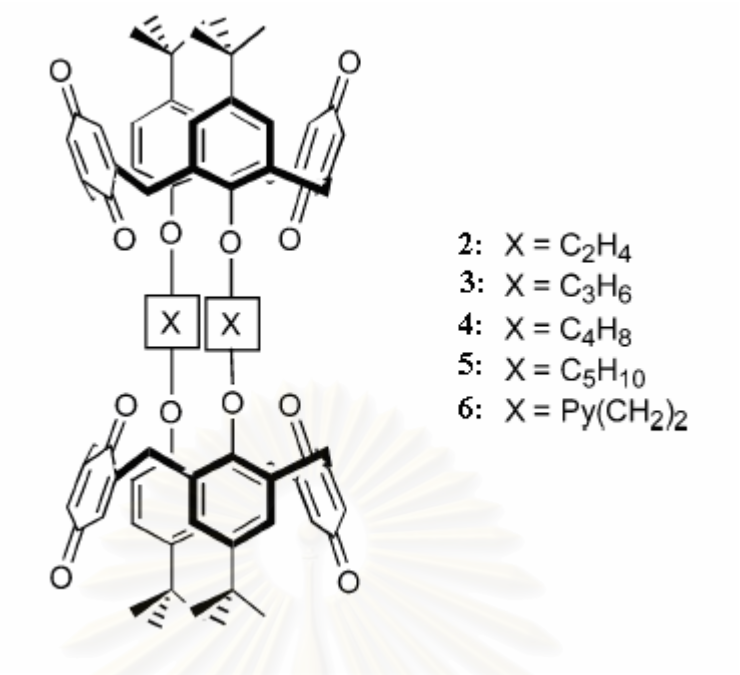

Figure 1.9 Double calix[4]arenes receptors: **2**, **3**, **4**, **5** and **6** [45]

1.6 Objective and the scope of this research

The objective of this research is to synthesize chromoionophores, employing calix[4]arene as a building block. The synthesis of double calix[4]arene containing indoaniline connecting through the wide rim, **L1**, **L2**, and **L3** have been described. Binding ability and selectivity towards alkali metal ions will be evaluated by means of UV-visible spectroscopy. The target molecules are shown below.

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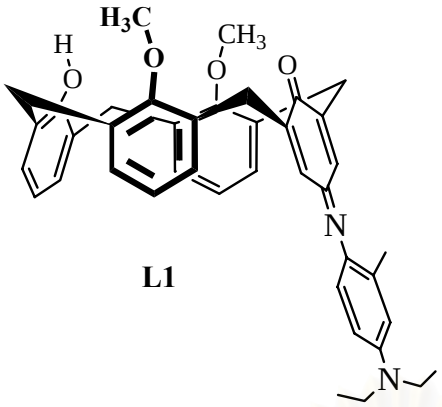
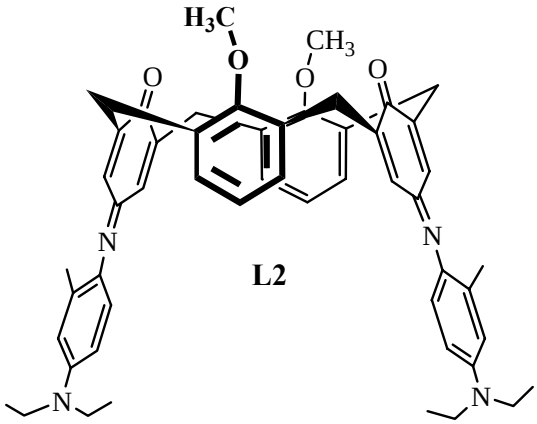
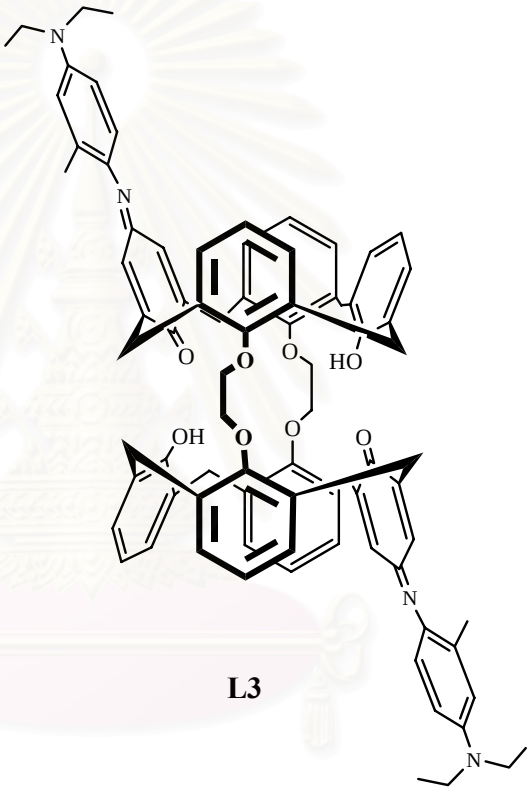


L1



L2



L3

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CHAPTER II

EXPERIMENTAL SECTION

2.1 General procedures

2.1.1 Analytical instrument

Nuclear magnetic resonance (NMR) spectra were recorded on a Varian 400 MHz nuclear magnetic resonance spectrometer. In all cases, samples were dissolved in deuterated chloroform and DMSO-d_6. The chemical shifts were recorded in part per million (ppm) using a residue proton solvents as internal reference. Elemental analysis was carried out on CHNS/O analyzer (Perkin Elmers PE 2400 series II). ESI mass and MALDI-TOF mass spectra were recorded on the Bruker and Biflex Bruker Mass spectrometer, respectively. Absorption spectra were measured by a Varian Cary 50 UV-vis spectrophotometer. IR spectrum of the samples were recorded on a Nicolet Impact 410 FTIR spectrophotometer at room temperature with the potassium bromide (KBr) disk method.

2.1.2 Materials

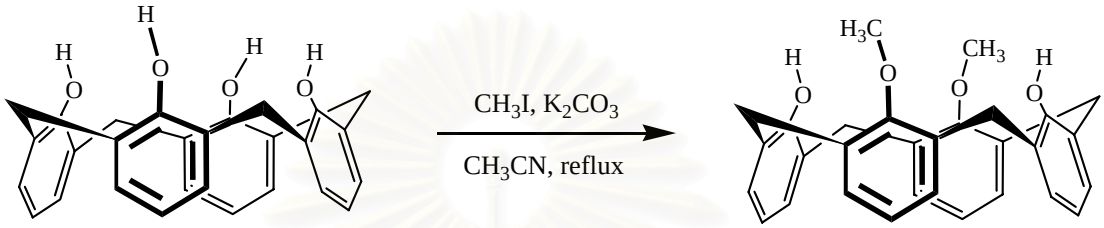
All materials were reagent grades purchased from Fluka, BDH, Aldrich, Carlo Erba and Merck or Lab-Scan were used without further purification. Commercial grade solvents such as acetone, dichloromethane, hexane, methanol and toluene were purified by distillation before used. Acetonitrile and dichloromethane for set up the reaction were dried over calcium hydride and freshly distilled under nitrogen atmosphere prior to use.

Column chromatography was carried out on silica gel (Kieselgel 60, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was performed on silica gel plates (Kieselgel 60, F_{254}, 1mm, Merck). Compounds on TLC plates were detected by the UV-light. Methanol and acetonitrile for UV-visible measurements (AR grade, Merck) were dried with molecular sieves. *p-tert*-Butyl calix[4]arene and calix[4]arene were synthesized using methods described in the literatures.[46-47]

All synthesized compounds were characterized by ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, mass spectrometry and elemental analysis.

2.2 Synthesis

2.2.1 Preparation of 25,27-dimethoxy-26,28-dihydroxycalix[4]arene (1a)



1a

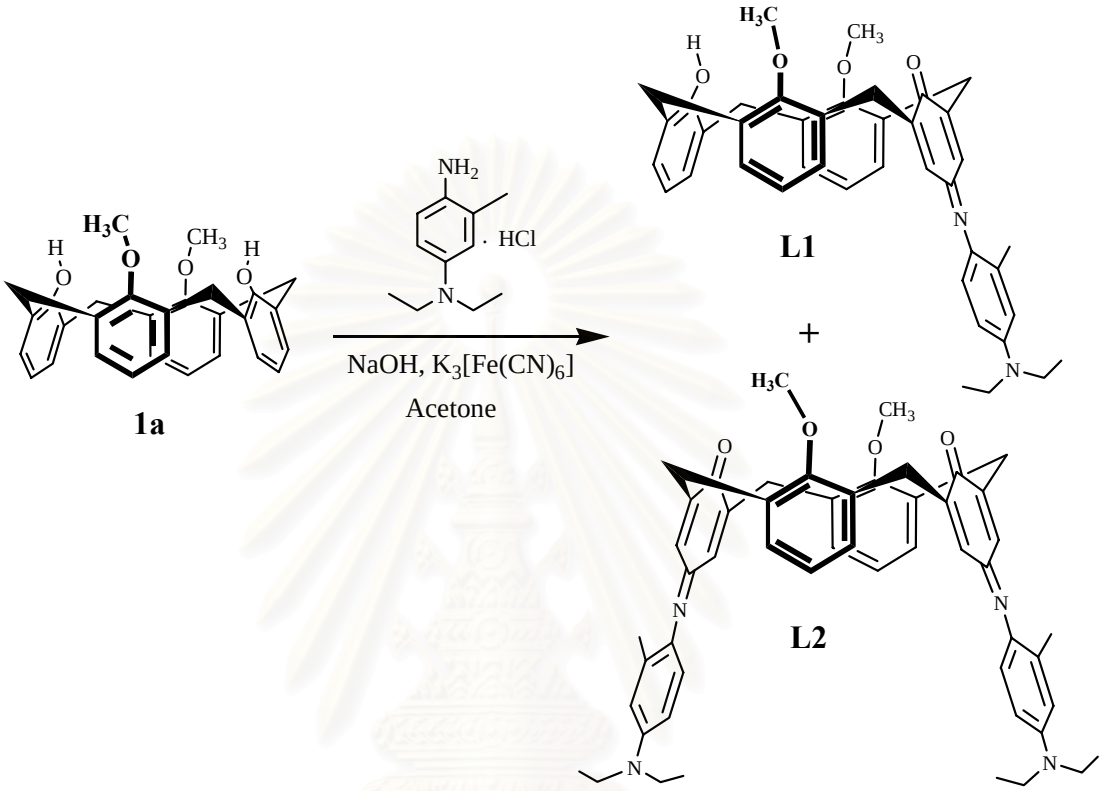
In a 250 mL two-necked round bottom flask equipped with a magnetic bar, calix[4]arene (4.016 g, 9.5 mmol), anhydrous potassium carbonate (1.444 g, 10.4 mmol) and acetonitrile (130 mL) were stirred under nitrogen atmosphere at room temperature for 30 mins. Methyl iodide (1.24 mL, 19.8 mmol) was then added, and the mixture was heated at reflux for 21 h. The mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (50 mL) and treated with 2 M hydrochloric acid and extracted with dichloromethane (2 x 25 mL), dried over anhydrous sodium sulphate, filtered and evaporated to dryness. The methanol was added to precipitate a white powder. White powder product **1a** was filtered from the organic solvent (3.224 g, 76 %).

Characterization data for 1a

^{1}H NMR spectrum (400 MHz, $CDCl_3$) : δ (in ppm)

δ 7.78 (s, 2H, ArO*H*), 7.12 (d, *J* = 7 Hz, 4H, *m*-*H*ArOCH$_3$), 6.92 (d, *J* = 8 Hz, 4H, *m*-*H*ArOH), 6.78 (t, *J* = 8 Hz, 2H, *p*-*H*ArOCH$_3$), 6.74 (t, *J* = 8 Hz, 2H, *p*-*H*ArOH),4.36 (AB, 4H$_A$, ArC*H*$_2$Ar), 4.02 (s, 6H, OC*H*$_3$), 3.46 (AB, 4H$_B$, ArC*H*$_2$Ar).

2.2.2 Preparation of 5-((4'-Diethylamino)-2'-mehtylphenyl)imino)-25,27-dimethoxy-28-hydroxy-26-one (L1) and 5,17-Bis((4'-Diethylamino)-2'-methylphenyl)imino)-25,27-dimethoxy-26,28-dione (L2)



In a 250 mL two-necked round bottom flask equipped with a magnetic bar, 25,27-dimethoxy-26,28-dihydroxycalix[4]arene **1a** (0.226 g, 0.5 mmol), *N*,*N*′-dimethyl-2-methyl-1,4-phenylenediamine monohydrochloride (0.430 g, 2 mmol) and NaOH (0.200 g, 5 mmol, in 2 mL H_2O) in acetone (50 mL) were stirred under nitrogen atmosphere at room temperature for 30 mins. The aqueous solution of $K_3[Fe(CN)_6]$ (1.317 g, 2 mmol) was then added dropwise and the mixture was stirred at room temperature for 2 h. The water (100 mL) was added into the mixture. Organic solvent was removed by a rotary evaporator. Crude product was filtered from the aqueous, dried in *vacuo*, and chromatograph on silica gel using mixtures of ethylacetate/CH_2Cl_2 as eluents to provide compounds **L1** (0.037g, 14%) and **L2** (0.124 g, 48%).

Characterization data for L1

^{1}H NMR spectrum (400 MHz, $CDCl_3$: δ (in ppm)

δ 7.23-6.80 (br, 6H, *m-H*ArCH$_3$, *m-H*ArOH), 6.95 (br, 1H, *o-H*ArNCH$_3$), 6.44 (t, *J* = 8 Hz, 3H, *p-H*ArOH, *p-H*ArOCH$_3$), 6.22 (br, 1H, *m-H*ArNR), 5.29 (s, 2H, *m-H* quinone), 3.38 (q, *J* = 7.2 Hz, 4H, CH$_3$C*H*$_2$NAr), 2.14 (s, 3H, C*H*$_3$ArNR), 1.20 (t, J = 6.8 Hz, 6H, C*H*$_3$CH$_2$NAr).

^{13}C NMR spectrum (100 MHz, DMSO-*d*$_6$+$CDCl_3$): δ (in ppm)

δ 12.44, 18.57, 28.70, 28.90, 43.80, 58.70, 112.68, 115.31, 118.71, 121.52, 122.44, 123.15, 126.38, 126.80, 128.80, 129.10, 129.68, 130.36, 131.23, 136.50, 146.58, 147.39, 152.01, 155.82, 187.00.

