การสังเคราะห์และศึกษาการเกิดสารประกอบเชิงซ้อนของคาลิกซ์[4]เอรีนที่มีสทิลบีนและคราวน์อีเทอร์

นางสาวอาริสา ใจอยู่

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
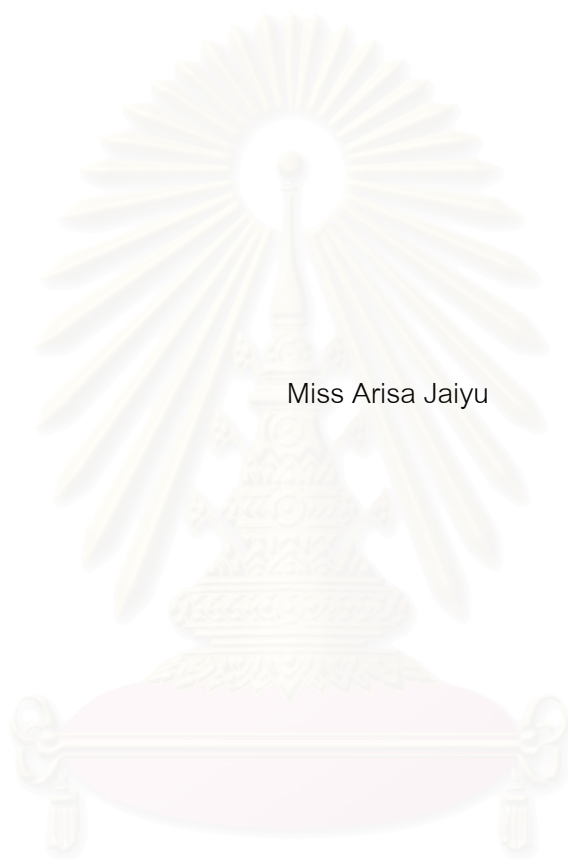สาขาวิชาเคมี   ภาควิชาเคมี
คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
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SYNTHESIS AND COMPLEXATION STUDY OF CALIX[4]ARENE CONTAINING STILBENE

AND CROWN ETHER

Miss Arisa Jaiyu

A Dissertation Submitted in Partial Fulfillment of the Requirements

for the Degree of Doctor of Philosophy Program in Chemistry

Department of Chemistry

Faculty of Science Chulalongkorn University

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Thesis Title   SYNTHESIS AND COMPLEXATION STUDY OF CALIX[4]ARENE CONTAINING STILBENE AND CROWN ETHER

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Field of Study   Chemistry

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อาริสา ใจอยู่ : การสังเคราะห์และศึกษาการเกิดสารประกอบเชิงซ้อนของคาลิกซ์[4]เอรีนที่มี สทิลบีนและคราวน์อีเธอร์ (SYNTHESIS AND COMPLEXATION STUDY OF CALI[4]ARENE CONTAING STILBENE AND CROWN ETHER) อ. ที่ปรึกษา : รศ.ดร. มงคล สุขวัฒนาสินิทธ์ 113 หน้า.

ได้ทำการสังเคราะห์อนุพันธ์ของคาลิกซ์[4]เอรีนที่มีสทิลบีนเป็นสะพานเชื่อมโดยใช้ปฏิกิริยารีดักชันคู่ควบ ภายในโมเลกุลของบิสเบนซาลดีไฮด์คาลิกซ์[4]เอรีนด้วยเปอร์เซ็นต์ผลิตภัณฑ์สูงภายใต้สภาวะที่เจือจางและมี ไทเทเนียมเตตระคลอไรด์มากเกินพอ สายเตตระและเพนตะเอทิลลีนไกลคอลถูกต่อเข้ากับหมู่ฟีนอลิกของคาลิกซ์ [4]เอรีนให้เป็นสทิลบีนคาลิกซ์[4]เอรีนคราวน์อีเธอร์-5และ -6 ตามลำดับ ซึ่งสะพานสทิลบีนบนคาลิกซ์[4]เอรีนช่วย ป้องกันการต่อของสายโพลีอีเธอร์ในรูปโคนคอนฟอร์เมชันได้อย่างมีประสิทธิภาพ ทำให้ได้ผลิตภัณฑ์เป็น 1,3-อัล-เทอเนตสทิลบีนคาลิกซ์[4]เอรีนคราวน์อีเธอร์ ซึ่งมีสมบัติในการสกัดและความจำเพาะเจาะจงกับซีเซียมไอออนที่ดีกว่า โคนคาลิกซ์[4]เอรีนคราวน์อีเธอร์และคราวน์อีเธอร์ทั่วไป

ความพยายามในการต่อคราวน์อีเธอร์ลงบนทรานส์ไอโซเมอร์ของเมตาสทิลบีนคาลิกซ์[4]เอรีนไม่เป็น ผลสำเร็จ จากการวิเคราะห์คอนฟอร์เมชันและการสังเคราะห์อนุพันธ์ที่ไม่ใช่คราวน์แสดงให้เห็นว่า สะพานเชื่อม ทรานส์เมตาสทิลบีนมีขนาดค่อนข้างยาวจนทำให้คาลิกซ์[4]เอรีนอยู่ในรูปพินช์โคนคอนฟอร์เมชัน ที่มีริมไฮดรอกซี แคบเกินกว่าที่จะยอมให้วงเฟนนิลพลิกเป็น 1,3-อัลเทอเนต ผลที่ได้จากงานนี้ทำให้เกิดความเข้าใจถึงปัจจัยที่ สามารถใช้เป็นแนวทางการสังเคราะห์อนุพันธ์คาลิกซ์[4]เอรีน ที่มีคอนฟอร์เมชันเป็น โคน พินช์โคน พาเชียลโคน และ 1,3-อัลเทอเนต

ภาควิชา เคมี   ลายมือชื่อนิสิต..
สาขาวิชา เคมี ลายมือชื่ออาจารย์ที่ปรึกษา..............................
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> ARISA JAIYU : SYNTHESIS AND COMPLEXATION STUDY OF CALIX[4]ARENE CONTAINING STILBENE AND CROWN ETHER.   THESIS ADVISOR : ASSOC. PROF. DR. MONGKOL SUKWATTANASINITT, 113 pp.

A series of stilbene-bridged calix[4]arenes were synthesized in high yields through an intramolecular reductive McMurry coupling of bisbenzaldehyde calix[4]arene using high dilution condition and a large excess of $TiCl_4$. Tetra- and pentaethylene glycol chains were tethered to the opposite phenolic groups of calix[4]arene to form stilbene-bridged calix[4]arene crown-5 and crown-6 respectively. The presence of stilbene bridge over the calix[4]arene rim effectively prevents the connection of the polyether chains in the cone conformation resulting in the exclusive formation of 1,3 alternate stilbene-bridged calix[4]arene crown product. Comparing to the cone conformation, the 1,3 alternate calix[4]arene crown ethers have greater extractability and selectivity toward Cs^+.

The attempts to construct the crown ethers for *trans*-isomer of *m*-stilbene-bridged calix[4]arene from *m-trans*-stilbene-bridged calix[4]arene have not been successful, yielding only intractable materials. Extensive conformation analyses and synthesis of non crown analogues revealed that the length of *m-trans*-stilbene-bridge is so long that force calix[4]arene into a pinched cone conformation in which the hydroxyl rim is too narrow to allow the phenyl ring flip. The results from this work provide a very logical and reliable insight for the synthesis of cone, pinched cone, partial cone and 1,3-alternate calix[4]arene derivatives.

Department   Chemistry Student's signature..

Field of study Chemistry Advisor's signature..

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CONTENTS

List of Abbreviations and Signs

Å	Angstrom
mp	Melting point
˚C	Degree Celsius
^{13}C-NMR	Carbon nuclear magnetic resonance
^{1}H-NMR	Proton nuclear magnetic resonance
δ	Chemical Shift
K	Binding Constant
g	Gram
mL	Milliliter
mM	Millimolar
mmol	Millimole
M	Molar
AA	Atomic Absortion
UV-Vis	Ultra violet-visible
µL	Micro litter

List of Numbered Compound

o-1   *ortho*-Bisbenzaldehyde calix[4]arene

m-1   *meta*-Bisbenzaldehyde calix[4]arene

p-1   *para*- Bisbenzaldehyde calix[4]arene

o-cis-2   *ortho-cis*-Stilbene-bridged calix[4]arene

o-trans -2 *ortho-trans*-Stilbene-bridged calix[4]arene

m-cis-2   *meta-cis*-Stilbene-bridged calix[4]arene

m-trans-2 *meta-trans*-Stilbene-bridged calix[4]arene

p-cis-2   *para-cis*-Stilbene-bridged calix[4]arene

o-cis-3   *ortho-cis*-Stilbene-bridged calix[4]arene crown-5

o-trans-3 *ortho-trans*-Stilbene-bridged calix[4]arene crown-5

m-cis-3   *meta-cis*-Stilbene-bridged calix[4]arene crown-5

p-cis-3   *para-cis*-Stilbene-bridged calix[4]arene crown-5

o-cis-4   *ortho-cis*-Stilbene-bridged calix[4]arene crown-6

m-cis-4   *meta-cis*-Stilbene-bridged calix[4]arene crown-6

p-cis-4   *para-cis*-Stilbene-bridged calix[4]arene crown-6

5   *meta-cis*-Stilbene-bridged calix[4]arene diethylene glycol ethyl ether

6   *meta-cis*-Stilbene-bridged calix[4]arene triethylene glycol monomethylether

7   *meta-trans*-Stilbene-bridged calix[4]arene diethylene glycol ethyl ether

8   *meta-trans*-Stilbene-bridged calix[4]arene triethylene glycol monomethylether; cone conformation

9   *m-trans* Stilbene-bridged calix[4]arene triethylene glycol monomethylether;patial cone conformation

10   Stilbene bridged *tert*-butyl calix[4]arene

11   Azobenzene bridged tert-butyl calix[4]arene

12   *O,O′*-Dimethylcalix[4]arene crown-5

13   *O,O′*-Dimethylcalix[4]arene crown-6

14   Phenanthrene bridged calix[4]arene crown ether

Structure of all compounds was shown in Appendix C.

List of Schemes

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CHAPTER I

INTRODUCTION

In biological system, ion transportation was controlled by ion pump through membrane containing natural ionophores. The well known ion pump is Na/K pump that relies on the conformational switch of proteins entrenched in the membrane to select binding with sodium or potassium ion using ATP in the process.[1-3] The chemists use supramolecular chemistry, a combination of organic synthesis of molecular architectures and coordination chemistry, for understanding and mimicking the biologal system.[4] Supramolecular chemistry may also lead to assembly of molecular devices defined as structurally organized chemical systems built for specific functions.[5-7]

1.1 Supramolecular Chemistry

Study of supramolecular structures has recently become one of the most interesting subjects in science covering chemistry, physics, biology which focus on the noncovalent interaction of molecules such as hydrogen bonding, metal coordination, hydrophobic forces, van der Waals forces, π-π interactions, and electrostatic interaction to assemble molecules into multimolecular complexes.[8] Supramolecular structures are common and important in biological systems observed in various combinations between receptor-ligand, antigen-antibody, DNA-protein, sugar-lectin, RNA-ribosome, etc. Chemists have demonstrated that artificial supramolecular systems can be designed to exhibit molecular recognition. One of the earliest examples of this system is crown ethers which were selectively bind specific cations. However a number of artificial systems have since been established.[9-11]

1.2 Crown ethers

Crown ethers are heterocyclic molecules consisting of repeating $-OCH_2CH_2$ units (**Figure 1.1**). Crown ethers are known as alkali metal ion receptor.[12-15] The binding properties are depending on the shape and size of the crown ethers; for examples, 18-crown-6 has high affinity for potassium cation 15-crown-5 for sodium

cation and 12-crown-4 for lithium cation. The oxygen atoms are ideally situated to coordinate with the cation in the interior of the ring, whereas the exterior of the ring is hydrophobic. The result is that the complexed cation is soluble in nonpolar solvents. The applications of crown ether are separation of metal ion and phase transfer catalysis.[16-18]

| 12-crown-4 | 15-crown-5 | 18-crown-6 |
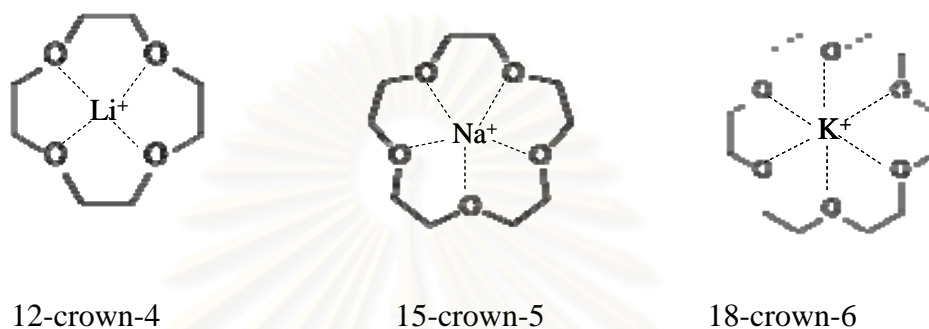
Figure 1.1 A various size of crown ethers and complexation with metal ion

1.3 Calix[4]arene

Calix[4]arenes, a well-established class of flexible macrocyclic compounds, are characterized by a three dimensional basket or cup structure that has a wide upper rim and narrow lower rim and a central annulus.[19-21] (**Figure 1.2**).
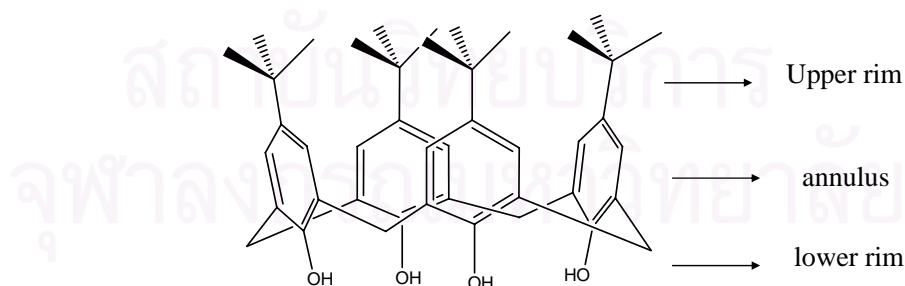
Figure 1.2 *p-tert*-butyl calix[4]arene structure

A calix[4]arene derivative is frequently used as a building block for construction of highly selective host molecules[20] because calix[4]arene can easily be functionalized both at the phenolic OH group (lower rim)[22-25] and the *para* position

of the phenol rings (upper rim).[21, 26-29] The rotation of the bonds between phenol rings brings about variable conformations of calix[4]arene. Four main conformations of calix[4]arene have been recognized that is one with the aryl groups all *syn* to each other, one with three aryl group *syn* and one *anti*, one with adjacent pairs of aryl groups *syn* and *anti* and one with all adjacent pairs of aryl groups *anti*. These were name as cone, partial cone, 1,2-alternate and 1,3-alternate with idealized structures having C_{4v}, C_s, C_2h, D_{2d} symmetry, respectively (**Figure 1.3**).[30-33]

The structures of these conformers can be easily distinguished by the characteristic ^1H NMR patterns arising from the ArCH$_2$Ar methylene protons judging from the symmetry of each conformer, cone, partial cone, 1,2-alternate, and 1,3-alternate will appear as a pair of doublets, two pairs of doublets, one singlet and pair of doublets, and one singlet, respectively.[34-35]
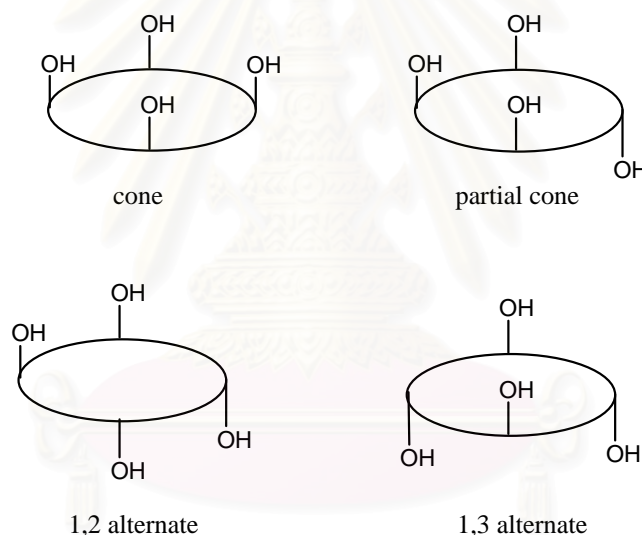
Figure 1.3 Calix[4]arene conformation

However, sometime the actual molecule of calix[4]arene have a conformation different from these four main conformations as the result of torsion changes in the aryl group orientation.[36-39] For example, the cone conformation sometime assumes a pinched cone structure in which one pair of aryl groups become almost parallel while the other pair splay outward.[21]

The binding properties of calix[4]arene toward alkali metal ion, alkaline earth metal ion, ammonium cation can be tuned by conformational change of the

calix[4]arene. It is now well-established that the efficiency and selectivity in metal ion binding by calixarene ionophores depends not only on the ring size of the calixarenes but also on the nature of the binding groups attached and, especially for calix-[4]arene derivatives, on the conformation of the macrocycle (cone, partial cone, 1,3-alternate, 1,2-alternate).[19]

In case of calix[4]arene crown-6 (**Figure 1.4**), the cone conformation hardly extract or bind with Cs^+ while the 1,3 alternate conformation have the high extractability toward Cs^+.[24] A dramatic increase in the binding and extraction of cesium cation is observed for all ligands in the 1,3-alternate conformation due to the cation-π interaction of phenyl rings of calix[4]arene and Cs^+ that performed well in 1,3 alternate conformation.[40-41]

1,3 alternate conformatiom   cone conformation

Figure 1.4 Conformation of calix[4]arene crown-6[24]

In some case, calix[4]arene conformation can be changed by complexing with a cationic guest (**Figure 1.5**).[19] When Li^+, Na^+ or ammonium cation was added into tetra-*O*-methyl calix[4]arene solution, the partial cone conformation of calix[4]arene was changed to cone conformation. Because of the absence of the intramolecular hydrogen bonding of the tetra-*O*-methyl calix[4]arene, the conformation is not locked and it is easy to rotate. So, the tetra-*O*-methylation of calix[4]arene can complex with many cations in different conformations and does not show selectivity.
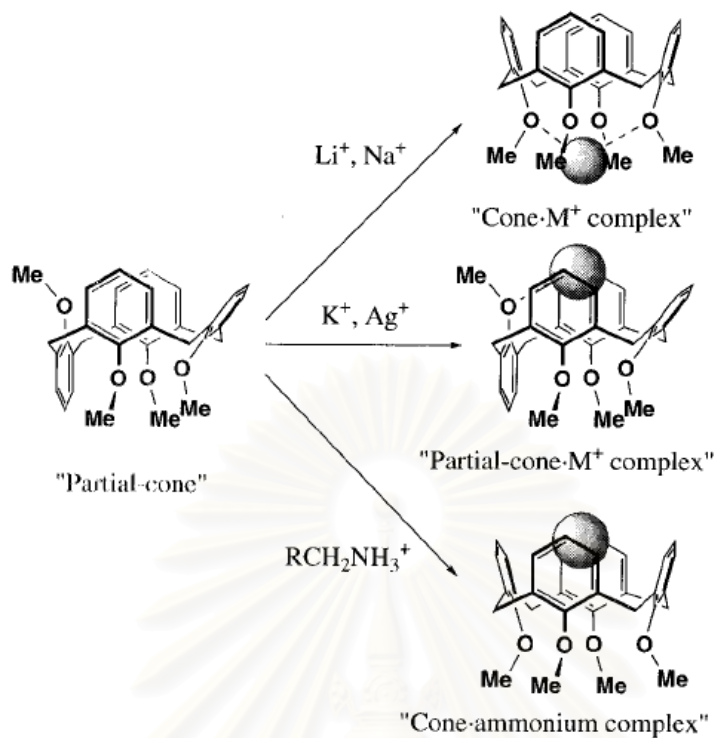
Figure 1.5 Inclusion of metal cation and of ammonium[19]

The common receptor such as calix[4]arene and crown ether were combined with azobenzene and stilbene (**Scheme 1.1**) that have different molecular lengths between various isomers and photo-switchability between *cis* and *trans* isomer to control the conformation and binding properties of the receptors.

cis-azobenzene   *trans*-azobenzene

cis-stilbene   *trans*-stilbene
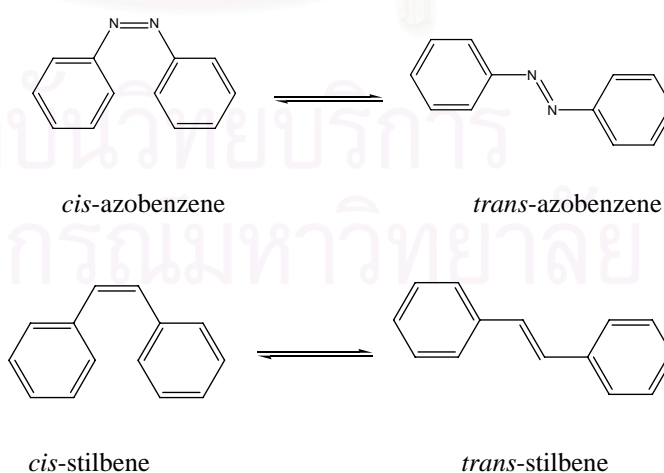
Scheme 1.1 *cis* and *trans* isomer of azobenzene and stilbene

In 1979, Ueno and coworkers[42] found that dipyridyl *cis*-azobenzene-capped *β*-cyclodextrin can bind 4,4′-bipyridyl, whereas *trans*-azobenzene-capped *β*-cyclodextrin cannot bind at all. They suggested that 4,4'-bipyridyl is too large to be included in the cavity of *trans*-azobenzene-capped *β*-cyclodextrin but can be included in the expanded cavity of *cis*- azobenzene-capped *β*–cyclodextrin. (**Figure 1.6**).
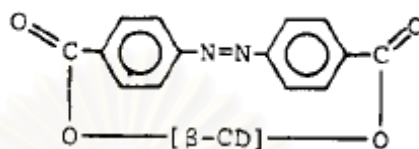
Figure 1.6 Azobenzene-capped β–cyclodextrin[26]

In 1980, Shinkai and coworkers[43] investigated the extractability of *cis* and *trans*-azobenzene crown ether (**Scheme 1.2**). They found that the extractability of *trans*-azobenezene crown ether is in the order $K^+ > Na^+ > Li^+ > Rb^+, Cs^+$ whereas that of *cis*-azobenezene crown ether is in the order $K^+ > Na^+ > Rb^+ > Li^+, Cs^+$; (ii) large alkali metal ions such as Rb^+ and Cs^+ are hardly extracted by *trans*-azobenezene crown ether, (iii) *trans*-azobenezene crown ether extracts Li^+ which cannot be extracted by *cis*- azobenezene crown ether. They also prepared azobis(benzo) crown ether and studied about their binding ability.[44] From the extraction study, *cis*-azobis(benzo) crown ether can bind with K^+, Rb^+ and Cs^+ well while the *trans* form can bind with Li^+ and Na^+ (**Scheme 1.3**) .
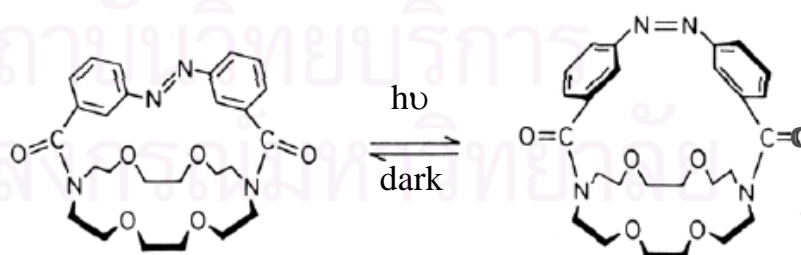
Scheme 1.2 *cis* and *trans* isomer of azobenzene crown ethers[43]
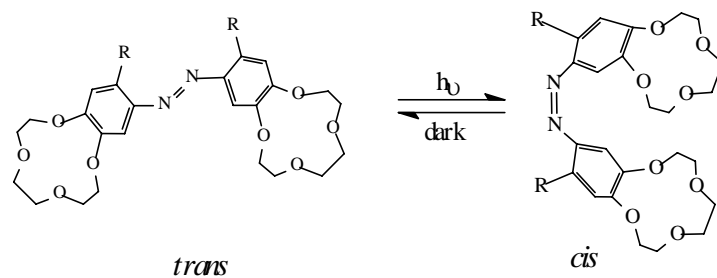
Scheme 1.3 *cis* and *trans* isomer of azobis(benzo) crown ether[44]

In 1997, Vicens and coworkers synthesized the calix[4]arene crown ether containing azobenzene.[45-46] Extraction of Cs^+ and Rb^+ proved that *cis*-azo calix[4]crown ether exhibits a greater binding ability than *trans*-azo calix[4]crown ether (**Scheme 1.4**). The results indicated that azobenzene can control conformation and binding properties of receptors.
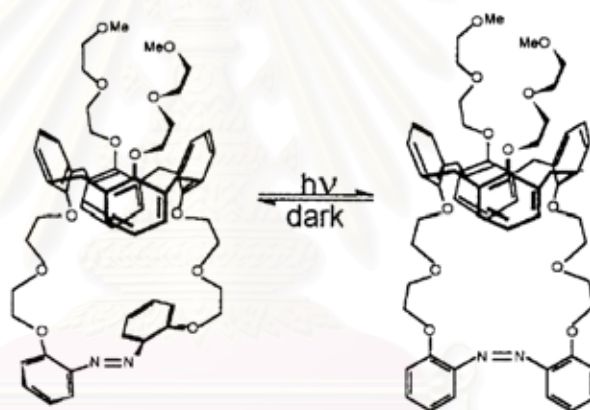
Scheme 1.4 *cis- and trans*-azo calix[4]crown ether[45-46]

In 2001, calix[4]arene crown ethers containing azobenzene (**Figure 1.7**) were prepared.[47-48] The X-ray structure showed that the conformation of *o-trans*-azobenzene crown ether calix[4]arene was cone while that of the *m-trans*-isomer was pinched cone. The *m-trans* derivative preferred to bind K^+ while the *m-cis* derivative preferred to bind Na^+. Although the *m-cis*- and *m-trans*-isomers of these azobenzene derivatives displayed different selectivity in binding alkali metal ions, their thermal isomerization prevented them from being good candidates for controllable receptors.[47-48]

Unlike azobenzenes, the stilbene analogues have been found not to undergo thermal isomerization.[49] Therefore, the stilbene-bridged calix[4]arene derivatives were synthesized (**Figure 1.8**). The result showed that the stilbene bridge can be used

to control the conformations of calix[4]arene between cone and pinched cone. Unfortunately, these stilbene derivatives can not bind with any alkali metal ion.[48, 50-51]
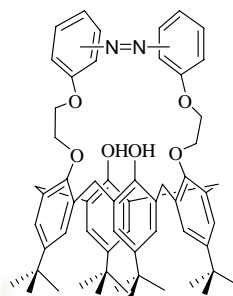
Figure 1.7 Azobenzene crown ether *p-tert*-butylcalix[4]arenes
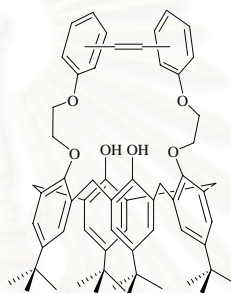
Figure 1.8 Stilbene crown ether *p-tert*-butylcalix[4]arenes

This dissertation presents the synthesis of a new series of calix[4]aene derivatives containing crown ether cavity and stilbene bridge on the opposite rims of calix[4]arene **(Figure 1.9)**. The design of the synthsized molecules uses crown ether as a cavity for hosting the alkali metal ions and various regioisomers of stilbenes as molecular bridges controlling the conformations of the calix[4]arene platform which may also be triggered by UV light. The binding properties of these new calix[4]arene derivatives should be interesting especially in terms of their selectivity and switchability.
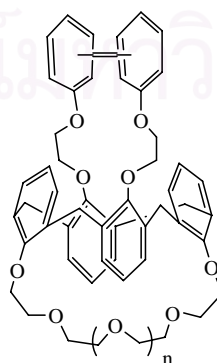
n=1, 2

Figure 1.9 Structures of the targeted stilbene-bridged crown ether calix[4]arenes

The outlines of this research include 1) synthesis of the proposed calix[4]arene crown ethers containing a stilbene bridge, 2) characterization and conformational analysis of the synthesized compounds, 3) study of binding properties toward alkali metal ions in comparison to the well known ionophore, 18-crown-6,[52] 3) study of photoisomerization of the synthesized compounds.

1.4 Study of a complexation process by NMR spectroscopy[53-54]

Dynamic NMR is the NMR spectroscopy of samples that undergo physical or chemical changes with time. The timescales studied can be varied from picoseconds to centuries and the techniques used for their study depend on the timescale. NMR can be used to determine the equilibrium and the rate constants which can be used to calculate the thermodynamic parameters of the system.

Chemical exchange refers to any process in which a nucleus exchanges between two or more environments in which its NMR parameters (e.g. chemical shift, scalar coupling, or relaxation) differ. Dynamic NMR deals with the effects in a broad sense of chemical exchange processes on NMR spectra and conversely with the information about the changes in the environment of magnetic nuclei that can be derived from observation of NMR spectra.

There are two main types of chemical exchange processes *i.e.* intramolecular and intermolecular exchanges. The examples of intramolecular exchange are motions of side chains in proteins, helix-coil transitions of nucleic acids, unfolding of proteins and conformational equilibrium. The process is truly unimolecular involving one reagent and one product that can be expressed as the following chemical equation:

$$A \underset{}{\overset{K_{eq}}{\rightleftharpoons}} B$$
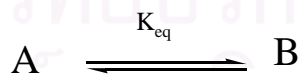
The intermolecular exchange on the other hand involves two reagents *e.g.* binding of small molecules to macromolecules (host-guest complexation), protonation/deprotonation equilibrium, isotope exchange processes and enzyme catalyzed reactions.

$$H+G \rightleftharpoons C$$

The chemical exchange process is usually driven by the intermolecular forces, such as ion-ion, ion-dipole, hydrogen bonding, solvophobic interactions, $\pi-\pi$ stacking, vander waals forces, charge transfer and others. Only the intermolecular exhanges in host-guest systems are discussed here. The equilibrium association constant (K) between host and guest is given by K= [C]/[H][G] with a unit of M^{-1}or L/mol. The Equilibrium Dissociation constant (K_d) corresponding to the reverse process, which is frequently used in biochemistry, is hence given as K_d= [H][G]/[C] with a unit of M or mol/L.

To obtain the K value for particular host-guest association equilibrium, we need to measure the equilibrium concentrations of host, guest and complex. Often, if just one of these concentrations can be measured, the others can be obtained using mass balance equations. Initially, the host and guest were mixed at analytical concentrations of H_0 and G_0, respectively. At equilibrium, the concentrations of free host, free, guest and complex are H, G and C, respectively that give H_0= H + C and G_0= G + C. Therefore, if C can be determined, H and G can immediately be calculated.

In a slow chemical exchange process, the proton resonances of the complex and the free host are simultaneously observed, the integrated proton signals (I_c and I_h) can be used to obtain the respective concentrations (C and G). For instance, $H = H_0 I_h/(I_h+I_c)$ and $C = H_0 I_c/(I_h+I_c)$. From the equilibrium concentrations obtained in this manner, the K value can be calculated directly. The derived equation for calculation of K is shown below.

$$K = (n_c / [H]_0)/ (1-n_c)(R-n_c)$$
$$\text{where } R=[G]_0/[H]_0 \text{ and } n_c = I_c/(I_c+I_h)$$

The determination of K value for a fast chemical exchange process is more complicated because only one set of signals is observed. An observed chemical shift (δ) is a molar average of those for the free host (δ_H) and complex (δ_C); thus, $\delta = X_H \cdot \delta_H + X_C \cdot \delta_C$. For any combination of analytical concentrations H_0 and G_0 the molar fractions of free host (X_H) and complex (X_C) at the equilibrium depend on the K value. The procedure relies on measuring δ as a function of variable H_0 and G_0 values. Practically, one of the initial concentrations is kept constant e.g H_0 is constant while G_0 is varied. To obtain the binding constant (K) data is fitted to a mathematical model

describing the 1:1 binding between host and guest. Many software packages can do this, including Excel and any plotting software packages. In this dissertation EQNMR was used.

The equilibrium constant (K) is related to the equilibrium concentration of the complex (C) as follows.

$$K = \frac{C}{(H_0-C)(G_0-C)}$$

and

$$C = \frac{[KG_0+KH_0+1] \pm \sqrt{(KG_0+KH_0+1)^2 -4K^2H_0G_0}}{2K}$$

The fitting software starts by inputting a guessing K and experimental δ values. It then calculates C from the guessing K. The C values is in turn used for calculation of the molar fractions, $X_C = C/H_0$ and $X_H = 1-X_C$, and δ. The program will give an optimum K by simulating δ_c that give the minimum differences between the experimental and calculated chemical shifts.

CHAPTER II

EXPERIMENTAL

2.1 Synthesis

All reagents were purchased from Sigma-Aldrich, Fluka® (Switzerland) Merck® (Germany), and Acros (Belgium). *p-tert*-Butylcalix[4]arene[56] and picrate salts were prepared according to the literatures.[57] For general reaction, solvents such as methylene chloride and acetonitrile were reagent grade stored over molecular sieves. In anhydrous reactions, solvents such as THF and toluene were dried by standard procedures and distilled before use. All column chromatography were operated using silica gel 60, Merck®. Solvents such as methylene chloride, hexane, ethyl acetate and methanol used for extraction and chromatography were commercial grade and distilled before use. The extraction except diethyl ether and chloroform which was reagent grade. Deionized water was used in all experiments unless specified otherwise. All reactions were carried out under positive pressure of N_2 filled in rubber balloons. The products were characterized by a melting point apparatus (Electrothermal 9100, Fisher Scientific, USA), elemental analyzer (PE 2400 Series II, Perkin-Elmer, USA.), mass spectrometer (Quattro Micro 2000, Micromass, France) Fourier transform infrared spectrometer (FTIR), Impact 410, Nicolet, USA and nuclear magnetic resonance spectrometer (400 MHz, Mercury 400, Varian, USA).. Deuterated chloroform ($CDCl_3$) was used in most NMR spectra unless specified otherwise. The UV-Visible spectra were obtained from UV-Vis spectrophotometer (Cary 100 Bio, Varian, Australia) using spectral grade acetonitrile as a solvent.

2.1.1 Preparation of tert- butyl calix[4]arene[56]

Polymerisation

Cracking

Over all 58 % yield
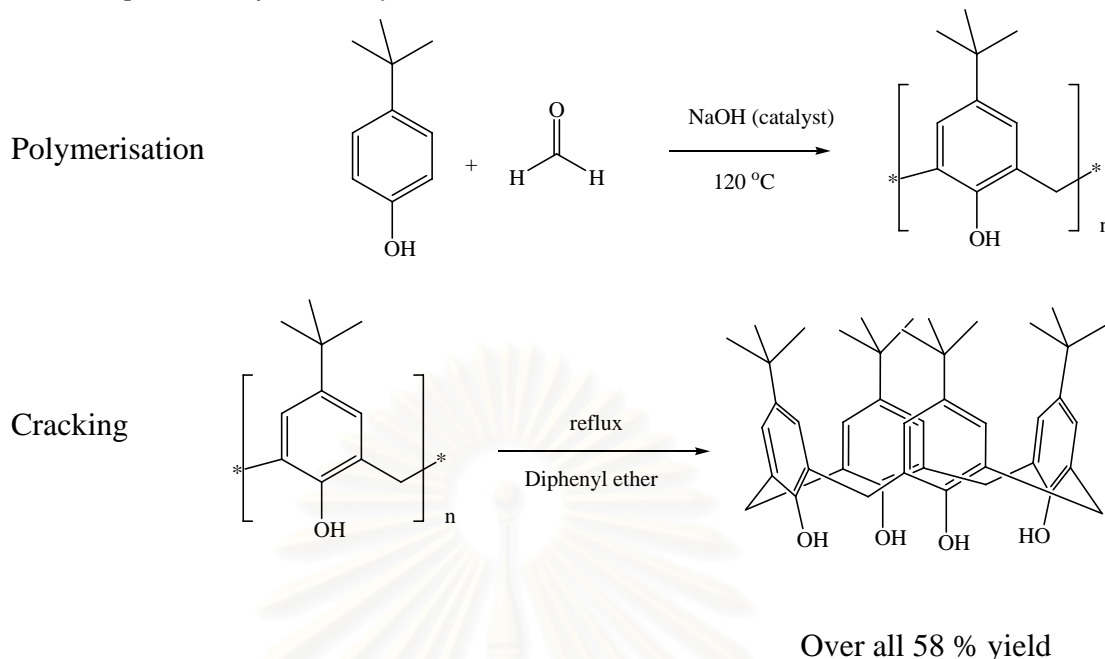
First step: *polymerisation*

In a 1 L round-bottomed flask equipped with a magnetic stirring bar, a mixture of *p-tert*-butylphenol (0.17 mol, 25.00 g), 37% formaldehyde in ethanol (0.20 mol, 15.50 mL) and sodium hydroxide (7.50 mmol, 0.30 g) was stirred and heated at 100-120 °C on a heating mantle. The flask was left open to allow the water by-product to escape from the reaction mixture. The stirring and heating was continued until a colourless liquid turned into a spongy crispy yellow solid as the water evaporated. The reaction was then allowed to cool to room temperature. Over heating resulted in low yield of the desired product in the following step due to the formation of green polymeric materials. The small amount of green polymer by-product, if formed, was disposed and only the yellow part of the precursor was brought to the next step, cracking. The precursor prepared should be used within one or two days to assure the high yield of *p-tert*-butylcalix[4]arene.

Second step: cracking

Two batches of the yellow polymer fromed in the first step were crushed into powder. In a 2 L two-necked round-bottomed flask equipped with a magnetic stirring bar, condenser and a Dean-Stark trap, the precursor from polymerisation process

(25.00 g) was stirred in diphenyl ether (250 mL). The reaction flask and the Dean-Stark side arm were wrapped with a heating jacket and cotton wool in aluminium foil in order to maintain the temperature. The mixture was refluxed on a heating mantle. The "pop" sound was produced indicating the removal of water from the reaction. When the "pop" sound was completely subsided, the reaction was allowed to cool to room temperature (around 2.5 hours). The pale brown product was precipitated out by addition of ethyl acetate (400 mL). The product was filtered and washed with ethyl acetate (400 mL) and 25% acetic acid in ethyl acetate (300 mL) yielding a white solid. The *p-tert*-butylcalix[4]arene was further purified by crystallisation in toluene giving a white crystal as a product in 58% yield.

2.1.2 Preparation of calix[4]arene[58]
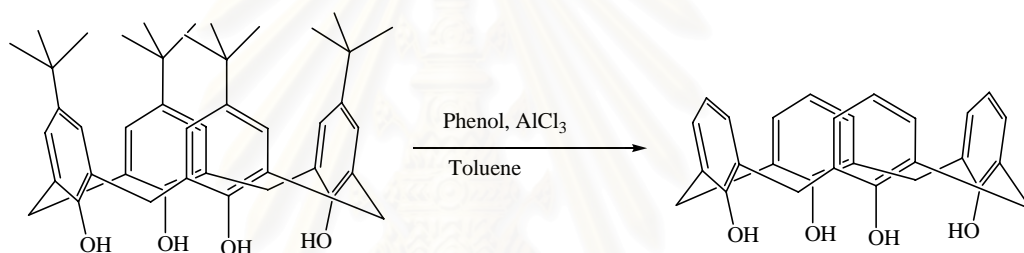
60 % yield

In a 500 mL round-bottomed flask with a magnetic stirring bar, a mixture of *tert*-butyl calix[4]arene (0.04 mol, 26 g), phenol (0.19 mol, 18 g) in anhydrous toluene (200 mL) was cooled to 0 °C in an ice bath. $AlCl_3$ (0.21 mol, 28 g) was slowly added to the reaction mixture. The reaction mixture was allowed to warm to room temperature and stirred for 1 hour. HCl (3 M, 150 mL) was added to the reaction mixture at 0 °C and extracted with water (2x30 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure until the white solid was precipitated and methanol (200 mL) was poured into the residue. The product was precipitated out as a white solid. The precipitate was filtered and washed with cold toluene and methanol. The calix[4]arene was further purified by crystallization in toluene giving a white solid as a product in 60 % yield.

2.1.3 Preparation of (2-Bromoethoxy)benzaldehyde[(59)]

ortho 73%,

meta 65%

para 79%
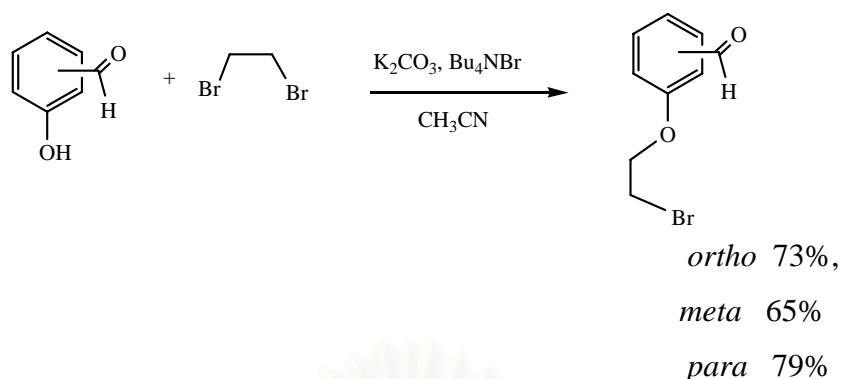
In a 1 L round-bottomed flask equipped with a magnetic bar and a reflux condenser, hydroxybenzaldehyde (0.20 mol, 24.40 g), K_2CO_3 (0.21 mol, 29.00 g) and Bu_4NBr (0.02mol, 6.40 g.) were dissolved in CH_3CN (800 mL). The mixture was stirred for 30 minutes at room temperature and dibromoethane (1.60 mol, 78 mL) was then added all at once to avoid the disubstitution by-product. The mixture was refluxed for 48 hours and allowed to cool to room temperature. The mixture was filtered and washed with CH_2Cl_2. The filtrate was combined and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (150 mL) and then extracted with aqueous NaOH (4 M, 4 x 25 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The product was further purified by a column chromatography using 20% ethyl acetate in hexane as an eluent yielding a white solid as the product and *m*-isomer yielded yellow liquid. (73%, 65%, 79% yield for *ortho*, *meta* and *para* derivatives, respectively).

