การสังเคราะห์ ไพรีนิลคาลิกซ์[4]เอรีน-คาลิกซ์[4]พิร์โรลเพื่อใช้เป็นฟลูออร์โรจินิกเซ็นเซอร์สำหรับแอนไอออน

นายปรีชา เทียมปัญญา
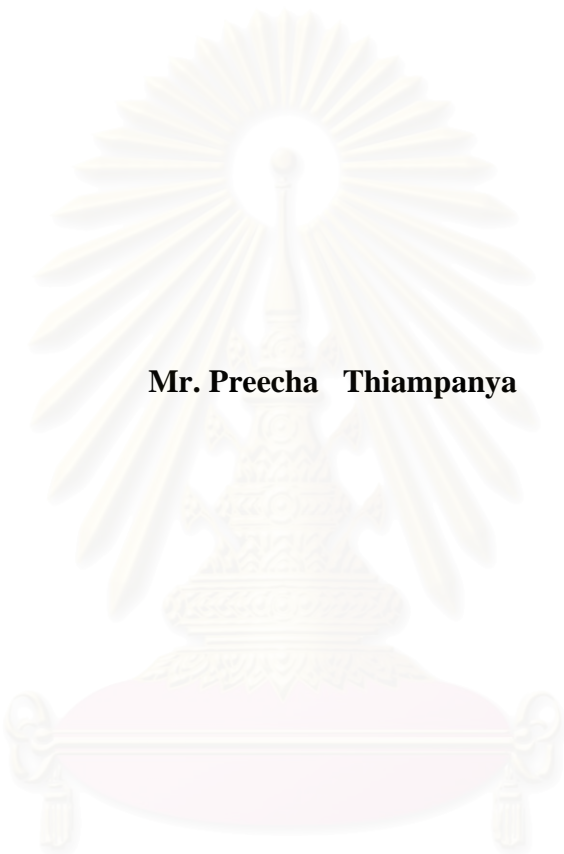
วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
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SYNTHESIS OF PYRENYLCALIX[4]ARENE-CALIX[4]PYRROLE AS FLUOROGENIC SENSOR FOR ANION

Mr. Preecha   Thiampanya

A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science Program in Chemistry

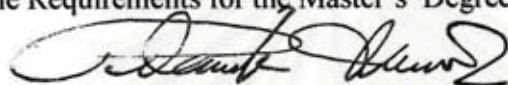**Department of Chemistry**

Faculty of Science

Chulalongkorn University

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Thesis Title	SYNTHESIS OF PYRENYLCALIX[4]ARENE-CALIX[4]PYRROLE AS FLUOROGENIC SENSOR FOR ANION
By	Mr.Preecha Thiampanya
Field of Study	Chemistry
Thesis Advisor	Associate Professor Buncha Pulpoka, Ph.D.

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

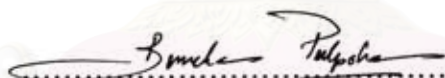.. Dean of the Faculty of Science

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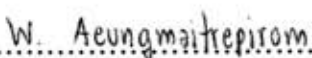
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ปรีชา เทียมปัญญา : การสังเคราะห์ ไพรีนิลคาลิกซ์[4]เอรีน-คาลิกซ์[4]พิร์โรลเพื่อใช้เป็นฟลูออร์โรจินิกเซ็นเซอร์สำหรับแอนไอออน
(SYNTHESIS OF PYRENYLCALIX[4]ARENE-CALIX[4]PYRROLE AS AS FLUOROGENIC SENSOR FOR ANION)
อ. ที่ปรึกษา :รศ.ดร.บัญชา พูลโภคา; 82 หน้า.

ได้ทำการสังเคราะห์และพิสูจน์เอกลักษณ์ด้วยเทคนิคทางสเปกโทรสโกปีของสารประกอบไพรีนิลคาลิกซ์[4]เอรีน-คาลิกซ์[4]พิร์โรล (7) สำหรับใช้เป็นเซ็นเซอร์ฟลูออร์โรจินิก จากการวิเคราะห์โครงสร้างพบว่าหน่วยคาลิกซ์[4]เอรีนและคาลิกซ์[4]พิร์โรลมีรูปร่างเป็นกรวยและ 1,3-อัลเทอเนตตามลำดับโดยมีสายเชื่อมไกลโคลิกต่ออยู่ในลักษณะทรานส์บนวงคาลิกซ์[4]พิร์โรล จากการศึกษาการเกิดสารประกอบเชิงซ้อนกับแอนไอออนของสาร 7 ด้วยเทคนิคสเปกโทรสโกปีเรืองแสงพบว่าในทุกสารประกอบเชิงซ้อนที่ศึกษามีความเข้มของการเรืองแสงของมอนอเมอร์ที่ความยาวคลื่น 376 และ 396 นาโนเมตรเพิ่มขึ้นเนื่องจากกระบวนการพีอีที จากการศึกษาการไทเทรตด้วยแอนไอออนด้วยเทคนิคเรืองแสงพบว่าลิแกนด์ 7 จับฟลูออไรด์ได้ดีที่สุด ตามด้วยอะซีเตต โบรไมด์ เบนโซเอต และคลอไรด์ โดยมีค่าลอการิทึมของค่าคงที่การเกิดสารประกอบเชิงซ้อนเป็น 3.45, 3.25, 1.74, 1.62 และ 1.28 ตามลำดับ นอกจากนี้ยังพบว่าเมื่อเติมเกลือฟลูออไรด์ลงในสารละลายของลิแกนด์ 7 ทำให้สีของสารละลายเปลี่ยนไปและการเรืองแสงยังลดลงในช่วงความยาวคลื่นที่ตามองเห็นได้

ภาควิชา..................เคมี.................. ลายมือชื่อนิสิต..ปรีชา..เทียมปัญญา..
สาขาวิชา..................เคมี.................. ลายมือชื่ออาจารย์ที่ปรึกษา..................
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PREECHA THIAMPANYA: SYNTHESIS OF PYRENYLCALIX[4]ARENE-CALIX[4]PYRROLE AS FLUOROGENIC SENSOR FOR ANION .
THESIS ADVISOR:ASSOC.PROF.BUNCHA PULPOKA, Ph.D, 82 pp.

A fluorogenic sensor for anion, pyrenylcalix[4]arene-calix[4]pyrrole (**7**), was successfully synthesized and characterized by spectroscopic techniques. It was revealed that the conformations of calix[4]arene and calix[4]pyrrole of **7** are in cone and 1,3-alternate manners, respectively. The glycolic spacers are in *trans*-position. Anion complexation studies of ligand **7** were carried with tetrabutylammonium salts by fluorescence spectroscopy. The spectra of all complexes exhibited an increase of monomer fluorescence emission at wavelengths of 376 and 396 nm when excited at 343 nm by a PET-based mechanism. According to fluorescence titrations, fluorogenic sensor **7** formed complexes with high affinity to fluoride following by acetate, chloride, bromide, benzoate, ions with logK of 3.45, 3.25, 1.74, 1.62 and 1.28 respectively. An addition of excesses fluoride ion to a solution of **7** resulted in a color change of solution of **7** and fluorescence quenching at visible region.

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

Department...............Chemistry.................. Student's signature. *Preecha Thiampanya*

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

Academic year............ 2006................... Co-advisor's signature...

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CONTENT

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

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LIST OF ABBREVATION AND SIGNS

Å	Angstrom
Bu_4NF	Tetrabutylammonium fluoride
Bu_4NCl	Tetrabutylammonium chloride
Bu_4NBr	Tetrabutylammonium bromide
Bu_4NI	Tetrabutylammonium iodide
Bu_4NCH_3COO	Tetrabutylammonium acetate
$Bu_4NPhCOO$	Tetrabutylammonium benzoate
Bu_4NPF_6	Tetrabutylammonium hexafluorophosphate
Bu_4NNO_3	Tetrabutylammonium nitrate
$Bu_4NH_2PO_4$	Tetrabutylammonium hydrogenphosphate
Bu_4NClO_4	Tetrabutylammonium perchlorate
δ	Chemecal shift
equiv	Equivalent
g	Gram
mg	Milligram
^{1}H-NMR	Proton Nuclear Magnetic Resonance
Hz	Hertz
IR	Infrared spectroscopy
λ	wavelength
M	Molar
MALDI-TOF	Matrix Assistant Laser Desorption/Ionization-Time of Flight
mL	Milliliter
mmol	Millimole
ppm	Part per million
RT	Room temperature
s,d,t,m	Splitting patterns of 1H-NMR (singlet, doublet, triplet and multiplet)
TFA	Trifluoro acetic acid
TsCl	Toluene-4-sulfonyl chloride

st   stretching

em   emission

CHAPTER I

INTRODUCTION

1. Supramolecular Chemistry

Supramolecular chemistry is one of the most popular and fastest growing areas of experimental chemistry and it seems to remain that way for the foreseeable future. For many years, chemists have synthesized molecules and investigated their physical and chemical properties. The field of *supramolecular chemistry*, however, has been defined as 'chemistry beyond the molecule', and involves investigation of new mlecular systems. The components are held together by *intermolecular forces, non by covalent bonds*.[1] Chemists working in this area can be thought of as architects combining individual covalently bonded molecular building blocks, designed to be held together by intermolecular forces, in order to create functional architectures. The definition of supramolecular chemistry is depicted in the Figure 1.1. [1]
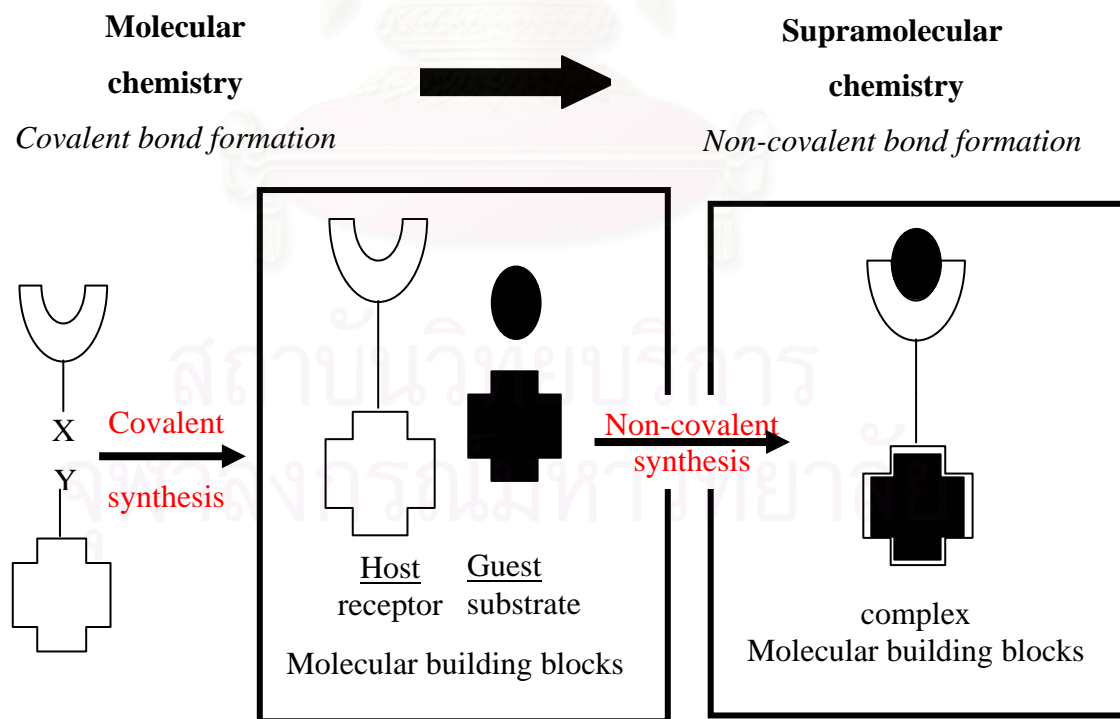
Figure 1.1 Supramolecular chemistry.

Supramolecular chemistry is a highly interdisciplinary field of science covering the chemical, physical, and biological features of greater complexity than molecules themselves. This introduction describes a generalized approach to supramolecular science and provides an indication of the wide ranging interests of chemists and inorganic chemistry are required for the synthesis of the pre-designed supramolecular components, and physical chemistry is used to fully understand their properties. Finally, a degree of technical experties can lead to functioning devices ready for application to real world.

In the complexation of supramolecular molecules, the glue used by supramolecular chemists to hold molecules together is non-covalent, and there are a number of such interactions that can be utilized. They include:

(i)   electrostatics (ion-ion, ion-dipole and dipole-dipole);

(ii)   hydrogen bonding;

(iii) π-π stacking interaction;

(iv)   dispersion and induction forces (van der Waals forces);

(v)   hydrophobic or solvatophobic effects.

1.1. Cation Receptors

Recognition of cation is one of the most interesting subjects in recent years. Due to various metal ions belong to metalloenzyme or it is well know that some heavy metal ions are toxic for organism, and early detection in the environment is desirable.[2]

Some of many applications of cationic receptors are to get rid of metallic pollutants in the environment and to study a metal ion playing an important role in living systems. Over the last two decades, the search for new material as chemical receptor for metal ion has been an area of rapid development. Many molecular platforms such as crown ethers,[3,4] cryptands,[5] cyclodextrins,[6] porphyrins[7] and calixarenes[8] are used to construct well-defined structures. Especially, attention has been paid on calixarene since it has binding ability toward alkaline and alkali earth metal ions that play various important roles in biochemistry and environmental science.

1.2. Anion Receptors

The synthesis of anion receptors possessing high affinity and adequate selectivity for various targeted substrates represents an ongoing challenge in the area of supramolecular chemistry. Anion recognition is often affected by hydrogen bonding interaction. Such interactions are weak and this is one of the reasons that anion recognition is more challenging to achieve than cation complexation.[9,10] Appreciated as being more difficult to achieve than cation recognition, this challenge continues to attract the attention of the researchers within the molecular recognition community due to the important role anions play in various biological as well as environmental systems.

Compared to relatively well-developed cation receptors,[11] development of anion receptors is only emerging as a research area of significant importance.[12] The slow development of anion recognition can be related to some inherent differences between anions and cations:[13]

i.   Anions are relatively large and therefore require (macrocyclic) receptors with a much larger binding site. The smallest anions, F^-, has the same ionic radius (1.33 Å) as a moderate size cation (K^+).

ii. Anions have many different shapes, e.g., spherical halides, linear SCN^-, trigonal planar NO_3^-, and tetrahedral $H_2PO_4^-$.

iii. Anions are more strongly hydrated than cations of equal size, whereas the

iii. solvation by organic solvents is generally less favorable.

iv. Several anions are presented only in a narrow pH window, e.g., $H_2PO_4^-$, and CO_3^{2-} anions in acidic and basic environment, respectively.

1.3. Bifunctional receptors

Ligand which simultaneously bind cation and anion have been a topic of current interest in supramolecular chemistry. Ditopic receptors have been prepared by attaching both cation and anion binding sites on a core molecule, either a rigid framework or a non-rigid one.

Reinhoudt and coworkers[1] have synthesized a receptor that consists of a calix[4]arene with cation binding ester groups at the lower rim and anion binding ureas groups at the upper rim. This receptor displays a very elegant ion-pair binding. In the chloroform solution, the two urea groups are hydrogen bonded together and so are not available for hydrogen bonding to any putative anionic guest species. However, when sodium cations are added, they bind the ester groups of the calixarene, causing the lower rim to contract. This force apart the urea groups at the upper rim apart which are then available for binding anionic species such as chloride anion
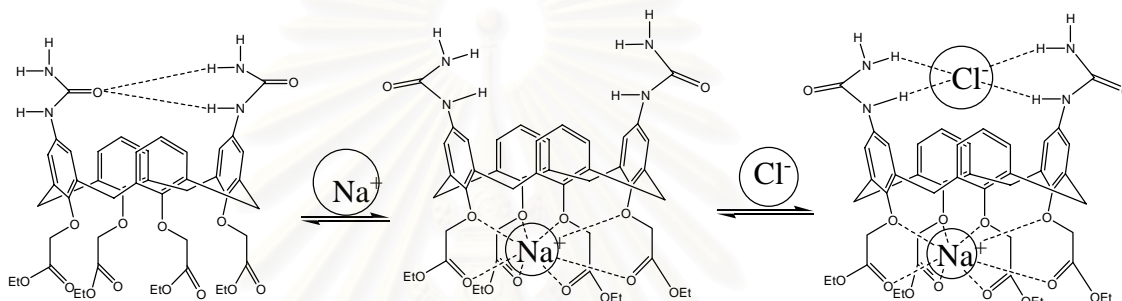
Figure 1.2 Anion and cation cooperative binding of 5,17-diureidocalix[4]-tetra-(ethylester).

In 2003, Pan Tongraung and coworkers[14] had synthesized calixarenes containing urea and crown/urea moieties (a) and (b). It was showed that (a) and (b) formed complexes with $H_2PO_4^- > Cl^- > Br^- > NO_3^-$. However, upon addition of Na^+, compared with the former Bu_4N^+, the binding ability of (b) towards $H_2PO_4^-$ was increase due to ion-pair enhancement.

(a)   **(b)**
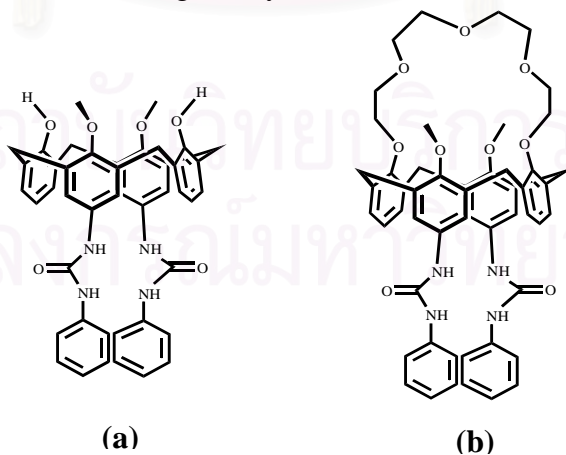
Figure 1.3 Calixarene containing (a) urea and (b) crown urea moieties as bifunctional receptor.

2. Selective Ion Sensor Design

In a related advanced supramolecular concept, recognition sites can be coupled to certain groups that are capable of "reporting" the anion coordination process. In this case, the binding process is transduced into a signaling event. Receptors specifically designed for sensing purposes are generally called chemosensors. One basic design principle in these new multicomponent systems is that the sensing event has to be related with an easy to measure signal. In fact, many chemosensors display changes in either color or fluorescence in the presence of a certain guest although changes in electrochemical properties such as the oxidation potential of redox active groups have also been widely used. In this sensing process, information at the molecular level, such as the presence or not of a certain guest in solution, is amplified to a macroscopic level; hence, sensing might open the door to the determination (qualitative or quantitative) of certain guests. These ideas connect in some way with supramolecular concepts such that of molecular devices (in this case sensor devices) in which the final operation (anion signaling) performed by the device results from the sum of the basic functions of the components, the binding site (coordination), and the reporting unit (transduction of the coordination event).
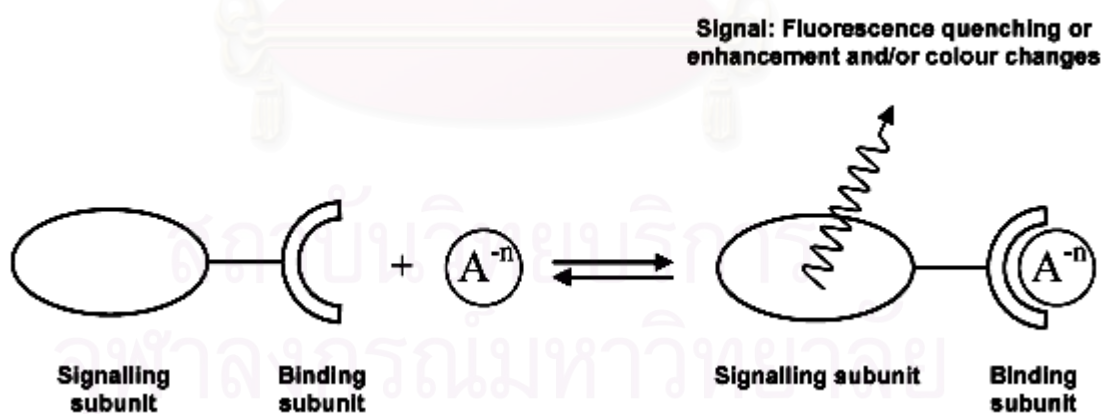
Figure 1.4 Anion chemosensor based on the binding site-signaling subunit approach.[15]

Fluorescence detection has been widely used as a versatile tool in analytical chemistry, biochemistry, cell biology, etc. In relation to the use of fluorescence for sensing or detecting, the principal advantage over other light-based methods such as absorbance is its high sensibility. This is so because the emission fluorescence signal is proportional to the substance concentration whereas in absorbance measurements the substance concentration is proportional to the absorbance, which is related to the ratio between intensities measured before and after the beam passes through the sample. Therefore, in fluorescence, an increase of the intensity of the incident beam results in a larger fluorescence signal whereas this is not so for absorbance. Fluorescence techniques can measure concentrations even one million times smaller than absorbance techniques.

There are excellent reviews dealing with the study of mechanisms involving the photophysics of fluorogenic chemosensors, and it is not our intention to explain exhaustively those mechanisms. However, it is interesting to understand the basis of the nature of the photoinduced processes that are responsible for the photophysical changes upon anion coordination. These effects are specifically related with the use of the binding site-signaling subunit approach and the displacement approach.

2.1.) Photoinduced Electron Transfer (PET)

This photoinduced process has been extensively studied and widely used for sensing purposes of cations and anions. As described above, fluorescence in a molecule is observed when an excited electron, for instance in the lowest unoccupied molecular orbital (LUMO), goes to the highest occupied molecular orbital (HOMO), releasing the excess of energy as light. Over this scheme, it might happen that an orbital from another part of the molecule or from another molecular entity could have energy between that of the HOMO and that of the LUMO of the fluorophore. When this "alien" orbital is full (for instance, if we have a donor group), a PET from this full orbital to the HOMO of the fluorophore can take place. A further electron transfer from the LUMO of the fluorophore to the external orbital retrieves the stable ground state. Following this sequence, fluorescence quenching occurs because the transition from the excited to the ground state takes place following a nonradiative path (see Figure 1.5 (a)). What is macroscopically observed is a decrease of the emission intensity or no fluorescence at all. A similar

process can take place when there is an empty orbital from another part of the molecule or from another molecular entity between both the HOMO and the LUMO of the fluorophore. In this case, a PET from the excited LUMO to the empty orbital can occur, followed by a further electron transfer from this orbital to the HOMO of the fluorophore. Again, deexcitation occurs without radiation and fluorescence quenching is observed (see Figure 1.5 (b)). The design of anion chemosensors tries to take advantage of such PET effects in such a way that the presence of the anion should induce the appearance or the removal of energy levels between the HOMO and the LUMO of the fluorophore inducing quenching or enhancement of the fluorescence emission.

(a)   (b)
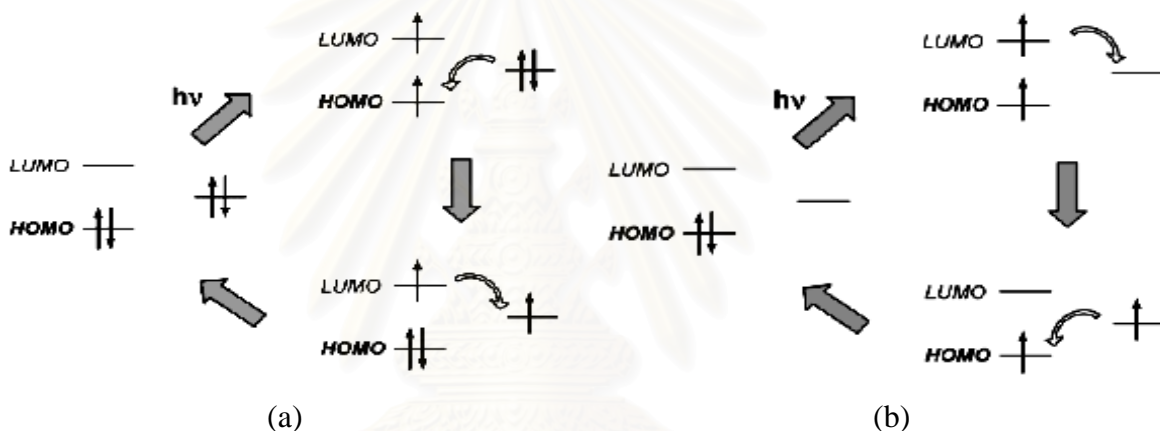
Figure 1.5 PET process with the participation of the HOMO and LUMO of the fluorophore and (a) an external molecular orbital (b) empty external molecular orbital.