ESI-MS spectrum : $C_{41}H_{42}N_2O_4$ + 2·H_2O , m/z = 663.34: Cald., m/z = 662.83.

Elemental Analysis

Anal calc. for $C_{41}H_{42}N_2O_4$+Na^+: C, 75.77; H, 6.52; N, 4.31.

Found: C, 75.31; H, 6.72; N, 4.52.

Characterization data for L2

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ (in ppm)

δ 5.28 (s, 4H, *m-H* quinone), 3.40 (q, *J* = 7.2 Hz, 8H, CH$_3$C*H*$_2$NAr), 2.13 (s, 6H, C*H*$_3$ArNR), 1.20 (t, J = 6.8 Hz, 12H, C*H*$_3$CH$_2$NAr).

^{13}C NMR spectrum (400 MHz, $CDCl_3$): δ (in ppm)

δ 12.46, 18.60, 32.92, 43.83, 58.71, 112.85, 113.06, 117.93, 122.48, 123.08, 129.12, 129.15, 131.26, 137.82, 146.59, 147.41, 152.00, 155.83, 184.46.

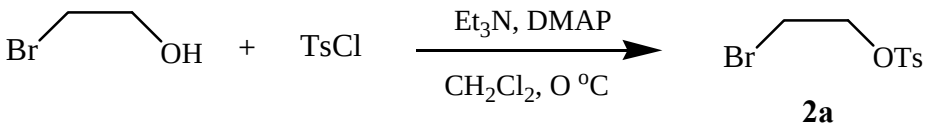
ESI-MS spectrum : $C_{52}H_{56}N_4O_4$, m/z = 801.53: Cald., m/z = 801.04.

Elemental Analysis

Anal calc. for $C_{52}H_{56}N_4O_4$: C, 77.97; H, 7.05; N, 6.99.

Found: C, 77.02; H, 6.99; N, 6.87.

2.2.3 Preparation of 2-bromoethyl-4-eththylbenzenesulfonate (2a)



2a

In a 250 mL two-necked round bottom flask equipped with a magnetic bar, 2-bromoethanol (5.004 g, 40 mmol), triethylamine (4.103 g, 40.5 mmol), a catalytic amount of DMAP and dichloromethane (160 mL) were stirred under nitrogen atmosphere at room temperature for 30 mins. Toluene-4-sulfonylchloride (TsCl) (8.098 mL, 40.5 mmol) was added dropwise and the mixture was stired at 0 ^{o}C for 4 h. The solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (50 mL) and treated with 2 M hydrochloric acid until no bubble, extracted with dichloromethane (2 x 25 mL) and washed with water (5 x 15 mL). The organic layer was dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure. The product was chromatographed on silica column with 30% hexane:CH_2Cl_2 to give **2a** as a yellow liquid after evaporation (7.930 g, 71%).

Characterization data for 2a

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ (in ppm)

δ 7.80 (d, *J* = 8.4 Hz, 2H, H_AAr), 7.36 (d, *J* = 8.0 Hz, 2H, H_BAr), 4.27 (t, *J* = 6.8 Hz, 2H, BrC*H2*), 3..36 (t, *J* = 6.4 Hz, 2H, OCH_2), 2.44 (s, 3H, ArCH_3).

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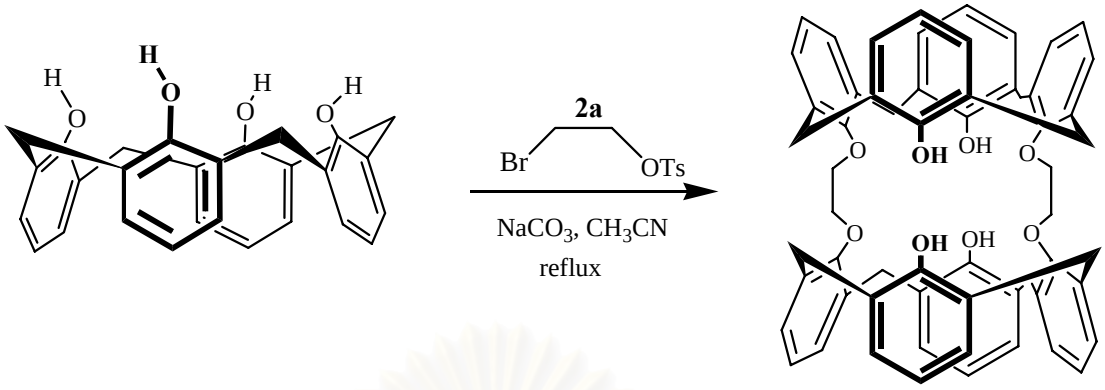
2.2.4 Preparation of Double Calix[4]arene (3a)



3a

In a 100 mL two-necked round bottom flask equipped with a magnetic bar, calix[4]arene (4.511 g, 10.6 mmol), anhydrous sodium carbonate (3.387 g, 31.9 mmol) and acetonitrile (60 mL) were stirred under nitrogen atmosphere at room temperature for 30 mins. Compound **2a** (1.65 mL, 26.55 mmol) was then added dropwise and the mixture was heated at reflux for 5 days. The mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (50 mL) and treated with 2 M hydrochloric acid and extracted with dichloromethane (2 x 25 mL). The organic layer was extracted with water (25 mL), dried over anhydrous sodium sulphate, filtered and evaporated to dryness. The methanol was subsequently added to precipitate a white powder **3a** (1.421 g, 32%).

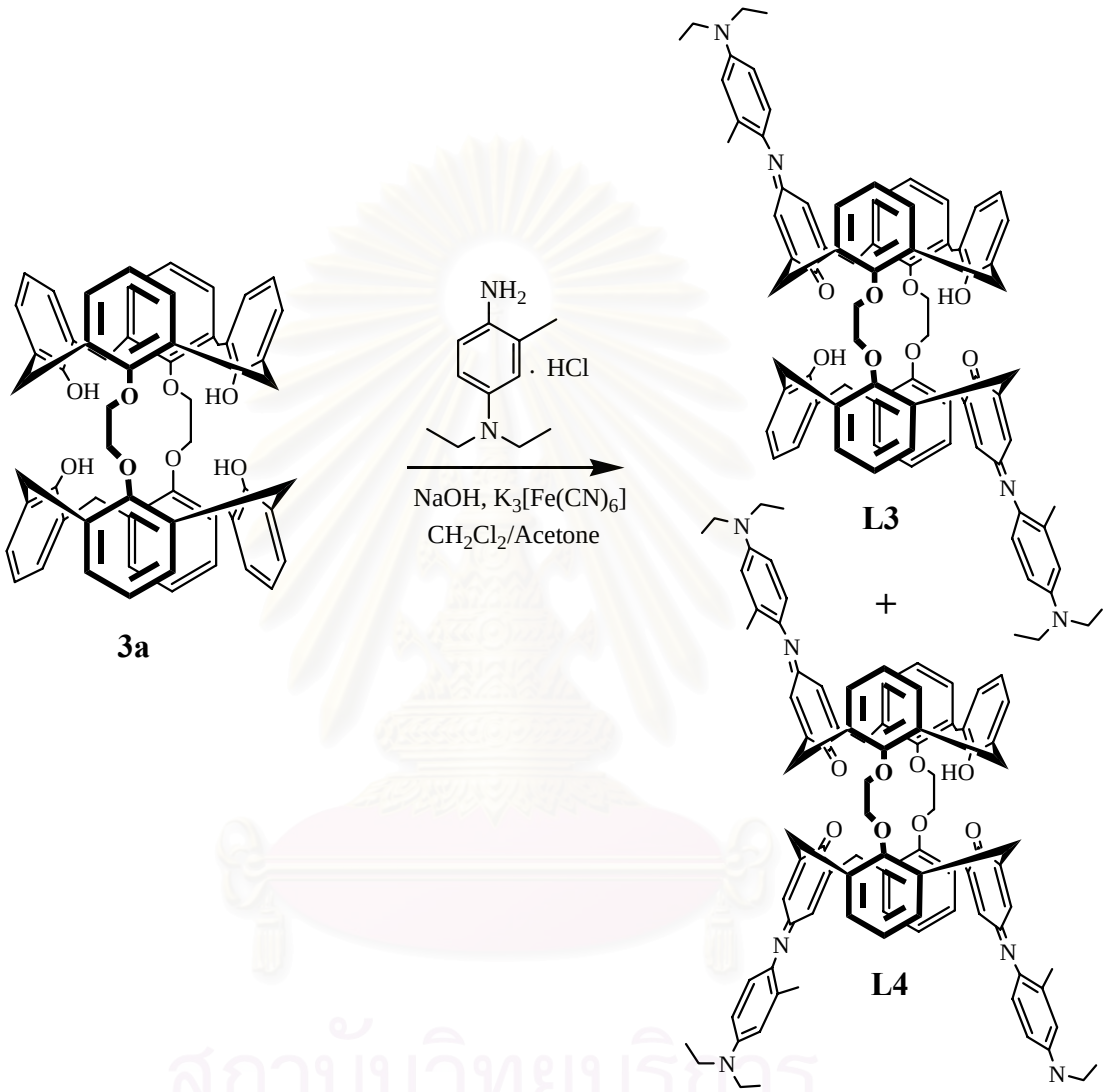
Characterization data for 3a

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ (in ppm)

δ 8.00 (s, 4H, ArO*H*), 6.97 and 6.90 (dd, *J* = 7.2 Hz, *J* = 7.6 Hz,16H, m-*H*ArOR, m-*H*ArOH), 6.71 (t, J = 7.2 Hz, 4H , *p*-*H*ArOR), 6.54 (t, *J* = 8.0 Hz, 4H , *p*-*H*ArOH), 4.58 (s, 8H, OCH_2CH_2O), 4.52 (AB, 4H_A, ArCH_2Ar,), 3.41 (AB, 4H_B, ArCH_2Ar,).

MALDI-TOF spectrum : $C_{60}H_{52}O_8 + Na^+$, m/z = 923.08: Cald., m/z = 924.06.

2.2.5 Preparation of Double calix[4]diquinone (L3) and Double calix[4]triquinone (L4)



In a 250 mL one necked round bottom flask equipped with a magnetic bar, double calix[4]arene **3a** (0.225 g, 0.25 mmol) in CH_2Cl_2 (200 mL) was stirred under nitrogen and warmed for 30 mins. In a 500 mL two necked round bottom flask equipped with a magnetic bar, *N,N'*-dimethyl-2-methyl-1,4-phenylenediamine monohydrochloride (0.859 g, 4 mmol) and NaOH (0.25 g, 6.25 mmol, in 2 mL H_2O) in acetone were stirred under nitrogen atmosphere at room temperature for 60 mins. The aqueous solution of $K_3[Fe(CN)_6]$ (1.317 g, 2 mmol) was then added dropwise and the mixture was stirred at room temperature for 2 h. The water (100 mL) was added into the mixture. Organic solvent was removed by a rotary evaporator. Crude product

was filtered from the aqueous, dried in *vacuo*, and chromatographed on silica gel using mixtures of MeOH/CH_2Cl_2 as eluents to provide compound **L3** (0.067 g, 21%) and **L4** (stick on the column).

Characterization data for L3

^{1}H NMR spectrum (400 MHz, $CDCl_3$) : δ (in ppm)
δ 7.29 (d, J = 6.4, 2H, *m-H*ArNR), 6.57-7.22 (m, 22H, *m-H*ArOCH$_3$, *m-H*ArOH, *p-H*ArOCH$_3$, *p-H*ArOH, m-*H*ArN, m-*H*ArCH$_3$), 6.04 (br, 4H, m- *H* quinone), 4.78-4.28 (m, 16H, OHArC*H*$_2$ArOR, OC*H*$_2$C*H*$_2$O), 3.56-3.11 (m, 16H, CH$_3$C*H*$_2$NAr, ROArC*H*$_2$quinonoe), 2.39 (s, 6H, C*H*$_3$ArNR), 1.25 (t, J = 6.8 Hz, 12H, C*H*$_3$CH$_2$NAr).

ESI-MS spectrum : $C_{82}H_{80}N_4O_8$+ Na^+, m/z = 1,271.50: Cald., m/z = 1,272.55.

Characterization data for L4

ESI-MS spectrum : $C_{93}H_{94}N_6O_8$ + Na^+, m/z = 1,446.54: Cald., m/z = 1,446.79.

2.3 Complexation studies

2.3.1 Complexation between compounds L1 and L2 with alkali metal ions using UV spectrophotometric titration

A solution of 1x10^{-5} M of a ligand in a 0.01 M tetraethyl ammonium chloride were prepared by adding 5 mL of a stock solution of ligand (1x10^{-4} M) in a 50 mL volumetric flask. A solution of 5.33x10^{-5} M of an alkali metal ion (Li^+, Na^+, K^+, Rb^+ and Cs^+ as chloride salt) in dried methanol were prepared in a 50 mL volumetric flask.

UV-vis spectra of all ligands and cation complexes were recorded at ambient temperature. The spectrum was recorded from 200-800 nm. The solution of a guest was added directly to 2.00 mL of the ligand (1x10^{-5} M) in a cuvette by a volumetric pipette.

2.3.2 Complexation between compound L3 with alkali metal ions using UV spectrophotometric titration

A solution of $1x10^{-5}$ M of a ligand in a 0.01 M tetraethyl ammonium chloride were prepared by adding 5 mL of a stock solution of ligand ($1x10^{-4}$ M) in a 50 mL volumetric flask. A solution of $5.33x10^{-5}$ M of an alkali metal ion (Li^+, Na^+, K^+, Rb^+ and Cs^+ as chloride salt) in dried methanol were prepared in a 50 mL volumetric flask.

UV-vis spectra of **L3** and cation complexes were recorded at ambient temperature. The spectrum was recorded from 200-800 nm. The solution of a guest was added directly to 2.00 mL of $1x10^{-5}$ M ligand in a cuvette by a microburette. The mixture was stirred for 30 seconds after each addition and its spectral variation was recorded. The volume added were 0.001 mL (5 additions), 0.01 mL (1 addition), 0.02 mL (4 additions), 0.1 mL (4 additions) and 0.2 mL (5 additions) which lead to 20 spectra including the ligand spectrum. The stability constants were calculated from spectrometric data using SIRKO program. **Table 2.1** shows concentrations of cations in titration experiments.