2-(2-bromoethoxy)benzaldehyde ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.67 (t, 2H, C$\underline{H}_2$Br, *J* = 6.0 Hz), 4.38 (t, 2H, C$\underline{H}_2$OAr, *J* = 6.0 Hz), 6.92 (d, 1H, Ar$\underline{H}$, *J* = 8.5 Hz), 7.03 (t, 1H, Ar$\underline{H}$, *J* = 7.5 Hz), 7.52 (dt, 1H, Ar$\underline{H}$, *J* = 8.5, 2.0 Hz), 7.81 (dt, 1H, Ar$\underline{H}$, *J* = 7.5, 2.0 Hz), 10.50 (s, 1H, ArC$\underline{H}$O,)

3-(2-bromoethoxy)benzaldehyde ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.65 (t, 2H, C$\underline{H}_2$Br, *J* = 6.0 Hz), 4.33 (t, 2H, C$\underline{H}_2$OAr, *J* = 6.0 Hz), 7.13–7.47 (m, 4H, Ar$\underline{H}$), 9.95 (s, 1H, ArC$\underline{H}$O)

4-(2-bromoethoxy)benzaldehyde ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.65 (t, 2H, C$\underline{H}_2$Br, *J* = 6.0 Hz), 4.36 (t, 2H, C$\underline{H}_2$OAr, *J* = 6.0 Hz), 7.00 (d, 2H, ArC$\underline{H}$, *J* = 9.0 Hz), 7.84 (d, 2H, ArC$\underline{H}$, *J* = 9.0 Hz), 9.88 (s, 1H, ArC$\underline{H}$O)

2.1.4 Preparation of bisbenzaldehyde calix[4]arene
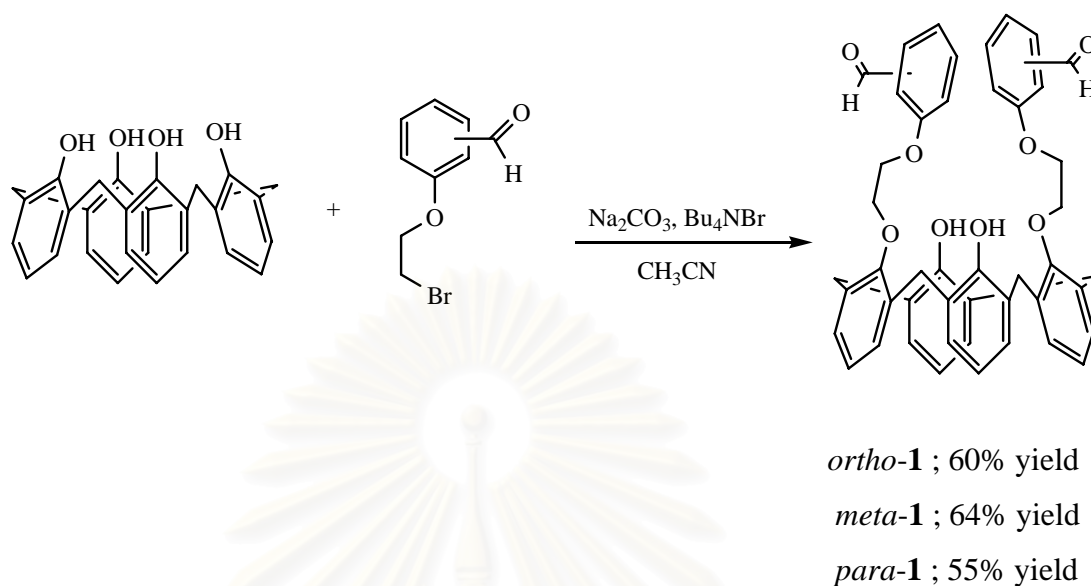
ortho-**1** ; 60% yield

meta-**1** ; 64% yield

para-**1** ; 55% yield

In a two-necked 1 L round-bottomed flask equipped with a magnetic bar and a reflux condenser, calix[4]arene (7.8 mmol, 5.00 g) and Na_2CO_3 or K_2CO_3 (57.9 mmol, 8.00 g) were dissolved in CH_3CN (300 mL). The mixture was stirred for 30 minutes at room temperature and (2-bromoethoxy)-benzaldehyde (17.5 mmol, 4.00 g) was then added dropwise. The mixture was refluxed for 5 days and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH_2Cl_2. The filtrate was combined and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (150 mL) and extracted with aqueous HCl (2 M, 4 x 25 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The product was further purified by crystallization in CH_2Cl_2/hexane yielding a white solid as the product (60%, 64%, 55% for *ortho*, *meta* and *para* derivatives, respectively when Na_2CO_3 was used as a base but the desired product can not isolate when K_2CO_3 was used as a base)

ortho-bisbenzaldehyde calix[4]arene **1**:   ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.38, 4.33 (d, 8H, ArCH$_2$Ar, J = 13 Hz) 4.42, 4.41 (broad, 8H, -OCH$_2$CH$_2$O-), 6.65, 6.76 (t, , 4H, calix –ArH, J = 7.5 Hz), 7.04, 6.76 (d, 4H, calix-ArH, J = 7.5 Hz), 7.02, 7.49 (t, 4H, aldehyde- ArH, J = 7.6 Hz), 7.85, 6.93 (d, 4H, aldehyde- ArH, J = 7.6 Hz), 7.89 (s, 2H, OH), 10.53 (s, 2H, CHO)

meta-bisbenzaldehyde calix[4]arene **1**:   ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.38, 4.42 (d, 8H, ArCH$_2$Ar, J = 13 Hz) 4.31, 4.29 (broad, 8H, -OCH2CH2O-) 6.67, 6.77 (t, 4H, calix-ArH, J = 7.5 Hz), 6.94, 7.06 (d, 4H calix-ArH), 7.42-7.54 (m, 6H, ArH), 7.39 (s, 2H, aldehyde- ArH), 7.95 (s, 2H, OH), 9.94 (s, 2H, CHO)

para-bisbenzaldehyde calix[4]arene **1**:   ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.38, 4.38 (d, 8H, ArCH$_2$Ar, J = 13 Hz) 4.30 (broad, 8H, -OCH2CH2O-) 6.67, 6.78 (t, , 4H, calix-ArH, J = 7.5 Hz), 6.94, 7.06 (d, 4H, calix-ArH, J = 7.5 Hz), 7.00, 7.84 (t, 4H, aldehyde-ArH, J = 8.7 Hz), 7.85 (s, 2H, OH), 9.90 (s, 2H, CHO)

2.1.5 Preparation of the Stilbene-Bridged Calix[4]arene[(52)]
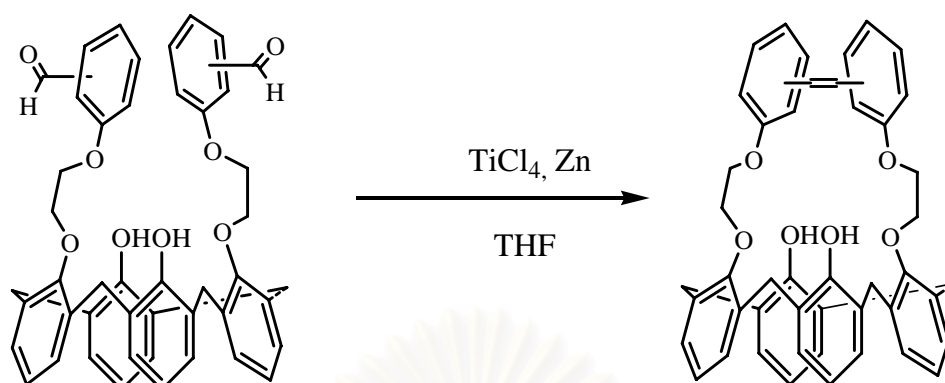
ortho-*cis*-**2** ; 62% *trans* 15%

meta-*cis*-**2** ; 37% *trans* 37%

para-cis-**2** ; 87%

(yield for opimized condition)

TiCl$_4$ (28 mmol, 5.27 g) was feeded under N$_2$ atmosphere in to a dried two-necked 500 mL round-bottomed flask equipped with a magnetic bar, anhydrous THF (200 mL) was added dropwise. After a completion of THF addition, activated Zn powder (56 mmol, 3.88 g) was added cautiously. The starting Ti(IV) was bright yellow which was gradually turned to green and finally to deep purple or black colour of Ti(0) upon refluxing with Zn powder. After 1 hour of reflux, the *bis*benzaldehyde 1 (1.39 mmol, 1.00 g) in THF (100 mL) was added dropwise for 3 hours. The mixture was refluxed for additional 24 hours and it was allowed to cool to room temperature. A solution of K$_2$CO$_3$ (15% w/v) was added to quench the excess TiCl$_4$. The mixture was slowly turned from grey to white or pale yellow. The precipitate was filtered over celite and washed with acetone and CH$_2$Cl$_2$. The acetone washing prior to wash with CH$_2$Cl$_2$ is necessary to avoid the formation of muddy sticky gum. The filtrate was evaporated and the residue was dissolved in CH$_2$Cl$_2$ (150 mL) and then extracted with water (2x25 mL). The organic phase was dried over anhydrous Na$_2$SO$_4$ and the solvent was removed to give the crude product. The reaction produced both *cis*- and *trans*-isomers for *o*- and *m*-isomer which were separated by column chromatography using dichloromethane as eluent (*cis*-isomer has a higher R$_f$ value). For *p*-isomer, only *cis*-isomer was formed and isolated. (62% and 15% *for ortho-cis* and *ortho-trans* derivatives, 37% and 37% for *meta-cis* and *meta-trans* derivatives and 87% for *para-cis* derivatives)

o-cis-stilbene-bridged calix[4]arene **2**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.30, 4.35 (d, 8H, ArCH$_2$Ar, J = 13.3 Hz), 4.20, 4.29 (broad, 8H, -OCH$_2$CH$_2$O), 6.71 (s, 2H, CH=CH), 6.87, 7.22 (d, 4H, stilbene-ArH, J = 7.8 Hz), 6.93, 7.01 (d, 8H, calix-ArH, J = 7.8 Hz), 6.76, 6.60 (t, 4H, calix-ArH, J = 7.8 Hz), 6.83, 7.19 (t, 4H, stilbene-ArH, , J = 7.8 Hz), 8.10 (s, 2H, OH)

o-trans-stilbene-bridged calix[4]arene **2**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.30, 4.35 (d, 8H, ArCH$_2$Ar, J = 13.3 Hz), 4.48, 4.79 (broad, 8H, -OCH$_2$CH$_2$O-), 7.75 (s, 2H, CH=CH), 6.85, 7.50 (d, 4H, stilbene-ArH, J = 7.8 Hz), 7.18 (t, 4H, stilbene-ArH), 6.94-6.96 (m, 10H, calix-ArH), 6.65, 6.79 (t, 4H, calix-ArH, J = 7.8 Hz), 8.44 (s, 2H, OH)

m-cis--stilbene-bridged calix[4]arene **2**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.35, 4.33 (d, 8H, ArCH$_2$Ar, J = 13.3 Hz), 3.96, 4.17 (broad, 8H, -OCH$_2$CH$_2$O-), 6.69 (s, 2H, CH=CH), 6.92, 6.89 (d, 4H, stilbene-ArH, J = 7.8 Hz), 7.27 (t, 2H, stilbene-ArH), 6.75 (s, 2H, stilbene-ArH), 7.00, 7.07 (d, 8H, calix-ArH, J = 7.8 Hz), 6.63, 6.81 (t, 4H, calix-ArH, J = 7.8 Hz), 8.30 (s, 2H, OH)

m-trans--stilbene-bridged calix[4]arene **2**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.40, 4.42 (d, 8H, ArCH$_2$Ar), 4.29, 4.65 (broad, 8H, -OCH$_2$CH$_2$O-),7.78 (s, 2H, CH=CH), 6.92, 7.16 (d, 4H, stilbene-ArH), 7.29 (t, 2H, stilbene-ArH), 7.26 (s, 2H, stilbene-ArH), 6.59, 7.10 (d, 8H, calix-ArH), 6.59, 6.77 (t, 4H, calix-ArH), 5.62 (s, 2H, OH,)

p-cis--stilbene-bridged calix[4]arene **2**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.39, 4.46 (d, 8H, ArCH$_2$CH$_2$Ar, J = 13.3 Hz), 6.65 (s, 2H, OH), 6.67, 6.73 (t, 4H, Ar-calix, J = 7.8 Hz), 6.73, 7.10 (d, 8H, Ar-calix, J = 7.8Hz), 6.76 (s, 2H, CH=CH,), 6.92 (br, 8H, Stilbene-ArH)

2.1.6 Preparation of ditosylate ester of tetraethylene glycol
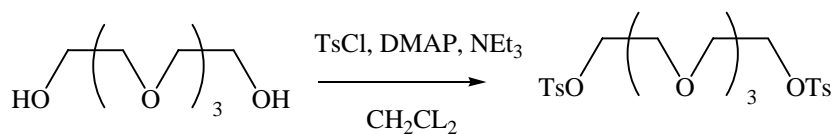
72% yield

In a 250 mL, round bottom flask with a magenetic stirrer, tetraehylene glycol (0.05 mmol, 9 mL), tiethylamine (15 mL) , DMAP (catalytic amount) was dissolved in CH_2Cl_2. Tosylchloride (20 g, 0.10 mol) in CH_2Cl_2 (50 mL) was slowly dropped in the reaction mixture at $0\,^{\circ}C$. Then, The reaction mixture was allowed to warm to room temperature and stirred until the reaction was completed. (Monitoring by TLC). The solvent was evaporated under reduced pressure and extracted with water (2x25 mL). The organic phase was corrected and dried over anhydrous Na_2SO_4 and the solvent was removed to give the crude product. The product was further purified by column chromatography using 10% ethyl acetate in hexane as eluent yielding the colorless liquid as the desired product.(72% yield.)

ditosylate ester of tetraethylene glycol: ^{1}H-NMR (400 MHz, CDCl$_3$): δ 2.42 (s, 2H, ArCH$_3$,), 3.50 (br, 2H, OCH$_2$CH$_2$,), 3.63 (t, 2H OCH$_2$CH$_2$O, J = 4.7 Hz), 4.10 (t, 2H, OCH$_2$CH$_2$O, J = 4.7 Hz), 7.29 (d, 4H, ArH, J = 8.6 Hz), 7.74 (d, 4H, ArH, J = 8.6 Hz)

2.1.7 Preparation of the Stilbene-Bridged Calix[4]arene crown-5[(52)]

ortho-cis-**3**	80 %
ortho-trans-**3**	67%
meta-cis-**3**	84%
para-cis-**3**	80%

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, stilbene calix[4]arene 2 (0.4 mmol, 0.25 g), Cs$_2$CO$_3$ (2.8 mmol, 0.91 g) and Bu$_4$NBr (0.3, 0.09 g) were dissolved in CH$_3$CN (150 mL). The mixture was stirred for 30 minutes at room temperature and tetraethylene glycol di-*p*-toluene sulfonate (0.4 mmol, 0.2 g) in CH$_3$CN 50 mL was then added dropwisely by addition funnel and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH$_2$Cl$_2$. The filtrate was combined and the solvent was evaporated at reduced pressure. The resulting residue was dissolved in CH$_2$Cl$_2$ and then extracted with aqueous HCl (1 M, 2x15mL). The organic phase was separated and dried over anhydrous Na$_2$SO$_4$. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH$_3$OH in CH$_2$Cl$_2$ as eluent yielding the white solid as the desired product. (80%, 67%, 84%, and 80% for *ortho-cis, ortho-trans, meta-cis* and *para-cis* derivatives, respectively.)

ortho-cis stilbene-bridged calix[4]arene crown-5 **3** : ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.06, 3.42 (t, 8H, -OCH$_2$CH$_2$O-crown), 3.11 (t, 4H, ArOCH$_2$CH$_2$O-crown, J = 5.4 Hz), 3.45 (t, 8H, ArOCH$_2$CH$_2$O-crown J = 6.7 Hz) 3.56 (broad, 8H, ArOCH$_2$CH$_2$OAr), 3.87 (m, 8H, ArCH$_2$Ar), 6.86, 6.90 (t, 4H, calix-ArH J = 7.4 Hz), 6.79, 7.18 (d, 4H, stilbene-ArH J = 7.4 Hz), 6.90, 7.16 (t, 4H, stilbene-ArH J = 7.4 Hz), 6.55 (s, 2H, CH=CH), 6.98, 7.10 (d, 8H, calix-ArH J = 7.4 Hz); ^{13}C-NMR (400 MHz, CDCl$_3$) δ 38.1 (ArCH$_2$Ar), 68.3 (OCH$_2$), 68.8 (OCH$_2$), 69.7 (OCH$_2$), 69.8 (OCH$_2$), 70.7 (OCH$_2$), 72.7 (OCH$_2$), 122.8 (calix-ArC), 123.7 (calix-ArC), 129.2 (calix-ArC), 129.7 (calix-ArC), 133.4 (calix-ArC), 133.9 (calix-ArC), 156.1 (calix-ArC), 156.3 (calix-ArC), 129.1 (stilbene-ArC), 127.9 (stilbene-ArC), 117.3 (stilbene-ArC), 117.7 (stilbene-ArC), 121.7 (stilbene-ArC), 122.8(stilbene-ArC), 127.9 (stilbene-ArC), 129.1 (stilbene-ArC), 156.9 (stilbene-ArC), 126.7 (CH=CH) ; mp = 124-126 ^{o}C; FTMS Calcd for C$_{54}$H$_{54}$O$_9$ [ESI, M$^+$ NH$_4$] : 846.4106 Found: 864.4091

ortho-trans stilbene-bridged calix[4]arene crown-5 **3**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.16, 3.53 (t, 8H, OCH$_2$CH$_2$O-crown J = 7.0 Hz), 3.25, 3.65 (t, 8H, ArOCH$_2$CH$_2$O-crown, J = 5.5 Hz), 3.57, 3.64 (br, 8H, ArOCH$_2$CH$_2$OAr), 3.88 (br, 8H, ArCH$_2$Ar),6.91, 7.15 (d, 8H, calix-ArH, J = 7.8 Hz), 6.92 (m, 2H, ArH), 7.19 (t, 2H, ArH, J = 7.8 Hz), 6.84 (d, 2H, ArH, J = 7.8 Hz), 7.54 (d, 2H, ArH, J = 7.8 Hz) 6.65, 7.02 (t, 4H. ArH, J = 7.8Hz) ; ^{13}C-NMR (400 MHz, CDCl$_3$) δ 37.9 (ArCH$_2$Ar), 65.8 (OCH$_2$), 68.1 (OCH$_2$), 68.3 (OCH$_2$), 69.8 (OCH$_2$), 70.5 (OCH$_2$), 72.6 (OCH$_2$), 129.3 (calix-ArC), 129.3 (calix-ArC), 133.9 (calix-ArC), 134.1 (calix-ArC), 134.1 (calix-ArC), 139.3 (calix-ArC), 156.2 (calix-ArC), 158.5 (calix-ArC), 111.1 (stilbene-ArC), 115.3 (stilbene-ArC), 122.6 (stilbene-ArC), 122.7 (stilbene-ArC), 129.1 (stilbene-ArC), 156.1 (stilbene-ArC), 121.4 (CH=CH) FTMS Calcd for C$_{54}$H$_{54}$O$_9$ [ESI, M$^+$ NH$_4$] : 846.4106 Found: 864.4099

meta-cis stilbene-bridged calix[4]arene crown-5 **3** : ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.16, 3.46 (t, 8H, OCH$_2$CH$_2$O-crown, J = 6.6 Hz), 3.27, 3.52 (t, 8H, ArOCH$_2$CH$_2$O-crown, J = 4.7 Hz), 3.60 (br, 8H, ArOCH$_2$CH$_2$OAr), 3.87 (br, 8H, ArCH$_2$Ar), 6.65, 6.91 (t, 4H, calix-ArH, J = 7.5 Hz), 6.83, 6.89 (d, 4H, stilbene-ArH, J = 7.5 Hz), 7.27 (t, 2H, stilbene-ArH, J = 7.5 Hz), 6.63 (s, 2H, stilbene-ArH),6.78 (s, 2H, CH=CH,), 7.05, 7.13 (d, 8H, calix-ArH, J = 7.4 Hz); ^{13}C-NMR (400 MHz, CDCl$_3$) δ 38.1 (ArCH$_2$Ar), 67.0 (OCH2), 68.3 (OCH$_2$), 68.4 (OCH$_2$), 69.7 (OCH2), 70.7 (OCH$_2$),

72.8 (OCH$_2$), 129.5 (calix-ArC), 129.8 (calix-ArC), 130.0 (calix-ArC), 134.1 (calix-ArC), 134.2 (calix-ArC), 138.5 (calix-ArC), 156.1 (calix-ArC), 158.5 (calix-ArC), 109.9 (stilbene-ArC), 111.5 (stilbene-ArC), 116.5 (stilbene-ArC), 122.3 (stilbene-ArC), 111.5 (stilbene-ArC), 156.0 (stilbene-ArC), 122.4 (CH=CH) ; mp = 206-207 ^{o}C ;Anal. Calcd for C$_{54}$H$_{54}$O$_9$: C, 76.62 ;H, 6.38; Found: C, 76.68; H, 6.45

para-cis stilbene-bridged calix[4]arene crown-5 **3** ^{1}H NMR (400 MHz, CDCl$_3$)δ 3.32, 3.39 (t, 8H, OCH$_2$CH$_2$O-crown, J = 5.0 Hz), 3.59 (br, 8H, ArOCH$_2$CH$_2$O-crown), 3.79 (br, 8H, ArOCH$_2$CH$_2$OAr,), 3.92 (s, 8H, ArCH$_2$Ar), 6.52, 6.89 (t, 4H, calix-ArH, J = 7.5 Hz), 6.75, 6.86 (d, 8H, stilbene-ArH, J = 7.5 Hz), 6.78 (s, 2H, CH=CH), 7.08, 7.14 (d, 8H, calix-ArH, J = 7.5 Hz) ; ^{13}C-NMR (400 MHz, CDCl$_3$) δ 37.8 (ArCH2Ar), 68.9 (OCH$_2$), 68.9 (OCH$_2$), 69.4 (OCH$_2$), 70.5(OCH$_2$), 70.6 (OCH$_2$), 71.9 (OCH$_2$), 130.1 (calix-ArC), 130.5 (calix-ArC), 130.6 (calix-ArC), 131.3 (calix-ArC), 133.8 (calix-ArC), 134.0 (calix-ArC), 155.8 (calix-ArC), 156.4 (calix-ArC), 117.4 (stilbene-ArC), 121.8 (stilbene-ArC), 115.5 (stilbene-ArC), 158.0 (stilbene-ArC), 122.7 (CH=CH); mp. = 211 °C ; Anal. Calcd for C$_{54}$H$_{56}$O, C=76.62 % H=6.38 % found C=76.60 % H=6.38%

2.1.8 Preparation of the Stilben-Bridged Calix[4]arene crown-6[(52)]

2

o-cis-**4**   75%

m-cis-**4**   68%

p-cis-**4**   70%

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, stilbene calix[4]arene **2** (0.4 mmol, 0.25 g), Cs_2CO_3 (2.8 mmol, 0.91 g) and Bu_4NBr (0.3, 0.09 g) were dissolved in CH_3CN (150 mL). The mixture was stirred for 30 minutes at room temperature and pentaethylene glycol di-*p*-toluene sulfonate (0.4 mmol, 0.2 g) in CH_3CN 50 mL was then added dropwisely by addition funnel and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH_2Cl_2. The filtrate was combined and the solvent was evaporated at reduced pressure. The resulting residue was dissolved in CH_2Cl_2 and then extracted with aqueous HCl (1 M 2x15mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH_3OH in CH_2Cl_2 as eluent yielding the white solid as the desired product. (75%, 68%, 70% for *ortho*, *meta* and *para*, respectively.)

ortho-cis stilbene-bridged calix[4]arene crown-6 **4**: ^{1}H NMR (400 MHz, $CDCl_3$)δ 3.12 (t, 4H, OCH_2, J = 6.3 Hz) 3.19 (br, 4H, OCH_2), 3.42(br, 4H, OCH_2), 3.46 (br, 4H, OCH_2), 3.55 (t, 4H, OCH_2), 3.61 (br, 8H, OCH_2), 3.75 (br, 8H, $ArCH_2Ar$), 6.41 (s, 2H, CH=CH), 6.89, 7.02 (d, 8H, calix-ArH, J = 7.5 Hz), 6.82, 7.09 (t, 4H, calix-

ArH, J = 7.5 Hz), 6.75 (m, 2H, stilbene-ArH), 6.77 (m, 2H, stilbene-ArH, J = 7.5 Hz), 6.82 (m, 2H, stilbene-ArH), 7.20 (d, 2H, stilbene-ArH) ; ^{13}C-NMR (400 MHz, CDCl$_3$) δ 38.1 (ArCH$_2$Ar), 68.2 (OCH$_2$), 69.0 (OCH$_2$), 69.5 (OCH$_2$), 70.3 (OCH$_2$), 70.7 (OCH$_2$), 70.8 (OCH$_2$), 71.1 (OCH$_2$), 121.9 (ArC), 122.6 (ArC), 123.7 (ArC), 126.5 (ArC), 126.9 (ArC), 129.3 (ArC), 129.6 (ArC), 129.8 (ArC), 130.2 (ArC), 133.3 (ArC), 133.8 (ArC), 134.0 (ArC), 134.3 (ArC), 156.2 (ArC), 156.3 (ArC), 156.9 (ArC); mp = 116-118 ^{o}C ; Anal. Calcd for C$_{56}$H$_{58}$O$_{10}$ C=75.53 %, H = 6.51 % found C = 75.54 % H = 6.56 %

meta-cis stilbene-bridged calix[4]arene crown-6 **4**: ^{1}H NMR (400 MHz, CDCl$_3$)δ 3.35 (br, OCH$_2$, 8H), 3.46 (br, OCH$_2$, 4H), 3.53 (br, OCH$_2$, 4H), 3.61 (t, OCH$_2$, 4H, J = 6.1 Hz), 3.64-3.71 (m, OCH$_2$, 12H), 3.85 (s, ArCH$_2$Ar, 8) 6.63, 7.27 (t, calix-ArH, 4H), 7.07, 7.12 (d, calix-ArH, 8H), 6.82, 6.91 (d, stilben-ArH, 4H, J = 7.4 Hz), 6.90 (t, stilben-ArH, 2H, J = 7.4 Hz), 6.64 (s, stilben-ArH, 2H), 6.78 (s, CH=CH, 2H) ; ^{13}C-NMR (400 MHz, CDCl$_3$) δ 38.0(ArCH$_2$Ar), 61.7 (OCH$_2$), 66.9 (OCH$_2$), 68.3 (OCH2), 68.9 (OCH$_2$), 69.4 (OCH$_2$), 72.7 (OCH$_2$), 112.9 (calix-ArC), 130.1 (calix-ArC), 130.3 (calix-ArC), 134.0 (calix-ArC), 134.3 (calix-ArC), 138.5 (calix-ArC), 156.3 (calix-ArC), 158.4 (calix-ArC), 111.3 (stilbene-ArC), 116.4 (stilbene-ArC), 112.4 (stilbene-ArC), 122.6 (stilbene-ArC), 122.6 (stilbene-ArC), 156.0 (stilbene-ArC), 122.2 (CH=CH) FTMS Calcd for C$_{56}$H$_{58}$O$_{10}$ [ESI, M$^+$ NH$_4$] : 908.4368 Found: 908.4352

para-cis stilbene-bridged calix[4]arene crown-6 **4**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.54 (br, OCH$_2$, 4H), 3.81 (br, OCH$_2$, 4H), 3.87 (br, OCH$_2$,4H), 3.91 (br, OCH$_2$,8H), 3.97 (t, OCH$_2$,4H), 4.46 (br, OCH$_2$,4H), 3.87 (s, ArCH2Ar, 8H), 6.19, 6.78 (t, calix-ArH, 4H, J = 7.5 Hz), 7.02, 7.19 (d, calix-ArH, 8H, J = 7.5 Hz), 7.07, 7.14 (d, stilbene-ArH, 8H, J = 7.5 Hz), 6.70 (s, CH=CH, 2H) ^{13}C-NMR (400 MHz, CDCl$_3$) δ 38.2 (ArCH$_2$Ar), 65.1 (OCH$_2$), 68.4 (OCH$_2$), 68.8 (OCH$_2$), 69.7 (OCH$_2$), 69.8 (OCH$_2$), 70.8 (OCH$_2$), 72.8 (OCH$_2$), 117.3 (ArC), 121.7 (ArC), 122.8 (ArC), 126.8 (ArC), 127.9 (ArC), 129.1 (ArC), 129.3 (ArC), 129.7 (ArC), 133.9 (ArC), 152.2 (ArC), 156.0 (ArC), 158.4 (ArC)(ArC); mp. = 256-257 °C; FTMS Calcd for C$_{56}$H$_{58}$O$_{10}$ [ESI, M$^+$ NH$_4$] : 908.4368 Found: 908.4375

2.1.9 Preparation of tosylate ester of diethyleneglycol monoethylether

77%
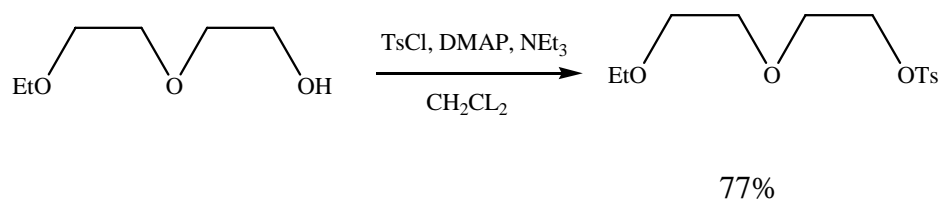
In a 250 mL, round bottom flask with a magenetic stirrer, diethylene glycol monoethylether (0.07 mol,10 g) tiethylamine (10 mL), DMAP (catalytic amount) was dissolved in CH_2Cl_2 (50 mL). Tosylchloride (0.07 mol, 14.3 g) in CH_2Cl_2 (50 mL) was slowly dropped in the reaction mixture at 0 °C. Then, The reaction mixture was allowed to warm to room temperature and stirred until the reaction was completed. (Monitoring by TLC). The solvent was evaporated under reduced pressure and extracted with water (2X30mL). The organic phase was corrected and dried over anhydrous Na_2SO_4 and the solvent was removed to give the crude product. The product was further purified by column chromatography using 10% ethyl acetate in hexane as eluent yielding the white solid as the desired product.(77% yield.)

tosylate ester of diethyleneglycol monoethylether: ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.23 (t, 3H, CH$_3$), 2.49 (s, 2H, ArC$\underline{H}_3$), 3.53 (m, 2H, OC$\underline{H}_2$CH$_3$,), 3.62, 3.57 (br, 4H, OCH$_2$CH$_2$O), 3.74, 4.21 (t, 4H, OC$\underline{H}_2$C$\underline{H}_2$O, J = 4.9 Hz), 7.34 (d, 4H, Ar$\underline{H}$, J = 8.3 Hz), 7.80 (d, 4H, Ar$\underline{H}$, J = 8.3 Hz)

2.1.10   Preparation of the m-cis-stilbene-bridged calix[4]arene diethylene glycol ethyl ether[(52)]
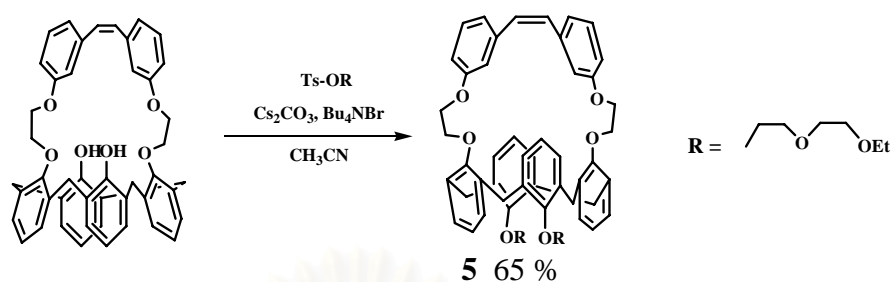
5 65 %

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, *m-cis*-2 (0.4 mmol, 0.25 g), Cs$_2$CO$_3$ (2.8 mmol, 0.91 g) and Bu$_4$NBr (0.3 mmol, 0.09 g) were dissolved in CH$_3$CN (100 mL). The mixture was stirred for 30 minutes at room temperature and diethyleneglycol monoethylether mono-*p*-toluenesulfonate (1.2 mmol, 0.6 g) was added and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH$_2$Cl$_2$. The filtrate was combined and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in CH$_2$Cl$_2$ and then extracted with aqueous HCl (1 M). The organic phase was separated and dried over anhydrous Na$_2$SO$_4$. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH$_3$OH in CH$_2$Cl$_2$ as eluent yielding the white solid as the desired product. (65% yield)

m-cis-stilbene calix[4]arene diethylene glycol ethyl ether **5**: ^{1}H-NMR (400 MHz, CDCl$_3$) δ 1.25 (t, 6H, CH$_2$CH$_3$), 3.85 (s, 8H, ArCH2Ar), 3.24 (t, 4H, OCH$_2$, J = 6.2 Hz), 3.34 (br, 8H, OCH$_2$), 3.52-3.60 (m, 12H, OCH$_2$), 3.68 (t, 4H, OCH$_2$), 6.60 (t, 2H, calix-ArH, J = 7.8 Hz), 7.28 (t, 2H, calix-ArH, J = 7.8 Hz), 7.12 (d, 4H, calix-ArH, J = 7.8 Hz), 7.05 (d, 4H, calix-ArH, J = 7.8 Hz), 6.63 (s, 2H, stilbene-ArH), 6.83 (br, 2H, stilbene-ArH),6.83 (br, 2H, stilbene-ArH), 6.92 (d, 2H, stilbene-ArH, J = 7.0 Hz), 6.83 (s, 2H, CH=CH) ; ^{13}C-NMR (400 MHz, CDCl$_3$) δ 38.0 (ArCH2Ar), 21.5 (CH3), 66.1 (OCH2), 68.3 (OCH2), 68.5 (OCH2), 69.9 (OCH2), 70.7 (OCH2), 72.7, 129.2 (calix-ArC), 129.5 (calix-ArC), 129.5 (calix-ArC), 134.1 (calix-ArC), 134.2 (calix-ArC), 139.5 (calix-ArC), 156.3 (calix-ArC), 158.65 (calix-ArC), 111.2 (stilbene-ArC), 111.5 (stilbene-ArC), 115.5 (stilbene-ArC), 121.6 (stilbene-ArC), 122.9 (stilbene-ArC), 156.2(stilbene-ArC), 122.7(CH=CH) FTMS Calcd for C$_{58}$H$_{64}$O$_{10}$ [ESI, M$^+$ NH$_4$] : 938.4838 Found: 938.4838

2.1.11 Preparation of monotosylate ester of tiethyleneglycol monomethylether
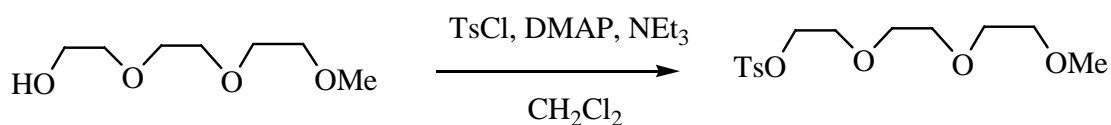

89% yield

In a 250 mL, round bottom flask with a magenetic stirrer, triethylene glycol monomethyl ether (61 mmol, 10.0 g), tiethylamine (17 mL), DMAP (catalytic amount) was dissolved in CH_2Cl_2 (50 mL). Tosylchloride (60 mmol, 11.5 g) in CH_2Cl_2 (100 mL) was slowly dropped in the reaction mixture at 0 ^{o}C. Then, The reaction mixture was allowed to warm to room temperature and stirred until the reaction was completed. (Monitoring by TLC). The solvent was evaporated under reduced pressure and extracted with water. The organic phase was corrected and dried over anhydrous Na_2SO_4 and the solvent was removed to give the crude product. The product was further purified by column chromatography using 10% ethyl acetate in hexane as eluent yielding the pale yellow liquid as the desired product.(89 % yield.)

monotosylate ester of tiethyleneglycol monomethylether: ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.44 (s, 3H, ArCH$_3$), 3.53 (t, 2H, OCH$_2$, J = 4.9 Hz), 3.59-3.60 (m, 8H, OCH$_2$), 3.68 (t, 2H, OCH$_2$, J = 4.9 Hz), 4.17 (t, 2H, OCH$_2$), 3.36 (s, 3H, OCH$_3$), 7.33 (d, 2H, ArH, J = 8.3 Hz), 7.79 (d, 2H, ArH, J = 8.3 Hz)

2.1.12 Preparation of m-cis stilbene-bridged calix[4]arene triethylene glycol monomethylether
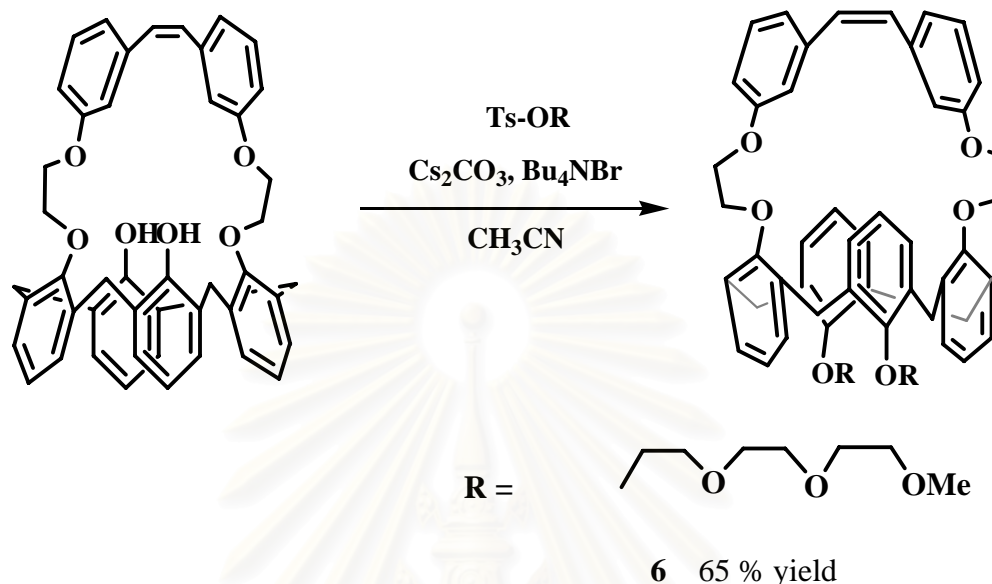
6 65 % yield

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, *m-cis stilbene calix[4]arene* (0.1 mmol, 0.10 g), Cs_2CO_3 (1.1 mmol, 0.33 g) and Bu_4NBr (0.1 mmol, 0.03 g) were dissolved in CH_3CN (50 mL). The mixture was stirred for 30 minutes at room temperature and monotosylate ester of tiethyleneglycol monomethylether (0.4 mmol, 0.12 g) was added and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH_2Cl_2. The filtrate was combined and the solvent was evaporated at reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (50 mL) and then extracted with aqueous HCl (1 M 2x15mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH_3OH in CH_2Cl_2 as eluent yielding the white solid as the desired product (65% yield).

m-cis stilbene-bridged calix[4]arene triethylene glycol monomethylether **6**: ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.22 (t, 4H, OCH$_2$, J = 6.2 Hz), 3.37 (br, 8H, OCH$_2$CH$_2$O), 3.39 (s, 3H, OCH$_3$), 3.57 (m, 8H, OCH$_2$), 3.67 (m, 12H, OCH$_2$), 3.85 (s, 8H, ArCH$_2$Ar), 6.59 (t, 2H, calix-ArH, J = 7.5 Hz), 6.62 (t, 2H stilbene-ArH, J = 7.5 Hz), 6.81 (br, 2H, calix-ArH), 6.83 (br, 2H, CH=CH), 6.90 (d, 2H, stilbene-ArH, J = 7.5 Hz), 7.05 (d, 4H, calix-ArH), 7.11 (d, 4H, calix-ArH, J = 7.5 Hz), 7.28 (t, 2H, stilbene-ArH, J = 7.5 Hz) ;^{13}C-NMR (400 MHz, CDCl$_3$) 37.8 (ArCH$_2$Ar), 58.9 (OCH$_3$), 66.8 (OCH$_2$), 68.2 (OCH$_2$), 68.9 (OCH$_2$), 69.2 (OCH$_2$), 70.4 (OCH$_2$), 70.6 (OCH$_2$), 71.8 (OCH$_2$), 76.7 (OCH$_2$), 77.0 (OCH$_2$), 77.3 (OCH$_2$), 111.1 (ArC), 116.3 (ArC), 122.1 (ArC), 122.3 (ArC), 122.6 (ArC), 129.4 (ArC), 129.7 (ArC), 130.0 (ArC), 130.1 (ArC), 130.2 (ArC), 134.1 (ArC), 138.4 (ArC), 155.7 (ArC), 156.2 (ArC), 158.3 (ArC)

2.1.13 Preparation of the m-trans- stilbene-bridged calix[4]arene diethylene glycol ethyl ether[(52)]

7 20 %

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, *m-trans*-2 (0.4 mmol, 0.25 g), Cs$_2$CO$_3$ (2.8 mmol, 0.91 g) and Bu$_4$NBr (0.3, 0.09 g) were dissolved in CH$_3$CN (100 mL). The mixture was stirred for 30 minutes at room temperature and diethyleneglycol monoethylether mono-*p*-toluenesulfonate (1.2 mmol, 0.6 g) was added and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH$_2$Cl$_2$. The filtrate was combined and the solvent was evaporated at reduced pressure. The resulting residue was dissolved in CH$_2$Cl$_2$ and then extracted with aqueous HCl (1 M). The organic phase was separated and dried over anhydrous Na$_2$SO$_4$. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH$_3$OH in CH$_2$Cl$_2$ as eluent yielding the white solid as the desired product. (20% yield)

m-trans-stilbene-bridged calix[4]arene diethylene glycol ethyl ether **7**: ^{1}H-NMR (400 MHz, CDCl$_3$) δ 1.250 (t, 6H, CH$_2$<u>CH$_3$</u>), 3.47, 3.62 (d, 8H, ArCH$_2$Ar, J = 13 Hz), 3.79 (br, 4H, OCH$_2$), 3.96 (br, 4H, OCH$_2$), 3.86 (br, 4H, OCH$_2$), 3.71 (br, 4H, OCH$_2$), 4.52 (br, 4H, OCH$_2$), 4.01 (br, 4H, OCH$_2$), 3.58 (q, 4H, <u>CH$_2$</u>CH$_3$, J = 7.0 Hz), 6.47 (t, 2H, calix-ArH, J = 7.8 Hz), 6.67 (t, 2H, calix-ArH, J = 7.8 Hz), 6.99 (d, 4H, calix-ArH, J = 7.8 Hz), 7.19 (d, 4H, calix-ArH, J = 7.8 Hz), 7.03 (br, 2H, stilbene-ArH), 7.18 (s, 2H, stilbene-ArH),7.34 (br, 2H, stilbene-ArH), 7.35 (t, 2H, stilbene-ArH, J = 7.0 Hz), 7.59 (s, 2H, CH=CH); ^{13}C-NMR (400 MHz, CDCl$_3$) δ 37.9 (ArCH2Ar), 15.1 (CH3), 66.7 (OCH2), 66.9 (OCH2), 68.3 (OCH2), 68.8 (OCH2), 69.2 (OCH2), 69.8 (OCH2), 70.6 (OCH2), 130.0(calix-ArC), 130.1 (calix-ArC), 130.2 (calix-ArC), 134.1 (calix-ArC), 134.1 (calix-ArC), 138.4 (calix-ArC), 156.4 (calix-ArC), 158.4 (calix-ArC), 111.1 (stilbene-ArC), 116.4 (stilbene-ArC), 122.4 (stilbene-ArC), 122.5 (stilbene-ArC), 129.9 (stilbene-ArC), 155.7(stilbene-ArC), 122.1 (CH=CH); mp = 120-122 ^{o}C; Anal. Calcd C58H64O10 C= 75.63 % H = 7.00 % found 75.68 % H= 6.86 %

2.1.14 Preparation of m-trans stilbene-bridged calix[4]arene triethylene glycol monomethylether

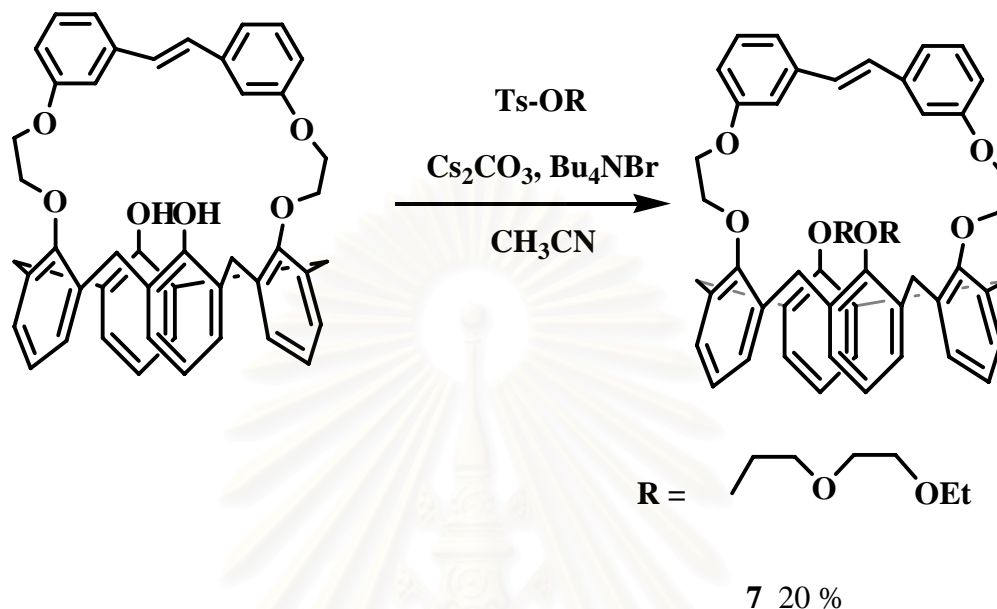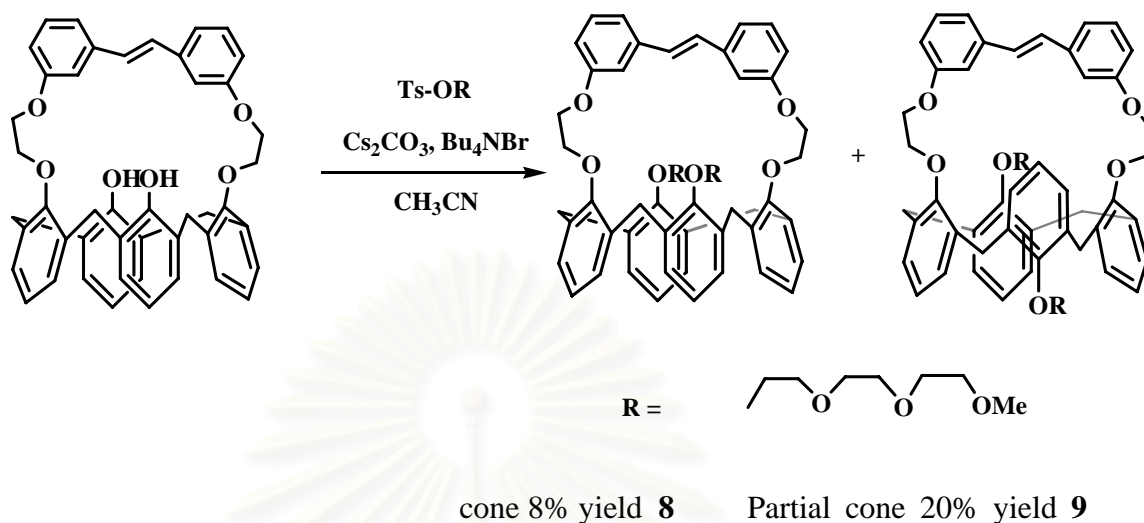cone 8% yield **8**   Partial cone 20% yield **9**

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, *m-trans* stilbene calix[4]arene (0.1 mmol, 0.10 g), Cs_2CO_3 (1.2 mmol, 0.40 g) and Bu_4NBr (0.1, 0.05 g) were dissolved in CH_3CN (50 mL). The mixture was stirred for 30 minutes at room temperature and monotosylate ester of tiethyleneglycol monomethylether (0.4 mmol, 0.15 g) was added and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH_2Cl_2. The filtrate was combined and the solvent was evaporated at reduced pressure. The resulting residue was dissolved in CH_2Cl_2 and then extracted with aqueous HCl (1 M 2x15mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH_3OH in CH_2Cl_2 as eluent yielding the white solid as the desired product (20% and 8% for partial cone and cone, respectively).