2.2) Electronic Energy Transfer (EET)

Another mechanism that may be responsible for the fluorescence quenching by certain molecular entities is the EET. When the external molecular group has some empty or half-filled energy levels between the HOMO and the LUMO of the fluorophore, a simultaneous exchange of two electrons (from the LUMO to the foreign orbital and from the foreign orbital to the HOMO) can occur (see Figure 1.6). The double electron exchange restores the fluorophore to its ground state following a nonradiative process therefore resulting in a fluorescence quenching. The occurrence of this double and

simultaneous electron transfer requires a close contact between the fluorophore and the molecular group. Thus, flexible linkers may favor the occurrence of an intramolecular energy transfer process of this type.
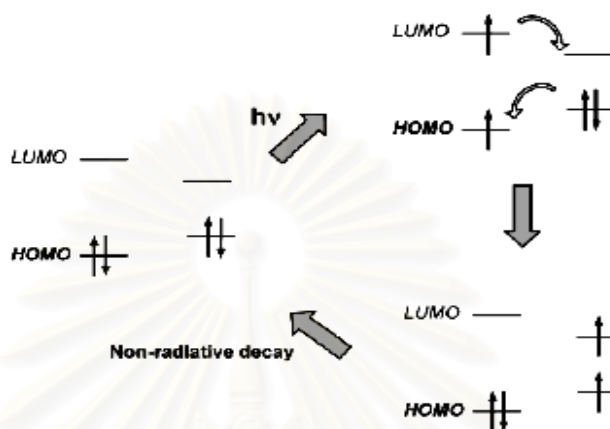
Figure 1.6 EET process with the participation of the HOMO and LUMO of the fluorophore and an external molecular orbital.

3. Fluorescent Sensors based on Calix[4]arene and Calix[4]pyrrole

Calixarenes are cavity-shaped cyclic molecules obtained from the base-catalyzed condensation of *p-tert*-butylphenol and formaldehyde. Among calixarenes, calix[4]arene is the most interesting platform due to its ease of synthesis, functionalization, its conformation and its promise as selective complexing agents in sensors. The "vase like shape" of calix[4]arene ("calic" means vase in Greek) can behave as platform for inclusion of guest molecule due to their flexible cavities.

In solution, calix[4]arene exists in 4 conformers called cone, partial cone, 1,2-alternate, and 1,3-alternate (see Figure 1.7). Each of them has its own specific properties and characteristic utilization in host-guest chemistry. Calix[4]arene is a very attractive compound that can be used as a platform for designing more sophisticated structure for binding ions and neutral molecules.
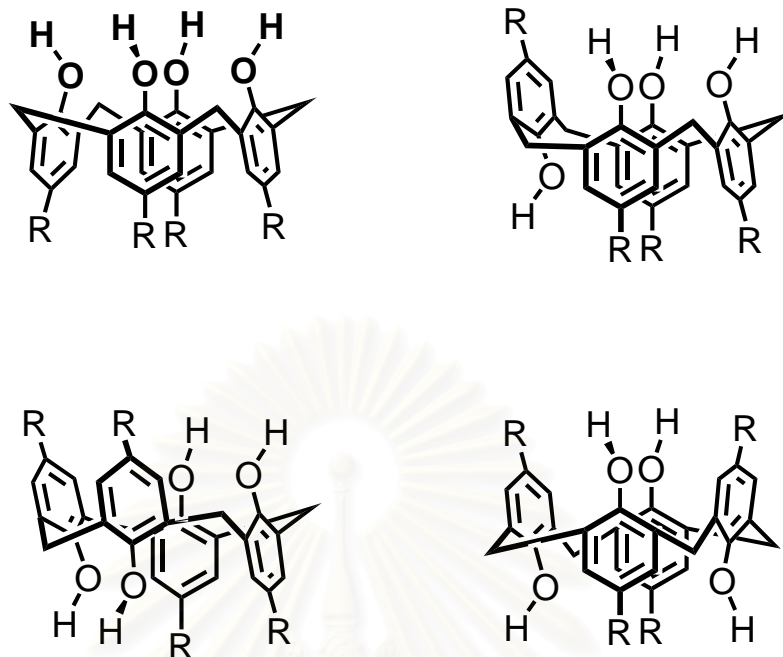
Figure 1.7 Conformations adopted by calix[4]arene

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

Fluorescent chemosensors for ion typically consist of an ion recognition unit (ionophore) and a fluorogenic unit (fluorophore) linked to the ionophore through a proper spacer. As recognition moieties for cations and anions, calixarenes with appropriate appended groups have been good candidates because of their high selectivity toward specific cations and anion, and their potential applications as fluorescence sensing agents have recived increasing interest.[16,17] Calix[4]arenes have two reactive sites: (1) phenolic OHs (lower rim) and (2) *para* positions (upper rim) to the hydroxy groups which can be easily functionalized with various cation-ligating groups such as carboxylic acid, amide, crown ether, and azacrown ether. In particular, amide groups as a functional group are known to capture not only cations through oxygen atoms but also anions and amide N-H. The fluorophores of calix[4]arene-based fluorescent sensors can be the pyrenyl,[18,19]

anthracenyl,[20] dansyl,[21] naphthalenyl,[22,23] coumarinyl[24] or 5-nitro-salicylaldehyde[25] groups which are appended at upper rim or lower rim of calix[4]arene platform. Most such calixarene-based fluorescence sensors were reported to utilize photophysical changes produced by cation binding: PET (photoinduced electron transfer); PCT (photoinduced charge transfer); excimer/exciplex formation and extinction; or energy transfer.

As for realizing high sensitivity, fluorometric sensing has been used. The pyrenyl group has often been used as an effective fluorescence probe because of its high detection sensitivity. Host molecules containing plural pyrenyl groups show an intramolecular excimer emission due to π-π stacking of the pyrene rings in the free state. Their structures change upon the addition of guest molecules as a direct result of complexation, which results in a decrease of the excimer emission intensity with an increase of monomer emission intensity. Since the degree of structural change highly depends on the kind of guest molecules, these compounds show selectivity toward specific molecules. Thus, a certain event that brings about structural changes in response to specific guest molecules is important in the molecular design of new fluorophores. Indeed, a variety of detection systems for guest molecules and ions using fluorescence changes in intramolecular excimer emission or fluorescence quenching of various pyrene functionalized ligands have been developed. Host molecules with more than one pyrenyl group exhibit intramolecular excimer emission by two different mechanisms. One results from π-π stacking of the pyrene rings in the free state, which results in a characteristic decrease of the excimer emission intensity and a concomitant increase of monomer emission intensity. The other mechanism is due to interaction of an excited pyrene (Py*) unit with a ground-state pyrene (Py) unit. Some pyrene-containing hosts exhibit excimer emission due to the former mechanism and some due to the latter.

The first example of a fluorescent sensor based on calix[4]arene is a calix[4]arene bearing two pyroyloxy at the distal hydroxyl groups (Figure 1.8 (a)). The eximer formation was observed in the absence of cation.[18] The methylamide linker was used to anchor the pyrene unit to calix[4]arene framework at lower rim but the disubstituted compound exhibits only a monomer emission at 398 nm because the hydrogen bonding between the phenolic OH oxygens and the amide hydrogens prevents close approach of

two pyrene groups (Figure 1.8 (b)).[19] The *O*-alkylation of the remained phenolic OH can provide calix[4]aren-based fluorescent sensor in cone (Figure 1.8 (c))[19] or 1,3-alternate conformations (Figure 1.8 (d)).[26] Both can also form excimers in the absence of cation and eximer fluorescence is quenched upon binding of cations.

(a) (b)

(c) (d)
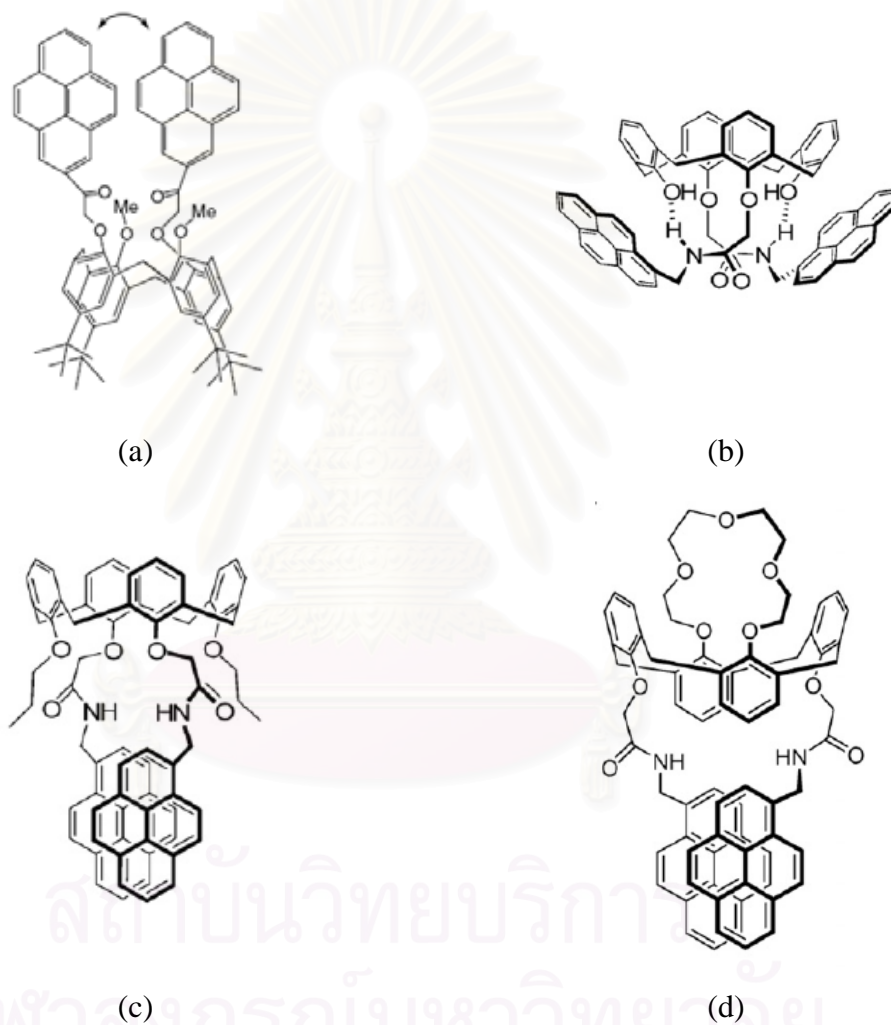
Figure 1.8 Fluorogenic pyrene cation sensors based on calix[4]arene.

However, the development of fluorescent sensor base on calix[4]arene for anion is much slower that for cation. A few fluorescent calix[4]arene anionophores was reported during the past decade.[27,28]

(a)   (b)   (c)
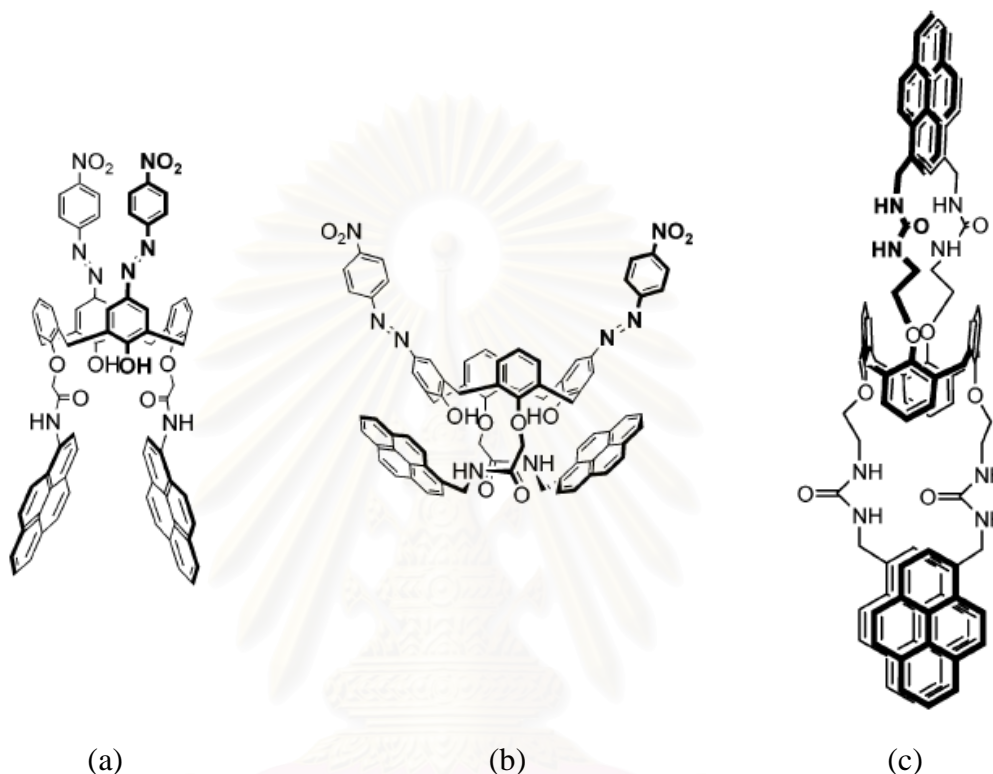
Figure 1.9 Fluorogenic pyrene anion sensors based on calix[4]arene.

The calix[4]arene sensors containing both chromogenic unit (4-nitrophenylazo) and fluorogenic moiety (pyrene) as sensing units and amide linkages as anion binding units were developed.[27] The color changes upon anion complexations, especially F⁻, were observed for both di(4-nitrophenylazo)-bis[N-(1-pyrenyl)-amidomethoxy)calix[4]arene (Figure 1.9 (a)) and di(4-nitrophenylazo)-bis[N-(1-pyrenylmetyl)-amidomethoxy)calix[4]arene (Figure 1.9 (b)) but the excimer formation was only revealed for the former. The fluorescence quenching of both compounds are different upon F⁻ binding. The blue shift fluorescence quenching was observed for the first case while the second one produced a red shift. A urea unit was used to serve as anion binding unit and incorporated on 1,3-alternate calix[4]arene scaffold.[28] A

tetra(pyrenylurea)calix[4]arene (Figure 1.9 (c)) was reported to be a chloride selective fluorescent sensor. Its excimer emission is quenched with a simultaneous rise in monomer emission solely by the chloride anion among a wide variety of anions tasted.

It is well known that among the various neutral anion receptors described in many literatures, calix[4]pyrroles, which are readily accessible from pyrrole and ketone, have been identified as one of the most attractive hosts for the binding of halide anions, especially for fluoride ions. The crystal structure of the free macrocyclic has a 1,3-alternate conformation with alternating pyrrole rings oriented 'up' and 'down' (Figure 1.11a). On binding a halide anion, however, crystallographic and NMR experiment indicated that the pyrrole rings align with all four N-H groups convergent, forming hydrogen bonds with the bound guest (Fig. 1.11 b).
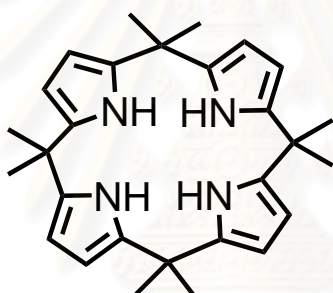
Figure 1.10 *meso*-octamethylcalix[4]pyrrole.
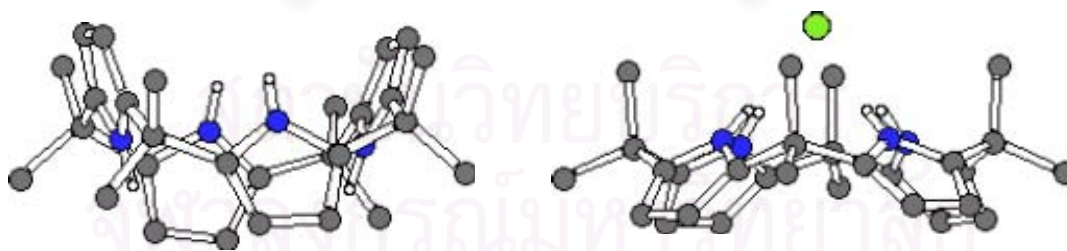
Figure 1.11 Crystal of (a) free *meso*-octamethylcalix[4]pyrrole and (b) *meso*-octamethylcalix[4]pyrrole with a bound chloride anion perched above the macrocyclic plane.[29]

The attempt for construction of anion receptor based on calix[4]arene appended calix[4]pyrrole was realized. In 1996, the first calix[4]arene-capped calix[4]pyrrole, calix[4]arene-calix[4]pyrrole pseudo dimer (Figure 1.12),[30] was obtained as the result of a template mediated condensation between a keto-functionalized calixarene and pyrrole by Sessler and co-workers. From its ^{1}H-NMR spectroscopic studies, this receptor contained a strong hydrogen bonding between the pyrrole NH groups and the calixarene oxygen atoms. Addition of tetrabutylammonium fluoride to the ligand solution caused no changes on the ^{1}H-NMR spectrum.

A year later, the same group[31] has achieved the first synthesis of the expanded calix[n]pyrrole, n = 5. In its complexation studies with tetrabutylammonium chloride, the calix[5]arene-calix[5]pyrrole shows a small downfield shift in the NH proton caused by weaker internal hydrogen bonding array compared with its corresponding tetrameric dimer.

(a)   (b)
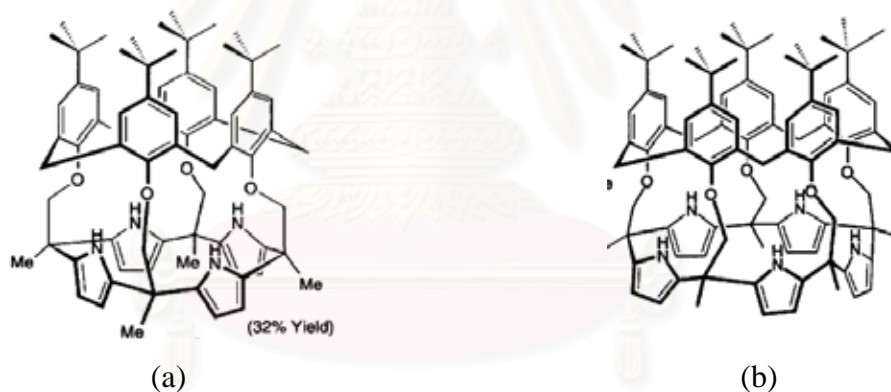
Figure 1.12 Molecular structures of calix[n]arene-calix[n]pyrrole pseudo dimers (a) n=4
(b) n=5

However, Ruangchaitaweesuk[32] successed to synthesize calix[4]arene-capped calix[4]pyrroles by replacing the methylene bridges between 2 subunits with triethylene glycol chains. The calix[4]arene-calix[4]pyrrole pseudo-dimers can act as the selective anion receptors.

Objectives and scope of the research

The target of this work are to synthesize fluorogenic sensor for anion by incorporation of a calix[4]pyrrole serving as anion binding unit and a pyrene group acting as fluorophore onto calix[4]arene framework, pyrenylcalix[4]arene-calix[4]pyrrole, and study its complexation properties.
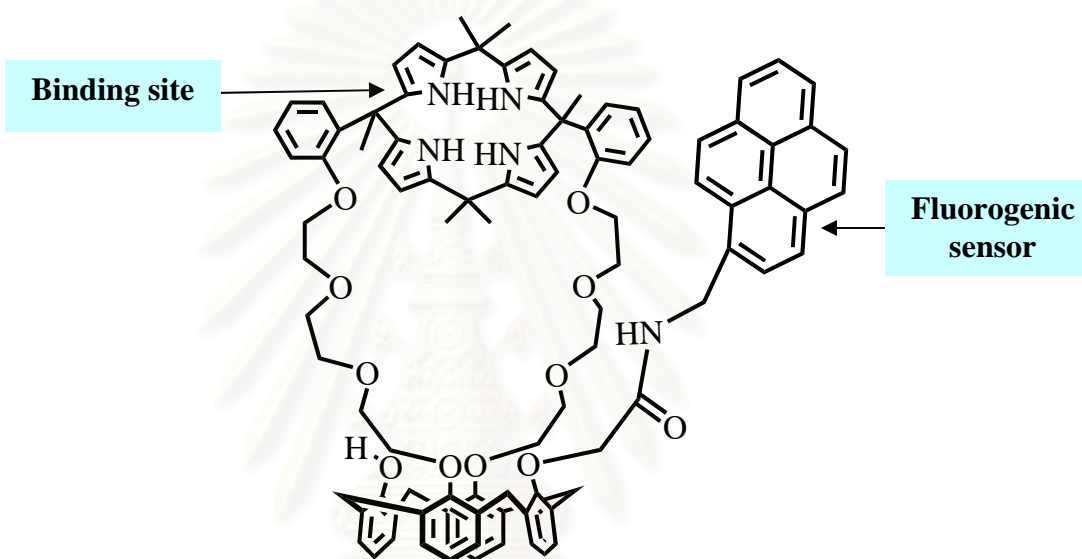
CHAPTER II

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 except 1,3-dipyrenyl-calix[4]arene-calix[4]pyrrole was dissolved in deuterated acetonitrile. Elemental analysis was carried out on CHNS/O analyzer (Perkin Elmers PE2400 series II). MALDI-TOF Mass spectra were recorded on a Biflex Bruker Mass spectrometer. Absorption spectra were measured by a Varian Cary 50 UV-Vis spectrophotometer. Fluorescence spectra were measured by a Varian Cary Eclipse spectrofluorometer controlled with a personal computer data processing unit. The light source is a pulsed xenon lamp and a detector is a photomultiplier tube.

2.1.2 Materials

All materials were standard analytical grade, purchased from Fluka, Alddrich or Merck and used without further purification. Commercial grade solvents such as acetone, hexane, dichloromethane, methanol and ethyl acetate were distilled before used. Acetonitrile was dried over CaH_2 and freshly distilled under nitrogen prior to use.

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

Starting materials such as *p-tert*-butylcalix[4]arene were prepared according to the literature procedure.[33] The compounds were characterized by ^{1}H-NMR spectroscopy, infrared spectroscopy, mass spectroscopy and elemental analysis.

2.2 Synthesis

2.2.1 Preparation of triethyleneglycol ditosylate (1)
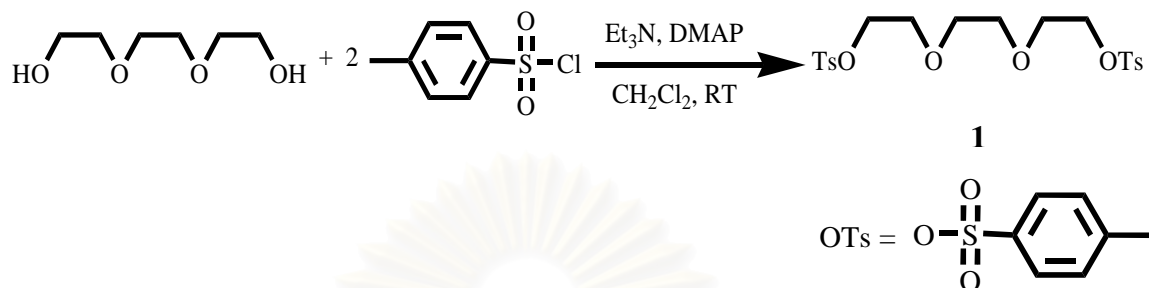
Into a 250 mL two-necked round bottom flask, a solution of triethyleneglycol (3.00 g, 28 mmol), triethylamine (11.8 mL, 85 mmol) and a catalytic amount of 4-dimethylaminopyridine in 50 mL of dichloromethane was chilled to 0 ˚C with an ice bath. The solution of tosylchloride (11.86 g, 62 mmol) in dichloromethane (100 mL) was then added dropwise. The reaction mixture was stirred for 4 hours at room temperature under nitrogen atmosphere. After the reaction was completed, the solution of 3 M hydrochloric acid was added until the pH of the solution reached to 1 and then extracted with dichloromethane (2 × 50 mL). The residue was dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. The residue was dissolved in a minimum amount of dichloromethane and methanol was added to precipitate. Compound **1** was obtained as a white solid (7.66 g, 65% yield).

