ไดคาร์บอกซิเลตแอนไอออนรีเซปเทอร์ที่ควบคุมโดยไอออนโลหะแอลคาไล

นางสาวเอื้อมพร รัตนสิงห์

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DICARBOXYLATE ANION RECEPTORS CONTROLLED BY ALKALI METAL IONS

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ได้สังเคราะห์ไดคาร์บอกซิเลตแอนไอออนรีเซปเทอร์ 2 ประเภท ประเภทแรกประกอบด้วยหมู่ยูเรียได้แก่สาร **2a 2b** และ **2c** ส่วนประเภทที่สองประกอบด้วยไดเอซาคราวน์อีเทอร์และหมู่ไธโอยูเรียได้แก่สาร **4** จากนั้นได้ศึกษาการเกิดสารประกอบเชิงซ้อนของลิแกนด์ **2a** กับไดคาร์บอกซิเลตแอนไอออนชนิดต่างๆ เช่น ออกซาเลต มาโลเนต ซัคซิเนต กลูทาเลต อะดิเปต พิมิเลต ซับเบอเรต และ อะซิเลต กระทำโดยการไทเทรตด้วยเทคนิคโปรตอนนิวเคลียร์แมกเนติกเรโซแนนซ์ (เอ็นเอ็มอาร์) พบว่าลิแกนด์ **2a** สามารถเกิดสารประกอบเชิงซ้อนกับไดคาร์บอกซิเลตในอัตราส่วน 1:1 และมีค่าคงที่ของการรวมตัวกับกลูทาเลตมากที่สุด จากการศึกษาการเกิดสารประกอบเชิงซ้อนของลิแกนด์ **4** และไดคาร์บอกซิเลตไอออนด้วยเทคนิคยูวี-วิสิเบิลสเปก โทรโฟโตเมทรี พบว่าลิแกนด์ **4** เกิดการเปลี่ยนแปลงของสเปกตรัมอย่างชัดเจน และยังสามารถเห็นการเปลี่ยนแปลงของสีของสารละลาย **4** ได้ด้วยตาเปล่าเมื่อจับกับไดคาร์บอกซิเลตแอนไอออน และสามารถเกิดสารประกอบเชิงซ้อนกับไดคาร์บอกซิเลตในอัตราส่วน 1:1 โดยลิแกนด์ **4** มีค่าคงที่ของการรวมตัวกับอะดิเปตมากที่สุด นอกจากนี้ยังศึกษาผลของโซเดียมไอออนต่อการเกิดสารประกอบเชิงซ้อนกับไดคาร์บอกซิเลตแอนไอออน พบว่า โซเดียมไอออนทำให้ค่าคงที่ของการรวมตัวของลิแกนด์ **4** กับ ไดคาร์บอกซิเลตแอนไอออนมีค่าเพิ่มขึ้น

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Dicarboxylate anion receptors have been synthesized and can be separated into two classes. One class consists of urea units, **2a**, **2b** and **2c**, and the other class contains a diazacrown ether unit and thiourea units, **4**. Complexation studies of ligand **2a** with various dicaboxylate anions such as oxalate, malonate, succinate, glutarate, adipate, pimelate, suberate and azelate were carried out by ^{1}H NMR titrations. Ligand **2a** was able to form 1:1 complexes with all dicarboxylate anions and the complex between ligand **2a** and glutarate possessed the highest association constants. Complexation studies between ligand **4** and dicarboxylate anions by UV-vis titration showed a dramatic color change which could be detected by naked eyes. The complexes of ligand **4** and dicarboxylate anions were 1:1 stoichiometry and ligand **4** formed the most stable complex with adipate. The effect of sodium ion towards anion binding abilities of ligand **4** was also investigated. In the presence of sodium ion, association constants of ligand **4** and dicarboxylate anions were found to increase.

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LIST OF SYMBOLS AND ABBREVIATION

K_a	Association constant
p	para
o	ortho
AcO^-	acetate
^1H NMR	Proton Nuclear Magnatic Resonance
UV-vis	Ultravisible-visible
IR	Infrared spectroscopy
Nm	nanometer
Equiv.	Equivalent
Å	Angstrom
δ	Chemical shift
Hz	Hertz
g	Gram
mmol	Millimole
mL	Milliliter
M	Mole
s, d, t, q, m	Splitting pattern of ^1H NMR (singlet, doublet, triplet, quartet and multiplet)
J	Coupling constant
^OC	Degree Celcius
ppm	part per million

CHAPTER I

INTRODUCTION

1.1 Supramolecular chemistry

The basis of supramolecular chemistry is the binding or complexation event, which is the action of the host molecule binding with a guest molecule to form a host-guest complex or supramolecule [1-2]. The host is an enzyme or synthetic compounds processing a central hole or cavity. The guest is monoatomic cations or simple inorganic anions. In more complexes biological interactions, the guest is called a substrate and can be a food particle, hormone, pheromone or neurotransmitter.

Supramolecular chemistry is characterized by the specificity and selectivity of its reactions. The term used to describe this is molecular recognition, as if the reactions will only happen when the molecule recognizes each other. Therefore, a supramolecular interaction can only happen when the host and guest complement each other. (e.g. hydrogen bond donor/acceptor, Lewis acids/base, hardness or softness etc.) An analogy to the mechanism is the lock and key scenario coined by Emil Fischer in 1894. The host molecule serves as the lock and the guest molecule serves as the key [3]. Only when the key matches the lock will open.

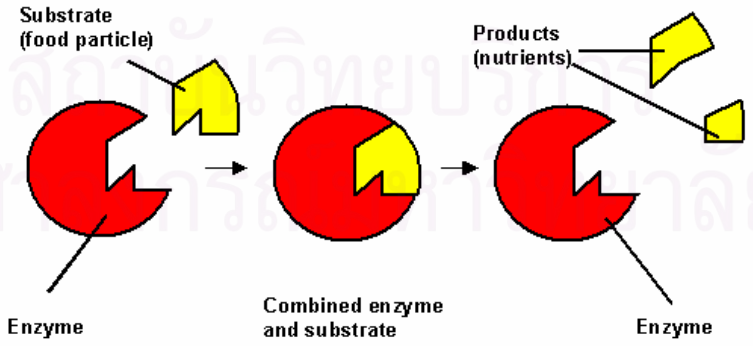


Figure 1.1 Example of a lock and key scenario in biological systems.

1.2 Anion receptor

Anion species play a very important role in chemistry and in biology. Their binding features went unrecognized, whereas the complexation of metal ions and, more recently, of cationic molecules was extensively studied. The coordination chemistry of anions may be expected to yield a great variety of novel structures and properties of both chemical and biological significance. Anionic substrates have specific features. They are large, compared with cation and they possess a range of geometries [4]: spherical, linear, planar, tetrahedral and octahedral. Therefore, a higher degree of design may make receptors complementary to their anionic guests. A well-designed anion receptor molecule would gain both high selectivity and great sensitivity. Geometry and basicity of anions should be considered for complementary of hosts and anions.

Reinhoudt and co-worker produced a series of acyclic tripodal receptors containing amide groups (compounds **1-2**) [5]. Compound **1** can bind $H_2PO_4^-$ with an association constant of 6.1 x 10^3 M^{-1} in acetonitrile. The increase electrophilicity of sulfonamide NH moieties in compound **2**, in combination with reorganization of the binding site by π-stacking, enhances $H_2PO_4^-$ binding with receptor **2** (K_a = 1.4 x 10^4 M^{-1}).

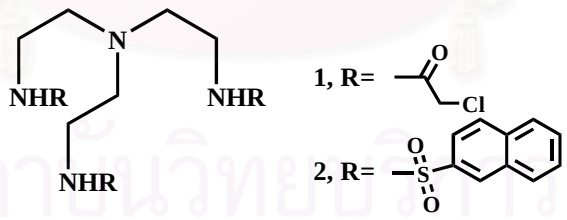
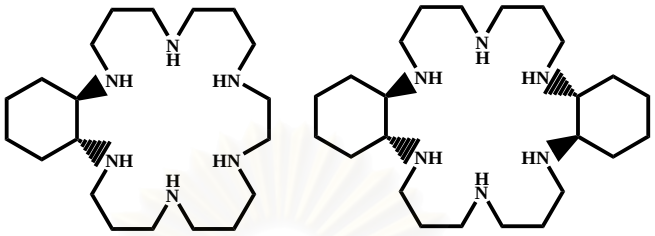


Figure 1.2 Structures of compounds **1**and **2**

Gotor and coworkers have examined the anion complexation properties of two chiral hexaazamacrocycles **3** and **4** [6]. These receptors were synthesized using a chemoenzymatic approach [7]. Protonation constants for the macrocycles were determined and association constants for the macrocycles with a variety of chiral anions measured by potentiometric titration with K values being determined for complexes containing 3, 4, 5 and 6 protons in 0.1 M Me_4Cl aqueous solution at 298 K.

hexaprotonated receptor **3** was found to preferentially bind D-tartarate (log K_a = 4.10) over its enantiomer (log K_a = 3.49) whilst hexaprotonated receptor **4** preferentially binds *N*-Ac-D-aspartate (log K_a = 5.34) over *N*-Ac-L-aspartate (log K_a = 4.57).



3 **4**

Figure 1.3 Structures of compounds **3** and **4**.

1.3 Anion receptors based on urea and thiourea

Despite lacking of the electrostratic complementary, ureas and thioureas have been shown to provide a strong binding site for carboxylates, using a bidentate hydrogen bonding motif. Thiourea derivatives showed stronger anion binding ability by means of stronger hydrogen bond than that of the corresponding urea because of the higher acidity of the former [8]. The higher acidity of the thiourea hydrogen dominates the weaker hydrogen bond accepting ability of sulfur as compare to oxygen [9-10].

A wide variety of urea containing anion receptors have been reported recently. These include a simple anion sensor system containing a single urea group linked to a chromophore or fluorophore through urea containing clefts to more complex macrocyclic systems. Thiourea is an especially good hydrogen bond donor and is an excellent anion receptor for carboxylate anions. Nishizawa and co-worker prepared thiourea-base chromophores with *p*-nitropheyl units, **5** and **6** [11]. As a result; compounds **5** and **6** were found to be more highly selective for acetate than other anions in 1% water: 99% acetonitrile. The binding properties of **5** and **6** with acetate showed that increasing the concentration of AcO^- produced a significant bathochromic shift in the UV-vis spectra. The stability constant of the acetate complex of **5** was 5.6 x 10^3 M^{-1}, much weaker than that of **6**, 3.5 x 10^5 M^{-1}. It was evident that increasing a *p*-nitropheyl group into the (*p*-nitropheyl)thiourea moiety enhanced the hydrogen bonding ability.

Likewise, chromophore **6** was then applied to the colorimetric determination of acetic acid in commercially available brands of vinegar. The results agreed well either the specification provided by the suppliers.

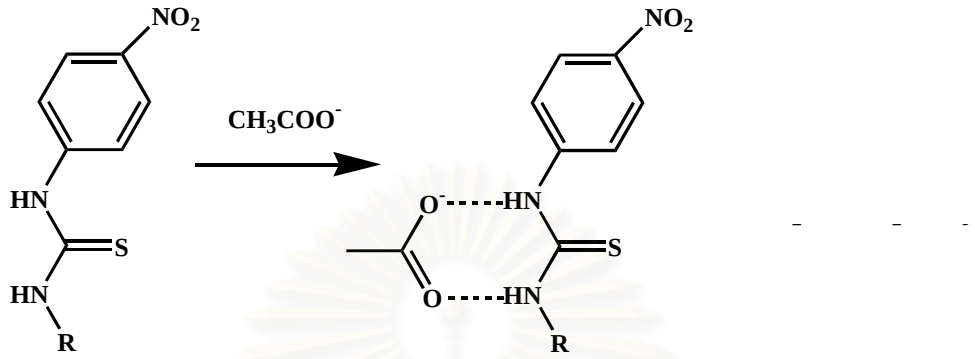


Figure 1.4 Compounds **5** and **6** were binding with acetate anion.

Hong and co-worker have recently reported anion coordination with a nitro-azophenol thiourea base sensor, compound **7** [12]. Association constants for anion binding were determined by ^{1}H NMR and UV-vis titrations in $CDCl_3$. $H_2PO_4^-$ (K_a = 2.6 x 10^4 M^{-1}) and AcO^- (K_a = 1.9 x 10^4 M^{-1}) gave stronger complexes with compound **3** than other anions due to their high basicity. Moreover, $H_2PO_4^-$ with four oxygens makes the strongest complexes *via* multitopic hydrogen-bonding interactions and these results agreed with those obtained by ^{1}H NMR. Large downfield shifts of thiourea NH resonances (>2.5 ppm) were detected upon complexation with $H_2PO_4^-$ and AcO^-. Broadening of the phenol OH resonance was also observed, indicating its participation in hydrogen-bonding interactions with anions.

In the absence of anions, the UV-vis absorption spectrum of **7** showed an absorption maximum peak at 376 nm. With addition of $H_2PO_4^-$, the peak at 376 nm decreased while a new peak appeared at 529 nm, concomitant with a solution colour change from light yellow to deep red. This may be due to electronic excitation through change transfer from the donor oxygen of the phenol to an acceptor substituent ($-NO_2$) of the chromophore. The excited state would be more stabilized by anion binding, resulting in a bathochromoc shift in the absorption maxima as well as colour change. Changing the substituent at the thiourea moiety of **7** from butylgroups to nitrobenzene groups in compound **8** allowed the easy colorimetric differentiation of F^-, $H_2PO_4^-$ and

AcO^- which have similar basicity. The degree of a red shift for **4** was determined to be $H_2PO_4^-$ >> AcO^- ≈ F^- >Br^- ≈ Cl^- > HSO_4^- ≈ I^- in $CHCl_3$, the maximum red-shift value (λ_{max} = 538 nm) for $H_2PO_4^-$ can be understood on the basis of the guest basicity and the structure of the complex.

Later, Hong and coworkers changed the signaling unit in compound **7** from nitro-azobenzene to indoaniline [13]. Compound **9**, a new chromogenic indoaniline-thiourea-based sensor, showed significant colour and UV-vis spectral changes upon binding anions. Upon addition of $H_2PO_4^-$ or HSO_4^-, the colour of the $CHCl_3$ solution changed from blue-green to deep blue. The association constants obtained from UV-vis titration for complexes of **9** with $H_2PO_4^-$ and HSO_4^- in $CHCl_3$ are 1.1 x 10^4 M^{-1} and 2.5 x 10^4 M^{-1}, respectively. However, addition of AcO^- or F^-, more basic anions, caused a less intense colour change. In addition, in the case of Cl^-, Br^- and I^-, no detectable colour changes were observed. This sensor, thus, allows the selective colorimetric detection of tetrahedral oxoanions such as $H_2PO_4^-$ and HSO_4^-. In the same manner as for compound **7**, compound **9** possesses four NH urea moieties and would preferably bind anions with tetrahedral geometry ($H_2PO_4^-$ and HSO_4^-).

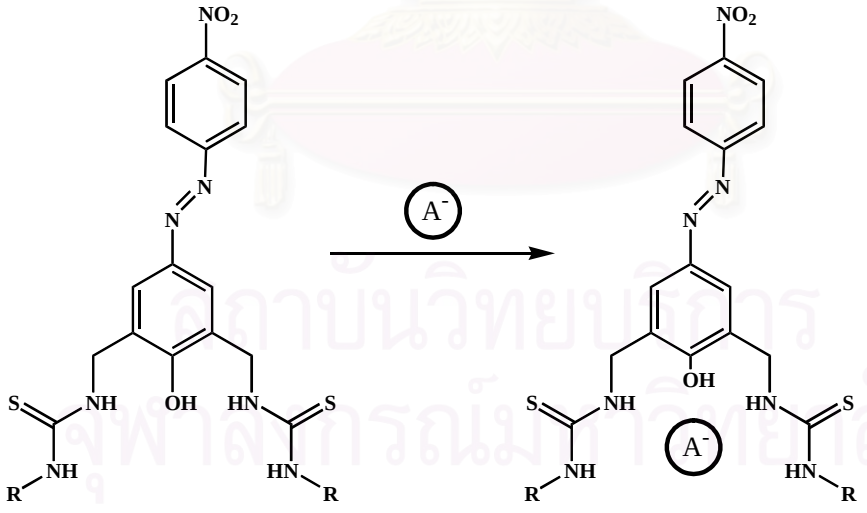
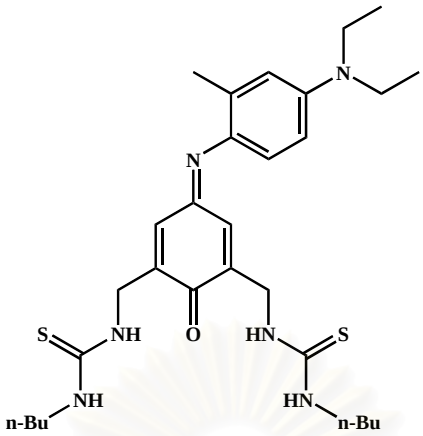


Figure 1.5 Binding of compounds **7** and **8** with anions.



9

Figure 1.6 Compound **9.**

1.4 Anion sensors

Anion sensors consistent of 3 parts: receptor unit, spacer and signaling unit. The receptor unit can bind anions with non-covalent interactions such as amide, urea and thioureas [14-15]. The spacer joins the signaling and receptor units together and must permit communication between the two of them. The signaling unit is responsive to the guest binding [16-18], which generates a signal in the form of an emission of electromagnetic radiation (photochemical sensing), a current (electrochemical sensing) or an otherwise externally measurable change (e.g. in color [19-22] or pH). The binding event must trigger intrinsically a change in the properties of the bound complex compared to the free guest or receptor, which results in signal generation.

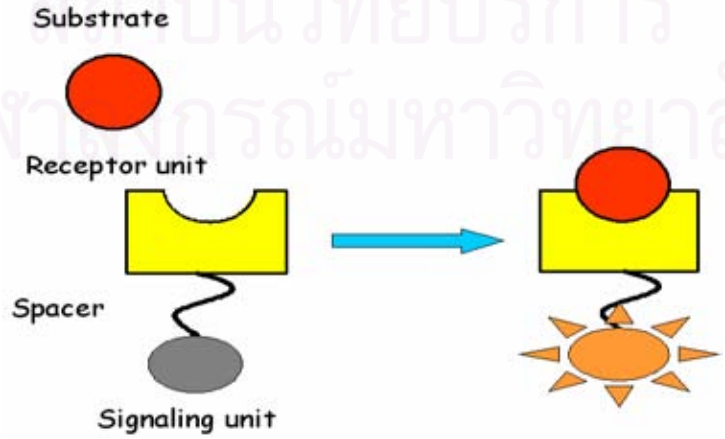


Figure 1.7 Representation of a chemical sensor.

Compounds **10** and **11** were especially designed for the recognition of bis-carboxylates such as glutarate, malonate and pyrophosphate [23]. For glutarate, the fluorescence emission of **10** was quenched by ca. 70% for malonate, the quenching was about 86%, and for pyrophosphate, the quenching was 95%. Similar quenching effects were observed for compound **11**. These bis-carboxylates form 1:1 complexes with both receptors (Figure 1.8). Other anions such as AcO^-, $H_2PO_4^-$ and F^- formed 2:1 anion:receptor complexes and also gave quite large fluorescence emission quenching (ca. 70-98%).

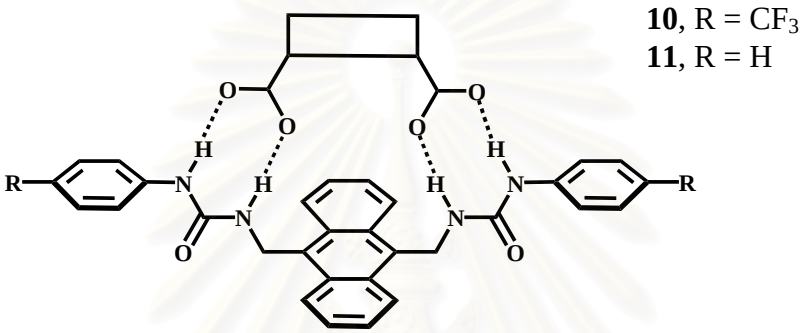


Figure 1.8 Schematic representation of the interaction of compounds **10** and **11** with bis-carboxylates.

1.5 Ditopic receptors

An exciting area of coordination chemistry is concerned with the syntheses of host molecules that contain binding sites for anionic and cationic guest species cavalently linked together and fashioned to be selective for target alkali/transition metal salts [24-26] and zwitterionic guests such as amino acids. Many of this synthetic receptor is unchanged molecules that operate in organic solvents. Under these conditions, target salts may exist as associated ion pairs that can hinder the single-ion recognition process. Two strategies can be employed to simultaneously bind both ions of the target salt. The dual-receptor strategy uses a binary mixture of anion and cation receptors; alternatively, a single ditopic receptor can be designed with specific cation and anion binding sites. These salt-binding receptors can be organic or organometallic molecules. They are prototypes for more complicated self-assembly systems that may eventually be used as components in molecular machines. The complexation of one changed guest can influence, through electrostatic and conformation effect, the

subsequent coordination of the pairing ion where the binding affinity for anions is modified as a result of the cations complexation, or *vice versa* [27-32].

Smith and co-workers have shown that alkali metal cations can successfully compete with neutral anion receptors for guest anions [33]. For example, a ^{1}H NMR titration showing dihydrogen phosphate complexation by **12** in CD_3CN is shown in **Figure 6** in the absence and presence of potassium tetraphenylborate. The potassium ions sequester the initial additions of dihydrogen phosphate until the cations and anions are at the same concentration. Only then do the added anions interact with the host receptor. Smith found that the ion-sequestering ability of the alkali metal cations is the order $Cs^+ < K^+ < Na^+$ matching their ion-pairing ability. In analogous receptors containing crown ether groups, the anion binding ability of the receptor was either enhanced or suppressed depending upon the nature of the receptor and the ion-pairing ability of the cationic guest.

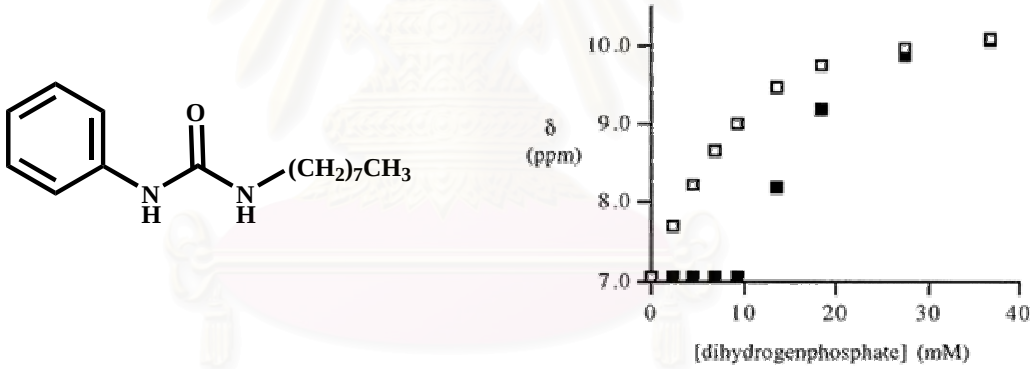


Figure 1.9 Compound **12** and chemical shift for aryl-NH in **12** in CD_3CN and upon addition of tatrabutylammonium dihydrogen phosphate: presence (solid square), and absence (outline square) of potassium tetraphenylborate.