Table 2.1 The concentrations of alkali metal ions (M^+) were used in UV-vis titration with **L3.**

Point	M^+/**L3**	[**L3**] mM	[M^+] mM	V of M^+ (mL)	V_{total} (mL)
1	0.00	0.01	0	0.000	2.000
2	0.53	0.009990	0.005328	0.002	2.002
3	1.07	0.009980	0.010645	0.004	2.004
4	1.60	0.009970	0.015952	0.006	2.006
5	2.13	0.009960	0.021248	0.008	2.008
6	2.67	0.009950	0.026534	0.010	2.010
7	5.33	0.009901	0.052805	0.020	2.020
8	10.67	0.009804	0.104575	0.040	2.040

9	16.00	0.009709	0.155339	0.060	2.060
10	21.33	0.009615	0.205127	0.080	2.080
11	26.67	0.009524	0.253967	0.100	2.100
12	53.33	0.009091	0.484845	0.200	2.200
13	80.00	0.008696	0.695648	0.300	2.300
14	106.67	0.008333	0.888883	0.400	2.400
15	133.33	0.008000	1.066660	0.500	2.500
16	186.67	0.007407	1.382707	0.700	2.700
17	240.00	0.006897	1.655162	0.900	2.900
18	293.33	0.006452	1.892461	1.100	3.100
19	346.66	0.006061	2.100997	1.300	3.300
20	400.00	0.005714	2.285700	1.500	3.500

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CHAPTER III

RESULTS AND DISCUSSION

3.1 Design concept

One attractive research field is the construction of optical sensors. Such a system generally consists of two parts. One is the cation-binding part employing various combinations of O, N or S as donor atoms. The other is the chromophore part which converts the binding event into an optical signal. These two parts can be either covalently attached or intermolecularly linked. According to previous studies, calix[4]arenes functionalized with appropriate cation-ligating groups, such as carboxylic acid, amide, crown ether, and azacrown ether groups, are good candidates for cation receptors due to their high selectivity toward specific cations.[48]

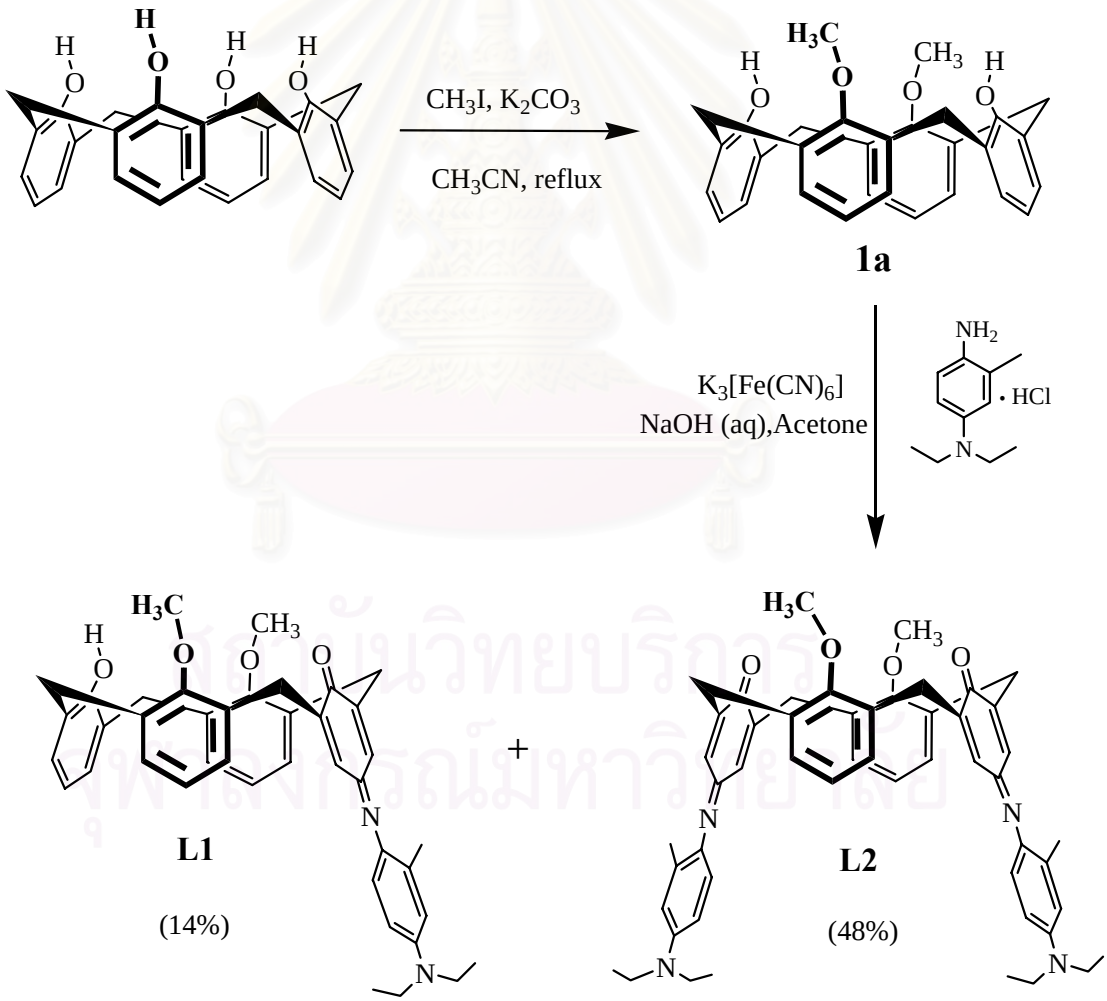
During our studies on the calix[4]arene-alkali metal ion interactions, this system offers a unique possibility of controlled change of molecular structure and hence change of complexation ability. Such a system is double calix[4]arenes with preorganised cavity for binding metal ions. It has been found that metal ions exclusively bound in the cavity of a double calix[4]arene through π-cation and ion-dipole interactions.[49-50] The objectives of our studies are to synthesize double calix[4]arene derivatives and to measure their abilities to bind alkali metal ions.

Indoaniline dyes are blue in color and typical donor-acceptor chromophores. Complexation of three new chromogenic calix[4]arene-indoaniline derivatives toward alkali metal ions have been studied by measuring their UV-vis spectra change.[51-52] Therefore, the connection between double calix[4]arene with the indoaniline dye will provide indoaniline-derived calix[4]arenes which were expected to bind and sense alkali metal ions.

3.2 Synthesis and characterization of indoaniline-derived calix[4]arenes

3.2.1 Synthesis and characterization of compounds L1 and L2

Recently, indoaniline derivatives have been used as chromogenic sensors.[24-25] These intense blue dyes can be easily prepared by the reaction of (*N*,*N*′-dialkylamino)aniline with phenols under oxidative conditions.[53] Calix[4]arenes which prove themselves to be very useful scaffolds for sensor design were coupled with indoaniline to yield remarkable chromoionophores. Synthesis of compounds **L1** and **L2** have been carried out by following the literature procedure and are outlined in **Scheme 3.1**.[39]



Scheme 3.1 Synthesis pathway for compounds **L1** and **L2**

The first step to synthesize **L1** and **L2** was the selective functionalization of two phenolic hydroxyl groups on the narrow rim of the calix[4]arene. The dimethoxy **1a** was prepared by alkylation of calix[4]arene with 2 equivalents of CH_3I in the presence of ten equivalents of potassium carbonate as a base in refluxing acetonitrile.

A reaction of 25,27-dimethoxy-26,28-dihydroxycalix[4]arene **1a** (**Figure A1**) with *N*,*N*′-dimethyl-2-methyl-1,4-phenylenediamine monohydrochloride under alkali conditions in the presence of $K_3[Fe(CN)_6]$ as an oxidizing agent afforded two types of indoaniline-derived calix[4]arenes: **L1** "monoquinone" with one hydroxyl group and two methoxy groups while and **L2** "diquinone" with two quinone and two methoxy groups. Compounds **L1** and **L2** were separated by column chromatography using ethylacetate/CH_2Cl_2 as eluents. ^{1}H NMR spectra of **L1** and **L2** are shown in **Figure A2** and **A3**, respectively.

^{1}H NMR spectrum of compound **L1** shows a triplet of C*H*$_3$CH$_2$NAr, a singlet of C*H*$_3$ArNR and a quartet of CH$_3$C*H*$_2$NAr at 1.20, 2.14 and 3.38 ppm, respectively, as well as a singlet peak of the quinone protons appear at 5.29 ppm. Unfortunately, the other NMR peaks were so broad because the conformational interconversion is somewhat slow on the NMR time scale as shown in **Figure A2**.

In the case of ^{1}H NMR spectrum of compound **L2**, it has the same pattern as **L1**. It showed a triplet of C*H*$_3$CH$_2$NAr, a singlet of C*H*$_3$ArNR and a quartet of CH$_3$C*H*$_2$NAr at 1.20, 2.13 and 3.40 ppm, respectively, as well as a singlet peak of the quinone protons appear at 5.28 ppm. However, other NMR peaks were so broad because of the conformation interconversion. The ^{1}H NMR spectrum of **L2** is shown in **Figure A3**.

Mass spectrum of **L1** and **L2** show signals at 663.34 and 801.53 m/z indicating the existence of **L1** and **L2**, respectively (**Figures A4, A5**). Moreover, the results from elemental analysis agree with the proposed structure.

Besides indoaniline, the oxidation of *N*,*N*′-dimethyl-2-methyl-1,4-phenylenediamine monohydrochloride also provided an azo indoaniline. A suitable crystal for X-ray study solid is obtained unexpectedly. It was grown by slow evaporation of a CH_2Cl_2/MeOH solution of the azo indoaniline. The ORTEP diagram is illustrated in **Figure 3.1**.

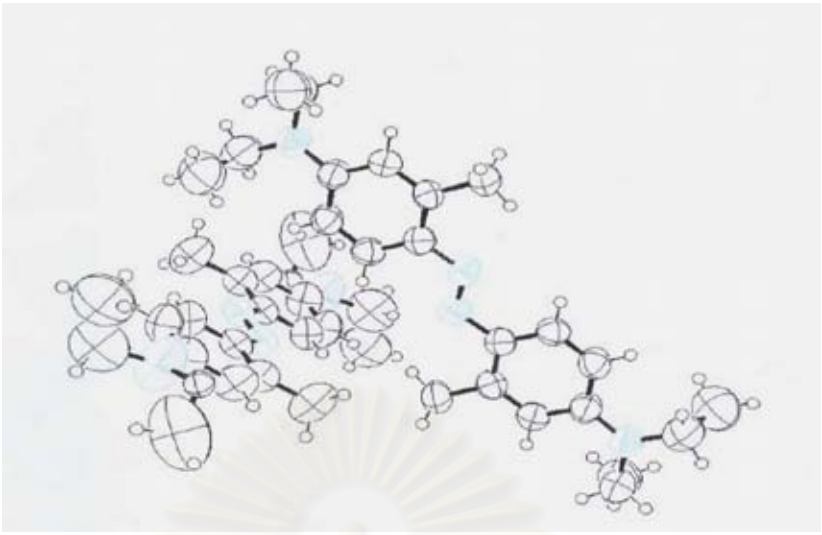


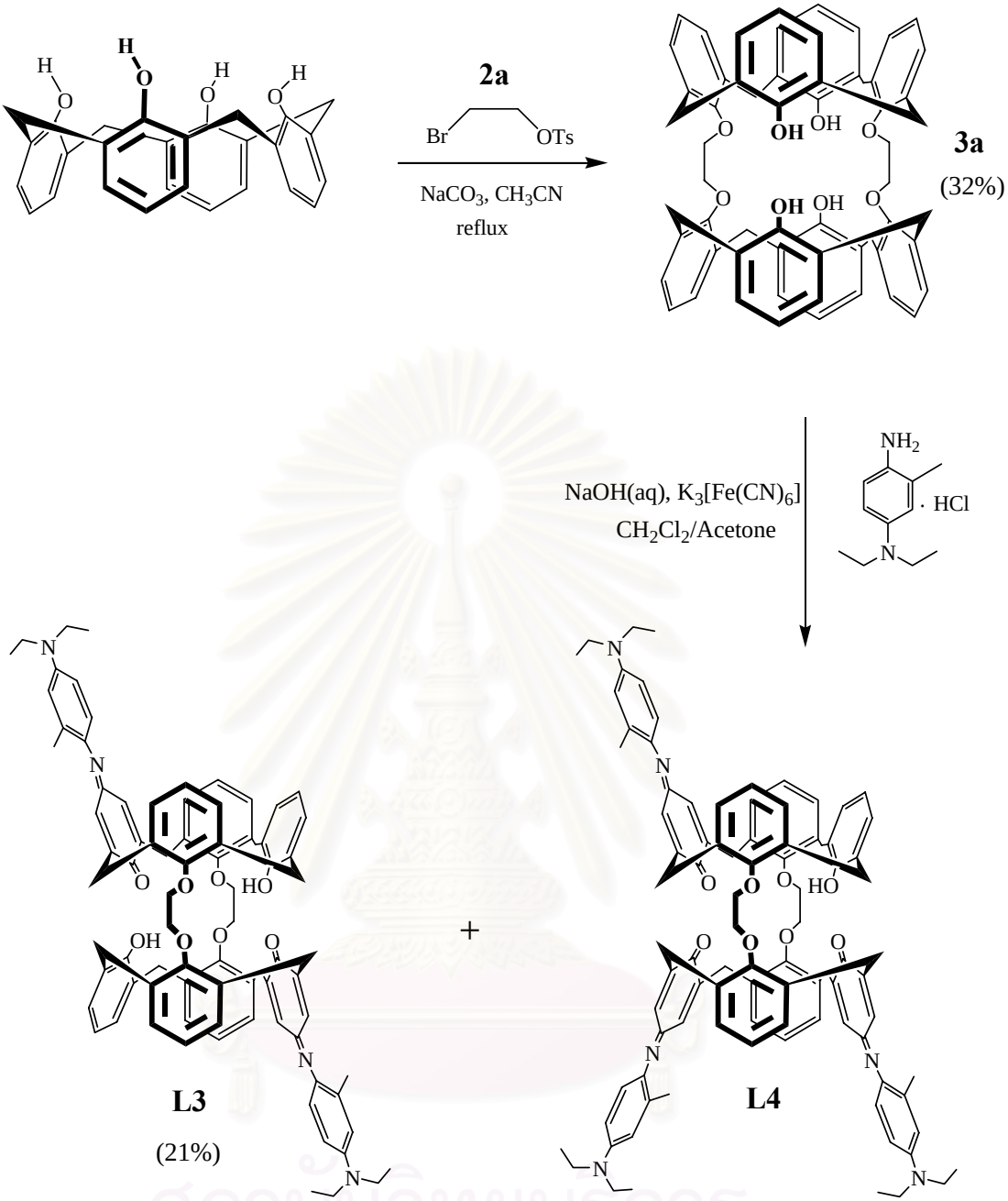
Figure 3.1 X-ray crystal structure of azo indoaniline

3.2.2 Synthesis and characterization of compounds L3 and L4

3.2.2.1 Synthesis and purification of compound L3

The synthesis of double calix[4]arene **3a** was carried out by adapting the method described by Kerdpaiboon et al. Nucleophilic substitution reaction of calix[4]arene with 2-bromoethyl-4-eththylbenzenesulfonate **2a** in acetonitrile using anhydrous sodium carbonate as base refluxed for 5 days. The white crystalline solid of double calix[4]arene is obtained in 32% yield. From ^{1}H NMR spectrum in **Figure A7**, this compound is in cone conformation due to the presence of ArCH_2Ar protons as two doublet at 4.52 and 3.41 ppm. The bridging glycolic protons (OCH_2CH_2O) appear at 4.58 ppm. The result from mass spectrometry shows signal at 923.08 m/z (**Figure A8**) that agrees with the proposed structure.