Characteristic data for 1: ^{1}H NMR spectrum (CDCl$_3$, δ(ppm), 400 MHz): 7.77 (d, J_{H-H} = 8.2 Hz, 4H, *o*-Ar**H**), 7.32 (d, J_{H-H} = 8.2 Hz, 4H, *m*-Ar**H**), 4.10 (t, J_{H-H} = 4.7 Hz, 4H, SO$_2$OC**H$_2$**CH$_2$OCH$_2$), 3.60 (t, J_{H-H} = 4.7 Hz, 4H, SO$_2$OCH$_2$C**H$_2$**OCH$_2$), 3.50 (s, 4H, SO$_2$OCH$_2$CH$_2$OC**H$_2$**), 2.42 (s, 6H, Ar-C**H$_3$**); **IR spectrum (KBr pellet (cm^{-1})):** 2800-3000 (CH, st), 1150-1200 (C-O-C, st)

2.2.2 Preparation of 2-(8-tosyltriethyleneglycol)acetophenone (2)

1   **2**
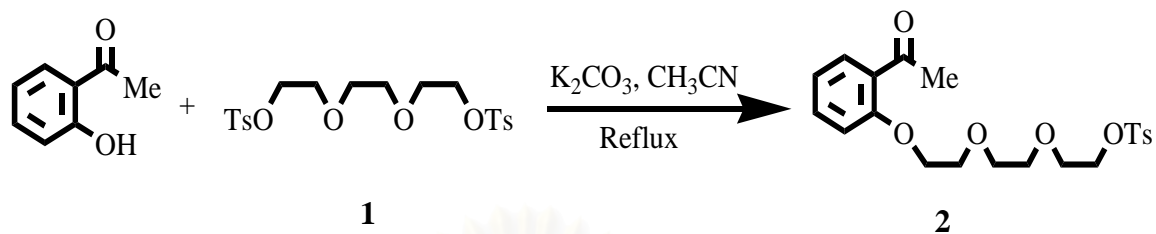
Into a 250 mL two-necked round bottom flask, 2-hydroxyacetophenone (1.36 g, 10 mmol) and K_2CO_3 (13.82 g, 100 mmol) were suspended in dried acetonitrile (50 mL). The mixture was stirred at room temperature under nitrogen atmosphere for 1 hour. A solution of triethyleneglycol ditosylate (**1**) (9.16 g, 20.0 mmol) in dried acetonitrile (100 mL) was then added dropwise. The reaction mixture was stirred and refluxed under nitrogen atmosphere for 18 hours. After the reaction was completed monitoring by TLC, the solution was allowed to cool to room temperature. The solvent was evaporated to dryness under reduced pressure. The obtained residue was dissolved in dichloromethane (100 mL) and extracted with 3 M HCl (1 × 100 mL) and water (2 × 100 mL), respectively. The combined organic layer was dried over anhydrous Na_2SO_4 and filtered off to give yellow oil. Compound **2** was purified by column chromatography (silica gel, CH_2Cl_2 : EtOAc; 90:10) and obtained as a colorless oil (2.53 g, 30%).

Characteristic data for 2: ^{1}H-NMR spectrum (CDCl$_3$, δ(ppm), 400 MHz): 7.82 (d, J_{H-H} = 4.0 Hz, 2H, Ar$_{tosyl}$**H**), 7.77 (dd, J_{H-H} = 1.6, 8.0 Hz, 1H, Ar**H**), 7.47 (t, J_{H-H} = 2.0, 8.0 Hz, 1H, Ar**H**), 7.36 (d, J_{H-H} = 4.0 Hz, 2H, Ar$_{tosyl}$**H**), 7.03 (t, $J_{H-H,}$ = 8.0 Hz, 1H, Ar**H**), 6.98 (d, J_{H-H} = 8.0 Hz, 1H, Ar**H**), 4.25 (t, J_{H-H} = 4.8 Hz, 2H, SO$_2$OC**H**$_2$), 4.18 (t, J_{H-H} = 4.8 Hz, 2H, ArOC**H**$_2$), 3.91 (t, J_{H-H} = 4.8 Hz, 2H, C**H**$_2$O), 3.73-3.64 (m, 6H, C**H**$_2$O), 2.66 (s, 3H, COC**H**$_3$), 2.46 (s, 3H, ArC**H**$_3$).

Elemental analysis: *Anal.Calcd.* for C$_{21}$H$_{26}$O$_7$S: C, 59.70%; H, 6.20%
Found: C, 59.78%; H, 6.29%

2.2.3 Preparation of 1,3-calix[4]-diacetophenone (3)
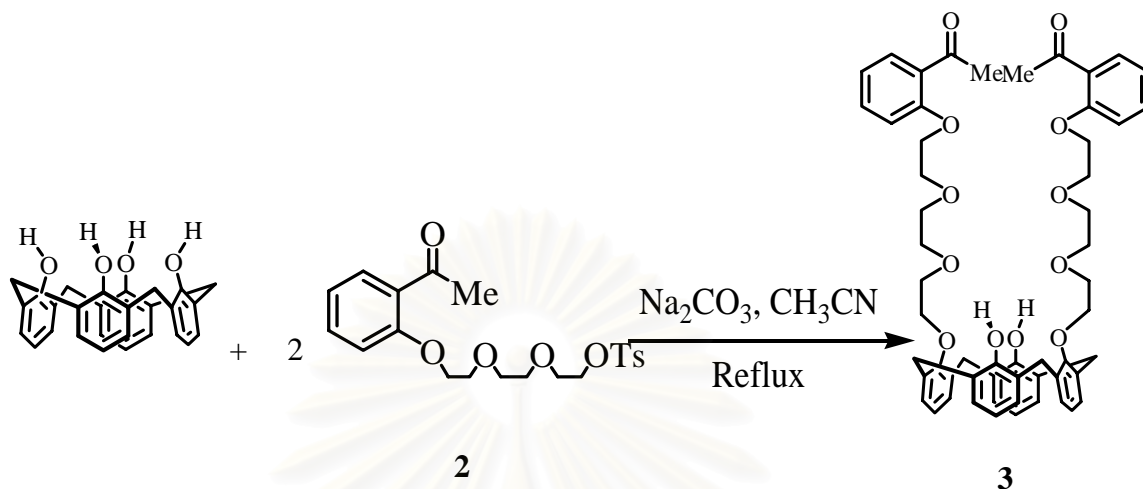
Into a 250 mL two-necked round bottom flask containing calix[4]arene (2.40 g, 5.7 mmol), Na$_2$CO$_3$ (6.00 g, 56.6 mmol) and acetonitrile (50 mL), a solution of 2-(8-tosyltriethyleneglycol)acetophenone (**2**) (4.78 g, 11.3 mmol) in acetonitrile (100 mL) was added dropwise. The reaction mixture was refluxed with stirring under nitrogen atmosphere for 7 days. After cooling to room temperature, the solvent was removed under reduced pressure to give yellow oil. The residue was dissolved in dichloromethane (100 mL) and extracted with 3 M HCl (1×100 mL) and water (2×100 mL), respectively. The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered off and evaporate to dryness under reduced pressure. The residue was dissolved in a minimum amount of dichloromethane and methanol was added to precipitate 1,3-calix[4]-diacetophenone (**3**) as a white solid (4.47 g, 85%)

Characteristic data for (3): ^{1}H-NMR spectrum (CDCl$_3$, δ(ppm), 400 MHz): 7.78 (t, J_{H-H} = 2.0 Hz, 2H, Ar**H**COCH$_3$), 7.45 (t, J_{H-H} = 2.0, 8.0 Hz, 2H, Ar**H**COCH$_3$), 7.26 (s, 2H, ArO**H**), 7.07 (d, J_{H-H} =7.6 Hz, 4H, Ar**H**OCH$_2$), 7.02 (t, J_{H-H} = 7.4 Hz, 2H, Ar**H**COCH$_3$), 6.89 (d, J_{H-H} = 7.6 Hz, 4H, Ar**H**OH), 6.86 (d, J_{H-H} = 8.8 Hz, 2H, Ar**H**COCH$_3$), 6.75 (t, J_{H-H} = 7.4 Hz, 2H, Ar**H**OCH$_2$), 6.67 (t, J_{H-H} = 7.4 Hz, 2H, Ar**H**OH), 4.43 (AB system, J_{H-H} = 13.0 Hz, 4H, ArC**H**$_2$Ar), 4.19 (t, J_{H-H} = 4.2 Hz, 4H, OC**H**$_2$), 4.08 (t, J_{H-H} = 4.2 Hz, 4H,

OCH$_2$), 3.99 (t, J_{H-H} = 4.2 Hz, 4H, OCH$_2$), 3.90-3.89 (m, 8H, OCH$_2$), 3.78-3.82 (m, 4H, OCH$_2$), 3.36 (AB system, J_{H-H} = 13.0 Hz, 4H, ArCH$_2$Ar), 2.67 (s, 6H, ArCOCH$_3$).

Elemental analysis: *Anal.Calcd.* for C$_{56}$H$_{60}$O$_{12}$: C,72.71%; H, 6.54%

Found: C,71.72%; H, 6.41%

2.2.4 Preparation of 1,3-calix[4]arene-bis-dipyrroethane (4)

3   +   80 $\overset{\text{H}}{\underset{}{\text{N}}}$ $\xrightarrow[\text{2 hrs}]{\text{TFA, RT}}$ 4
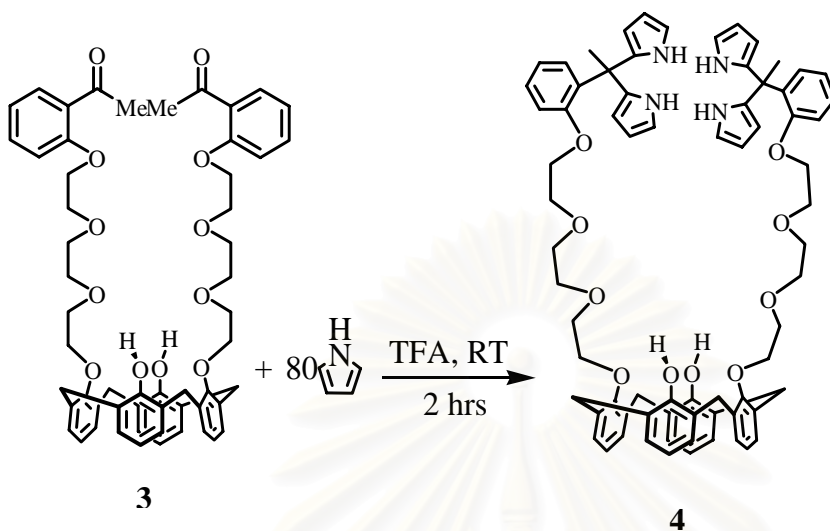
Into a 100 mL two-necked round bottom flask, a solution of 1,3-calix[4]-diacetophenone (**3**) (4.23 g, 4.6 mmol) in pyrrole (25.5 mL, 365 mmol) was degassed by bubbling with nitrogen for 15 min, and CF$_3$COOH (0.07 mL, 0.9 mmol) was then added. The solution was stirred in darkness for 10 min at room temperature. Then the reaction mixture was diluted with CH$_2$Cl$_2$ (100 mL), washed with 0.1 M NaHCO$_3$ (2 × 100 mL) and water (2× 100 mL). The organic layer was dried over anhydrous Na$_2$SO$_4$ and the solvent was removed in vacuo. The obtained residue was purified by column chromatography over silica gel (CH$_2$Cl$_2$:EtOAc:NEt$_3$ = 95:5:1) to give 3.22 g of the 1,3-calix[4]-bis-dipyrroethane (**4**) as a transparent viscous oil (61% yield).

Characteristic data for 4: ^{1}H-NMR spectrum (CDCl$_3$, δ(ppm), 400 MHz): 8.86 (s, 4H, N**H**), 7.74 (s, 2H, Ar**OH**), 7.32-7.26 (m, 2H, Ar**H**), 7.22-7.17 (m, 2H, Ar**H**), 7.10 (d, $J_{\text{H-H}}$ = 7.6 Hz, 4H, Ar**H**OCH$_2$), 6.95 (t, $J_{\text{H-H}}$ = 8.0 Hz, 2H, Ar**H**C$_{py}$CH$_3$), 6.90 (d, $J_{\text{H-H}}$ = 8.0 Hz, 4H, Ar**H**OH), 6.75 (t, $J_{\text{H-H}}$ = 7.6 Hz, 2H, Ar**H**C$_{py}$CH$_3$), 6.71 (t, $J_{\text{H-H}}$ = 7.6 Hz, 4H, Ar**H**OCH$_2$), 6.60-6.64 (m, 4H, **H**$_{py}$), 6.09-6.13 (m, 4H, **H**$_{py}$), 5.90-5.94 (m, 4H, **H**$_{py}$), 4.44 (AB system, $J_{\text{H-H}}$ = 13.0 Hz, 4H, ArC**H**$_2$Ar), 4.15-4.19 (m, 4H, OC**H**$_2$), 3.96 (t, $J_{\text{H-H}}$ = 4.6 Hz, 4H, OC**H**$_2$), 3.87 (t, $J_{\text{H-H}}$ = 4.6 Hz, 4H, OC**H**$_2$), 3.78 (t, $J_{\text{H-H}}$ = 4.6 Hz, 4H, OC**H**$_2$),

3.70 (t, $J_{\text{H-H}}$ = 4.6 Hz, 4H, OC**H**$_2$), 3.39 (AB system, $J_{\text{H-H}}$ = 13.0 Hz, 4H, ArC**H**$_2$Ar), 3.36 (d, $J_{\text{H-H}}$ = 4,8 Hz, 4H, OC**H**$_2$), 2.67 (s, 6H, ArC$_{py}$C**H**$_3$)

Elemental analysis: *Anal.Calcd.* for C$_{72}$H$_{76}$N$_4$O$_{10}$: C,74.72%; H, 6.62%; N, 4.84%

Found: C,73.38%; H, 6.61%; N, 4.66%

2.2.5 Preparation of calix[4]arene-calix[4]pyrrole (5)

4   **5**
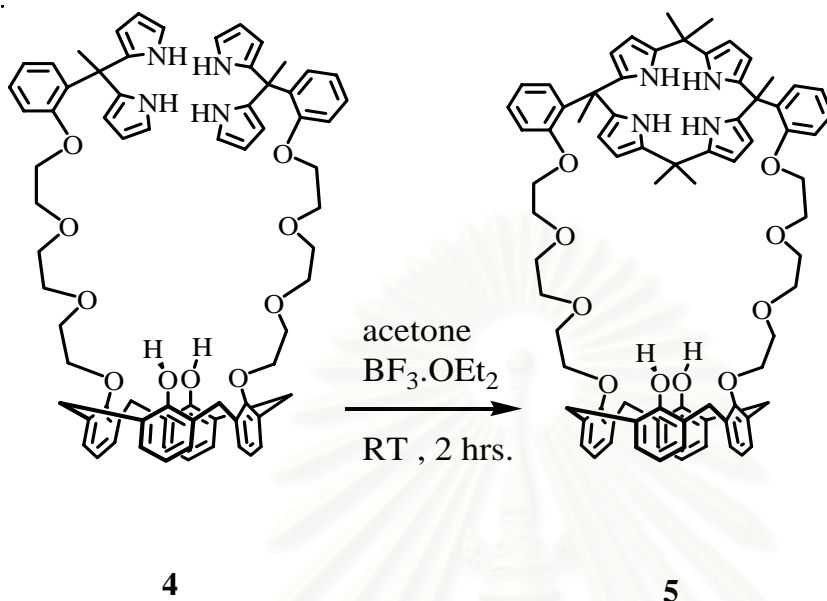
A solution of 1,3-calix[4]-bis-dipyrroethane (0.13 g, 0.1 mmol) in acetone (30 mL) was added with $BF_3.OEt_2$ (0.01 mL, 0.04 mmol). The solution was stirred for 2 hours at room temperature. The solvent was removed by rotary evaporator under reduced pressure. The obtained residue was dissolved with CH_2Cl_2 and extracted with saturated $NaHCO_3$ solution. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by silica gel pack using CH_2Cl_2:EtOAc (95:5) as eluent. The product containg fractions were conbined and dried under vacuo. The obtained solid was dissolved in dichloromethane and recrystalized with methanol to give 0.05 g of **5** as a white solid (37% yield).

Characteristic data for (5): **^{1}H-NMR spectrum** (CDCl$_3$, δ(ppm), 400 MHz): 7.98 (s(br), 4H, N**H**), 7.91 (s, 2H, ArO**H**), 7.23 (t, J_{H-H} = 8.4 Hz, 2H, Ar**H**), 7.08 (d, J_{H-H}=7.6 Hz, 4H, Ar**H**), 6.94 (d, J_{H-H}= 7.6 Hz, 8H, Ar**H**), 6.85 (d, J_{H-H} = 8.0 Hz, 2H, Ar**H**), 6.78 (t, J_{H-H} = 7.6 Hz, 4H, Ar**H**), 6.68 (t, J_{H-H} = 7.6 Hz, 2H, Ar**H**), 5.91 (s, 4H, **H**$_{py}$), 5.67 (s(br), 4H, **H**$_{py}$), 4.40 (AB system, J_{H-H} = 13.0 Hz, ArC**H$_2$**Ar), 4.20 (t, J_{H-H} = 4.8 Hz, 4H, OC**H$_2$**), 4.09 (t, J_{H-H} = 5.0 Hz, 4H, OC**H$_2$**), 3.89 (t, J_{H-H} = 4.6 Hz, 4H, OC**H$_2$**), 3.83 (s, 4H,

OCH$_2$), 3.57 (s, 4H, OCH$_2$), 3.39 (AB system, J_{H-H} = 13.0 Hz, 4H, ArCH$_2$Ar), 3.13 (s, 4H, OCH$_2$), 2.09 (s, 6H, ArCCH$_3$), 1.55 (s, 12H, (CH$_3$)$_2$CPy$_2$)

Elemental analysis: *Anal.Calcd.* for C$_{78}$H$_{84}$N$_4$O$_{10}$: C,75.70%; H, 6.84%; N, 4.53%

Found: C,75.65%; H, 6.73%; N, 4.56%

MALDI-TOF mass (m/z) [M+Na$^+$] : 1259.65

2.2.6 Preparation of *N*-(1-pyrenylmethyl)chloroacetamide (6)

6
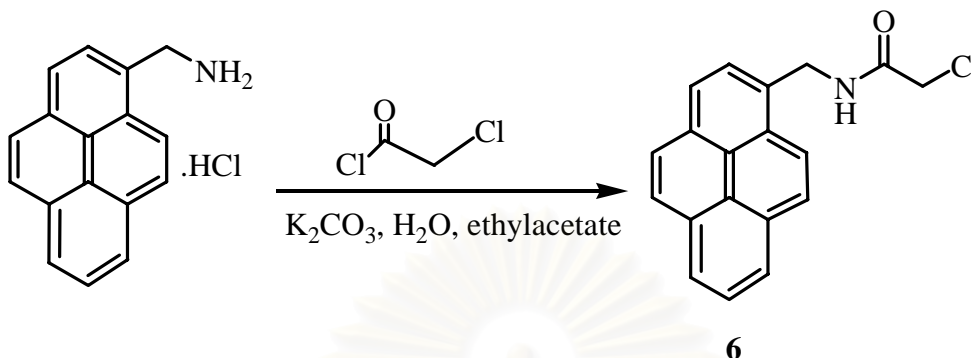
Into a suspension of 1-pyrenemethylamine hydrochloride (0.60 g, 2.2 mmol) and potassium carbonate (1.24 g, 9.0 mmol) in a mixture of water (100 mL) and ethyl acetate (100 mL), a solution of chloroacetyl chloride (0.075 mL, 2.8 mmol) in ethyl acetate (10 mL) was added dropwise. The reaction mixture was stirred at room temperature for 2 hours under inert atmosphere. Then, the organic phase was separated and dried over anhydrous magnesium sulfate. After the solvents were evaporated off under vacuo, the obtained solid was purification by column chromatography (SiO_2, ethyl acetate/hexane 1:3) to give a white solid (0.25 g, 75%).

Characteristic data for 6: **^{1}H-NMR spectrum** (CD_3CN, δ(ppm), 400 MHz): 8.02-8.31 (m, 9H, Ar**H**), 6.95 (s (br), 1H, N**H**), 5.23 (d, J_{H-H} = 5.4 Hz, 2H, NHC**H$_2$**), 4.19 (s, 2H, COC**H$_2$**)

2.2.7 Preparation of pyrenylcalix[4]arene-calix[4]pyrrole (7)
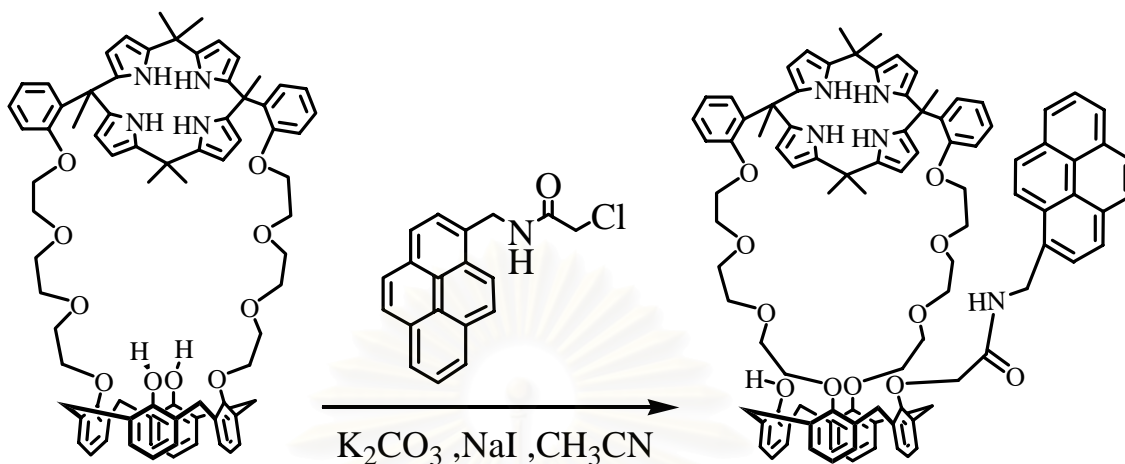
Into a suspension of calix[4]arene-calix[4]pyrrole (**5**) (20 mg, 0.016 mmol), anhydrous potassium carbonate (88 mg, 0.064 mmol) and a catalytic amount of sodium iodide in 15 mL of dried acetonitrile, a solution of N-(1-pyrenylmethyl)chloroacetamide (**6**) (10.8 mg, 0.035 mmol) in 10 mL of dried acetonitrile was added. The reaction mixture was refluxed for 30 hrs. After removal of the solvent in vacuo, the obtained solid was dissolved in CH_2Cl_2 (10 mL) and extracted with $NaHCO_3$ solution (10 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography using CH_2Cl_2:EtOAc (97:3) as eluent to afford **7** in 66% yield (19 mg).

Characteristic data for 7 : ^{1}**H-NMR spectrum** (CD$_3$CN, δ(ppm), 400 MHz): 8.02-8.31 (m, 9H, pyrene-**H**), 7.95 (s, 1H, ArO**H**), 7.23 (t, J_{H-H} = 8.4 Hz, 2H, Ar**H**), 7.08 (d, J_{H-H} = 7.6 Hz, 4H, Ar**H**), 6.94 (d, J_{H-H} = 7.6 Hz, 4H, Ar**H**), 6.85 (d, J_{H-H} = 8.0 Hz, 2H, Ar**H**), 6.78 (t, J_{H-H} = 7.6 Hz, 4H, Ar**H**), 6.68 (t, J_{H-H} = 7.6 Hz, 6H, Ar**H**), 5.91(s, 4H, **H**$_{py}$), 5.67 (s, 4H, **H**$_{py}$), 5.23 (d, J_{H-H} = 5.4 Hz, 2H, NHC**H**$_2$pyrene), 4.40 (AB system, J_{H-H} = 13.0 Hz, 4H, ArC**H**$_2$Ar), 4.20 (t, J_{H-H} = 4.8 Hz, 4H, OC**H**$_2$), 4.09 (t, J_{H-H} = 5.0 Hz, 4H, OC**H**$_2$), 3.89 (t, J_{H-H} = 4.6 Hz, 8H, OC**H**$_2$), 3.43 (t, J_{H-H} = 5.2 Hz, 8H, OC**H**$_2$, ArC**H**$_2$Ar), 3.13 (s, 4H, OC**H**$_2$), 2.09 (s, 6H, ArCC**H**$_3$), 1.55 (s, 12H, (C**H**$_3$)$_2$CPy$_2$).

MALDI-TOF mass (m/z): 1506.98

2.2.8 Preparation of calix[4]diquinone-calix[4]pyrrole (8)

5   Tl(CF$_3$CO$_2$)$_3$ **8**

CF$_3$CO$_2$H
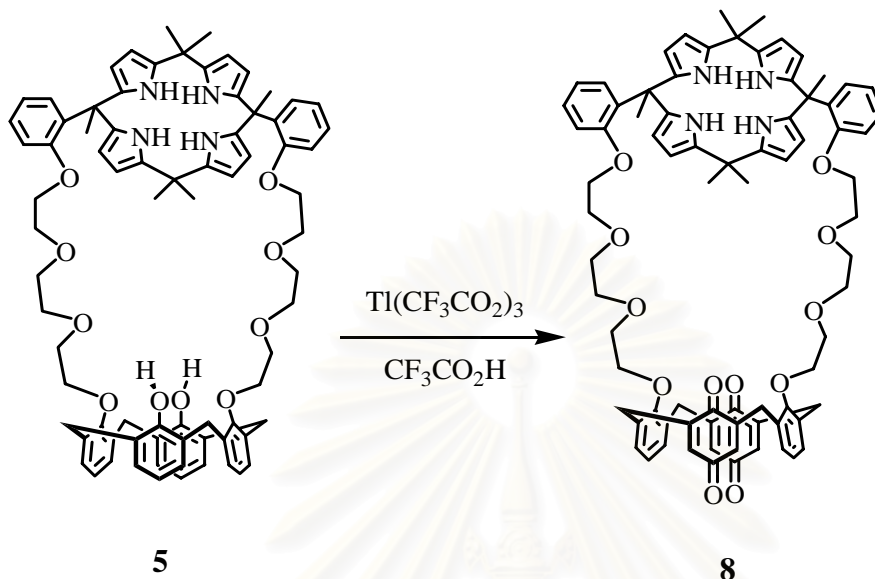
Into a 50 mL two-necked round-bottom flask containing a suspension of thallium trifluoroacetate (0.084 g, 0.194 mmol) in trifluoroacetic acid (3 mL) stirred in the darkness under nitrogen atmosphere for 1 hour a solution of calix[4]arene-calix[4]pyrrole (**5**) (0.024 g, 0.02 mmol) in trifluoroacetic acid (2 mL) was then added. The mixture was stirred for additional 2 hrs. The solution was then poured into ice. Chloroform (30 mL) was added and then stirred for 30 minutes. The organic layer was separated and washed with water until the pH of aqueous phase reached to **7**. The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in a minimum amount of chloroform, and methanol was added to precipitate a yellow solid.