Miyaji and co-workers reported chromogenic molecular switch **13** as a new ditopic ferrocene receptor for anions and cations [34]. Upon addition of F^- to a solution of **13** in accetonitrile, a new absorbance appeared at 472 nm (K_a = 9,340 M^{-1}). Addition of K^+ to the solution of **13.F**$^-$ caused a reverse behavior. The colour of the solution turned colourless. This implied that the colour change was controlled by F^- 'switches on' and K^+ 'switches off'. This result was confirmed by NMR studied in acetonitrile. When K^+ was added to the solution of **13.F**$^-$, large upfield shifts of the proton of the

urea-NH occurred and shifted to the position of the free receptor. The results from ^{1}H NMR and UV-vis studied, therefore, supported the fluoride binding center of **13** that caused the colour quenching process. This receptor may thus be applied as an optical device at the molecular level.

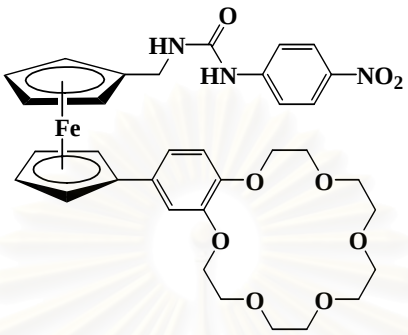


Figure 1.10 Compound **13**

In order to form an ion-pair successfully, Smith and coworkers have synthesized a variety of compounds including the strapped crown ether diamide clef receptors **14** (Figure 7) that is capable of binding a solvent separated ion-pair ($Na^{+}/CHCl_3/Cl^{-}$) and **15** (Figure 7) that is capable of recognizing KCl contact ion-pairs [35-36]. The association constant of receptor **15** with chloride is enhanced from 35 M^{-1} in DMSO-d_6 at 295 K to 460 M^{-1} in the presence of 1 equivalent of potassium tetraphenylborate. Addition of sodium to the receptor only increases its affinity for chloride to a K_a of 50 M^{-1} under the same conditions. X-ray crystal structures of the NaCl and KCl complexes reveal that the sodium cation is bound more closely to the crown ether than the potassium cation so increasing ion-dipole repulsion between chloride and crown ether oxygens (Figure 7).

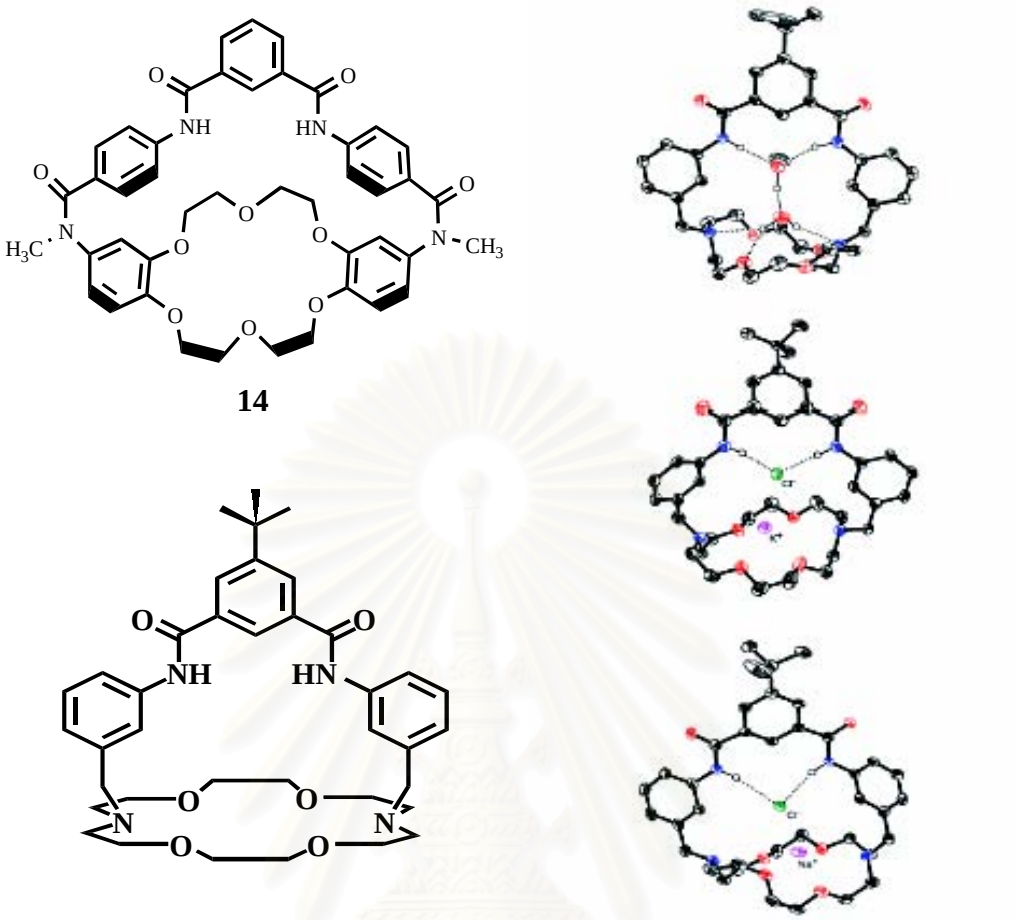


Figure 1.11 X-ray crystal structures of **14** and **15** with water and methanol (top), complexes of **15** with KCl (middle) and NaCl (bottom).

1.6 Photoactive Components

Photochromic molecules and their photoisomerization reactions have been the object of extensive investigation in the field of molecular photochemistry. Incorporation of a photochromic component into a supramolecular structure can lead to artificial photoresponsive species that may be quite valuable as model systems for theoretical studied and as photochemical molecular devices. The basic requirements for the design of an artificial photoresponsive supramolecular system are as follows: (a) a component of the supramolecular system must be able to absorb light (b) as a consequence of light excitation, the chromophoric component (or another component) must undergo a structural change (c) such a molecular structural change must cause a “functional”

change (that is a change in some properties relevant to a function) in another component or in the whole supramolecular structure.

1.6.1 Olefin-type compounds

The photoinduced *cis-trans* isomerization of olefin-type compounds is a important natural process [37-39] and an extensively investigated reaction in molecular photochemistry [40]. In general, the *trans*- isomer is the thermodynamically more stable form for free molecules, and the thermal *cis*→*trans* isomerizations can be slow or fast, depending on the compound and the experimental conditions. Both *trans*→*cis* and *cis*→*trans* isomerizations usually be obtained by irradiation with light of an appropriate wavelength. The reaction mechanism is excited state twisting about the –C=C- double bond. Stibene have a double-bond twist in the excited state, *trans*- and *cis*- isomers are shown in Figure 8. The mechanism of *trans*- and *cis*-isomerization of stibene was proposed as a rotation of the weaken double bond by an excitation of high-amplitude torsional vibration or by excitating an electron from a π-bonding to a π^*-antibonding orbital as rotation.

Figure 1.12 *Trans*- and *cis*- isomerization of stibene.

1.6.2 Azobenzene

Azobenzene is isostructural with stibene and the *trans*- and *cis*- isomers are shown in Figure 9. The same as stibene, the *trans*- isomer of azobenzene is more stable than the *cis*- isomer. Azobenzene have an absorption band ($\pi\pi^*$) in the ultraviolet region (~320 nm) is accompanied by a weak band ($n\pi^*$) near 450 nm. On conversion to the *cis* isomer, the $\pi\pi^*$ band shifts to shorter wavelengths and there is an increase in the intensity of the $n\pi^*$ absorption. Two possible mechanisms of *trans*- and *cis*-isomerization of azobenzene [41] are (i) twisting about the –N=N- double bond, as in

stibene. (ii) in-plane inversion at one of the two nitrogen atoms. The in-plane mechanism is responsible for the dark isomerization, whereas it is not yet clear whether photoisomerization takes place exclusively *via* inversion [42-43] or *via* twisting and inversion depending on the excited state populated by light excitation [44-45].

Photoinduced isomerization of azobenzene involves a large structural rearrangement and a big change in the dipole moment. The isomerization causes a decrease in the distance between the para carbon atoms from about 9.0 Å in the *trans*- form to 5.5 Å in the *cis*- form. The *trans*- form is planar and has no dipole moment, whereas the *cis*- form is non-planar and exhibits a dipole moment of 3.0 D [46]. These properties are useful for probes of conformational dynamic of macromolecules by site-specific photo labeling.

Figure 1.13 *Trans*- and *cis*- isomerization of azobenzene.

Shinkai and co-worker synthesized azobis(benzocrown ether) **16**, show in Figure 11, which possessed a butterfly-like motion. The *trans*-form isomerized by UV light irradiation to the *cis*- form, and the *cis*- form was isomerized thermally reversible to the *trans*-form [47]. The binding ability of photoresponsive **16** was determined by solvent extraction of alkali metal salts. The results consistently suggest that *cis*-**16** form stable 1:2 cation/crown complexes with large alkali metal cations (K^+, Rb^+ and Cs^+), wheras *trans*-13 form stable 1:1 cation/crown complexes with small alkali metal cations (Li^+ and Na^+).

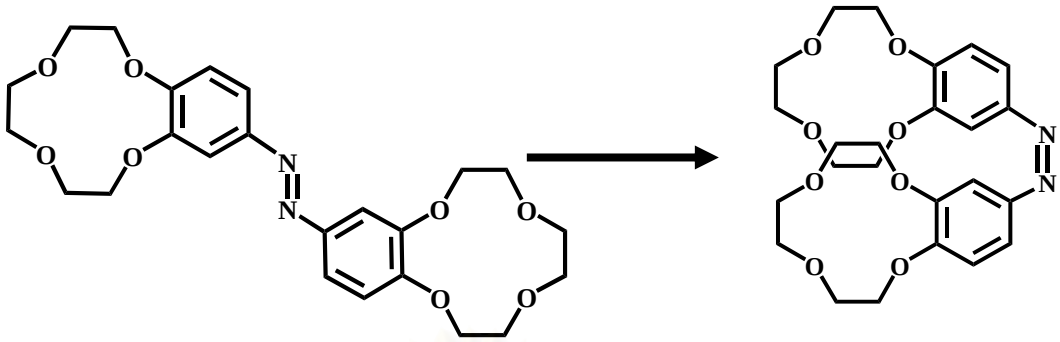


Figure 1.14 *Trans-cis* isomerization of azobenzene capped with crown ether (**16**).

1.7 Anion sensor of dicarboxylate anions

This reaction and the citric cycle [48] (known as Kreb's cycle) occur inside mitochondria. The cycle consists of dicarboxylate anions such as α-ketoglutarate, fumarate, malate, oxaloacetate and succinate are importance intermediates for generating ATP (adenosine triphosphate). Thus dicarboxylate anions are important for living cells.

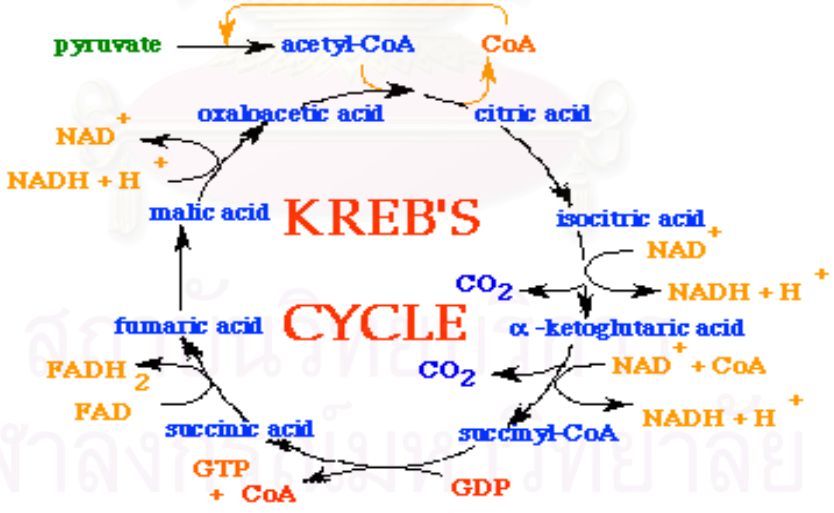


Figure 1.15 The citric acid cycle.

Fluorescence sensors for dicarboxylate anions have been reported by Mei and Wu [49]. The fluorescence quenching and a new emission of compound **17** (Figure 12) through photoinduced electron transfer (PET) process by different dicarboxylate anions

has been studied. Its sensitivity for recognition depends strongly on the chain length of dicarboxylate anions and the distance between urea units. ^{1}H NMR spectra indicate that a 1:1 complex is formed between compound **17** and a dicarboxylate anions through hydrogen bonding interactions. Results also indicate that multiple hydrogen bonding interactions may affect the stability of complexes and play an important role in molecular recognition.

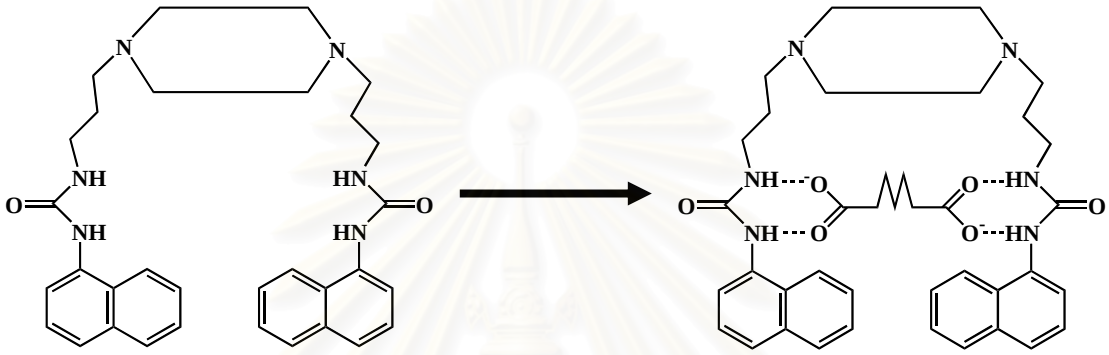


Figure 1.16 Structure of compound **17** and it complexation with pimelate anion.

1.8 Objectives and scope this research

The main goals of this research are to synthesize azobenzene and crown ether containing urea and thiourea groups. The azobenzene compounds employed NH-based donor urea or thiourea to serve as anion receptor. Complexation studies of these compounds with dicarboxylate anions such as oxalate, malonate, succinate, glutarate, adipate, pimelate, suberate and azelate are carried out by ^{1}H-NMR titrations. The binding abilities of the crown ether derivative towards dicarboxylate anions in the presence and absence of a metal ion will be investigated by UV-vis titration.

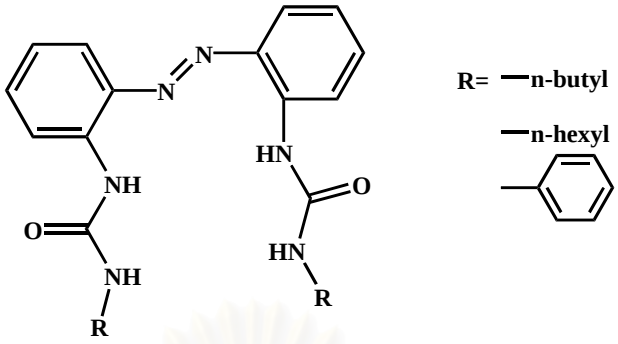


Figure 1.17 Structure of azobenzene containing urea derivatives.

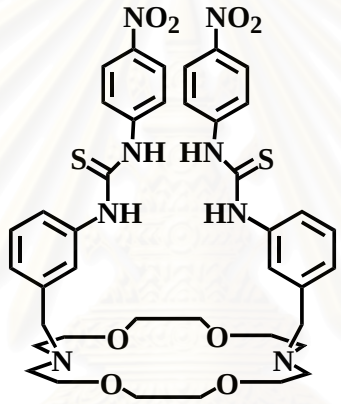


Figure 1.18 Structure of diazacrown ether containing thiourea.

CHAPTER II

EXPERIMENTAL SECTION

2.1 General procedure

2.1.1 Analytical instruments

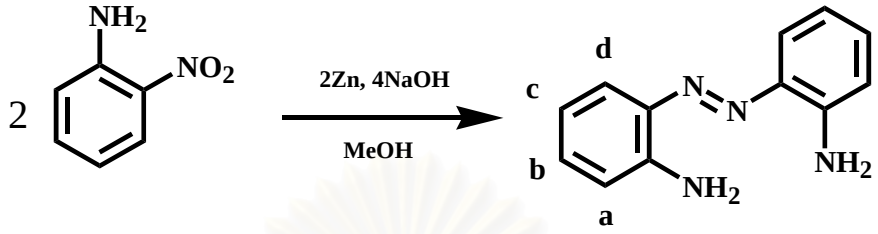
^{1}H NMR spectra were recorded on a Varian 400 MHz nuclear magnetic resonance spectrometer. In all cases, samples were dissolved in deuterated chloroform, acetonitrile or dimethyl sulfoxoxide, and chemical shifts were recorded using a residual proton signal as internal reference. Elemental analysis was analyzed on a Perkin Elmer CHON/S analyzer (PE2400 series II). UV- vis absorption spectra were acquired on a Varian Cary 50 UV- vis spectrophotometer. Infrared spectra were obtained on a Nicolet Impact 410 using KBr pellet. All melting points were taken on an Electrothermal 9100 apparatus.

2.1.2 Materials for synthesis

All materials were standard analytical grade, purchased from Fluka, Aldrich, Carlo Erba, BHD or Merck, and used without further purification. Commercial grade solvents such as acetone, dichloromethane, methanol, hexane and ethyl acetate were distilled before used. Chromatographic separations were performed on silica gel columns (kieselgel 60, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was carried out using silica gel plates (kieselgel 60 F_{254}, 1 mm, Merck). Synthesis of 2,2′-diaminobenzene,**1a** was carried out according to the literature procedure. The products were characterized by ^{1}H NMR spectroscopy and elemental analysis.

2.2 Synthesis of azobenzene derivatives

2.2.1 Preparation of 2, 2′-diaminoazobenzene , 1



1

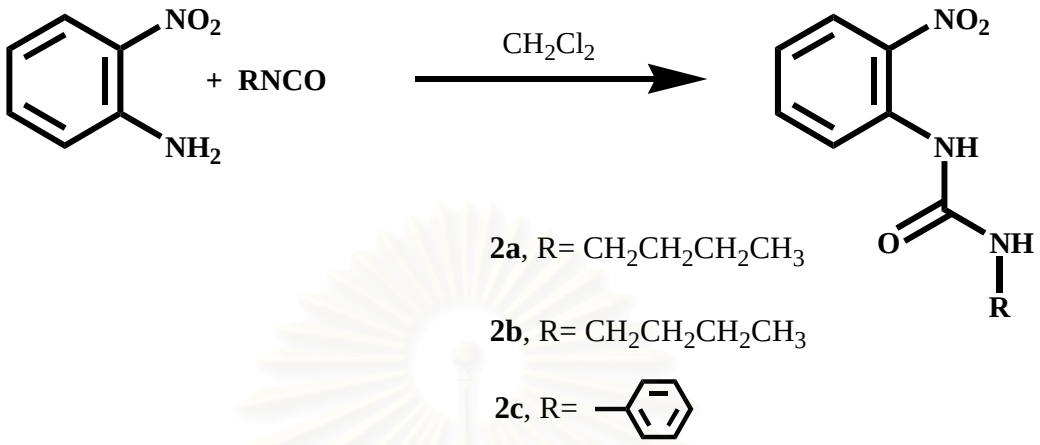
trace

In a 250 mL two-necked round bottom flask equipped with a magnetic bar and a reflux condenser, *o*-nitroaniline (0.6914 g, 5.0 mmol), zinc powder (0.6617g, 10.1 mmol), a solution of sodium hydroxide (0.8800 g, 22.00 mmol) in 25 mL of water were mixed in methanol (100 mL) and stirred. The mixture was refluxed under nitrogen for 10 hours. The reaction mixture was filtered while hot and washed with a small amount of methanol. The combined filtrate was neutralized by addition of 3 M hydrochloric acid and filtrated. The solvent was removed under reduced pressure on a rotary evaporator to give a brown residue. The product was eluted through a silica gel column with dichloromethane as eluent to give a orange solid. The product **1** was dried in *vacuo* and kept in a desiccator.