Cone m-trans stilbene-bridged calix[4]arene triethylene glycol monomethylether **8**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 3.61 (d, $ArCH_2Ar$, J = 13 Hz), 3.47 (d, $ArCH_2Ar$, J = 13 Hz), 3.38 (br, 4H, OCH_2), 3.57 (br, 4H, OCH_2), 3.69 (br, 4H, OCH_2), 3.78 (br, 4H, OCH_2), 3.86 (br, 4H, OCH_2), 3.95 (br, 4H, OCH_2), 4.00 (br, 4H, OCH_2), 4.52 (br, 4H, OCH_2), 6.47, 6.66 (t, 4H, calix-ArH, J = 7.5 Hz), 6.99 (d, 4H, calix-ArH, J = 7.5 Hz), 7.02 (br, 2H, stilbene-ArH, J = 7.5 Hz), 7.18 (d, 4H,

calix-ArH, J = 7.5 Hz), 7.22 (s, sH, stilbene-ArH), 7.34 (br, 4H, stilbene-ArH), 7.59 (s, 2H, CH=CH)

Partial cone m-trans stilbene-bridged calix[4]arene triethylene glycol monomethylether **9**: ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.13 (d, 2H, ArCH$_2$Ar J = 13.4 Hz), 4.19 (d, 2H, ArCH$_2$Ar J = 13.4 Hz), 3.70, 3.77 (d, 4H, ArCH$_2$Ar, J = 13 Hz), 3.37 (s, 3H, OCH$_3$), 2.94 (br, 2H, OCH$_2$), 3.09 (br, 2H, OCH$_2$CH$_2$O), 3.24 (br, 5H, OCH$_3$), 3.32 (br, 2H, OCH$_2$), 3.56 (br, 2H, OCH$_2$), 3.68 (br, 4H, OCH$_2$), 3.78 (m, 4H, OCH$_2$), 3.94 (br, 2H, OCH$_2$), 4.04 (br, 4H, OCH$_2$), 4.11 (br, 2H, OCH$_2$), 4.57 (br, 2H, OCH$_2$), 6.27 (d, 2H stilbene-ArH, J = 7.5 Hz), 6.49 (t, 2H stilbene-ArH, J = 7.5 Hz), 7.12 (d, 2H stilbene-ArH, J = 7.5 Hz), 7.20 (s, 2H stilbene-ArH), 7.60 (s, 2H, CH=CH)d), 6.79 (t, 1H, calix-ArH, J = 7.5 Hz), 6.87 (t, 1H, calix-ArH, J = 7.5 Hz), 6.99 (d, 2H stilbene-ArH, J = 7.5 Hz), 7.04 (d, 2H stilbene-ArH, J = 7.5 Hz), 7.12 (d, 2H stilbene-ArH, J = 7.5 Hz), 7.26-7.32 (m, 6H, ArH); ^{13}C NMR 31.3 (ArCH$_2$Ar), 35.2 (ArCH$_2$Ar) 58.9 (OCH$_3$) 59.0 (OCH$_2$), 68.6 (OCH$_2$), 68.9 (OCH$_2$), 69.6 (OCH$_2$), 69.9 (OCH$_2$), 70.0 (OCH$_2$), 70.6 (OCH$_2$), 70.6 (OCH$_2$), 70.7 (OCH$_2$), 71.6 (OCH$_2$), 71.8 (OCH$_2$), 71.9 (OCH$_2$), 74.0 (OCH$_2$), 74.6 (OCH$_2$) 117.9 (calix-ArC), 119.1 (calix-ArC), 120.6 (calix-ArC), 121.9 (calix-ArC), 122.0 (CH=CH), 122.5 (stilbene-ArC), 128.5(stilbene-ArC), 128.8 (stilbene-ArC), 129.2 (stilbene-ArC), 129.6 (stilbene-ArC), 129.6 (calix-ArC), 130.7 (calix-ArC), 131.8 (calix-ArC), 133.2 (calix-ArC), 134.1 (calix-ArC), 137.4 (calix-ArC), 139.0 (calix-ArC), 160.7 (calix-ArC), 156.9 (calix-ArC), 155.7 (calix-ArC), 154.2 (stilbene-ArC)

2.1.15 Preparation of O,O′-dimethylcalix[4]arene [(60)]
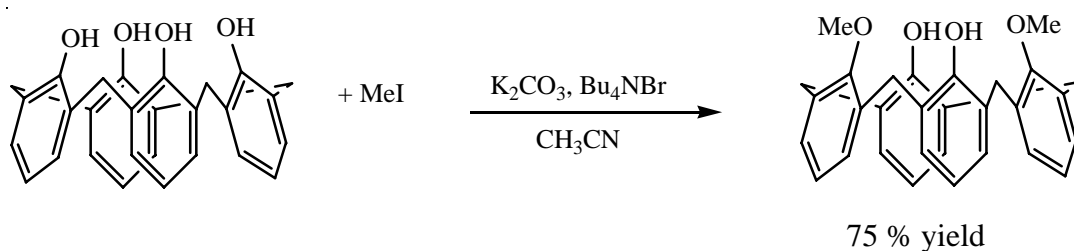
75 % yield

In a two-necked 1 L round-bottomed flask equipped with a magnetic bar and a reflux condenser, calix[4]arene (7.8 mmol, 5.00 g) and K_2CO_3 (18.9 mmol, 2.5 g) were dissolved in CH_3CN (300 mL). The mixture was stirred for 30 minutes at room temperature and iodomethane (17.5 mmol, 4.00 g) was then added dropwise. The mixture was refluxed for 3 days and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH_2Cl_2. The filtrate was combined and the solvent was evaporated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (150 mL) and extracted with aqueous HCl (2 M, 4 x 25 mL). The organic phase was separated and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The product was further purified by crystallization in CH_2Cl_2/hexane yielding a white solid as the product (75% yield).

dimethyl calix[4]arene ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.41 (d, 4H, ArCH$_2$Ar, J = 13 Hz), 4.30 (d, 4H, ArCH$_2$Ar, J = 13 Hz), 3.98 (s, 6H, OMe), 6.68 (t, 2H, calix-ArH, J = 7.4 Hz), 6.72 (t, 2H, calix-ArH, J = 7.4 Hz), 6.87 (d, 4H, calix-ArH, J = 7.4 Hz), 7.07 (d, 4H, calix-ArH, J = 7.4 Hz), 7.76 (s, 2H, OH)

2.1.16 Preparation of O,O′-dimethylcalix[4]arene crown-5 and crown-6[60]
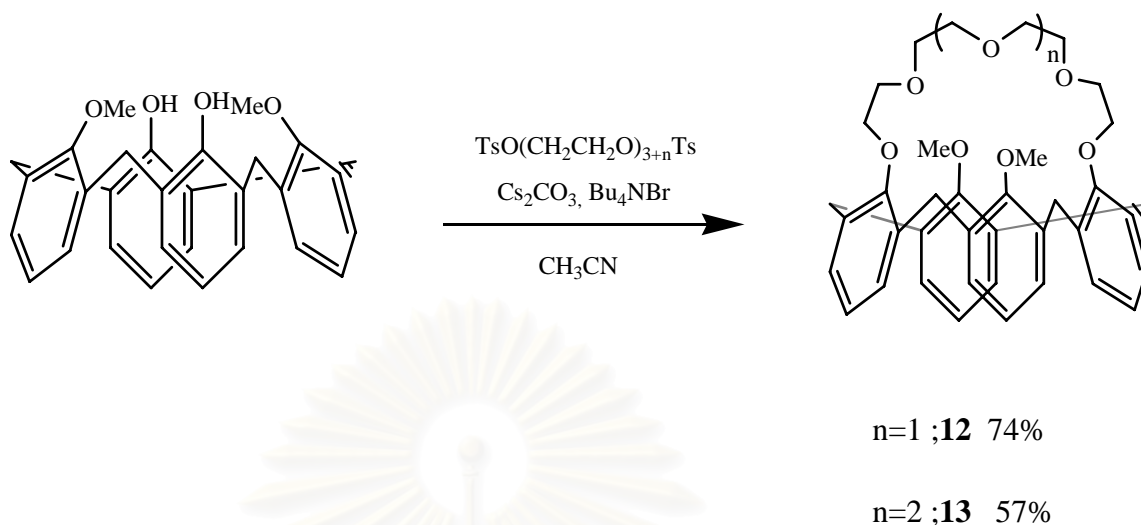
TsO(CH$_2$CH$_2$O)$_{3+n}$Ts
Cs$_2$CO$_3$, Bu$_4$NBr

CH$_3$CN

n=1 ;**12** 74%

n=2 ;**13** 57%

In a 250 mL, 2 necked round bottom flask equipped with a magnetic stirring bar and a reflux condenser, calix dimethoxy (0.4 mmol, 0.25 g), Cs$_2$CO$_3$ (2.8 mmol, 0.91 g) and Bu$_4$NBr (0.3, 0.09 g) were dissolved in CH$_3$CN (150 mL). The mixture was stirred for 30 minutes at room temperature and tetraethylene glycol di-p-toluene sulfonate or pentaethylene glycol di-p-toluene sulfonate (0.4 mmol, 0.2 g) in CH$_3$CN 50 mL was then added dropwisely by addition funnel and reflux for 24 hr. and then allowed to cool to room temperature. The mixture was filtered and washed with acetone and CH$_2$Cl$_2$. The filtrate was combined and the solvent was evaporated at reduced pressure. The resulting residue was dissolved in CH$_2$Cl$_2$ and then extracted with aqueous HCl (1 M). The organic phase was separated and dried over anhydrous Na$_2$SO$_4$. The solvent was evaporated under reduced pressure. The product was further purified by column chromatography using 2 % CH$_3$OH in CH$_2$Cl$_2$ as eluent yielding the white solid as the desired product (74 % and 57% for **10** and **11**, respectively).

O,O'-dimethylcalix[4]arene crown-5 **12** ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.19, 4.42 (d,, 8H ArCH$_2$Ar, J = 13 Hz), 3.57, 3.75 (br, 8H, OCH$_2$CH$_2$O), 3.92 (br, 4H, calixOCH$_2$), 3.99 (br, 4H, calixOCH$_2$CH$_2$), 4.13 (s, 6H, OCH$_3$) 6.42 (t, 2H, Calix-ArH), 6.53 (d, 4H, Calix-ArH, J = 7.1 Hz), 6.89 (t, Calix-ArH, 2H, J = 7.1 Hz), 7.12 (d, Calix-ArH, 4H, J = 7.1 Hz); ^{13}C NMR(400 MHz, CDCl3), 31.2 (ArCH$_2$Ar), 70.8, 71.0 (OCH$_2$CH$_2$O), 73.0 (calixOCH$_2$), 71.5(calixOCH$_2$CH$_2$), 61.2 (OCH$_3$) 122.4 (Calix-ArC), 122.5 (Calix-ArC), 127.6 (Calix-ArC), 128.3 (Calix-ArC), 133.5 (Arcalix), 136.6 (Arcalix), 155.3 (Arcalix), 159.2(Arcalix); mp = 195-197 $^{\circ}$C Anal. Calcd C$_{38}$H$_{54}$O$_7$ C = 74.43 % H = 6.93, found C = 70.94 % H= 6.82 %

O,O'-dimethylcalix[4]arene crown-6 **13** ^{1}H-NMR (400 MHz, CDCl$_3$) δ 3.19 (d, ArCH$_2$Ar, 4H, J = 13 Hz), 3.60 (br, OCH$_2$, 4H), 3.70 (m, OCH2, 4H), 3.80 (m, OCH$_2$, 4H), 3.92 (br, OCH$_2$, 8H), 4.07 (br, OCH$_2$, 6H), 4.46 (d, ArCH$_2$Ar, 4H, J = 13 Hz), 6.36 (m, 6H, ArH), 6.93 (t, 2H, ArH, J = 7.4 Hz), 7.15 (d, 4H, ArH, J = 7.4 Hz) ;^{13}C NMR (400 MHz, CDCl$_3$) 31.2 (ArCH$_2$Ar), 70.7,71.5, 71.4 (OCH$_2$CH$_2$O), 73.0 (calixOCH$_2$), 70.81(calixOCH$_2$CH$_2$), 61.2, (OCH$_3$) 122.4 (Calix-ArC), 122.5 (Calix-ArC), 127.7(Calix-ArC), 128.3 (Calix-ArC), 133.7 (Arcalix), 136.7 (Arcalix), 155.3 (Arcalix), 159.2(Arcalix); mp = 180-181 $^{\circ}$C; Anal. Calcd C$_{40}$H$_{46}$O$_8$ C= 73.50 % H= 7.20 %found 73.68 % H = 7.03 %

2.1.17 Preparation of metal picrate salts[57]
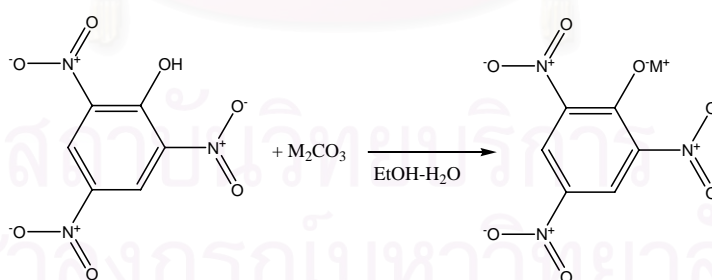
In a 50 mL Erlenmayer flask, picric acid (8.73 mmol, 2.0 g) was dissolved in ethanol (20 mL). The solution was stirred at room temperature. The metal carbonate (4.36 mmol) was dissolved in small amount of ethanol (if the metal carbonate cannot completely dissolve in ethanol, tiny amount of water was added as a co-solvent). Then the metal carbonate solution was added drop wise into the stirring picric acid solution. The mixture was heated to slowly evaporate the ethanol. As a result, the picrate salt was obtained as yellow crystal in quantitative yield.

2.2. Liquid-Liquid extraction

2.2.1 Liquid-Liquid Extraction of metal picrate by UV-Vis Spectroscopy[52]
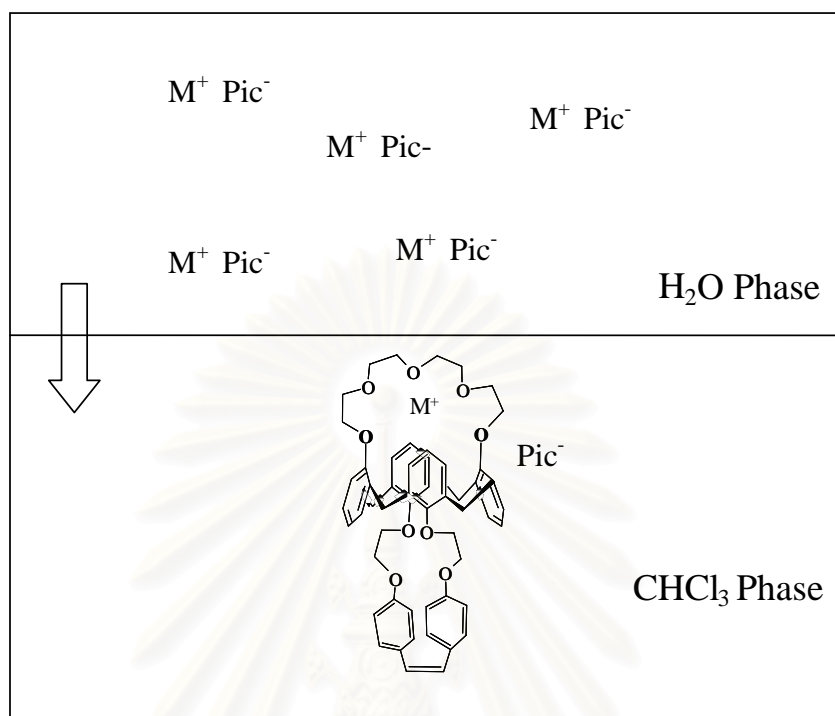
The alkali metal ion extraction at the aqueous|CHCl$_3$ interface by stilbene-bridged calix[4]arene crowns **3** and **4** were investigated in comparison with compounds **5**, **6**, **7**, **8**, **10**, **11**, **13**, **15** and 18-crown-6. The extraction was carried out by thorough mixing a chloroform solution (5 mM, 1 mL) of the ligand with an aqueous solution of the metal picrate (5 mM, 1 mL) for 24 hours. After centrifugation, the aqueous phase (35 μL) was pipetted out and diluted to 5 mL. The concentration of the remaining metal ion in the aqueous phase was determined from the UV absorbance of picrate ion at 354 nm in the diluted solution. The %extraction was calculated from ([A$_0$-A]/[A$_0$])×100 whereas A$_0$ and A were the absorbance of the aqueous metal picrate solutions before and after extraction, respectively.

2.2.2 Experimental procedure for Liquid-Liquid Extraction by Atomic Absorption

The alkali metal ion extraction at the aqueous|CHCl$_3$ interface by stilbene-bridged calix[4]arene crowns-5 and crown-6 were investigated in comparison with compounds calix crown-5 and calix crown-6 and 18-crown-6. The extraction was carried out by thorough mixing a chloroform solution (5 mM, 1 mL) of the ligand with an aqueous solution of the potassium or cesium nitrate (5 mM, 1 mL) for 24 hours. After centrifugation, the aqueous phase (30 μL for K and 200 μL for Cs) was pipetted out and diluted to 5 mL. The concentration of the remaining metal ion in the aqueous phase was determined from the atomic absorption in the diluted solution. The calibration curve was created by standard solution in 1-10 ppm for potassium and 10-50 ppm for cesium. The %extraction was calculated from $([C_0-C]/[C_0])\times100$ whereas C_0 and C were the concentration(ppm) of the aqueous metal ion solutions before and after extraction, respectively.

2.3 Solid-Liquid Extraction[52]
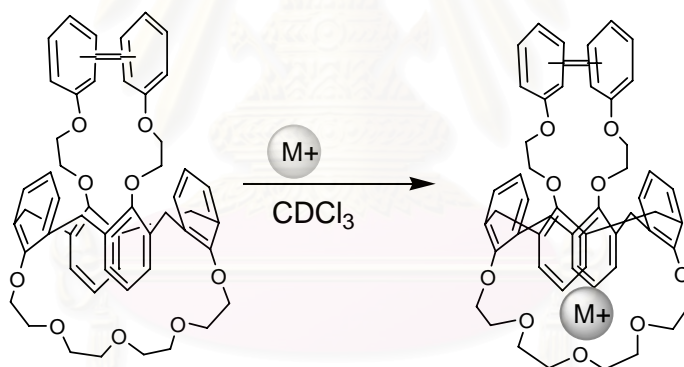
An excess amount of metal picrate was added into a solution of stilbene bridged calix[4]arene crown-5 or crown-6 in CDCl$_3$. The color of the solution gradually changed from colorless to yellow indicating the dissolution of metal picrate into the chloroform solution due to the complexation of the metal cation with the host compounds. The mixtures were analyzed by ^{1}H NMR before and after sonication for 1-3 hour.

2.4 NMR titration
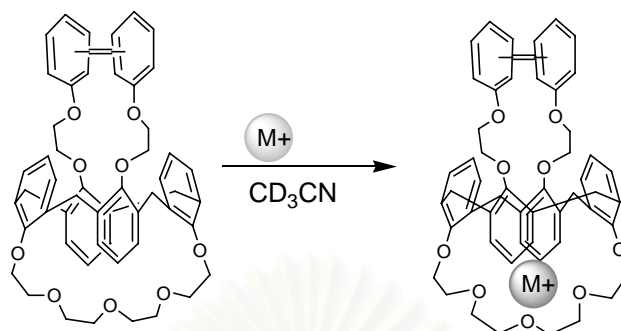
In an NMR tube, **3** (0.002 g) were dissolved into acetonitrile-*d* (0.70 mL) to make a 3.3 mM of the host solution. The mixture was titrated with metal picrate solution (23.6 mM) which was prepared by dissolving metal picrate or metal perchlorate into CD$_3$CN (1.0 mL) in a vial capped with a rubber septum. The guest solution (10 μL) was added stepwise into the host solution until the ^{1}H NMR spectrum was no more change. If the complexation is fast exchange, the complexation constant was determined by using EQNMR curve fitting program. If the complexation is slow exchange, the binding constant was determined by the equation below.

$K = (n_c/[H]_0)/ (1-n_c)(R-n_c)$ where $R=[G]_0/[H]_0$

$n_c = I_c/(I_c+I_h)$

I_c = integration of complex

I_h= integration of host

2.5 Photoisomerization

In an NMR tube, **3** (0.002 g) were dissolved into acetronitrlie-*d* (0.70 mL). The solution was then exposed to the UV light using Hanovia 450 W medium pressure mercury lamp at 5 cm distance. The NMR spectra of the solution were collected at every 10 minutes.

3.1 Synthesis

The synthesis of stilbene-bridged crown ether calix[4]arenes, **3** and **4,** followed the retro synthesis shown in Scheme 3.1. The synthesis was started from the preparation of bromoethoxybenzaldehyde from a nucleophilic substitution of hydroxybenzaldehyde on dibromoethane. The reaction of two equivalents of bromoethoxybenzaldehyde with two phenol rings of calix[4]arene gave bis-benzaldehyde calix[4]arene, **1**. The intramolecular reductive coupling of the bezaldeyde moieties of **1** led to the formation of stilbene-bridged calix[4]arene, **2**. The stilbene-bridged crown ether calix[4]arenes, **3** and **4** was obtained through the reactions between the remaining phenolic hydroxyl groups of **2** and the ditosylate esters of tetra- and pentaethylene glycols, respectively. The ditosylate esters of the glycols were prepared from tosylation of the corresponding glycols.
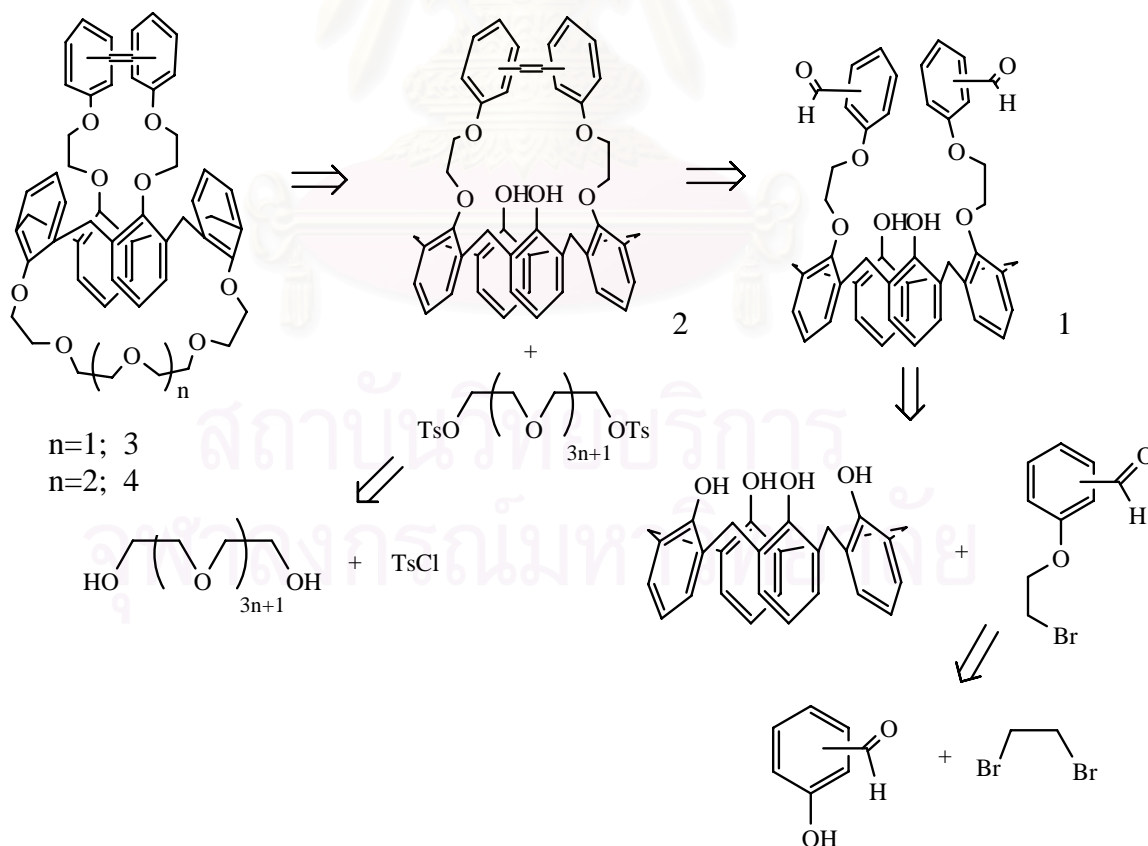
Scheme 3.1 Retro synthesis of stilbene-bridged crown ether calix[4]arenes

3.1.1 Preparation of bisbenzaldehydecalix[4]arenes

Three isomers of (2-bromoethoxy)benzaldehydes, *ortho*, *meta* and *para*, were prepared in 73, 65 and 79% yields, respectively, via nucleophillic substitution between the corresponding isomers of hydroxybenzaldehydes and dibromoethane (**Scheme 3.2**). Dibromoethane was used in excess (eight equivalents) to limit the disubstitution of hydroxybenzaldehyde on dibromoethane. If the products were stored for a long period of time, it should be extracted with a NaOH solution (10% w/v) prior to use in the subsequent synthesis to remove the carboxylic acid formed by autoxidation of the aldehyde groups.

ortho 73%

meta 65%

para 79%
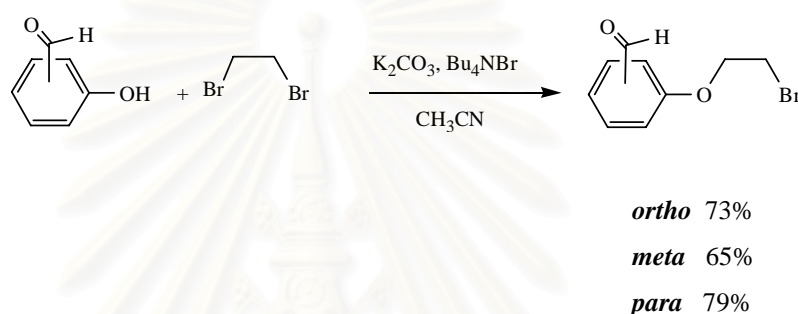
Scheme 3.2 Synthesis of (2-bromoethoxy)benzaldehydes

Initially, K_2CO_3 was used as a base to deprotonate the phenolic proton of calix[4]aene to form an oxygen nucleophile for the nucleophilic substitution reaction on bromoethoxybenzaldehyde. The desired disubstituted calix[4]arene product was obtained along with trisubstituted calix[4]arene as a by product. When Na_2CO_3, a weaker base, was used as a base instead of K_2CO_3, the reaction gave less amount of the by- product that in turn facilitated the crystallization in the purification step. The bisbenzaldehyde calix[4]arenes were isolated in moderate yields (**Scheme 3.3**). The bisbenzaldehyde calix[4]arene products were characterised by ^{1}H NMR spectroscopy. A doublet pair ^{1}H NMR signal of methylene bridge proton was corresponding to 1,3 di-*o*-alkylation product. The strong trend for the 1,3-di-*o*-alkylation can be explained by the stabilization of the corresponding monoanion of the monoether by two intramolecular hydrogen bond and by steric hindrance.[61-62]
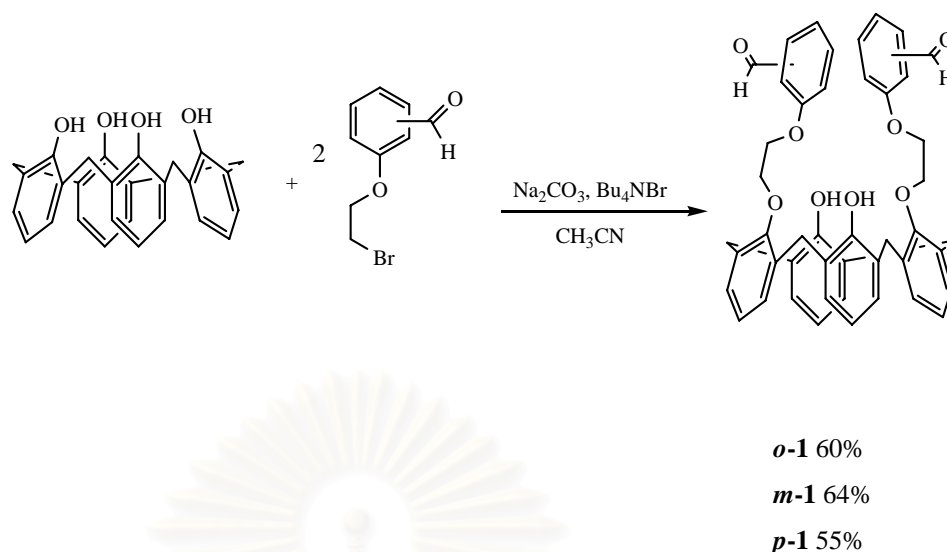
Scheme 3.3 Synthesis of bisbenzaldehyde calix[4]arenes **1**

3.1.2 Preparation of stilbene-bridged calix[4]arenes 2

The stilbene bridge was constructed from an intramolecular reductive coupling (McMurry coupling) of two aldehyde groups in bis-benzaldehyde calix[4]arenes **1**. A high dilution condition (7 mM of bisbenzaldehydes) was used to minimize the intermolecular coupling. However, when the reaction was performed with 3 equivalents of TiCl$_4$, the expected stilbenes **2** were obtained in relatively low yields (**Scheme 3.4**). Significant amounts of side products such as pinacols, dimers and intractable polymers were observed.
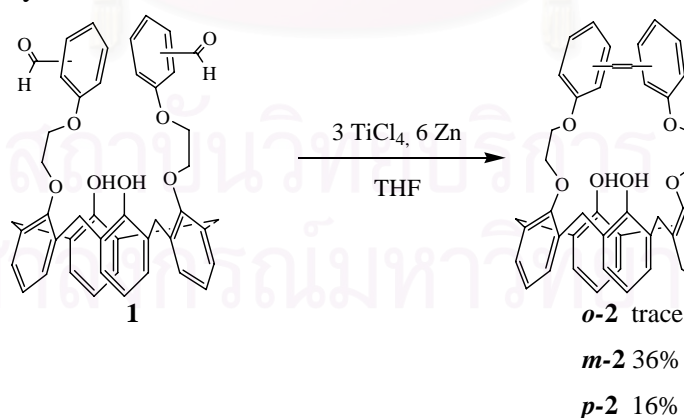
Scheme 3.4 Synthesis of the stilbene-bridged calix[4]arenes **2**

Among three regioisomers of **1**, the coupling of the *meta* isomer gave the highest yield of the desired stilbene. The explanation of this result was brought to light only after all the x-ray structures of **1** were obtained (**Figure 3.1**). Only *m*-**1** has

proper orientation of the benzaldehyde units for the intramolecular coupling. On the other hand, the aldehyde groups of the other two isomers, *o*- and *p*-**1**, turning outward the calix[4]arene cavity, are not organized for the intramolecular coupling.

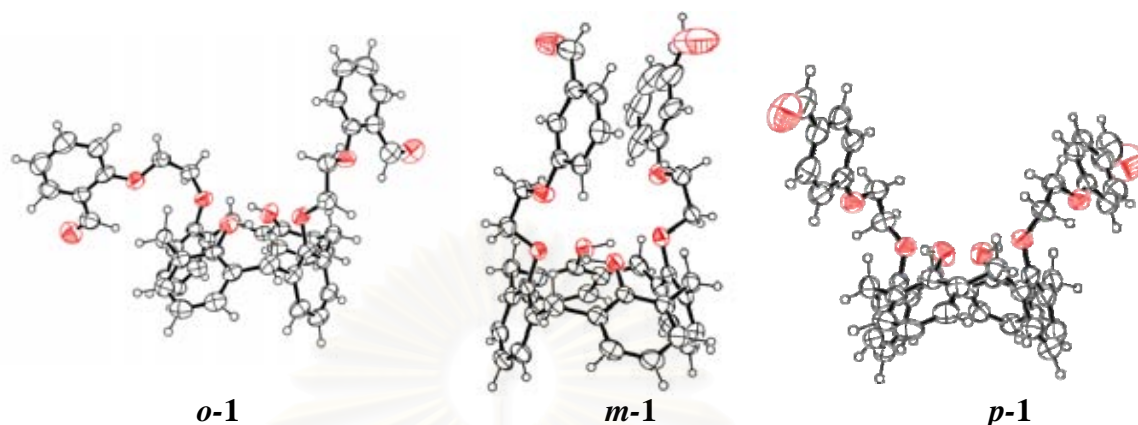*o*-**1**   *m*-**1**   *p*-**1**

Figure 3.1 X-ray structures of **1**

To improve the yields of the desired stilbenes, it is necessary to ponder on the mechanism of the reductive McMurry coupling reaction. The proposed mechanism begins with a single electron transfer of Ti(0) to one of the aldydehyde group of **1** to form **1*** radical. The radical proceeds to form a C-C bond through either intra- or intermolecular radical addition to another aldehyde group (Scheme 4.5). The intra- and intermolecular addition are competing and their rate constants are be represented by k_{intra} and k_{inter}. The reaction rate of the intra- and intermolecular C-C bond formation can be described as $k_{intra}[1^*]$ and $k_{inter}[1][1^*]$, repectively, that gives $k_{intra}/k_{inter}[1]$ as the intra/inter product ratio. Use of higher concentration of Ti should promote the formation of **1*** with and expense of **1** resulting in greater intra/inter product ratio.

The pinacol side product is presumably derived from the hydrolysis of the Ti(II) complex (**Scheme 3.5**). Despite using anhydrous THF as the solvent for the reaction, trace amount of water impurity can become significant under high dilution condition. Excess Ti should also help cutting down this problem by reacting with water.
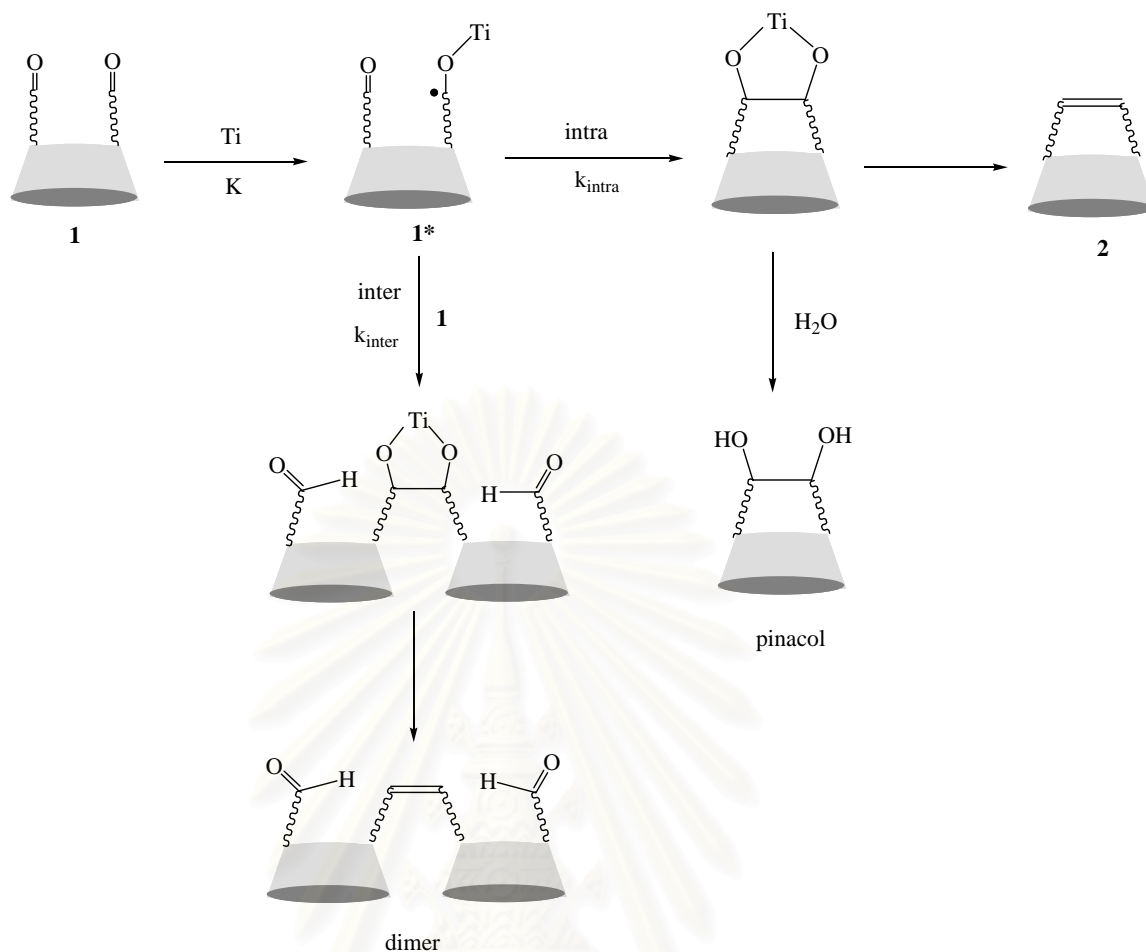
Scheme 3.5 The mechanism of Reductive McMurry couping reaction[63-64]

The McMurry coupling reaction was performed using various amounts of $TiCl_4$. Upon increasing equivalents of $TiCl_4$, the yields of **2** linearly increased (**Figure 3.2**) while the dimer and pinacol side products decreased and eventually unobservable. The concentration of **1** can be described as $[1^*]/K[Ti]$ that give $Kk_{intra}[Ti]/k_{inter}[1^*]$ as the intra/inter product ratio. Applying the steady state approximation ($[1^*]$ is constant), the intra/inter product ratio is linearly proportional to $[Ti]$. To obtain the same %yields of **2**, the amounts of $TiCl_4$ required for coupling of **o-1** and **p-1** are higher than that of **m-1** suggesting that the k_{intra}/k_{inter} of **o-1** and **p-1** are lower than that of **m-1**. These results agree well with the orientation of the aldehyde groups revealed by the x-ray structures described previously. It is also important to note here that the use of large excess of $TiCl_4$ (20 or 40 equivalents) markedly improved the yields of all isomers of **2** from the previous work.
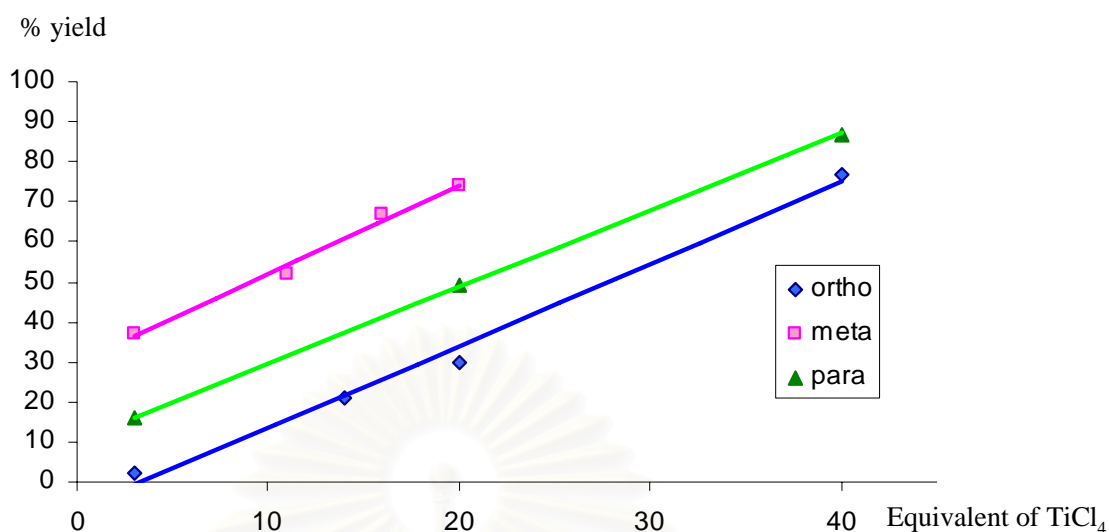
Figure 3.2 Effects of TiCl$_4$ amounts used in McMurry coupling of **1** to the yields of **2**

The reductive coupling of **1** yielded stereoisomeric mixtures of *cis*- and *trans*-stilbene **2**. The mixtures of *cis* and *trans* products were successfully separated by silica gel column using CH$_2$Cl$_2$ as an eluent. The assignment of *cis*- and *trans*-isomers was accomplished based on the vinylic ^{1}H NMR signals in reference to the parent *cis*- and *trans*-stilbenes (**Table 3.1**). The *cis*-isomer was assigned to the isomer possessing vinylic proton signal at the lower chemical shift than that of the *trans* analogue. The structure of ***m-trans*-2** obtained from X-ray crystallography confirmed the assignment of ^{1}H-NMR spectrum (**Figure 3.3**).

Table 3.1 Chemical shifts of the vinylic protons of **2** and stilbene in CDCl$_3$

Compound	^{1}H-NMR (ppm)	
	cis-isomer	*trans*-isomer
***o*-2**	6.72	7.75
***m*-2**	6.70	7.78
***p*-2**	6.76	*NA*
Stilbene	6.57	7.15

NA = not available

Figure 3.3 X-ray structure of *m-trans*-**2**

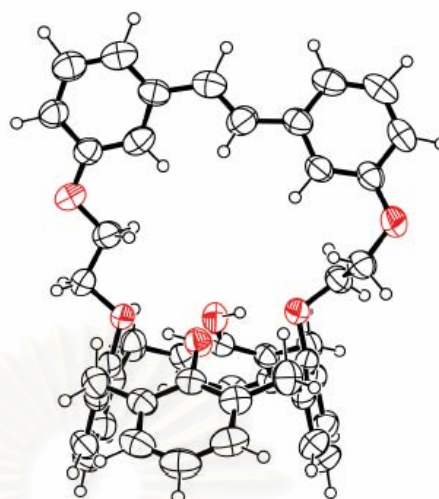Generally, *trans*-stilbene is thermodynamically more stable than its *cis*-isomer. In this work, the McMurry coupling of **1** however gave *cis*-**2** in preference to the *trans*-**2** (**Table 3.2**). The preference of the *cis*-isomer can be attributed to the rigidity of calix[4]arene structure and the molecular length of the stilbene unit.[35] The distance between two opposite hydroxyl groups calculated from AM1 is around 4.10 Å. The minimum molecular lengths of various isomers of stilbene calculated from AM1 are tabulated in **Table 3.3**. The absence of *p-trans*-**2** suggest that molecular length of *p-trans*-stilbene is probably too long to fit on the narrow rim of calix[4]arene with short ethylene chains.