2.3 Anion complexation studies of ligand 7 by fluorescence titration

Fluorescence spectra were recorded with a Varian Cary Eclipse spectrofluorometer. Stock solutions (2.4 mM) of the tetrabutylammonium anions were prepared by dissolving the given amounts of salts in CH_3CN. Stock solutions of **7** (0.04 mM) were prepared in CH_3CN. For all measurements, excitation was carried out at 343 nm with excitation and emission slit widths at 5 nm. Fluorescence titration experiments were performed using 6 μM solutions of **7** in CH_3CN and various concentrations of tetrabutylammonium anion in CH_3CN. The variations in fluorescence intensity I_F were recorded as a function of concentration of salt. The ligand concentration was kept constant and equal to 6 μM. The excitation wavelength was that of the absorption maximum of the complex, and the fluorescence intensities were in all cases monitored at 343 nm. After calculating the concentrations of the free ligands and complexed forms of **7** from the fluorescence titration experiments, the association constants (K_s) were obtained using the following equation $I_F^o/(I_F - I_F^o) = [a/(b-a)][(1/K_s[M]) + 1]$ where I_F^o is the fluorescence intensity of the solutions containing free ligand and I_F is the ligand complexed with anion at the chosen emission wavelength are measured and are related to the initial concentration of the ligand $[a/(b-a)]$. When $I_F^o/(I_F - I_F^o)$ is plotted against the reciprocal of the anion concentration $[M]^{-1}$, the correlation coefficients were ≥0.98, the stability constant is given by the ratio intercept/slope.[34,35,36]

CHAPTER III

RESULTS AND DISCOUSSION

3.1 Synthesis and characterization of calix[4]arene-calix[4]pyrrole derivatives and pyrenylcalix[4]arene-calix[4]pyrrole

3.1.1 Synthesis and characterization of 1,3-calix[4]-diacetophenone (3)

The synthetic pathway of 1,3-calix[4]-diacetophenone **3** (Scheme 3.1) started with a preparation of triethyleneglycol ditosylate **1** by tosylation of triethyleneglycol in the presence of triethylamine as base and a catalytic amount of DMAP in dichloromethane at room temperature for 4 hours. A white solid of compound **1** was obtained in 65% yield by precipitating with methanol. The ^{1}H-NMR spectrum of compound **1** showed the characteristic peaks of tosyl groups; a singlet of C**H**$_3$ at 2.42 ppm and two doublets of Ar**H** at 7.77 and 7.32 ppm ($J_{H-H} = 8.2$ Hz).
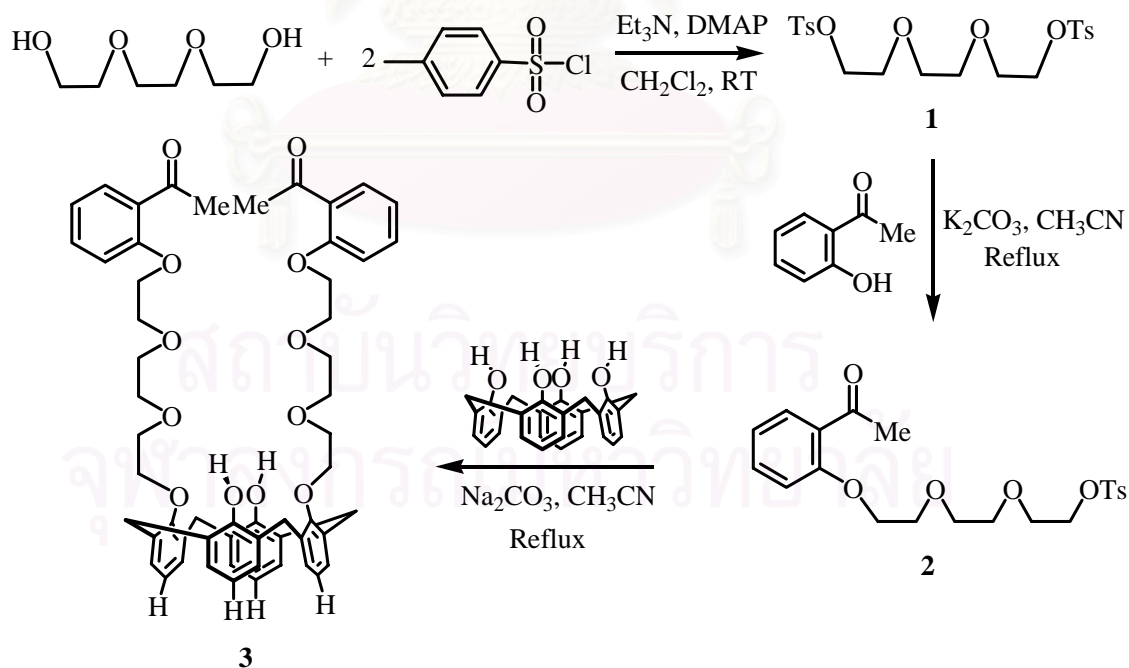
Scheme 3.1 Synthetic pathway of 1,3-calix[4]-diacetophenone (**3**) .

The nucleophilic substitution reaction of 2-hydroxyacetophenone with triethylene glycol ditosylate (**1**) using excess K_2CO_3 as base in acetonitrile provided 2-(8-tosyltriethyleneglycol)acetophenone (**2**) as a colorless oil (30% yield). The ^{1}H-NMR spectrum of **2** showed the characteristic peaks of tosyl groups; a singlet of C**H**$_3$ at 2.46 ppm and two doublets of Ar**H** at 7.82 and 7.36 ppm (J_{H-H} = 4.0 Hz), and the characteristic peaks of the acetophenone unit, a singlet of C**H**$_3$ at 2.66 ppm, two doublets of Ar**H** at 7.77 and 6.98 ppm (J_{H-H} = 8.0 Hz) and two triplets of Ar**H** at 7.47 and 7.03 ppm (J_{H-H} = 8.0 Hz).

A condensation of 2 equi. of 2-(8-tosyltriethyleneglycol)acetophenone (**2**) with calix[4]arene was carried out by using K_2CO_3 as a base in acetonitrile for 7 days. A white solid of compound **3** was obtained in 85% yield by precipitation with methanol in dichloromethane. From the ^{1}H-NMR spectrum, the substitution occurred in distal manner due to the presence of only AB-system of methylene bridge protons of calix[4]arene unit (ArC**H**$_2$Ar) as two doublets at 3.36 and 4.43 ppm (J_{H-H} = 13.0 Hz). These two doublets also indicated that compound **3** exists in cone conformation. The elemental analysis was in accordance with the structure of **3**.

3.1.2 Synthesis and characterization of 1,3-calix[4]arene-bisdipyroethne (4)
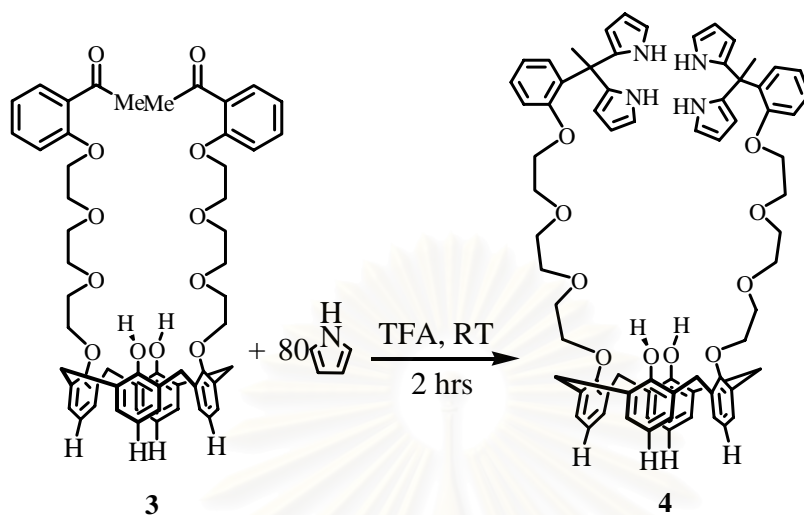
Scheme 3.2 Synthetic pathway of 1,3-calix[4]arene-bisdipyrroethane (**4**)

The synthesis of 1,3-calix[4]arene-bisdipyrroethane **4** was accomplished by treating 1,3-calix[4]-diacetophenone (**3**) with 80 times excess pyrrole in a presence of catalytic amount of trifluoroacetic acid for 10 minutes according to conventional procedure.[37] After purification by column chromatography on silica (dichloromethane/ethyl acetate/ triethylamine = 95/5/1), compound **4** was obtained as a viscouse oil in 61% yield. The ^{1}H-NMR spectrum of **4** showed the characteristic peaks of NH pyrrole as a singlet at 8.86 ppm and three multiplets of the pyrrolic protons of the dipyrrolethane at 6.62, 6.11 and 5.92 ppm, respectively. On the other hand, elemental analysis was not in good agreement with the structure due to its instability at room temperature.

3.1.3 Synthesis and characterization of calix[4]arene-calix[4]pyrrole (5)

Due to the highly selective anion binding of calix[4]pyrrole[38] and its easy modification of calix[4]arene to obtain a specific conformer and selective cation binding ability, the calix[4]arene-calix[4]pyrrole (**5**) was synthesized to serve as the intermediate to further modification as depicted in Scheme 3.3.
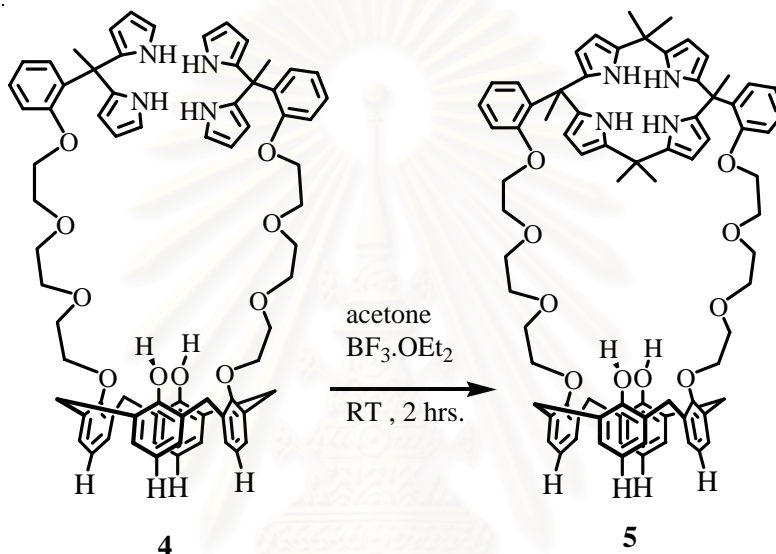
Scheme 3.3 The synthesis of calix[4]arene-calix[4]pyrrole (**5**).

The synthesis of compound **5** was accomplished by the condensation of 1,3-calix[4]arene-bisdipyrroethane (**4**) with a dry acetone in the presence of $BF_3.OEt_2$ as a catalyst at room temperature for 2 hours. The compound **5** was separated on column chromatography and recrystallized with methanol afford a white solid (37%). The ^{1}H-NMR spectrum showed a broad signal of NH at 7.98 ppm, the singlet signal of OH at 7.91 ppm and two singlet peaks of β-pyrrolic protons at 5.91 and 5.67 ppm. Calix[4]arene exists in cone conformation due to a doublet signal of ArC**H**$_2$Ar of calix[4]arene at 3.39 and 4.40 ppm (J_{H-H} = 13.0 Hz). MALDI-TOF MS supported the structure of desired product **5** showing an intense line at m/z 1259.65 [M+Na$^+$] and the elemental analysis result was in good agreement with the proposed structure.

The configuration of calix[4]pyrrole unit exists in 1,3-alternate conformation and the phenyltriethylene glycol spacers between calix[4]arene and calix[4]pyrrole link in trans geometry according to the previous report.[39]

3.1.4 Synthesis and characterization of pyrenylcalix[4]arene-calix[4]pyrrole (7)

The construction of anion sensor of compound **7** was accomplished by the reaction of calix[4]arene-calix[4]pyrrole (**5**) with *N*-(1-pyrenylmethyl)chloroacetamide (**6**) using K_2CO_3 as a base in a refluxing acetonitrile with a catalytic amount of NaI for 30 hrs. The compound **7** was separated by column chromatography as a yellow solid (66%). The ^{1}H-NMR spectrum of **7** exhibits two doublets at 4.40 ppm in AB pattern, corresponding to protons of the methylene bridge, which suggests that **7** is in the cone conformation. The protons of the pyrene unit present at 8.02-8.31 ppm as a multiplet signal.
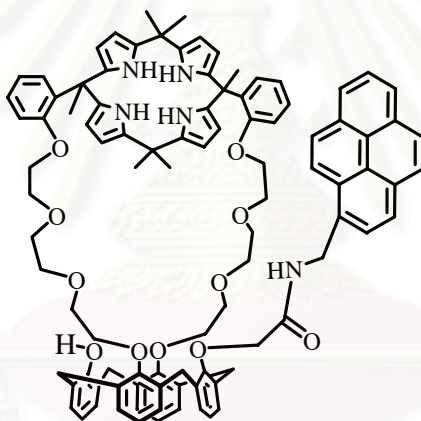

Figure 3.1 The structure of pyrenylcalix[4]arene-calix[4]pyrrole **7**.

3.1.5 Synthesis and characterization of calix[4]diquinone-calix[4]pyrrole (8)

The synthesis of calix[4]diquinone-calix[4]pyrrole (**8**) was show in Scheme 3.4.
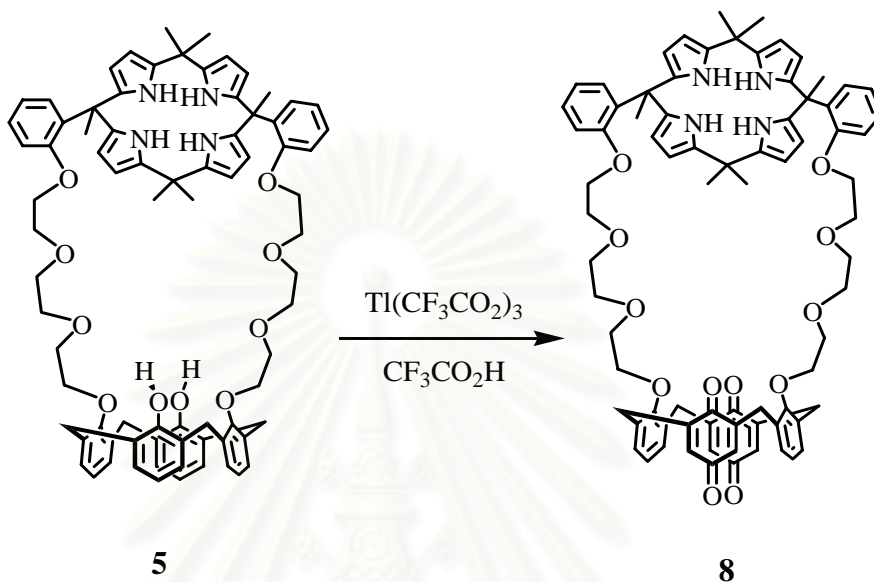
Scheme 3.4 Synthetic pathway of calix[4]diquinone-calix[4]pyrrole (**8**).

The oxidation of compound **5** with thallium trifluoroacetate in trifluoroacetic acid was stirred in the dark under nitrogen atmosphere for 2 hrs. After work-up and precipitation with methanol in dichloromethane, a yellow crystalline solid was obtained. The obtained compound was characterized by ^{1}H-NMR spectroscopy and the result indicated that the desired product was not obtained. From the ^{1}H-NMR spectrum at 7.51 and 7.75 ppm act as doublet of doublet spectrum may be refered to some derivative of benzoquinone was obtained.[40] It's can also be described for the bad condition to synthesized calix[4]diquinone-calix[4]pyrrole.

3.2 Anion complexation studies of pyrenylcalix[4]arene-calix[4]pyrrole (7)

Compound **7** contains the calix[4]pyrrole which can binds anions and *N*-(1-pyrenylmethyl)acetamide as a fluorophore . Thus the complexation studies of pyrenylcalix[4]arene-calix[4]pyrrole with F^-, Cl^-, Br^-, I^-, CH_3COO^-, $PhCOO^-$, $H_2PO_4^-$, ClO_4^-, NO_3^-, PF_6^-, were carried out in acetonitrile. The anion recognition *via* H-bonding interactions can also be easily monitored by anion complexation induced change in fluorescence intensity by fluorimetric titrations.

3.2.1 Complexation studies of compound 7 to determine the selectivity

First of all, the anion binding ability of compound **7** was investigated by measuring the fluorescence intensity changes of **7** upon additions with the excess (400 equiv.) tetrabutylammonium salts. The obtained spectra are shown in Figure 3.2.
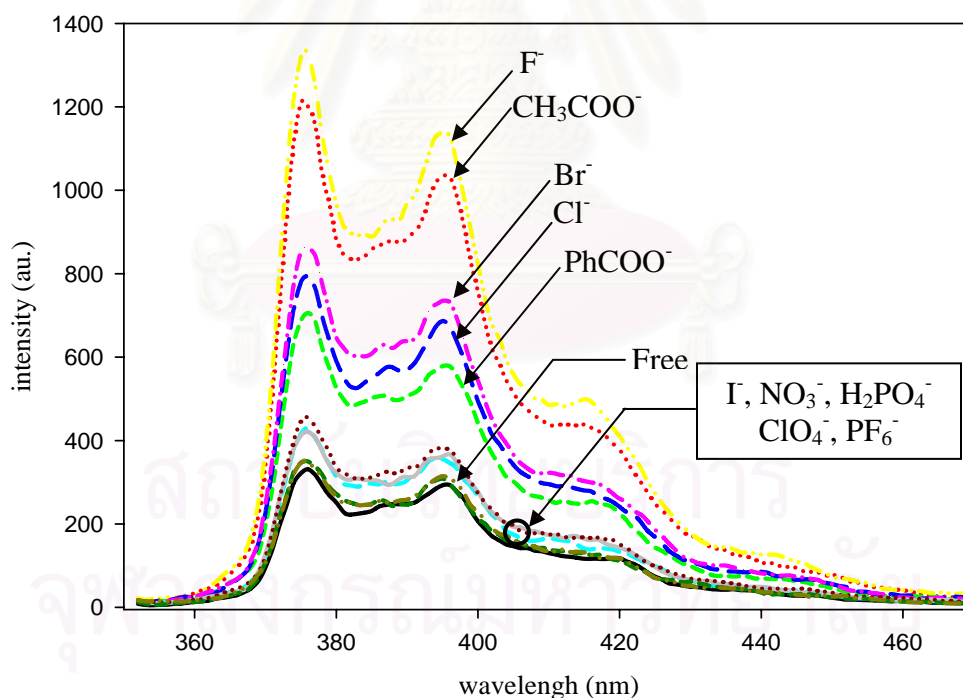

Figure 3.2 Fluorescence changes of pyrenylcalix[4]arene-calix[4]pyrrole (**7**) (6.0 μM) with various tetrabutylammonium salts (2.4 mM).

The spectrum of compound **7,** in the absence of anions, displays a monomer fluorescence emissions (λ_{em} = 376 nm and λ_{em} = 396 nm) when irradiated at 343 nm in CH_3CN. Thus both fluorescence intensity were assigned to the pyrenyl chromophore.[41] An increase of intensity was observed in both the 376 nm and 396 nm emission intensities upon adding the anion, but no other spectral shifts, or the formation of isobestic points, were observed. Table 3.1 shows the changes of fluorescence intensities of **7** in the presence of large excesses of tetrabutylammonium anions of both wavelengths. Compound **7** exhibits much greater responses to F⁻, AcCOO⁻, Br⁻, Cl⁻, PhCOO⁻, respectively among the anions studied. This responses can be viewed as involving the initial interaction of anions with the calix[4]pyrrole moiety in **7** through hydrogen bonding to give the anion·**7** complex.[42] The enhancement of the monomeric fluorescence bands of **7** observed upon anion complexation is also due to a PET-based mechanism.[43] This mechanism can be propose by upon recognition of anion, the anion reduces the effect of PET quenching from calix[4]pyrrole group to the pyrenyl fluorophore, by 'blocking' the pathway of the electron transfer then the emission intensity of the complex were enhance.[43]

Table 3.1 Fluorescence changes (I-I_0) of pyrenyl-calix[4]arene-calix[4]pyrrole (**7**) upon the addition of various anion.

λ_{em} (nm)	Fluorescence Changes ($I - I_0$)									
	F⁻	Cl⁻	Br⁻	I⁻	CH_3COO^-	PhCOO⁻	NO_3^-	$H_2PO_4^-$	ClO_4^-	PF_6^-
376	**997**	**462**	**531**	98	**870**	**375**	90	123	19	19
396	**846**	**447**	**442**	62	**741**	**286**	69	87	15	21

I_0: fluorescence emission intensity of free **7.**

I: fluorescence emission intensity of anion-complexed **7.**

3.2.2 Determination the stability constants of anion bindings of 7 towards tetrabutylammonium salts

Compound **7** was also studied the complexation with various anions whether it can act as a fluorogenic sensor. Various tetrabutylammonium salts, (i.e., Bu_4NF, Bu_4NCl, Bu_4NBr, Bu_4NI, Bu_4NCH_3COO, $Bu_4NPhCOO$, Bu_4NNO_3, $Bu_4NH_2PO_4$, Bu_4NClO_4 and Bu_4NPF_6), were chosen to study by using a acetonitrile as a solvent. The fluorescence spectra were recorded after the addition of the solutions of the anions.

Figure 3.3 shows changes in emission spectra of fluoroionophore (recorded in acetonitrile at a concentration 6.0×10^{-6} M of the ligand) upon addition of tetrabutylammonium fluoride (2.3×10^{-3} M in acetonitrile). The fluorimetric titration was performed 2 times and the maxima fluorescence intensities are reported in Table 3.2. When $I_F^o/(I_F - I_F^o)$ are plotted against the reciprocals of the F$^-$ concentration $[M]^{-1}$ (Figure 3.4-3.5), the stability constants are obtained from the ratio of intercept/slope (Table 3.3) and the average log K is 3.45.
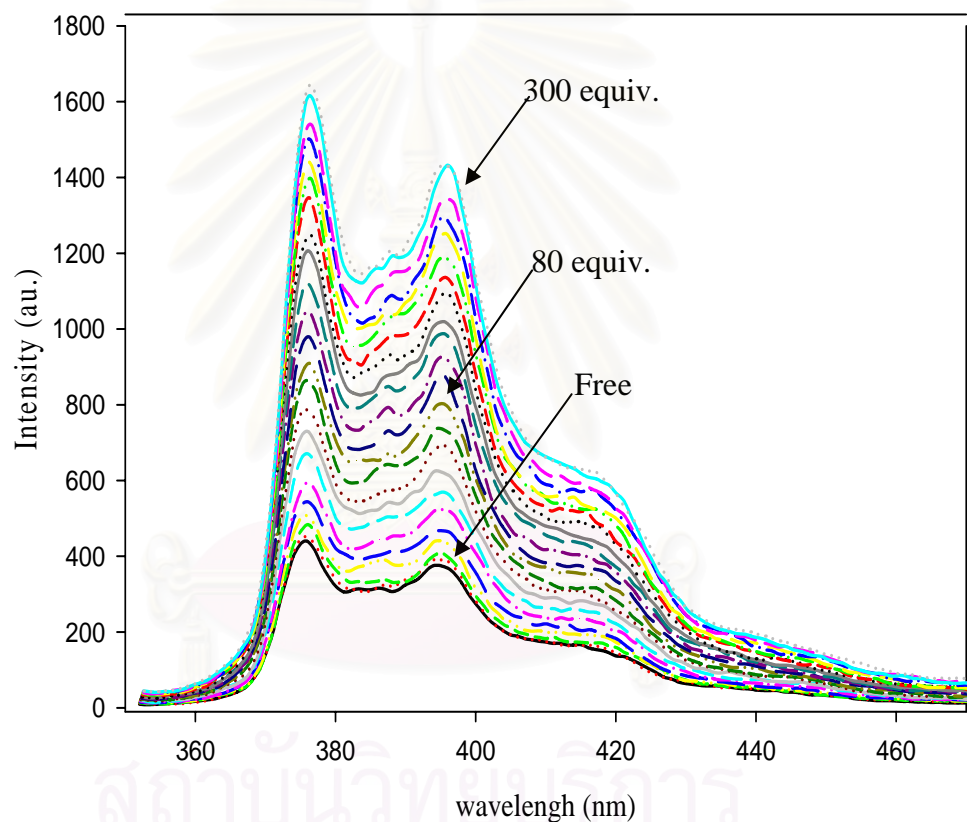

Figure 3.3 Fluorescence emission spectra of **7** (6.0 μM) upon additions of various amounts of tetrabutylammonium fluoride in CH₃CN. The excitation wavelength was 343 nm.