Characterization data for 1:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 8.05 (d, 2H, *J* = 8.4 Hz, -N=NAr-H_dNH_2), 7.29 (t, 2H, *J* = 7.6 Hz, -N=NAr-H_aNH_2), 6.74 (d, 2H, *J* = 8.0 Hz, -N=NAr-H_bNH_2), 6.64 (t, 2H, *J* = 8.0 Hz, -N=NAr-H_cNH_2); 5.07 (s, broad, 4H, -ArNH_2)

2.2.2 Preparation of 2a, 2b and 2c



Typically into a 50 mL two-necked round bottom flask equipped with a magnetic bar, an appropriate (2.7 mmol) was added to a solution of 2-nitroaniline (0.1383 g, 1.0 mmol), in dichloromethane (10 mL) and stirred overnight at room temperature under nitrogen. The solvent was removed under reduced pressure on a rotary evaporator to give a yellowish residue. The product was eluted through a silica gel column with dichloromethane as eluent to give a orange-yellow residue. Recrytallization from dichloromethane/hexane gave the product **2a, 2b and 2c** as yellow solids (in 19%, 26% and 19%, respectively). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 2a:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 8.59 (d, 2H, *J* = 8.4 Hz, -N=NAr-H_dNH_2), 8.11 (d, 2H, *J* = 8.0 Hz, -N=NAr-H_aNH_2), 7.52 (t, 2H, *J* = 7.2 Hz, -N=NAr-H_bNH_2), 6.98 (t, 2H, *J* = 7.2 Hz, -N=NAr-H_cNH_2); 9.73 (s, broad, 4H, -ArNHC=O), 4.8 (s, broad, 4H, -C=ONHCH_2-), 1.47 (q, 2H, J = 7.2 Hz, -NH$(CH_2)_3CH_3$), 1.40-1.20 (m, 4H, J = 7.6 Hz, -NH$(CH_2)_3CH_3$), 0.89 (t, 3H, J = 6.8 Hz, -NH$(CH_2)_3CH_3$)

IR spectrum (KBr (cm^{-1})): 1649 (C=O)

Melting point: 112.3-114.1 ^oC

Elemental analysis:

Anal. calcd for $C_{22}H_{30}O_2N_6$	C, 55.69; H, 6.37; N, 20.23
Found	C, 58.80; H, 7.72; N, 15.07

Characterization data for 2b:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 8.73 (d, 2H, *J* = 9.2 Hz, -N=NAr-H_dNH_2), 8.23 (t, 2H, *J* = 8.8 Hz, -N=NAr-H_aNH_2), 6.74 (d, 2H, *J* = 8.0 Hz, -N=NAr-H_bNH_2), 6.64 (t, 2H, *J* = 4.0 Hz, -N=NAr-H_cNH_2); 5.07 (s, broad, 4H, -ArNH_2), 3.24 (q, 2H, J = 6.4 Hz, -NH$(CH_2)_3CH_3$), 1.54-1.20 (m, 4H, J = 7.6 Hz, -NH$(CH_2)_3CH_3$), 0.85 (t, 3H, J = 8.3 Hz, -NH$(CH_2)_3CH_3$)

IR spectrum (KBr (cm^{-1})): 1649 (C=O)

Melting point: 98.0-99.7 °C

Elemental analysis:

Anal. calcd for $C_{26}H_{38}O_2N_6$	C, 58.85; H, 7.22; N, 15.84
Found	C, 58.83; H, 8.42; N, 15.66

Characterization data for 2c:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 8.72 (d, 2H, *J* = 9.2 Hz, -N=NAr-H_dNH_2), 7.22 (d, 2H, *J* = 8.0 Hz, -N=NAr-H_aNH_2), 7.67 (t, 2H, *J* = 8.8 Hz, -N=NAr-H_bNH_2), 7.45 (t, 2H, *J* = 7.2 Hz, -N=NAr-H_aNH_2); 10.05 (s, broad, 4H, -ArNH_2C=O), 6.82 (s, broad, 4H, -C=ONHCH_2-), 7.37 (d, 2H, *J* = 8.8 Hz, -NH-Ar-H_e), 7.15 (t, 2H, *J* = 8.0 Hz, -NH-Ar-H_f), 7.18 (t, 2H, *J* = 7.4 Hz, -NH-Ar-H_g)

IR spectrum (KBr (cm^{-1})): 1649 (C=O)

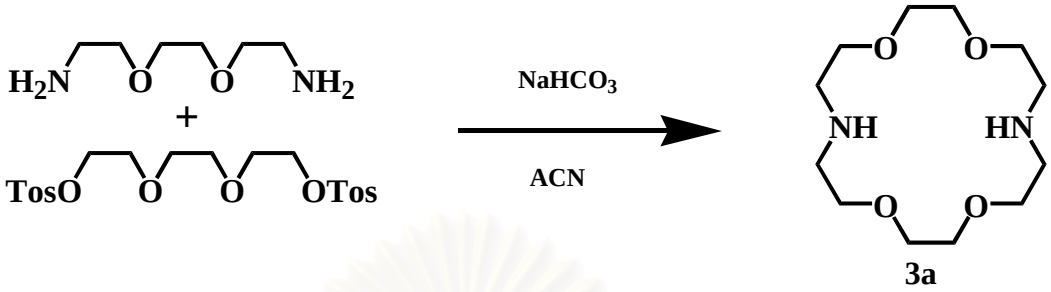
Melting point: 177.8-179.1 °C

Elemental analysis:

Anal. calcd for $C_{26}H_{22}O_2N_6$	C, 60.37; H, 4.31; N, 16.33
Found	C, 60.67; H, 4.71; N, 16.28

2.3 Synthesis of diazacrown ether containing thiourea (4)

2.3.1 Preparation of 1,4,10,13,-tetraoxa-7,16-diazacyclooctadecane (3a)



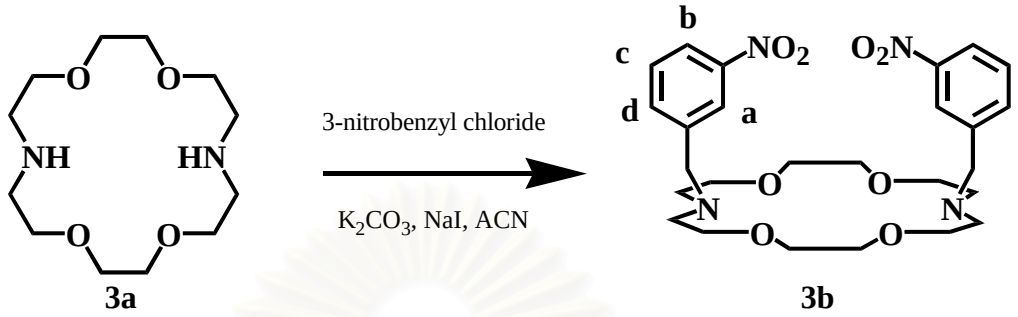
3a

In a 50 mL two-necked round bottom flask equipped with a magnetic bar, a mixture of triethylene glycol ditosylate (5.2 g, 9.6 mmol) and sodium carbonate (10.6 g, 96 mmol) in acetonitrile (75 mL) were stirred and refluxed for 1 hour. A solution of diethylene glycolamine **(**1.43 g, 9.6 mmol) in acetonitrile (25 mL) was slowly added in the mixture. The white precipitate was filtered. The solvent was removed by a rotary evaporation to give a yellow oil. The product was purified by Al_2O_3 column chromatography with THF:ethanol 10:1 as eluent to give a colorless solution. Addition of hexane gave a white solid of **3a** (35% yield).

Characterization data for 3a:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 3.63 (t, 16H, *J* = 5.2 Hz, -CH_2O-), 2.83 (t, 8H, *J* = 4.8 Hz, -CH_2NH-), 2.72 (s, broad, 2H, -NH)

2.3.2 Preparation of 7,16-bis(3-nitrobenzyl)1,4,10,13,-tetraoxa-7,16-diaza cyclooctadecane (3b)

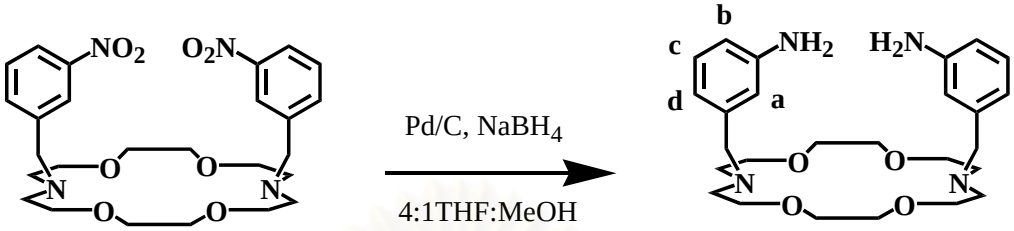


In a 250 mL two-necked round bottom flask equipped with a magnetic bar, a mixture of diazacrown ether (**3a**) (1.01g, 4.99mmol), sodium carbonate (2.43 g, 16 mmol) and a catalytic amount of sodium iodide in acetonitrile (75 mL) were stirred. The solution of 3-nitrobenzyl chloride **(**1.55 g, 9 mmol) in acetonitrile (30 mL) was slowly added in the mixture after stirred and refluxed overnight. The white precipitate was filtered. The solvent was removed by a rotary evaporation to give a yellow oil. The yellow oil was extracted with dichloromethane/water. The organic layer was dried over anhydrous magnesium sulphate and filtered. The solvent was removed to give yellow oil. The product was purified with Al_2O_3 column chromatography with 30% hexane: dichloromethane as eluent to give a yellow solution. Addition of hexane gave a yellow solid of **3b** (58% yield).

Characterization data for 3b:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 8.29 (s, 2H, H_a), 8.09 (d, 2H, *J* = 8.4 Hz, H_b), 7.73 (d, 2H, *J* = 7.6 Hz, H_d), 7.48 (t, 2H, *J* = 8.0 Hz, H_c); 3.84 (s, 4H,-CH_2N-), 3.67 (t, 16H, *J* = 6.0 Hz, -CH_2O-), 2.87 (t, 8H, *J* = 6.4 Hz, -CH_2NH-)

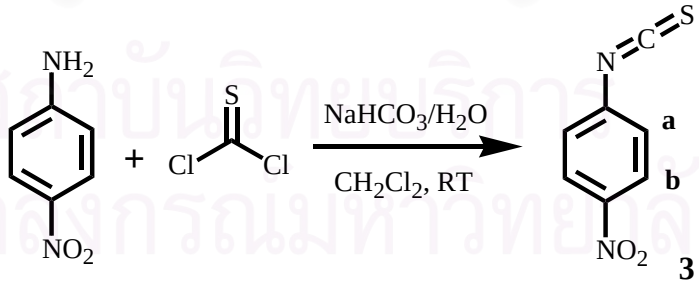
2.3.3 Preparation of 1,4-bis(3-aminobenzyl)1,4,10,13,-tetraoxa-7,16-diaza cyclooctadecane (3c)



3b **3c**

In a 100 mL two-necked round bottom flask equipped with a magnetic bar, a solution of bis(nitrobenzyl)diazobenzene (**3b**) (0.45 g, 0.8 mmol) in THF:methanol 4:1 (50 mL) was stirred. The solution was added palladium/charcoal and sodium borohydride (0.10 g, 2.6 mmol) and was stirred for 30 minutes. The black precipitate was filtered. The solvent was removed by a rotary evaporation to give a yellow oil. The yellow oil was extracted with dichloromethane/water. The organic layer was dried over anhydrous magnesium sulphate and filtered. The solvent was removed to give a yellow oil of **3c** (95% yield). This air sensitive product was immediately used in the next step.

2.3.4 Preparation of 4-nitrophenyl thioisocyanate (3)



3

In a 250 mL one-necked round bottom flask equipped with a magnetic bar, 4-nitroaniline (2.1489 g, 15.56 mmol), a solution of sodium bicarbonate (2.9616 g, 35.25 mmol) in deionized water (30 mL) and dichloromethane (60 mL) were stirred for 10 minutes at room temperature. Thiophosgine (1.80 mL, 23.61 mmol) was added dropwise and the mixture was stirred overnight. The organic phase was separated and

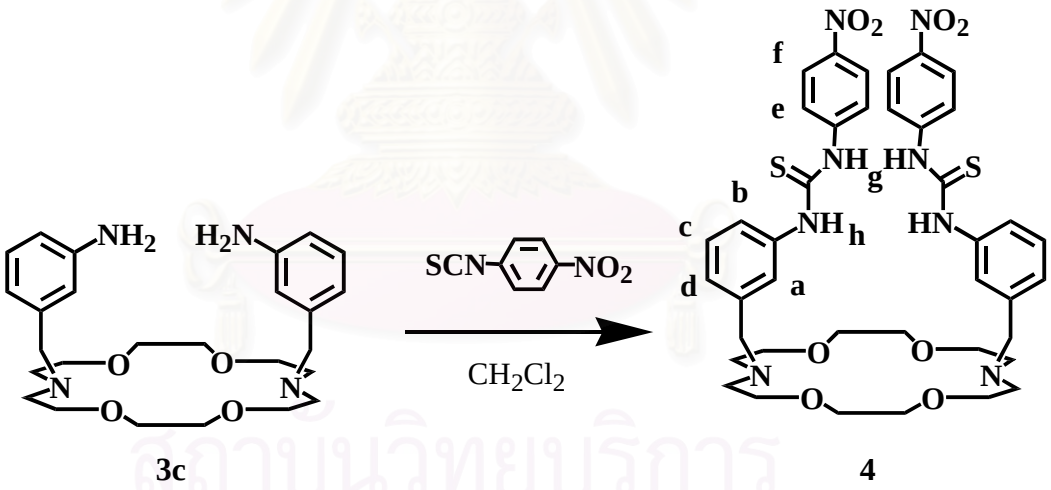
the aqueous layer was extracted with dichloromethane. The combined organic layer was washed with deionized water and dried over anhydrous sodium sulphate. After filtration of sodium sulphate, the solvent was evaporated by a rotary evaporation to give 4-nitrophenyl thioisocynate, **3**, as a yellow solid (93% yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 3:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 8.22 (d, 2H, *J* = 7.0 Hz, SCN*Ar*-H_bNO_2), 7.33 (d, 2H, *J* = 5.2 Hz, SCN*Ar*-H_aNO_2)

Melting point: 111 -116 ^oC

2.3.4 Preparation of [1,4-bis(N-(4-nitrophenyl)-N'-3-benzyl)thiourea] 1,4,10,13,-tetraoxa-7,16-diazacyclooctadecane (4)



3c **4**

In a 50 mL two-necked round bottom flask equipped with a magnetic bar, a mixture of bis(aminobenzyl)diazobenzene (**3c**) (3.70 g, 0.8 mmol) and 4-nitrophenyl thioisocyanate (2.89 g, 1.6 mmol) in dichloromethane (25 mL) were stirred overnight. The yellow precipitate was filtered. Recrystallization from hexane gave a yellow solid of **4** (49% yield). The product was dried in *vacuo* and kept in a desiccator.

Characterization data for 4:

^{1}H NMR spectrum ($CDCl_3$): δ (ppm) = 10.369 (s, broad, 2H, H_g), 10.291 (s, broad, 2H, H_h), 8.21 (d, 2H, *J* = 9.2 Hz, H_f), 7.73 (d, 2H, *J* = 9.2 Hz, H_e), 7.44 (s, 2H, H_a), 7.37 (d, 2H, *J* = 8.4 Hz, H_b), 7.30 (t, 2H, *J* = 7.2 Hz, H_c), 7.48 (d, 2H, *J* = 7.6 Hz, H_d); 3.63 (s, 4H,-CH_2N-), 3.53 (t, 16H, *J* = 6.0 Hz, -CH_2O-), 2.71 (t, 8H, *J* = 5.6 Hz, -CH_2NH-)

IR spectrum (KBr (cm^{-1})): 1640 (C=S)

Melting point: 107.9-109.1 ^oC

Elemental analysis:

Anal. calcd for $C_{40}H_{48}O_8N_8S_2$	C, 57.68; H, 5.81; N, 13.45
Found	C, 57.59; H, 5.92; N, 13.33

2.4 Complexation studies with dicarboxylate anions

2.4.1 Preparation of tetrabutylammonium salts

In a 50 mL two-necked round bottom flask equipped with a magnetic bar, 0.8 M solution of tetrabutylammonium hydroxide in methanol (5.0 mL, 4.00 mmol) was added to a stirred solution of a dicarboxylic acid (2.00 mmol) in methanol (15 mL) and stirring was continued overnight at room temperature under nitrogen. The solvent was removed by a rotary evaporation and the solid was dried for several days under high *vacuum* over P_2O_5. Tetrabutylammonium salts were stored under *vacuo* before used.

2.4.2 ^{1}H NMR titration studies for complexes of ligand 2a with dicarboxylate anions

Typically, a 0.01 M solution of a ligand ($7.0x10^{-6}$ mol) in CD_3CN (0.7 mL) was prepared in a 5-mm NMR tube. An initial ^{1}H NMR spectrum of the solution of ligand was recorded. A 0.14 M stock solution of guest molecules ($4.2x10^{-5}$ mol) in CD_3CN (0.3 mL) was prepared in a vial (shown in **Table 2.1**). The solution of a guest molecule was added *via* a microsyringe (10 μL portion) to the NMR tube. ^{1}H NMR spectra were recorded after each addition.

Table 2.1 The amounts of tetrabutylammonium salts that used in anion complexation studies with ligand **2a**.

Ligand	Anions	
	Name	Weight (gram)
2a	Acetate	0.01266
	Oxalate	0.02406
	Malonate	0.02465
	Succinate	0.02524
	Glutalate	0.02583
	Adipate	0.02642
	Pimatate	0.02701
	Suberate	0.02760
	Azelate	0.02819

2.4.3 Binding studies of 4 toward dicarboxylate anions.

2.4.3.1 UV-vis titration studies for complexes of ligand 4 with dicarboxylate anions

Typically, a stock solution of $2.0x10^{-5}$ M solution of ligand **4** ($2.0x10^{-6}$ mol) in acetonitrile (AR grade) was prepared in a 100 mL a volumetic flask, ionic strength being kept constant at 0.01 M using tetrabutyl ammonium perchlorate. The solution of the ligand was pipetted into a 1 cm pathlenght quartz cuvette and absorption spectra of the ligand were recorded from 250 to 600 nm at room temperature with a Varian Cary 50 UV-vis spectrophotometer. A solution of a guest in 25 mL of 0.01 M tetrabutyl ammonium perchlorate in acetonitrile was prepared in a volumetic flask (shown in **Table 2.2**). The solution of the guest was added directly to the cuvette by a microburette (200 μL portion) and stirred for 30 seconds and absorption spectra of the solution were recorded after each addition. The change in absorbance with solution of a guest was followed until the absorbance of a new peak was constant. Stability constants were refined from spectrophotometric data using the Sirko program [50].

Table 2.2 The amounts of tetrabutylammonium salts that used in anion complexation studies with ligand **4**.

Ligand	Anions	
	Name	Concentration (mM)
4	Malonate	1.00
	succinate	1.00
	Glutalate	0.30
	Adipate	0.30
	Pimatate	0.30
	Suberate	1.00

2.4.3.2 UV-vis titration studies for complexes of ligand 4 with sodium ion

Typically, a stock solution of $2.0x10^{-5}$ M solution of ligand 4 ($2.0x10^{-6}$ mol) in acetonitrile (AR grade) was prepared in a 100 mL a volumetic flask, ionic strength being kept constant at 0.01 M using tetrabutyl ammonium perchlorate. The solution of the ligand was pipetted into a 1 cm pathlenght quartz cuvette and absorption spectra of the ligand were recorded from 250 to 600 nm at room temperature with a Varian Cary 50 UV-vis spectrophotometer. A solution of sodium perchlorate in 25 mL of $6.7x10^{-4}$ M tetrabutyl ammonium perchlorate in acetonitrile was prepared in a volumetic flask. The solution of the guest was added directly to the cuvette by a microburette (200 μL portion) and stirred for 30 seconds and absorption spectra of the solution were recorded after each addition. The change in absorbance with solution of a guest was followed until the absorbance of a new peak was constant. Stability constants were refined from spectrophotometric data using the Sirko program [50].

2.4.3.3 UV-vis titration studies for complexes of ligand 4 with dicarboxylate anions in the presence sodium ion

Typically, a stock solution of $2.0x10^{-5}$ M solution of ligand **4** ($2.0x10^{-6}$ mol) in acetonitrile (AR grade) was prepared in a 100 mL a volumetic flask, ionic strength being kept constant at 0.01 M using tetrabutyl ammonium perchlorate. The solution of the ligand was pipetted into a 1 cm pathlenght quartz cuvette and absorption spectra of the ligand were recorded from 250 to 600 nm at room temperature with a Varian Cary 50 UV-vis spectrophotometer. A solution of anion and sodium perchlorate in 25 mL of 0.01 M tetrabutyl ammonium perchlorate in acetonitrile was prepared in a volumetic flask (shown in Table 2.4). The solution of guests were added directly to the cuvette by a microburette (200 μL portion) and stirred for 30 seconds and absorption spectra of the solution were recorded after each addition. The change in absorbance with solution of a guest was followed until the absorbance of a new peak was constant. Stability constants were refined from spectrophotometric data using the Sirko program [50].

Table 2.4 The amounts of tetrabutylammonium salts that used in anion complexation studies with ligand **4**.

Ligand	Sodium perchlorate 0.01 M (mL)	Anions	
		Name	Concentration (M)
4	8.00	Malonate	0.20
	8.00	succinate	0.20
	8.00	Glutalate	0.20
	5.00	Adipate	0.13
	8.00	Pimatate	0.20
	8.00	Suberate	0.20

CHAPTER III

RESULTS AND DISSCUSION

3.1 Synthesis and characterization of azobenzene derivatives and diaza crown ether.

3.1.1 Synthesis and characterization of 2,2'-diaminoazobenzene derivatives, (2a, 2b, 2c).

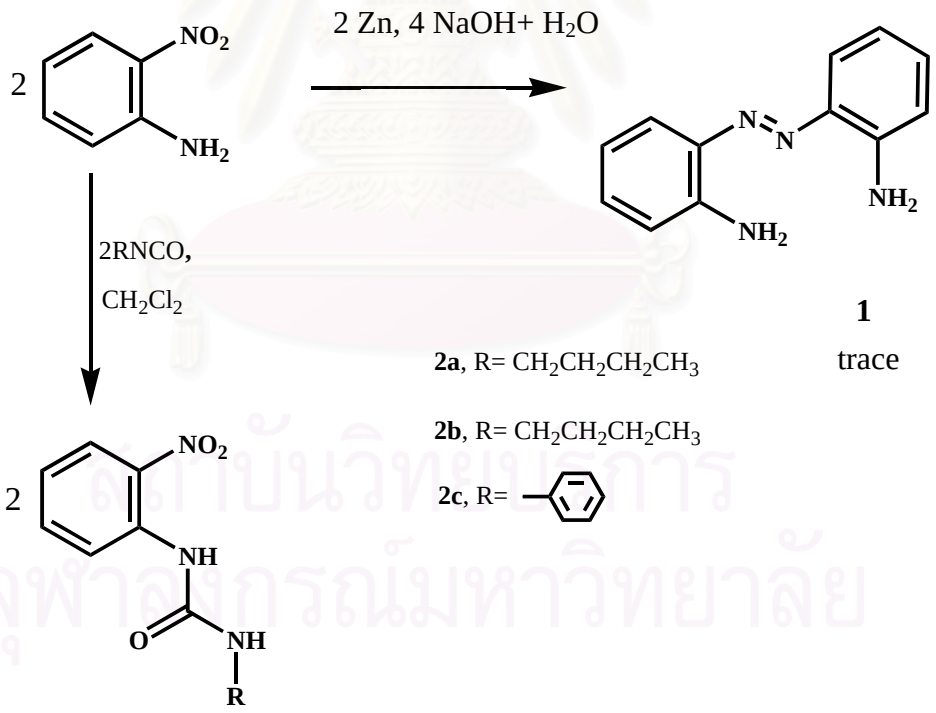
Azobenzene derivatives exhibit photoinduced reversible *cis-trans* isomerisms and the structural change is considerably large. Therefore, conformations of azobenzene-containing compounds are changed (or controlled) by photoinduced configurational changes of azobenzene units. We then connected an azobenzene unit to an anion receptor unit to form a photo-switchable anion receptor and sensor.

It is known that the azobenzene can be synthesized from a reductive coupling of two nitro groups using zinc as an oxidizing agent [51]. Syntheses of compounds **2a-c** are outlined in Scheme 3.1. Synthesis of 2,2'-diaminoazobenzene (**1**) was carried out from 2-nitroaniline in the presence of aqueous sodium hydroxide and zinc. Workup and purification by column chromatography resulted in an orange solid of **1**. The ^{1}H NMR spectrum of 2,2'-diaminoazobenzene (**1**) showed an amine proton signal at 5.07 ppm. The aromatic protons appeared as two doublets at 6.74 and 8.05 ppm and two triplets at 6.64 and 7.29 ppm.

The final product **2a** was obtained by 2-nitroaniline with 2.5 equiv. of n-butyl isocyanate in dichloromethane overnight. The crude product was obtained as a bright yellow solid in 19% yield after entensive purification by column chromatography and recrystallization. The ^{1}H NMR spectrum of **2a** showed characteristic peaks of a butyl group as a quartet at 1.47 ppm (J = 7.2 Hz), a multiplet at 1.20-1.40 ppm, a triplet at 0.89 ppm (J = 7.6 Hz) and two singlet peaks due to urea protons (-N=NArNHCONH-) at 9.73 and 4.80 ppm. IR spectra showed a C=O stretching band at 1649 cm^{-1}.

A similar coupling reaction between 2-nitroaniline and n-hexyl isocyanate gave compound **2b** which was purified by column chromatography and recrytallization. The ^{1}H NMR spectrum of **2b** showed characteristic peaks of a hexyl group as a quartet at 3.24 ppm (J = 6.4 Hz), a multiplet at 1.20-1.54 ppm (J = 7.6 Hz), a triplet at 0.85 ppm (J = 8.3 Hz) and two singlet peaks due to urea protons (-N=NArNHCONH-) at 10.05 and 5.07 ppm. IR spectra showed a C=O stretching band at 1649 cm^{-1}.