Synthesis of compounds **L3** and **L4** were carried out as shown in **Scheme 3.2**. [39] The synthesis of double calix[4]arene coupled with indoaniline is more complicate than that of **L1** and **L2** because the solubility of **3a** is very poor. The only way to synthesize compound **L3** and **L4** was to dissolve **3a** with warming in a large amount of CH_2Cl_2. Finally, coupling with indoaniline under alkali conditions in the presence of $K_3[Fe(CN)_6]$ as an oxidizing agent was carried out in dried acetonitrile. The purification of dark blue crude was performed using a silica gel column and employing mixture of MeOH/CH_2Cl_2 as eluents. **L3** was obtained as a blue solid in 21% yield while most of **L4** was stuck on the silica gel column.



Scheme 3.2 Synthesis pathway for compounds **L3** and **L4**

^{1}H NMR spectrum of **L3** shows a triplet of C*H*$_3$CH$_2$NAr and a singlet of CH$_3$ArNR at 1.25 and 2.39 ppm, respectively, as well as a singlet peak of the quinone protons appear at 6.04 ppm. The other ^{1}H NMR peaks were so broad, because the conformational interconversion is somewhat slow on the NMR time scale as shown in **Figure A9**. However, the result from mass spectrometry shows signal at 1,271.50 m/z that agrees with the proposed structure (**Figure A10)**.

3.2.2.2 Attempts to purify compound L4

In the case of **L4**, unfortunately, this compound stuck to the silica gel column. After the silica gel was stirred with methanol overnight, only a small amount of **L4** is obtained. The result from mass spectrometry is shown in **Figure A11**. The desired product **L4** is not yet pure. The purification of **L4** is a challenging task to pursue.

3.3 Cation complexation studies

3.3.1 Complexation studies of compounds L1 and L2 with Li^+, Na^+, K^+, Rb^+ and Cs^+.

Compounds **L1** and **L2** contain monoquinone and diquinone moieties, respectively which can possibly bind alkali metal ions. Thus complexation studies of compounds **L1** and **L2** with Li^+, Na^+, K^+, Rb^+ and Cs^+ using Cl^- as a counteranion were carried out in polar solvents such as methanol and acetonitrile. Compounds **L1** and **L2** consisted of quinone and indoaniline group as two different chromophores (**Scheme 3.1**). The cation recognition *via* ion-dipole interactions can also be easily monitored by cation complexation induced change in UV-vis spectra. However, upon addition of alkali metal ions to compounds **L1** and **L2** did not disturb the UV-vis spectrum significantly as shown in **Figure 3.2**. Therefore, only **L3** was subjected to titration.

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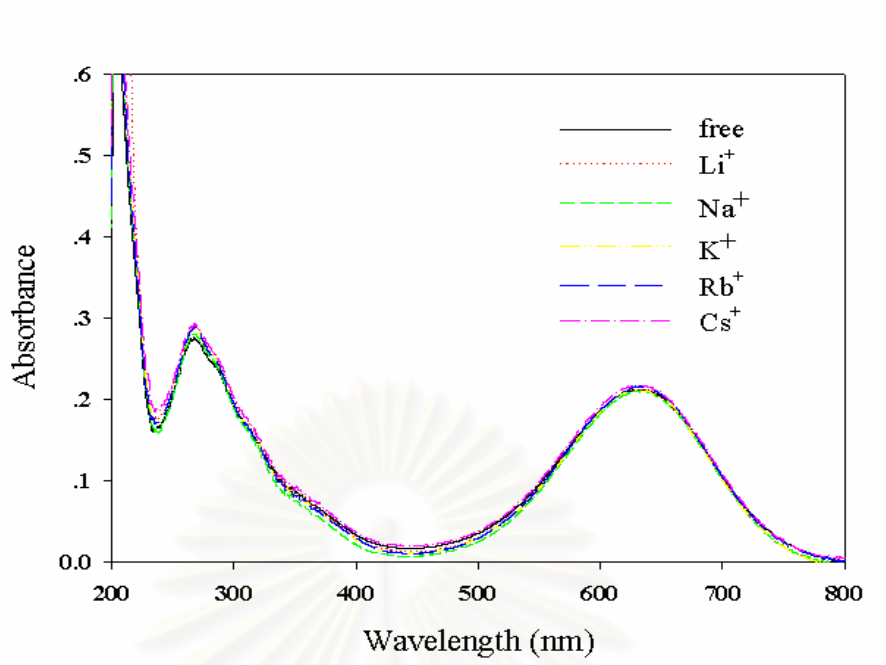

Figure 3.2 A change of ligand spectrum upon addition of 400 equiv. of alkali metal ions to a solution of **L1** in 99% MeOH ; [**L1**] = 1 x 10^{-5} M

3.3.2 Complexation studies of compound L3 with Li^+, Na^+, K^+, Rb^+ and Cs^+.

This absorbance range may be used as a criterion of complex formation because strong complexation usually results in large change in both absorption position and intensity. These findings consider that a metal ion, which is encapsulated in the cavity of **L3**, could cause a significant ion-dipole interaction with two quinone carbonyl groups of the chromophores and then would induce some intense spectral change in absorption.

Regarding the double calix[4]diquinone, compound **L3** absorbs at 280 and 643 nm in MeOH (**Figure 3.3**). The two possible chromophores in the compound are the *phenolic* groups of calix[4]arene and the *indoaniline* groups. From the literature [54-55] the phenolic group of calix[4]arene shows peak maxima at 270-290 nm. Therefore, the peak maxima at 280 nm must be originated from phenolic group of calix[4]arene. Another peak maximum at 643 nm in this compound **L3** is belonging to indoaniline chromophore. However, the changes of ligand spectra with alkali metal

ions are more significant at 643 nm. Therefore, only the peak at 643 nm is monitored for complexation studies.

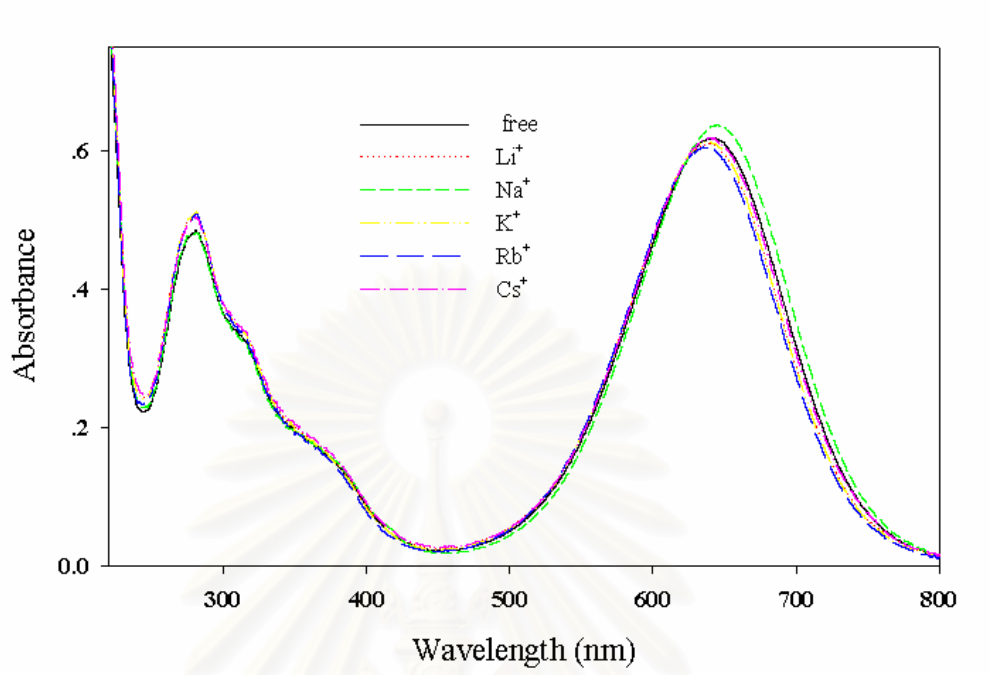

Figure 3.3 A change of ligand spectrum upon addition of 400 equiv. of alkali metal ions to a solution of **L3** in 99% MeOH; [**L3**] = 1 x 10^{-5} M

The alkali metal ions studied are Li^+, Na^+, K^+, Rb^+ and Cs^+. Free **L3** exhibited absorption band at 643 nm. The λ_{max} changes ($\Delta\lambda_{max}$) upon the metal ion addition are listed in **Table 3.1** as well. As seen in **Figure 3.3** both hypsochromic and bathochromic shifts were found depending on the systems studied. For Li^+, K^+, Rb^+ and Cs^+ cause hypsochromic shift while Na^+ results in bathochromic shift. These indicate the formation of metal complexes.

Table 3.1 (-) and (+) in wavelength changes denote hypsochromic shift and bathochromic shift respectively.

compound	λ_{max} (nm)	metal-induced wavelength changes ($\Delta\lambda_{max}$/nm)				
		Li^+	Na^+	K^+	Rb^+	Cs^+
L3	643	-3.00	+3.00	-4.10	-3.00	-3.00

In donor-acceptor chromophores, the electronic excitation is mostly accompanied by the UV spectra shifting in the direction of the acceptor constituents of the chromoionophore. With respect to the UV spectra shifting, addition of Li^+, K^+, Rb^+ and Cs^+ to **L3** show a lower wavelength shifting of spectra. Since it can be postulated that the amine nitrogen atoms of chromophore are positively polarized when **L3** complexes with the metal ions. The ion-dipole and ion-ion interactions take place. Moreover, hydroxyl can be formed hydrogen bonding with oxygen quinone as shown in **Figure 3.4**(a). Therefore, the exited states are more destabilized by cation than the ground states. Such effect causes a hypsochromic shift.

Among the metal ions studies, K^+ gave the most significant changes with respect to the blue shift $\Delta\lambda_{max}$ = -4.10 nm. Judging from the magnitude of this blue shift, it is concluded that the K^+ is encapsulated in the double calix[4]diquinone cavity with aid of the conjugated indoaniline. However the color does not change significantly as expected.

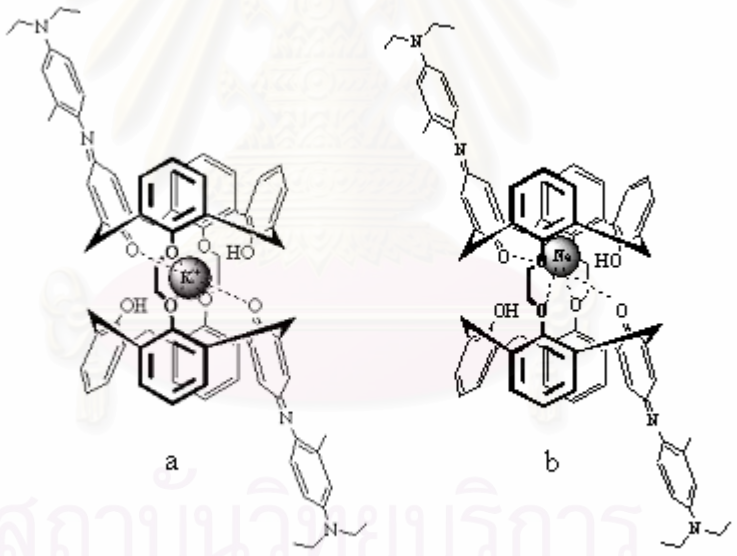

Figure 3.4 Proposed structures of the complexes between **L3** and K^+ (a) and Na^+ (b)

Surprisingly, wavelength changes of **L3** was found to undergo a bathochromic shift, $\Delta\lambda_{max}$ = +3.00 nm, only for addition of Na^+. This red shift behavior is ascribed to a suitable cavity for the sodium ion together with π-cation interactions driven by the electron donation of the indoaniline chromophores (**Figure 3.4** (b)). [56-57]

3.3.3 Complexation studies of compound L3 to determine stability constants

Stability constants of **L3** toward five alkali metal ions, Li^+, Na^+, K^+, Rb^+ and Cs^+, were determined at least twice by titrating the **L3** with ~ 400 equiv. of alkali metal ions using Cl^- as a counteranion and Et_4NCl as a supporting electrolyte. The calculation with SIRKO shows that the change in ligand spectrum fitted with the model of 1:1 ligand to all metal complexes. Typical spectra during titration are shown in **Figures 3.5-3.9** and the value of stability constants are collected in **Table 3.2**.