Table 3.2 The fluorescence intensity of compound **7** with adding F^- (I^0_F = 312.23 and
319.62 respectively)

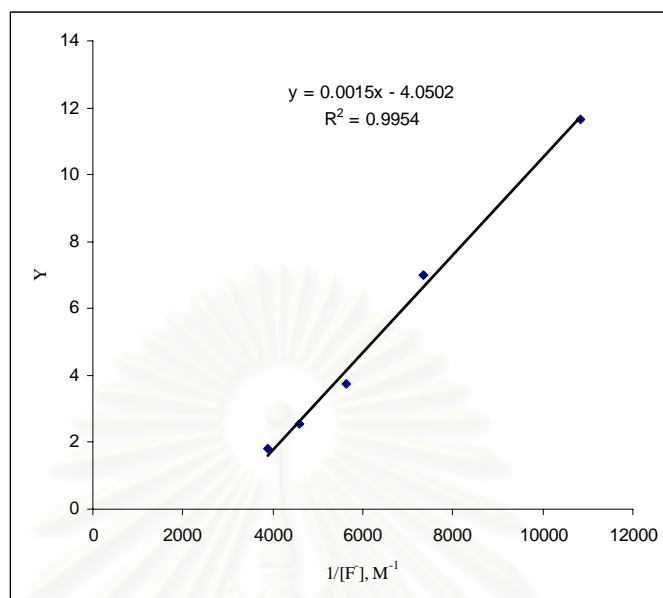| Titration entry	Equiv. F^-	$[F^-]$ (mM)	I_F (a.u.)	I_F-I^0_F (a.u.)	I^0_F/I_F-I^0_F	$1/[F^-]$ (M^{-1})
1	16	0.092	342.09	30.09	10.36	10833.3
	24	0.136	359.79	47.79	6.52	7361.1
	32	0.178	398.84	86.84	3.59	5625.0
	40	0.218	438.84	126.71	2.46	4583.3
	48	0.257	489.21	177.21	1.76	3888.9
2	16	0.092	343.89	24.27	13.16	10833.3
	24	0.136	361.52	41.90	7.62	7361.1
	32	0.178	396.84	76.38	4.18	5625.0
	40	0.218	446.07	126.45	2.52	4583.3
	48	0.257	486.87	167.25	1.91	3888.9

Figure 3.4 The linear plot between $Y\{ = I^0_F/(I_F-I^0_F)\}$ and $1/[F^-]$ for the first fluorimetric titration.
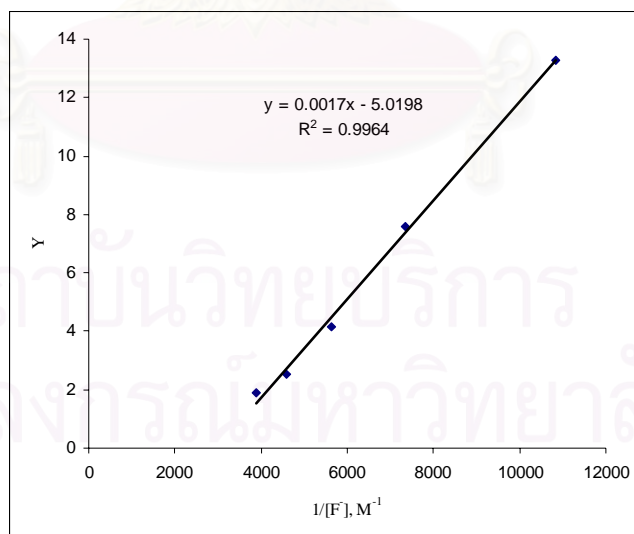

Figure 3.5 The linear plot between $Y\{ = I^0_F/(I_F-I^0_F)\}$ and $1/[F^-]$ for the second fluorimetric titration.

Table 3.3 The stability constant of **7** toward F⁻

Titration entry	Intercept	slope	R^2	Log K
1	-4.0502	0.0015	0.9954	3.43
2	-5.0198	0.0017	0.9964	3.47
Average				3.45

Figure 3.6 shows changes in emission spectra of fluoroionophore **7** (recorded in acetonitrile at a concentration 6.0×10^{-6} M of the ligand) upon addition of tetrabutylammonium chloride (2.3×10^{-3} M in acetonitrile). The fluorimetric titration was performed 2 times and the maxima fluorescence intensities are reported in Table 3.4. When $I_F^o /(I_F - I_F^o)$ were plotted against the reciprocals of the Cl$^-$ concentration [M]$^{-1}$ (Figure 3.7-3.8), the stability constants were obtained from the ratio of intercept/slope (Table 3.5) with the average log K of 1.74.
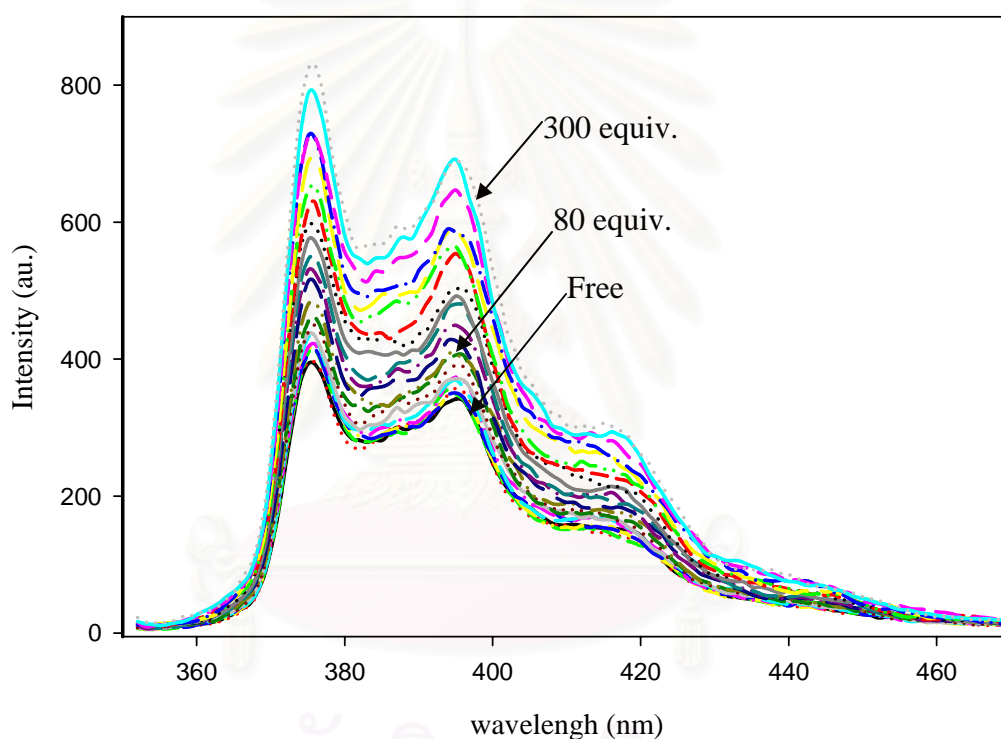

Figure 3.6 Fluorescence emission spectra of **7** (6.0 μM) upon additions of various amounts of tetrabutylammonium chloride in CH$_3$CN. The excitation wavelength was 343 nm.

Table 3.4 The fluorescence intensity of compound **7** with adding Cl$^-$ (I^0_F = 281.35 and 307.55 respectively).

| Titration entry	Equiv. Cl$^-$	[Cl$^-$] (mM)	I_F (a.u.)	I_F-I^0_F (a.u.)	I^0_F/I_F-I^0_F	1/[Cl$^-$] (M^{-1})
1	40	0.218	348.21	62.21	4.18	4583.3
	48	0.257	363.93	82.93	3.38	3888.8
	72	0.366	391.62	110.62	2.54	2731.5
	96	0.465	427.25	146.25	1.92	2152.8
	128	0.582	452.04	171.04	1.64	1718.8
	160	0.686	495.25	214.25	1.31	1458.3
2	24	0.136	365.12	58.12	5.28	7361.1
	32	0.178	389.35	82.35	3.72	5625.0
	40	0.218	403.78	96.78	3.17	4883.3
	56	0.295	431.89	124.89	2.45	3392.9
	180	0.745	609.81	302.81	1.01	1342.6
	260	0.945	699.88	392.88	0.78	1057.7
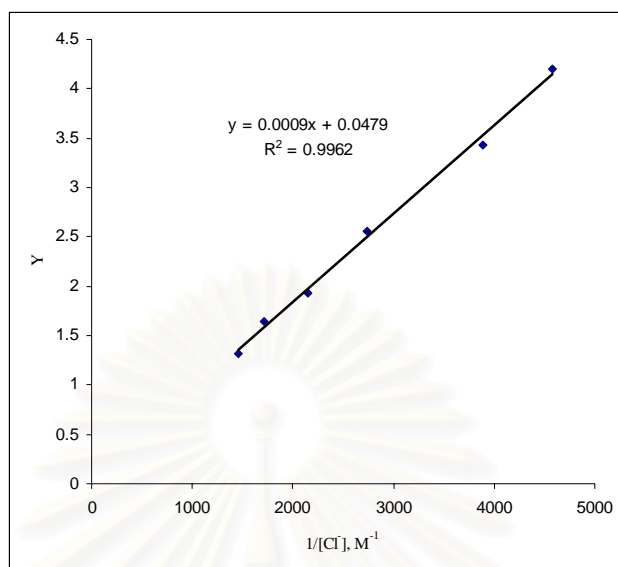
Figure 3.7 The linear plot between $Y\{ = I^0_F/(I_F-I^0_F)\}$ and $1/[Cl^-]$ for the first fluorimetric titration.
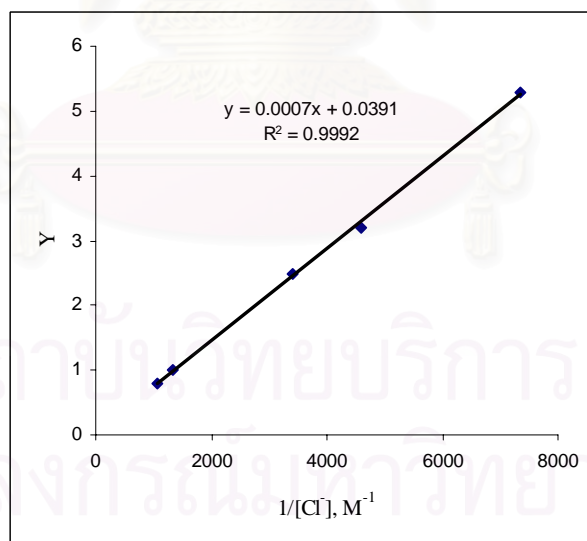

Figure 3.8 The linear plot between $Y\{ = I^0_F/(I_F-I^0_F)\}$ and $1/[Cl^-]$ for the second fluorimetric titration.

Table 3.5 The stability constant of **7** toward Cl⁻ .

Titration entry	intercept	slope	R^2	log K
1	0.0479	0.0009	0.9962	1.73
2	0.0392	0.0007	0.9992	1.75
Average				1.74

Figure 3.9 shows changes in emission spectra of fluoroionophore **7** (recorded in acetonitrile at a concentration 6.0×10^{-6} M of the ligand) upon addition of tetrabutylammonium bromide (2.3×10^{-3} M in acetonitrile). The fluorimetric titration was performed 2 times and the maxima fluorescence intensity was reported in Table 3.6. When $I_F^o / (I_F - I_F^o)$ were plotted against the reciprocals of the Br$^-$ concentration $[M]^{-1}$ (Figure 3.10 - 3.11), the stability constants were obtained from the ratio of intercept/slope (Table 3.7) with the average log K of 1.62.
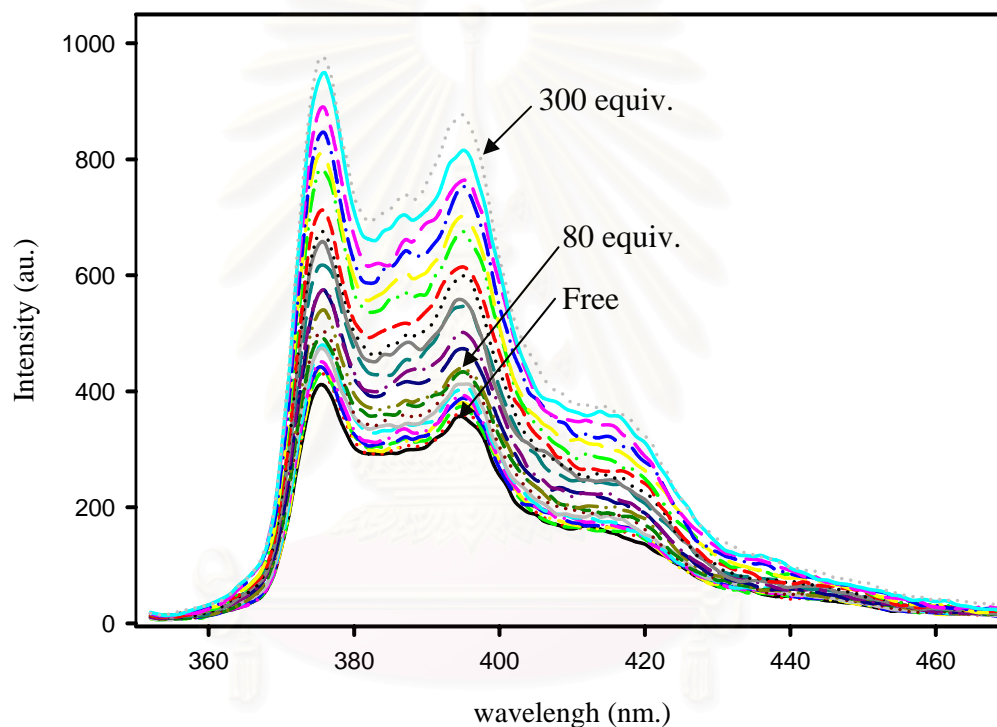

Figure 3.9 Fluorescence emission spectra of **7** (6.0 μM) upon additions of various amounts of tetrabutylammonium bromide in CH$_3$CN. The excitation wavelength was 343 nm.

Table 3.6 The fluorescence intensity of compound **7** with adding Br$^-$ (I^0_F = 276.40 and 281.56 respectively).

| Titration entry	Equiv. Br$^-$	[Br$^-$] (mM)	I_F (a.u.)	I_F-I^0_F (a.u.)	I^0_F/I_F-I^0_F	1/[Cl$^-$] (M^{-1})
1	40	0.218	340.48	64.08	4.31	4583.3
	48	0.257	340.61	64.21	4.30	3888.9
	64	0.331	353.60	77.20	3.58	3020.8
	80	0.400	377.77	101.37	2.72	2500.0
	160	0.686	448.75	172.35	1.60	1458.3
	200	0.800	482.77	206.37	1.33	1250.0
2	24	0.136	313.63	32.63	8.61	7361.1
	40	0.218	330.88	49.88	5.63	4583.3
	48	0.257	338.92	57.92	4.85	3888.9
	72	0.366	367.20	86.20	3.25	2731.5
	128	0.582	440.01	159.01	1.76	1718.8
	144	0.635	473.26	192.26	1.46	1574.1
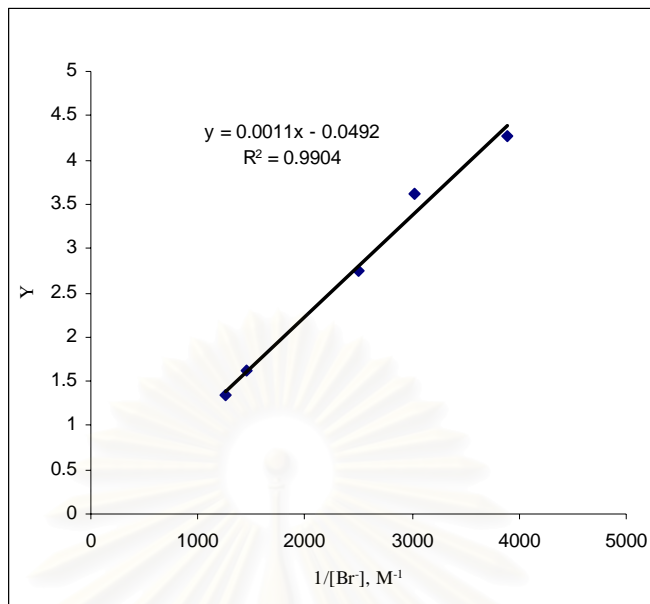
Figure 3.10 The linear plot between $Y\{=I^0_F/(I_F-I^0_F)\}$ and $1/[Br^-]$ for the first fluorimetric
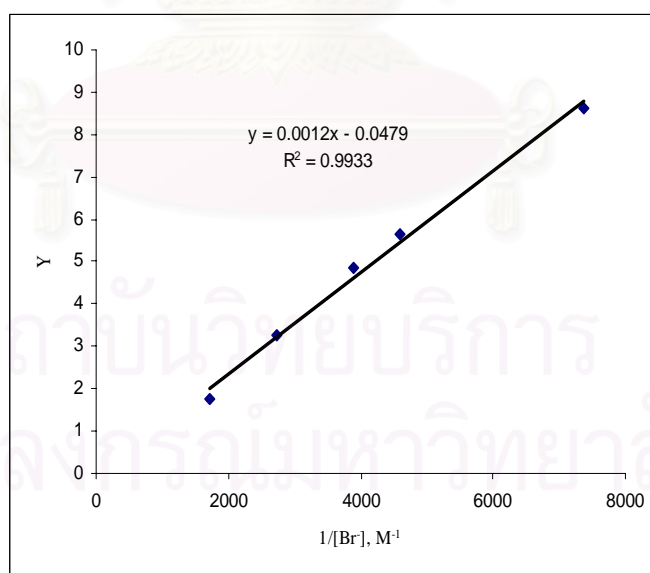
titration.

Figure 3.11 The linear plot between $Y\{=I^0_F/(I_F-I^0_F)\}$ and $1/[Br^-]$ for the second

fluorimetric titration.

Table 3.7 The stability constant of **7** toward Br⁻

Titration entry	intercept	slope	R^2	log K
1	-0.0492	0.0011	0.9904	1.65
2	-0.0479	0.0012	0.9933	1.60
Average				1.62

Figure 3.12 shows changes in emission spectra of fluoroionophore **7** (recorded in acetonitrile at a concentration 6.0×10^{-6} M of the ligand) upon addition of tetrabutylammonium acetate (2.3×10^{-3} M in acetonitrile). The fluorimetric titration was performed 2 times and the maxima fluorescence intensities are reported in Table 3.8. When $I_F^o /(I_F - I_F^o)$ were plotted against the reciprocals of the CH_3COO^- concentration $[M]^{-1}$ (Figure 3.13-3.14), the stability constants were obtained from the ratio of intercept/slope (Table 3.9) with the average log K of 3.25.
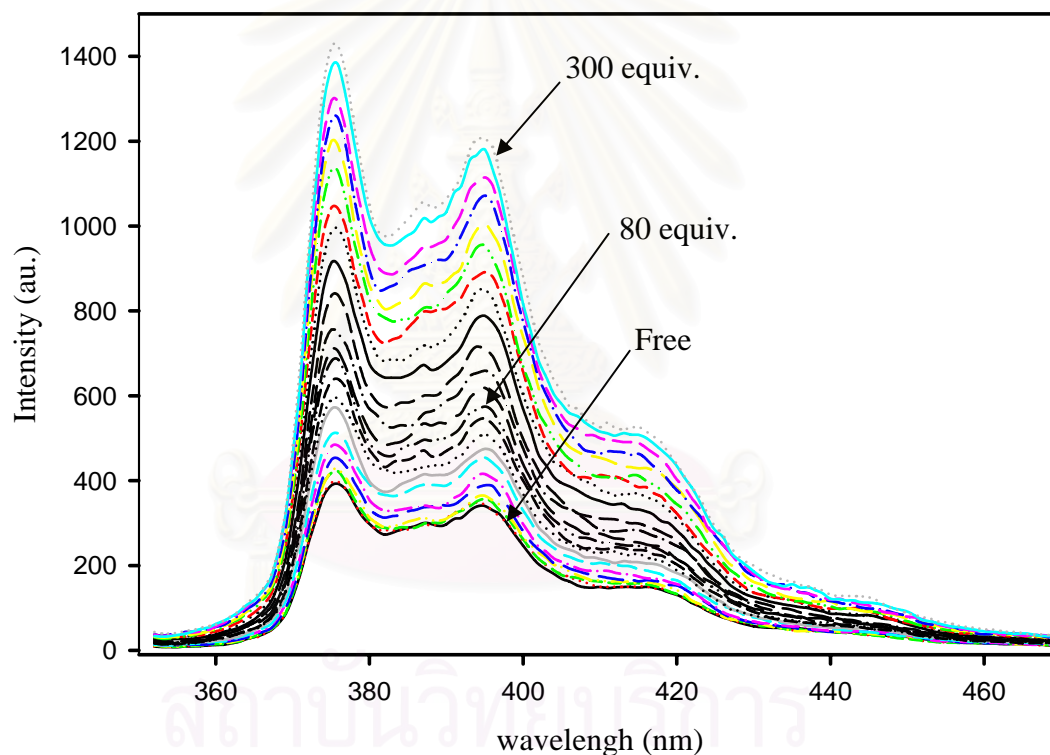

Figure 3.12 Fluorescence emission spectra of **7** (6.0 μM) upon additions of various amounts of tetrabutylammonium acetate in CH_3CN. The excitation wavelength was 343 nm.

Table 3.8 The fluorescence intensity of compound **7** with adding CH_3COO^- ($I^0_F = 272.85$ and 277.84 respectively).

| Titration entry	Equiv. CH_3COO^-	$[CH_3COO^-]$ (mM)	I_F (a.u.)	$I_F-I^0_F$ (a.u.)	$I^0_F/I_F-I^0_F$	$1/[CH_3COO^-]$ (M^{-1})
1	24	0.136	307.82	34.97	7.80	7361.1
	40	0.218	337.93	65.08	4.19	4583.3
	56	0.295	405.91	133.06	2.05	3392.9
	64	0.331	426.99	154.14	1.77	3020.8
	72	0.366	458.82	185.97	1.46	2731.5
	80	0.400	486.48	213.63	1.27	2500.0
2	32	0.178	318.89	41.89	6.61	5625.0
	48	0.257	347.94	70.94	3.90	3888.9
	56	0.295	383.59	106.59	2.59	3392.9
	64	0.331	411.15	134.15	2.06	3020.8
	72	0.366	439.78	162.78	1.70	2731.5
	80	0.400	459.73	182.73	1.51	2500.0
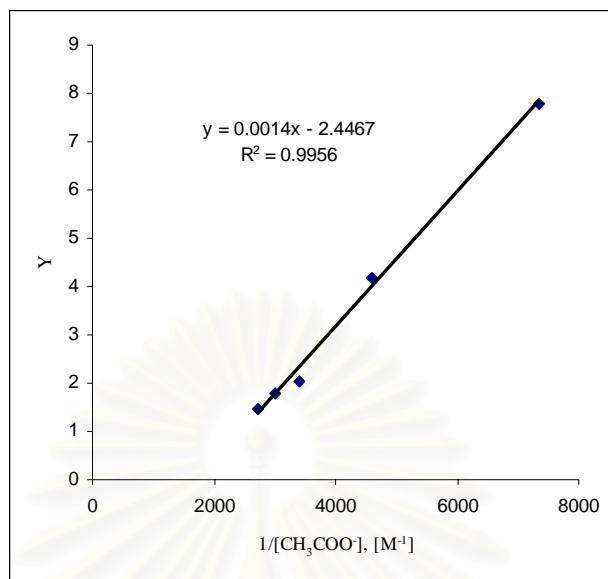
Figure 3.13 The linear plot between $Y\{=I^0_F/(I_F-I^0_F)\}$ and $1/[CH_3COO^-]$ for the first fluorimetric titration.