Reaction of 2-nitroaniline with phenyl isocyanate gave compound **2c** which was purified by column chromatography and recrytallization. The ^{1}H NMR spectrum of **2c** showed characteristic peaks of a phenyl group as a doublet at 7.37 ppm (J = 8.8 Hz), a triplet at 7.15 ppm (J = 8.0 Hz), a triplet at 7.18 ppm (J = 7.4 Hz) and two singlet peaks due to urea protons (-N=NArNHCONH-) at 10.05 and 6.82 ppm. IR spectra showed a C=O stretching band at 1649 cm^{-1}.



Scheme 3.1 The synthetic pathway of azobenzene containing ureas.

3.1.2 Synthesis and characterization of diazacrown ether derivatives.

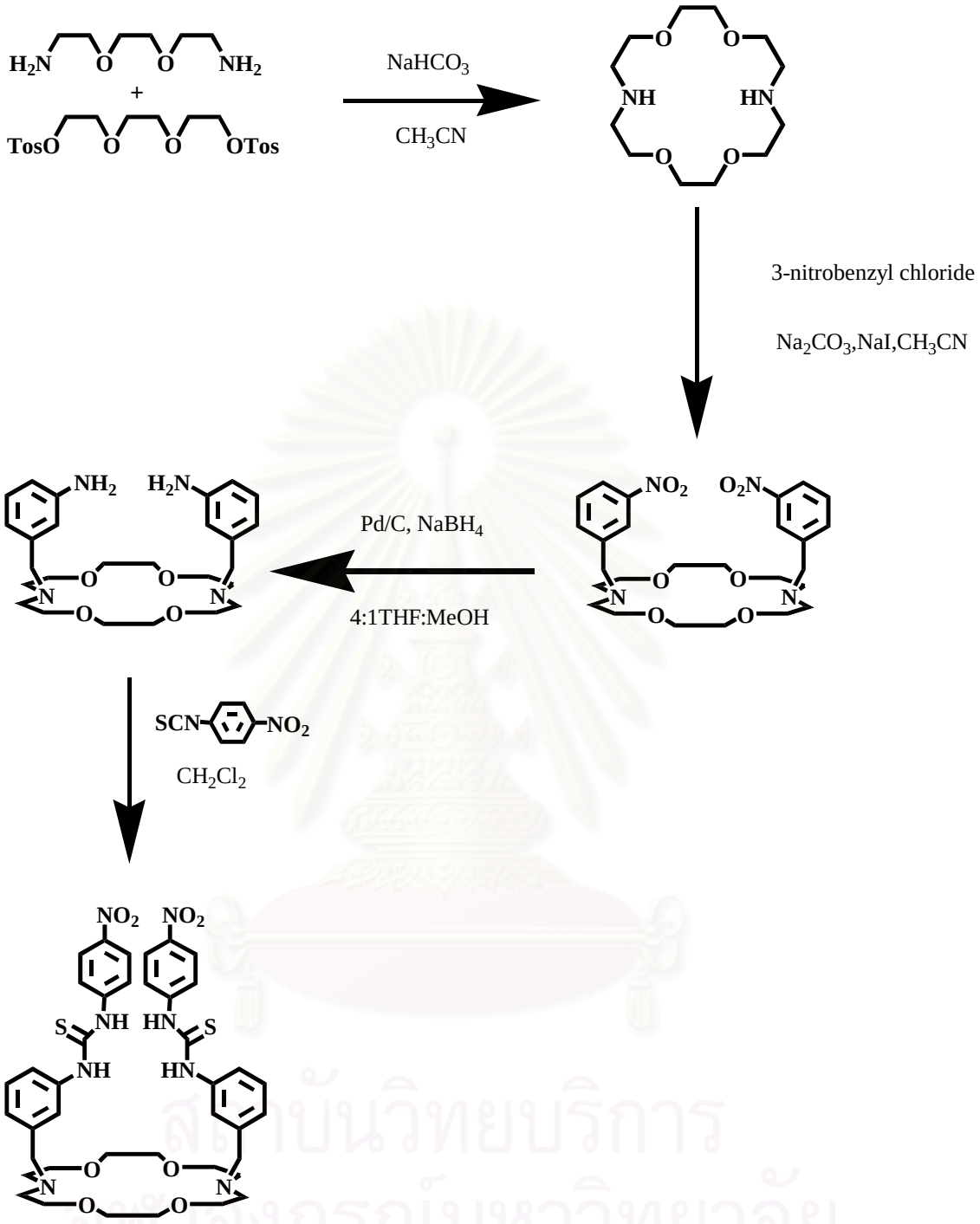
It is known that the crown ether have a cavity which an alkali metal ion can residue by attractive electrostatic ion-dipole interactions. The better the fit of the cation into the crown, the stronger the complex formed. We connected a crown ether and a sensory unit to an anion receptor unit to build a dicarboxylate anion receptor and sensor. The synthesis of receptor **4** was conducted according to Scheme 3.2.

Preparation of triethylene glycol ditosylate was carried out by a reaction between triethylene glycol and tosylchloride in the presence triethylamine and a catalyst amount of DMAP in CH_2Cl_2. Purification by column chromatography and recrytallization gave a white solid of triethylene glycol ditosylate. The ^{1}H NMR spectrum of the product showed a singlet of methyl protons at 2.48 ppm, a doublet of aromatic protons at 7.38 and 7.82 ppm and a triplet of bridging glycolic protons (OCH_2CH_2O) at 3.69 and 4.18 ppm.

The coupling reaction of triethylene glycol ditosylate with triethylamine in acetonitrile using anhydrous potassium carbonate as based afforded diaza crown ether, **3a**, as a white solid in 35% yield after Al_2O_3 column and recrytallization. The ^{1}H NMR spectrum of **3a** showed a singlet peak of NH protons at 2.72 ppm and ethylene protons appear at 2.83 and 3.63 ppm.

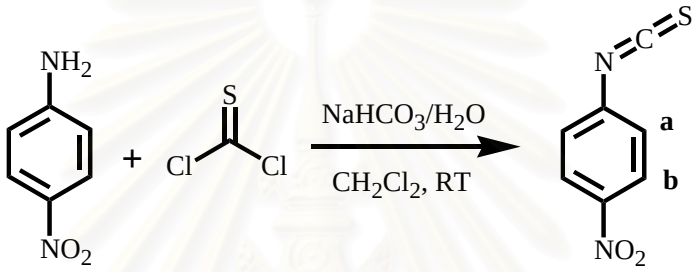
Bis(3-nitrobenzyl)diaza crown ether, **3b**, was synthesized by adding of a solution of 3-nitrobenzyl chloride into a mixture of diaza crown ether, sodium carbonate and sodium iodide. Compound 3b was obtained in 40% yield after Al_2O_3 column and recrytallization. The ^{1}H NMR spectrum of **3b** showed a singlet at 8.29 ppm, a doublet at 8.09 and 7.73 ppm, a triplet at 7.48 ppm of aromatic protons, a singlet of benzyl protons at 3.84 ppm and triplet of ethylene protons at 2.87 and 3.67 ppm.

Reduction of the nitro group to the amine group was carried out using sodium borohydride and palladium/charcoal in 4:1 THF:MeOH. The solution was extracted with dichloromethane/water and dried with magnesium sulphate to give a yellow oil (95% yield). This air sensitive amine product **3c** was immediately used in the next step.



Scheme 3.2 The synthetic pathway of receptor **4.**

The preparation of thioisocyanate is a common method in which the primary amine was reacted with thiophosgene to give chlorothioformamide (ClCSNHR) that loss HCl to obtain thioisocyanate (RNCS). In this case, the preparation of 4-nitrophenyl thioisocyanate was carried out by stirring a mixture of 4-nitroaniline with 1.5 equiv. of thiophosgene in the presence of 2.3 equiv. of sodium carbonate in CH_2Cl_2 at room temperature overnight (Scheme 3.3). A bright yellow solid of 4-nitrophenyl thioisocyanate was obtained in 93 % yield. The ^{1}H NMR spectrum of 4-nitrophenyl thioisocyanate showed the characteristic peak of the compound in accordance with the literature [52].



Scheme 3.3 The synthesis of 4-nitrophenyl thioisocyanate.

The final product **4** was obtained by reacting compound **3c** with 4-nitrophenyl thioisocyanate in dichloromethane under nitrogen atmosphere. The product precipitated and was recrytallized from hexane to obtain a yellow solid (49 % yield). The ^{1}H NMR spectrum of **4** showed two singlet peaks due to NH-thiourea at 10.37 and 10.29 ppm, and aromatic protons appeared at 7.30-7.75 ppm. The IR spectra showed a C=S stretching band at 1640 cm^{-1}.

3.2 Complexation studied with dicarboxylate anions.

Compound **2a** contains four urea groups and **4** contains thiourea groups as hydrogen bond donors for binding dicarboxylate anions. Binding of **2a** with dicarboxylate anions possessing various chain lengths was studied. Receptor **4** was subjected to the study of ion pair effects the binding of **4** with various dicarboxylate anions.

Compound **2a** possessed alkyl chains. Thus **2a** is soluble in aprotic solvents such as CD_3CN and $CDCl_3$ and protic solvents such as CD_3OH and DMSO-d_6. However, protic solvents can interact with anions. When $CDCl_3$ was used as solvent, NH signals of the urea group of **2a** disappeared upon the addition of dicarboxylate anions in $CDCl_3$. The association constants cannot be calculated using $CDCl_3$. Therefore, CD_3CN was used instead.

Receptor **4** has a *p*-nitrophenylthiourea moiety as a chromophore, thus the anion complexes were studied by UV-vis spectrophotometry. Anions were recognized on **4** by hydrogen bonding interactions and monitored by the change of UV-vis absorption spectra and with naked-eyes. Association constants can be calculated using the Sirko program.

3.2.1 Complexation studies of compound 2a with various dicarboxylate anions by ^{1}H NMR spectrophotometry.

^{1}H NMR spectra of compound **2a** with and without dicarboxylate anions in CD_3CN at room temperature were recorded by a Varian 400 MHz nuclear magnetic resonance spectrometer. The ^{1}H NMR spectra of **2a** showed a broad signal at 9.43 and 6.15 ppm of the urea NH protons. The signal at 9.43 ppm of the NH proton was adjacent to the aromatic signal at 6.15 ppm. When the dicarboxylate anions were added into the solution of **2a**, both signals of NH protons shifted remarkably downfield as shown in Table 3.1. Results indicated compound **2a** interacted with dicarboxylate anions by hydrogen bonding between urea and carboxylate groups.

Table 3.1 ^{1}H NMR chemical shifts (ppm) of **2a** (in CD_3CN) in the absence and presence of dicarboxylate anions (4 equiv.).

Anions	**H_a**	**H_b**
None	9.43	6.15
Malonate	-	-
Succinate	9.79	7.24
Glutarate	11.60	8.90
Adipate	10.14	7.65
Pimelate	11.80	9.12
Suberate	11.71	9.06
Azelate	11.04	8.48

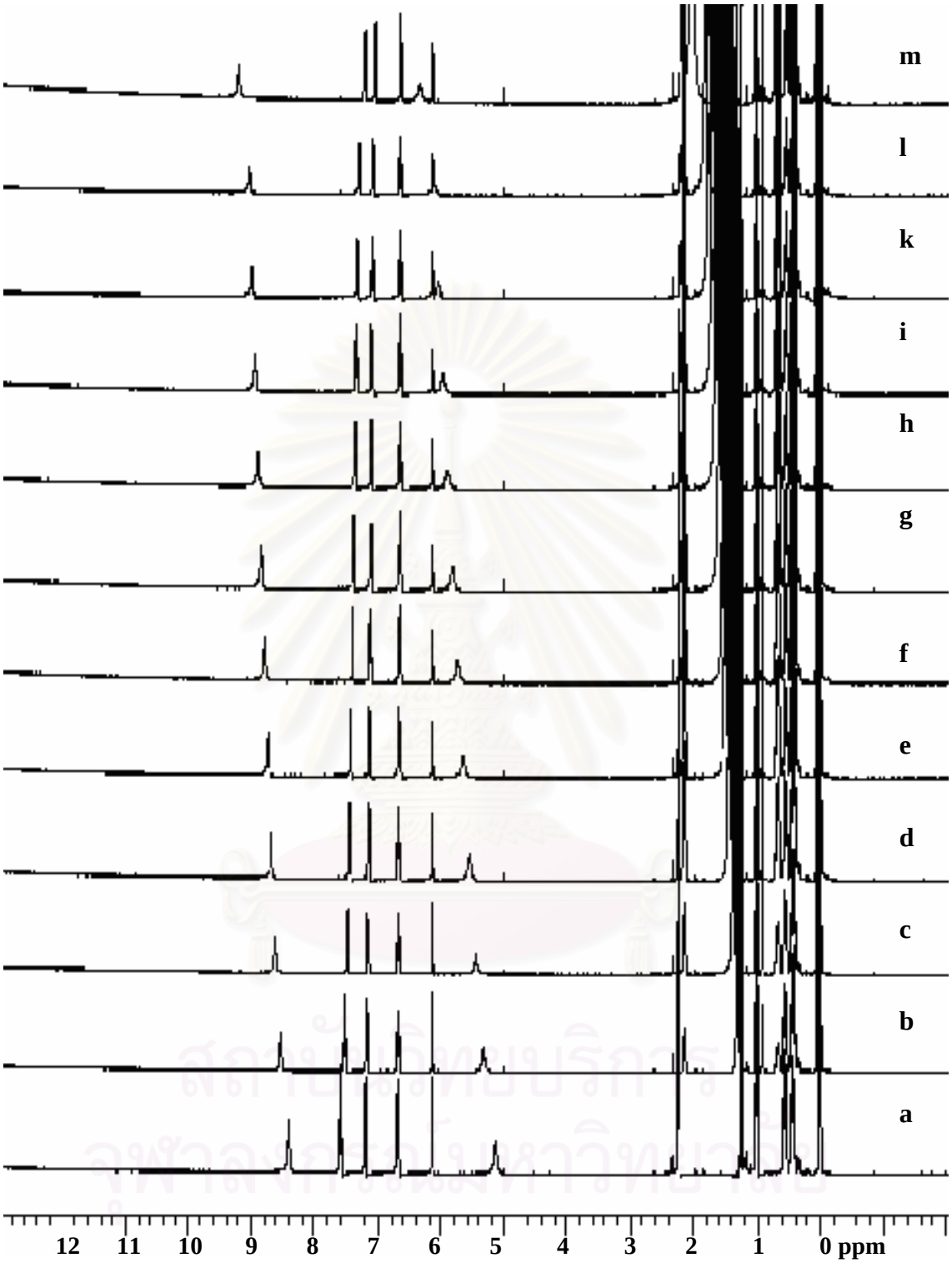


Figure 3.1 The spectra of compound **2a** was added adipate, a) **2a**, b) 0.2 equiv., c) 0.4 equiv., d) 0.6 equiv., e) 0.8 equiv., f) 1.0 equiv., g) 1.2 equiv., h) 1.4 equiv., i) 1.6 equiv., j) 1.8 equiv., k) 2.0 equiv., l) 3.0 equiv., m) 4.0 equiv..

Form Figure 3.1 indicates that **2a** formed complex with adipate in a 1:1 stoichiometry (Figure 3.2 and Figure 3.3). The 1:1 stoichiometry between **2a** and dicarboxylate anions can be confirmed by Job's plots [53] (Figure 3.4).

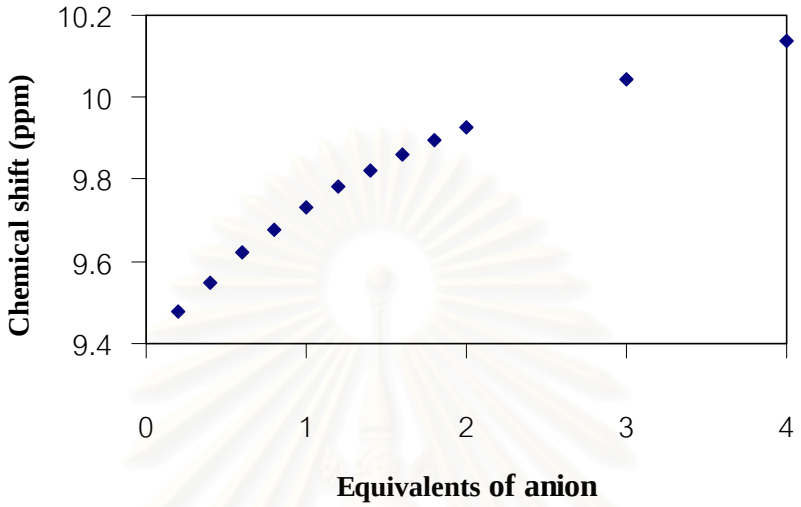


Figure 3.2 Titration curves between **2a** (NH_a) with adipate in CD_3CN.

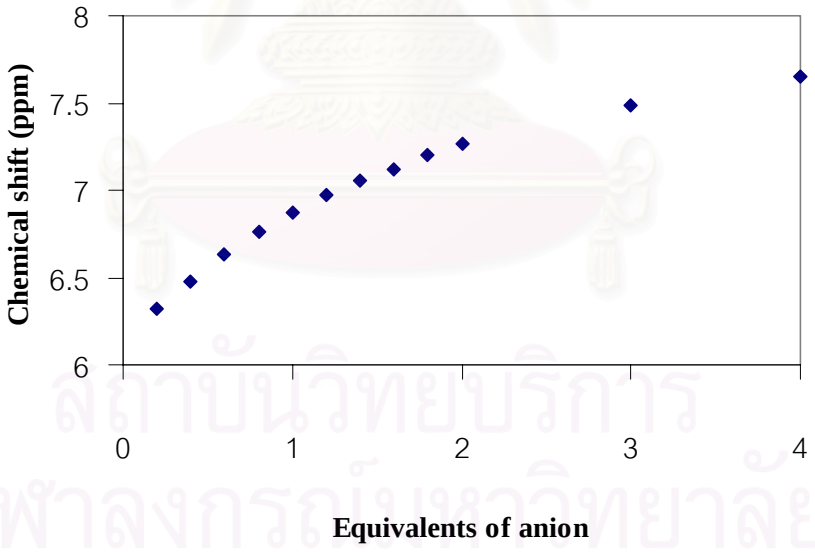


Figure 3.3 Titration curves between **2a** (NH_b) with adipate in CD_3CN.

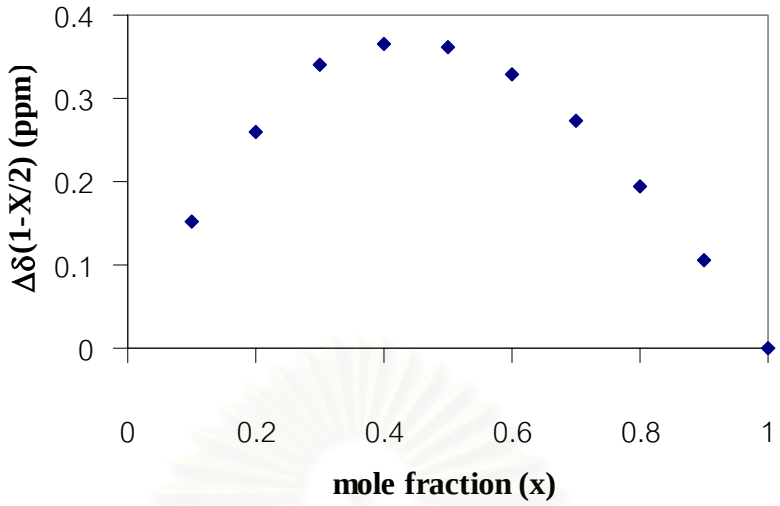


Figure 3.4 The Job's plots of compound **2a** with adipate.

Association constants calculated from the resulting titration curves using the EQNMR computer program [54] are shown in Table 3-2.

Table 3.2 Association constants of compound **2a** toward various dicarboxylate anions.

Anions	**Association constant**
Malonate [a]	138
Succinate	49,54
Glutarate	1144,193
Adipate	528,737
Pimelate	145,208
Suberate	382,450
Azelate	64,112

[a] calculated from the change in chemical shift of aromatic proton.

Compound **2a** was characterized by ^{1}H NMR spectrometry, IR spectrometry, elemental analysis and mass spectrophotometer. The results indicated that compound **2a** did contain an azobenzene unit. However, the analysis suggested the possible structure of **2a** as shown in fig 3.5. Thus, the photoisomerization of **2a** was not studied. Job's plots of compound **2a** with dicarboxylate anions showed that stoichiometries between **2a** and dicarboxylate anions were 1:1. Table 3.2 shows the association constants of **2a** towards various dicarboxylate anions. The possible structure for the complexation between **2a** and a dicarboxylate anion is proposed shown in Figure 3.5.

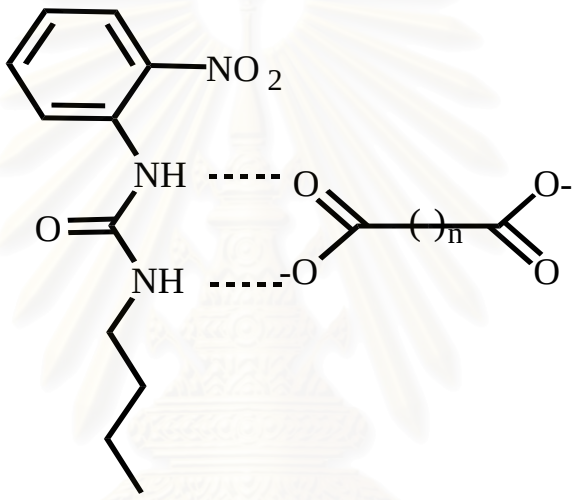


Figure 3.5 A possible structure for the complex between **2a** and a dicarboxylate anion.

3.2.2 Binding studies of 4 toward dicarboxylate anions.

Receptor **4** consists of diaza crown ether which can be bind the alkali metal ions, the thiourea unit for binding dicarboxylate anions and a *p*-nitrophenyl moiety as a chromophore. Complexation of **4** with dicarboxylate anions can be studied by UV-vis spectrophotometry in the absence and the presence of alkali metal ions. The characteristic spectra of the solution of **4** in the 0.01 M tetrabutylammonium perchlorate in CH_3CN showed a board band around 325 nm (Figure 3.6). The absorbance of this band follows Beer Lambert law and the molar coefficient is 24000 cm^{-1}. It was found that diaza crown ether can recognize sodium ion better than other alkali metal ions because of the size of the ionophoreic cavity fit to sodium ion. Thus, only sodium ion was studied as an affecter to dicarboxylate anion binding ability of **4**.