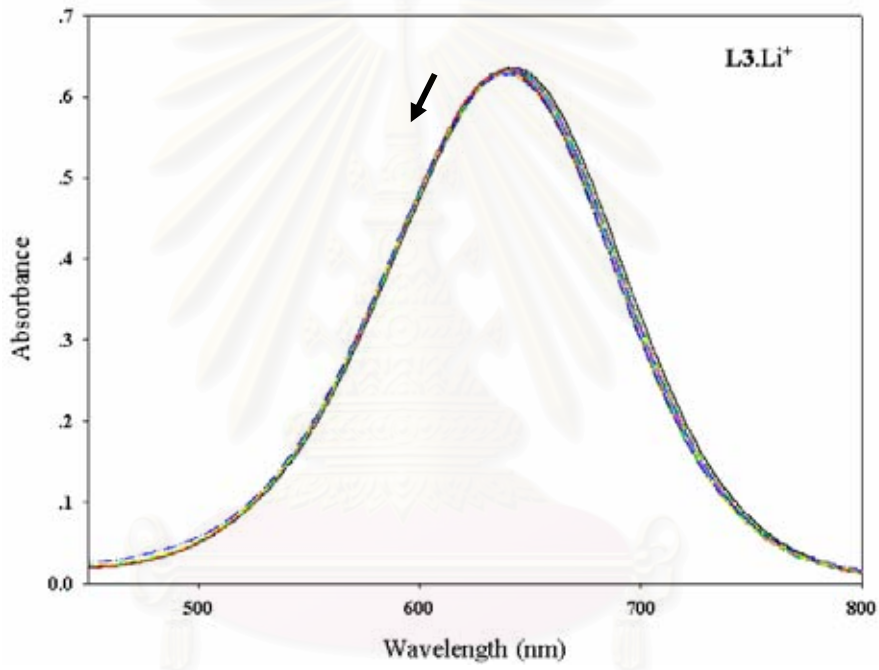

Figure 3.5 Hypsochromic band shifting of **L3** ($1x10^{-5}$ M) upon the addition of LiCl (0-400 equiv.)

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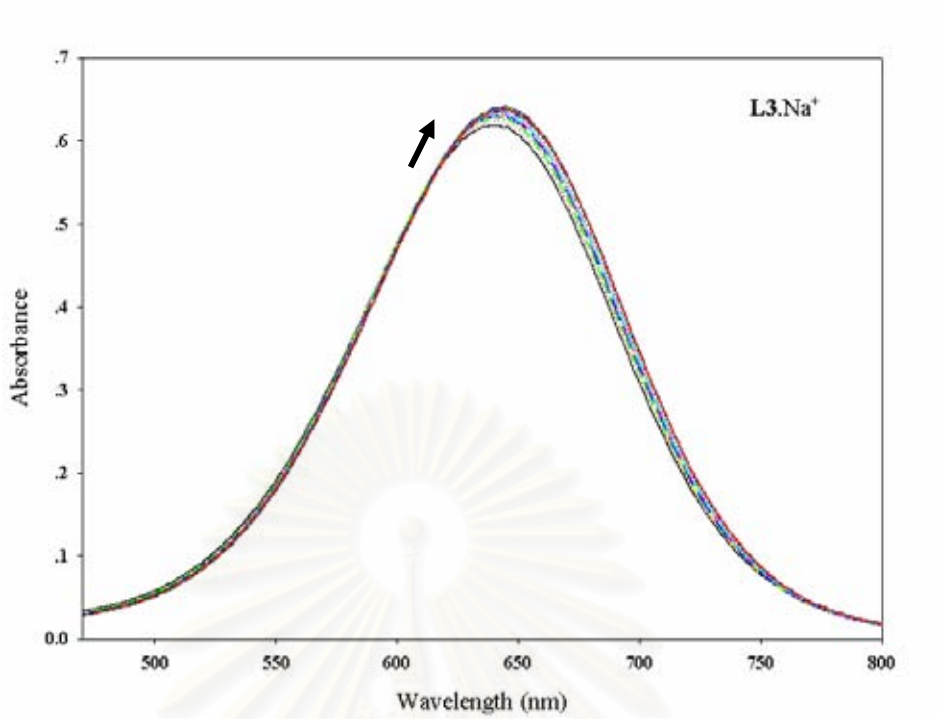

Figure 3.6 Bathochromic band shifting of **L3** ($1x10^{-5}$ M) upon the addition of NaCl (0-400 equiv.)

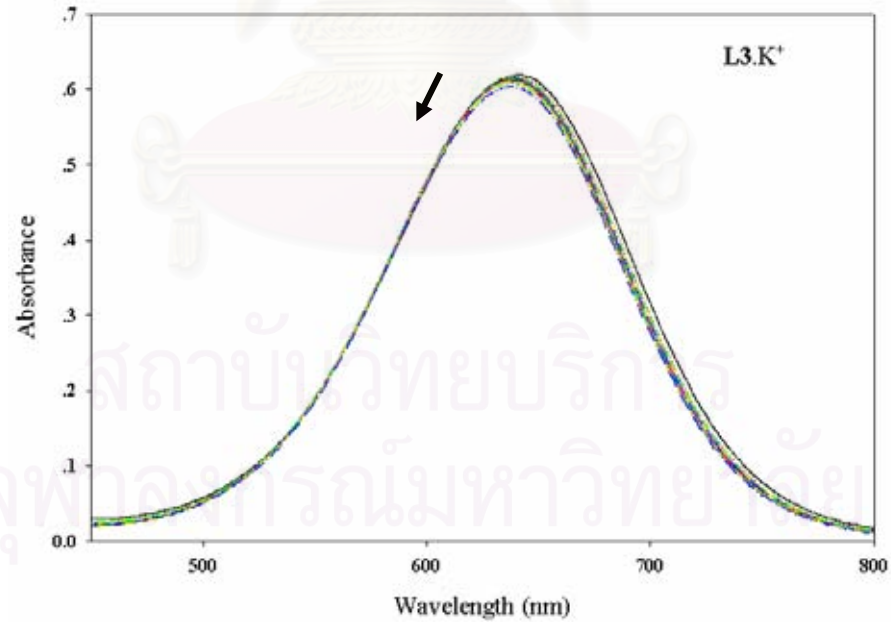

Figure 3.7 Hypsochromic band shifting of **L3** ($1x10^{-5}$ M) upon the addition of KCl (0-400 equiv.)

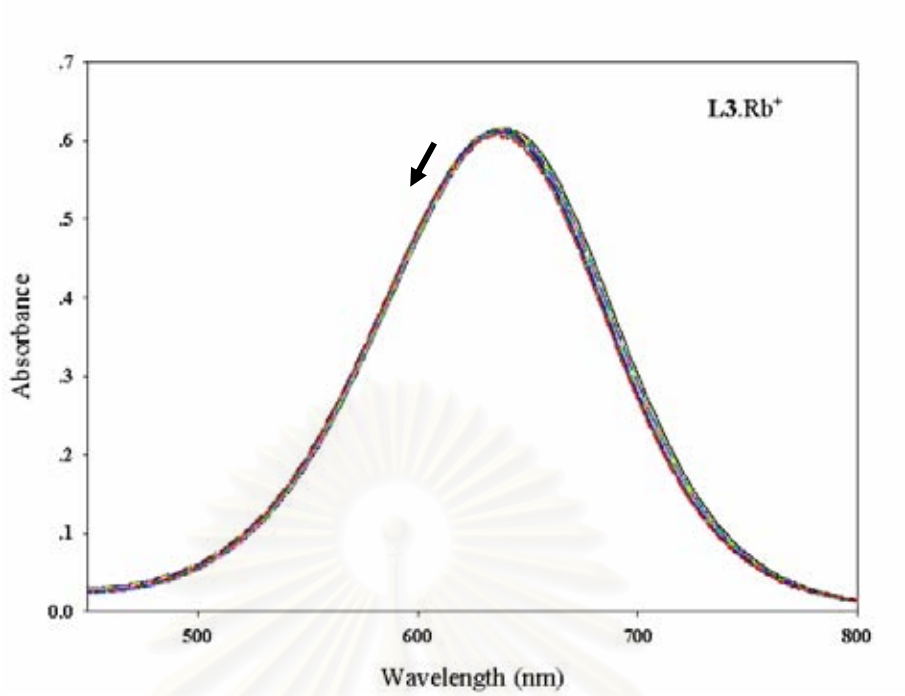

Figure 3.8 Hypsochromic band shifting of **L3** ($1x10^{-5}$ M) upon the addition of RbCl (0-400 equiv.)

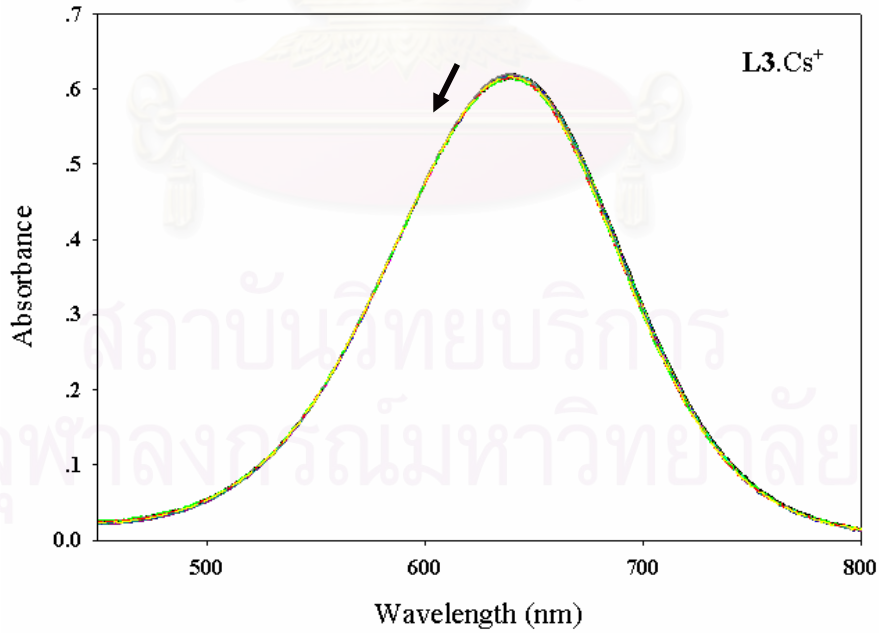

Figure 3.9 Hypsochromic band shifting of **L3** ($1x10^{-5}$ M) upon the addition of CsCl (0-400 equiv.)

Table 3.2 Stability constant data for the alkali metal complexes of **L3**

Compound	log *K**				
	Li^+	Na^+	K^+	Rb^+	Cs^+
L3	4.65 ± 0.04	3.51 ± 0.01	**4.97 ± 0.10**	3.93 ± 0.04	3.42 ± 0.04

* At 298 K. Conducted in methanol; 0.01 M tetraethylammonium chloride

The stability constants are found to be $K^+ > Li^+ > Rb^+ > Na^+ > Cs^+$, respectively. However, all of the cases of alkali metal ion complexation, no color change is observed upon excess addition of alkali metal cations to the solution of **L3**.

As can be seen from **Table 3.2**, compound **L3** shows relatively strong binding ability to the entire alkali metal ion examined, especially for K^+. The highest stability constants upon complexation of K^+ with **L3** indicate that the cavity of **L3** seems to be the best fit to the diameter of K^+ in terms of size (**Figure 3.10**) and spatial arrangement.

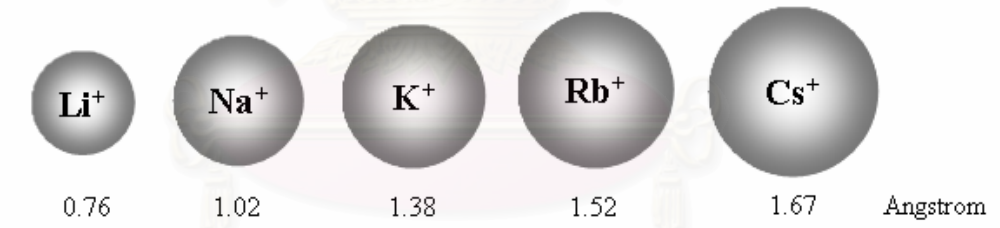

Figure 3.10 Illustration of the alkali metal ions size

Surprisingly, **L3** have good selectivity for Li^+ over Na^+, although the size of Na^+ should fit more appropriately in the cavity of **L3**. This indicates that the binding ability of **L3** to alkali metal ions effects on the other factors such as ion pairing. The structures of the complexes are not known exactly. They may be the subject of future NMR study. It might be presumed that “ion pairing effect”.[56] It was due to NaCl is strongly solvated by methanol molecules, so the complex formation would be suppressed, while LiCl is less solvated than NaCl.

CHAPTER IV

CONCLUSION

Compounds **L1**, **L2** and **L3** consistings “monoquinone”, “diquinone” and double calix[4]diquinone, respectively were synthesized by reacting 25,27-dimethoxy-26,28-dihydroxycalix[4]arene **1a** and double calix[4]arene **3a** with *N*,*N*′-dimethyl-2-methyl-1,4-phenylenediamine monohydrochloride to obtain the desired products.

Among the three host systems studied, only the double calix[4]diquinone **L3** displays significant shifts in UV-vis spectra towards complexation with alkali chloride while **L1** and **L2** did not produce significant change. Therefore, only receptor **L3** was subjected to the recognition investigation.

Addition of Li^+, K^+, Rb^+ and Cs^+ to the receptor **L3**, resulted in a blue shift due to cation-dipole interaction between metal ions and the ethylene glycol cavity. However, Na^+ resulted in a red shifted due to π-cation interaction between cation with benzene ring of calix[4]arene cavity.

Stability constants from UV-vis titrations in methanol solution revealed that **L3** generally forms complexes with Li^+, Na^+, K^+, Rb^+ and Cs^+ which the selectivity trend $K^+ > Li^+ > Rb^+ > Na^+ > Cs^+$ with the highest log*K* = 4.97 for K^+. In case of the higher selectivity of Li^+ than Na^+ can be described by “ion pairing effect”.

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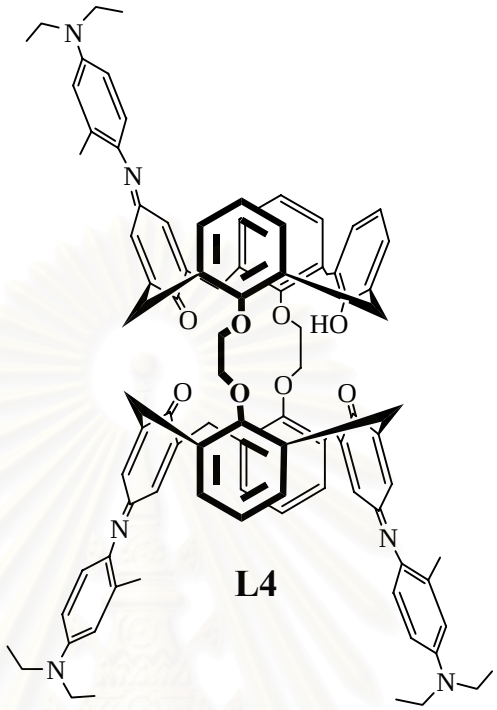
Suggestion for future works:

Future works should be aimed to purify double calix[4]triquinone **L4**.



L4

Furthermore, they should be focused on

(i) Growing the single crystal for X-ray crystal structure studies of compound **L3** and its metal complexes.