Table 3.2 Product ratio in the synthesis of stilbene-bridged calix[4]arenes

Products	% Yield		*cis*: trans ratio
	cis	*trans*	
o-**3**	62	15	75 : 25
m-**3**	37	37	50 : 50
p-**3**	87	0	100 : 0

Table 3.3 The minimum molecular lengths of various isomers of stilbene calculated from AM1 are tabulated .


cis-stilbene   *trans*-stilbene
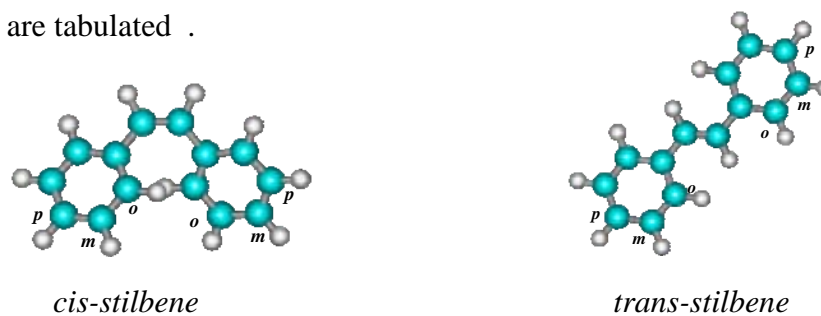
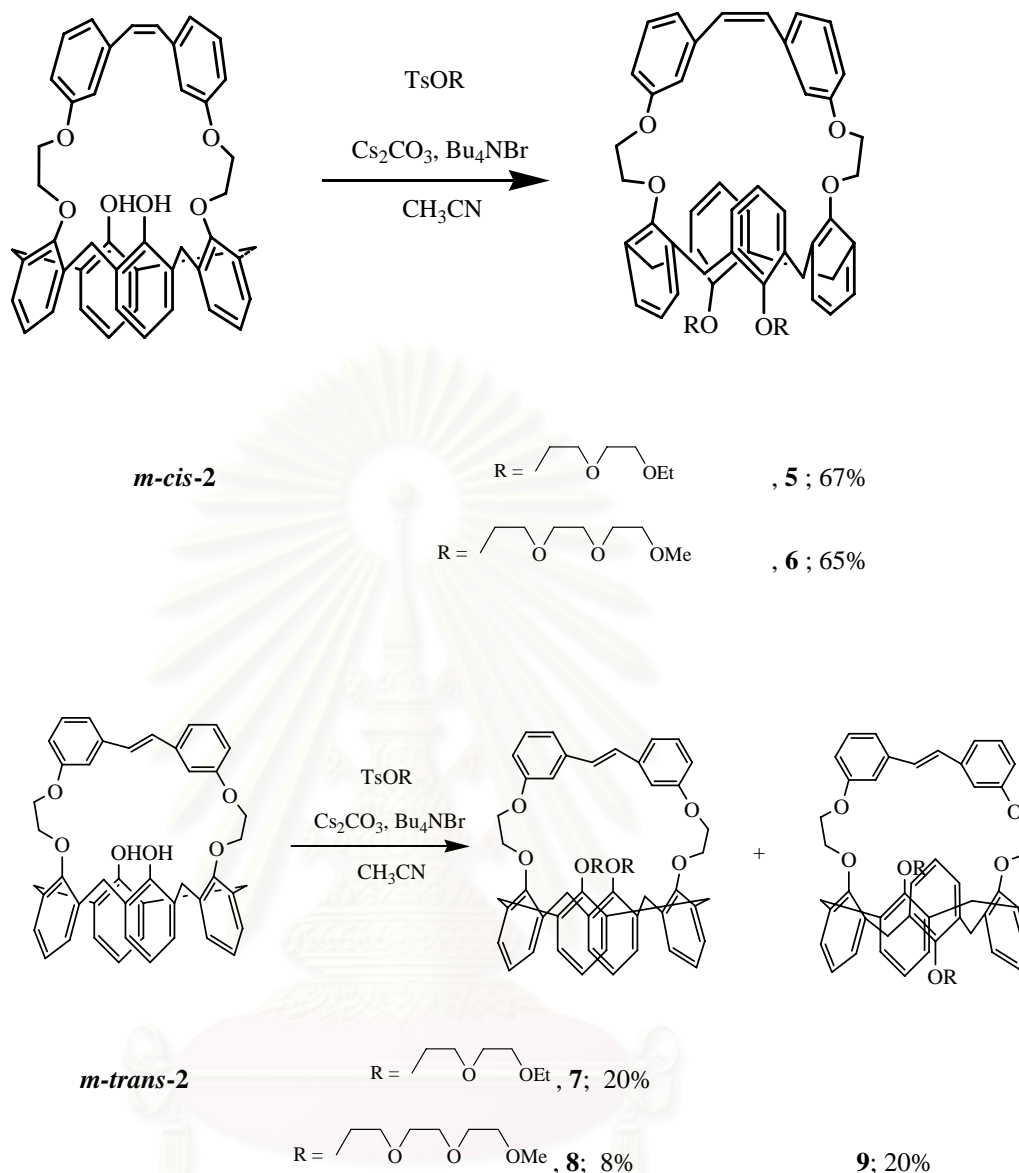|	molecular lengths of stilbene (Å)	
	cis	*trans*
o-o	3.07	5.23
m-m	4.81	7.98
p-p	6.94	9.36

3.1.3 Preparation of the stilbene-bridged crown ether calix[4]arenes (3, 4)

The reaction of **2** with tetra- and pentaethylene glycol ditosylate esters provided stilbene-bridged calix[4]arene crown-5 and crown-6 (**3** and **4**), respectively. As an intramolecular reaction, this reaction also performed under a high dilution condition to minimize the intermolecular reaction leading to the formation of polymers. Cs_2CO_3 was used as a base to facilitate the conformational flip of calix[4]arene from the cone into 1,3 alternate. For ***o*-2**, the synthesis of crown ethers was viable for both *cis* and *trans*-isomers. However, for ***m*-2,** only the *cis*-isomer could form the crown ethers while the *trans*-isomer yielded an intactable mixture. Only *cis*-isomers of ***p*-3** and **4** were synthesized since only ***p-cis*-2** was available (**Scheme 3.6**). The characteristic singlet ^{1}H NMR signal of the calix[4]arene methylene bridge protons observed in the spectra of **3** and **4** indicated that the stilbene-bridged calix[4]arene crowns were formed in the 1,3 alternate conformation .
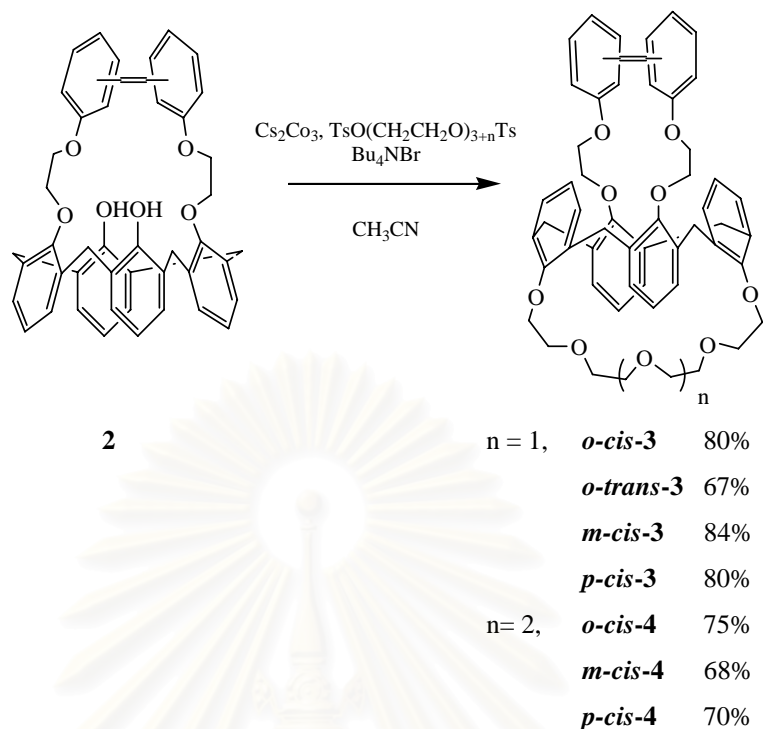
Scheme 3.6 Synthesis of the stilbene-bridged calix[4]arene crown-5 and crown-6

To investigate for the reasons of the infertile synthesis of **m-trans-3** and **4** from **m-trans-2** despite the same reaction worked well on **o-trans-2**, **m-cis** and **trans-2** were allowed to react with two equivalents of tosylate ester of di- or triethyleneglycol monoalkylether under the same condition. The products from the reaction of **m-cis-2** were the expected 1,3-alternate **5** and **6**. On the other hand, the reaction of **m-trans-2** with the tosylate ester of diethylenglycol monoethyl ether gave only poor yield of cone **7** (**Scheme 3.7**). The reaction of **m-trans-2** with the tosylate ester of triethyleneglycol monomethyl ether was even more surprising giving cone **8** as a minor product and partial cone **9** as a major product.

m-cis-2

R = ⟋⟍O⟍OEt , **5** ; 67%

R = ⟋⟍O⟍O⟍OMe , **6** ; 65%

m-trans-2

R = ⟋⟍O⟍OEt , **7**; 20%

R = ⟋⟍O⟍O⟍OMe , **8**; 8% **9**; 20%

Scheme 3.7 Alkylation of *m- cis* and *trans-2* with two equivalents of tosylate ester of diethyleneglycol monoethylether or triethylene glycol monomethylether

The conformations of the products were assigned according to the ^{1}H NMR signals of the methylene protons of calix[4]arene. The spectra of 1,3-alternate **5** and **6** show one singlet signals of the methylene protons while the corresponding signals in the spectra of cone **7** and **8** were one pairs of doublet characteristic to the cone calix[4]arene (**Figure 3.4**).[34-35]
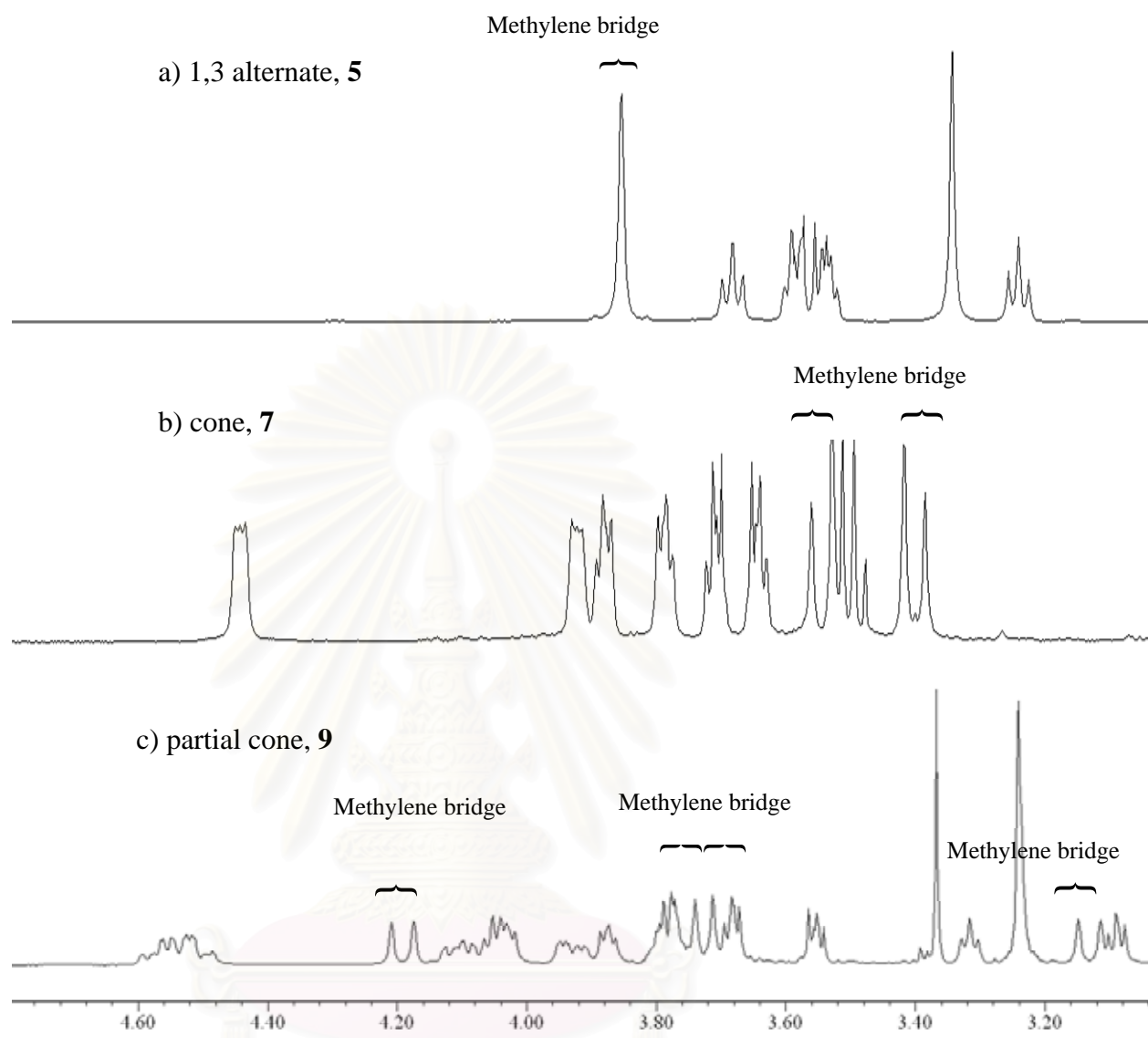
Figure 3.4 ^{1}H NMR signals of methylene protons of calix[4]arene in a)1,3-alternate **5**, b) cone **7** and c) partial cone **9**

Evidently, the phenyl rings of calix[4]arene platform in *m-cis-*2 can flip to form 1,3-alternate conformation but those in *m-trans*-**2** cannot. To gain insight of this difference, AM1 molecular modelling was used to optimize the structures of *m-cis-*2 and *m-trans-*2. The optimized structure of *m-cis-*2 is in the perfect cone conformation while that of *m-trans-*2 is in a pinched cone form (**Figure 3.5**). This AM1 optimized structure of *m-trans-*2 is in good agreement with its x-ray structure (**Figure 3.3**). The

distance between the two opposite hydroxyl groups of **m-trans-2** calculated from AM1 is 3.6 Å significantly shorter than that of **m-cis-2**. The contracted space between the oposite hydroxyl groups of **m-trans-2** is likely to responsible for the restriction of the phenyl ring flip. The diethylene glycol chains were thus connected to **m-trans-2** without any flipping of the phenyl rings.
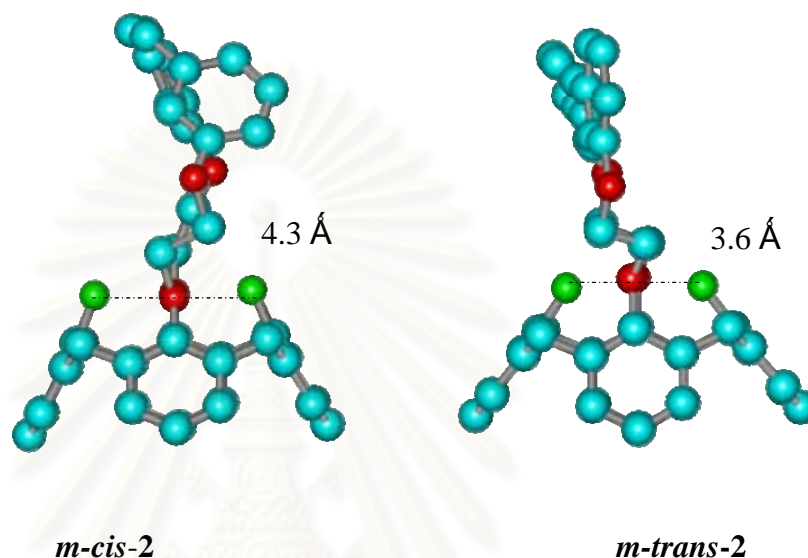

4.3 Å

3.6 Å

m-cis-**2**   **m-trans-2**

Figure 3.5 The AM1 optimized structure of **m-trans-2** and **m-cis-2** and the distance between the oxygen atoms in the two opposite hydroxyl groups

In case of triethylene glycol cahins, the reaction gave a partial cone **9** as a major product. It is logical to assume that the alkylation of the two glycol chains proceed one by one. As a longer substituent comparing to diethylene glycol, the first connected triethylene glycol chain is probably more readily to be forced away from the calix[4]arene cavity by the steric repulsion of the stilbene bridge creating more room for the remaining hydroxyl group to turn upside down to form the patial cone conformation.

3.1.4 Discrimination between cone and pinched cone calix[4]arene by chemical shifts of the hydroxyl protons

The circular shape of the hydroxyl rim of calix[4]arene is significantly distorted to form an elliptical shape upon the conformational change from cone to a pinched cone.   It is thus of interest to analyze the effect of this change to the strength of the intramolecular bonds of the hydroxyl groups. Chemical shifts of ^{1}H NMR signals were used for the analyses.

The chemical shift of the phenolic protons of *m-trans*-**2** appeared at significantly upfield position comparing to that of *m-cis*-**2** suggesting that the hydrogen bonds in the pinched cone conformation are weaker than those in the cone form. To confirm this hypothesis, the chemical shifts of phenolic protons of all isomers of **2,** synthesized in this work, and other two known series of stilbene and azobenzene-bridged *tert*-butylcalix[4]arenes (**10** and **11**)[47-48] were compiled (**Table 3.4**).
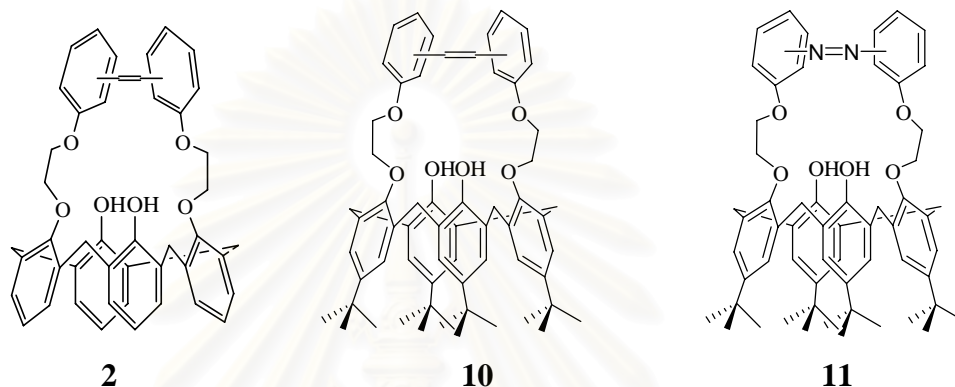

2   **10**   **11**

Table 3.4 Chemical shifts (ppm) of phenolic protons of various calix[4]arene derivatives

	2	**10**	**11**
o-cis	8.10	7.70	-
o-trans	8.44	8.43	7.61
m-cis	8.30	8.08	-
m-trans	5.62	6.60	6.07
p-cis	6.65	6.29	-

The x-ray structures are available for *m-trans*-**2,** *o-cis*-**10**, *o-trans*-**11** and *m-trans*-**11** (**Appendix B**). The conformations of *o-cis*-**10** and *o-trans*-**11** are cone while those of *m-trans*-**2** and *m-trans*-**11** are pinched cone. The phenolic protons of *o-cis*-**10** and *o-trans*-**11** gave the chemical shift at sinificantly lower field than those of *m-trans*-**2** and *m-trans*-**11**. These observations support the hypothesis regarding the weaker intramolecular hydrogen bonding within the pinched cone conformation. In

calix[4]arene, the hydrogen bonds form between the adjacent hydroxyl groups. The weaker hydrogen bonding in a pinched cone conformation should thus be attributed to the longer distance between the adjacent phenolic oxygens as illustrated by the hydroxyl rims of *m-cis*-**2** and *m-trans*-**2** optimized by AM1 (**Figure 3.6**).
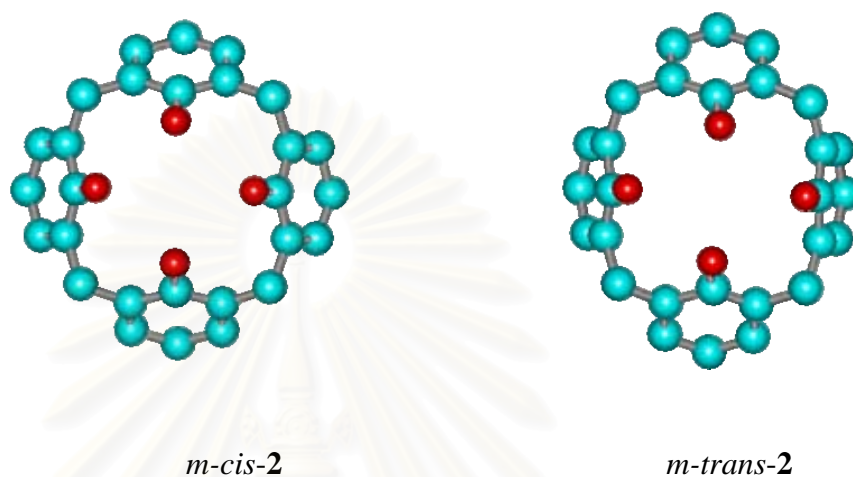

m-cis-**2**   *m-trans*-**2**

Figure 3.6 The hydroxyl rims of *m-cis*-**2** and *m-trans*-**2** optimized by AM1 (the stilbene unit and H was omitted for clarity.

Applying the above theory, the conformations of the rest of the isomers of **2**, **10** and **11** in Table 3.3 can be predicted based on the chemical shift values of the signals of the phenolic protons. The conformation *of o-cis*-, *o-trans*- and *m-cis*-isomers should be cone and those of *m-trans*- and *p-cis*-isomers should be pinched cone It is also conceivable to extend this theory for prediction of cone or pinched cone conformation of other di-*O,O'*-substituted calix[4]arene derivatives.

3.1.5 Preparation of the calix[4]arene crown-5 and crown-6

For comparison in the extraction study, calix[4]arene crowns without stilbene bridge analogous to **3** and **4** were synthesized (**Scheme 3.8**). Calix[4]arene was double methylated followed by alkylation with ditosylate ester of tetra- and pentaethylene glycols to form *O,O'*-dimethylcalix[4]arene crown-5 and crown-6 (**12** and **13**). Without the stilbene bridge, calix[4]arene crowns were obtained in the cone conformation exclusively.

75 % yield   n=1, **12** 74%

n=2, **13** 52%
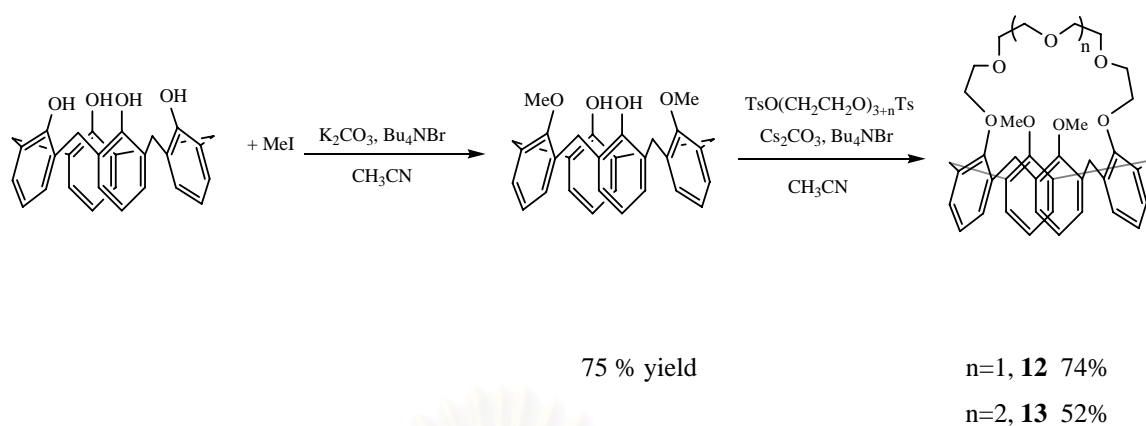
Scheme 3.8 Synthesis of *O,O'*-dimethylcalix[4]arene crown-5 and crown-6

3.2 Complexation study

3.2.1 Liquid-liquid extraction of alkali picrates

The alkali metal ion extraction at the $H_2O|CHCl_3$ interface by stilbene-bridged calix[4]arene crowns **3** and **4** were investigated in comparison with compounds **5, 6, 12, 13** and 18-crown-6. The extraction was carried out by thorough mixing a chloroform solution of the ligand (5 mM, 1 mL) with an aqueous solution of an alkali picrate (5 mM, 1 mL) for 24 hours. After centrifugation, the aqueous phase (35 μL) was pipetted out and diluted to 5 mL. The concentration of the remaining metal ion in the aqueous phase was determined indirectly from the absorbance of picrate ion at 354 nm in the diluted solution. The % extraction was calculated from ($[A_0-A]/[A_0])\times100$ whereas A_0 and A represent the absorbance of the aqueous solutions before and after extraction, respectively.

Four types of alkali ions (Li^+, Na^+, K^+ and Cs^+) were studied. Generally, the ligands containing a crown ether unit *i.e.* **3**, **4**, **12** and 18-crown-6 exhibit good extractability toward alkali ions larger than Na^+ (**Figure 3.7**). The stilbene-bridged calix[4]arenes **5** and **6** in which structures contain di- and triethylene glycol chains have poor extractability towards all alkali ions. The results indicate that the oxygen atoms present in the non-crown structures are not efficient for binding the alkali ions, probably due to the entropic factor. Despite containing a crown-6 unit, **13** shows rather poor extractability towards all alkali ions that will be rationalized later.

The stilbene-bridged calix[4]arene crown-5, **3**, possesses high K^+ extractability comparable to 18-crown-6 but it shows significantly greater K^+/Cs^+ selectivity. On the

other hand, the stilbene-bridged calix[4]arene crown-6, **4**, displays high Cs^+ extractability and impressively high Cs^+/K^+ selectivity. Comparing to **3**, the cone calix[4]arene crown-5 ether **12** shows lower K^+ extractability. Even more, the cone calix[4]arene crown-6 ether, **13**, has much lower Cs^+ extractability than **4**. The results strongly suggest that the 1,3-alternate calix[4]arene crown is more suitable for hosting K^+ and especially Cs^+ ions. The cation/π interaction that is more accessible through the 1,3-alternate conformation has been proposed to enhance the binding to a soft cation such as Cs^+.[40-41]
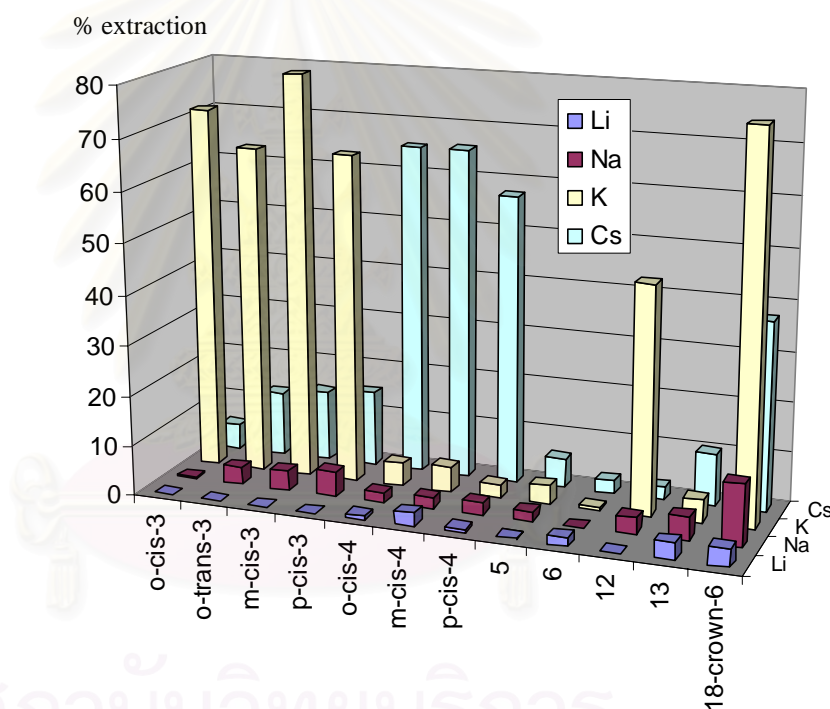
Figure 3.7 Alkali ion extractabilities at $H_2O|CHCl_3$ interface of some calix[4]arene derivatives synthesized in this work comparing to 18-crown-6

The extractabilities of *m-cis*-**3** and *p-cis*-**3** were confirmed by ^{1}H NMR using $CDCl_3$, in place of $CHCl_3$, as a solvent for the ligands . After extraction, the dueterated chloroform layer was separated, dried over Na_2SO_4 and analyzed by ^{1}H NMR spectroscopy. The spectra revealed that only the extraction of an aqueous solution of K^+ picrate led to signal shifts in the spectra of the ligands while the extractions of the solutions of orther alkali ions did not alter the spectra (**Figures 3.8 and 3.9**). The

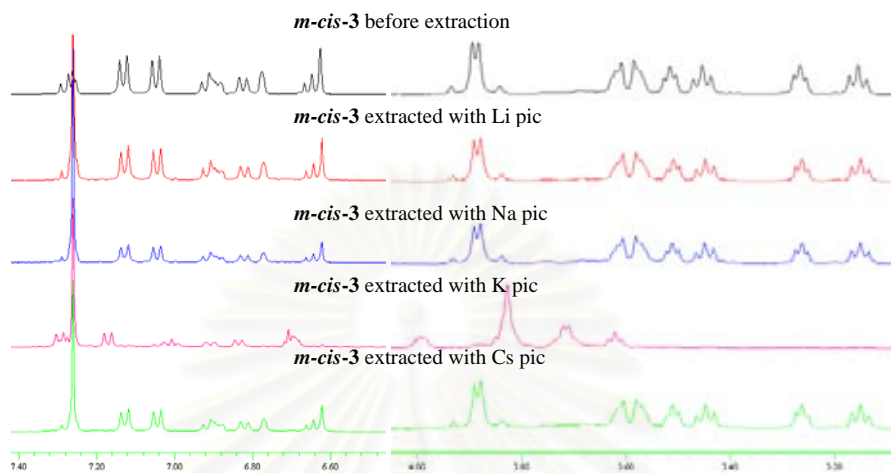results confirm that *m-cis*-**3** and *p-cis*-**3** can extract K$^+$ ion in preference to other alkali ions.

Figure 3.8 ^{1}H NMR spectra of *m-cis*-**3** before and after metal picrate extraction
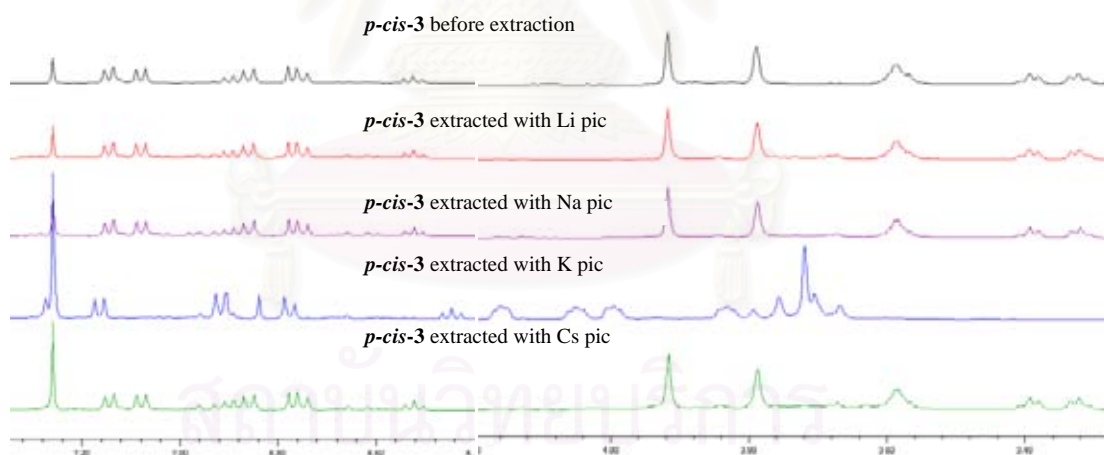

Figure 3.9 ^{1}H NMR spectra of *p-cis*-**3** before and after metal picrate extraction

3.2.2 Liquid-solid extration of alkali picrates

     Having high extracting ability, ligands **3** and **4** were also tested for solid-liquid extraction. An excess amount of potassium picrate was added into a solution of **3** or **4** in CDCl$_3$ and the mixture was sonicated. The color of the solution gradually turned yellow indicating the dissolution of metal picrate into CDCl$_3$ which is normally nonsolvent for the picrate salts. The changes in ^{1}H NMR spectra were used to justify

the nature of these complexation. For example, new set of proton signals were clearly observed after 1 hr of sonication *p-cis*-**3** with potassium picrate (compare **Figure 3.10a and b**) suggesting a partial association of the ligand to K$^+$, to form the expecting host-guest complex, in a slow exchange process. This new set of signals became stroger with the expenses of the original set of signals of the pure ligand as the sonication prolonged. The original signals of *p-cis*-**3** were completely replaced by the signals of the complex after 3 hr of sonication (**Figure 3.10c**) signifying a complete complexation of *p-cis*-**3** to K$^+$ in the solid-liquid extraction.
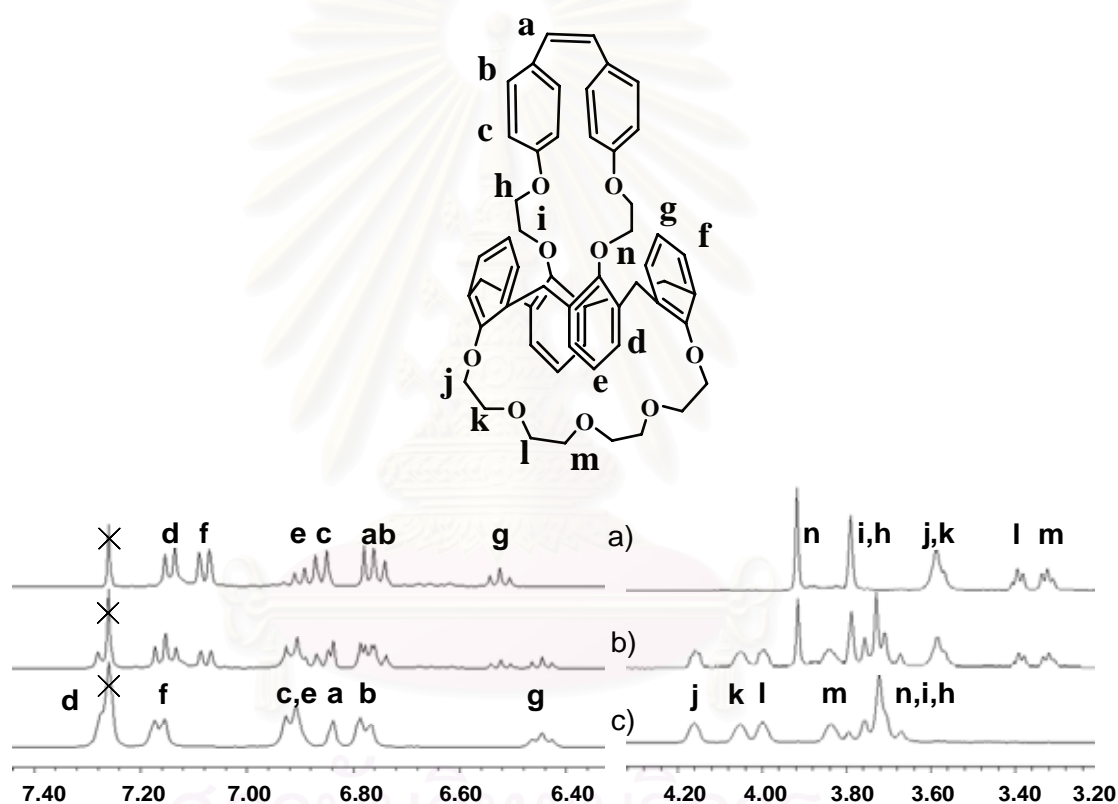
Figure 3.10 ^{1}H NMR spectra of a) *p-cis*-**3** b) partial complexation between *p-cis*-**3** and potassium picrate c) full complexation between *p-cis*-**3** and potassium picrate.

Upon complexation with K$^+$, the signals of the methylene protons in the crown ether chain of *p-cis*-**3** were significantly shifted down field while the other signals were shifted only slightly (**Figure 3.11**) suggesting that K$^+$ situated mostly within the crown ether loop. For the complexation between *p-cis*-**4** and Cs$^+$, sizeable shifts of

various signals including the calixarene aromatic protons were observed (**Figure 3.12**) implying the participation of cation-π interaction in the complexation.
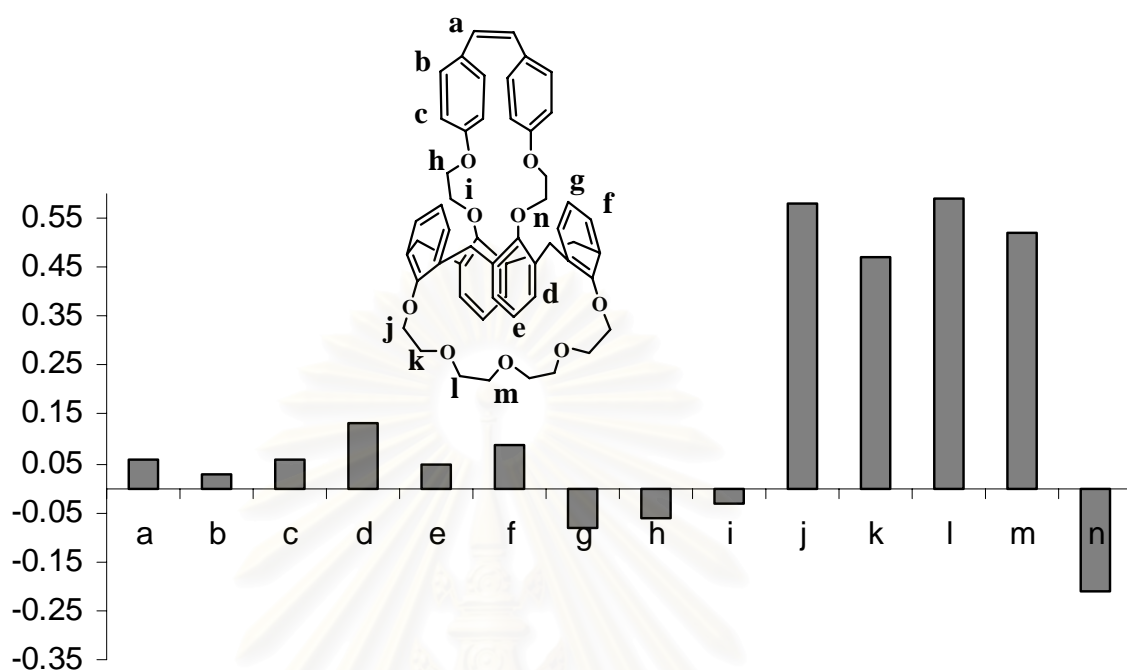

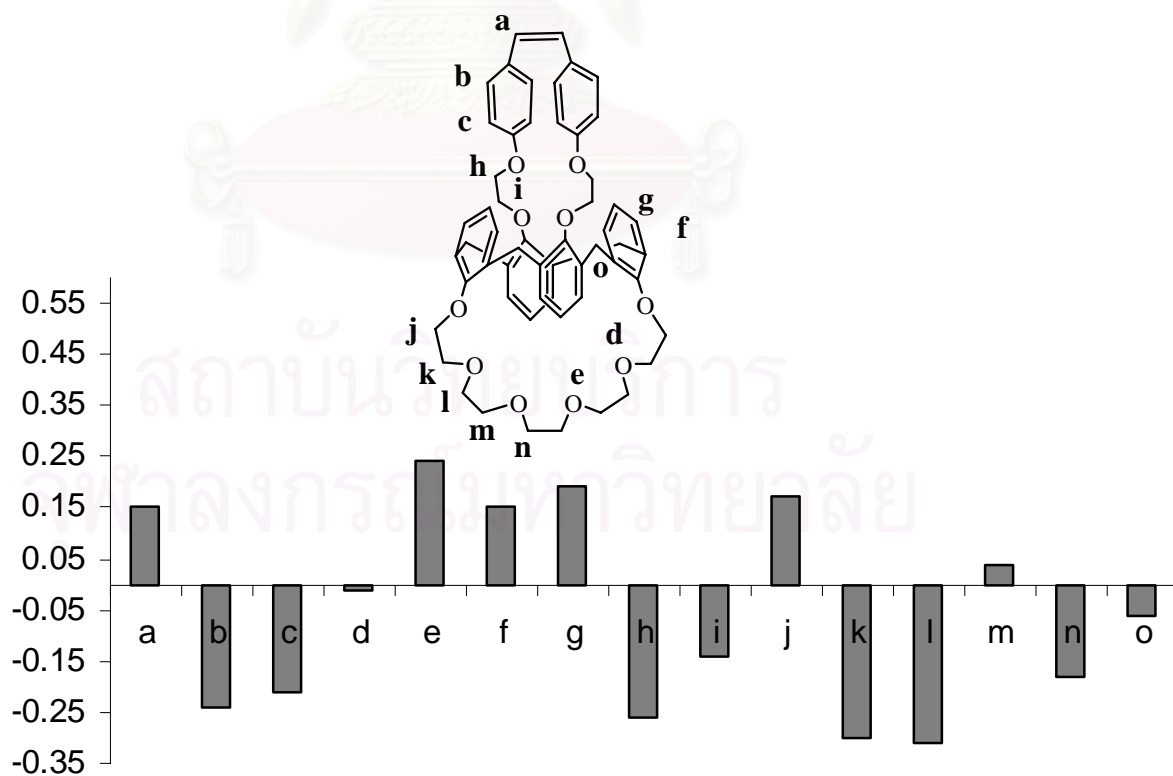**Figure 3.11** Δδ of *p-cis*-**3** complexed with potassium picrate.

Figure 3.12 Δδ of *p-cis*-**4** complexed with cesium picrat

The solid-liquid extractions of *p-cis*-**3** with other alkali metal picrate were also studied by ^{1}H NMR using a similar procedure. The extraction of Cs picrate by *p-cis*-**3** in CDCl$_3$ gave a yellow solution which showed two sets of proton signals belonging to the free host and the complex signifying a slow exchange process of this complexation (**Figure 3.13**). The complexation reached the completion slower than K$^+$ indicating a weaker ligand binding to Cs$^+$ comparing to K$^+$. Upon the extraction of sodium picrate, the signals in the spectrum of the ligand however became broaden especially in the region of the crown ether methylene protons. and no significant change in the spectrum of the ligand in the extraction of Li picrate. The results can be interpreted as the exchange rates for Na picrate with *p-cis*-**3** was faster than *p-cis*-**3** with K picrate and no complexation between Li$^+$ and *p-cis*-**3**. The binding order of *p-cis*-**3** to the alkali ions obtained in this solid-liquid extraction study is K$^+$ > Cs$^+$> Na$^+$> Li$^+$ matching the results from the liquid –liquid extraction described previously.
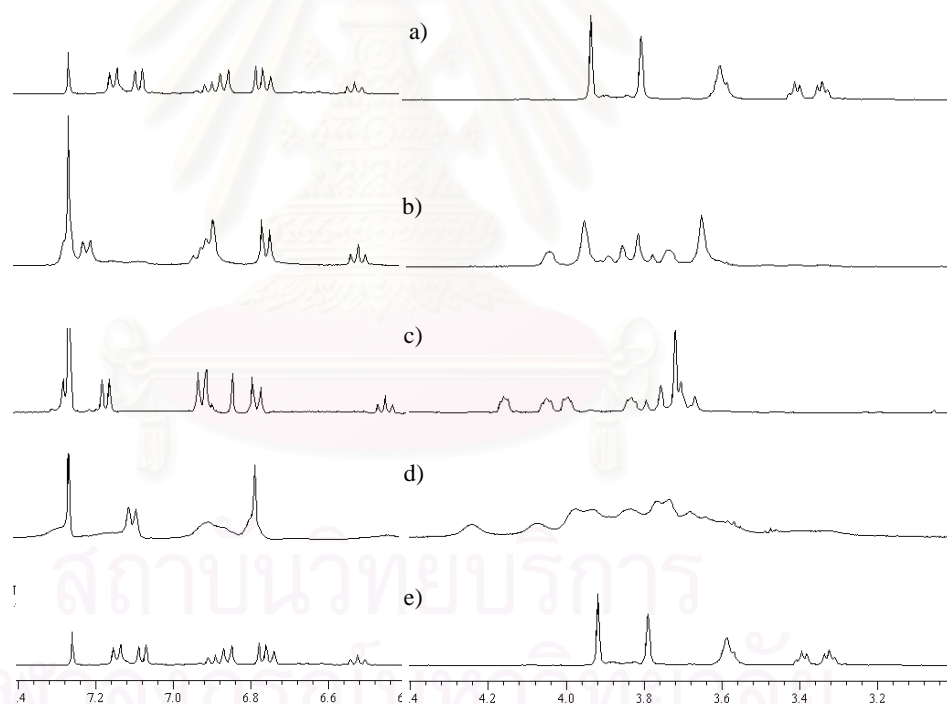

Figure 3.13 ^{1}H NMR spectra of a) *p-cis*-**3** b) *p-cis*-**3** + Cs picrate c) *p-cis*-**3** + K picrate d) *p-cis*-**3** + Na picrate and e) *p-cis*-**3** + Li picrate

3.2.3 Determination of complexation constants by ^{1}H NMR titration

The association constant (K) for **p-cis-3** and an alkali metal ion was obtained from ^{1}H NMR titration of the ligand with a metal picrate in CD_3CN. Titrated with K^+, the proton signals of **p-cis-3** splitted into two sets belonging to the starting ligand and the complex (**Figure 3.14**). The K value for such a slow process was determined simply by taking the integal ratio of the apropriate peaks that is $K = I_{7.39}/I_{7.18}$; whereas $I_{7.39}$ = integral at 7.39 ppm and $I_{7.18}$ = integral at 7.18 ppm, giving Log K = 3.15 (**Table 3.5**).