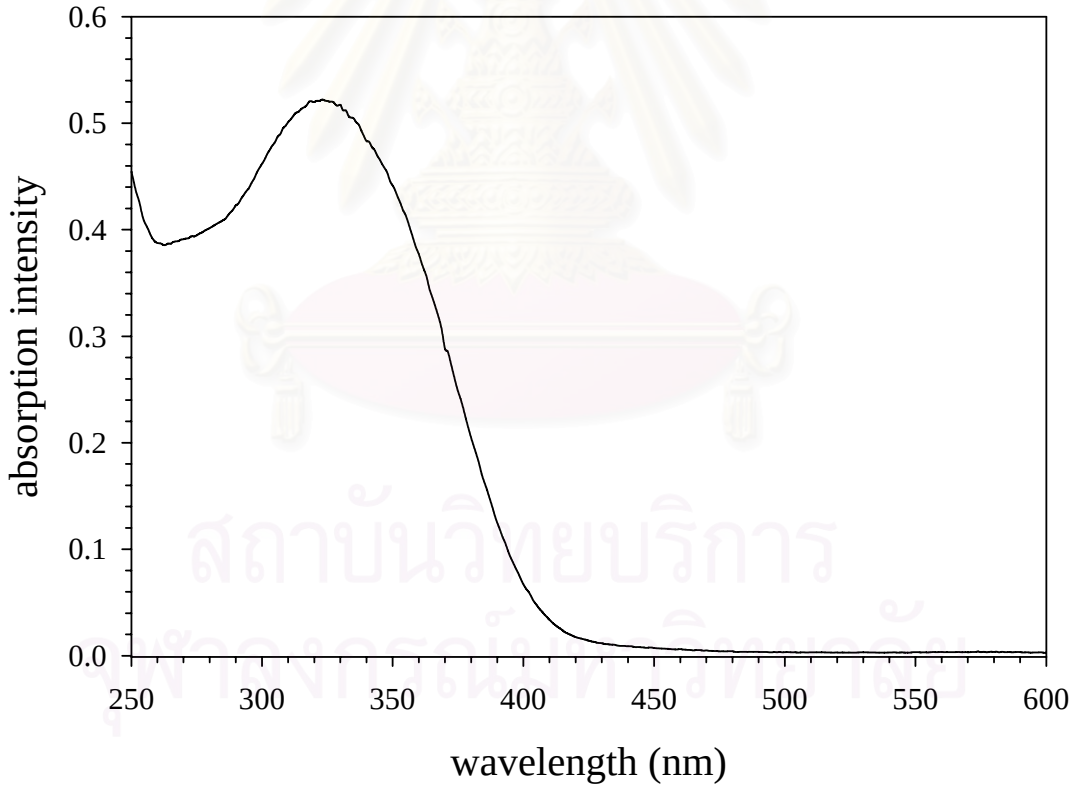


Figure 3.6 The UV-vis absorption spectra of receptor **4** ($2x10^{-5}$ M) containing 0.01 tetrabutylammonium perchlorate in acetonitrile.

3.2.2.1 UV-vis titration studies for complexes of ligand 4 with dicarboxylate anions.

This research interest is to study complexation of **4** with various dicarboxylate anions which have a different chain length. The receptor **4** ($2x10^{-5}$ M) was prepared using 0.01 tetrabutylammonium perchlorate in CH_3CN to control the ionic strength. Absorption spectra of receptor **4** were measured in the absence and presence of various dicarboxylate anions at room temperature. For example, the absorption spectra of titrations between **4** and adipate are shown in Figure 3.7 and suberate are shown in Figure 3.8. It was found that a new band was occurred when the solution of the guest was added in the solution of receptor **4** (shown in Table 3.3) and the association constant was calculated form absorption spectra by using the Sirko program (shown in Table 3.4).

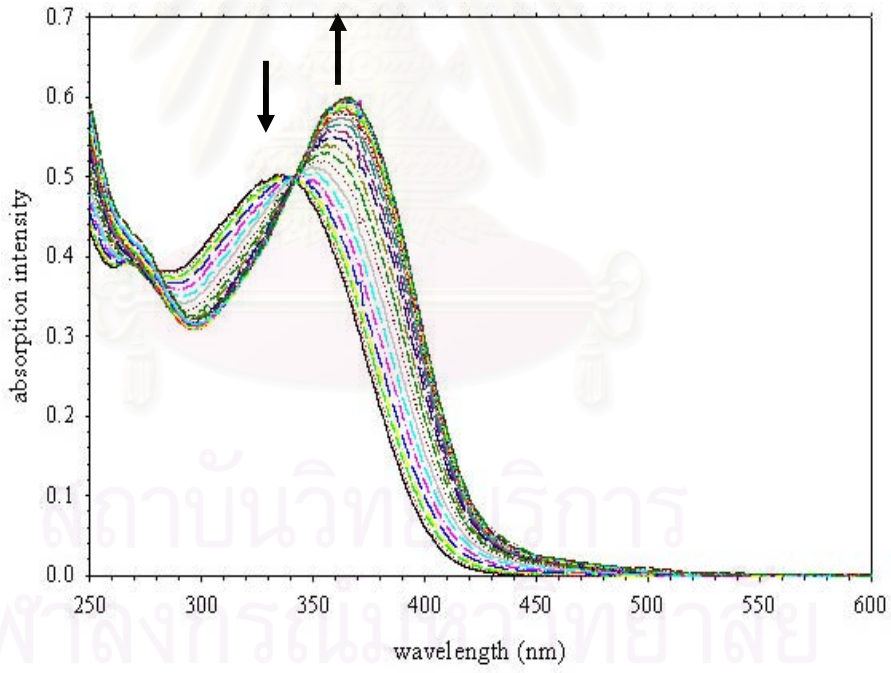


Figure 3.7 The UV-vis absorption spectra of receptor **4** ($2x10^{-5}$ M) upon addition of adipate.

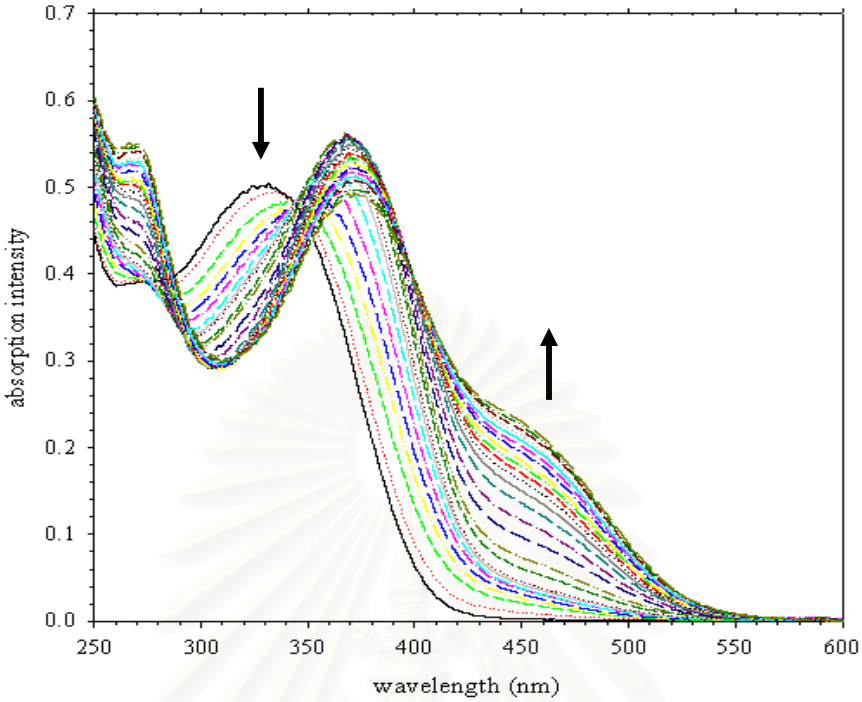


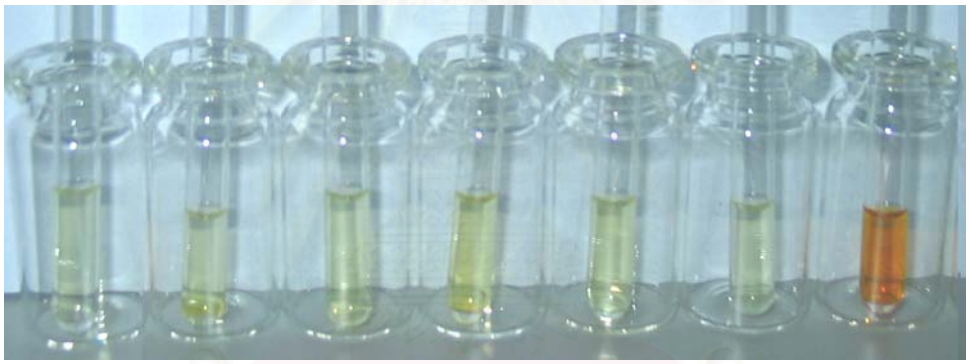
Figure 3.8 The UV-vis absorption spectra of receptor **4** ($2x10^{-5}$ M) upon addition of suberate.

Table 3.3 Wavelength of a new band appeared in the spectrum of **4** upon addition of various dicarboxylate anions.

Anions	**Wavelength (nm)**
Malonate	363
Succinate	362
Glutarate	363, 460
Adipate	368
Pimelate	355
Suberate	367,455

Table 3.4 Association constants of receptor **4** toward various dicarboxylate anions.

Anions	**log K_a (M^{-1})**
Malonate	3.80
Succinate	3.90
Glutarate	4.30
Adipate	5.40
Pimalate	4.22
Suberate	4.32
Azelate	5.28



a b c d e f g

Figure 3.9 Color of the solutions **4** (a) upon addition of b) malonate c) succinate d) glutarate e) adipate f) pimelate g) suberate.

Association constants of receptor **4** toward dicarboxylate anions can be calculated by the Sirko program [50] and shown in Table 3.4. Association constants depend on the chain length of dicarboxylate anions in which possesses highest association constant. Possible structures for the complexation between **4** and dicarboxylate anions are shown in Figure 3.10.

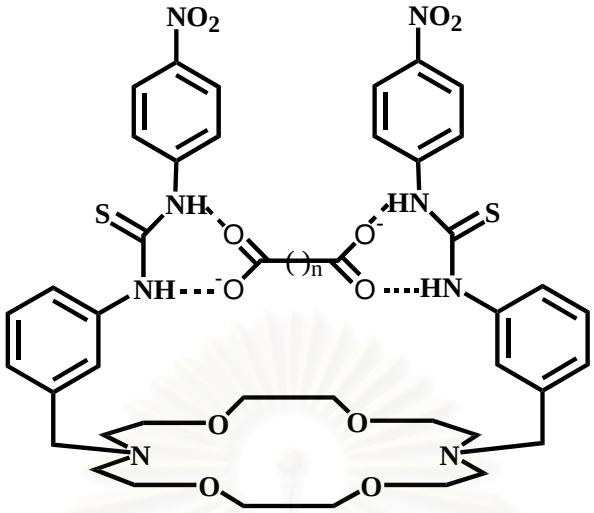


Figure 3.10 A Possible structure for the complex between **4** and dicarboxylate anions.

3.2.2.2 UV-vis titration studies for complexes of ligand 4 with sodium ion.

The absorption spectra of receptor **4** in the presence of sodium perchlorate salt were measured at room temperature. The results of titrations were found a little hypochromic effect when an excess amount of the sodium perchlorate was added (shown in Figure 3.11). This effect indicated that sodium ion sat in the cavity of the diazacrown ether. An association constant was calculated by Sirko program to be log K = 4.14.

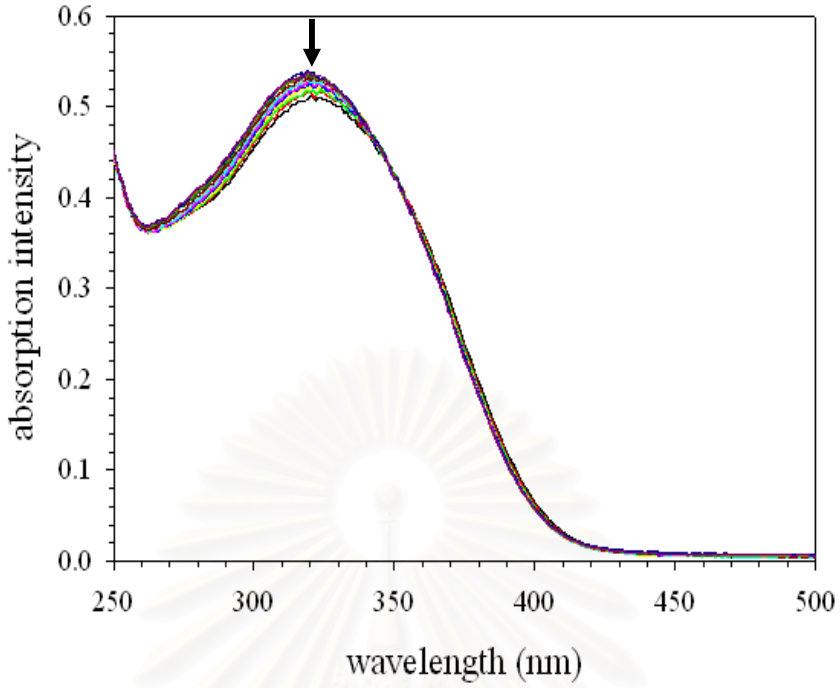


Figure 3.11 The UV-vis absortion spectra of receptor **4** ($2x10^{-5}$ M) upon addition the sodium perchlorate.

The changed spectra in Figure 3.11 are hypochromic effect with an increasing amount of sodium ion into the solution of receptor **4**. The results indicated that the sodium ion was sat in the cavity of diazacrown ether. The association constant (log K_a) of receptor **4** and sodium ion is 4.14 M^{-1}. A possible structure for the complexation between **4** with sodium ion is shown in Figure 3.12. Thus, the next experiment was studied the ion-pairing effect of sodium ion to improve the association constants of receptor **4** with dicarboxylate anions by electrostatic interactions of sodium ion with dicarboxylate anions.

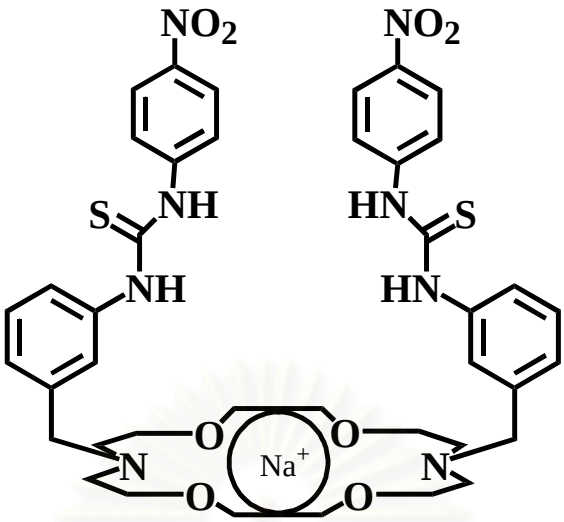


Figure 3.12 A possible structure for the complexation between **4** and sodium ion.

3.2.2.3 UV-vis titration studies for complexes of ligand 4 with dicarboxylate anion and sodium ion.

Dicarboxylate anions and sodium ion were added into the solution of receptor **4** to study an influence of an ion-pair effect to association constant. For example, the absorption spectrum of the titrations between **4** and suberate/sodium ion was shown in Figure 3.13. The association constant which calculated by the Sirko program (shown in Table 3.6) increased upon an addition of the anions/sodium ion.

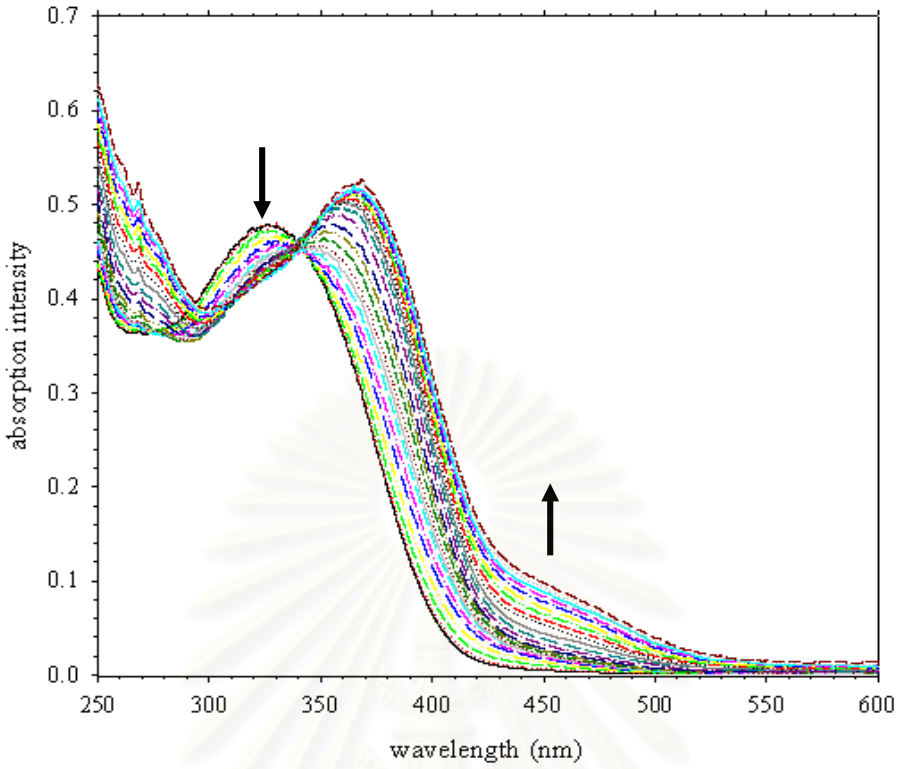


Figure 3.13 The UV-vis absorption spectra of receptor **4** ($2x10^{-5}$ M) upon addition of suberate and sodium ion.

Table 3.5 Association constants of receptor **4** toward with various dicarboxylate anions and sodium perchlorate.

Anions	**log K (M^{-1})**
Malonate	4.86
Succinate	4.99
Glutarate	4.22
Adipate	6.12
Pimalate	4.70
Suberate	5.06

The increasing of association constants in Table 3.6 results from the presence of sodium ion. The sodium ion in the cavity of diazacrown ether enhanced the binding ability of dicarboxylate anions with urea group by the ion pair interaction. A possible structure for the complexation between **4**, sodium ion and dicarboxylate anions is showed in Figure 3.14.

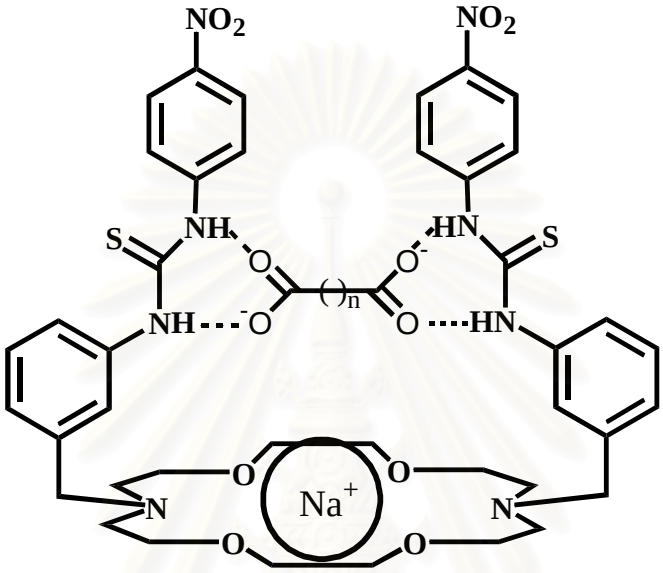


Figure 3.14 A possible structure for the complexation between **4**, sodium ion and dicarboxylate anions.

CHAPTER IV

CONCLUSION

Anions receptors containing urea groups (**2a**, **2b**, **2c**) have been synthesized. Coupling reactions between 2-nitroaniline with n-butylisocyanate, n-hexylisocyanate and phenylisocyanate gave **2a** (19 % yield), **2b** (26 % yield) and **2c** (63 % yield), respectively.

Diazacrown ether (**4**) containing thiourea groups have been synthesized in four steps. The first step, a coupling reaction between triethylene glycol ditosylate with triethylamine gave diaza crown ether, **3a** (35 % yield). The second step was the synthesis of the bis(3-nitrobenzyl)diaza crown ether, **3b** (40 % yield) by adding of a solution of 3-nitrobenzyl chloride into a mixture of diaza crown ether. In the third step, the nitro groups were reduced to amine groups by sodium borohydride to obtained **3c** in 95 % yield. Finally, the product **4** (49 % yield) was synthesized by a coupling between compound **3c** and 4-nitrophenyl thioisocyanate.

Complexation of **2a** with various dicarboxylate anions were studied by ^{1}H NMR titrations. The titration results showed that the highest association constant was obtained from the complex between **2a** and glutarate by using EQNMR computer program. The stoichiometries of all complexes from Job's plot were 1:1.

Complexes between receptor **4** and dicarboxylate anions were further investigated by UV-vis titrations. Calculated association constants between receptor **4** and dicarboxylate anions were showed that the receptor **4** formed the most stable complex with adipate and all complexes showed 1:1 stoichiometry. Upon an addition of suberate, the color of receptor **4** solution changed significantly from bright yellow to orange. Receptor **4** can possibly be used as a naked-eye sensor for suberate.

The ion-pair effect was studied by adding both sodium ion and dicaboxylate anions into the solution of receptor **4**. Association constants were found to be higher those in the absence sodium ion.

Suggestions for future work:

Future works should be focused on:

1. X-ray crystal structure of receptors (**2a-c** and **4**) and dicarboxylate anions complexes should be obtained in order to understand structures of synthetic receptors and their coordination chemistry with dicarboxylate anions.
2. The receptor **4** can possibly be used for binding amino acid. Therefore, the binding studies of **4** with amino acids should be carried out.

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APPENDICES

APPENDIX A

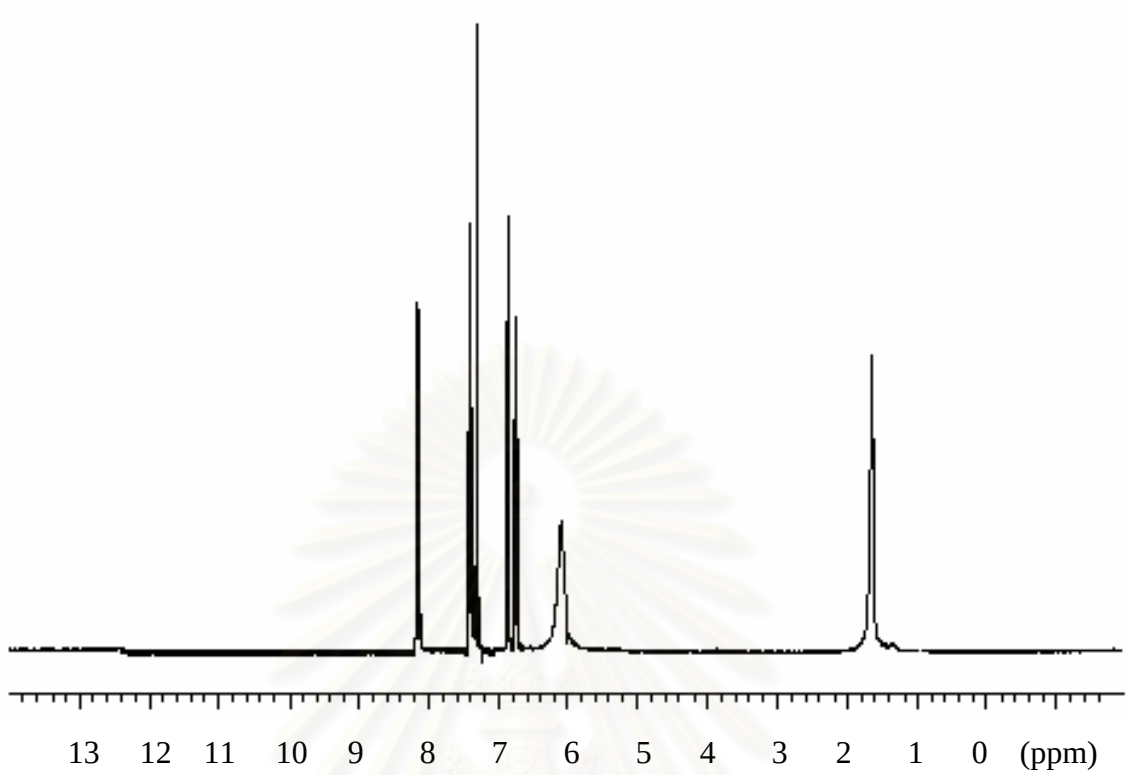

Figure A.1 The ^{1}H NMR spectrum of 2,2'-diaminoazobenzene, **1**, in $CDCl_3$ with 400 MHz.