(ii) Employing the synthesized compound for detecting other charge-transfer molecules such as resorcinol and catechol.

(iii) Employing the synthesized compound for detecting alkaline earth metal ions.

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APPENDICES

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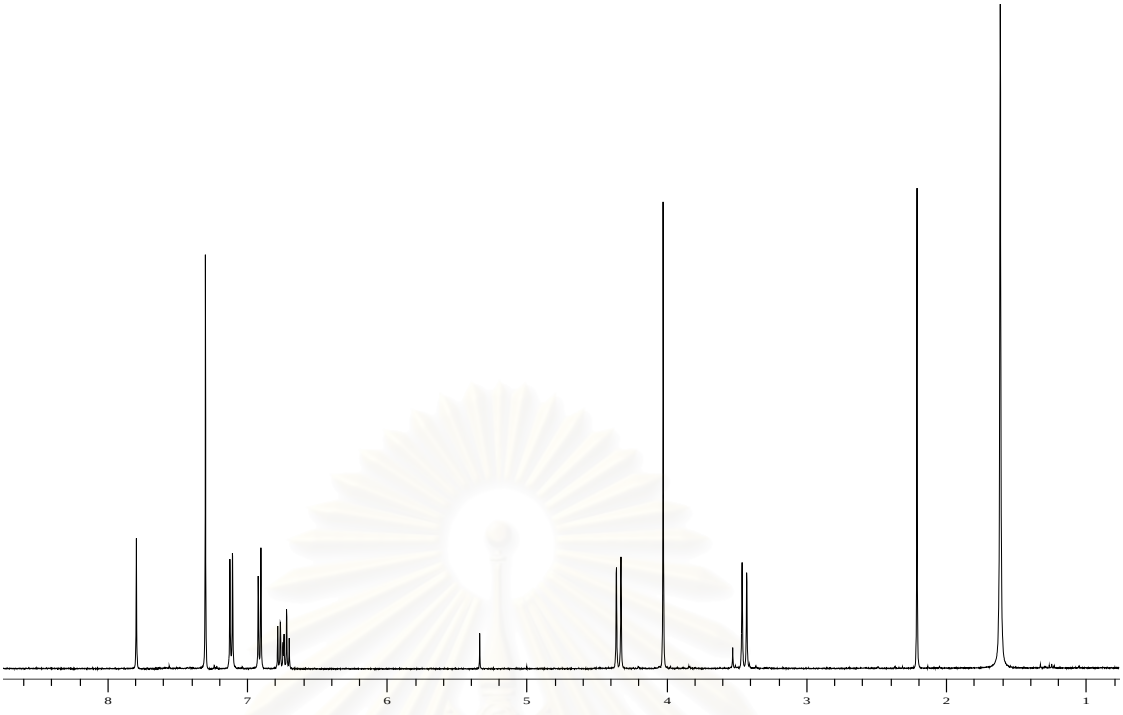

Figure A1: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 25, 27-dimethoxy-26, 28-dihydroxycalix[4]arene (**1a**)

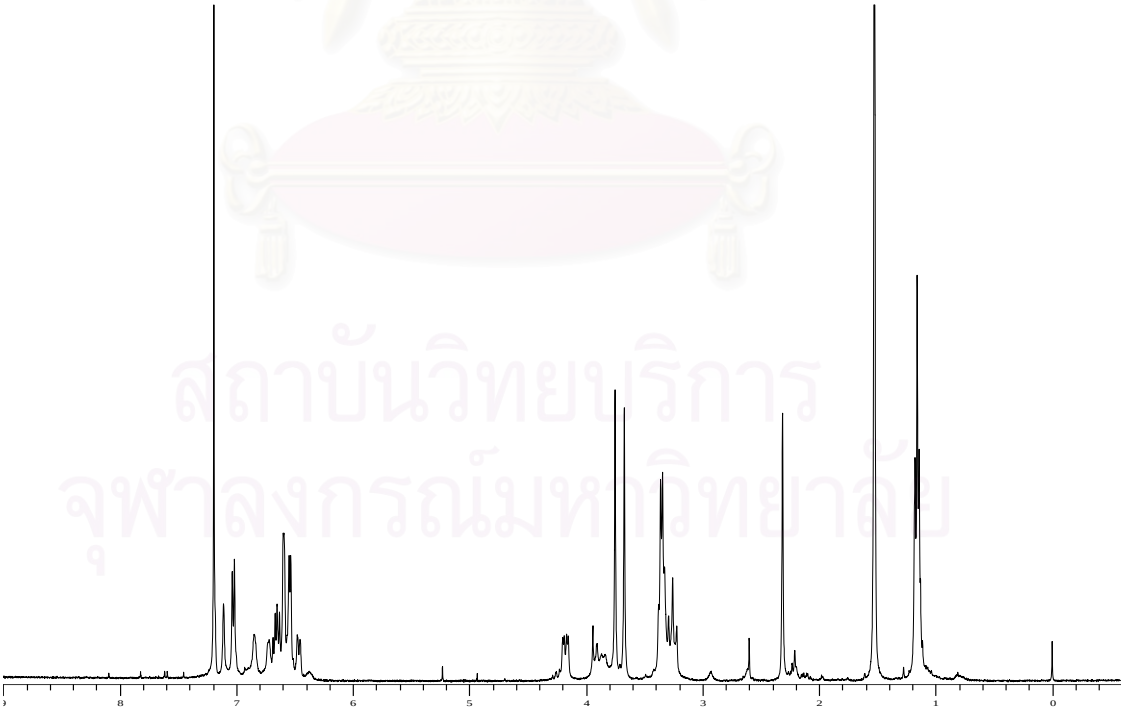

Figure A2: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 5-((4'-diethylamino)-2'-mehtylphenyl)imino)-25,27-dimethoxy-28-hydroxy-26-one (**L1**)

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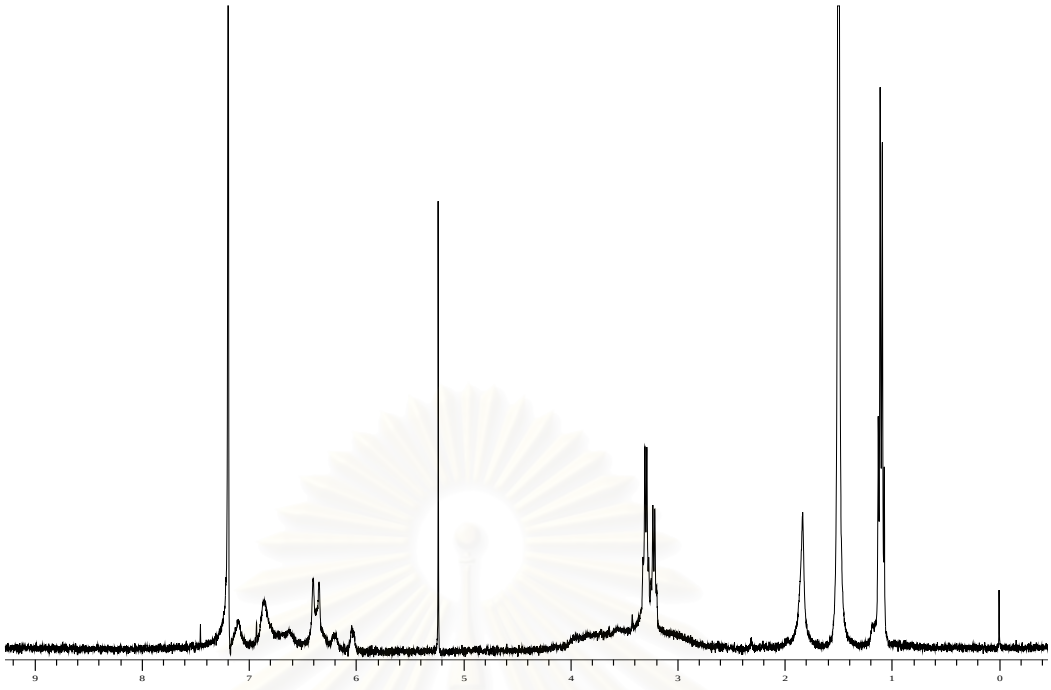

Figure A.3: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 5, 17-bis ((4'-diethylamino)-2'-mehtylphenyl)imino)-25,27-dimethoxy-26,28-dione (**L2**)

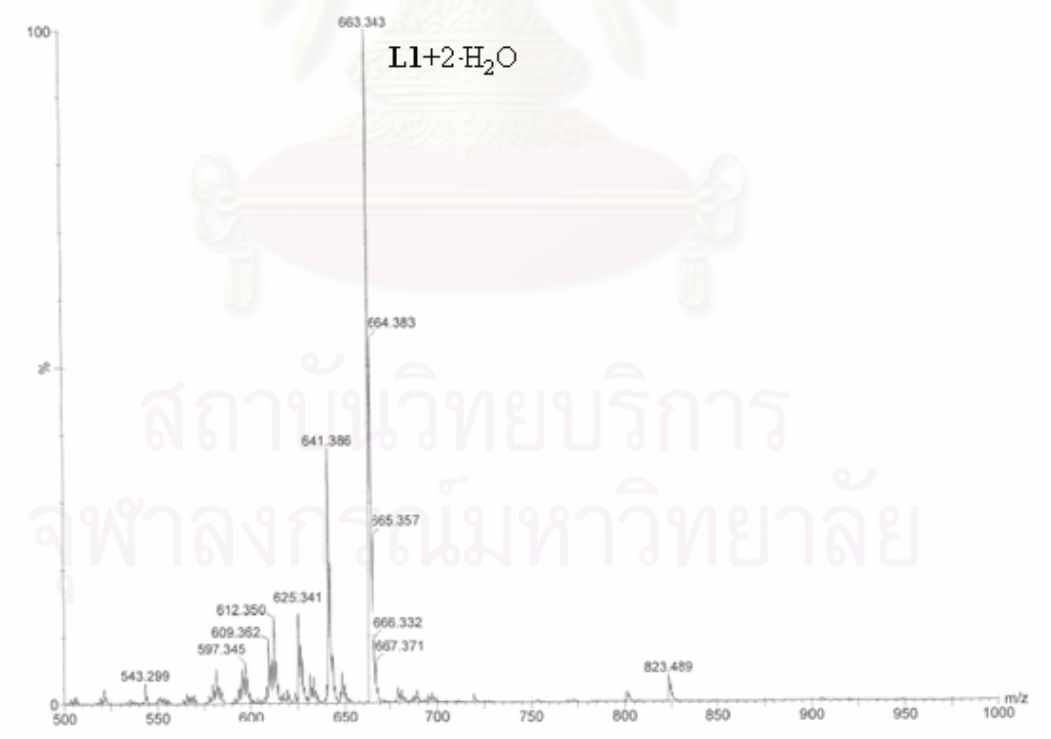

Figure A4: ESI-MS spectrum of 5-((4'-diethylamino)-2'-mehtylphenyl)imino)-25,27-dimethoxy-28-hydroxy-26-one (**L1**)

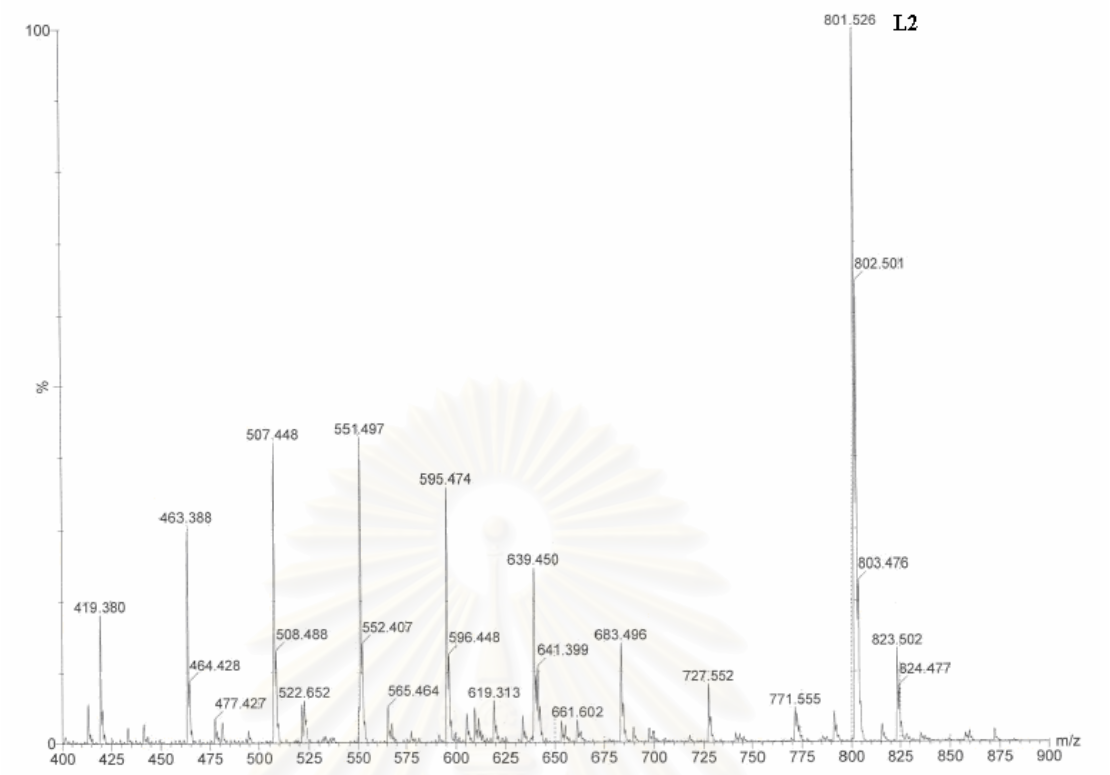

Figure A5: ESI-MS spectrum of 5, 17-bis ((4'-diethylamino)-2'- mehtylphenyl)imino)-25,27-dimethoxy-26,28-dione (**L2**)