The complexation of **p-cis-3** and Na picrate in CD_3CN is the fast exchange process in which the shifts in the proton signals corresponding to a weighted average of the complex and free ligand. (**Figure 3.15**). The shift of 1H NMR of **p-cis-3** on the addition of Na picrate was shown in **Figure 3.16**. EQNMR program was used for determination of the log K value being 2.23.

Initially, the titration of **p-cis-3** with Cs picrate produced a ^{1}H NMR spectrum with very broad signals that gradually became sharpen (**Figure 3.17**) indicating that the rate of association-dissociation process was in the same range of NMR time scale. The signals became very sharp when over one equivalent of Cs picrate was added. These phenomena prevent the calculation of K value at the experimental temperature.

No significant changes in the ^{1}H NMR spectrum of **p-cis-3** when the ligand was titrated with Li picrate, even with two equivalents of Li picrate, indicating no complexation between Li^+ and the ligand.

These results were in good agreement with the extractability obtained from the liquid-liquid and solid-liquid extractions. Wrapping these up, the complexation constant between **p-cis-3** with the alkali metal ion is probably in the order of $K^+>Cs^+>Na^+>Li^+$ and the rate of exchange process is probably in the reverse order.
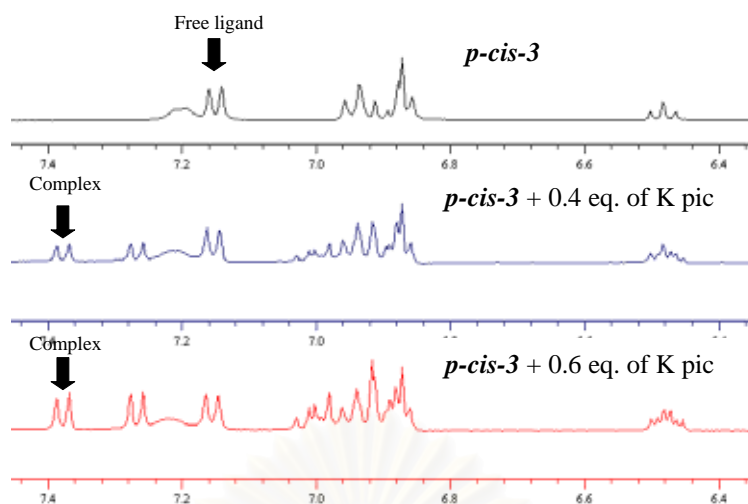
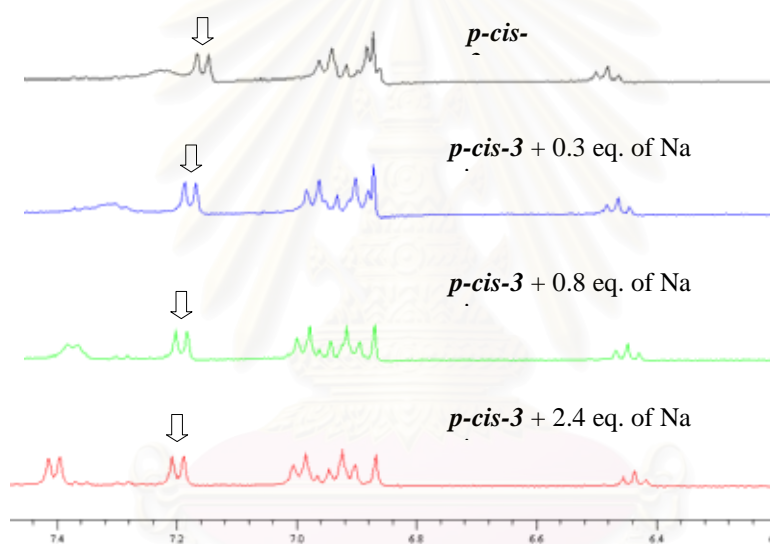**Figure 3.14** ^{1}H NMR titration spectra of *p-cis-***3** with potassium picrate

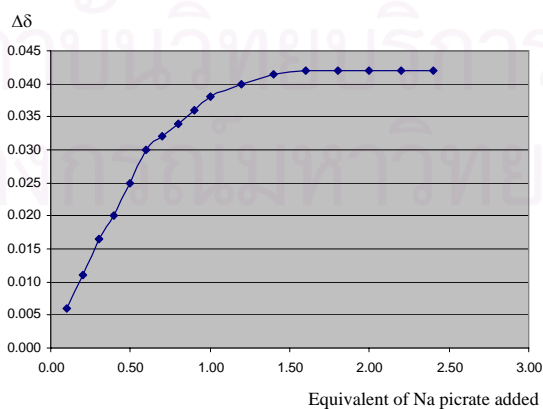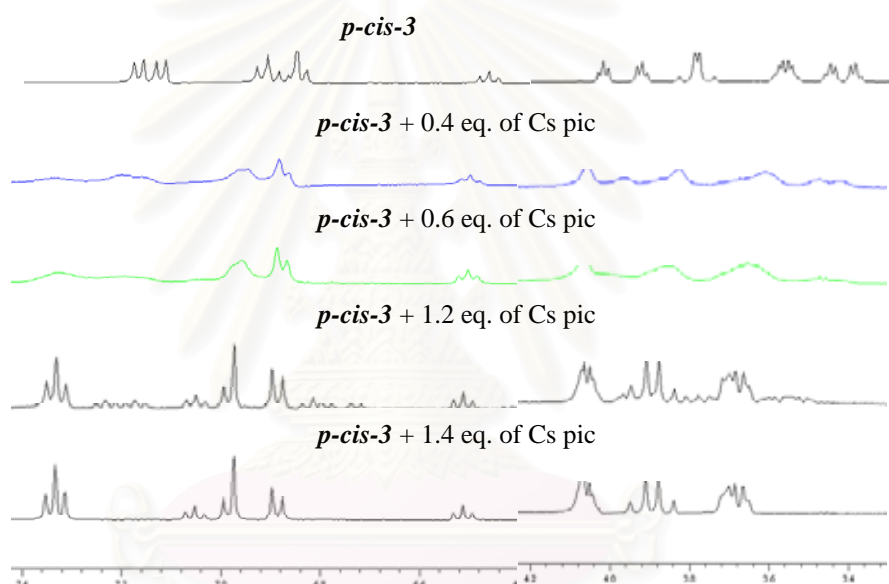**Figure 3.1**5 ^{1}H NMR titration spectra of *p-cis*-**3** with sodium picrate

Figure 3.16 $\Delta\delta$ of *p-cis*-**3** complexed with sodium picrate in NMR titration experiment

Table 3.5 log K of **p-cis-3** with alkali metal picrate

	Li	Na	K	Cs
p-cis-3	$<1^a$	2.23	3.15	*NA*

NA= not available

[a]No significant spectral changes even in the presence of a large excess of metal ion.

Figure 3.17 ^{1}H NMR titration spectra of **p-cis-3** with cesium picrate

3.2.4 Effect of anionic couter ions on liquid-liquid extraction of alkali ions

Picrate is an organic anion which is known to enhance the extraction of an alkali cation by an organic ligand soluble in organic solvents. To investigate the effect of anionic couter ions on the extractability of potassium ion, the liquid-liquid extractions of KPF_6 and $KClO_4$ at the $H_2O|CHCl_3$ interface by ligands **p-cis-3**, **12** and 18-crown-6 were conducted. The similar extractions of $CsNO_3$ by ligands **p-cis-4** and **13** were also performed. Due to the poor UV-Vis absorbance of these inorganic anions, the % extractions were determined by the atomic absorption spectroscopy. The ligands have lower extractability towards K^+ and Cs^+ with inorganic couter ions comparing to the

metal picrate (**Table 3.6**). It is however of sinificance to note the higher extractability of either K^+ or Cs^+ ions by the stilbene-bridged calix[4]arene crown ethers, **3** and **4**, over the other types of ligands including 18-crown-6 and their cone analogues, **12** and **13**.

Table 3.6 Extraction percentage of KPF_6, $KClO_4$, $CsNO_3$ from water to chloroform by calix[4]arene crown-5 derivatives , calix[4]arene crown-6 derivatives and 18-crown-6 at room temperature analyzed by Atomic Absorption Spectroscopy.

	KPF_6	$KClO_4$	$CsNO_3$
p-cis-**3**	33.0	34.5	-
12	2.0	6.1	-
18-crown-6	9.9	5.8	-
p-cis-**4**	-	-	21
13	-	-	12

The anion effect was also studied by ^{1}H NMR spectroscopy. The spectra of *p-cis*-**3** mixed with $KClO_4$ for 1 and 3 hours showed new set of signals with expenses of the signals of the pure ligand indicating a slow exchange process and probably strong complexation (**Figure 3.18**). Compare with the complex between *p-cis*-**3** and K picrate, the ^{1}H NMR spectra of complex between *p-cis*-**3** and $KClO_4$ was not different much.
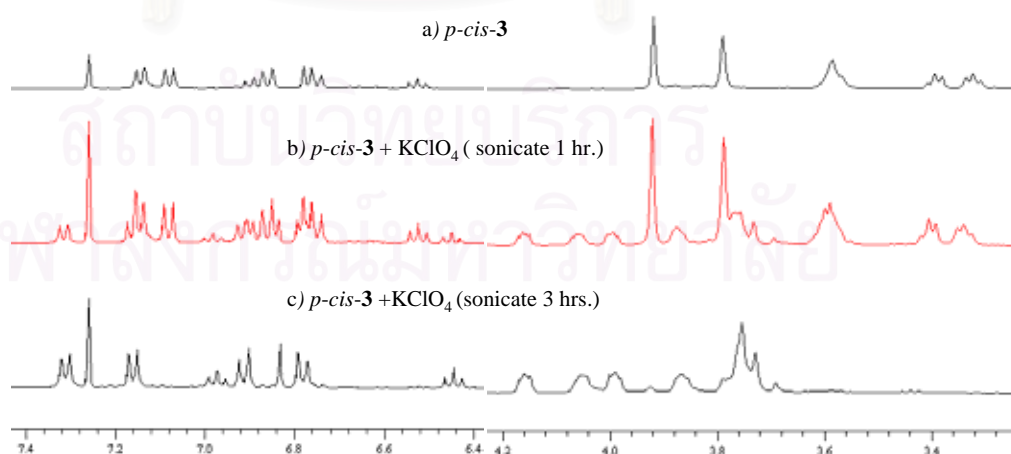
Figure 3.18   ^{1}H NMR spectra of *p-cis*-**3** a) before mixing b) after 1 hour and c) after 3 hours of mixing

3.3 Photoisomerization Study

In CD$_3$CN, the UV irradiation of **o-cis-3** and **m-cis-3** yielded unidentified mixtures with very complicated ^{1}H NMR spectra (**Appendix A.36-37**). In contrast, the UV irradiation of **p-cis-3** gave a new compound with very clean ^{1}H NMR spectrum (**Figure 3.19**). The number and pattern of ^{1}H NMR signals were not corresponding to the *p-trans*-stilbene crown ether. The competing photoisomerization reaction of *cis*-stilbene to form dihydrophenanthrene was reported.[65] ^{1}H NMR spectra showed that the new compound can interpreted as phenanthrene-bridged calix[4]arene crown ether **14** . These results indicated that the phenanthrene ring was formed from the photochemical electrocyclic ring closer of *cis*-stilbene followed by the dehydrogenation in the presence of air (**Scheme 3.9**).
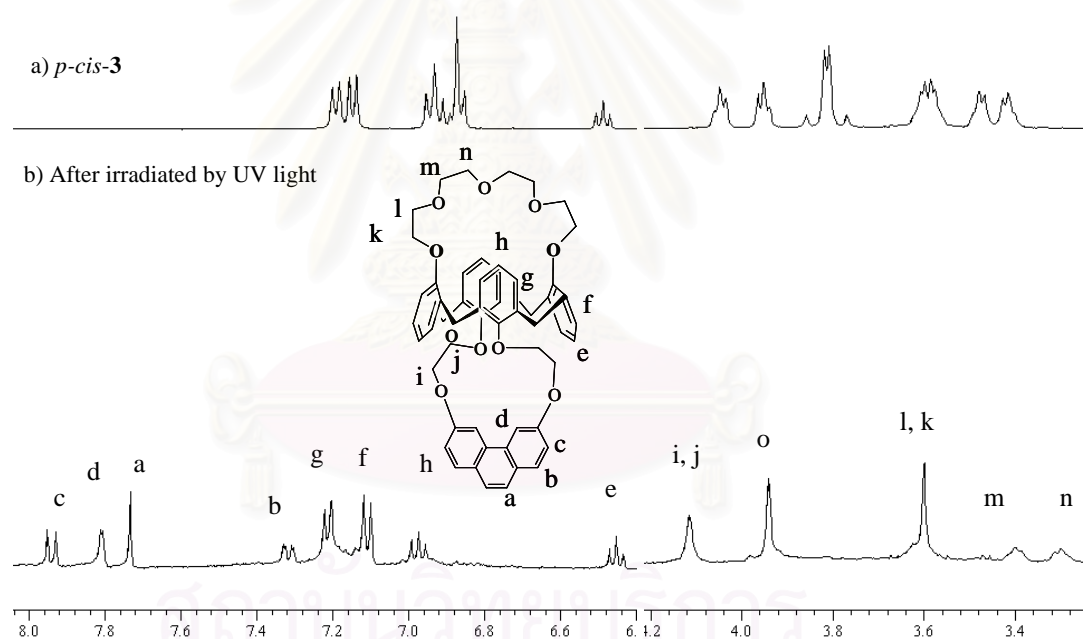
Figure 3.19 ^{1}H NMR of a) p-cis-3 b) p-cis-3 after irradiated by UV light
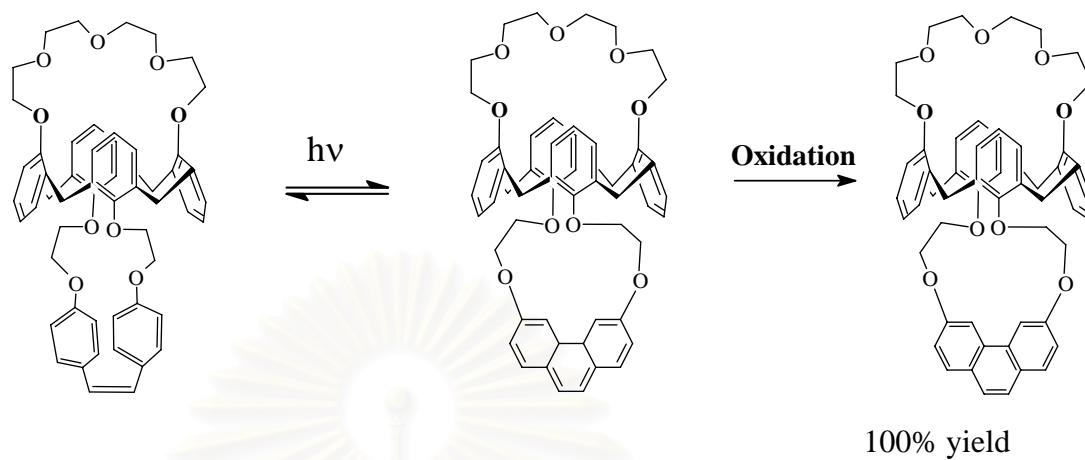
Scheme 3.9 Photoreaction of *p-cis*-**3** under UV light.

CHAPTER IV

CONCLUSION AND SUGGESTION

4.1 Conclusion

The series of *o*-, *m*- and *p*-stilbene-bridged calix[4]arenes were successfully synthesized through an intramolecular reductive McMurry coupling of the corresponding bisbenzaldehyde calix[4]arene in high yields using a large excess of $TiCl_4$ and high dilution condition. The rigid and narrow cavity of calix[4]arene platform prefers the shorter bridges that leads to the preference of the absence of *p-trans* and the formation of *o-cis* over *o-trans* stereoisomer. With assistance of some x-ray structures and extensive analyses of ^{1}H NMR spectra, the conformation of *o-cis-*, *o-trans* and *m-cis*-stilbene-bridged calix[4]arenes was designated as a cone while that of *p-cis* and *m-tran*-stilbene-bridged calix[4]arenes was assigned as a pinched cone.

The crown-5 and -6 ethers were successfully tethered over the stilbene-bridged calix[4]arenes, excepting the *m-trans* isomer, via coupling of tetra- and pentaethylene glycol chains to the remaining phenolic groups. The presence of stilbene bridge over the calix[4]arene rim effectively prevents the connection of the polyether chains in the cone conformation resulting in the exclusive formation of 1,3 alternate stilbene-bridged calix[4]arene crown ethers. The short distance between the two opposite hydroxyl groups in the severely distorted pinched cone conformation of *m-trans*-stilbene-bridged calix[4]arene is probably responsible for unsuccessful synthesis of *m-trans*-stilbene-bridged calix[4]arene crown ether.

In general, the stilbene-bridged calix[4]arene crown ethers have greater alkali ion extractability and selectivity, at the $H_2O|CHCl_3$ interface, than 18-crown-6 and the corresponding cone calix[4]arene crown ethers. The stilbene-bridged calix[4]arene crown-5 and -6 ethers possess excellent K^+/Cs^+ and Cs^+/K^+ selectivities, respectively. The complexation constants obtained from ^{1}H NMR titration showed that the complexation of the stilbene-bridged calix[4]arene crown-5 and K picrate in CD_3CN is in the slow exchange and have highest K compare with other alkali metal ion. The alkali ion extratabilities of the stilbene-bridged calix[4]arene crown ethers at the water|organic interface are higher for picrate salts comparing to the inoganic salts such as chlorate, hexafluorophosphate and nitrate.

The UV irradiation of *o-cis-* and *m-cis-*stilbene-bridged calix[4]arene crown-5 gave only mixtures of unidentified products. The photoreaction of *p-cis-*stilbene bridged calix[4]arene crown-5 however yielded phenanthrene-bridged calix[4]arene crown-5 exclusively. There was no observable photoisomerization from *cis-* to *trans* stereoisomer in all cases.

This work demonstrates that the stilbene bridges can be used to control the conformation of the calix[4]arene and thus binding properties of the calix[4]arene platform although the photo-switchability between *cis* and *trans* isomer of the bridge was not possible.

4.2   Suggestion for future works

The suggested of future work should be focused on

1. Synthesis of the   *m-cis* and *m-trans* stilbene bridged calix[4]arene containing binding unit such as urea or thiourea on the upper rim.
2. Crytallisation of compound **2** for study of calix[4]arene conformation

References

(1)   Shiver, D. F.; Atkins, P. W.; Langford, C. H. *Inorganic Chemistry*; Freeman, W. H., Ed., **1990**, 608.

(2)   Bertini, I.; Gray, H. B.; Lippard, S. J.; Valentine, J. S. *Bioinorganic Chemistry*; University Science Books, **1994**,107.

(3)   Kaim, W.; Schwederski, B. *Bioinorganic Chemistry: Inorganic Elements in the Chemistry of Life*; John Wiley & Sons, **1994**, 281.

(4)   Lehn, J.-M. Supramolecular Chemistry - Scope and Perspectives Molecules, Supermolecules, and Molecular Devices, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89-112.

(5)   Lehn, J.-M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH,   **1995**, 89.

(6)   Vogtle, F. *Supramolecular Chemistry*; John Wiley & Sons, **1991**, 313.

(7)   Reed, C. A. Molecular Architectures, *Acc. Chem. Res.* **2005**, *38*, 215-216.

(8)   Lehn, J. M. Supramolecular chemistry, Science, 1993, 260, 1762-1763.

(9)   Moore, D. S. Advances in DNA Sequence Specific Agents**,** *J. Am. Chem. Soc.* **1998**, *120*, 613-613.

(10)   Gordon, M.S.; Jensen, J. H**.** Understanding the Hydrogen Bond Using Quantum Chemistry, *Acc. Chem. Res.* **1996**, *29*, 536-543.

(11)   Huang, C.-H.; McClenaghan, N. D.; Kuhn, A.; Hofstraat, J. W.; Bassani, D. M. Enhanced Photovoltaic Response in Hydrogen-Bonded All-Organic Devices**,** *Org. Lett***, 2005**, *7*, 3409-3412.

(12)   Schultz, R. A.; Dishong, M. D.; Gokel, G. W. Crown-cation complex effects. 15. Lariat ethers. 4. Chain length and ring size effects in macrocyclic polyethers having neutral donor groups on flexible arms *J. Am. Chem. Soc.* **1982**, *104*, 625-626.

(13)   Grootenhuis, P. D. J.; Kollman, P. A. Molecular mechanics and dynamics studies of crown ether - cation interactions: free energy calculations on the cation selectivity of dibenzo-18-crown-6 and dibenzo-30-crown-10 *J. Am. Chem. Soc.* **1989**, *111*, 2152-2158.

(14)   Walkowiak,W.; Kang, S. I.; Stewart, L.; Ndip, G. E. Bartsch, R. A. Effect of ring size variation within lipophilic crown ether carboxylic acids on the

selectivity andefficiency of competitive alkali-metal cation solvent extraction into chloroform *Anal. Chem.* **1990**, *62*, 2022-2026.

(15)   Strzelbicki, J. Bartsch, R. A. Extraction of alkali metal cations from aqueous solutions by a crown ether carboxylic acid *Anal. Chem.* **1981**, *53*, 1894-1899.

(16)   Choi,K. Y.; Lee, C. Y. Kinetics of bulk free-radical polymerization of methyl methacrylate using potassium peroxydisulfate with 18-crown-6 as phase-transfer catalyst, *Ind. Eng. Chem. Res.* **1987**, *26*, 2079-2086.

(17)   Stott, P. E.; Bradshaw, J. S.; Parish, W. W. Modified crown ether catalysts. 3. Structural parameters affecting phase transfer catalysis by crown ethers and a comparison of the effectiveness of crown ethers to that of other phase transfer catalysts *J. Am. Chem. Soc.* **1980**, *102*, 4810-4815.

(18)   Sasaki, T.; Eguchi, S.; Ohno, M.; Nakata, F. Studies on reactions of isoprenoids. XXII. Crown ether catalyzed synthesis of dialkylvinylidenecyclopropane derivatives *J. Org. Chem.* **1976**, *41*, 2408-2411.

(19)   Ikeda, A.; Shinkai, S. Novel cavity design using calix[n]arene skeletons: toward molecular recognition and metal binding *Chem. Rev.* **1997,** 97, 1713-1734.

(20)   Gutsche, C. D. *Calixarenes* Revisited, Monograph in Supramolecular Chemistry, Stoddart, J. F., Ed.; The Royal Society of Chemistry: London, **1998**.

(21)   Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J. *Calixarenes 2001*; Kluwer Academic Publishers: Dordrecht, Holland, **2001**. 2-20.

(22)   Iwamoto,; K. Araki, K.; Shinkai, S. Syntheses of all possible conformational isomers of O-alkyl-p-t-butylcalix[4]arenas *Tetrahedron*, **1991***, 47*, 4325-4342.

(23)   Groenen, L. C.; Ruël, B. H. M.; Casnati, A.; Verboom, W.; Pochini, A.; Ungaro, R.;Reinhoudt, D. N. Synthesis of monoalkylated calix[4]arenes via direct alkylation *Tetrahedron*, **1991***, 47,* 8379-8384.

(24)   Groenen, L. C.; Ruël, B. H. M.; Casnati, A.; Timmerman, P.; Verboom, W.; Harkema, S.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. Syn-1,2-dialkylated calix[4]arenes : general intermediates in the NaH/DMF

tetraalkylation of calix[4]arenas *Tetrahedron Lett.* **1991***, 32,* 2675-2678.

(25)   Shinkai, S.; Fujimoto, K.; Otsuka, T.; Ammon, H. L. Syntheses and ion selectivity of conformational isomers derived from calix[4]arene *J. Org. Chem..* **1992**, *57*, 1516-1523.

(26)   Loon, J. D. V.; Arduini, A.; Coppi, L.; Verboom, W.; Pochini, A.; Ungaro, R.; Harkema, S.; Reinhoudt, D. N. Selective functionalization of calix[4]arenes at the upper rim *J. Org. Chem.***1990***, 55,* 5639-5646.

(27)   Ho, I.-T.; Lee, G.-H.; Chung, W.-S. Synthesis of upper-rim allyl- and *p*-methoxyphenylazocalix[4]arenes and their efficiencies in chromogenic sensing of Hg^{2+} ion *J. Org. Chem.* **2007,** *72***,** 2434-2442.

(28)   Ozturk, G.; Akkaya, E. U. Differential and substrate-selective reactivity of calix[4]arene derivatives with cyclenyl-Zn(II)modifications at the upper rim *Org. Lett***. 2004***, 6,* 241-243.

(29)   Chawla, H. M.; Pant, N.; Srivastava, B.; Upreti, S Convenient direct synthesis of bisformylated calix[4]arenes via *ipso* substitution *Org. Lett.* **2006**, *8*, 2237-2240.

(30)   Gutsche, C. D.; Bauer, L. J. Calixarenes. 13. The conformational properties of calix[4]arenes, calix[6]arenes, calix[8]arenes, and oxacalixarenes *J. Am. Chem. Soc.* **1985**, *107*, 6052-6059.

(31)   Gutsche, C. D.; Reddy,. P. A. Calixarenes 25. Conformations and structures of the products of arylmethylation of calix[4]arenes *J. Org. Chem.* **1991**, *56*, 4783-4791.

(32)   Iwamoto, K.; Araki, K., Shinkai, S. Conformations and structures of tetra-O-alkyl-*p-tert*-butylcalix[4]arenas. How is the conformation of calix[4]arenas immobilized? J. Org. Chem. **1991**, *56*, 4955-4962.

(33)   Iwamoto, K.; Shinkai, S. Synthesis and ion selectivity of all conformational isomers of [tetrakis(ethoxycarbonyl)methoxy]calix[4]arene *J. Org. Chem.* **1992**, *57*, 7066-7073.

(34)   Cornforth, J. W., P. D. Hart, G. A. Nicholls, R. J. W. Rees, and J. A. Stock.

Antituberculous effects of certain surface-active polyoxyethylene ethers, *J. Pharmacol.* **1955**, *10*, 73–86.

(35)   Cornforth, W. J.; Morgan,E. D.; Potts, K. T.; Preparation of antituberculous polyoxyethylene ethers of homogeneous structure, *Tetrahedron.* **1973**, *29*, 1659-1667.

(36)   Conner, M;. Janout, V.; Regen, S. L. Pinched-cone conformers of calix 4 arenes *J. Am. Chem. Soc.* **1991**, *113*, 9670-9671.

(37)   Evans, D. R.; Huang, M.; Fettinger, J. C.; Williams, T. L. Synthesis and characterization of diametrically substituted tetra-*O-t*-butylcalix[4]arene ligands and their chelated complexes of titanium, molybdenum, and palladium *Inorg. Chem.* **2002**, *41*, 5986-6000.

(38)   Cameron, B. R.; Veggel, F. C. J. M. V.; Reinhoudt, D. N. Transition metal complexes of lower rim 1,3-diphosphinite and 1,3-diphosphino calix[4]arenas *J. Org. Chem.* **1995**, *60*, 2802-2806.

(39) Scheerder, J.; Vreekamp, R. H.; Engbersen, J. F. J.; Verboom, W.; van Duynhoven, J. P. M.; Reinhoudt, D. N. The pinched cone conformation of calix[4]arenes: noncovalent rigidification of the calix[4]arene skeleton *J. Org. Chem.* **1996**, *61*, 3476-3481.

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

(41)   Ungaro, R.; Casnati, A.; Ugozzoli, F.; Pochini, A.; Dozol, J.; Hill. C.; Rouquette, H. 1,3-Dialkoxycalix[4]arene crown-6 in 1,3-alternate conformation cesium selective ligands that exploit cation-arene interaction, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1506-1509.

(42)   Ueno, A.; Yoshimura, H.; Saka, R.; Osa, T. Photocontrol of binding ability of capped cyclodextrin, *J. Am. Chem. Soc.* **1979**, *101*, 2779-2780.

(43)   Shinkai,S.; Nakaji,T.; Nishida,Y.; Ogawa,T.; Manabe,O. Photoresponsive crown ethers. 1. *cis-trans* isomerism of azobenzene as a tool to enforce

conformational changes of crown ethers and polymers, *J. Am. Chem. Soc.* **1980**, 102, 5860-5865.

(44)   Shinkai, S.; Ogawa, T.; Kusano, Y.; Manabe, O. Selective extraction of alkali metal cations by a photoresponive bis(crown ether)*, Chem. Lett.* **1980**, 283-286.

(45)   Saadioui, M.; Reynier, N.; Dozol, J.; Asfari, Z.; Vicens,J. Synthesis and complexation properties towards alkali cations of a photosensitive azo-modified calix[4]crown ether in the 1,3-alternate conformation, *J. Incl. Phenom.* **1997**, *29.* 153–165.

(46)   Saadioui, M.; Reynier, N.; Dozol, J.; Asfari, Z.; Vicens,J. Synthesis, characterisation and UV-Vis properties of azocalix[4]crowns, *J .Incl. Phenom* **1997**, *28***,** 223–244.

(47)   Pipoosanakaton, B.; Sukwattanasinitt, M.; Jaiboon, N.; Chaichit, N.; Tuntulani, T. Preparation of new azobenzene crown ether *p-tert*-butylcalix[4]arenes and their roles as switchable ionophores for Na$^+$ and K$^+$ ions, *Tetrahedron. Lett.* **2000**, *41*, 9095-9100.

(48)   Rojanathanes, R.; Pipoosananakaton, B.; Tuntulani, T.; Bhanthumnavin, W.; Orton, J. B.; Cole, S. J.; Hursthouse, M. B.; Grossel, M. C.; Sukwattanasinitt,   M. Comparative study of azobenzene and stilbene bridged crown ether *p**-tert**-*butyl calix[4]arene, *Tetrahedron* **2005**, *61,* 1317-1324.

(49)   March, J. *Advanced Organic Chemistry*, 4th ed.; John Wiley & Sons: New York, **1992**,1234.

(50)   Sukwattanasinitt, M.; Rojanathanes, R.; Tuntulani, T.; Sritana-Anant,Y.; Ruangpornvisuti, V. Synthesis of stilbene crown ether *p-tert*-butylcalix[4]arenas*, Tetrahedron. Lett*. **2001**, *42, 5291–5293.

(51)   Rojanathanes, R.; Tuntulani, T.; Bhanthumnavin, W.; Sukwattanasinitt, M. Stilbene-bridged *tert*-butylcalix[4]arene as photoswitchable molecular receptors**,** *Org. Lett.* **2005**, *7*, 3401-3404.

(52)   Jaiyu, A. Rojanathanes, R. Sukwattanasinitt, M. Stilbene-bridged 1,3-alternate calix[4]arene crown ether for selective alkali ion extraction,*Tetrahedron Lett.* **2007**, *48*, 1817–1821.

(53)   Roger S. Macomber*, An Introduction to NMR titration for studying rapid*

reversible   complexation, *J. Chem. Educ*. **1992**, *69*, 375-378.

(54)   Cohen,Y.; Avram, L.; Frish, L. Diffusion NMR spectroscopy in supramolecular and combinatorial chemistry: An old parameter - new insights *Angew. Chem. Int. Ed.* **2005**, *44*, 520-554.

(55)   Castro, R.; Godinez, L. A.; Criss, C. M.; Kaifer, A. E. Host properties of cyclodextrin and a water-soluble calix[6]arene probed with dimeric bipyridinium guests, *J. Org. Chem.* **1997**, *62*, 4928-4935.

(56)   Gutsche, C. D.; Iqbal, M. *p-tert-* Butylcalix[4]arene *Organic Syntheses, Coll.* **1990***, 68,* 234-236.

(57)   Memon, S.; Tabakci, M. Roundhill, D. M.; Yilmaz, M. Useful approach toward the synthesis and metal extractions with polymer appended thioalkyl calix[4]arenas *Polymer* **2005**, *46*, 1553-1560.

(58)   Gutsche, C. D.; Levine, J. A.; Sujeeth, P. K. Calixarenes. 17. Functionalized Calixarenes: The Claisen Rearrangement Route *J. Org. Chem.* **1985**, *50*, 5802-5806

(59)   Seangpprasertkji, R.; Asfari, Z.; Arnaud, F.; Weiss, J.; Vincens, J. *A* Schiff-base *p-tert*-butylcalix[4]arene synthesis and metal ion complexation *J. Incl. Phenom.* **1992**, *14*, 141-147.

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

(61)   Bohmer, V.; Wolff, A.; Vogt, W. A new route to chiral calix[4]arenes *via* 1,3-derivatization, *J. Chem. Soc. Chem. Commun*. **1990**, 968- 970.

(62)   No, K.; Kim, J. M.; Inherently chiral calix[4]arene*, Bull. Korean. Chem. Soc.* **1995**, *16*, 1122-1125.

(63)   Kingston, J. V.; Ozerov, O. V.; Parkin, S.; Brock, C. P.; Ladipo, F. T.; Mechanistic insight into fragmentation reactions of titanapinacolate complexes *J. Am. Chem. Soc.* **2002**, *124*, 12217-12224.

(64)   McMurry, J. E. Carbonyl-coupling reactions using low-valent titanium. *Chem. Rev.* **1989**, *89*, 1513-1524.

(65)   Petek,. H.; Yoshihara, K.; Fujiwara, Y.; Lin, Z.; Penn, J. H.; Frederick, J. H. Is
        the nonradiative decay of *cis*-stilbene due to the dihydrophenanthrene
        isomerization channel? Suggestive evidence from photophysical
        measurements on 1,2-dlphenylcycloaikenes *J. Phys. Chem.* **1990**, *94*, 7539-
        7543.