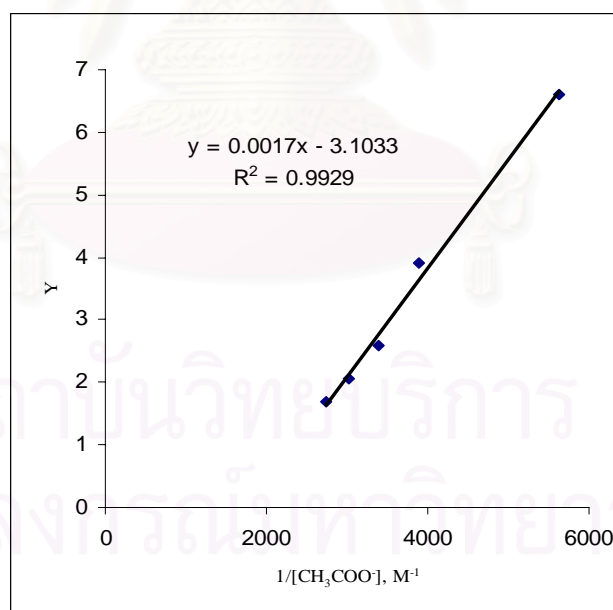**Figure 3.14** The linear plot between $Y\{=I^0_F/(I_F-I^0_F)\}$ and $1/[CH_3COO^-]$ for the second fluorimetric titration.

Table 3.9 The stability constant of **7** toward CH_3COO^-.

Titration entry	intercept	slope	R^2	log K
1	-2.4467	0.0014	0.9956	3.24
2	-3.1033	0.0017	0.9929	3.26
Average				3.25

Figure 3.15 shows changes in emission spectra of fluoroionophore **7** (recorded in acetonitrile at a concentration 6.0×10^{-6} M of the ligand) upon addition of tetrabutylammonium benzoate (2.3×10^{-3} M in acetonitrile). The fluorimetric titration was performed 2 times and the maxima fluorescence intensities are reported in Table 3.10. When $I_F^o/(I_F - I_F^o)$ were plotted against the reciprocals of the PhCOO$^-$ concentration $[M]^{-1}$ (Figure 3.16-3.17), the stability constants are obtained from the ratio of intercept/slope (Table 3.11) provided an average log K of 1.28.
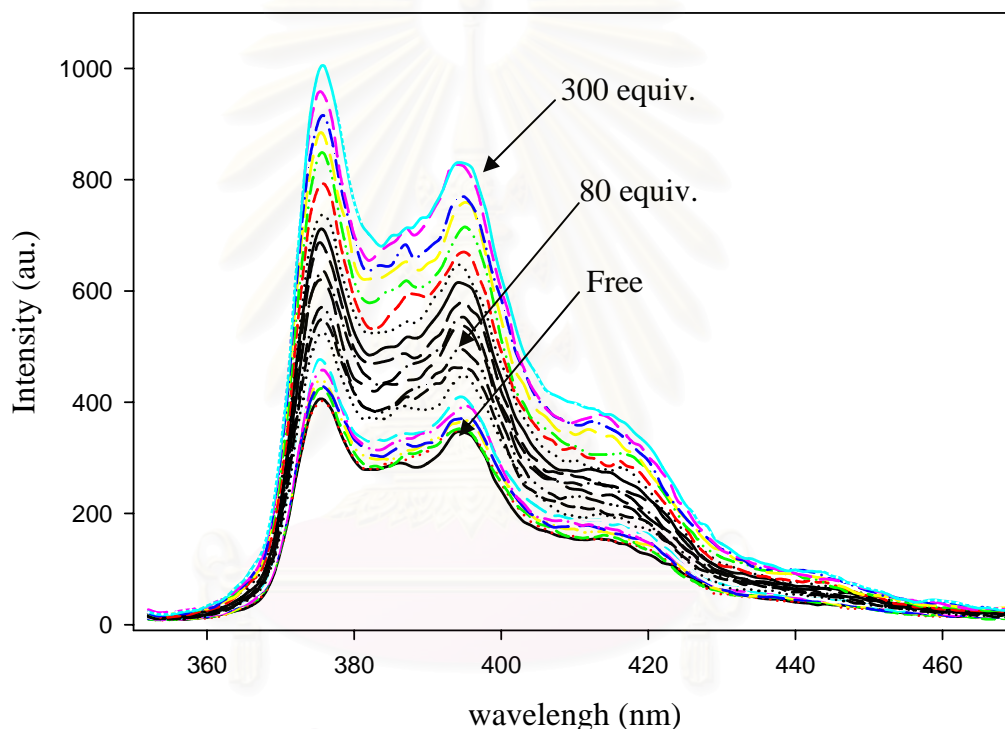

Figure 3.15 Fluorescence emission spectra of **7** (6.0 μM) upon additions of various amounts of tetrabutylammonium benzoate in CH₃CN. The excitation wavelength was 343 nm.

Table 3.10 The fluorescence intensity of compound **7** with adding PhCOO$^-$ (I^0_F = 278.88 and 277.42 respectively).

| Titration entry	Equiv. PhCOO$^-$	[PhCOO$^-$] (mM)	I_F (a.u.)	I_F-I^0_F (a.u.)	I^0_F/I_F-I^0_F	1/[PhCOO$^-$] (M^{-1})
1	32	0.178	339.05	61.05	4.55	5625.0
	40	0.218	351.55	73.55	3.77	4583.3
	64	0.331	390.31	112.31	2.47	3020.8
	96	0.465	433.28	155.28	1.79	2150.8
	112	0.525	450.23	172.23	1.61	1574.1
	160	0.686	535.28	257.28	1.08	1458.3
2	24	0.136	337.84	60.84	4.55	7361.1
	48	0.257	386.35	109.35	2.53	3888.9
	56	0.295	408.75	131.75	2.10	3392.9
	64	0.331	434.03	157.03	1.76	3020.8
	144	0.635	536.98	259.98	1.06	1574.1
	160	0.686	570.55	293.55	0.94	1458.3
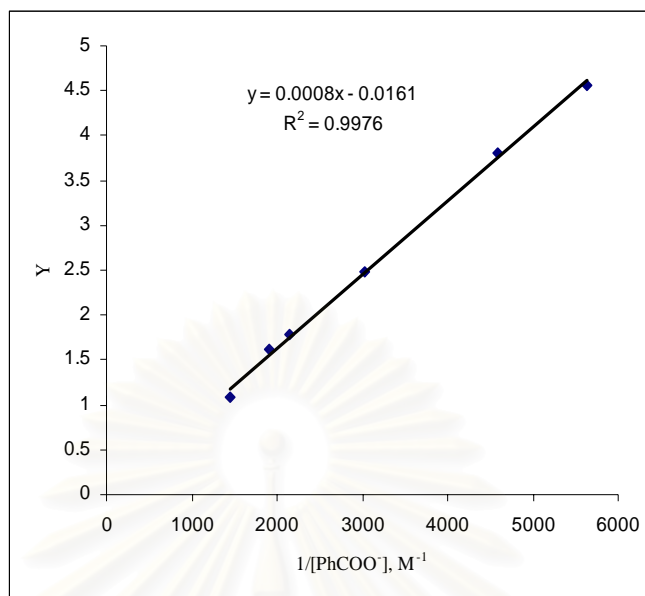
Figure 3.16 The linear plot between $Y\{=I^0_F/(I_F-I^0_F)\}$ and $1/[\text{PhCOO}^-]$ for the first fluorimetric titration.
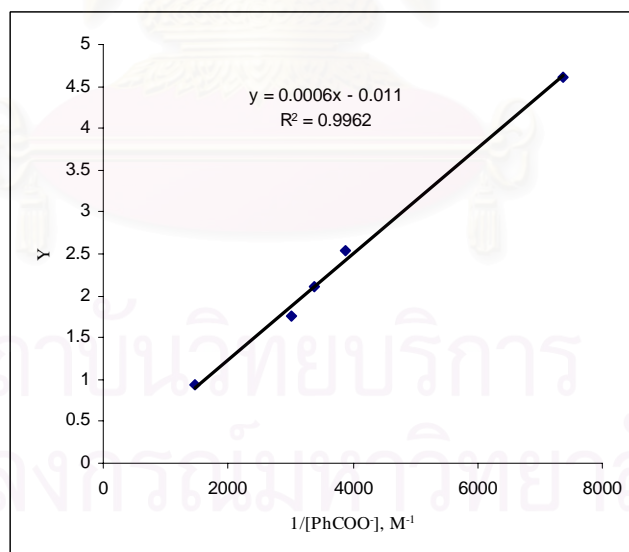

Figure 3.17 The linear plot between $Y\{=I^0_F/(I_F-I^0_F)\}$ and $1/[\text{PhCOO}^-]$ for the second fluorimetric titration.

Table 3.11 The stability constant of **7** toward PhCOO⁻.

Titration entry	intercept	slope	R^2	Log K
1	-0.0161	0.0008	0.9976	1.30
2	-0.0110	0.0006	0.9962	1.26
Average				1.28

3.2.3 Florescence and color changes of 7 by tetrabutylammonium salts.

When the excesses anions were added, a fluorescence emission of ligand **7** changed as shown in Figure 3.18. That are also confirmed the anions can complex with the ligand **7.**

    7   **7**.F⁻   **7**.Br⁻   **7**.Cl⁻   **7**.I⁻
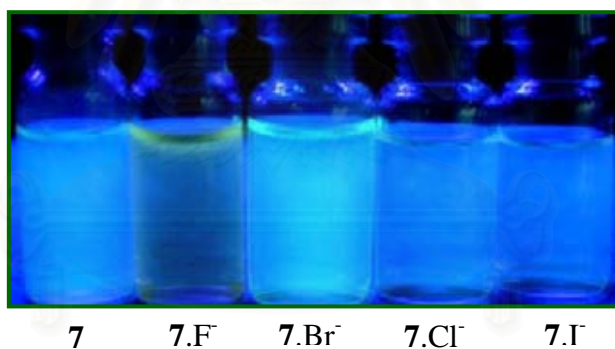
Figure 3.18 Fluorescence changes for **7** in the presence of F⁻, Br⁻,Cl⁻, I⁻.

Addition of excesses Bu$_4$NF to a solution of **7** did not only quenched markedly a fluorescence emission of compound **7** but also its color (Figure 3.19).
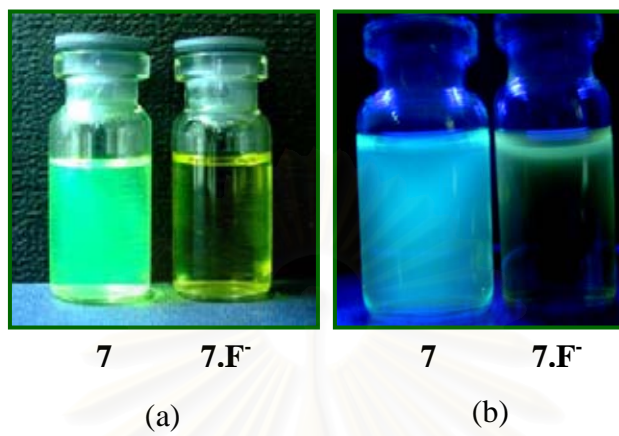

Figure 3.19 Visual changes for **7** in the presence of F$^-$: (a) color change; and (b) fluorescence change.

CHAPTER IV

CONCLUSION

The fluorescent anion sensor, pyrenylcalix[4]arene-calix[4]pyrrole (**7**), has been successfully synthesized in 4 steps starting from a condensation of 2-(triethyleneglycol tosylate)acetophenone (**2**) with calix[4]arene to afford 1,3-calix[4]-diacetophenone (**3**). After condensation of diketone **3** with pyrrole, the obtained 1,3-calix[4]-bis(dipyrrolethane) (**4**) was then cyclized with acetone to provide calix[4]arene-calix[4]pyrrole (**5**). In order to incorporate a fluorescent unit, **5** was reacted with *N*-(1-pyrenylmethyl)chloroacetamide (**6**) to obtain **7** in a total yield of 13%. Regarding the geometry of fluorogenic sensor **7**, the calix[4]arene unit constrains in cone conformation whereas calix[4]pyrrole one fixes in 1,3-alternate fashion with *trans*-linkages of the two units.

The complexation studies of the synthesized ligand **7** were carried out with tetrabutylammonium salts in CH_3CN by fluorescence spectroscopy. In all cases, the monomer fluorescence emissions (λ_{em} = 376 nm and λ_{em} = 396 nm) were increased when irradiated at 343 nm in the order of $F^->CH_3COO^->Cl^->Br^->PhCOO^-$ due to PET process. According to the fluorescence emission changes in the anions titration, the association constant of **7,** log K = 3.45 for F^- ion, logK = 3.25 for CH_3COO^-, logK = 1.74 for Cl^- ion, logK = 1.62 for Br^- ion and logK = 1.28 for $PhCOO^-$. Moreover, the addition of F^- ion into the solution of fluorogenic calix[4]arene **7** results notably in both color change and fluorescence quenching.

REFERENCES

1. Beer, P. D.; Gale, P. A.; Smith, D. K. Supramolecular Chemistry. UK : Oxford University Press, (1999).

2. Valeur, B.; Leray, I. Design principles of fluorescent molecularsensors for cation recognition. Coordination Chemistry Reviews (2000) : 3-40.

3. Perderson, C. J. Cyclic Polyethers and Their Complexes with Metal Salts. Journal of the American Chemical Society 87(1967) : 7017.

4. Kodansh Ltd. Their Characteristic and Application. Crown Compound, 53. Tokyo : 1982.

5. Dietrich, B.; Lehn, J-M.; Sauvage, J.-P. Diaza-polyoxa-macrocycles et macrobicycles. Tetrahedron Letters 10(1969) : 2885.

6. Stoddart, J. F. Cyclodextrins, Off-the-Shelf Components for the Construction of Mechanically Interlocked Molecular Systems. Angewandte Chemie International Edition in English 1992 : 846.

7. Kobayashi, N.; Mizuno, K.; Osa, T.A. A 'calix[4]arened' porphyrin as a new host and an oxygen carrier model. Inorganica Chimica Acta 224(1994) : 1.

8. Pochini, A.; Ungaro, R. Calixarenes and Related Hosts. Executive Eds, Comprehensive Supramolecular Chemistry, 524.: Elsevier, 1996.

9. Sessler, J. L.; Gebauer, A.; Gale, P. A. Anion Binding and Electrochemical Properties of Calix[4]pyrrole Ferrocene Conjugates. Gazzetta Chimica Italiana 127(1997) : 723.

10. Sessler, J. L.; Anzenbacher Jr. P.; Jursikova, K.; Miyaji, H.; Genge, J. W.; Tvermoes, N. A.; Allen, W. E.; Shriver, J. A. Functionalized Calix[4]pyrroles Pure and Applied Chemistry 70(1998) : 2401.

11. de Silva, S. A.; Zavaleta, A.; Baron, D. E.; allam, O.; Isidor, E. V.; Kashimura, N.; Percapio, J. M. A. Fluorescent Photoinduced Electron Transfer Sensor for Cationswith an Off-On-Off Proton Switch. Tetrahedral Letters 38(1997) : 2237.

12. Antonisse, M. G. M.; Reinhoudt, D. N. Neutral anion receptors: design and application. Cmemical communications 4(1998) : 443.

13. Atwood, J. L.; Steed, J. W. Supramolecular Chemistry of Anions. New York : Wiley-VCH , 1997.

14. Tongraung, P.; Chantarasiri, N.; Tuntulani, T.; Calix[4]arenes containing urea and crown/urea moieties: effects of the crown ether unit and Na+ towards anion binding ability. Tetrahedron Letters 44(2003) : 29.

15. Ramo´n, M.–M.; Fe´lix, S. Fluorogenic and Chromogenic Chemosensors and Reagents for Anions. Chemical. Reviews 103(2003) : 4419-4476.

16. Vicens, J. and Harrowfield, J. Calixarenes in the Nanoworld Dordrecht The Netherland : Springer, 2007.

17. Valeur, B.; Bernard, V.; Leray, I. Ion-responsive supramolecular fluorescent systems based on multichromophoric calixarenes. Inorganica Chimica Acta 360(2007) : 765-774.

18. Aoki, I.; Kawabata, H.; Nakashima, K.; Shinkai, S. Electrochemical detection of saccharides by redox cycle of a chiral ferrocenylboronic acid derivative: a novelmethod for sugar sensing. Journal of the chemical society,Chemical communication (1995) : 1771-1772.

19. Kim, S. K.; Kim, S. U.; Lee, S. H.; Ko, J.; Bartsch, R. A.; Kim, J. S. Indium(III)-Induced Fluorescent Excimer Formation and Extinction in Calix[4]arene-Fluoroionophores. Inorganic chemistry 44(2005) : 7866.

20. Jin, T. Aldehydes and ketones as dipolarophiles: application to the synthesis of oxapenams Chemical Communications 3(1999) : 249.

21. Perez-Jimenez, C.; Harris, S.; Diamond, D. A novel calix[4]arene tetraester with fluorescent response to complexation with alkali metal cations. Journal of the Chemical Society, Chemical Communications 5(1993) : 480.

22. Talanova, G. G.; Elkarim, N. S. A.; Talanov, V. S.; Bartsch, R. A. A Calixarene-Based Fluorogenic Reagent for Selective Mercury(II) Recognition. Analytical Chemistry 71(1999) : 3106-3109.

23. Leray, I.; Lefèvre, J.P.; Delouis, J.F.; Delaire, J.; Valeur, B. Synthesis and photophysical and cation-binding properties of mono- and tetranaphthylcalix 4 arenes as highly sensitive and selective fluorescent sensors for sodium. Chemistry

- A European Journal 7(2001) : 4590.

24. Leray, I.; Asfari, Z.; Vicens, J.; Valeur, B. Synthesis and binding properties of calix 4 biscrown-based fluorescent molecular sensors for caesium or potassium ions. Journal of the Chemical Society, Perkin Transactions 2, 8(2002) : 1429-1434.

25. Liang, Z.; Liang Zhi Liang; Zhi Liu, ZL. A new fluorescent chemosensor for copper(II) and molecular witch controlled by light. Tetrahedron Letters 48(2007) : 1629-1632.

26. Kim, S.K.; Lee, S.H.; Lee, J.Y.; Lee, J.Y.; Lee, R.A.; Bartsch, R.A.; Kim, J.S. An Excimer-Based, Binuclear, On-Off Switchable Calix[4]crown Chemosensor. Journal of the American Chemical Society 126(2004) : 16499-16506.

27. Kim, H.J. Kim, S.K.; Lee, J.Y.; Kim, J.S. Fluoride-Sensing Calix-luminophores Based on Regioselective Binding Journal of Organic Chemistry 71(2006) : 6611-6614.

28. Schazmann, B.; Alhashimy, N.; Diamond, D. Chloride Selective Calix[4]arene Optical Sensor Combining Urea Functionality with Pyrene Excimer Transduction Journal of the American Chemical Society 128(2006) : 8607-8614.

29. Gale, P. A.; Sessler, J. L.; Král, V.; Lynch, V. Calix[4]pyrroles Old Yet New Anion-Binding Agents. Journal of the American Chemical Society 118(1996) : 5140.

30. Gale, P. A.; Sessler, J. L.; Lynch, V.; Samsom, P. I. Synthesis of a new cylindrical calix[4]arene-calix[4]pyrrole pseudo dimmer. Tetrahedron Letters 37(1996) : 7881.

31. Gale, P. A.; Genge, J. W.; Kral, V.; McKervey, M. A.; Sessler, J. L.; Walker, A. First synthesis of an expanded calixpyrrole. Tetrahedron Letters 38(1997) : 8443.

32. Ruangchaitaweesuk, S. Synthesis of bis-calix[4]arene-calix[4]pyrrole as ion pair receptor. Master degree Chemistry Department of Chemistry Faculty of Science Chulalongkorn University Bangkok, 2004.

33. Gutche, C. D.; Iqbal, M. *p-tert*-butylcalixarene Organic Synthesis 68(1990) : 234.

34. Fery-Forgues, S.; Le Bris, M-T.; Guetté, J-P. ; Valeur, B. Ion-Responsive Fluorescent Compounds. 1. Effect of Cation Binding on Photophysical Properties of a Benzoxazinone Derivative Linked to Monoaza-I 5-crown-5. The Journal of Physical Chemistry 92(1988) : 6233-6237.

35. Bouson, J.; Valeur, B. Ion-responsive fluorescent compounds. 2. cation-streered intramolecular charge transfer in a crowned merocyanine. The Journal of Physical Chemistry 93(1988) : 3871-3876.

36. Bouson, J; Pouget, J.; Valeur, B. Ion-Responsive Fluorescent Compounds. 4. Effect of Cation Binding on the Photophysical Properties of a Coumarin Linked to Monoaza- and Diaza-Crown Ethers. The Journal of Physical Chemistry 97(1993), : 4552-4557.

37. Lee, C. H.; Lindsey, J. S. One-flask synthesis of meso-substituted dipyrromethanes and their application in the synthesis of trans-substituted porphyrin building blocks. Tetrahedron 50(1994) : 11427.

38. Miyaji, H.; Sato, W.; Sessler, J. L. *Angew. Chem. Int. Ed.* **2000**, *39*, 1777.

39. Anzenbacher, Jr. P.; Jursikova, K.; Shriver, J. A.; Miyaji, H.; Lynch, V. M.; Sessler, J. L.; Gale, P.A. Lithiation of *meso*-Octamethylcalix[4]pyrrole: A General Route to *C*-Rim Monosubstituted Calix[4]pyrroles Journal of Organic Chemistry 65(2000) : 7641.

40. Alexander, M.; David H. P.; Mark E. Thallium in Organic Synthesis. XLII. Direct Oxidation of 4-Substituted Phenols to 4,4-Disubstituted Cyclohexa-2,5-dienones Using Thallium(II1) Nitrate. Journal of Organic Chemistry 41(1976) : 282.

41. Franpise, M.; Winnik. Photophysics of Preassociated Pyrenes in Aqueous Polymer Solutions and in Other Organized Media Chemical Reviews 93(1993) : 587-614.