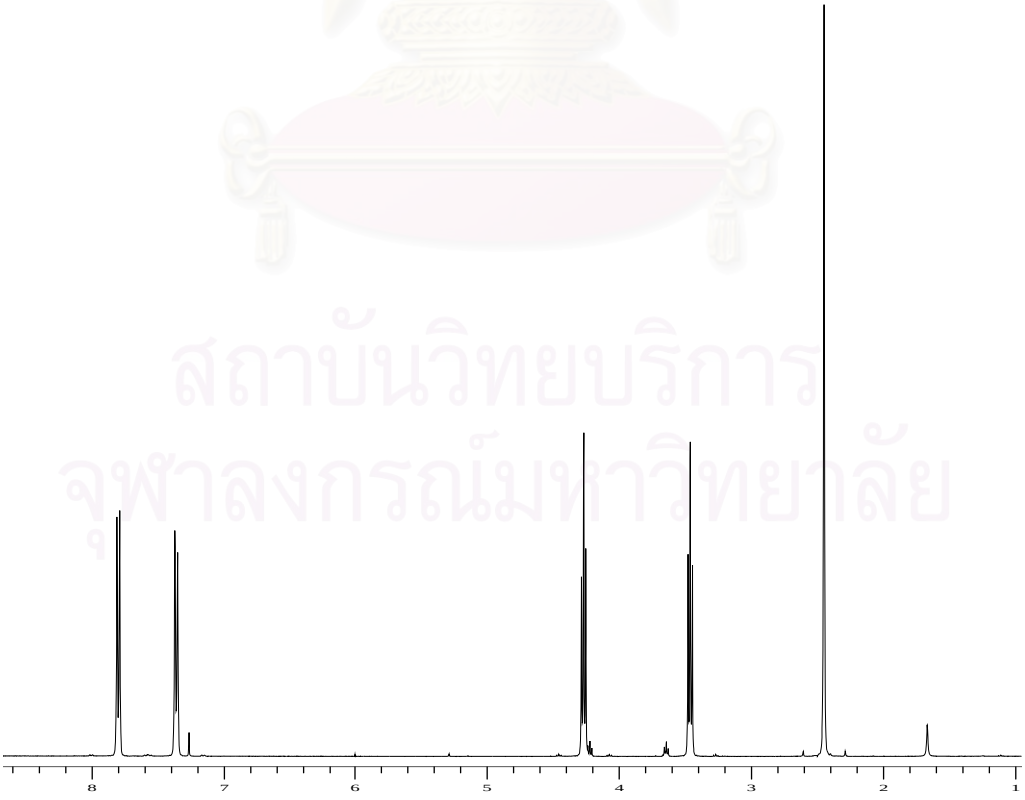

Figure A6: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2-bromoethyl-4-eththylbenzenesulfonate (**2a**)

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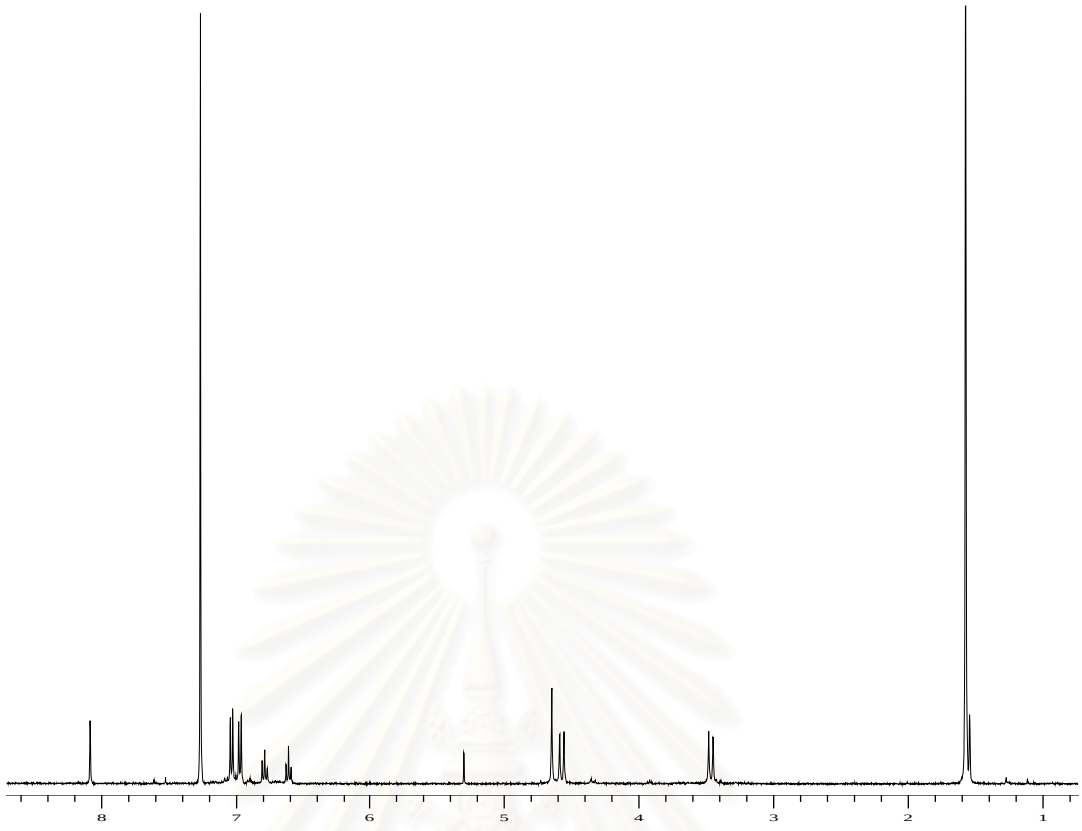

Figure A7: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of double calix[4]arene (**3a)**

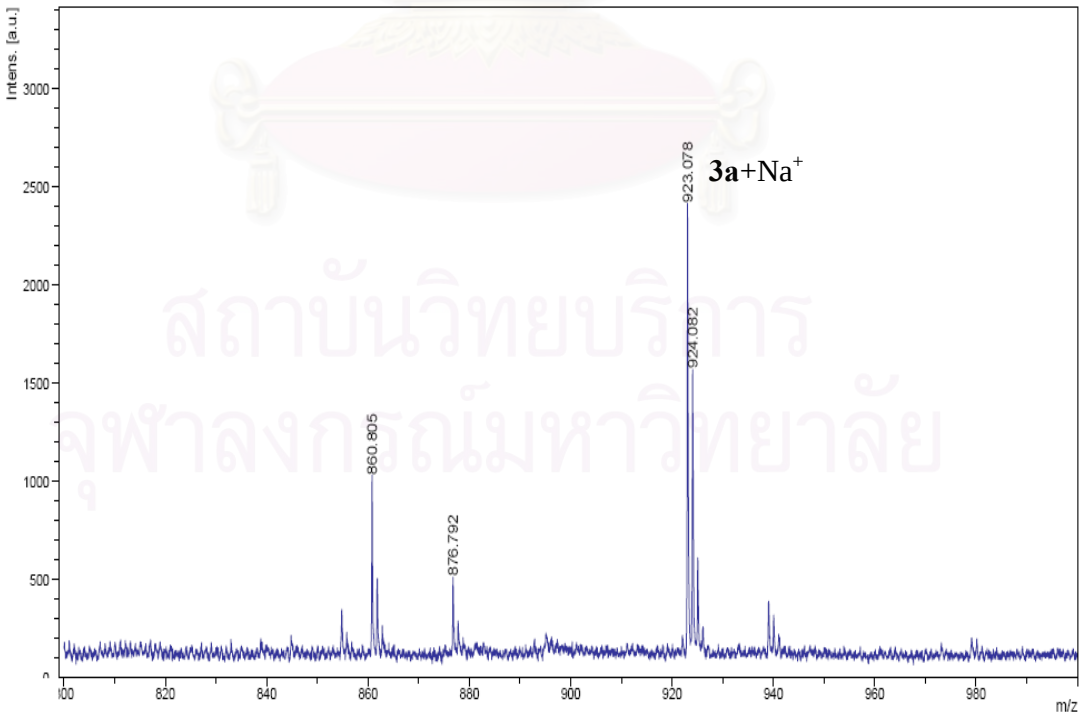

Figure A8: MALDI-TOF spectrum of double calix[4]arene(**3a)**

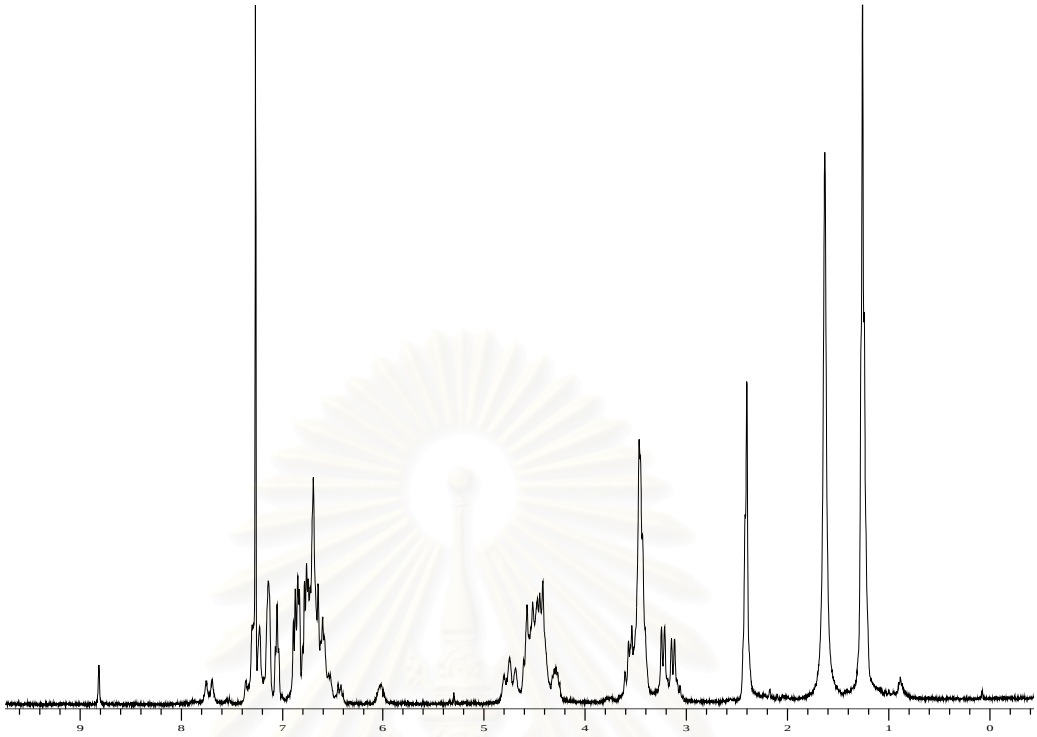

Figure A9: ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of double calix[4]diquinone(**L3**)

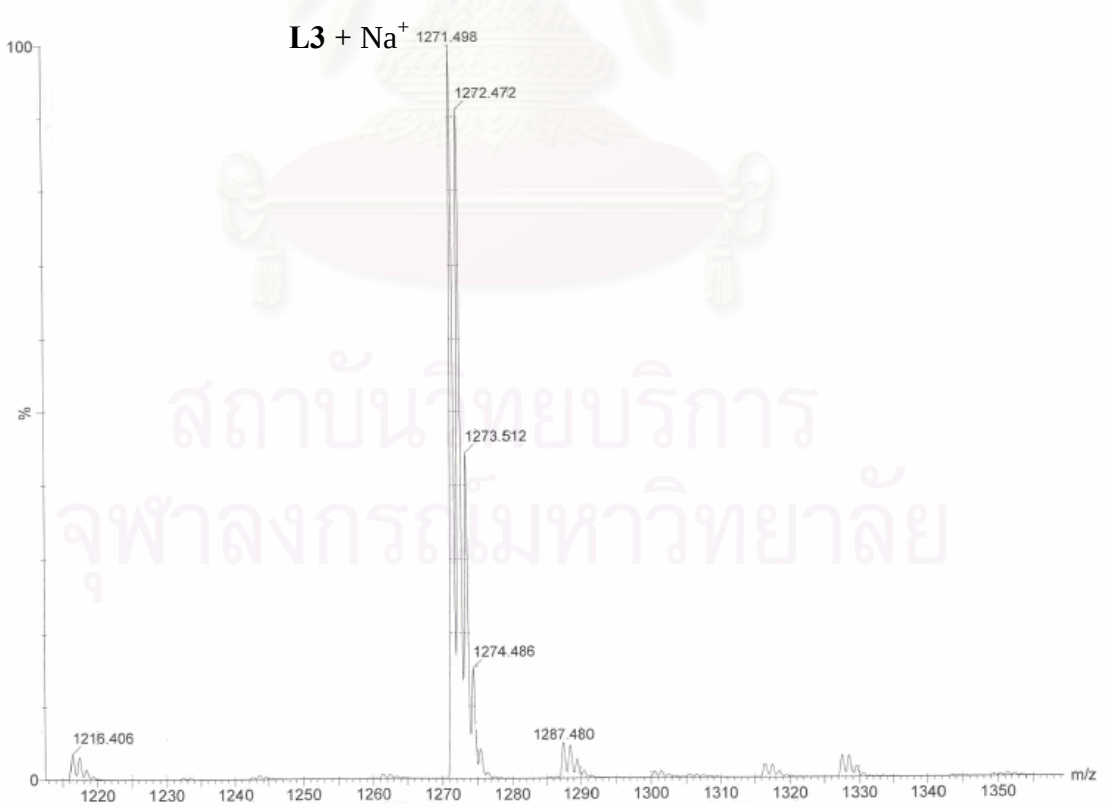

Figure A10: ESI-MS spectrum of double calix[4]diquinone (**L3)**

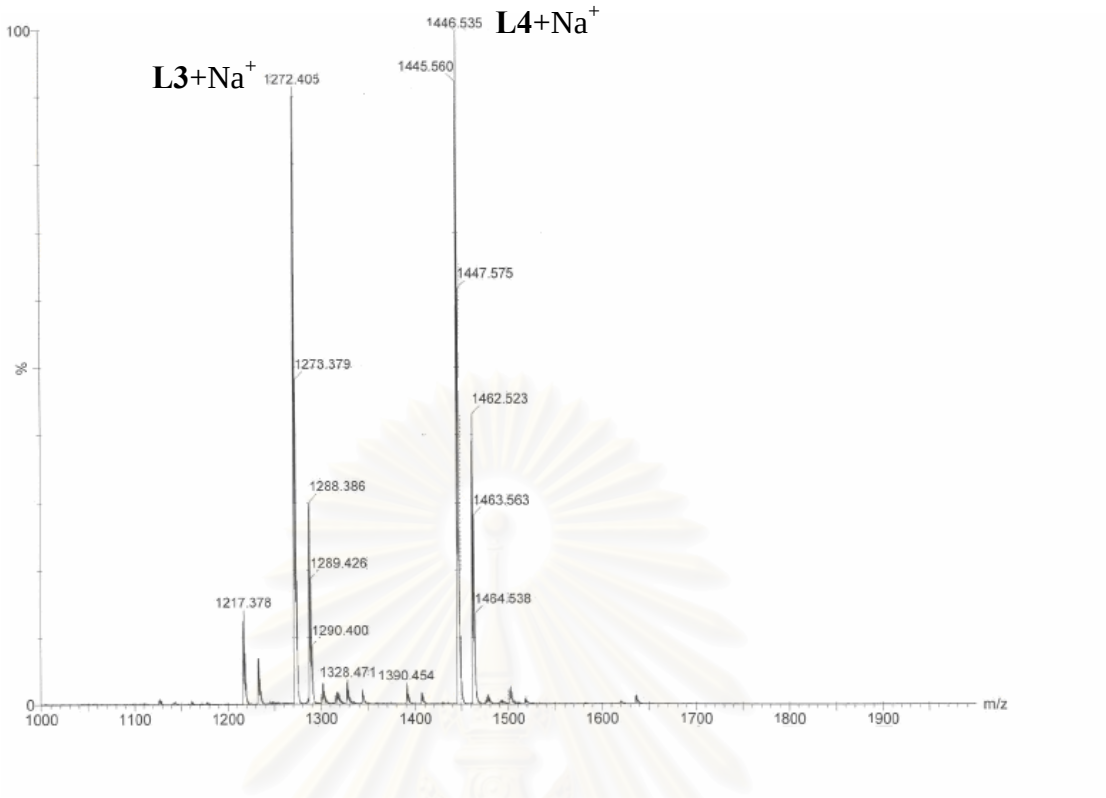

Figure A11: ESI-MS spectrum of double calix[4]triquinone (**L4**) in case of impurity from double calix[4]diquinone (**L3)**