APPENDICES
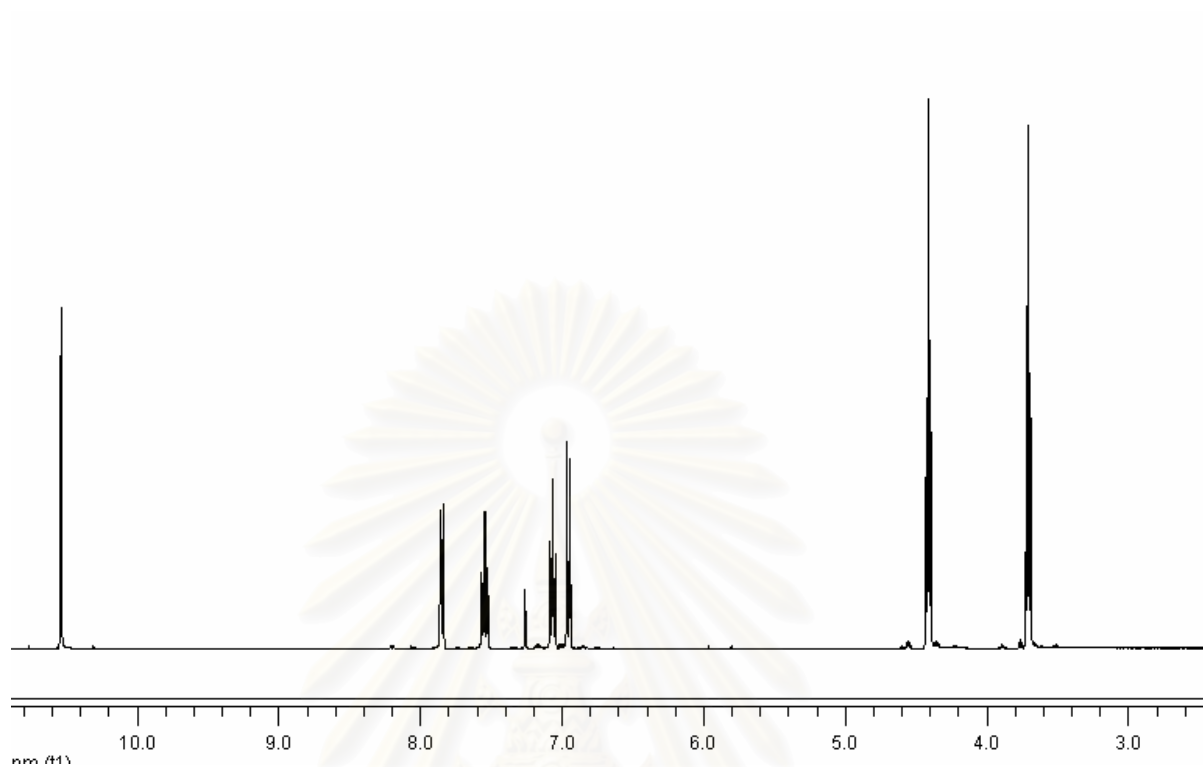
Figure A.1 ^{1}H NMR of *o*- (2-Bromoethoxy)benzaldehyde
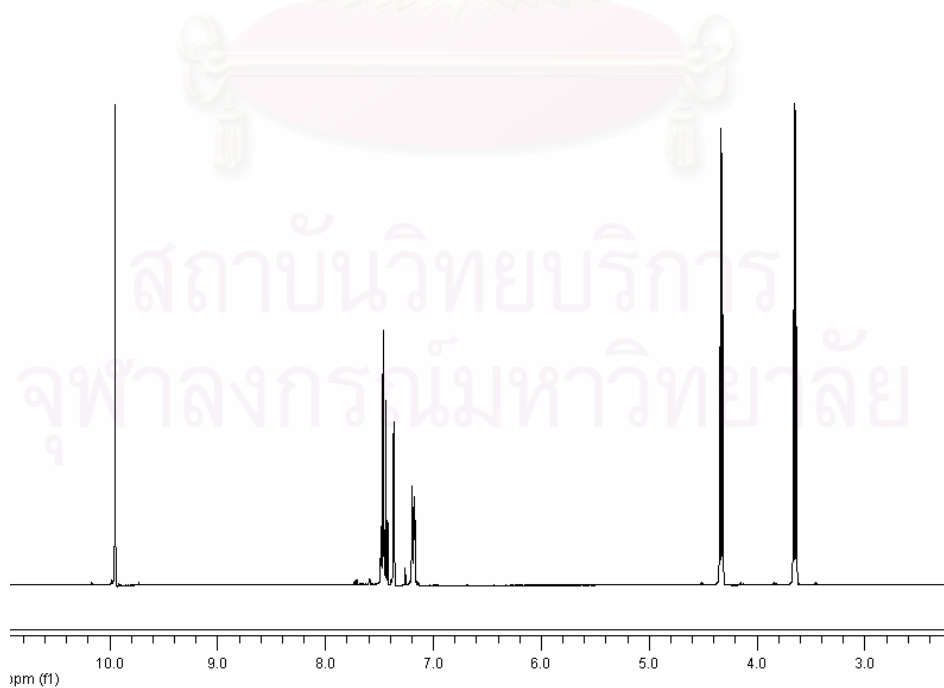
Figure A.2 ^{1}H NMR of *m*-(2-Bromoethoxy)benzaldehyde
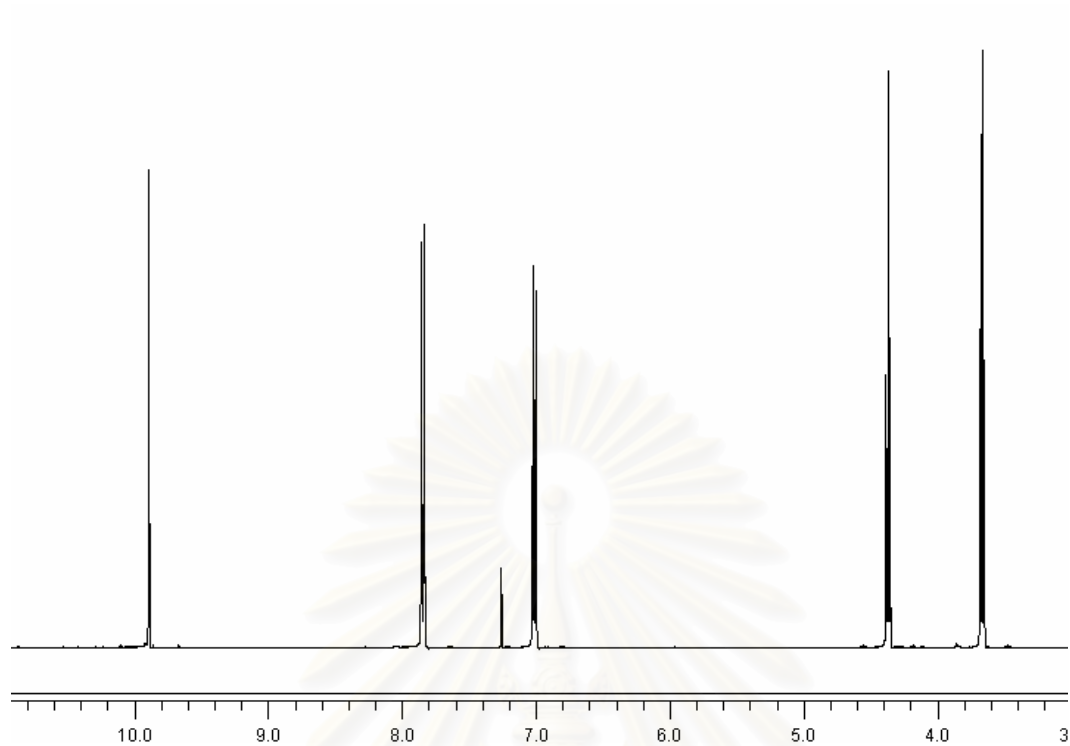
Figure A.3 ¹H NMR of *p*-(2-Bromoethoxy)benzaldehyde
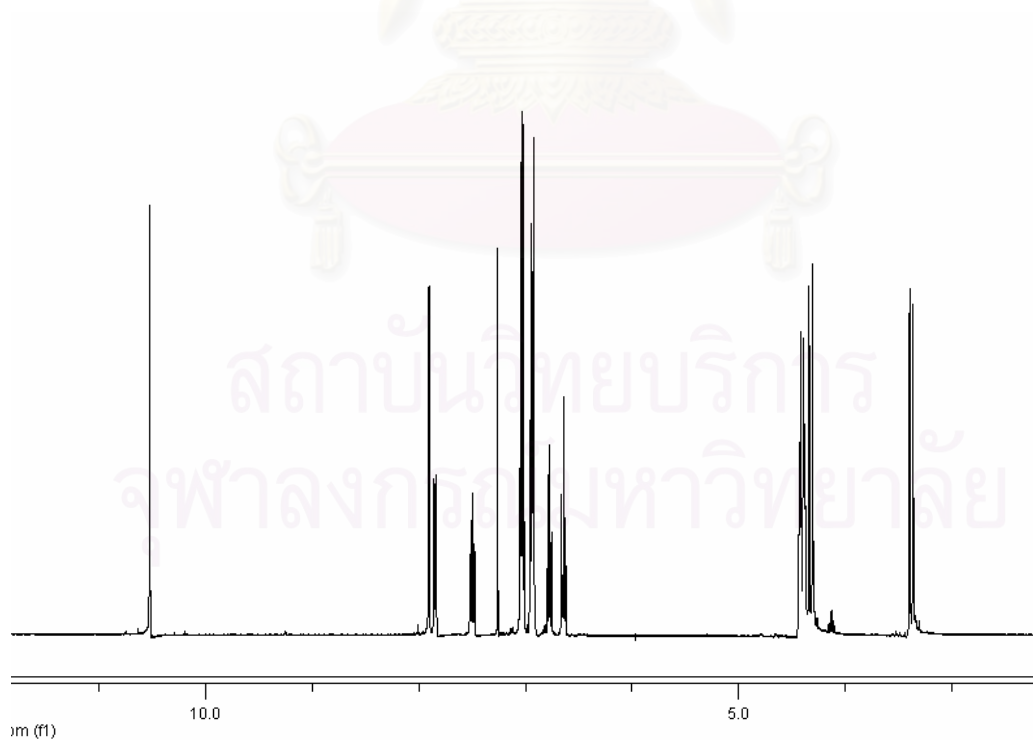
Figure A.4 ¹H NMR of   *o*-Stilbene-bridged calix[4]arene **1**
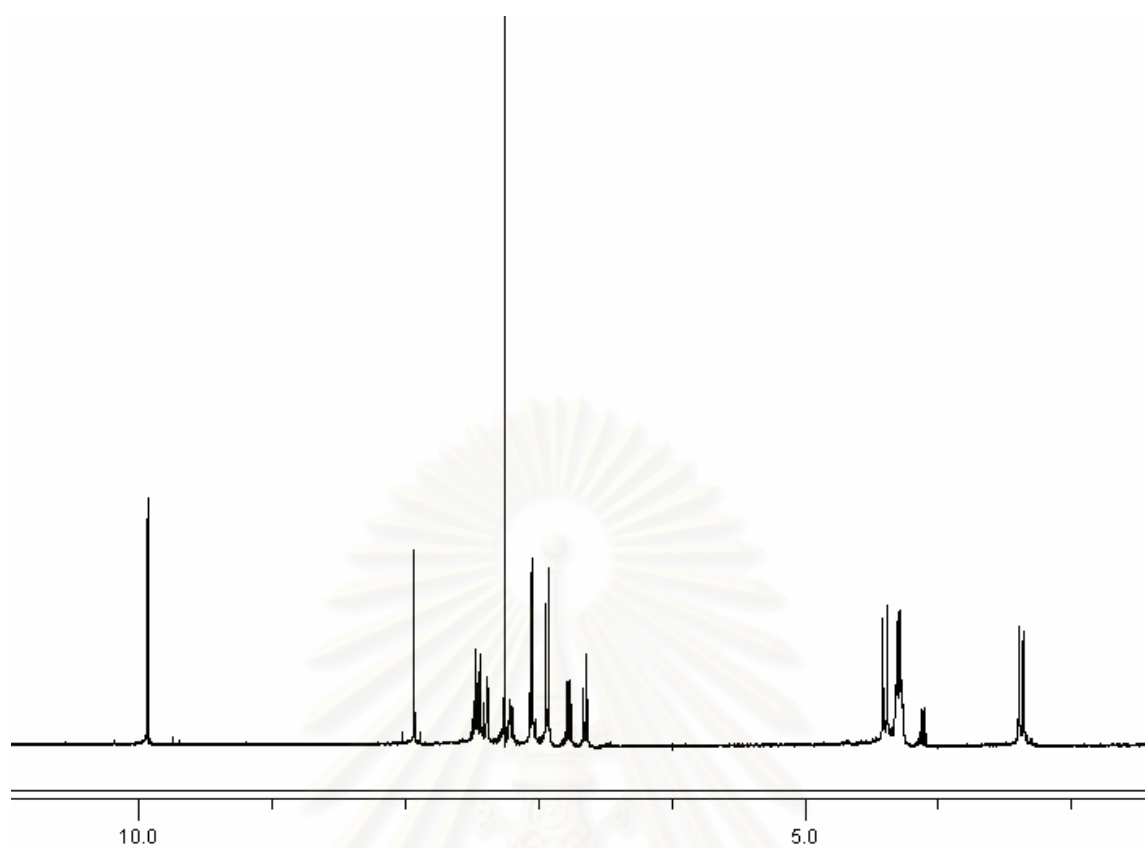
Figure A.5 ^{1}H NMR of *m*-Stilbene-bridged calix[4]arene **1**
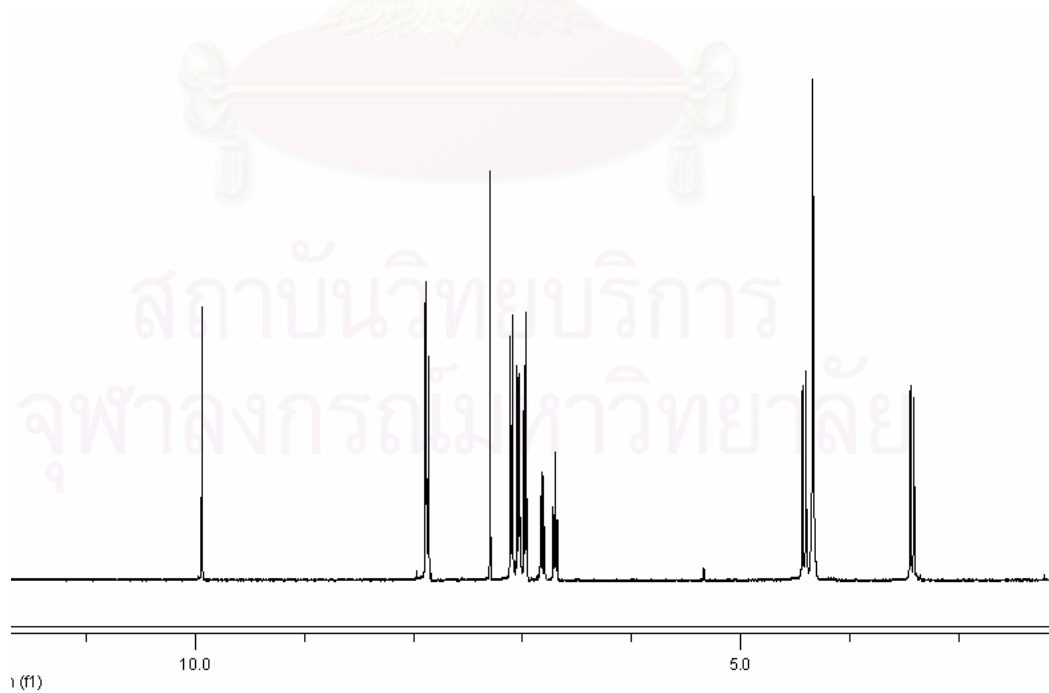
Figure A.6 ^{1}H NMR of *p*-Stilbene-bridged calix[4]arene **1**
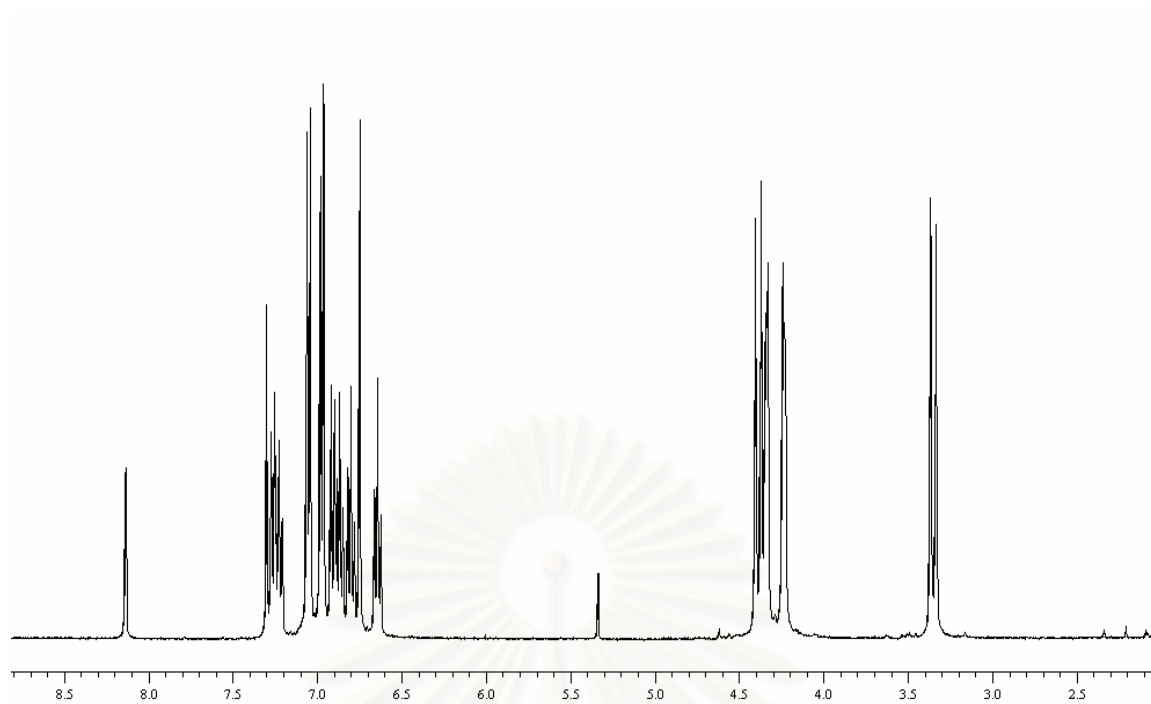
Figure A.7 ^{1}H NMR of *o-cis*-Stilbene bridged calix[4]arene **2**
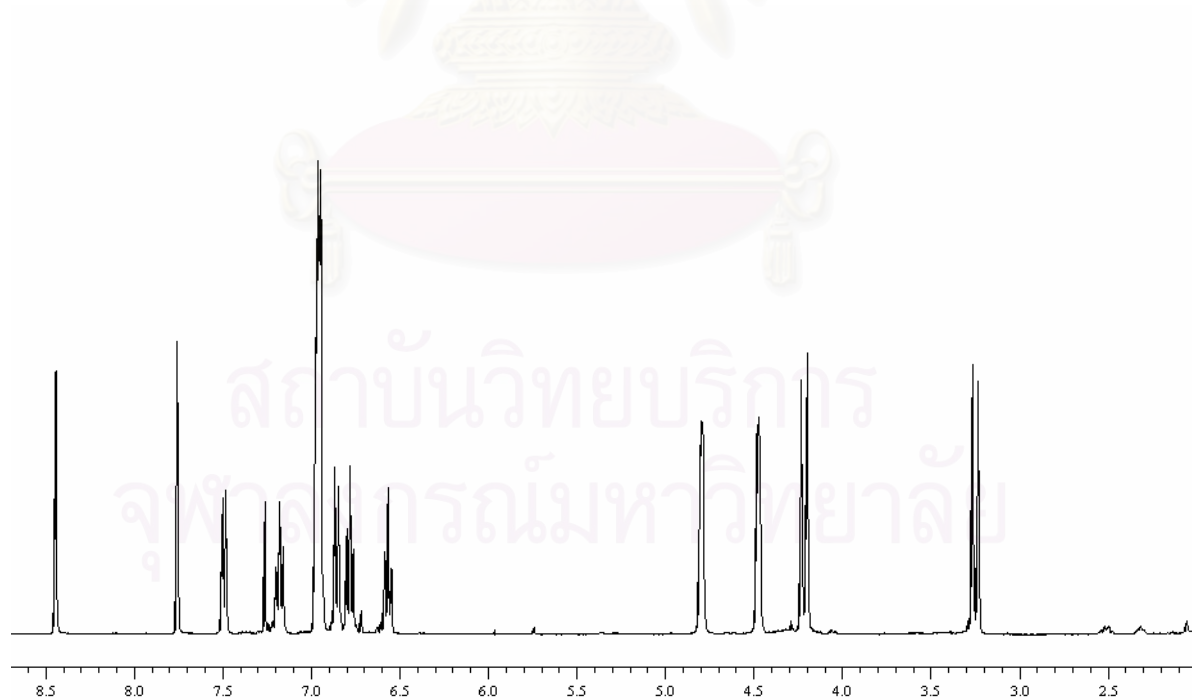
Figure A.8 ^{1}H NMR of *o-trans*-Stilbene bridged calix[4]arene **2**
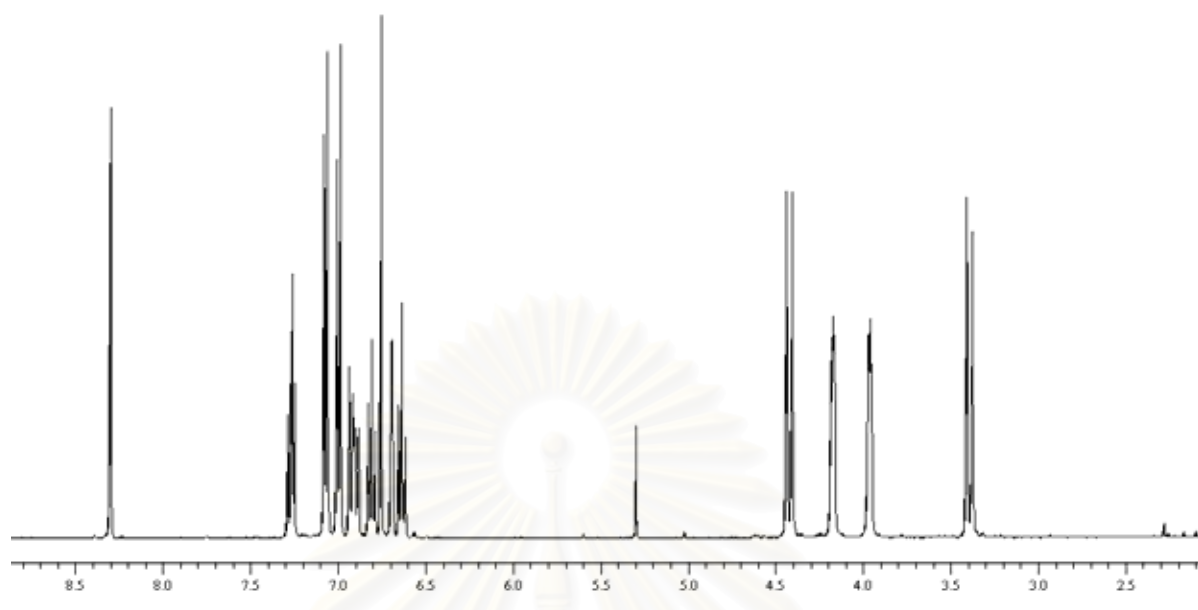
Figure A.9 ^{1}H NMR of *m-cis*-Stilbene bridged calix[4]arene **2**
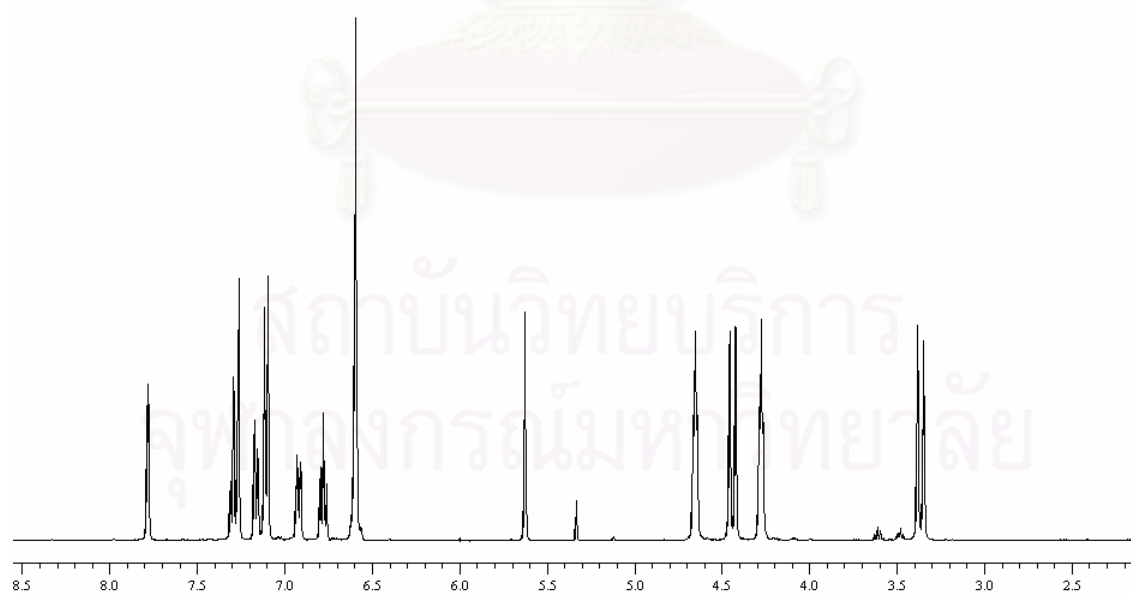
Figure A.10 ^{1}H NMR of *m-trans*-Stilbene bridged calix[4]arene **2**
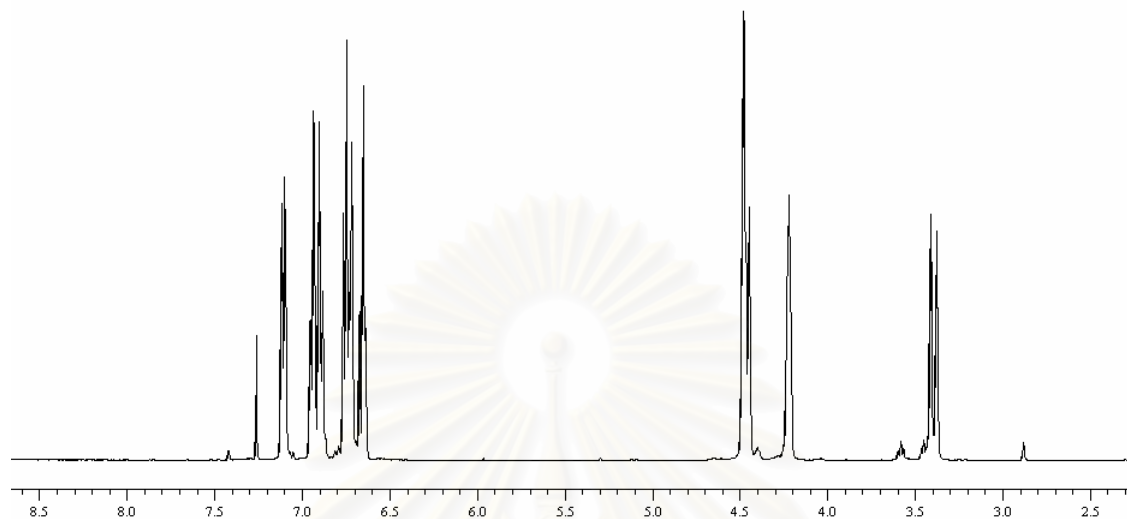
Figure A.11 [^1]H NMR of *p-cis*-Stilbene bridged calix[4]arene **2**
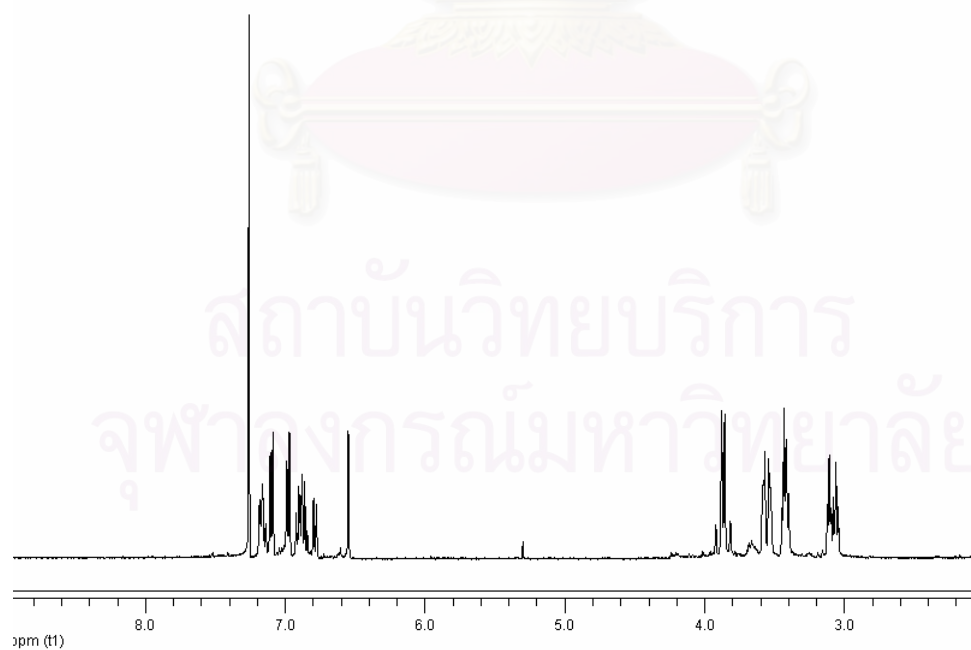
Figure A.12 [^1]H NMR of *o-cis*-Stilbene bridged calix[4]arene crown-5 **3**
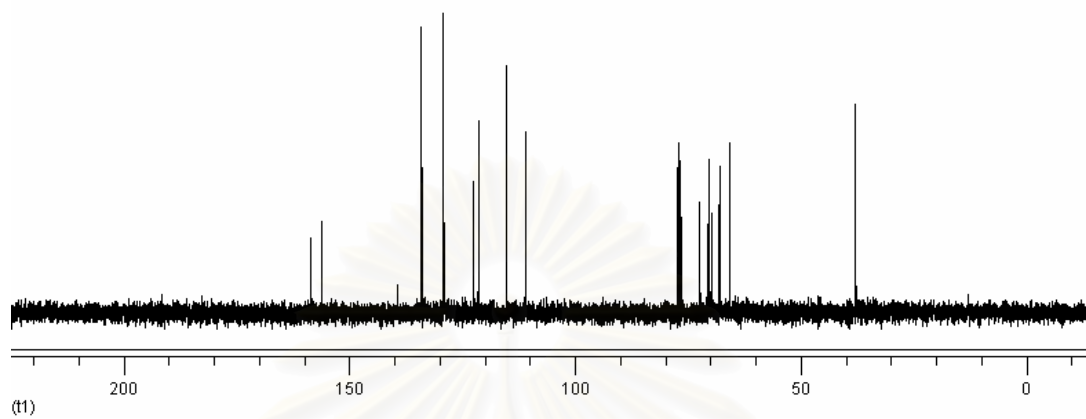
Figure A.13 ^{13}C NMR of *o-cis*-Stilbene bridged calix[4]arene crown-5 **3**
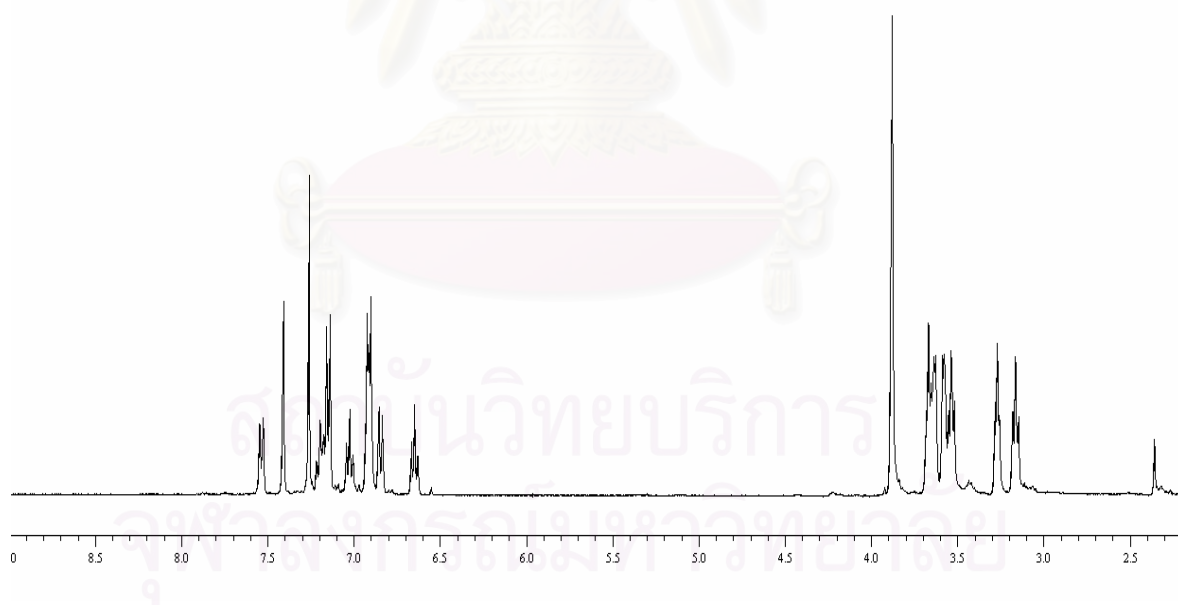
Figure A.14 ^{1}H NMR of *o-trans*-Stilbene bridged calix[4]arene crown-5 **3**
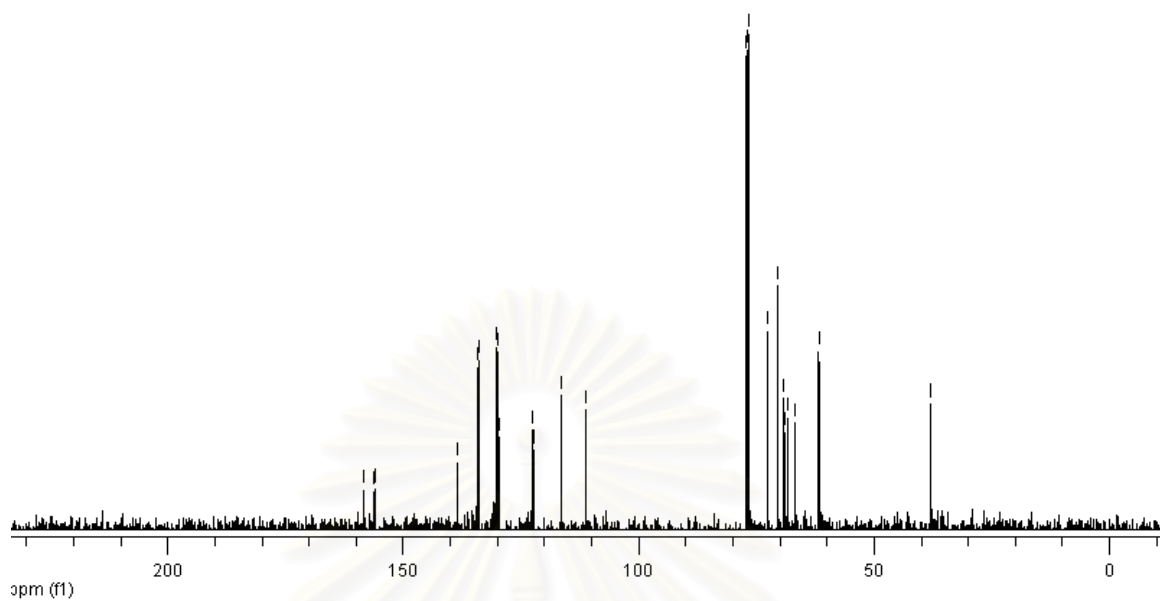
Figure A.15 ^{13}C NMR of *otrans*-Stilbene bridged calix[4]arene crown-5 **3**
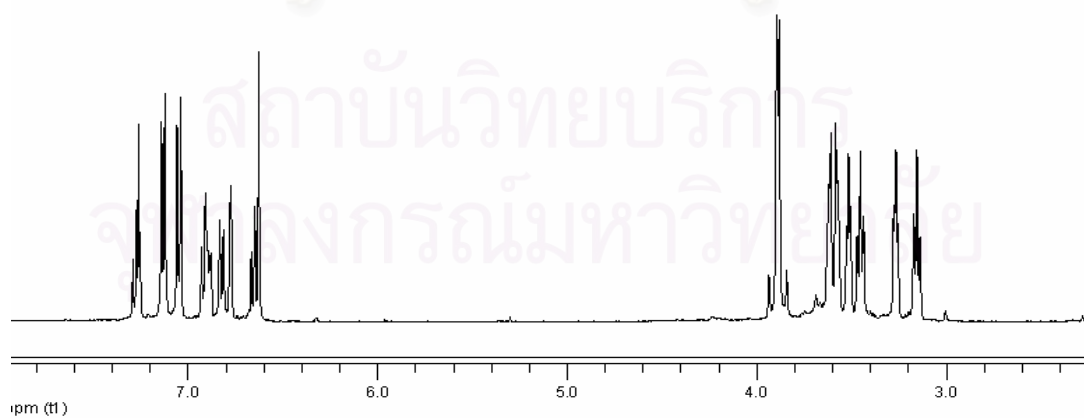
Figure A.16 ^{1}H NMR of *m-cis*-Stilbene bridged calix[4]arene crown-5 **3**
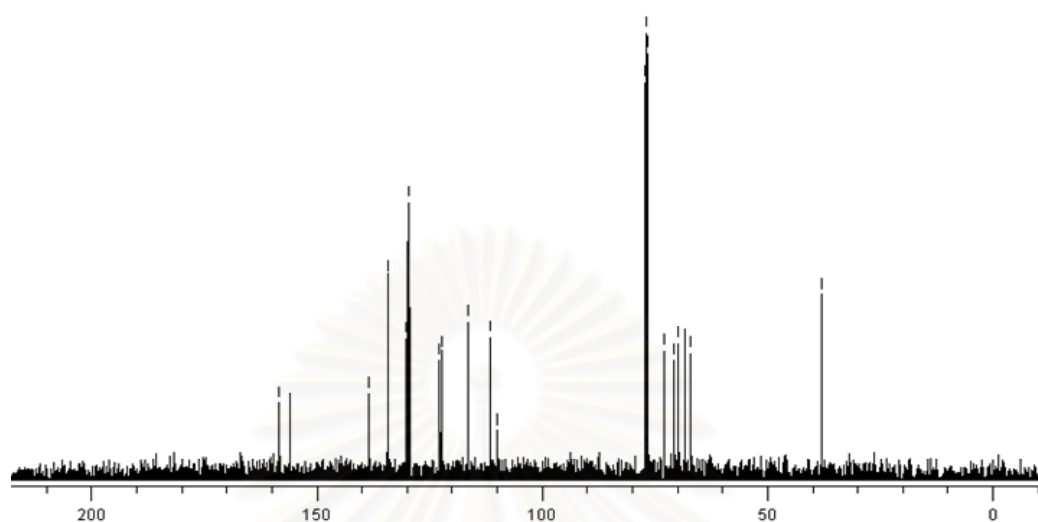
Figure A.17 ^{13}C NMR of *m-cis*-Stilbene bridged calix[4]arene crown-5 **3**
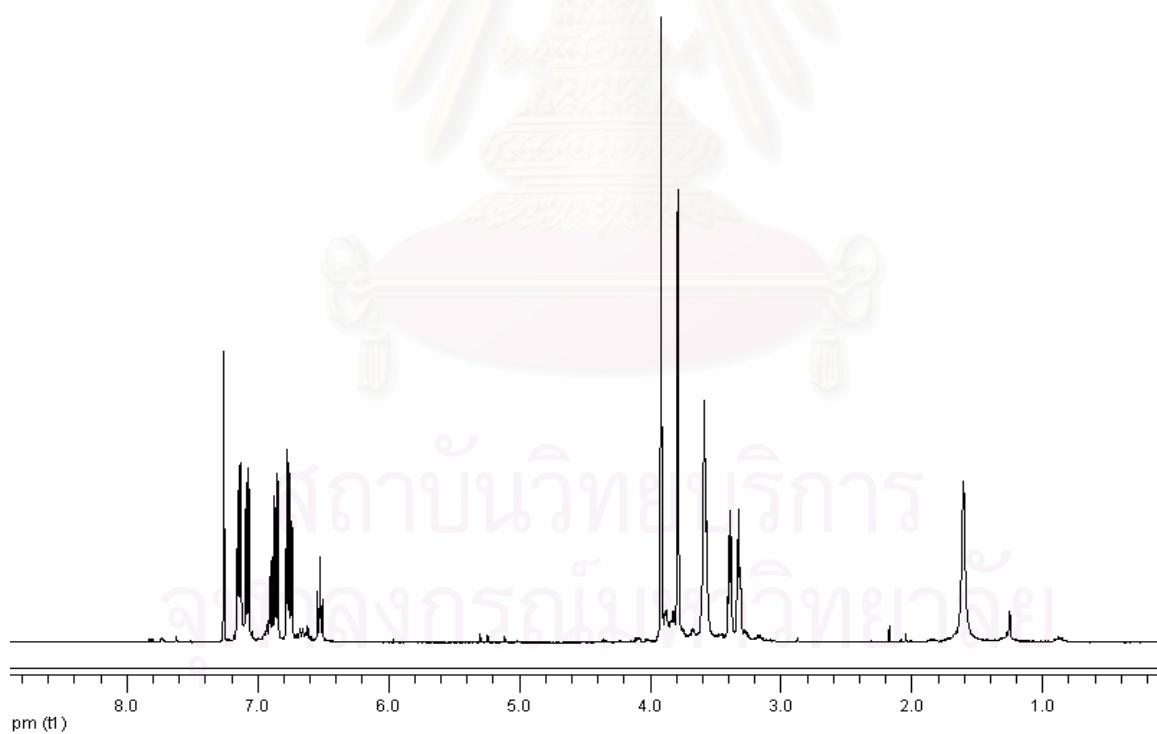
Figure A.18 ^{1}H NMR of *p-cis*-Stilbene bridged calix[4]arene crown-5 **3**
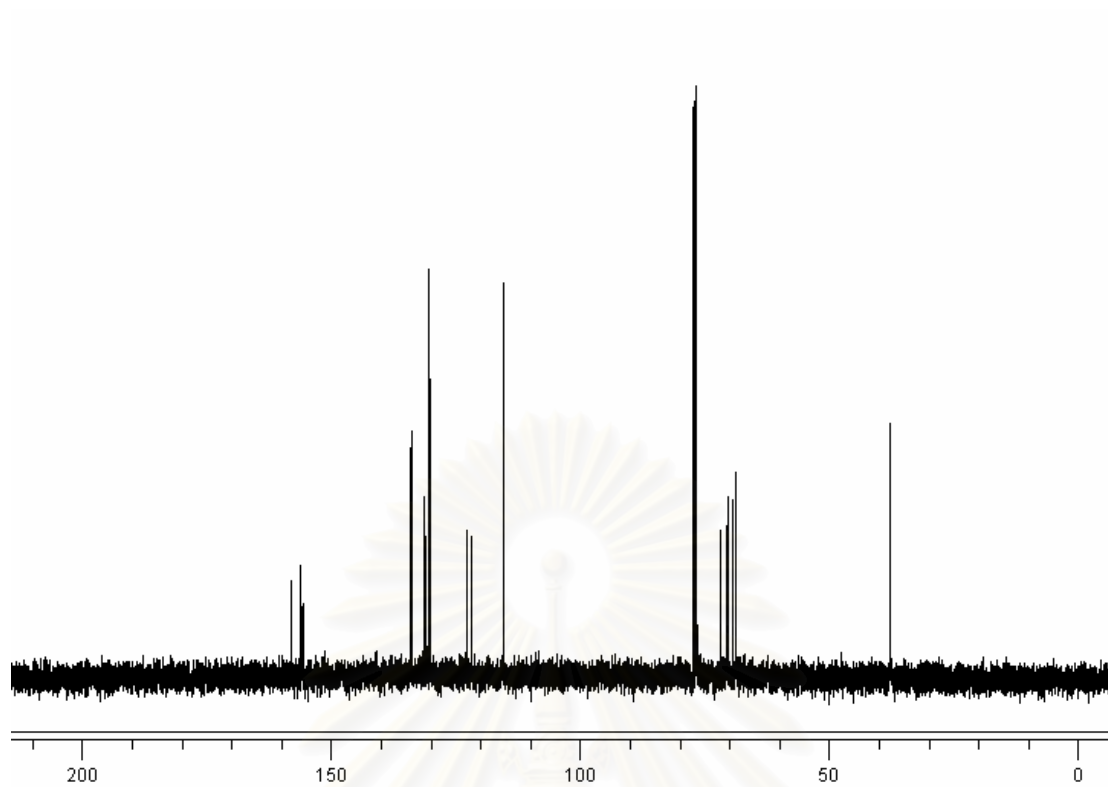
Figure A.19 ^{13}C NMR of *p-cis*-Stilbene bridged calix[4]arene crown-5 **3**
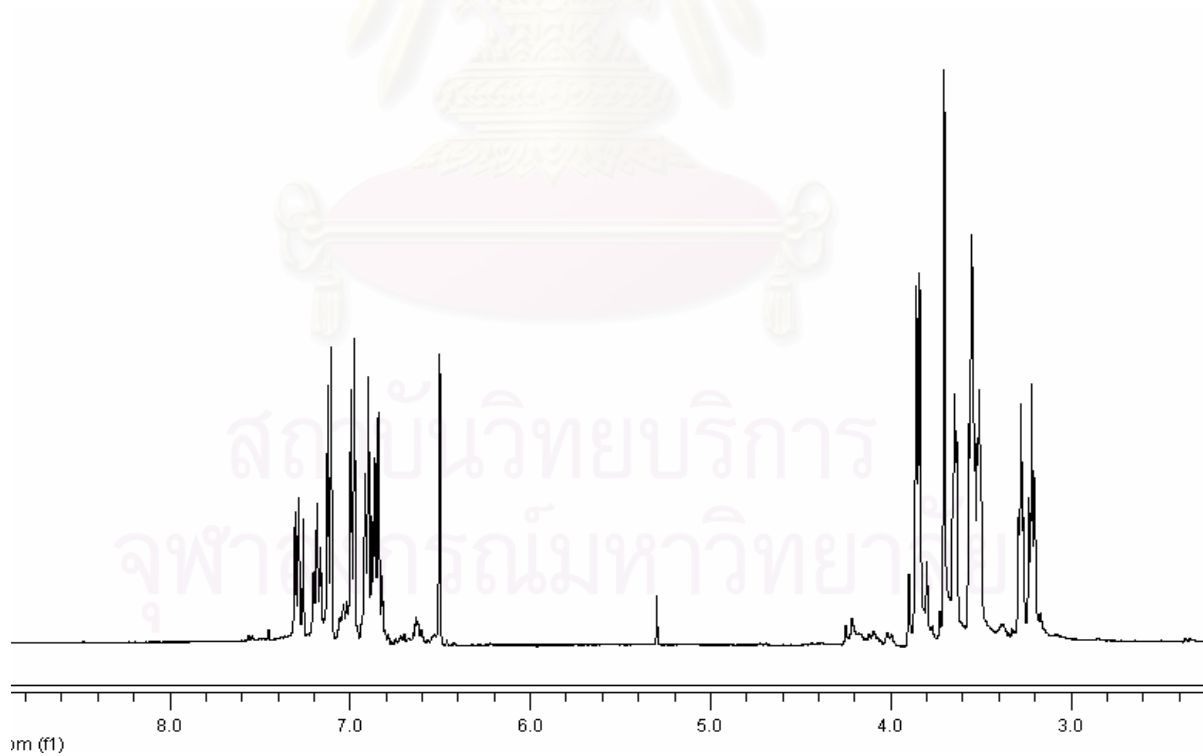
Figure A.20 ^{1}H NMR of *o-cis*-Stilbene bridged calix[4]arene crown-6 **4**

7.0   6.0   5.0   4.0   3.0

ppm (t1)
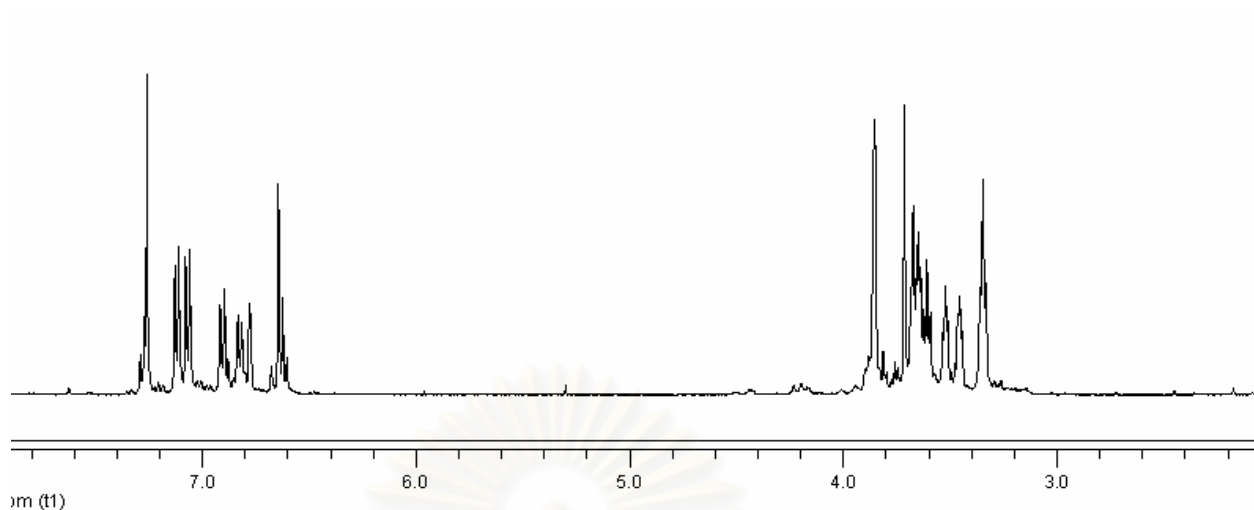
Figure A.21 ^{1}H NMR of *m-cis*-Stilbene bridged calix[4]arene crown-6 **4**