42. Gale, P. A.; Sessler, J. L.; Kral, V. Calixpyrroles. Chemical Communications 1(1998) : 1-8.

APPENDICES
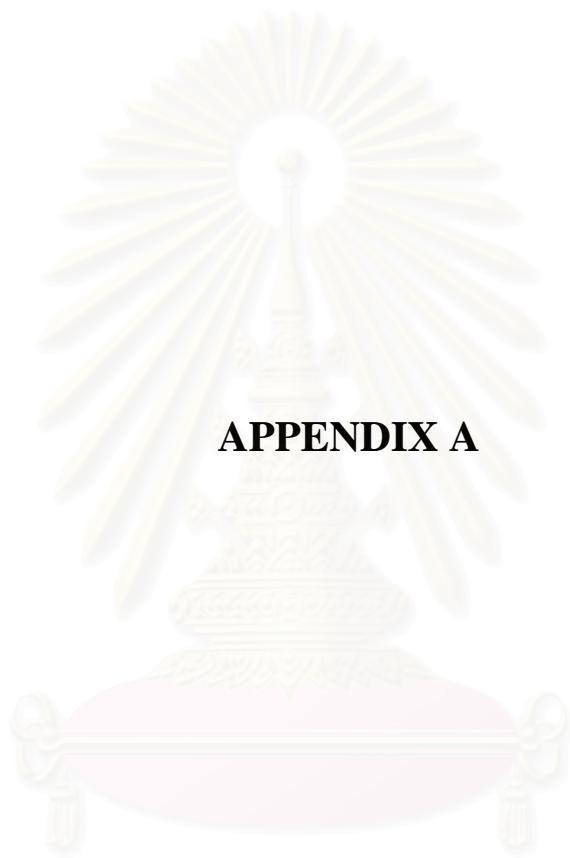
APPENDIX A
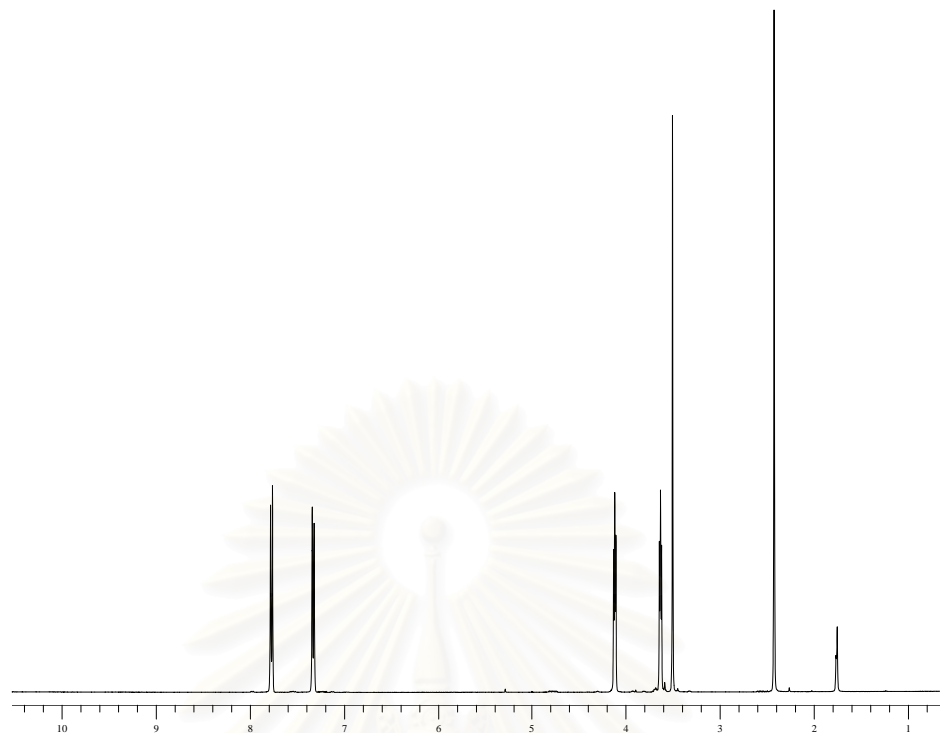
Figure A.1 ^{1}H-NMR (CDCl$_3$, 400 MHz) spectrum of triethyleneglycol ditosylate (**1**)
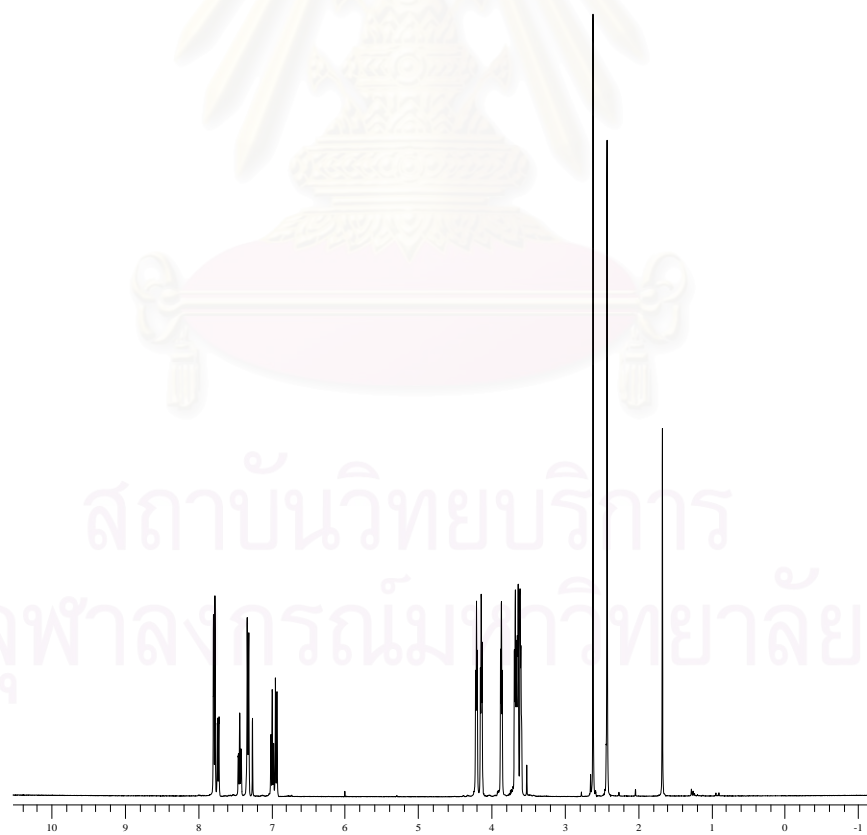
Figure A.2 ^{1}H-NMR (CDCl$_3$, 400 MHz) spectrum of 2-(8-tosyltriethyleneglycol)
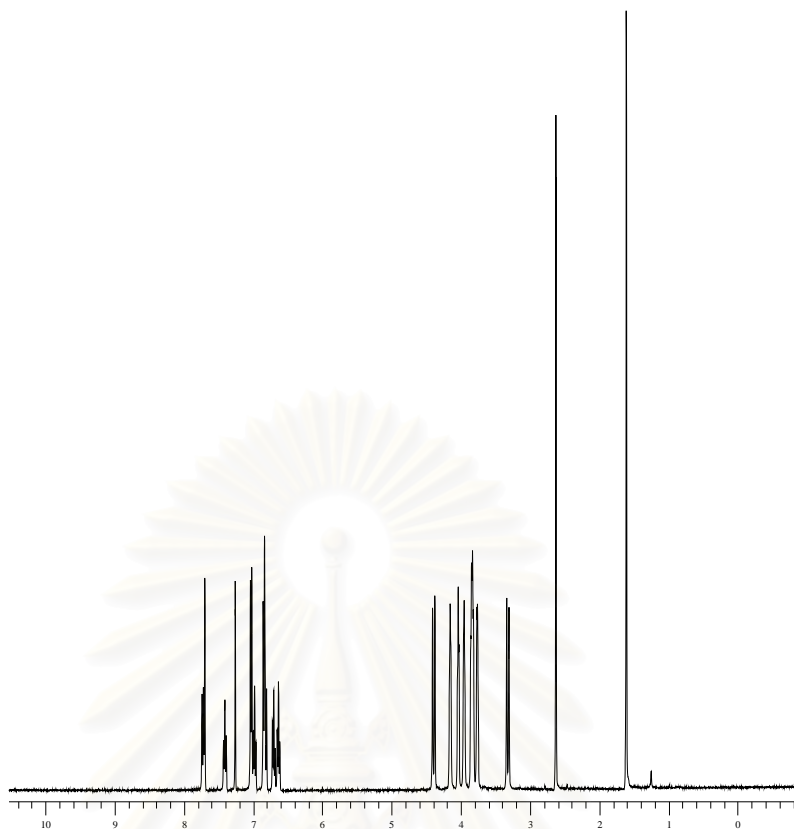
acetophenone (**2**)

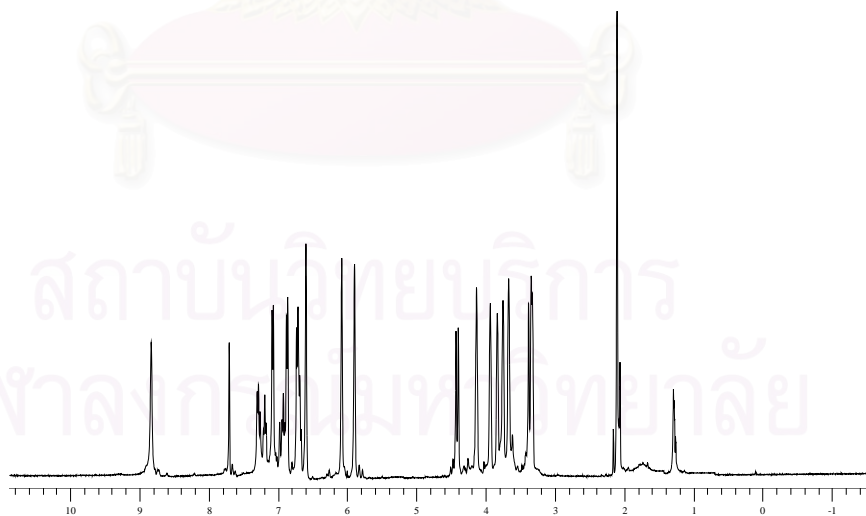**Figure A.3** ^{1}H-NMR (CDCl$_3$, 400 MHz) spectrum of 1,3-calix[4]-diacetophenone (**3**)

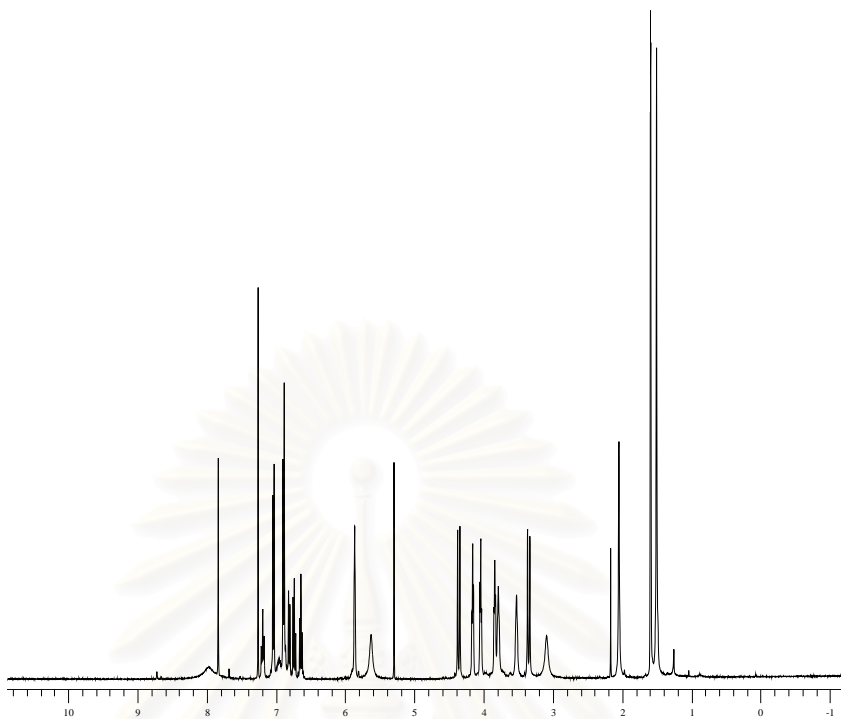**Figure A.4** ^{1}H-NMR (CDCl$_3$, 400 MHz) spectrum of 1,3-calix[4]-bis-dipyrroethane
(**4**)

Figure A.5 ^{1}H-NMR (CDCl$_3$, 400 MHz) spectrum of calix[4]arene-calix[4]pyrrole
(**5**)
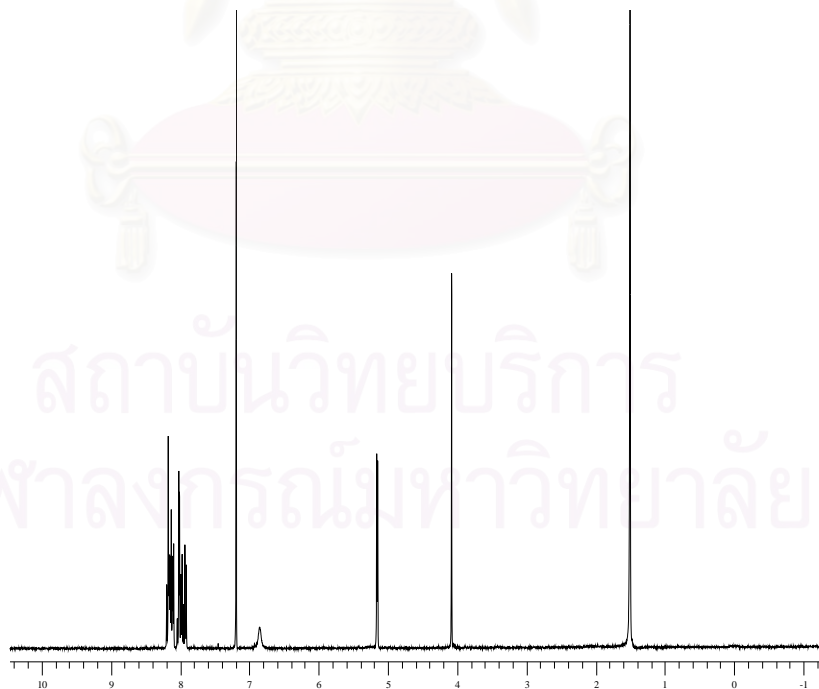
Figure A.6 ^{1}H-NMR (CD$_3$CN, 400 MHz) spectrum of *N*-(1-pyrenylmethyl)
chloroacetamide (**6**)
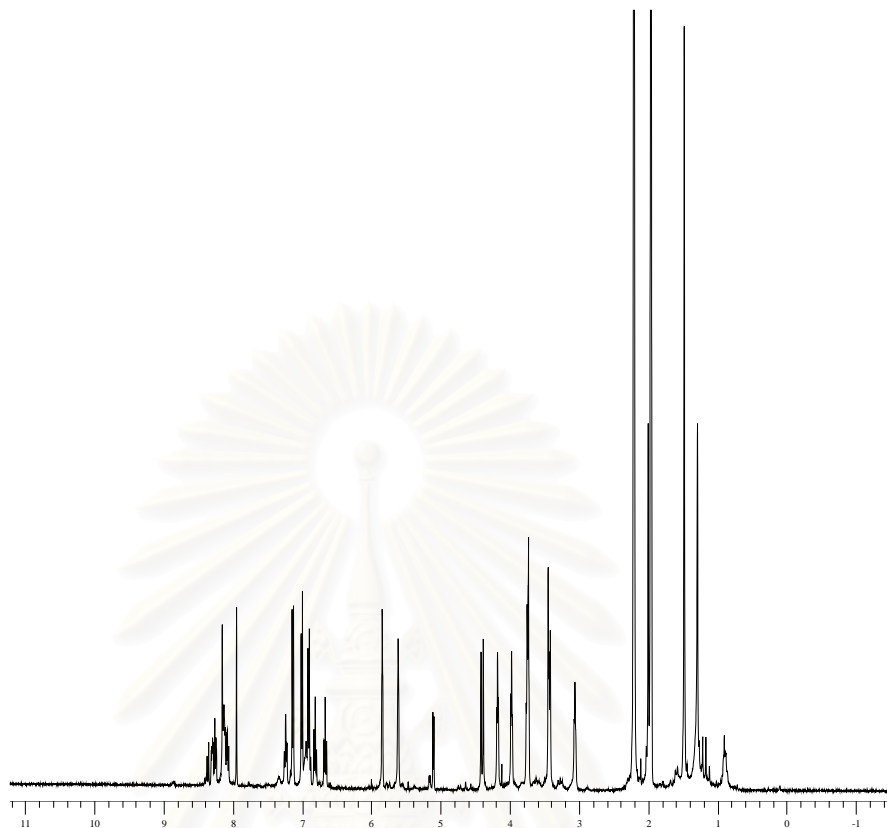
Figure A.7 ¹H-NMR (CD₃CN, 400 MHz) spectrum of 1,3-dipyrenyl-calix[4]arene-
calix[4]pyrrole (**7**)
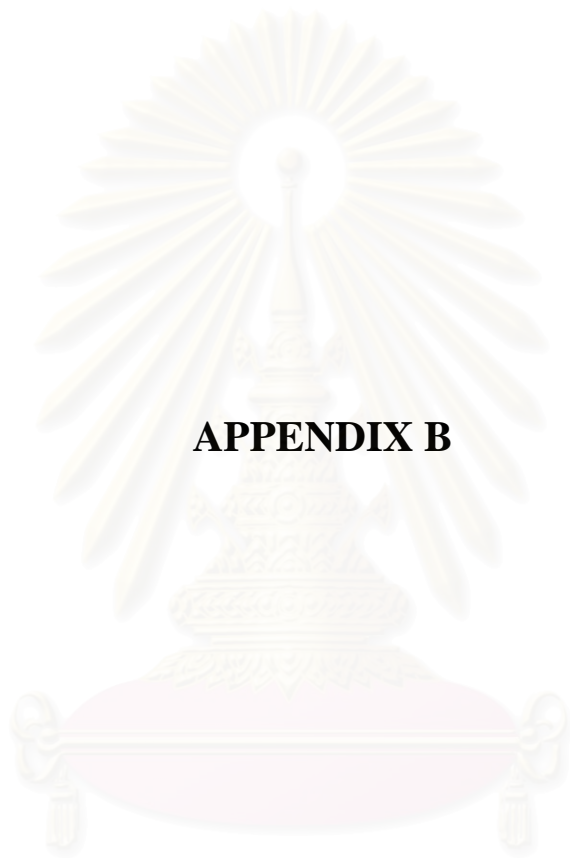
APPENDIX B
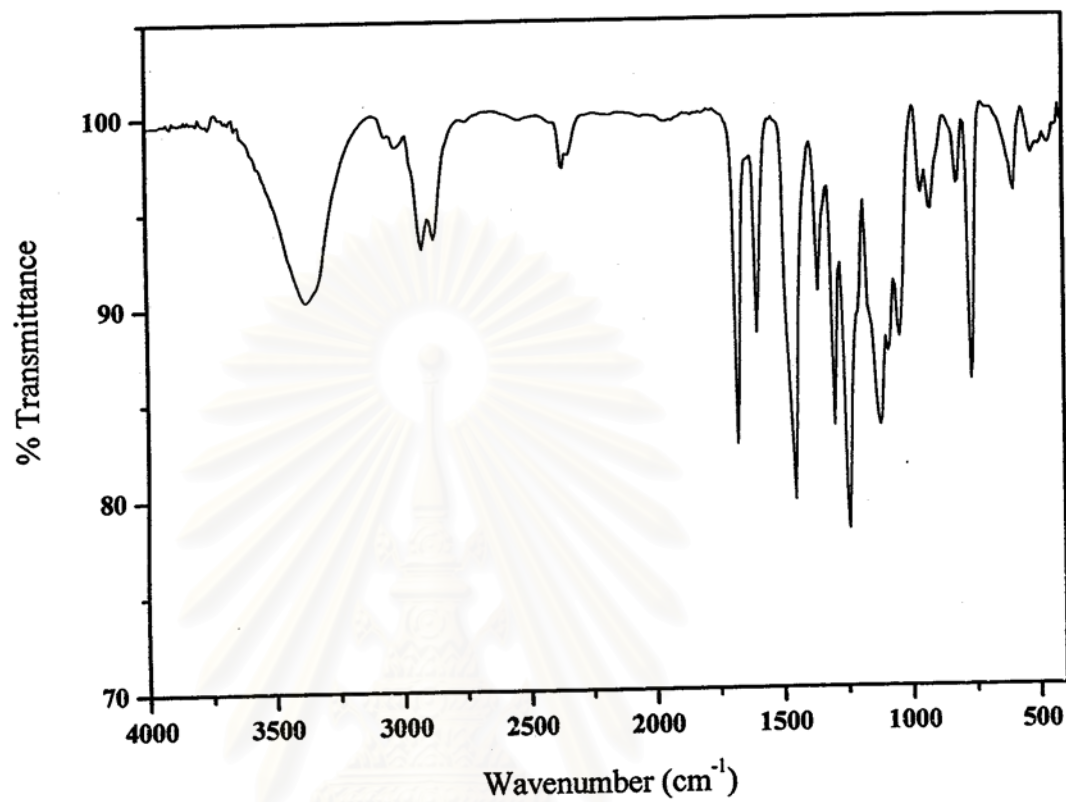
Figure C.1 IR spectrum of 1,3-calix[4]-diacetophenone (**3**)
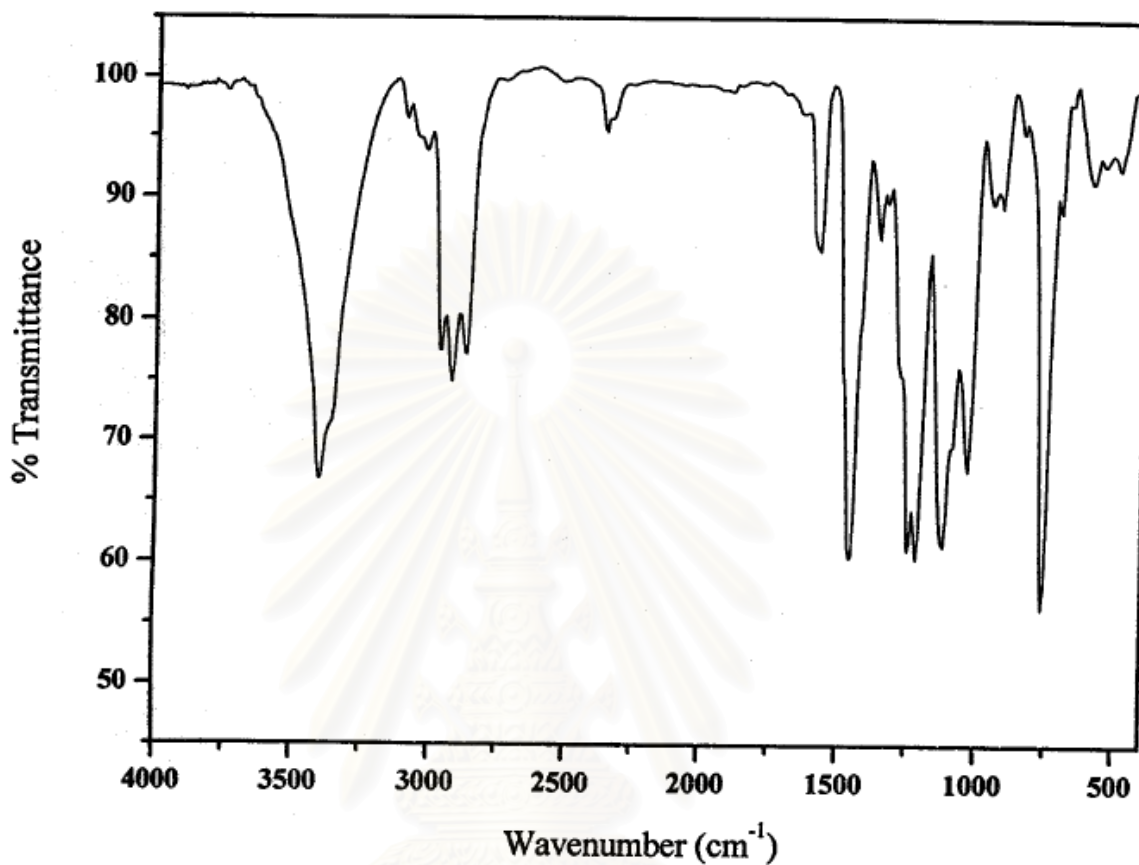
Figure C.2 IR spectrum of calix[4]arene-calix[4]pyrrole (**5**)
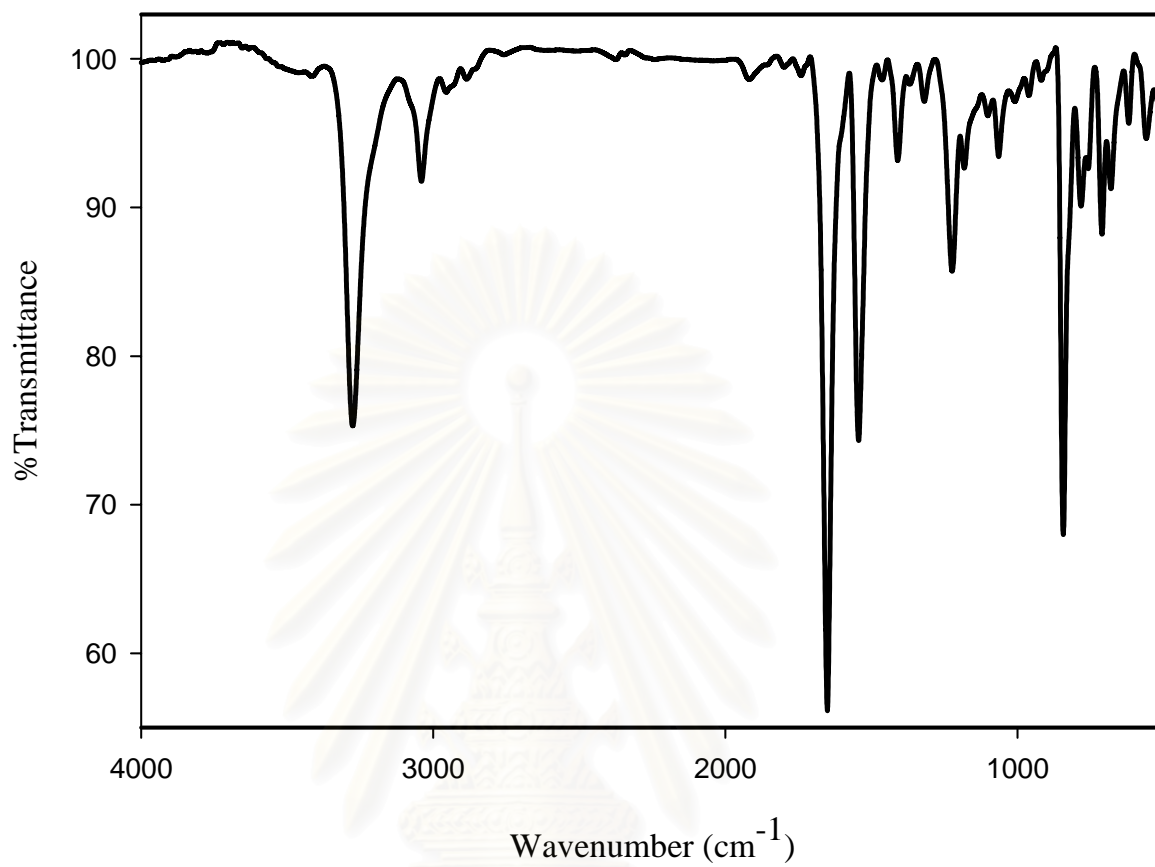
Figure C.2 IR spectrum of calix[4]arene-calix[4]pyrrole (**6**)
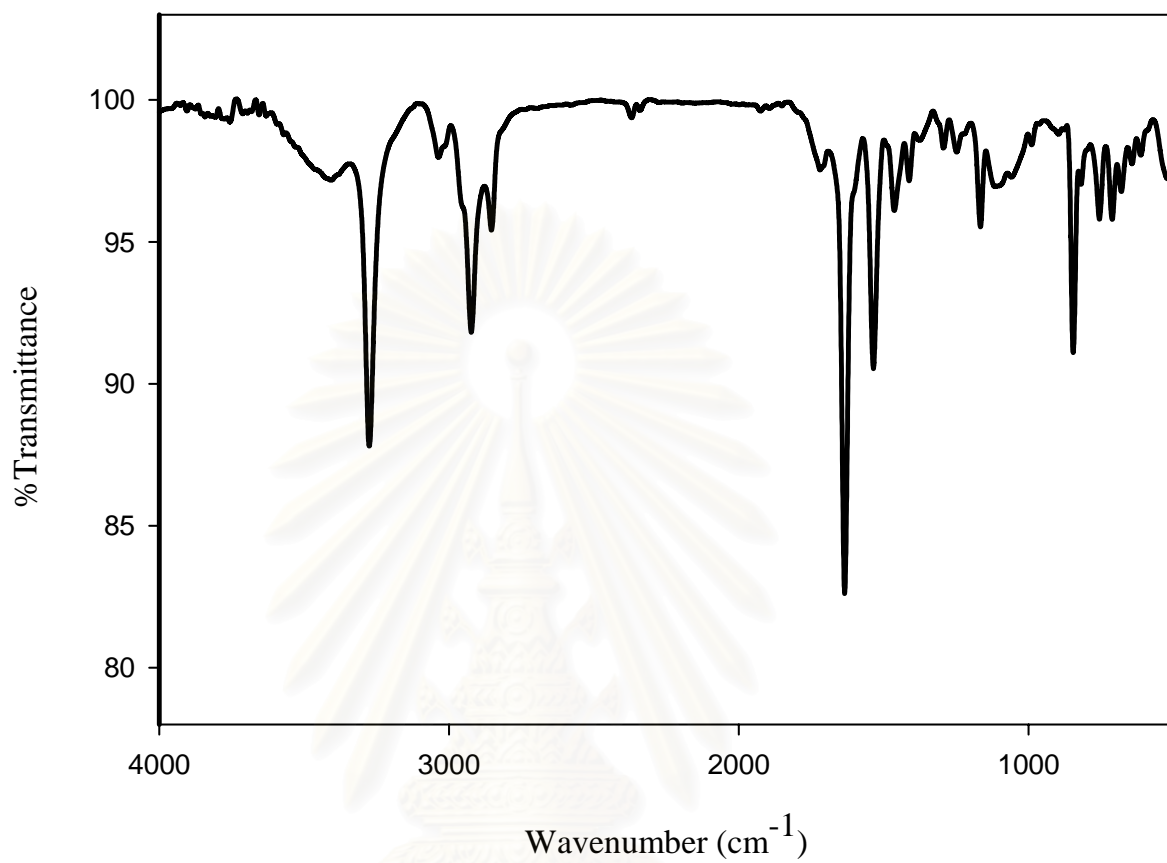
Figure C.2 IR spectrum of 1,3-dipyrenyl-calix[4]arene-calix[4]pyrrole (**7**)