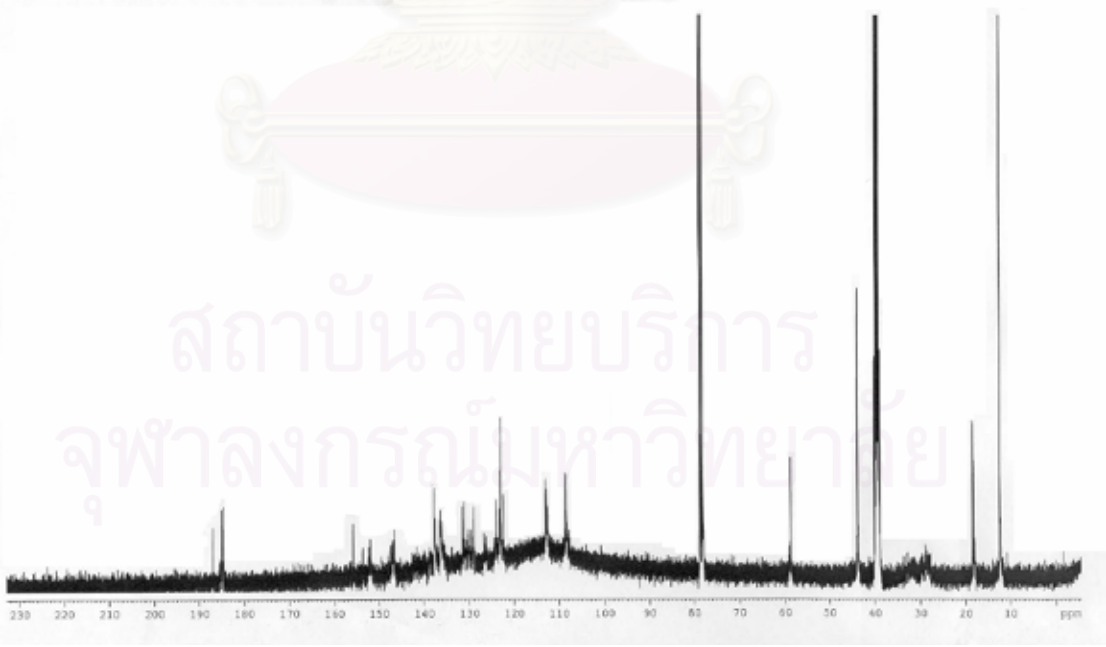

Figure A12: ^{13}C NMR spectrum of 5-((4'-diethylamino)-2'-mehtylphenyl)imino) -25,27-dimethoxy-28-hydroxy-26-one (**L1)**

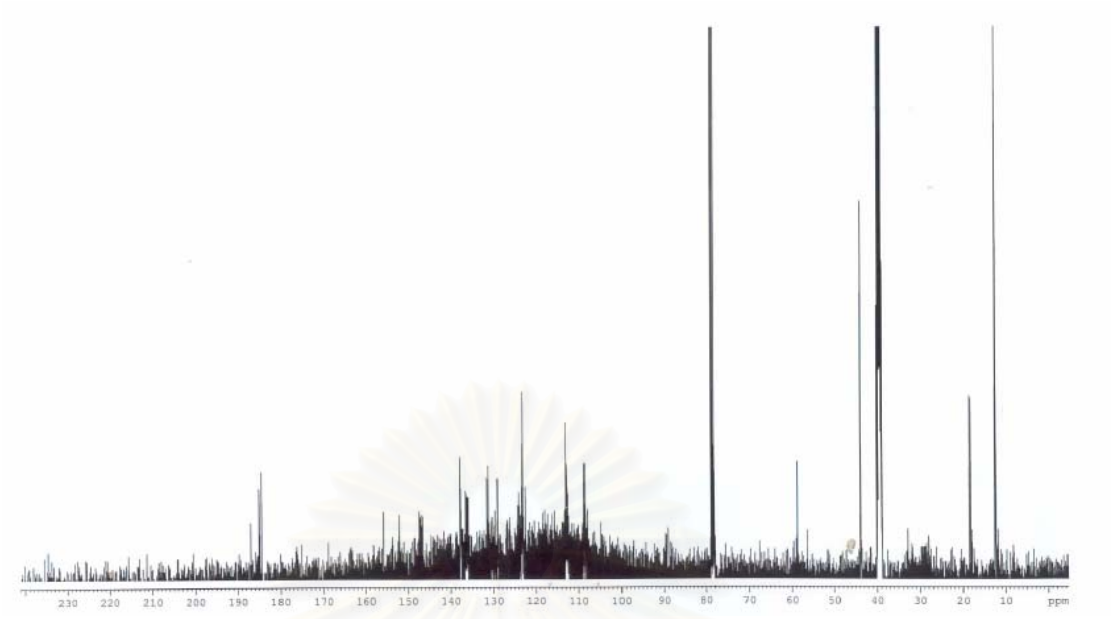

Figure A13: ^{13}C NMR spectrum of 5, 17-bis ((4'-diethylamino)-2'- mehtylphenyl) imino)-25,27-dimethoxy-26,28-dione (**L2**)

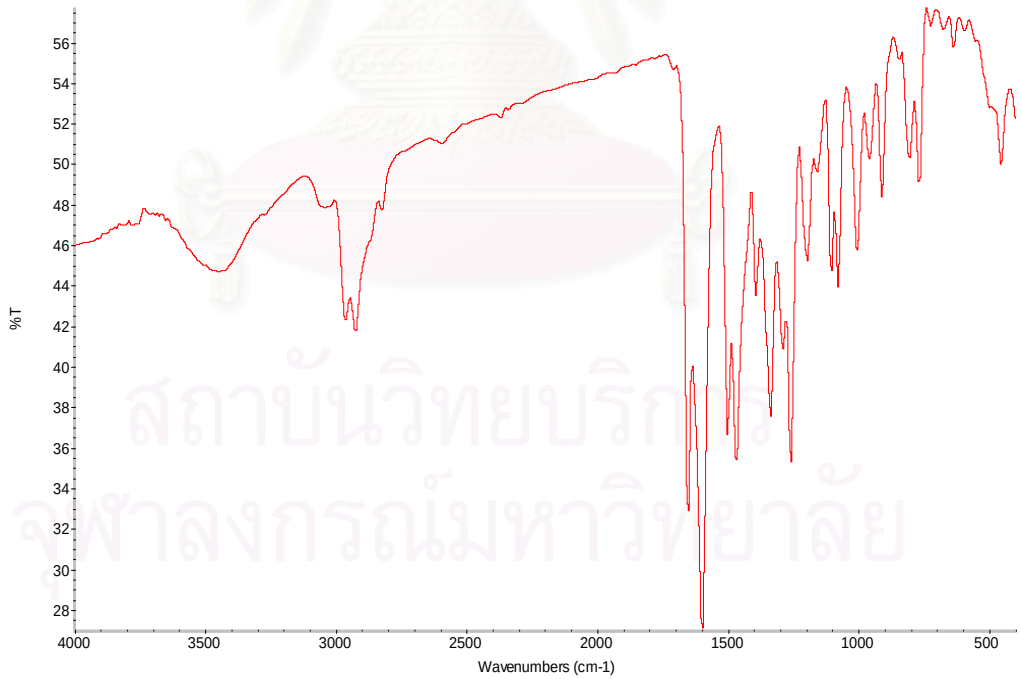

Figure A14: IR spectrum of 5-((4'-diethylamino)-2'-mehtylphenyl)imino) -25,27-dimethoxy-28-hydroxy-26-one (**L1**)

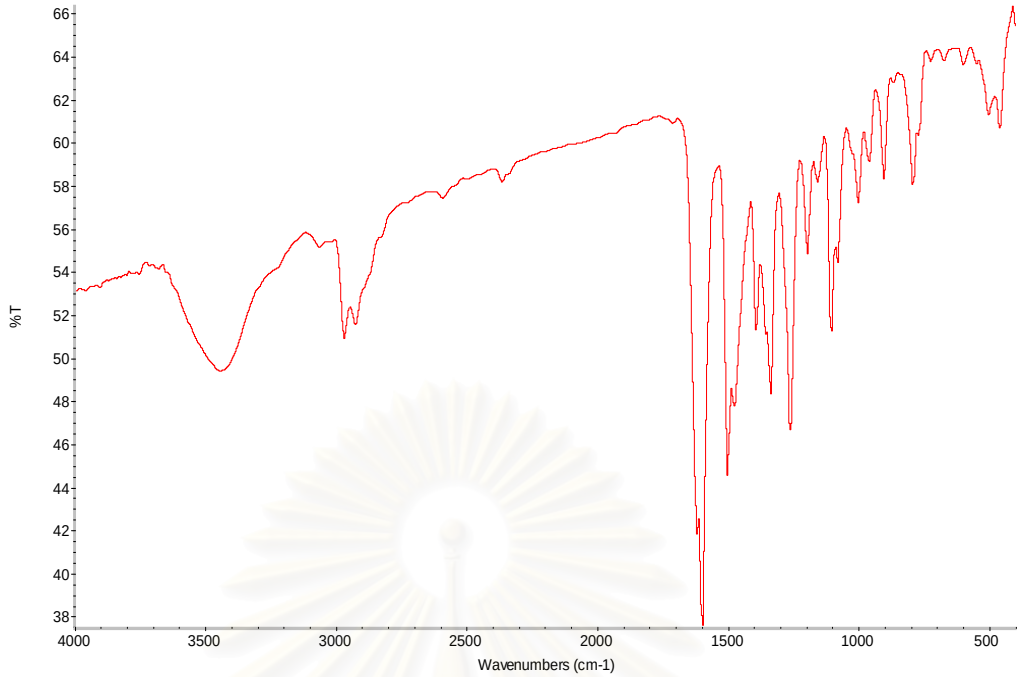

Figure A15: IR spectrum of 5, 17-bis ((4'-diethylamino)-2'- mehtylphenyl)imino) -25,27-dimethoxy-26,28-dione (**L2**)

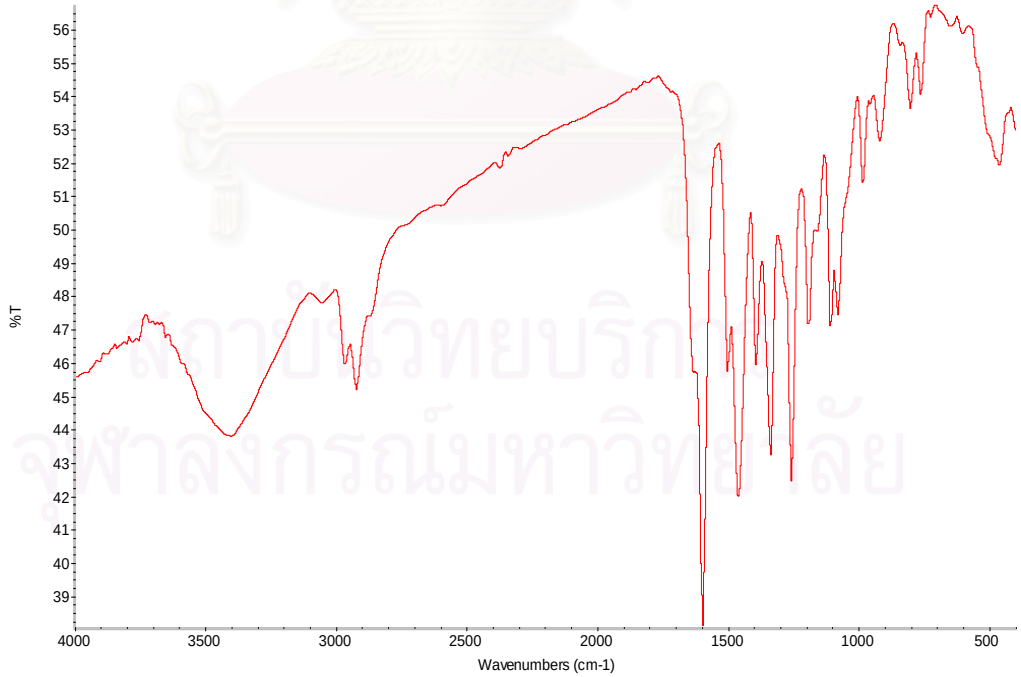

Figure A16: IR spectrum of double calix[4]diquinone (**L3**)

VITA

Mr. Sutiam Kruawan was born on October 16, 1978 in Surin, Thailand. He graduated with a high school diploma from Surawittayakarn School, Surin in 1994. He received his Bachelor's degree of Science in Chemistry from Mahasarakham University in 1998. Since 2004, 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 Associate Professor Dr.Thawatchat Tuntulani and Assistant Professor Dr.Boosayarat Tomapatanaget as co-supervisor. He finished his Master's degree of Science in the academic year 2006.

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