8.0   7.0   6.0   5.0   4.0   3.0

ppm (t1)
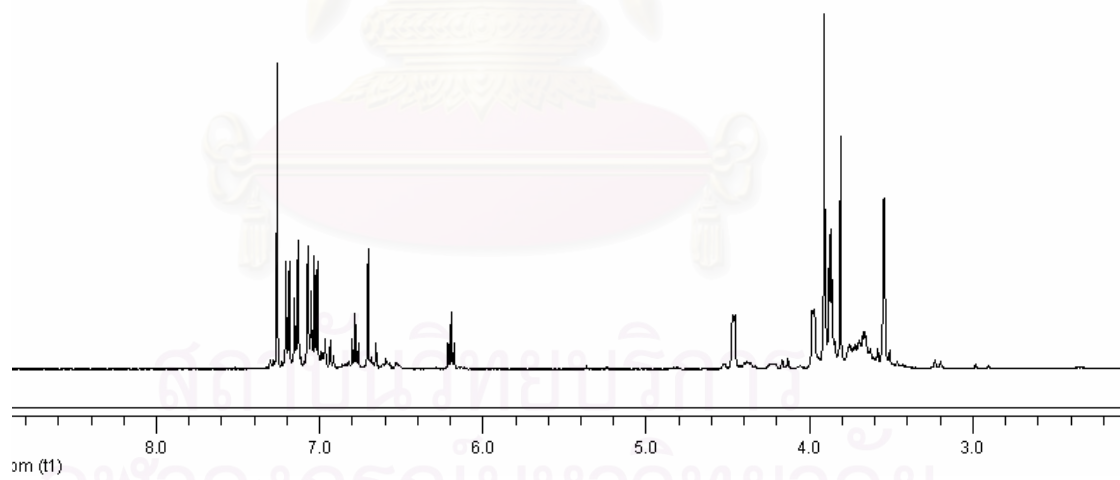
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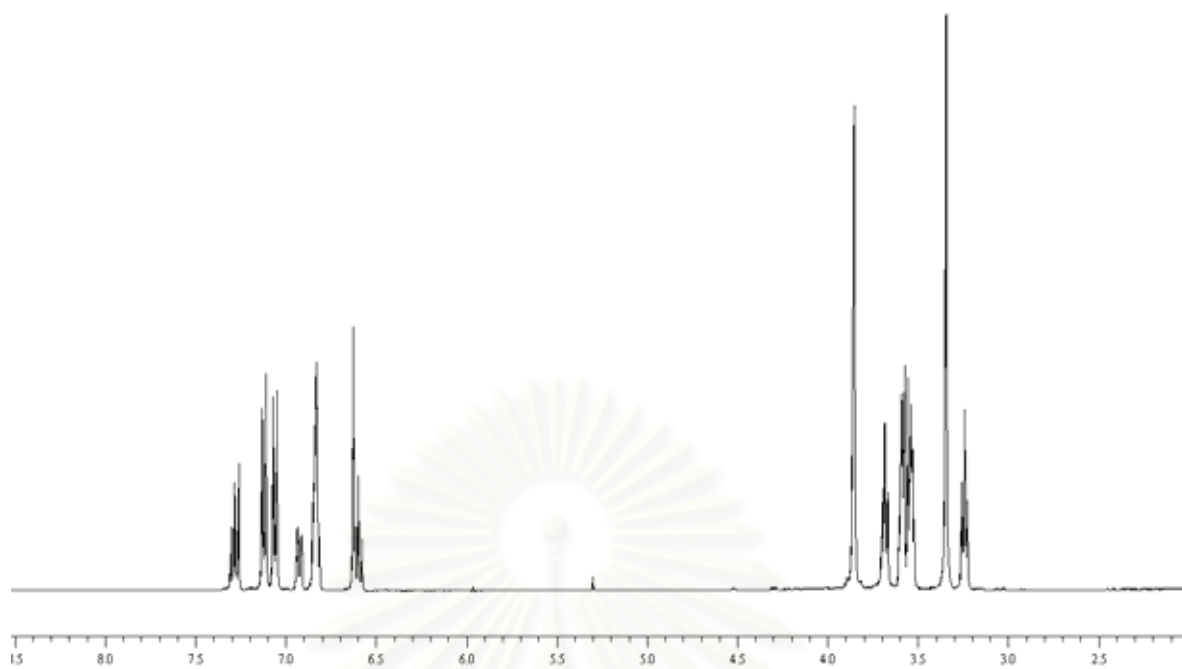
Figure A.23 ^{1}H NMR of *m-cis*-Stilbene calix[4]arene diethylene glycol ethyl ether **5**
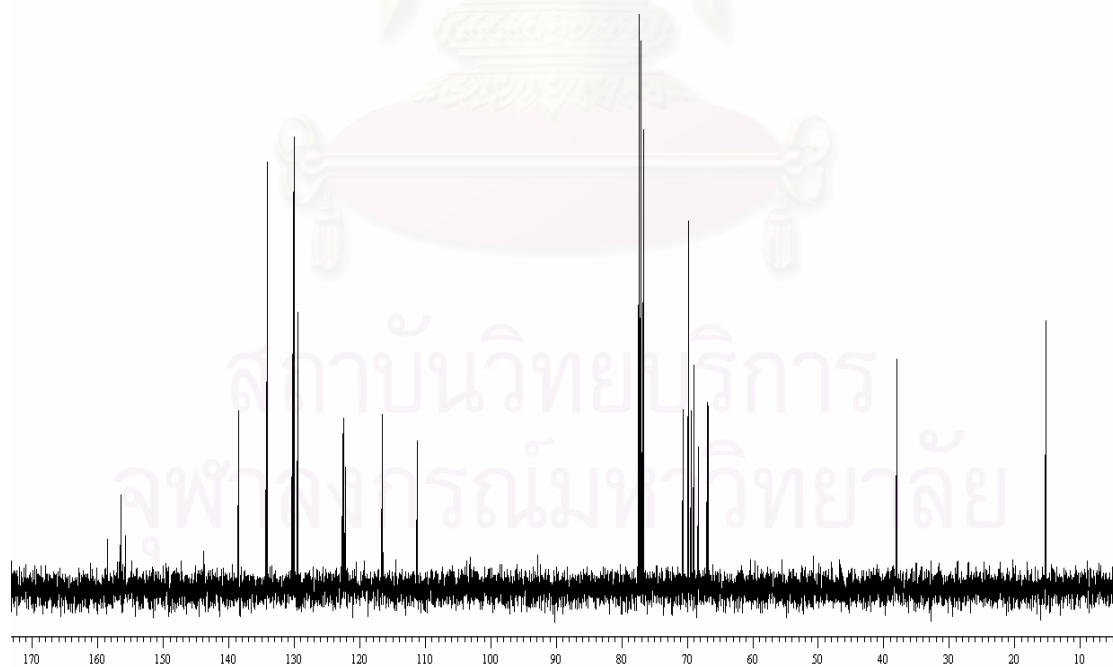
Figure A.24 ^{13}C NMR of *m-cis*-Stilbene calix[4]arene diethylene glycol ethyl ether **5**
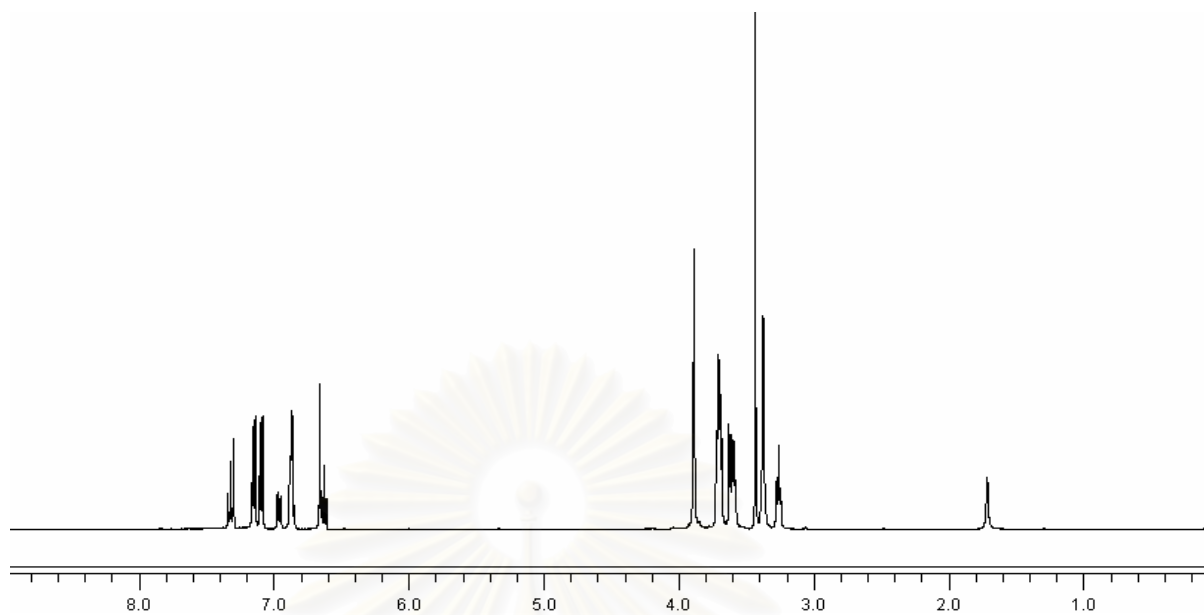
Figure A.25 ¹H NMR of *m-cis* Stilbene calix[4]arene triethylene glycol monomethylether **6**
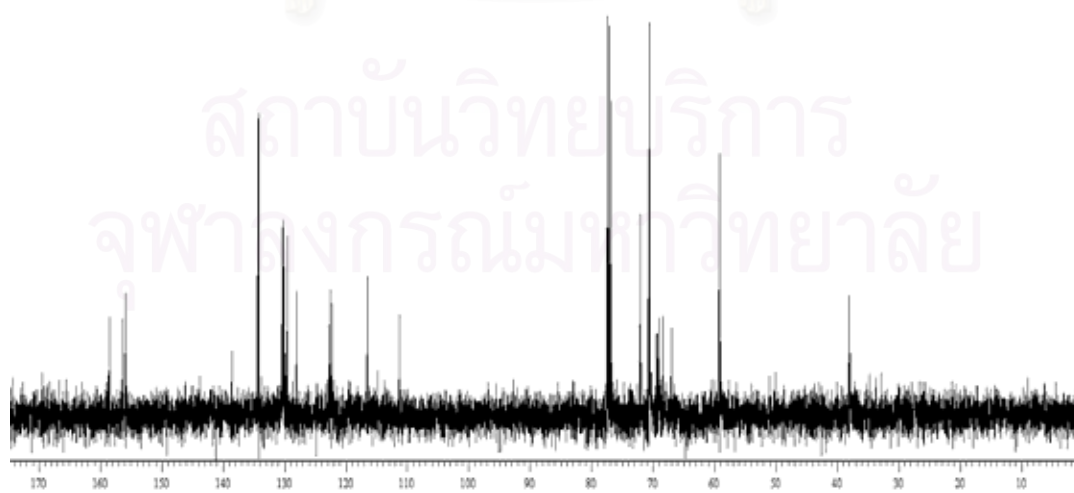
Figure A.26 ¹³C NMR of *m-cis* Stilbene calix[4]arene triethylene glycol monomethylether **6**
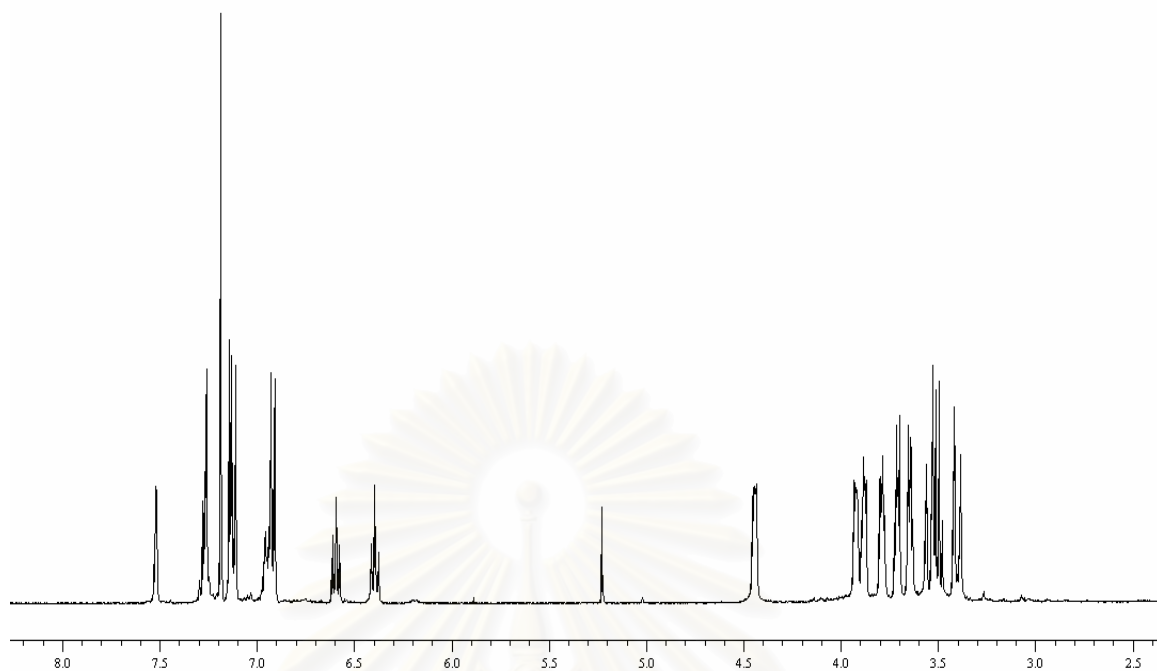
Figure A.27 ^{1}H NMR of *m-trans*-Stilbene calix[4]arene diethylene glycol ethyl
ether **7**
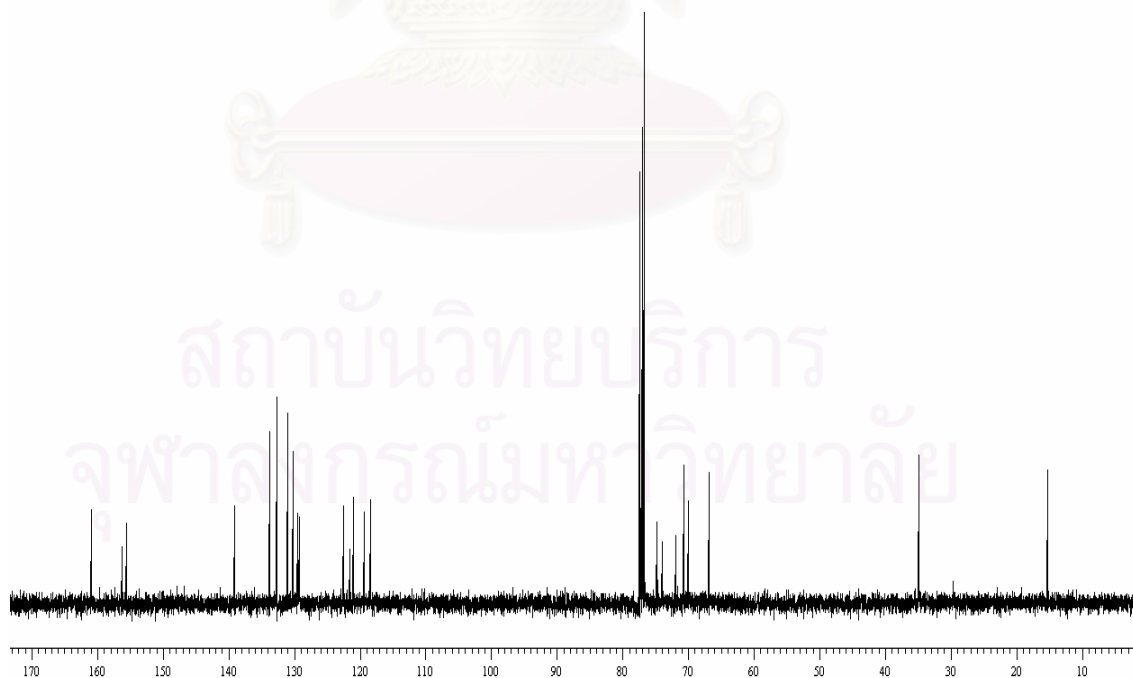
Figure A.28 ^{13}C NMR of *m-trans*-Stilbene calix[4]arene diethylene glycol ethyl ether **7**
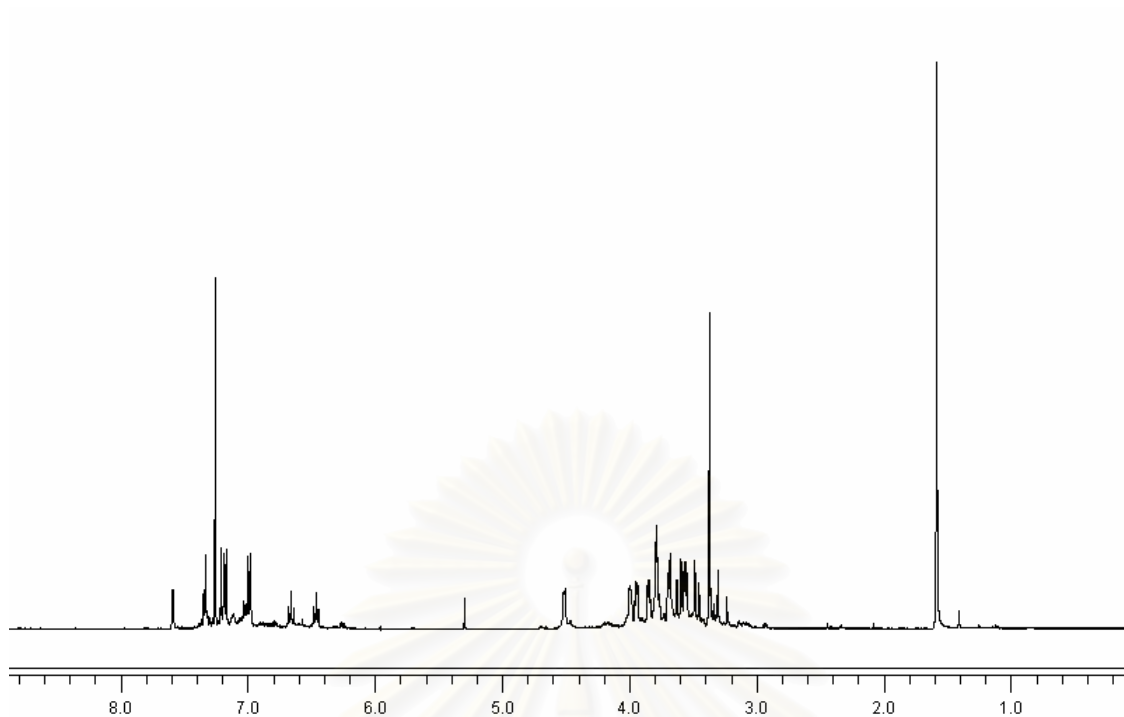
Figure A.29 ^{1}H NMR of *m-trans* Stilbene calix[4]arene triethylene glycol monomethylether cone conformation **8**
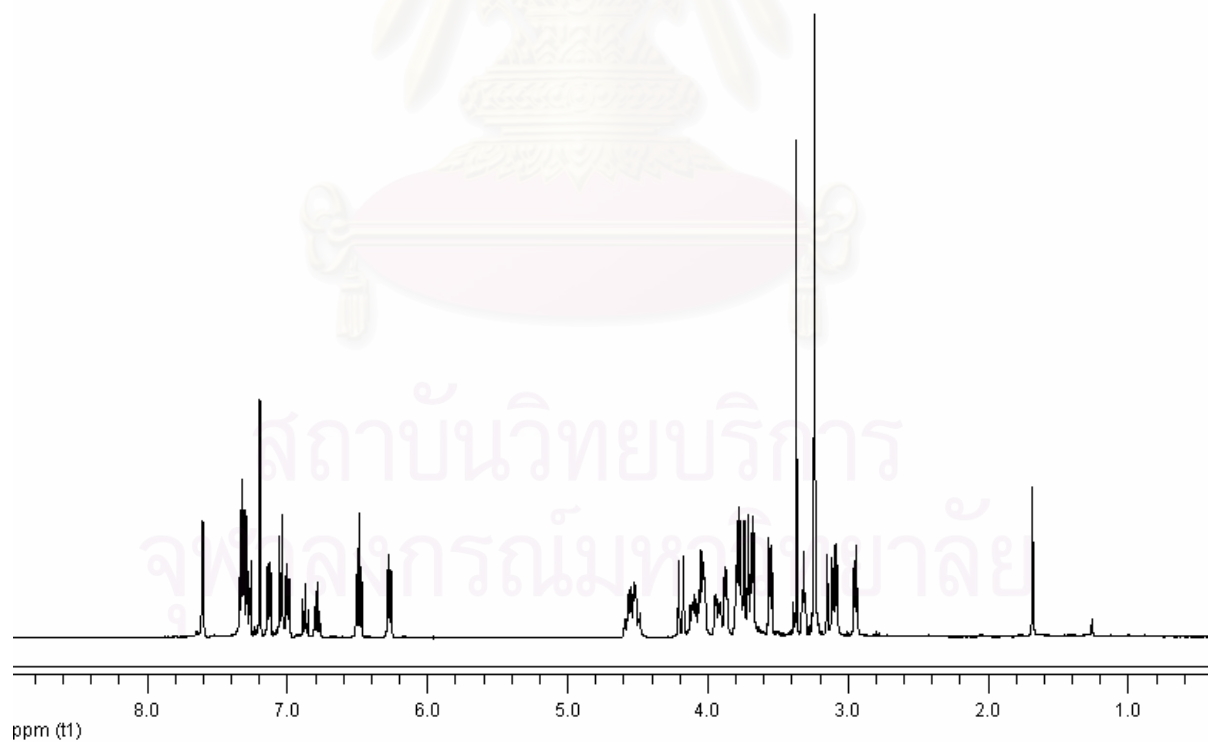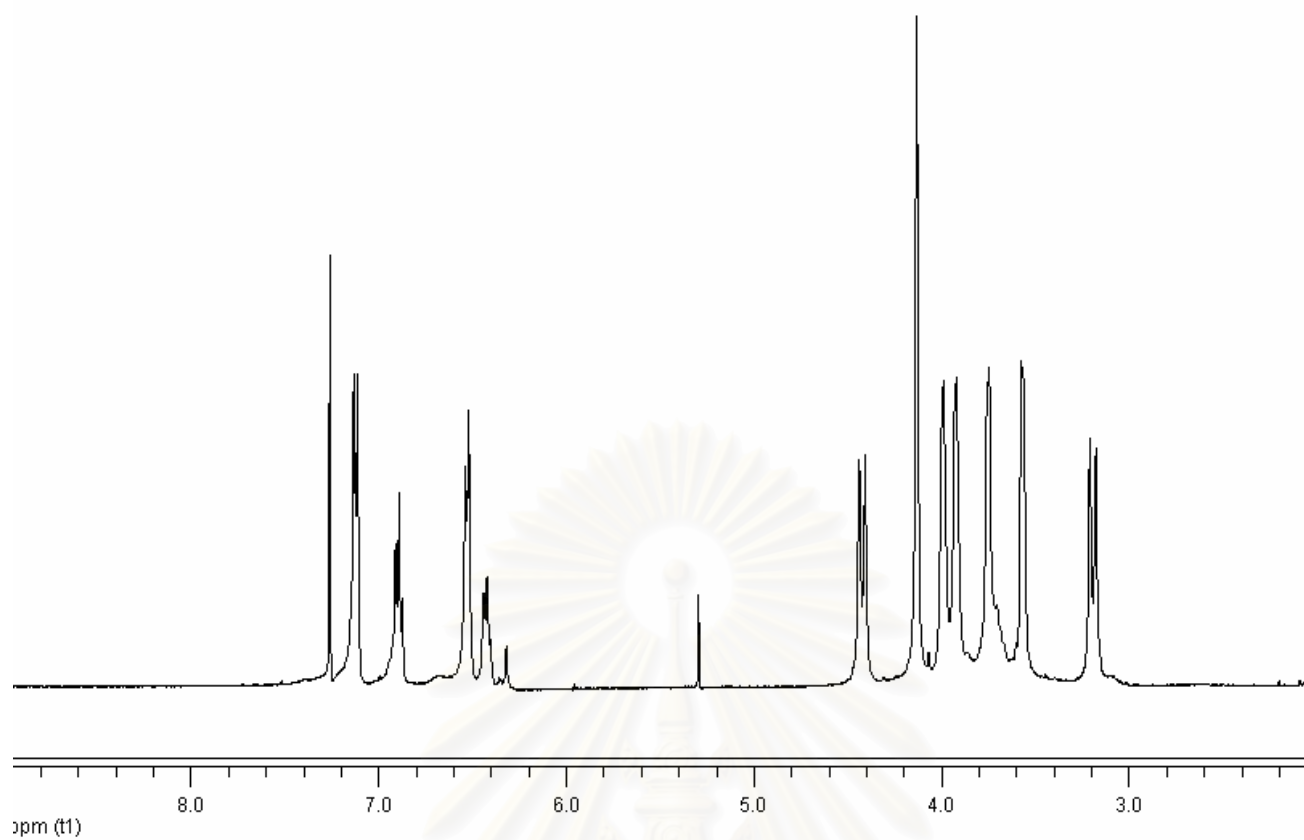

Figure A.30 ^{1}H NMR of *m-trans* Stilbene calix[4]arene triethylene glycol monomethylether partial cone conformation **9**
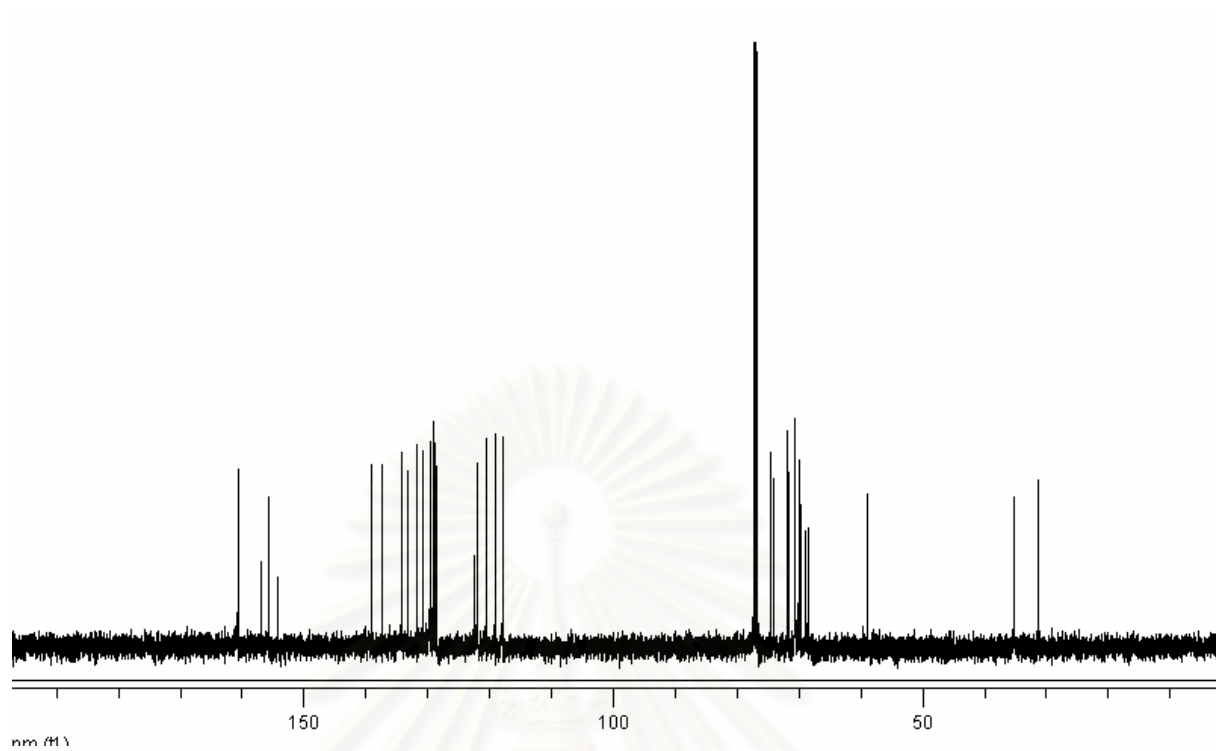
Figure A.31 ^{13}C NMR of *m-trans* Stilbene calix[4]arene triethylene glycol
monomethylether partial cone conformation **9**
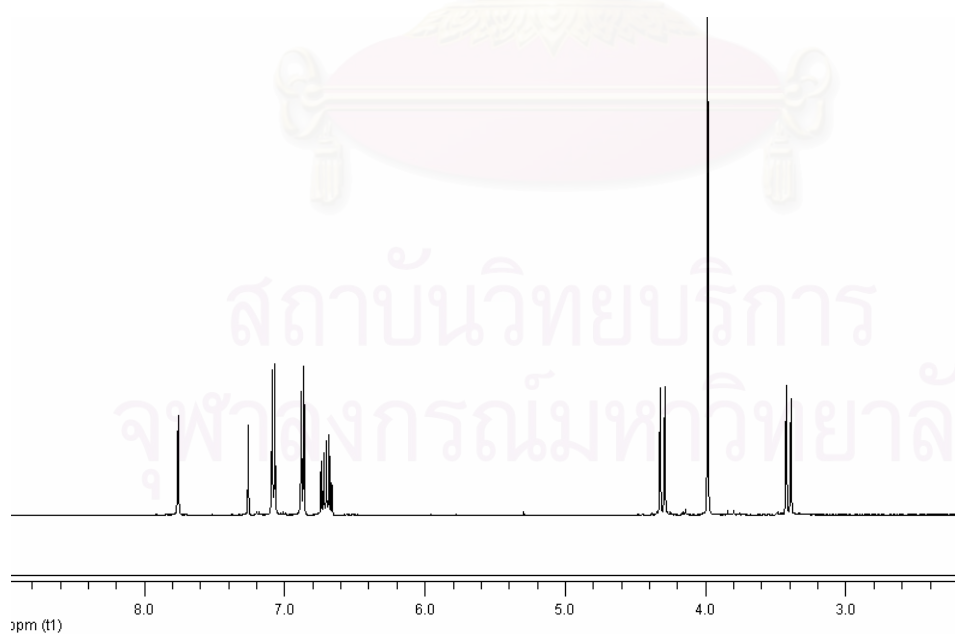
Figure A.32 ^{1}H NMR of dimethyl calix[4]arene

Figure A.33 ^{1}H NMR of O,O'-dimethylcalix[4]arene crown-5 **12**
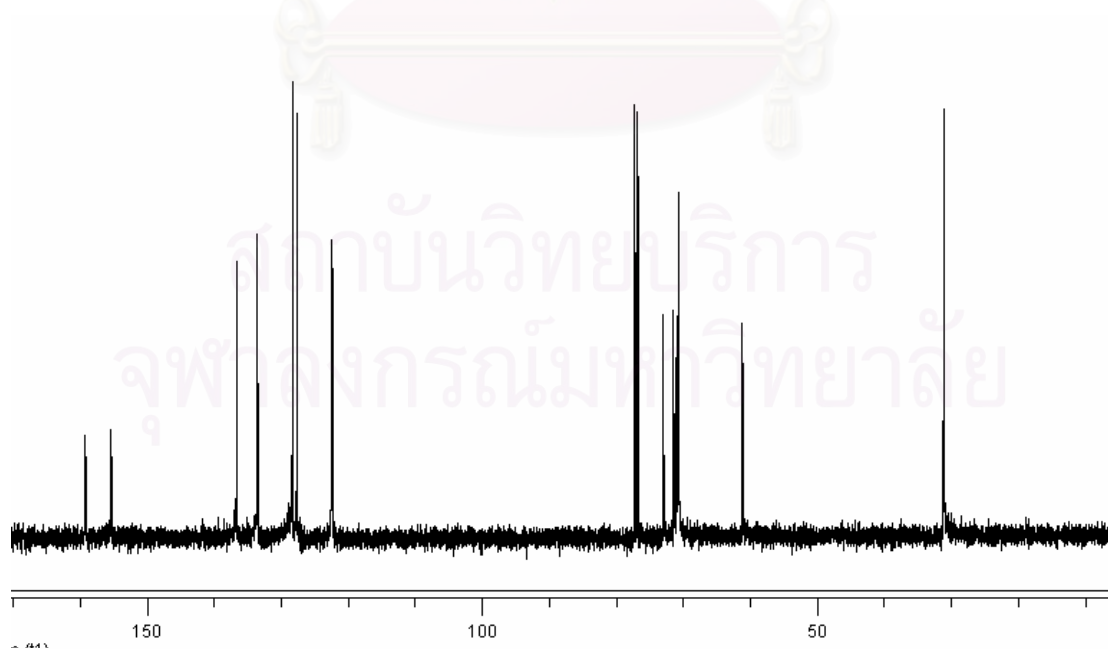
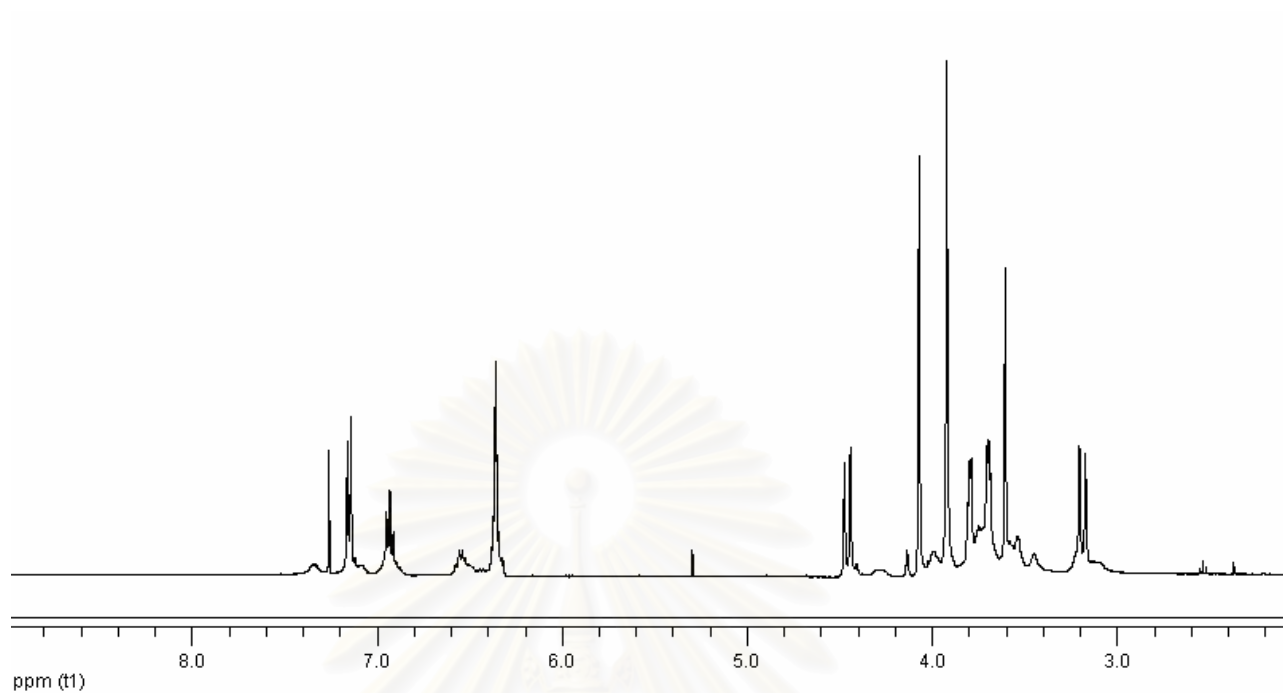**Figure A.34** ^{13}C NMR of O,O'-dimethylcalix[4]arene crown-5 **12**

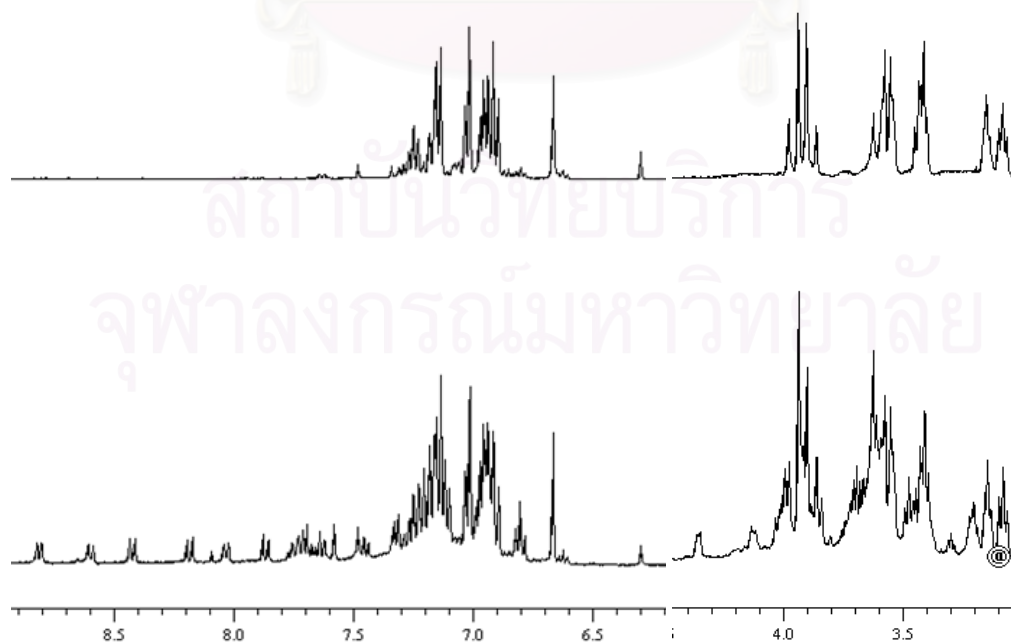**Figure A.35** ^{1}H NMR of *O,O′*-dimethylcalix[4]arene crown-5 **13**

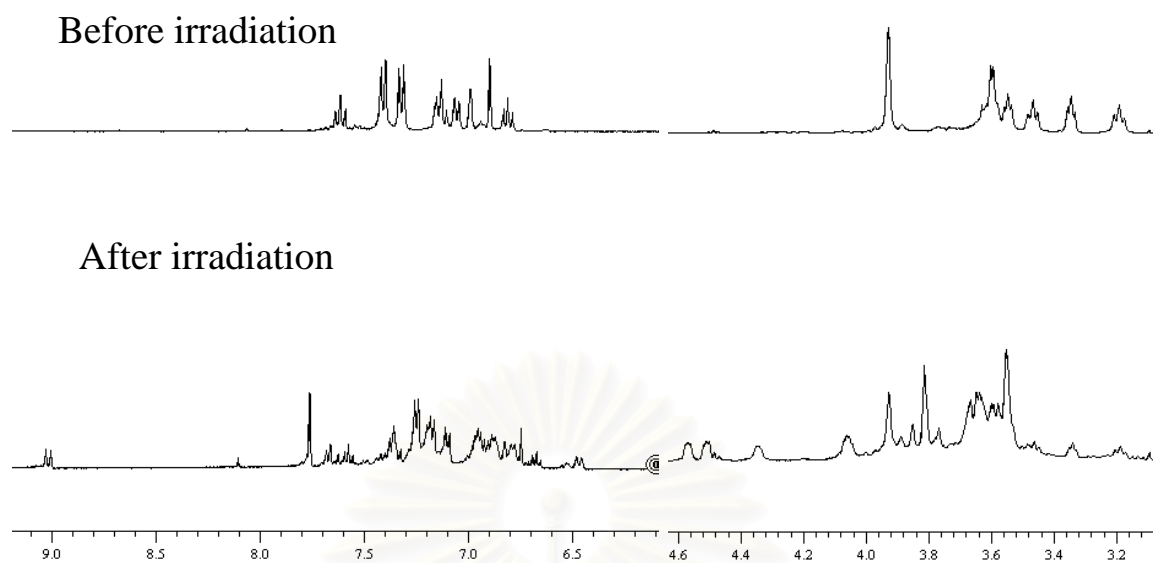**Figure A.36** ^{1}H NMR of *o-cis*-**3** before and after irradiated upon UV light

Before irradiation

After irradiation

Figure A.37 ^{1}H NMR of *m-cis-***3** before and after irradiated upon UV light

Figure B.1 X-ray structure of *m-trans*-**2**
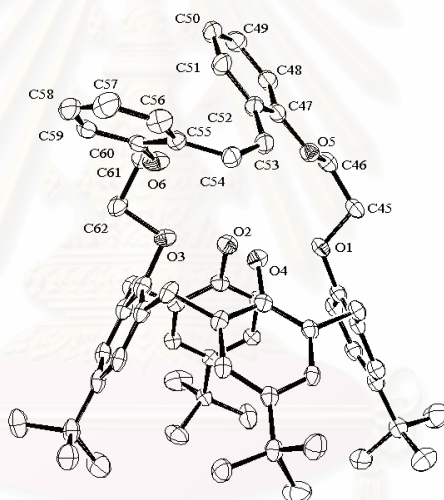

Figure B.2 X-ray structure of *o-cis*-**10**
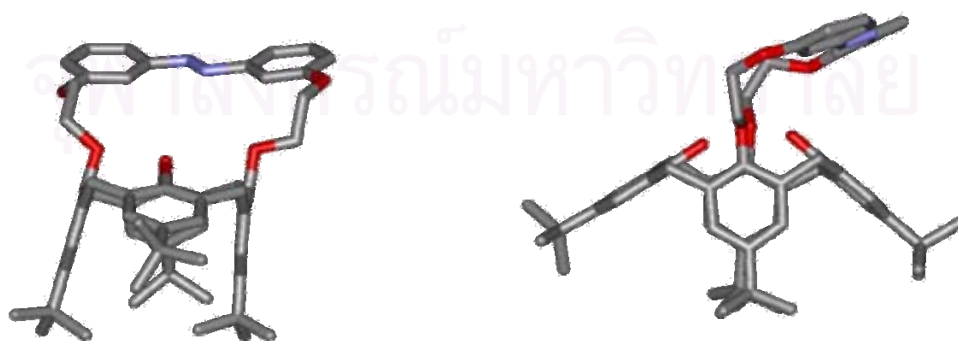
Figure B.2 X-ray structure of *m-trans*-**11**

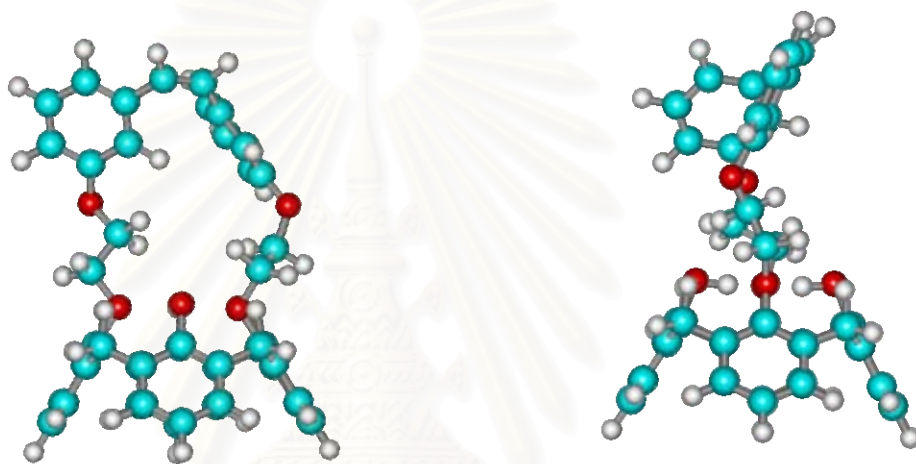**Figure B.3** X-ray structure of *o-trans*-**11**
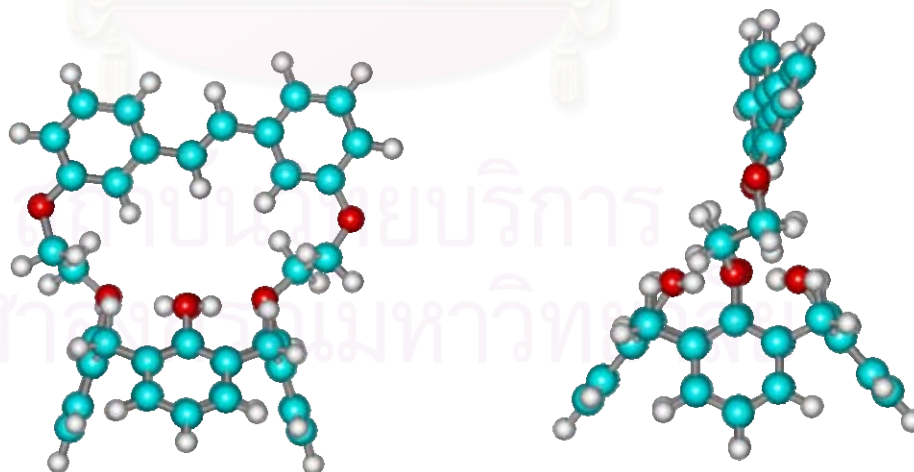

Figure B.4 AM1 structure of *m-cis*-**2**

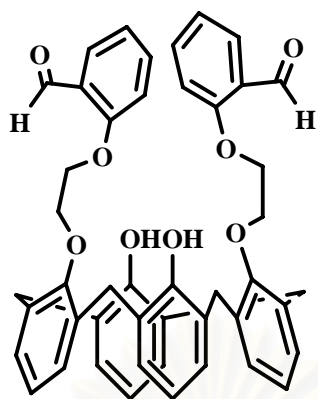**Figure B.5** AM1 stucture of *m-trans*-**2**

Figure C.1. *o-1: ortho*-Bisbenzaldehyde calix[4]arene
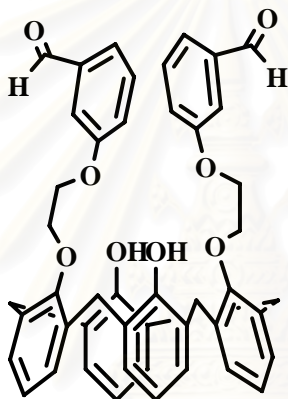

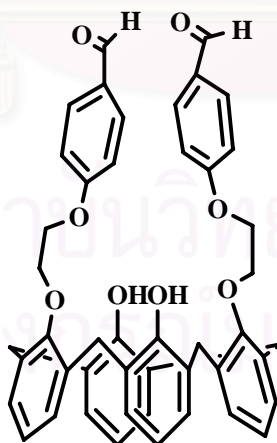**Figure C.2** *m-1: meta*-Bisbenzaldehyde calix[4]arene