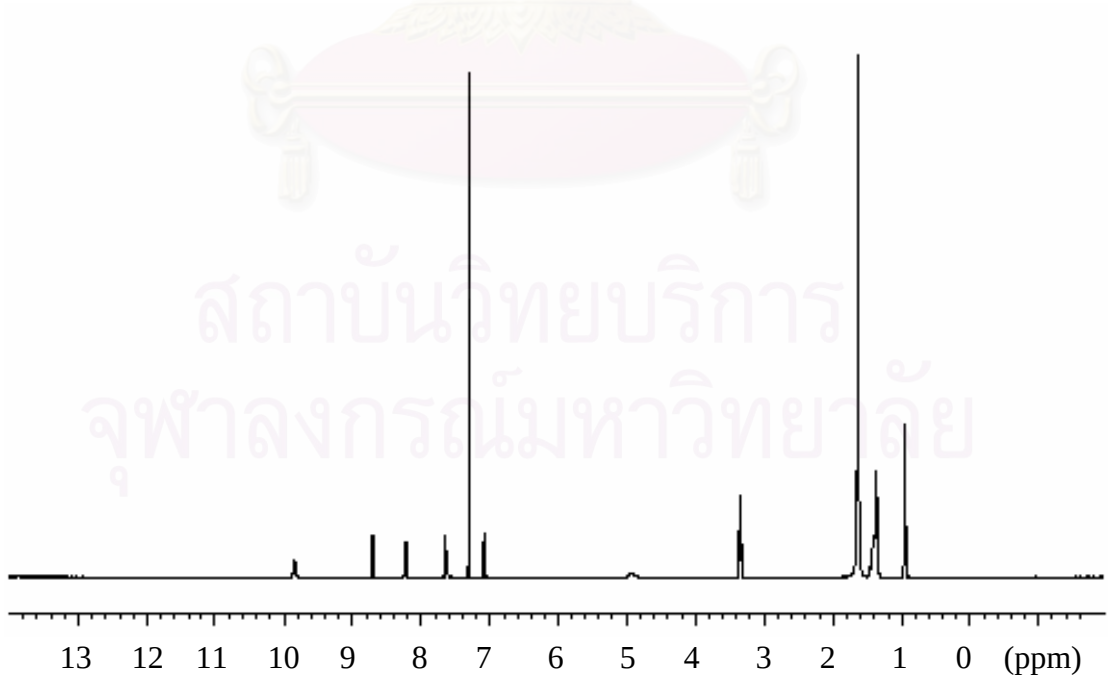

Figure A.2 The ^{1}H NMR spectrum of 2,2'-bis(*N*'-butyllereido)azobenzene, **2a**, in $CDCl_3$ with 400 MHz.

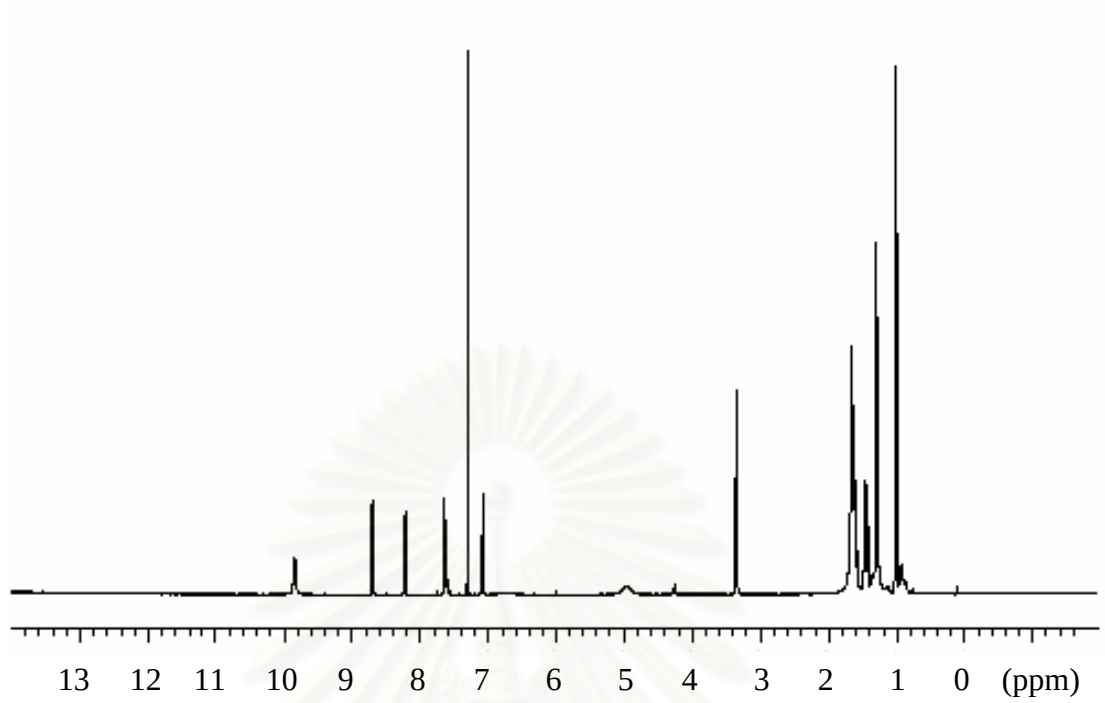

Figure A.3 The ^{1}H NMR spectrum of 2,2'-bis(*N*'-haxyllereido)azobenzene, **2b**,in $CDCl_3$ with 400 MHz.

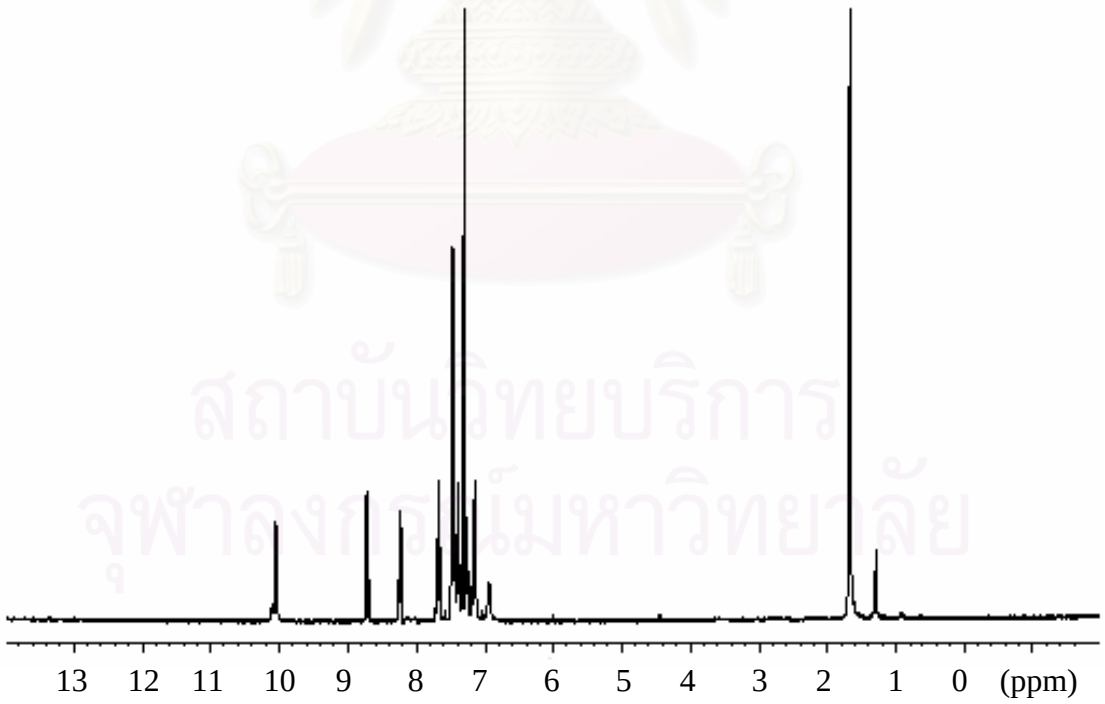

Figure A.4 The ^{1}H NMR spectrum of 2,2'-bis(*N*'-phenyllereido)azobenzene, **2c**, in $CDCl_3$ with 400 MHz.

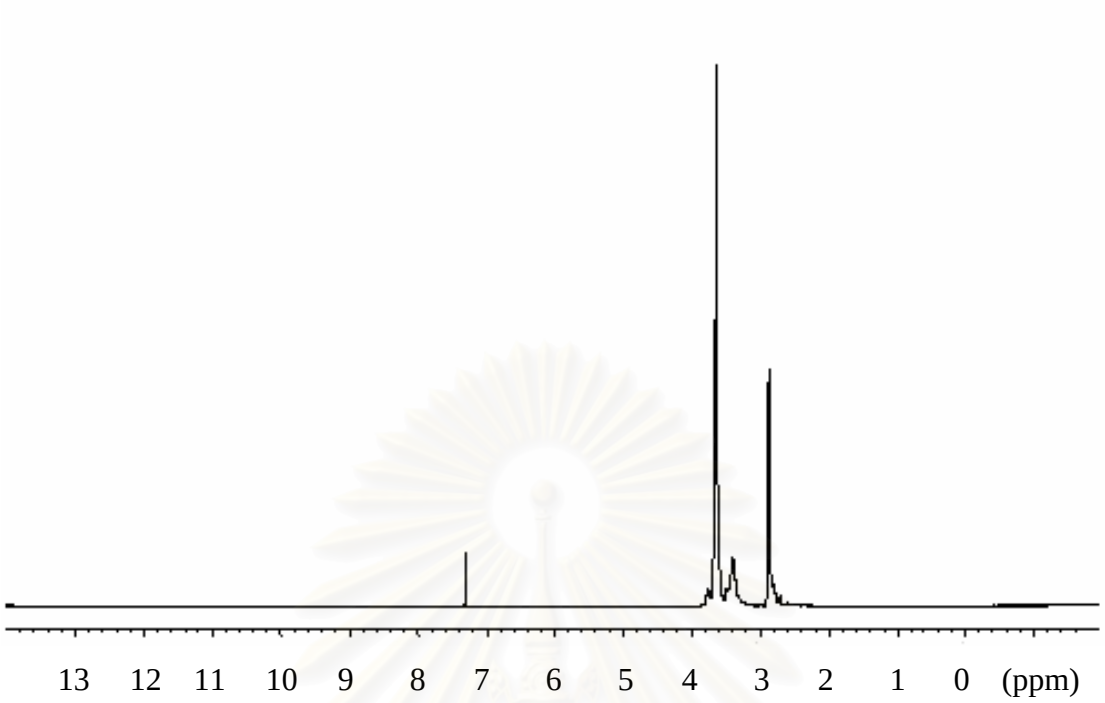

Figure A.5 The ^{1}H NMR spectrum of 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, **3a**, in $CDCl_3$ with 400 MHz.

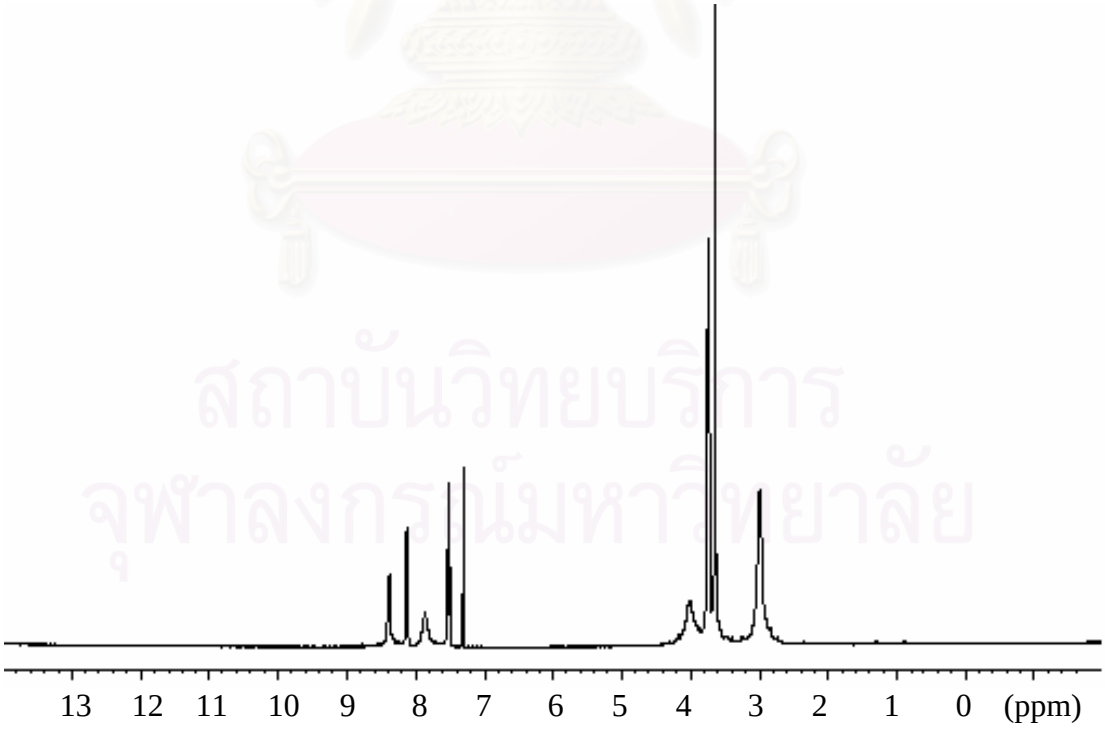

Figure A.6 The ^{1}H NMR spectrum of 7,16-bis(3-nitrobrnzyl)1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, **3b**, in $CDCl_3$ with 400 MHz.

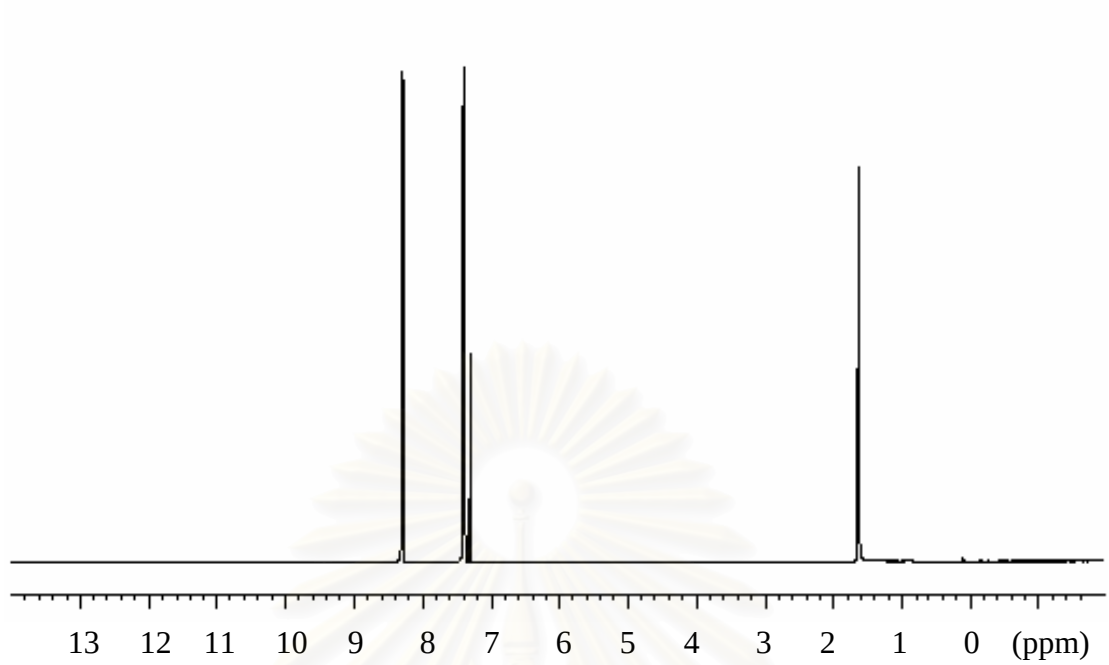

Figure A.7 The ^{1}H NMR spectrum of 4-nitrophenyl thioisocyanate, **3**, in $CDCl_3$ with 400 MHz.

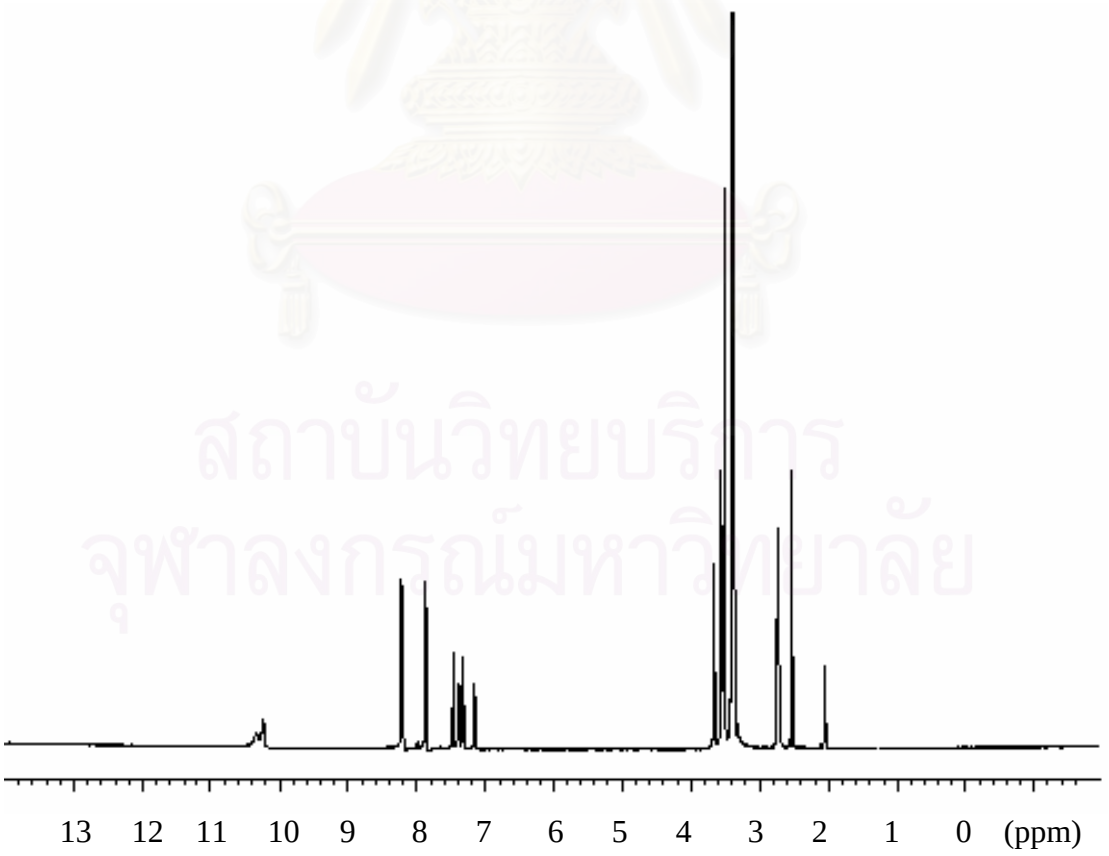

Figure A.8 The ^{1}H NMR spectrum of [1,4-bis(3-nitrobenzyl)-N'-3-benzyl]1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, **4**, in DMSO-d_6 with 400 MHz.

APPENDIX B

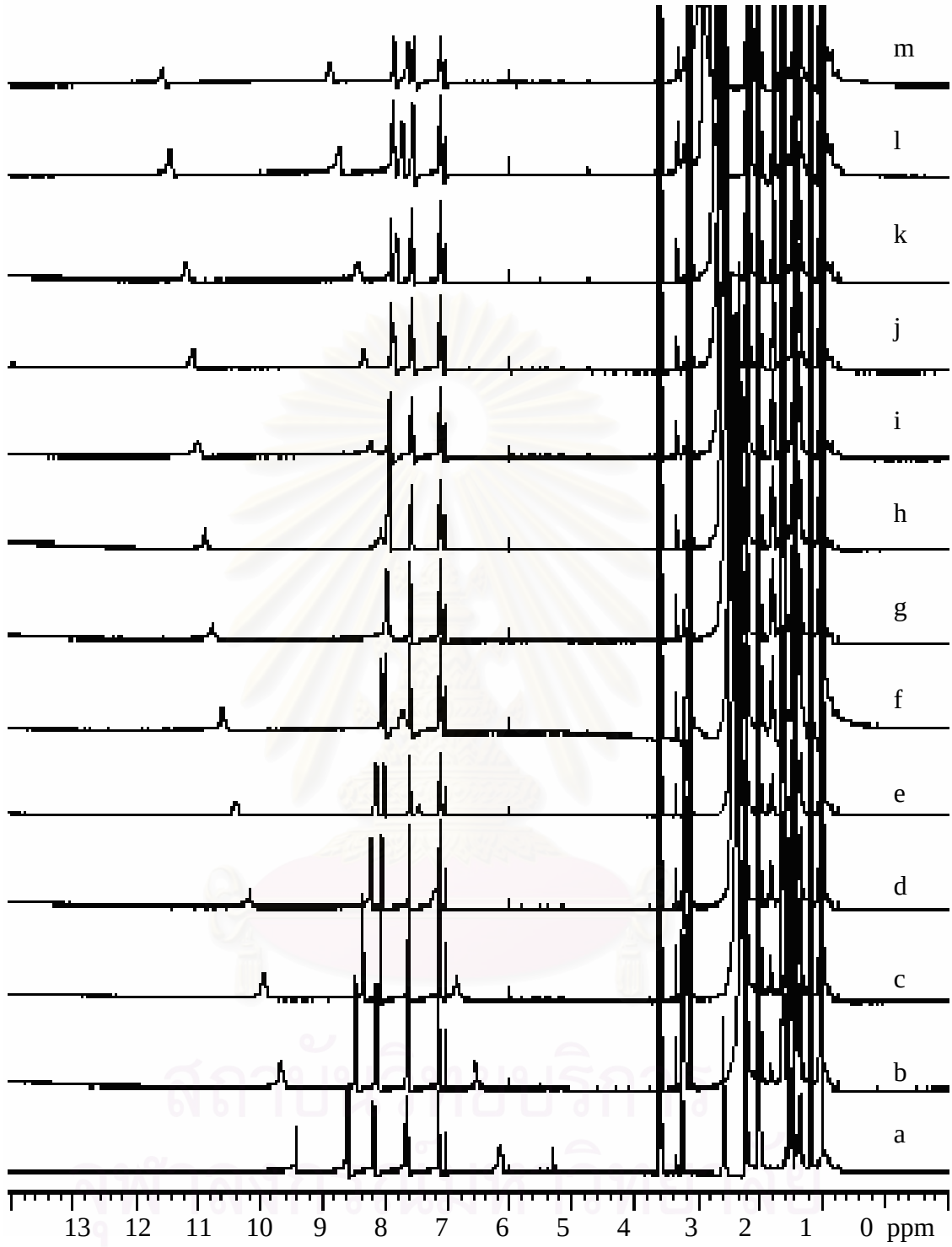

Figure B.1 The spectra of compound **2a** was added the glutarate, a) **2a**, b) 0.2 equiv., c) 0.4 equiv., d) 0.6 equiv., e) 0.8 equiv., f) 1.0 equiv., g) 1.2 equiv., h) 1.4 equiv., i) 1.6 equiv., j) 1.8 equiv., k) 2.0 equiv., l) 3.0 equiv., m) 4.0 equiv..