APPENDIX C

X:L

	X:L
	0.0 : 1.0
	8.0 : 1.0
	16.0 : 1.0
	24.0 : 1.0
	32.0 : 1.0
	40.0 : 1.0
	48 : 1.0
	56.0 : 1.0
	64.0 : 1.0
	72.0 : 1.0
	80.0:1.0
	96.0:1.0
	112.0:1.0
	128.0:1.0
	144.0:1.0
	160.0:1.0
	180.0:1.0
	200.0:1.0
	220.0:1.0
	240.0:1.0
	260.0:1.0
	280.0:1.0
	300.0:1.0
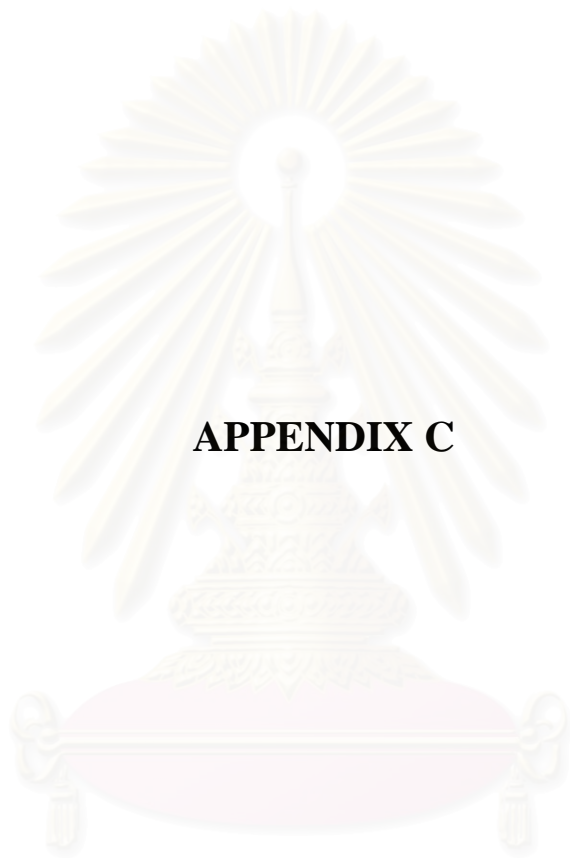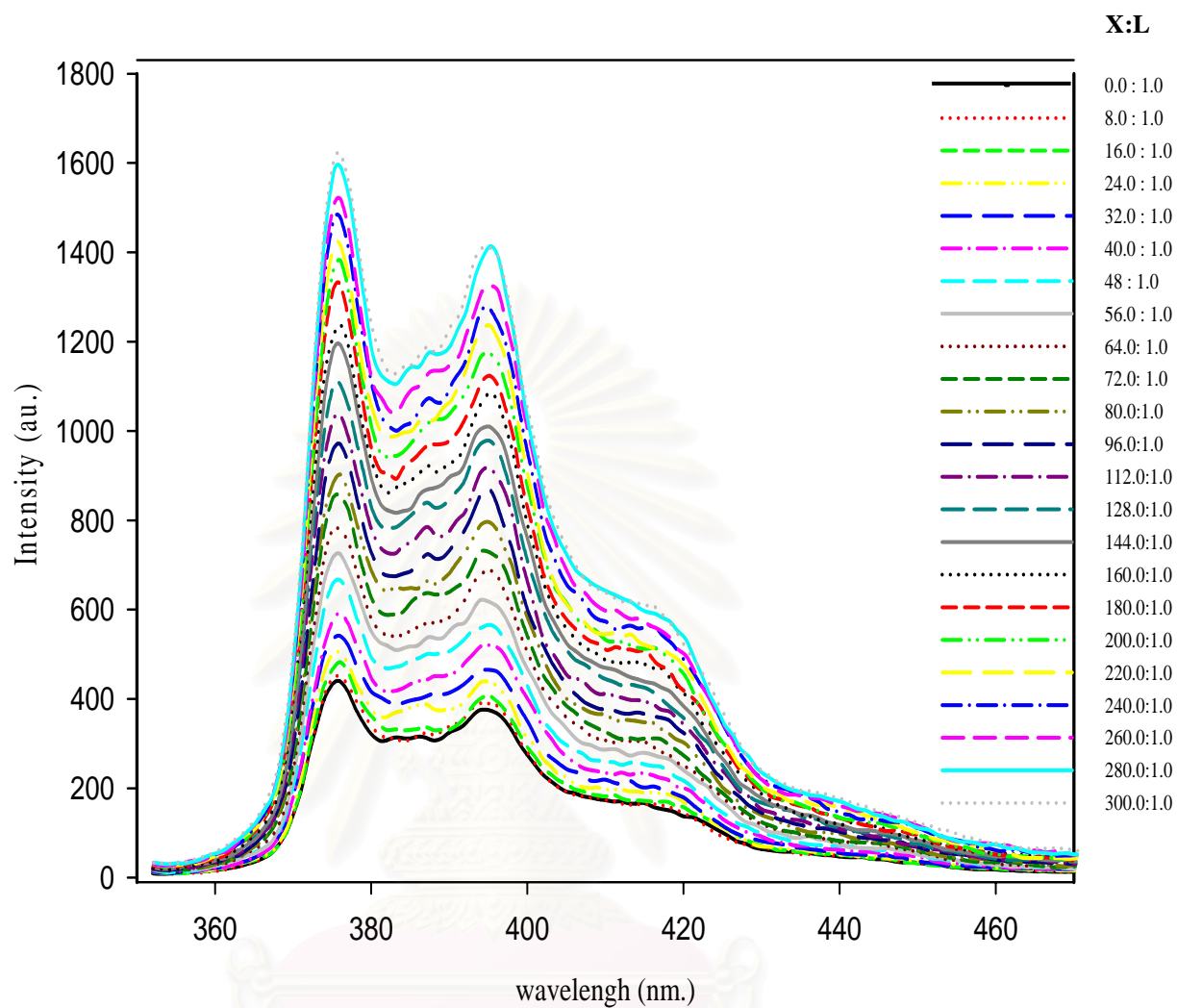
Figure C.1 Fluorescence titration of ligand **7** with Bu_4NF
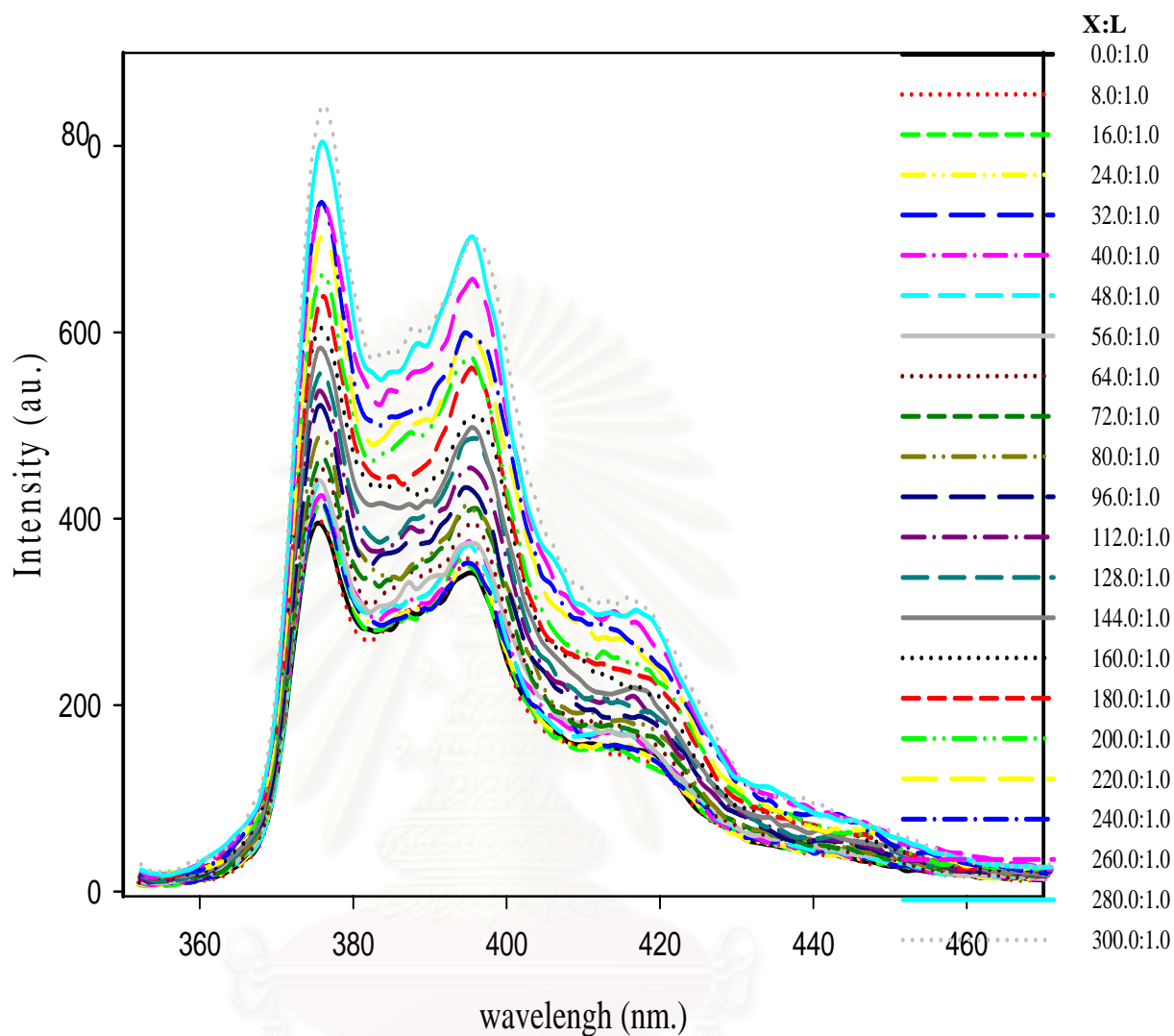
Figure C.2 Fluorescence titration of ligand **7** with Bu$_4$NCl
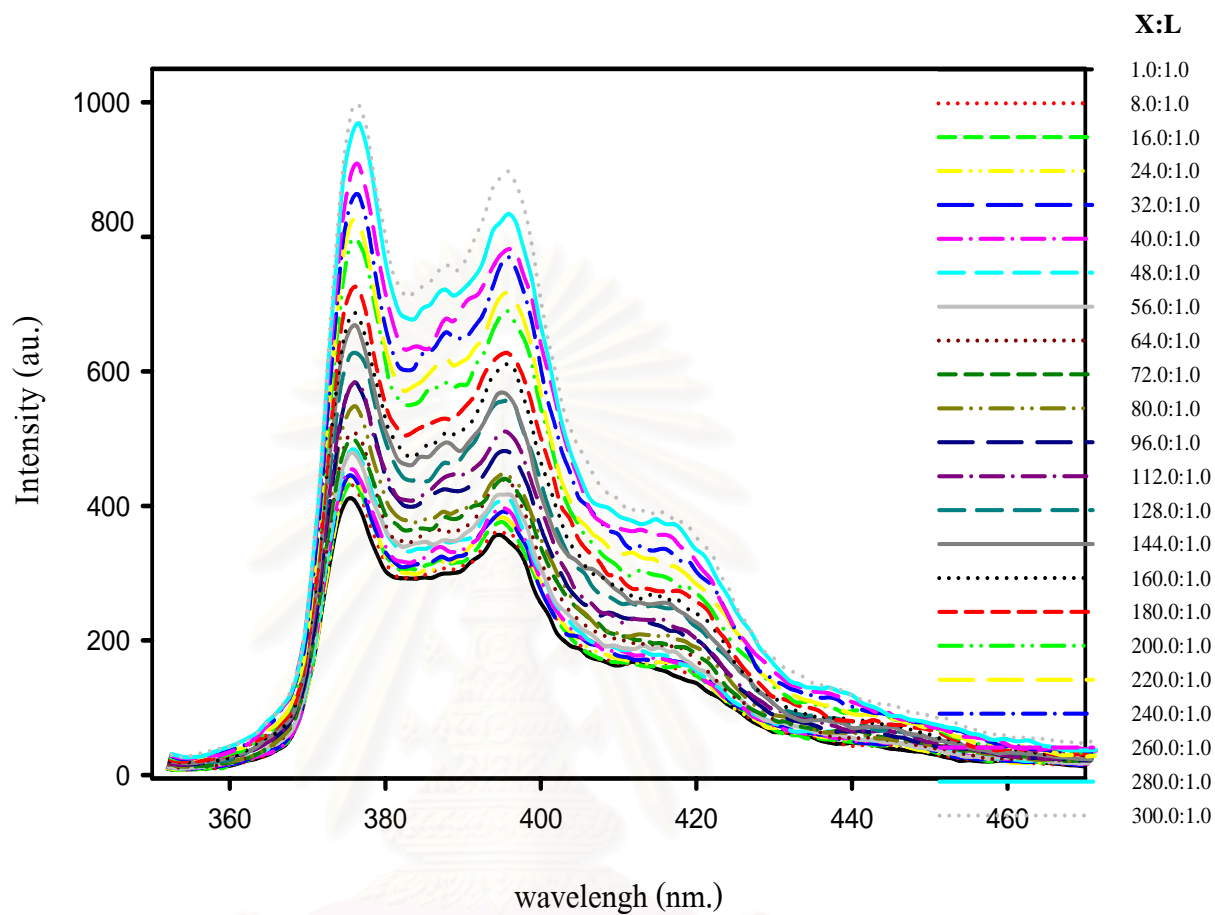
Figure C.3 Fluorescence titration of ligand **7** with Bu$_4$NBr.

X:L
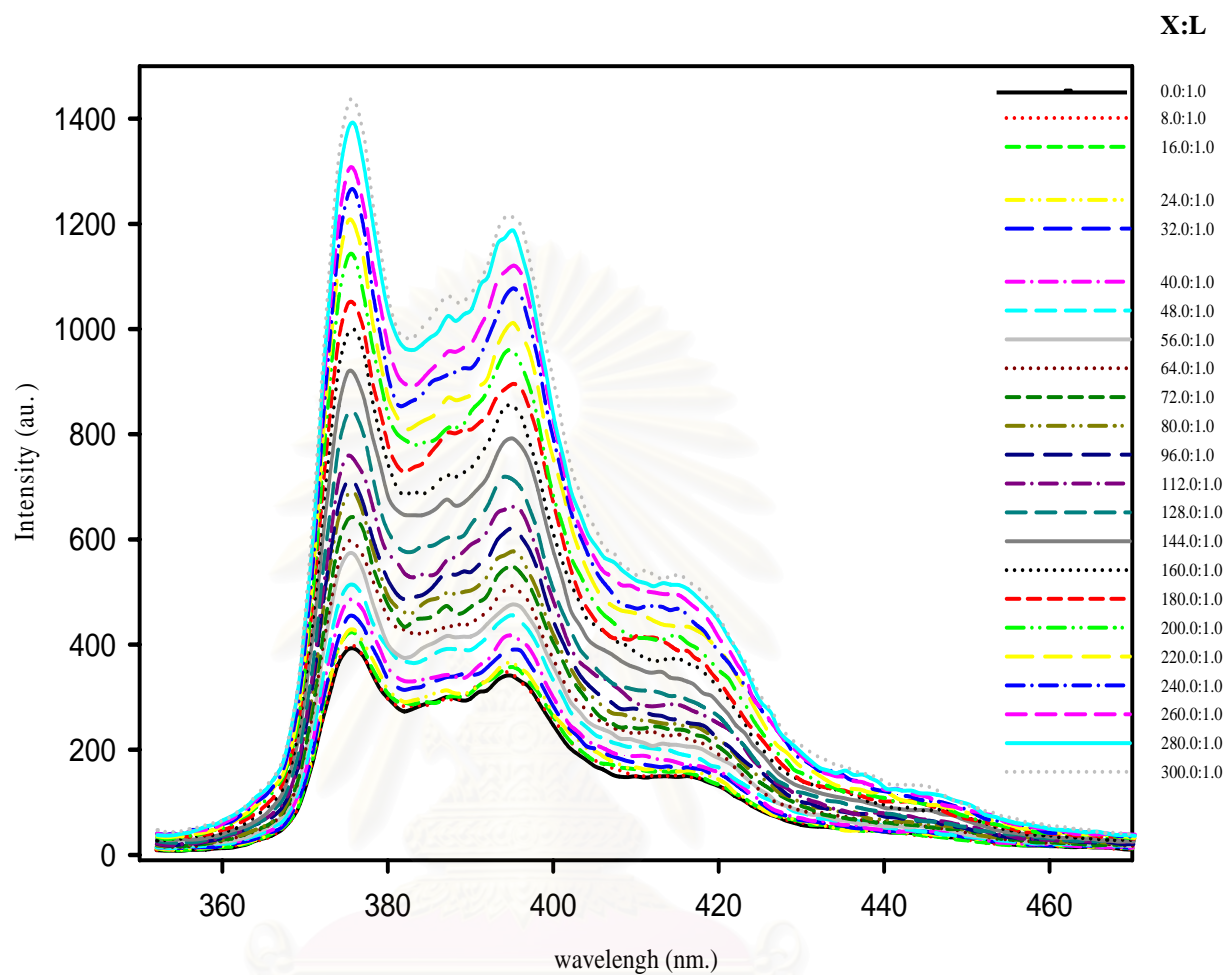
Figure C.4 Fluorescence titration of ligand **7** with Bu$_4$NCH$_3$COO
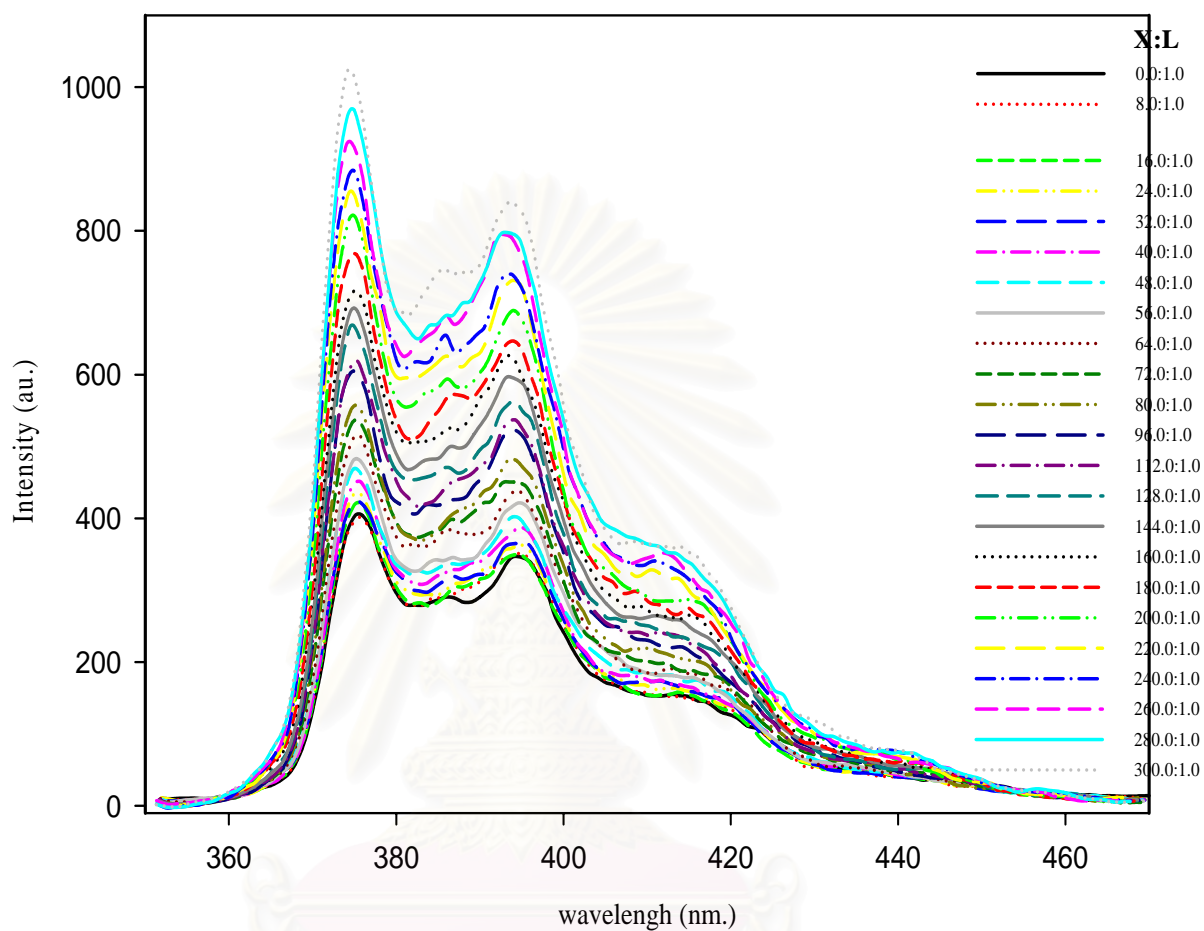
Figure C.5 Fluorescence titration of ligand **7** with Bu₄NPhCOO

VITAE

Mr.Preecha Thiampanya was born on January 27,1979 in Angthong, Thailand. He graduated with a high school diploma from Angthong Phattamaroj Witthayakhom School, Angthong in 1996. He received his Bachelor's degree of Science in Chemistry from Ramkhamheang University in 2001. He worked at the Center of protein structure and function, Faculty of Science, Mahidol University since 2002-2003. Since 2004, he has been a graduate student at the Department of Chemistry, Chulalongkorn University and become a member of the Supramolecular Chemistry Research Unit under Supervision of Associate Professor Dr. Buncha Pulpoka. He finished his Master's degree of Science in the academic year 2006.