Figure C.3 *p-1: para*- Bisbenzaldehyde calix[4]arene
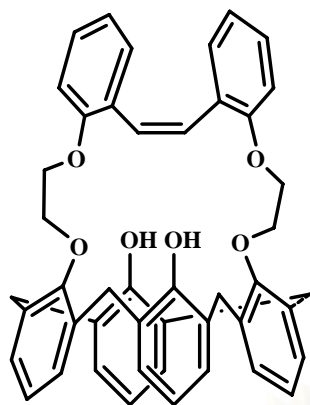
Figure C.4 *o-cis*-2: *ortho-cis*-Stilbene-bridged calix[4]arene
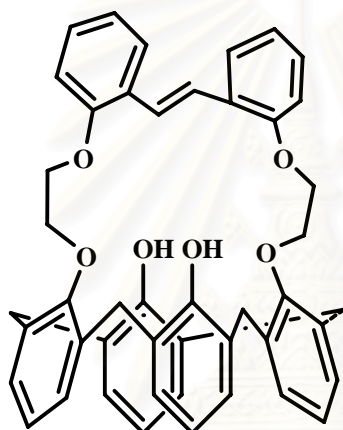
Figure C.5 *o-trans* -2: *ortho-trans*-Stilbene-bridged calix[4]arene
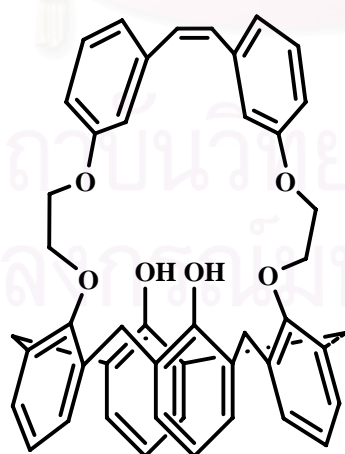
Figure C.6 *m-cis*-2: *meta-cis*-Stilbene-bridged calix[4]arene
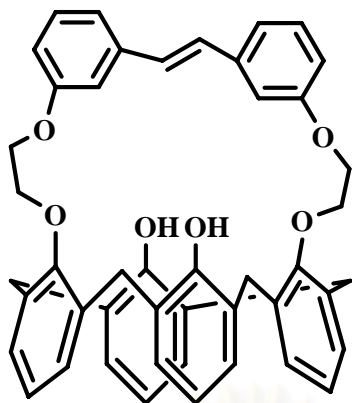
Figure C.7 *m-trans*-2: *meta-trans*-Stilbene-bridged calix[4]arene
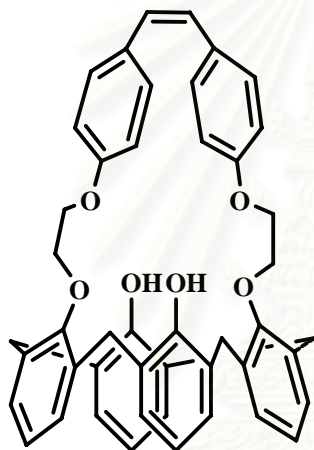
Figure C.8 *p-cis*-2: *para-cis*-Stilbene-bridged calix[4]arene
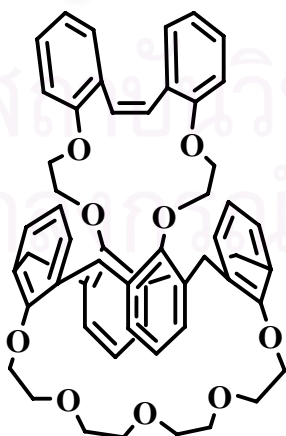
Figure C.9 *o-cis*-3: *ortho-cis*-Stilbene-bridged calix[4]arene crown-5
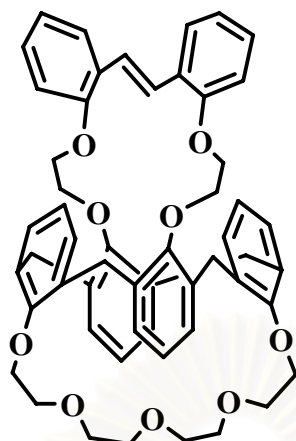
Figure C.10 *o-trans*-**3**: *ortho-trans*-Stilbene-bridged Calix[4]arene crown-5
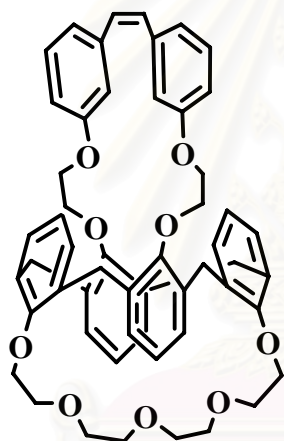
Figure C.11 *m-cis*-**3**: *meta-cis*-Stilbene-bridged calix[4]arene crown-5
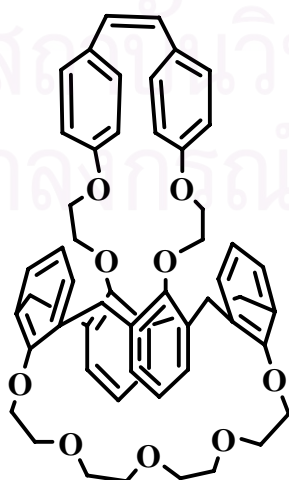
Figure C.12 *p-cis*-**3**: *para-cis*-Stilbene-bridged calix[4]arene crown-5
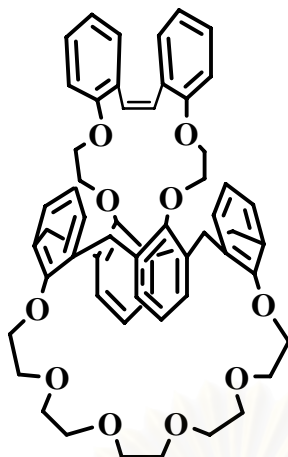
FigureC.13 *o-cis*-4: *ortho-cis*-Stilbene-bridged calix[4]arene crown-6
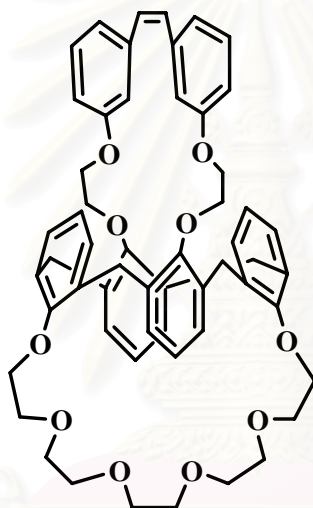
FigureC.14 *m-cis*-4: *meta-cis*-Stilbene-bridged calix[4]arene crown-6
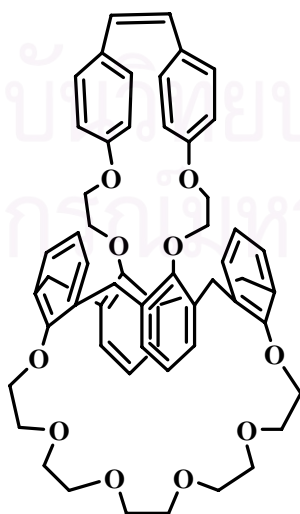
Figure C.15 *p-cis*-4: *para-cis*-Stilbene-bridged calix[4]arene crown-6

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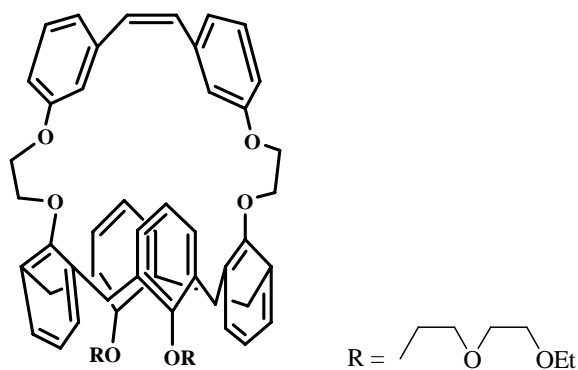
Figure C.16   5: *meta-cis*-Stilbene-bridged calix[4]arene diethylene glycol ethyl ether

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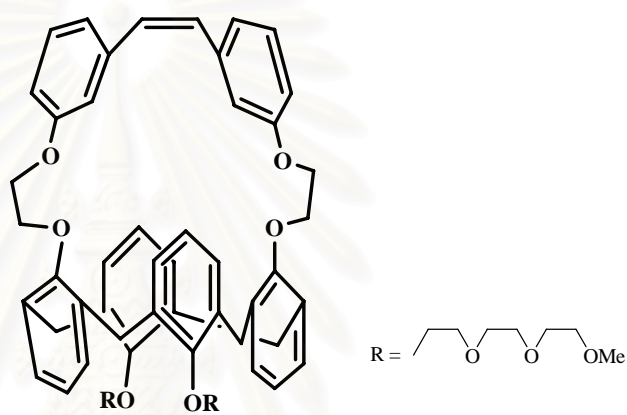
Figure C.17   6: *m-cis* Stilbene-bridged calix[4]arene triethylene glycol
monomethylether

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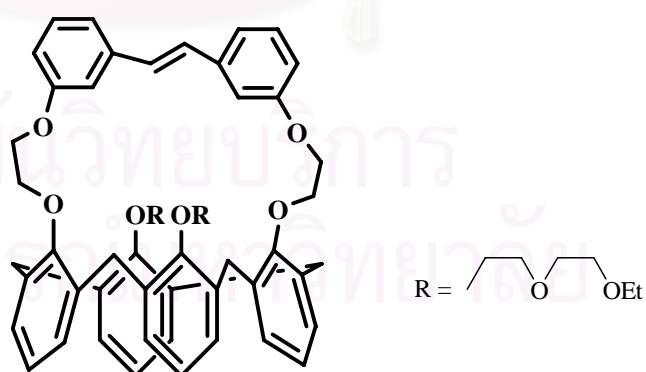
Figure C18 7: *m-trans*- Stilbene-bridged calix[4]arene diethylene glycol ethyl ether
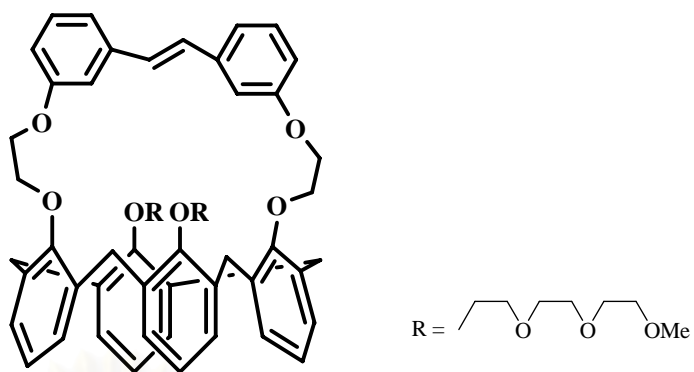
Figure C.19 8: *m-trans* Stilbene -bridged calix[4]arene triethylene glycol

monomethylether; cone conformation
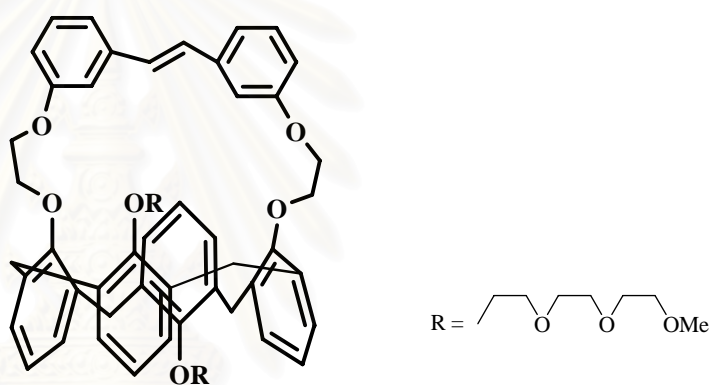
FigureC.20 9: *m-trans* Stilbene -bridged calix[4]arene triethylene glycol

monomethylether;patial cone conformation
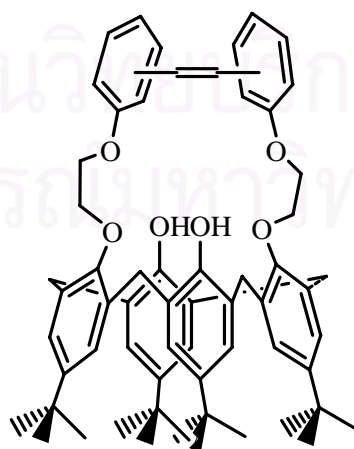
Figure C.21 10: stilbene bridged *tert*-butyl calix[4]arene
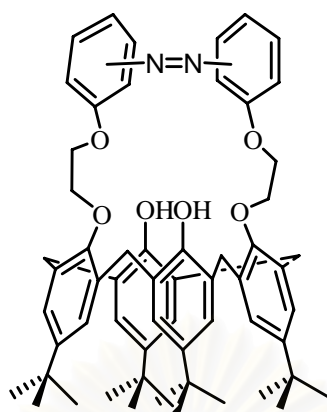
Figure C.22 11: azobenzene bridged tert-butyl calix[4]arene
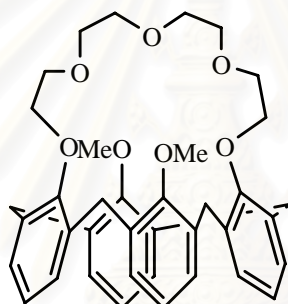
Figure C.23 12*: O,O′*-dimethylcalix[4]arene crown-5
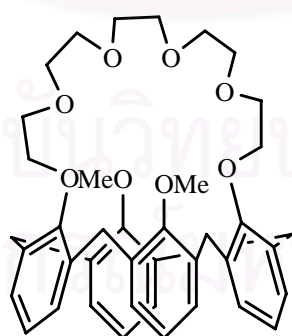
Figure C.24 13: *O,O′*-dimethylcalix[4]arene crown-6
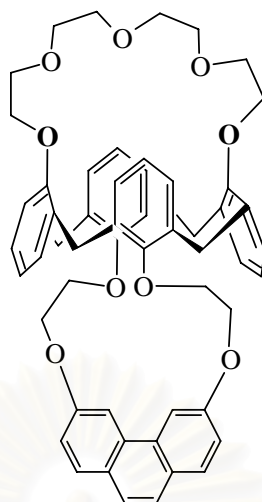
Figure C.25 14: phenanthrene bridged calix[4]arene crown ether

APPENDIX D

REPRINT

Jaiyu, A. Rojanathanes, R. Sukwattanasinitt, M. Stilbene-bridged 1,3-alternate calix[4]arene crown ether for selective alkali ion extraction, *Tetrahedron Letters* **2007**, *48*, 1817–1821.

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Stilbene-bridged 1,3-alternate calix[4]arene crown ether for selective alkali ion extraction

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Abstract—A series of stilbene-bridged calix[4]arenes was synthesized through an intramolecular reductive McMurry coupling of bis-benzaldehyde calix[4]arene in high yields. Tetra- and pentaethylene glycol chains were tethered to the phenolic groups of calix[4]-arene to form stilbene-bridged calix[4]arene crown-5 and crown-6, respectively. The presence of stilbene bridge over the calix[4]arene rim effectively prevented the connection of the polyether chains in the cone conformation resulting in the exclusive formation of 1,3-alternate stilbene-bridged calix[4]arene crown product. Compared to the cone analogues, the 1,3-alternate calix[4]-arene crown ethers showed a greater extraction ability and selectivity toward Cs^+.
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1. Introduction

Since its discovery, calix[4]arene has been extensively used as a molecular platform to construct artificial iono-phores.[1] Thanks to its preorganized basket structure and readily functionalizable phenolic groups, calix[4]-arene-based ionophores with variety of cavity shapes and sizes were readily synthesized.[2] Calix[4]arene crown ethers, a class of calix[4]arene derivatives containing polyether chain tethered across opposite phenolic rings, are known to be more selective alkali ionophores than their crown ethers counterparts.[3] Both crown ether chain length and calixarene conformation play important roles in regulating the complextion with metal ions.[4] The applications of calix[4]arene crown ethers for Na^+/K^+ pump mimicking,[5] Rb^+ transportation in radiopharmaceutical treatments,[6] and the removal of Cs^+ radioactive wastes were reported.[7]

We have recently synthesized and studied a series of azobenzene-bridged and stilbene-bridged *tert*-butylcalix-[4]arenes as photoswitchable ionophores[8] and molecular receptors.[9] We found that the incorporation of different isomers of rigid azobenzene or stilbene bridge on the narrow phenolic rim can regulate the calix[4]arene cavity shape. In this work, we would like to report the use of stilbene bridge to direct the synthesis of calix[4]arene crown ethers in a 1,3-alternate conformation for selective alkali ion extraction.

2. Results and discussion

Using reductive McMurry intramolecular coupling of bis-benzaldehyde calix[4]arenes **1** followed by condensation with the ditosylate ester of tetra- and pentaethylene glycol, stilbene-bridged calix[4]arene crown-5 and crown-6 were synthesized (Scheme 1). The reductive coupling yielded stereoisomeric mixtures of *cis* and *trans* stilbene **2** of which the cis isomer was predominant. By using a high dilution condition (7 mM of bisbenzalde-hydes) and a large excess of TiCl₄ and Zn (20 equiv), the yields of stilbene products were markedly improved from our previous work.[9] The mixtures of *cis* and *trans* stilbene-bridged calix[4]arene were separated by column chromatography and used in the next condensation step. Only cis form of the final products from the condensation were successfully synthesized except for *o*-**3** that the trans isomer was also obtained. The characteristic singlet NMR signal of the calix[4]arene methylene protons observed in the spectra of **3** and **4** indicated that the stilbene-bridged calix[4]arene crowns were formed in the 1,3-alternate conformation.[10]

To our surprise, the attempts to prepare *m-trans*-**3** and *m-trans*-**4** from *m-trans*-**2** by the same approach have
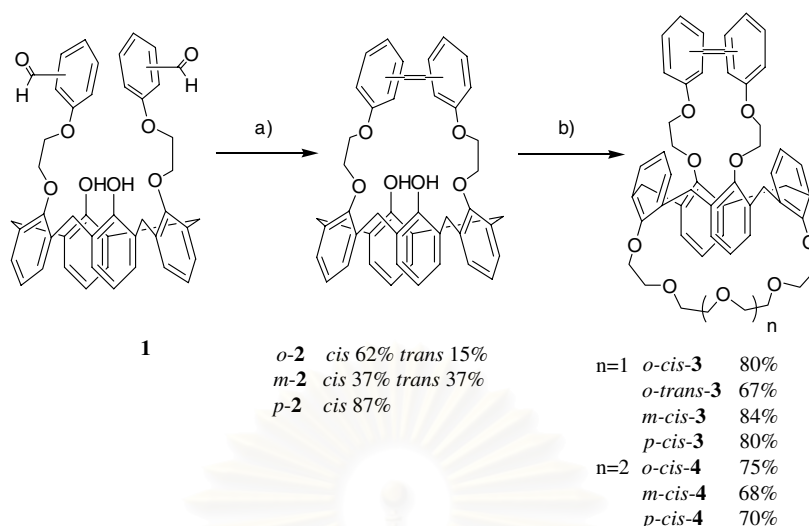
Scheme 1. Synthesis of stilbene calix[4]arene crown ether **3**, **4**.[11] Reagents: (a) TiCl$_4$, Zn, THF; (b) TsO(CH$_2$CH$_2$O)$_{(3+n)}$Ts, Cs$_2$CO$_3$, Bu$_4$NBr, CH$_3$CN.

been so far fruitless, yielding only intractable materials. To clarify these puzzling results, both *cis*- and *trans-m-***2** were condensed with 2 equiv of *p*-toluenesulfonate ester of diethyleneglycol monoethylether (Scheme 2). The products from *m-cis-***2** was the expected 1,3-alternate *m-cis-***5** but the reaction of *m-trans-***2** gave only a poor yield of the unexpected cone *m-trans-***6**. The cone conformation was assigned according to the characteristic NMR signals of the doublet pairs of the calix[4]arene methylene protons. The results suggested that the phenol ring flipping process required for the conversion of the conformation from cone to 1,3-alternate was somehow disallowed in *m-trans-***2**. Although our previous work has predicted that the calix[4]arene rims in *m-trans-***2** were distorted from the normal circular shape into an oval shape[9] we have never thought that this distortion would totally prevent the ring flipping process.

For comparison in the extraction study, calix[4]arene crowns without the stilbene bridge (**7** and **8**) containing the same crown sizes as **3** and **4** were also synthesized (Scheme 3). Without the stilbene bridge, calix[4]arene crowns were obtained in the cone conformation exclusively.

The alkali metal ion extraction at the aqueous CHCl$_3$ interface by stilbene-bridged calix[4]arene crowns **3** and **4** were investigated in comparison with compounds **5**, **7**, **8**, and 18-crown-6. The extraction was carried out by thorough mixing a chloroform solution (5 mM, 1 mL) of the ligand with an aqueous solution of the metal picrate (5 mM, 1 mL) for 24 h. After centrifugation, the aqueous phase (35 μL) was pipetted out and diluted to 5 mL. The concentration of the remaining metal ion in the aqueous phase was determined from
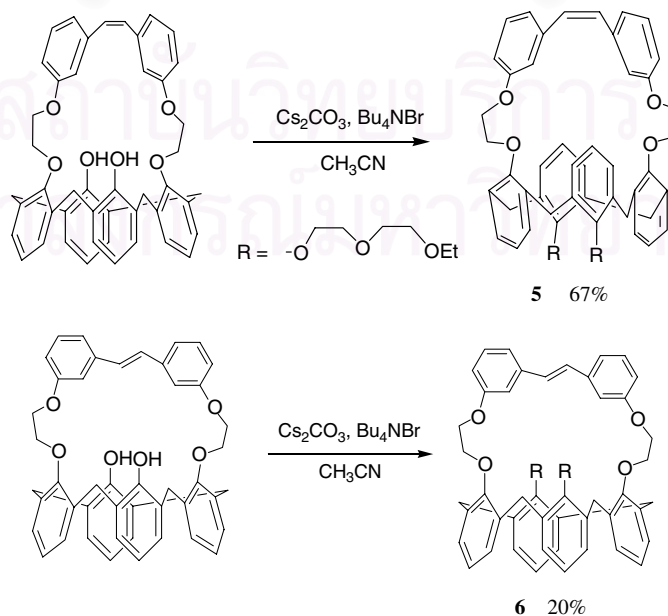
Scheme 2. Synthesis of stilbene calix[4]arene crown ether **5**, **6**.
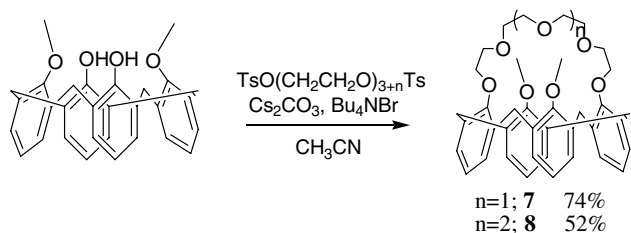
Scheme 3. Synthesis of calix[4]arene crown ether **7**, **8**.

the UV absorbance of picrate ion at 354 nm in the diluted solution. The % extraction was calculated from $([A_0 - A]/[A_0]) \times 100$, whereas A_0 and A were the absorbance of the aqueous metal picrate solutions before and after extraction, respectively.

Calix[4]arene crowns (**3**, **4**, and **7**) and 18-crown-6 generally showed a good extractability toward alkali ions larger than Na$^+$ (Fig. 1). While the calix[4]arene crown-5 such as **3** and **7** showed a significantly greater K$^+$/Cs$^+$ selectivity than that of 18-crown-6, the calix[4]arene crown-6 (compound **4**) displayed impressively high Cs$^+$/K$^+$ selectivity. Stilbene-bridged calix[4]arene **5** in which structure contains two linear diethylene glycol chains has poor extractability toward all alkali ions.

Figure 1. Extraction percentage of alkali metal picrates from water to chloroform by calix[4]arene derivatives and 18-crown-6 at room temperature.
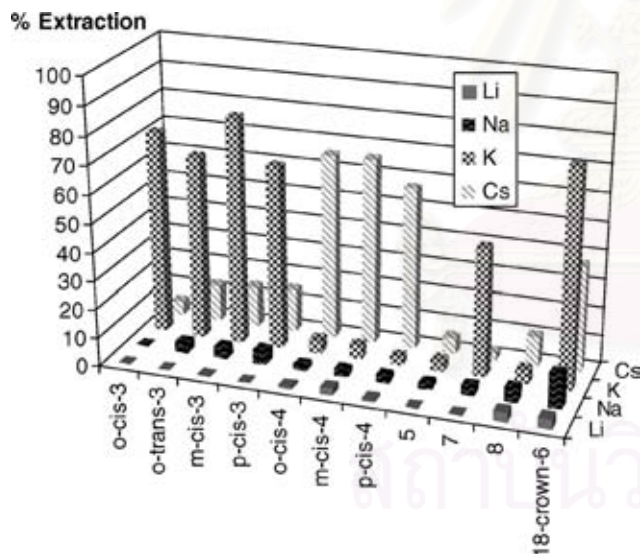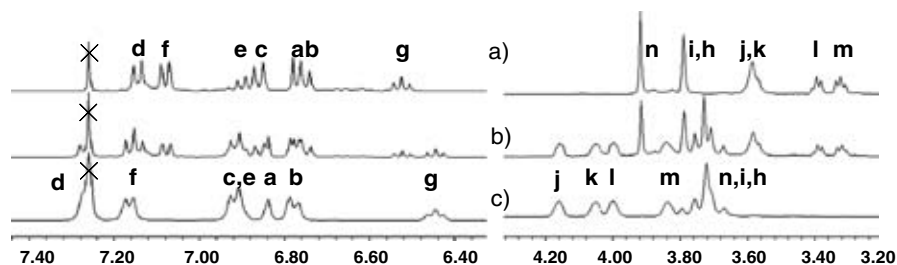
The result indicated that neither the six oxygen atoms present in the diethylene glycol chains nor in the crown oxygens on the same side with the stilbene bridge are suitable for hosting the alkali ions. The cone calix[4]-arene crown **8** has relatively much lower Cs$^+$ extractability compared to the 1,3-alternate stilbene-bridged calix[4]-arene crown **4**. The 1,3-alternate calix[4]arene crown was reported to have a suitable orientation of aromatic rings for cation/π interaction participating in the binding of Cs$^+$.[11]

Having a high extracting ability, ligands **3** and **4** were also tested for solid–liquid extraction. An excess amount of potassium picrate was added into a solution of **3** or **4** in CDCl$_3$ and the mixture was sonicated. The color of the solution gradually changed from colorless to yellow indicating the dissolution of metal picrate into CDCl$_3$, which is normally nonsolvent for picrate salts. The changes in ^{1}H NMR spectra were used to justify the nature of complexation. For example, a new set of proton signals was clearly observed after 1 h of sonication *p-cis*-**3** with potassium picrate salt (compare Fig. 2a and b) suggesting a partial association of the ligand to K$^+$, to form the expecting host–guest complex, in the slow exchange process. This new set of signals became stronger with the expenses of the original set of signals as the sonication prolonged. The original signals *p-cis*-**3** were completely replaced by the signals of the complex after 3 h of sonication (Fig. 2c) signifying a full complexation of the host molecules to K$^+$ in the solid–liquid extraction.

Upon complexation with K$^+$, the signals of the methylene protons in the crown ether moiety of *p-cis*-**3** were shifted significantly downfield while the other signals were shifted only slightly (Fig. 3a) indicating that K$^+$ situated mostly within the crown ether loop. For the complexation between *p-cis*-**4** and Cs$^+$, significant shifts of various signals including the calixarene aromatic protons were observed (Fig. 3b) suggesting the possibility of cation–π interaction involving in the complexation.

In summary, the incorporation of stilbene bridge to calix[4]arenes provided a sensible approach to synthesize calix[4]arene crown-5 and crown-6 in 1,3-alternate conformation. These 1,3-alternate calix[4]arene crowns have a greater extractability and selectivity than those of the corresponding cone calix[4]arene crowns. The stilbene-bridged calix[4]arene crown-5 has an excellent K$^+$/Cs$^+$ selectivity while the stilbene-bridged calix[4]arene
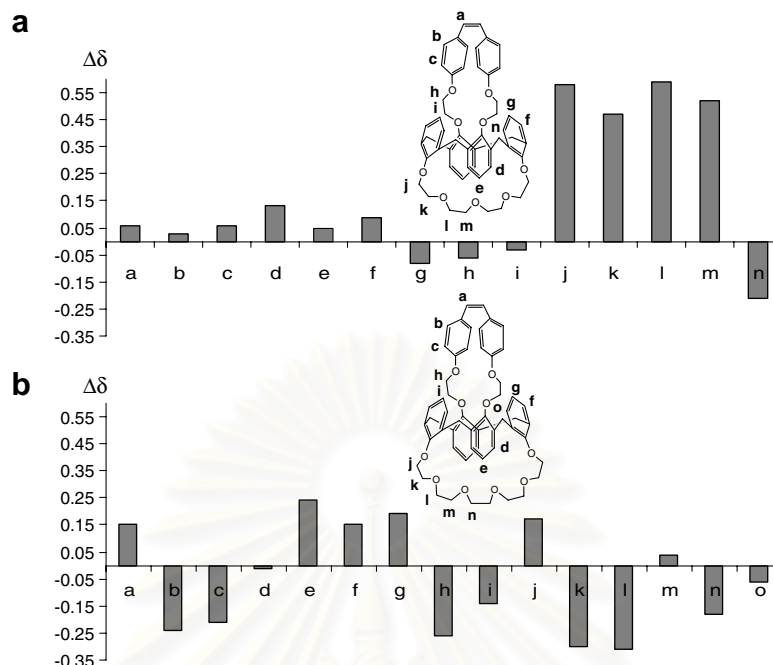

Figure 2. The ^{1}H NMR spectra of (a) *p-cis*-**3**, (b) partial complexation between *p-cis*-**3** and potassium picrate, and (c) full complexation between *p-cis*-**3** and potassium picrate.

Figure 3. (a) $\Delta\delta$ of *p-cis*-**3** complexed with potassium picrate and (b) $\Delta\delta$ of *p-cis*-**4** complexed with cesium picrate.

crown-6 has an excellent Cs^+/K^+ selectivity in the aqueous chloroform extraction. The metal selectivities of 1,3-alternate calix[4]arene crowns also significantly outperform 18-crown-6.

Acknowledgments

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.01.026.

References and notes

1. (a) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161–170; (b) Gutsche, C. D. *Calixarenes* Revisited. In *Monograph in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1989; (c) Böhmer, V. *Angew. Chem., In. Ed. Engl.* **1995**, *34*, 713–745; (d) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713–1734; (e) Gutsche, C. D. *Calixarenes* Revisited. In *Monograph in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: London, 1998; (f) Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J. *Calixarenes 2001*; Kluwer Academic: Dordrecht, Holland, 2001.

2. (a) Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767–2777; (b) Matsumoto, H.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 77–80; (c) Arduini, A.; Domiano, L.; Pochini, A.; Secchi, A.; Ungarro, R.; Ugozzoli, F.; Struck, O.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1997**, *53*, 3767–3776; (d) Bodenant, B.; Weil, T.; Businelli-Pourcel, M.; Fages, F.; Barbe, B.; Pianet, I.; Laguerre, M. *J. Org. Chem.* **1999**, *64*, 7034–7039; (e) Beer, P. D.; Hopkins, P. K.; McKinny, J. D. *Chem. Commun.* **1999**, 1253–1254; (f) Guillon, J.; Leger, J.-M.; Sonnet, P.; Jarry, C.; Robba, M. *J. Org. Chem.* **2000**, *65*, 8283–8289; (g) Tuntulani, T.; Poompradub, S.; Thavornyutikarn, P.; Jaiboon, N.; Ruangpornvisuti, V.; Chaichit, N.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **2001**, *42*, 5541–5544; (h) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486–516; (i) Liu, J.-M.; Zheng, Q.-Y.; Yang, J. L.; Chen, C.-F.; Huang, Z.-T. *Tetrahedron Lett.* **2002**, *43*, 9209–9212; (j) Yilmaz, A.; Memon, S.; Yilmaz, M. *Tetrahedron* **2002**, 7735–7740; (k) Cao, Y.-D.; Zheng, Q.-Y.; Chen, C.-F.; Huang, Z.-T. *Tetrahedron Lett.* **2003**, *44*, 4751–4755.

3. (a) Gbidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadl, A.; Reinhoudt, D. *J. Am. Chem. Soc.* **1990**, *112*, 6979–6985; (b) Nijenhuis, W. F.; Buitenhuis, E. G.; de Jong, F.; Sudholter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 7963–7968; (c) Yamamoto, H.; Shinkai, S. *Chem. Lett.* **1994**, 1115–1118; (d) Asfari, Z.; Bressot, C.; Vicens, J.; Hill, C.; Dozol, J.; Rouquette, H.; Eymard, S.; Lamare, V.; Toumois, B. *Anal. Chem.* **1995**, *67*, 3133–3139; (e) Geraci, C.; Chessari, G.; Piattelli, M.; Neri, P. *Chem. Commun.* **1997**, 921; (f) Kim, J.; Lee, W.; Suh, I.; Kim, J.; Yoon, I.; Lee, J. *J. Org. Chem.* **2000**, *65*, 7215–7217.

4. (a) Bocchi, C.; Careri, M.; Casnati, A.; Mori, G. *Anal. Chem.* **1995**, *67*, 4234–4238; (b) Asfari, Z.; Bressot, C.; Vicens, J.; Hill, C.; Dozol, J.; Rouquette, H.; Eymard, S.; Lamare, V.; Tournois, B. *Anal. Chem.* **1995**, *67*, 3133–3139; (c) Arnaud-Neu, F.; Caccamese, S.; Fuangswasdi, S.; Pappalardo, S.; Parisi, M. F.; Petringa, A.; Principato, G. *J. Org. Chem.* **1997**, *62*, 8041–8048; (d) Kim, J. S.; Pang, J. H.; Yu, I. Y.; Lee, W. K.; Suh, I. H.; Kim, J. K.; Cho, M. H.; Kim, E. T.; Ra, D. Y. *J. Chem. Soc., Perkin Trans. 2* **1999**, 837–840; (e) Casnati, A.; Ca, N. D.; Sansone, F.; Ugozzoli, F.; Ungaro, R. *Tetrahedron* **2004**, *60*, 7869–7876; (f) Luo, H.; Dai, S.; Bonnesen, P. V.;

Buchanan, A. C.; Holbrey, J. D.; Bridges, N. J.; Rogers, R. D. *Anal. Chem.* **2004**, *76*, 3078–3083; (g) van Leeuwen, F. W. B.; Beijleveld, H.; Miermans, C. J. H.; Huskens, J.; Verboom, W.; Reinhoudt, D. N. *Anal. Chem.* **2005**, *77*, 4611–4617.

5. (a) Reinhoudt, D. N.; Dijkstra, P. J.; in't Veld, P. J. A.; Bugge, K.-E.; Harkema, S.; Ungaro, R.; Ghidini, E. *J. Am. Chem. Soc.* **1987**, *109*, 4761–4762; (b) Dijkstra, P. J.; Brunink, J. A. J.; Bugge, K.-E.; Reinhoudt, D. N.; Harkema, S.; Ungaro, R.; Ugozzoli, F.; Ghidini, E. *J. Am. Chem. Soc.* **1989**, *111*, 7567–7575; (c) Beer, P. D.; Gale, P. A.; Chen, Z.; Drew, M. G. B.; Heath, J. A.; Ogden, M. I.; Powell, H. R. *Inorg. Chem.* **1997**, *36*, 5880–5893; (d) Bourgeois, J.-P.; Echegoyen, L.; Fibboli, M.; Pretsch, E.; Diederich, F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2118–2121.

6. (a) Brewer, K. *J. Am. Chem. Soc.* **1938**, *60*, 691; (b) Anderson, C. J.; Welch, M. J. *Chem. Rev.* **1999**, *99*, 2219–2234.

7. (a) *Radioactive Waste Management and Disposal*; Cecille, L., Ed.; Elsevier: New York, 1991; (b) Asfari, Z.; Pulpoka, B.; Saadioui, M.; Wenger, S.; Nierlich, M.; Thuery, P.; Reynier, N.; Dozol, J.-F.; Vincens, J. In *J. Mol. Recognit. Inclusion, Proc. 9th Int. Symp.*; 1998; pp 173–178; (c) Hill, C.; Dozol, J.-F.; Lamare, V.; Rouquette, H.; Eymard, S.; Tournois, B.; Vincens, J.; Asfari, Z.; Bressot, C. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *19*, 399–408; (d) McDowell, W. J.; Case, G. N.; McDonough, J. A.; Bartsch, R. A. *Anal. Chem.* **1992**, *64*, 3013–3017.

8. (a) Pipoosananakaton, B.; Sukwattanasinitt, M.; Jaiboon, N.; Chaichit, N.; Tuntulani, T. *Tetrahedron Lett.* **2000**, *41*, 9095–9100; (b) Sukwattanasinitt, M.; Rojanathanes, R.; Tuntulani, T.; Sritana-anant, Y.; Ruangpornvisuti, V. *Tetrahedron Lett.* **2001**, *42*, 5291–5293; (c) Rojanathanes, R.; Pipoosananakaton, B.; Tuntulani, T.; Bhanthumnavin, W.; Orton, J. B.; Cole, S. J.; Hursthouse, M. B.; Grossel, M. C.; Sukwattanasinitt, M. *Tetrahedron* **2005**, *61*, 1317–1324.

9. Rojanathanes, R.; Tutulani, T.; Bhabthumnavin, W.; Sukwattanasinitt, M. *Org. Lett.* **2005**, *7*, 3401–3404.

10. Spectroscopic data of stilbene calix[4]arene crown-5 or 6 (**3** and **4**); compound *o-cis*-**3**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.06, 3.42 (t, –OCH$_2$CH$_2$O-crown, 8H), 3.11, 3.45 (t, ArOCH$_2$CH$_2$O-crown, 8H), 3.56 (br, ArOCH$_2$CH$_2$OAr, 8H), 3.87 (m, ArCH$_2$Ar, 8H), 6.86, 6.90 (t, calix-ArH, 4H), 6.79, 7.18 (d, stilbene-ArH, 4H), 6.90, 7.16 (t, stilbene-ArH, 4H), 6.55 (s, CH=CH, 2H), 6.98, 7.10 (d, calix-ArH, 8H); ^{13}C NMR (400 MHz, CDCl$_3$) δ 38.1 (ArCH$_2$Ar), 68.3 (OCH$_2$), 68.8 (OCH$_2$), 69.7 (OCH$_2$), 69.8 (OCH$_2$), 70.7 (OCH$_2$), 72.7 (OCH$_2$), 122.8 (calix-ArC), 123.7 (calix-ArC), 129.2 (calix-ArC), 129.7 (calix-ArC), 133.4 (calix-ArC), 133.9 (calix-ArC), 156.1 (calix-ArC), 156.3 (calix-ArC), 129.1 (stilbene-ArC), 127.9 (stilbene-ArC), 117.3 (stilbene-ArC), 117.7 (stilbene-ArC), 121.7 (stilbene-ArC), 122.8 (stilbene-ArC), 127.9 (stilbene-ArC), 129.1 (stilbene-ArC), 156.9 (stilbene-ArC), 126.7 (CH=CH); mp = 124–126 °C; FTMS calcd for C$_{54}$H$_{54}$O$_9$ [ESI, M$^+$ NH$_4$]: 846.4106, found: 864.4091; compound *o-trans*-**3**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.16, 3.53 (t, OCH$_2$CH$_2$O-crown, 8H), 3.25, 3.65 (t, ArOCH$_2$CH$_2$O-crown, 8H), 3.57, 3.64 (br, ArOCH$_2$CH$_2$OAr, 8H), 3.88 (m, ArCH$_2$Ar, 8H), 6.65, 7.15 (d, calix-ArH, 8H); ^{13}C NMR (400 MHz, CDCl$_3$) δ 37.9 (ArCH$_2$Ar), 65.8 (OCH$_2$), 68.1 (OCH$_2$), 68.3 (OCH$_2$), 69.8 (OCH$_2$), 70.5 (OCH$_2$), 72.6 (OCH$_2$), 129.3 (calix-ArC), 129.3 (calix-ArC), 133.9 (calix-ArC), 134.1 (calix-ArC), 134.1 (calix-ArC), 139.3 (calix-ArC), 156.2 (calix-ArC), 158.5 (calix-ArC), 111.1 (stilbene-ArC), 115.3 (stilbene-ArC), 122.6 (stilbene-ArC), 122.7 (stilbene-ArC), 129.1 (stilbene-ArC), 156.1 (stilbene-ArC), 121.4 (CH=CH) FTMS calcd for C$_{54}$H$_{54}$O$_9$ [ESI, M$^+$ NH$_4$]: 846.4106, found: 864.4099; compound *m-cis*-**3**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.16, 3.46 (t, OCH$_2$CH$_2$O-crown, 8H), 3.27, 3.52 (t, ArOCH$_2$CH$_2$O-crown, 8H), 3.60 (br, ArOCH$_2$CH$_2$OAr, 8H), 3.87 (m, ArCH$_2$Ar, 8H), 6.65, 6.91 (t, calix-ArH, 4H), 6.83, 6.89 (d, stilbene-ArH, 4H), 7.27 (t, stilbene-ArH, 2H), 6.63 (s, stilbene-ArH, 2H), 6.78 (s, CH=CH, 2H), 7.05, 7.13 (d, calix-ArH, 8H); ^{13}C NMR (400 MHz, CDCl$_3$) δ 38.1 (ArCH$_2$Ar), 67.0 (OCH$_2$), 68.3 (OCH$_2$), 68.4 (OCH$_2$), 69.7 (OCH$_2$), 70.7 (OCH$_2$), 72.8 (OCH$_2$), 129.5 (calix-ArC), 129.8 (calix-ArC), 130.0 (calix-ArC), 134.1 (calix-ArC), 134.2 (calix-ArC), 138.5 (calix-ArC), 156.1 (calix-ArC), 158.5 (calix-ArC), 109.9 (stilbene-ArC), 111.5 (stilbene-ArC), 116.5 (stilbene-ArC), 122.3 (stilbene-ArC), 111.5 (stilbene-ArC), 156.0 (stilbene-ArC), 122.4 (CH=CH); mp = 206–207 °C; Anal. Calcd for C$_{54}$H$_{54}$O$_9$: C, 76.62; H, 6.38. Found: C, 76.68; H, 6.45; compound *p-cis*-**3**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.32, 3.39 (t, OCH$_2$CH$_2$O-crown, 8H), 3.59 (br, ArOCH$_2$CH$_2$O-crown, 8H), 3.79 (br, ArOCH$_2$CH$_2$OAr, 8H), 3.92 (s, ArCH$_2$Ar, 8H), 6.52, 6.89 (t, calix-ArH, 4H), 6.75, 6.86 (d, stilbene-ArH, 8H), 6.78 (s, CH=CH, 2H), 7.08, 7.14 (d, calix-ArH, 8H); ^{13}C NMR (400 MHz, CDCl$_3$) δ 37.8 (ArCH$_2$Ar), 68.9 (OCH$_2$), 68.9 (OCH$_2$), 69.4 (OCH$_2$), 70.5 (OCH$_2$), 70.6 (OCH$_2$), 71.9 (OCH$_2$), 130.1 (calix-ArC), 130.5 (calix-ArC), 130.6 (calix-ArC), 131.3 (calix-ArC), 133.8 (calix-ArC), 134.0 (calix-ArC), 155.8 (calix-ArC), 156.4 (calix-ArC), 117.4 (stilbene-ArC), 121.8 (stilbene-ArC), 115.5 (stilbene-ArC), 158.0 (stilbene-ArC), 122.7 (CH=CH); mp = 211 °C; Anal. Calcd for C$_{54}$H$_{56}$O: C, 76.62; H, 6.38. Found: C, 76.60; H, 6.38; compound *o-cis*-**4**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.12 (t, OCH$_2$, 4H) 3.19 (t, OCH$_2$, 4H) 3.42 (t, OCH$_2$, 4H), 3.46 (t, OCH$_2$, 4H), 3.55 (t, OCH$_2$, 4H), 3.61 (m, OCH$_2$, 8H), 3.75 (t, ArCH$_2$Ar, 8H), 6.41 (s, CH=CH, 2H), 6.89, 7.02 (d, calix-ArH, 8H), 6.82, 7.09 (t, calix-ArH, 4H), 6.75 (m, stilbene-ArH, 2H), 6.77 (m, stilbene-ArH, 2H), 6.82 (m, stilbene-ArH, 2H), 7.20 (d, stilbene-ArH, 2H); mp = 116–118 °C; Anal. Calcd for C$_{56}$H$_{58}$O$_{10}$: C, 75.53; H, 6.51. Found: C, 75.54; H, 6.56; compound *m-cis*-**4**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.35 (t, OCH$_2$, 8H), 3.46 (t, OCH$_2$, 4H), 3.53 (t, OCH$_2$, 4H), 3.61 (t, OCH$_2$, 4H), 3.64 (t, OCH$_2$, 4H), 3.67 (t, OCH$_2$, 4H), 3.71 (t, OCH$_2$, 4H), 3.85 (s, ArCH$_2$Ar, 8) 6.63, 7.27 (t, calix-ArH, 4H), 7.07, 7.12 (d, calix-ArH, 8H), 6.82, 6.91 (d, stilben-ArH, 4H), 6.90 (t, stilben-ArH, 2H), 6.64 (s, stilben-ArH, 2H), 6.78 (s, CH=CH, 2H); ^{13}C NMR (400 MHz, CDCl$_3$) δ 38.0 (ArCH$_2$Ar), 61.7 (OCH$_2$), 66.9 (OCH$_2$), 68.3 (OCH$_2$), 68.9 (OCH$_2$), 69.4 (OCH$_2$), 72.7 (OCH$_2$), 1129.9 (calix-ArC), 130.1 (calix-ArC), 130.3 (calix-ArC), 134.0 (calix-ArC), 134.3 (calix-ArC), 138.5 (calix-ArC), 156.3 (calix-ArC), 158.4 (calix-ArC), 111.3 (stilbene-ArC), 116.4 (stilbene-ArC), 112.4 (stilbene-ArC), 122.6 (stilbene-ArC), 122.6 (stilbene-ArC), 156.0 (stilbene-ArC), 122.2 (CH=CH) FTMS calcd for C$_{56}$H$_{58}$O$_{10}$ [ESI, M$^+$ NH$_4$]: 908.4368, found: 908.4352; compound *p-cis*-**4**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.54 (t, OCH$_2$, 4H), 3.81 (t, OCH$_2$, 4H), 3.87 (t, OCH$_2$, 4H), 3.91 (t, OCH$_2$, 8H), 3.97 (t, OCH$_2$, 4H), 4.46 (t, OCH$_2$, 4H), 3.87 (s, ArCH$_2$Ar, 8H), 6.19, 6.78 (t, calix-ArH, 4H), 7.02, 7.19 (d, calix-ArH, 8H), 7.07, 7.14 (d, stilbene-ArH, 8H), 6.70 (s, CH=CH, 2H) mp = 256–257 °C; FTMS calcd for C$_{56}$H$_{58}$O$_{10}$ [ESI, M$^+$ NH$_4$]: 908.4368, found: 908.4375. The experimental details are available in Supplementary data.

11. (a) Lamare, V.; Dozol, J. F.; Ugozzoli, F.; Casnati, A.; Ungaro, R. *Eur. J. Org. Chem.* **1998**, *8*, 1559–1568; (b) Kim, J. S.; Ohki, A.; Ueki, R.; Ishizuka, T.; Shimotashiro, T.; Maeda, S. *Talanta* **1999**, *48*, 705–710.

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