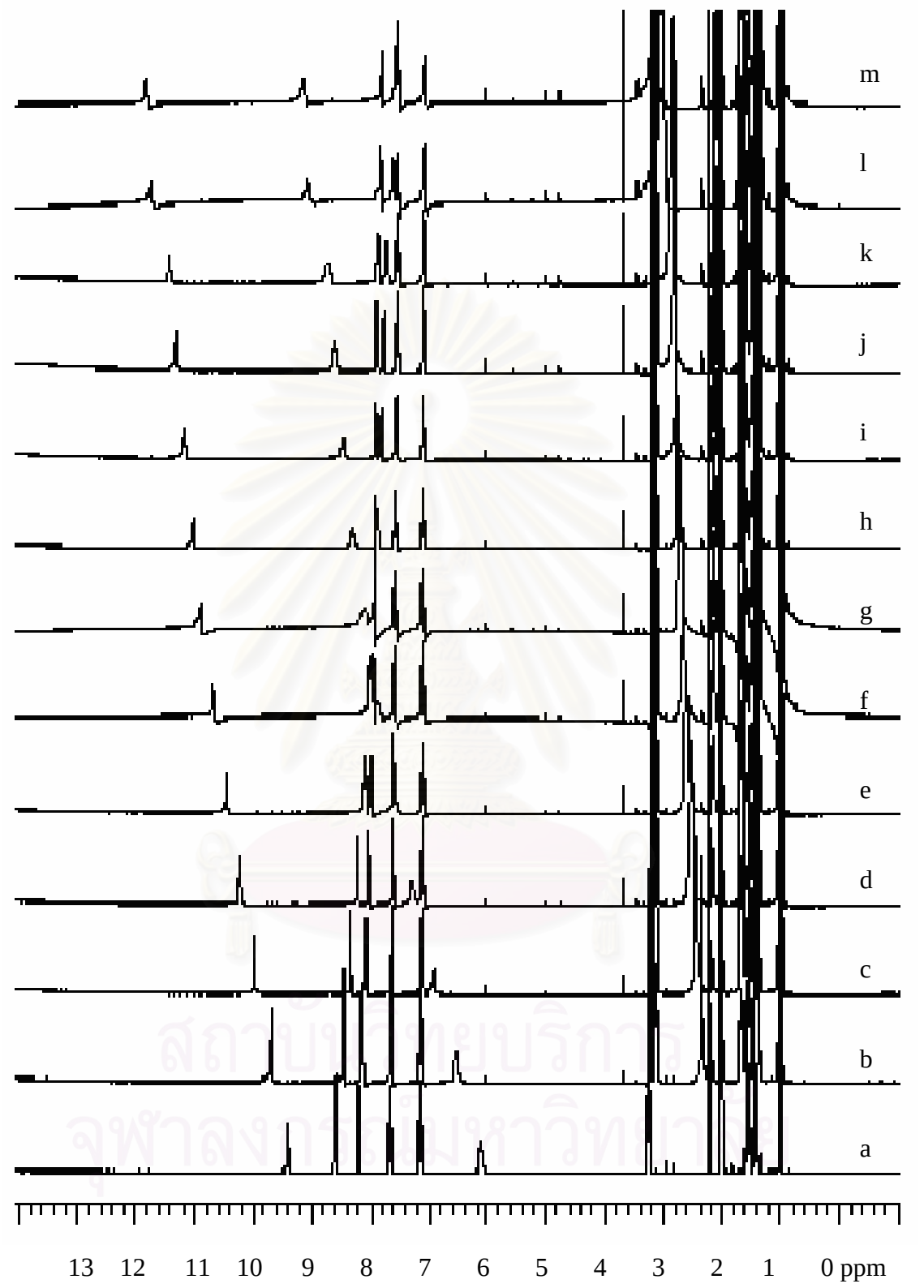

Figure B.2 The spectra of compound **2a** was added the pimelate, a) **2a**, b) 0.2 equiv., c) 0.4 equiv., d) 0.6 equiv., e) 0.8 equiv., f) 1.0 equiv., g) 1.2 equiv., h) 1.4 equiv., i) 1.6 equiv., j) 1.8 equiv., k) 2.0 equiv., l) 3.0 equiv., m) 4.0 equiv..

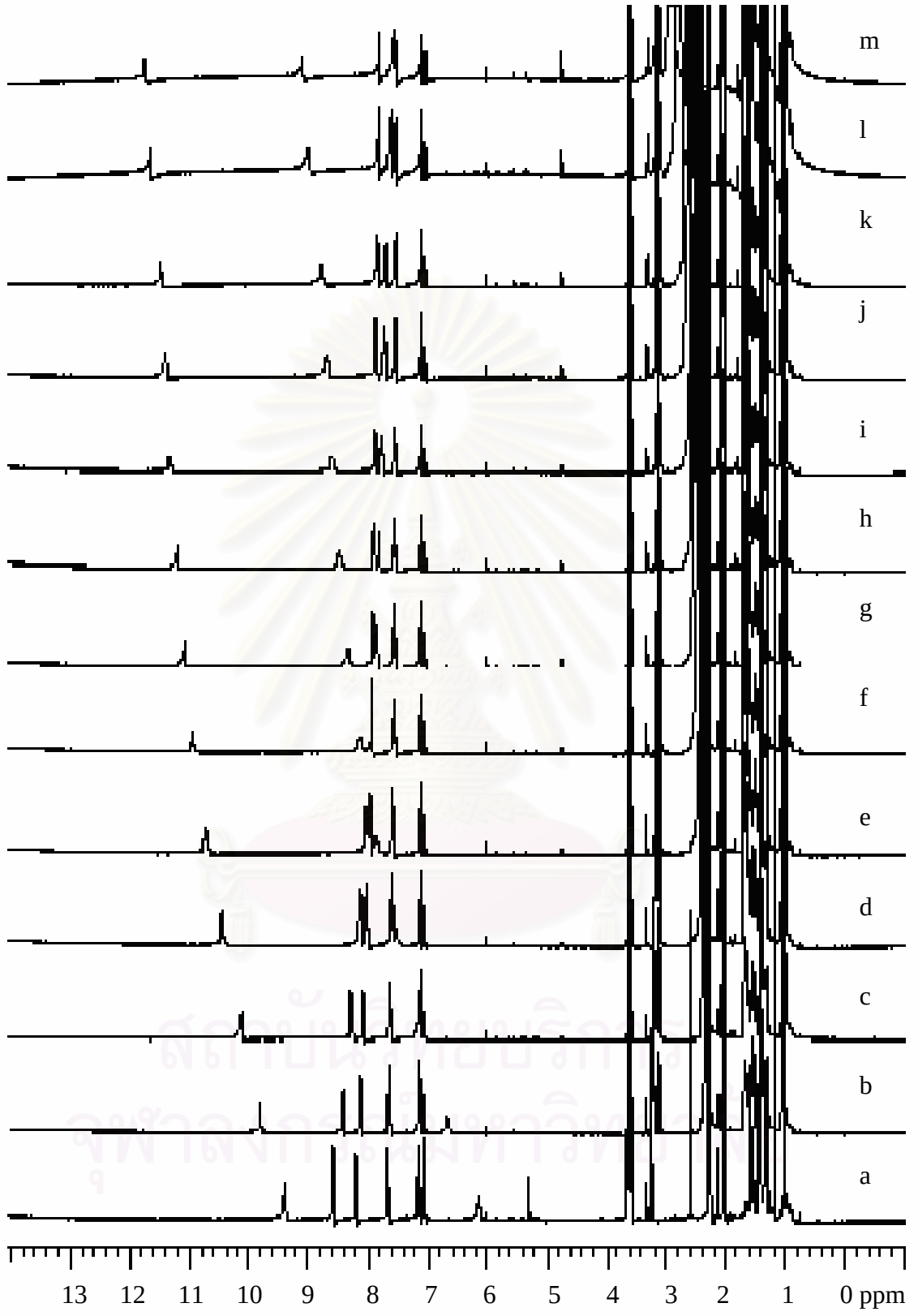

Figure B.3 The spectra of compound **2a** was added the suberate, a) **2a**, b) 0.2 equiv., c) 0.4 equiv., d) 0.6 equiv., e) 0.8 equiv., f) 1.0 equiv., g) 1.2 equiv., h) 1.4 equiv., i) 1.6 equiv., j) 1.8 equiv., k) 2.0 equiv., l) 3.0 equiv., m) 4.0 equiv..

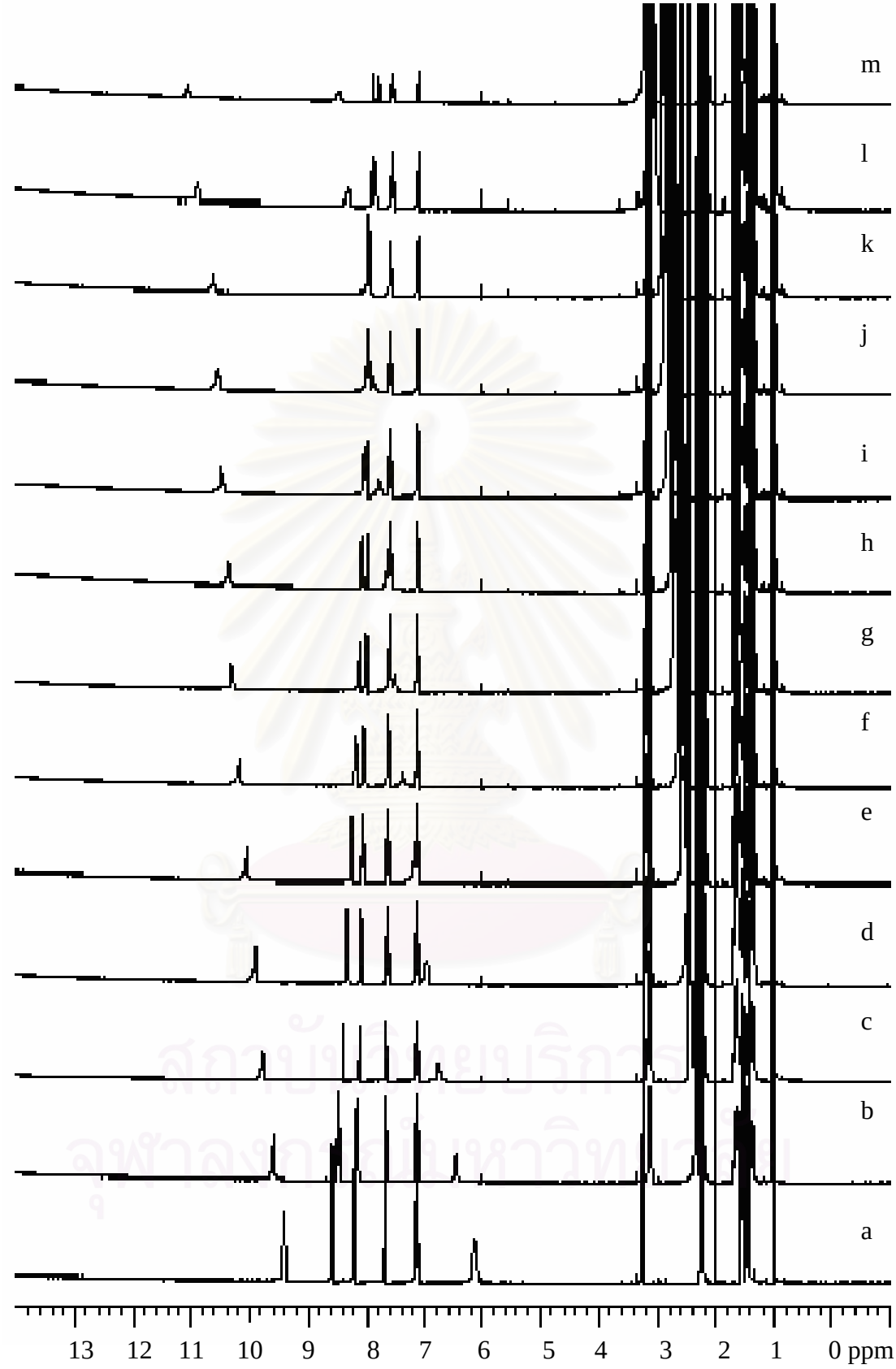

Figure b.4 The spectra of compound **2a** was added the azelate, a) **2a**, b) 0.2 equiv., c) 0.4 equiv., d) 0.6 equiv., e) 0.8 equiv., f) 1.0 equiv., g) 1.2 equiv., h) 1.4 equiv., i) 1.6 equiv., j) 1.8 equiv., k) 2.0 equiv., l) 3.0 equiv., m) 4.0 equiv..

APPENDIX C

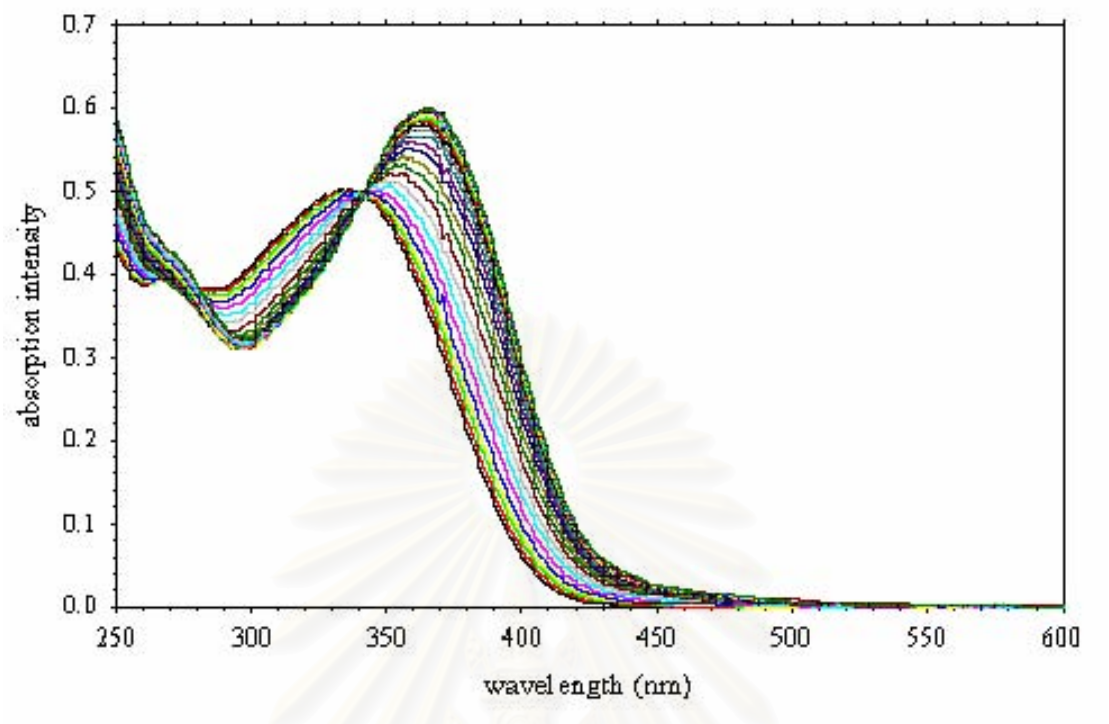

Figure C.1 UV-vis spectra of **4** with malonate in acetonitrile ([**4**]= $2x10^{-5}$ M, [malonate]= 0-35 equiv.)

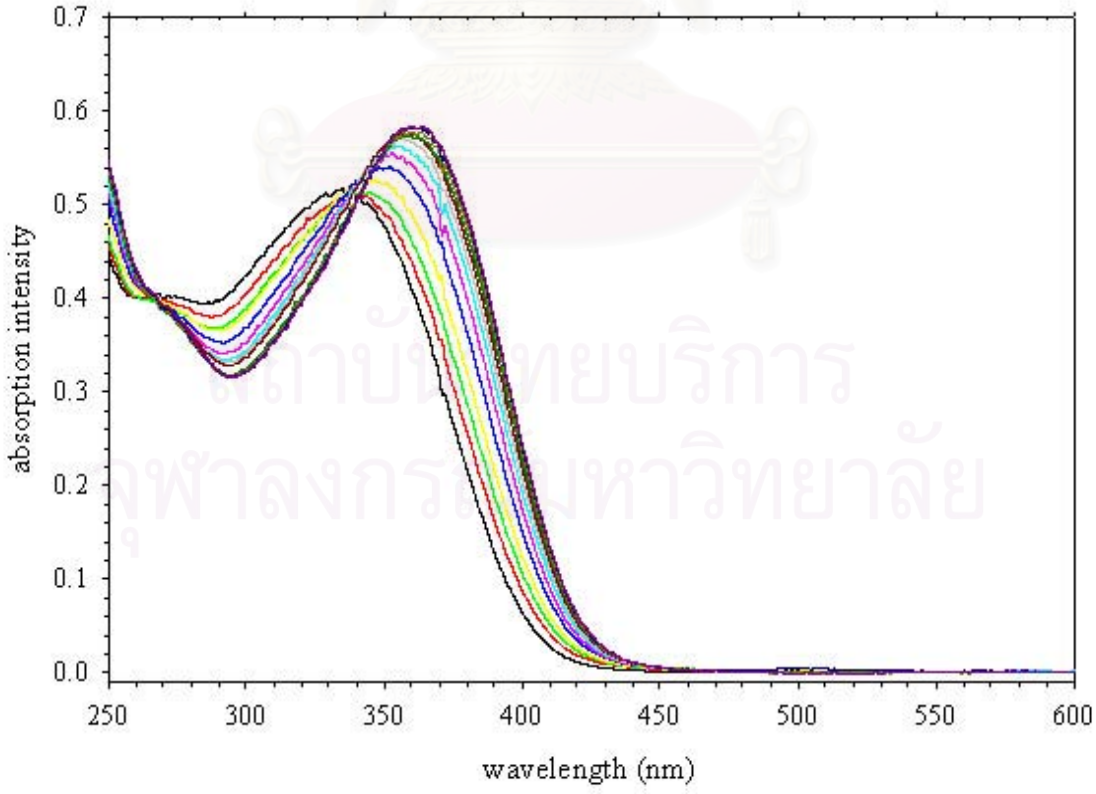

Figure C.2 UV-vis spectra of **4** with succinate in acetonitrile ([**4**]= $2x10^{-5}$ M, [succinate]= 0-25 equiv.)

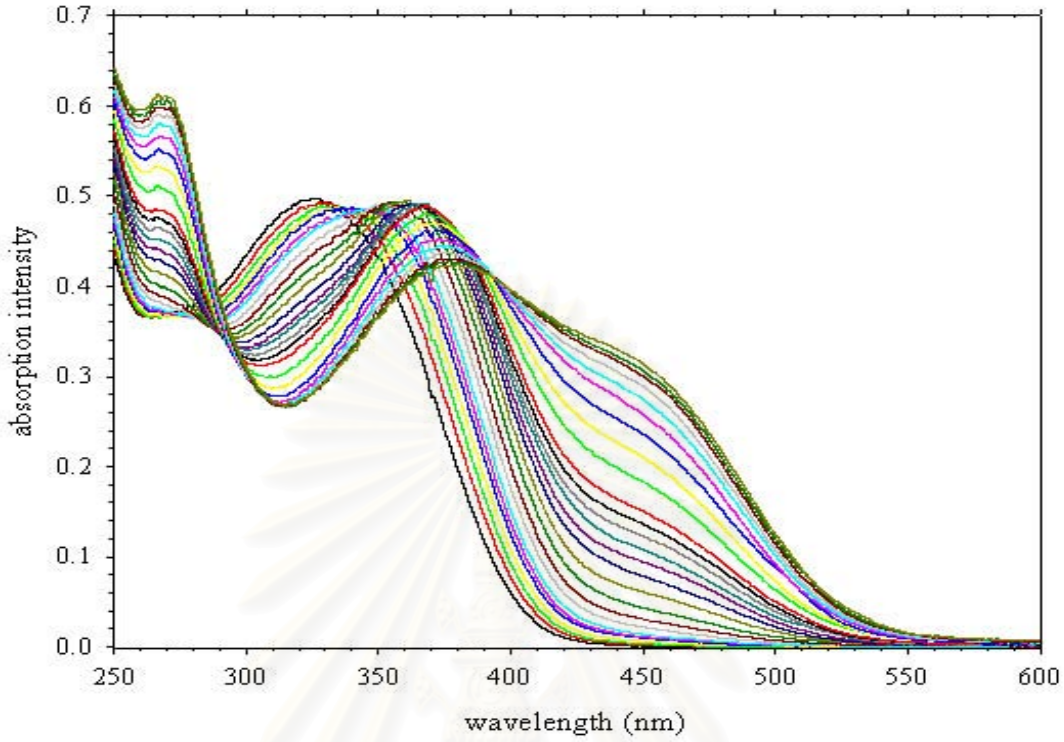

Figure C.3 UV-vis spectra of **4** with glutarate in acetonitrile ([**4**]= $2x10^{-5}$ M, [glutarate]= 0-10 equiv.)

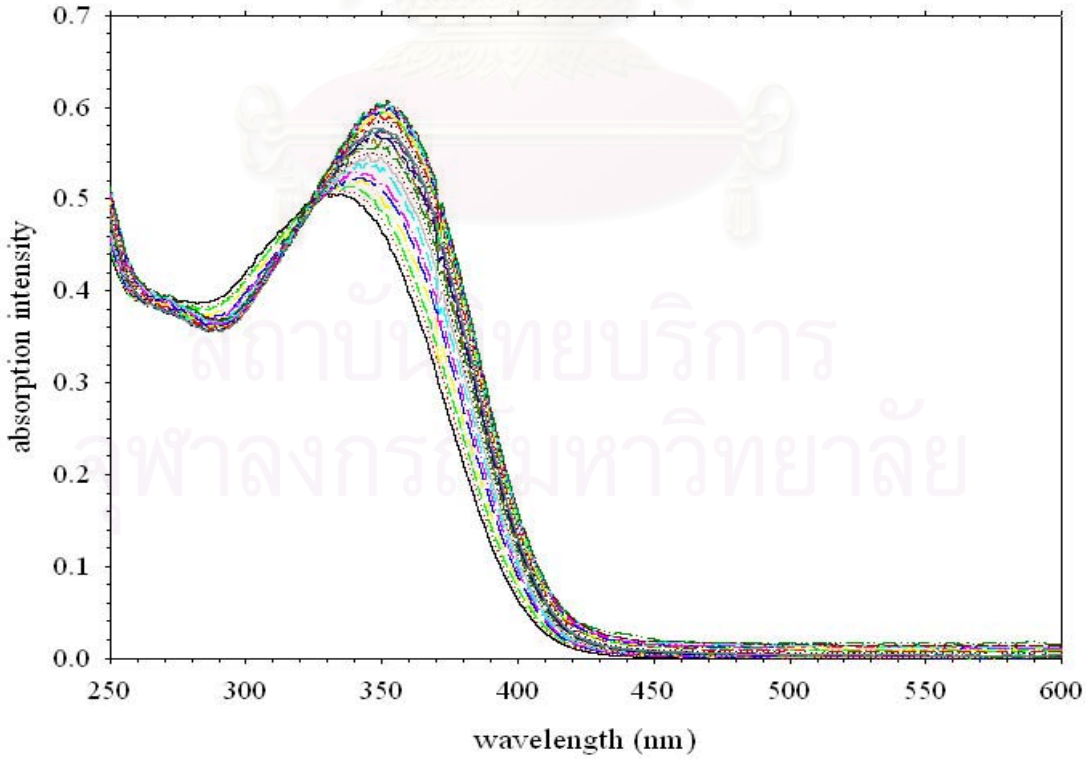

Figure C.4 UV-vis spectra of **4** with pimelate in acetonitrile ([**4**]= $2x10^{-5}$ M, [pimelate]= 0-10 equiv.)

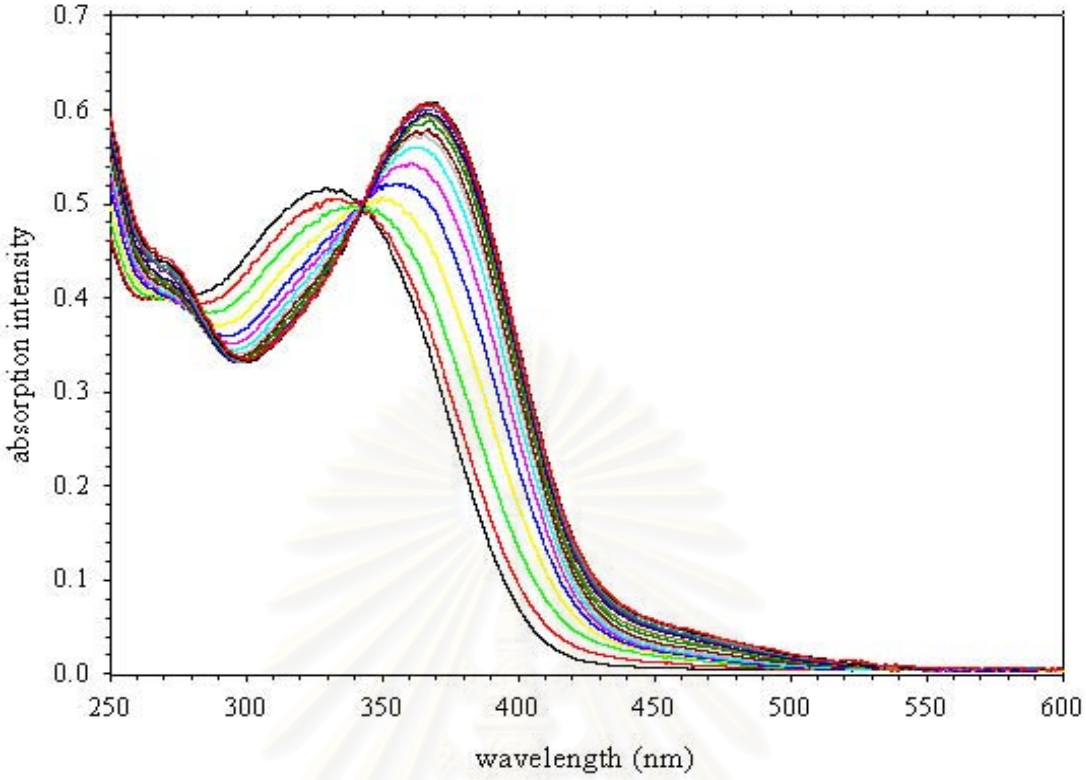

Figure C.5 UV-vis spectra of **4** with azelate in acetonitrile ([**4**]= $2x10^{-5}$ M, [azelate]= 0-10 equiv.)

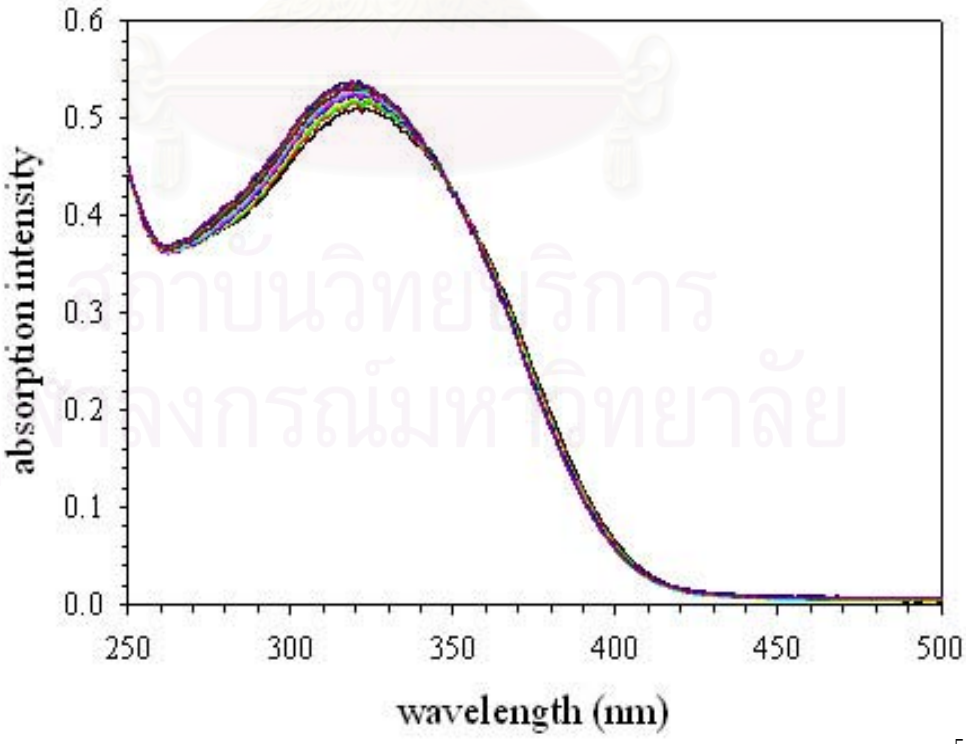

Figure C.6 UV-vis spectra of **4** with sodium perchlorate in acetonitrile ([**4**]= $2x10^{-5}$ M, [Na+]= 0-25 equiv.)

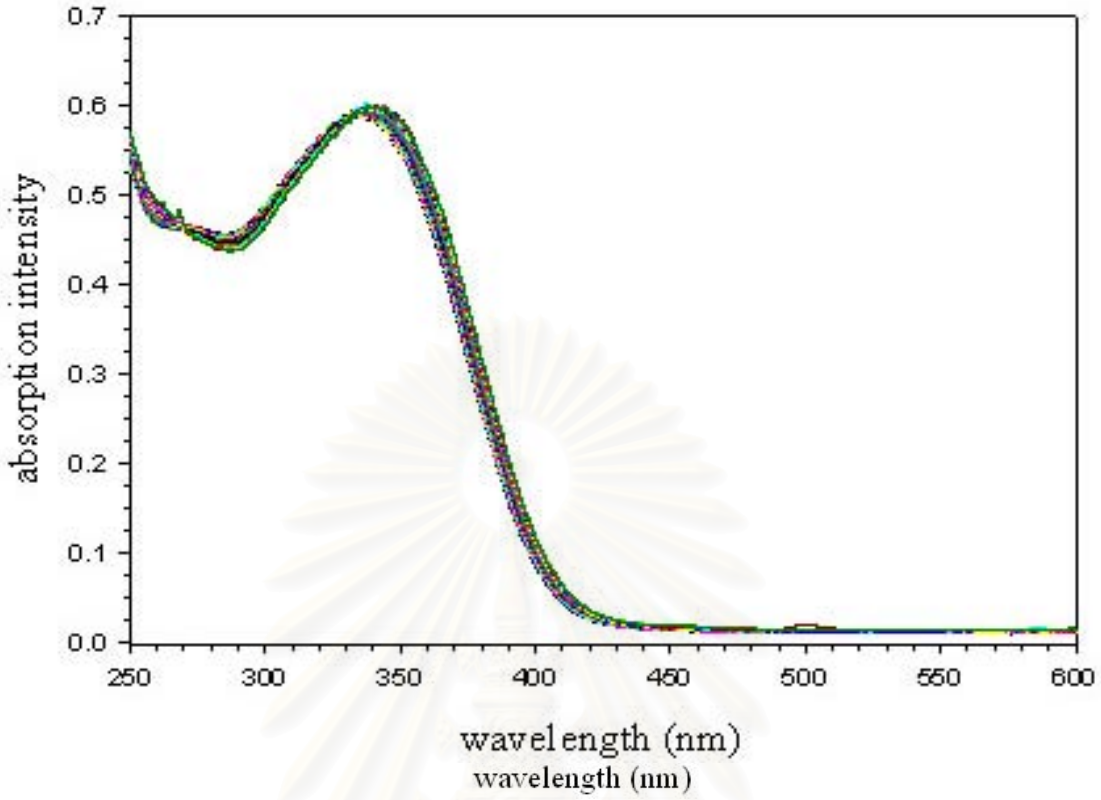

Figure C.7 UV-vis spectra of **4** with malonate in acetonitrile (**[4]**= $2x10^{-5}$ M, [malonate]= 0-8 equiv.)

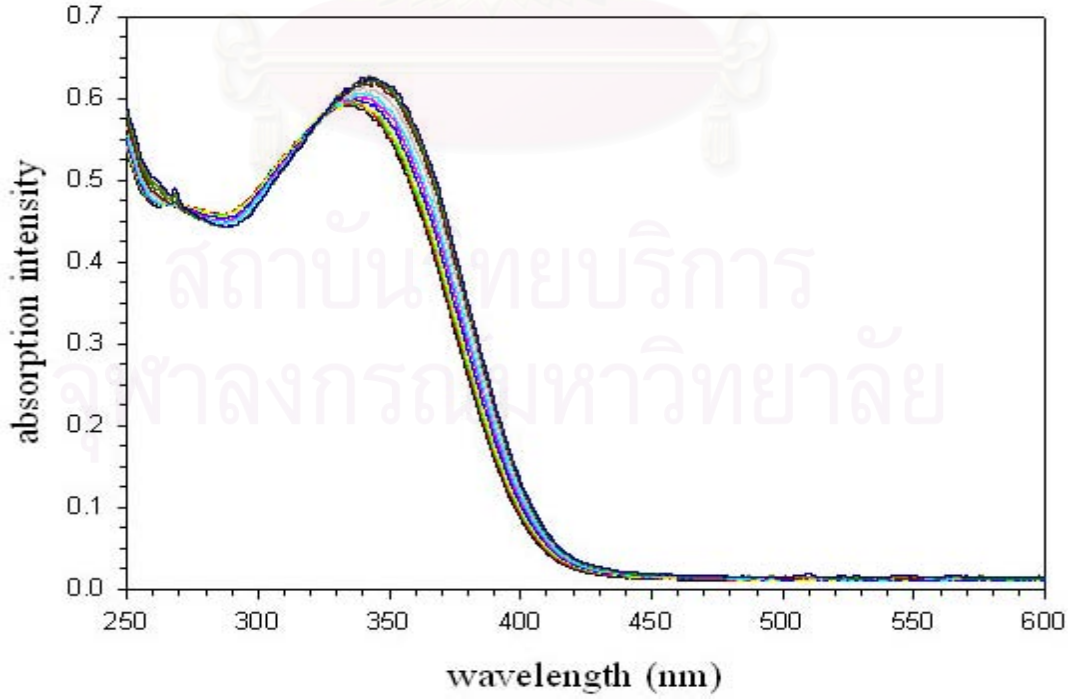

Figure C.8 UV-vis spectra of **4** with succinate in acetonitrile ([**4**]= $2x10^{-5}$ M, [succinate]= 0-10 equiv.)

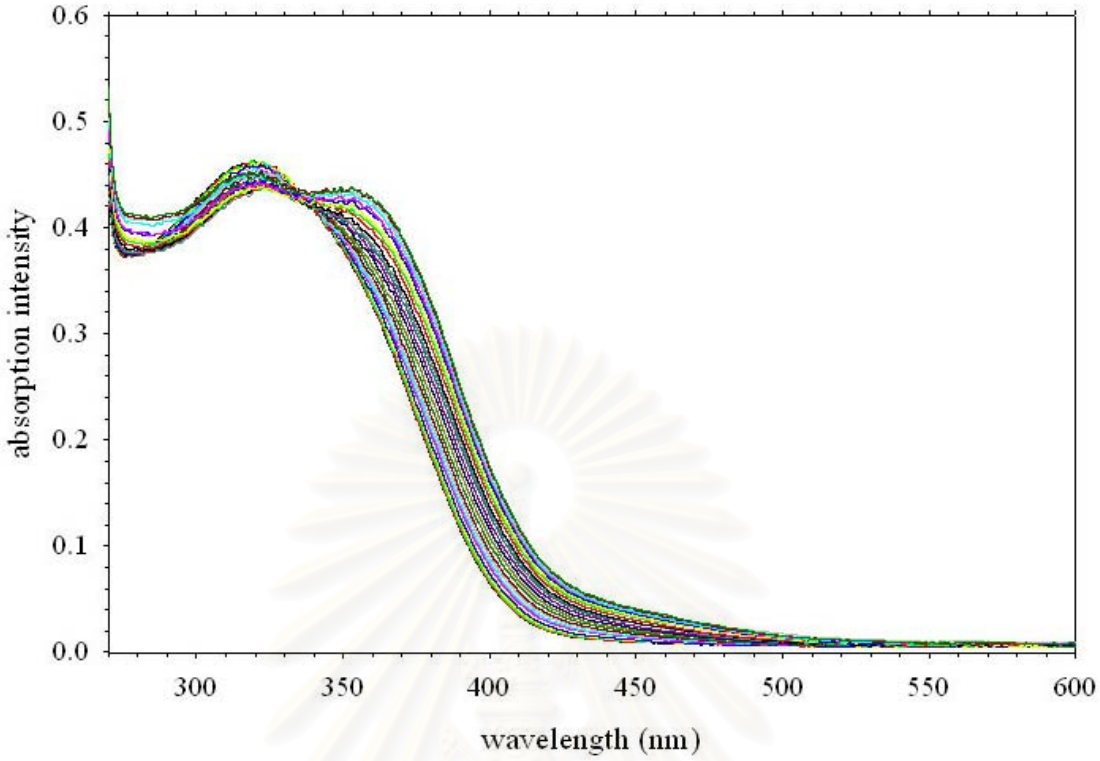

Figure C.9 UV-vis spectra of **4** with glutarate in acetonitrile ([**4**]= $2x10^{-5}$ M, [glutarate]= 0-8 equiv.)

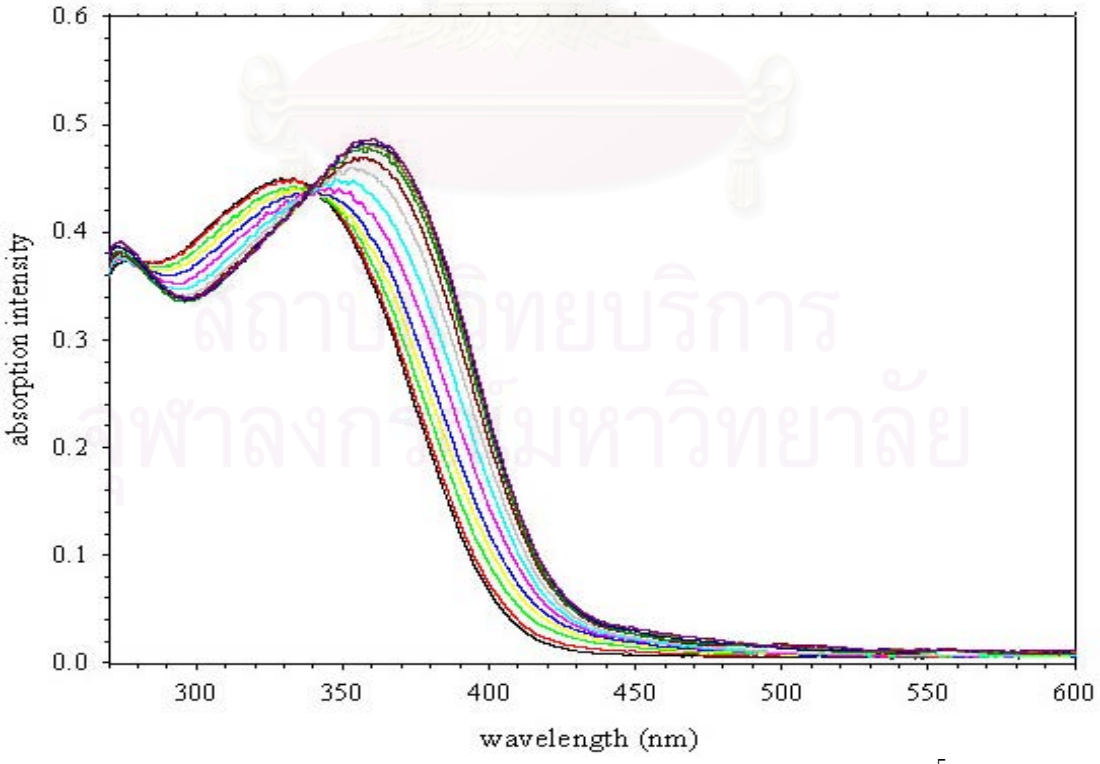

Figure C.10 UV-vis spectra of **4** with adipate in acetonitrile ([**4**]= $2x10^{-5}$ M, [adipate]= 0-5 equiv.)

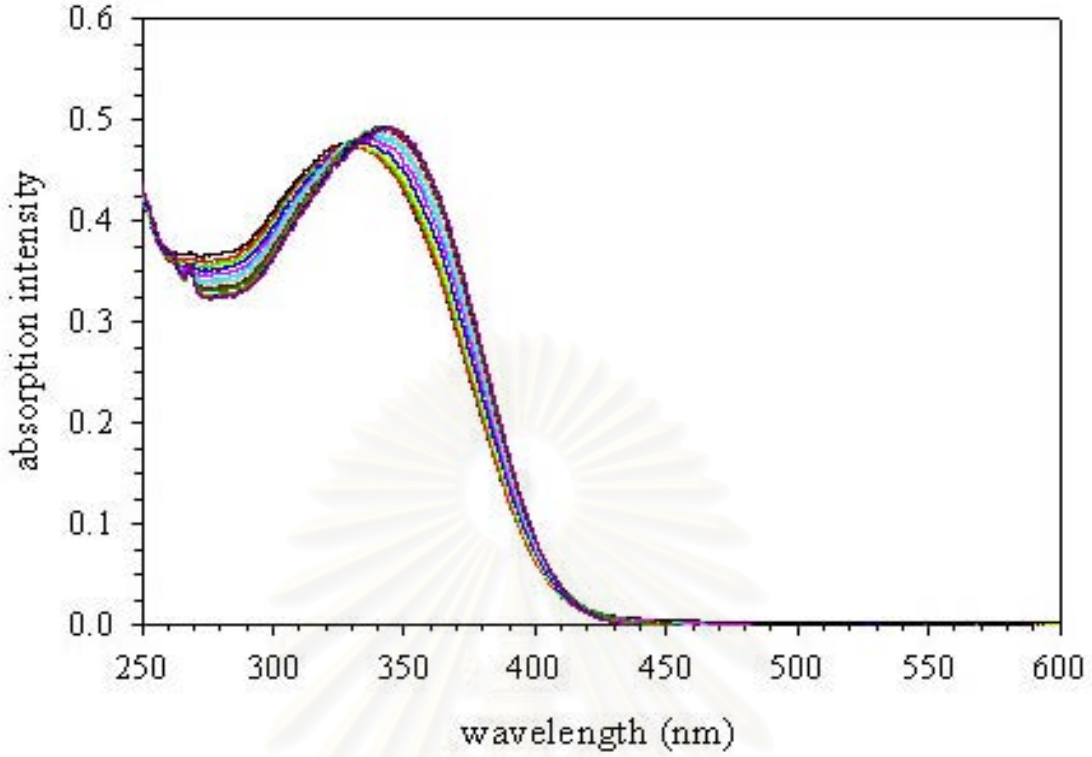

Figure C.11 UV-vis spectra of **4** with pimelate in acetonitrile ([**4**]= $2x10^{-5}$ M, [pimelate]= 0-8 equiv.)

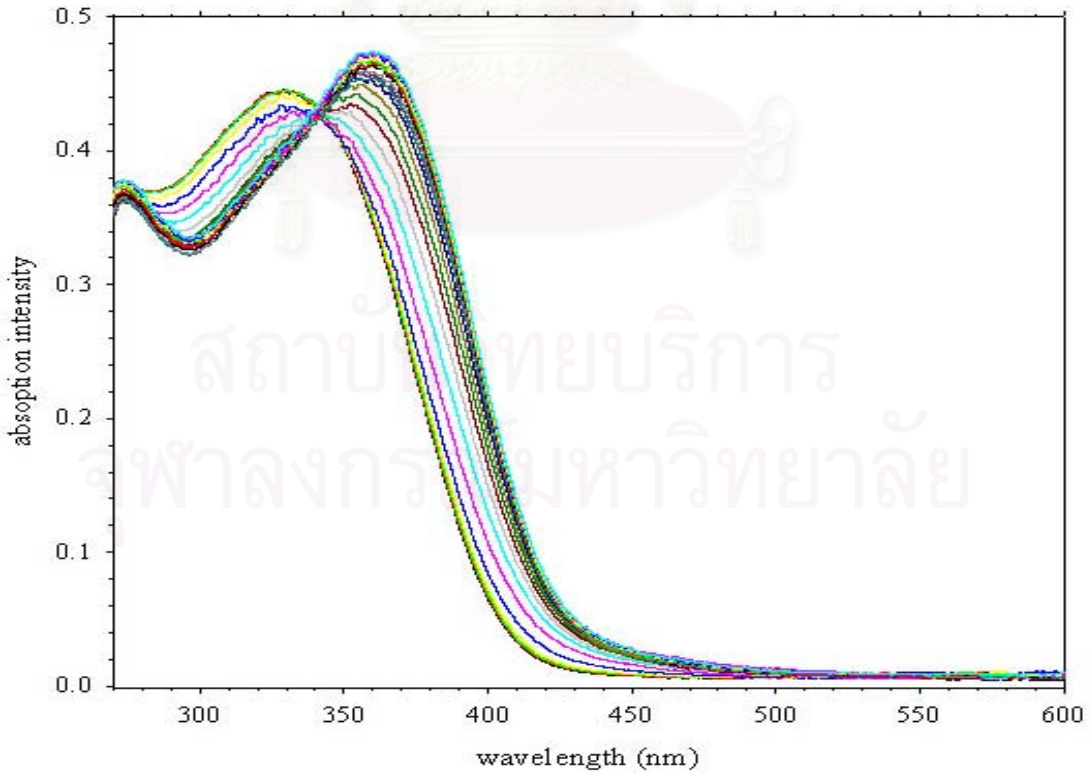

Figure C.19 UV-vis spectra of **4** with azelate in acetonitrile ([**4**]= $2x10^{-5}$ M, [azelate]= 0-10 equiv.)

VITAE

Miss Auamphon Rattanasing was born on April 22, 1979 in Ayutthaya, Thailand. She graduted with a diploma in the Institute of Analytical Chemistry Training, Chulalongkorn University in 2002.She received her Bachelor's degree of Science in Chemistry from Chulalongkorn University in 2002. Since 2002, she has been a graduate student at the Department of Chemistry, Chulalongkorn University and become a member of the Supramolecular Chemistry Research Unit under supervision of Associate Professor Thawatchai Tuntulani. She finished her Master's degree of Science in the academic year 2004.