

CHAPTER I

INTRODUCTION



1.1 Review of Supramolecular Chemistry

Supramolecular chemistry is a rapid-growing field of chemistry. Recently, it has interested several groups of scientists. Supramolecular chemistry is the chemistry of molecular assemblies and of the intermolecular bonds which are non-covalent intermolecular forces such as van der Waals interaction, hydrogen bonding, electrostatic forces, donor-acceptor interactions, etc. The concept of supramolecular chemistry can be simplified as shown in Figure 1.1.

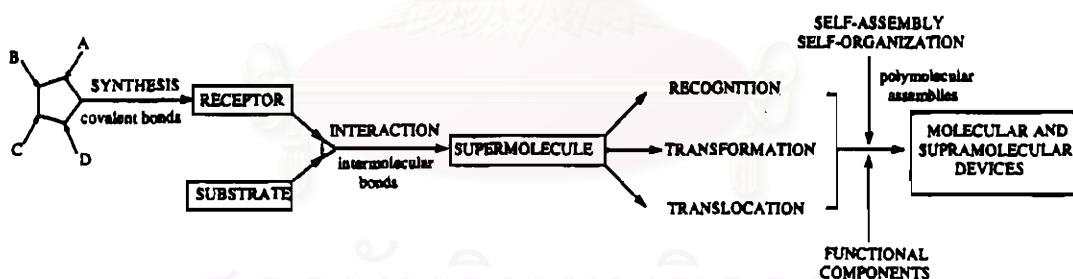


Figure 1.1 Simplified concept of supramolecular chemistry.

Supramolecules can be categorized by structures and nature of the intermolecular bonds. The structures of supramolecules are defined by their conformational, thermodynamical, kinetical and dynamical properties. Supramolecules may be distinguished by different degree of strength and directionality of intermolecular bonds: metal ion coordinates, electrostatic forces,

hydrogen bondings, van der Waals interactions, donor-acceptor interactions, etc. Bondings are classified in weak or moderate as in hydrogen bonds and strong or very strong interactions for metal ion coordination. In fact, intermolecular forces are weaker than covalent bonds. By this reason, supermolecules are thermodynamically less stable, kinetically more labile and dynamically more flexible than classical molecules. Supramolecular chemistry is then concerned with soft bonds and represents a “soft chemistry”.

Supramolecular chemistry can be divided into two general areas concerning:

- (1) supermolecules as oligomolecules that are result of the intermolecular association of a few components (a receptor and its substrate(s)) based on the principles of molecular recognition;
- (2) supramolecular assemblies as polymolecules that result from the spontaneous association of a large undefined number of components into a specific phase having more or less well-defined microscopic organization and macroscopic characteristics depending on its nature (such as films, layers, membranes, vesicles, micelles, mesomorphic phases, solid state structures, etc.). It thus covers the rational, coherent approach to molecular associations, from the smallest, the dimer, to the largest, the organized phase, and to their designed manipulation.

1.2 Molecular Recognition

Molecular recognition is defined by the energy and the information involved in the binding and selection of substrate(s) by a given receptor molecule; it may also involve a specific fraction. Mere binding is not recognition, although it is often taken as such. One may say that recognition is binding with a purpose, like

receptors are ligands with a purpose. It implies a pattern recognition process through a structurally well-defined set of intermolecular interactions. Binding of substrate to receptor forms a complex or supermolecule characterized by its (thermodynamic and kinetic) stability and selectivity, i.e., by the amount of energy and of information brought into operation.

Information may be stored in the architecture of the receptor, in its binding sites and in the ligand layer bound substrate: it is read out at the rate of formation and dissociation of the supermolecule. In addition to size and shape, a receptor is characterized by the dimensionality, the connectivity and the cyclic order of its structural graph; conformation, chirality and dynamics also come into play. The binding sites are characterized by their electronic properties (charge, polarity, polarisability, van der Waals attraction and repulsion), their size, shape, number, and arrangement in the receptor framework as well as their eventual reactivity that may allow the coupling of complexation with other process (such as protonation, deprotonation, oxidation or reduction). The ligand layer acts through its thickness, its lipo- or hydrophilicity and its overall polarity, being exo/endo-lipo/polarophilic. In addition, stability and selectivity depend on medium and result from a subtle balance between solvation (of both receptor and substrate) and complexation (i.e., "solvation" of substrate by receptor). Finally, for charged complexes medium-dependent cation-anion interactions influence markedly the binding stability and selectivity.

High recognition by a receptor molecule consists in a large difference between the binding free energies of a given substrate and of the other substrates. It results in a marked deviation from the statistical distribution. In order to achieve large differences in affinity several factors must be taken into account:

- 1) strike (shape and size) complementary between substrate and receptor, i.e. presence of convex and concave domains in the correct location on substrate and on receptor;
- 2) interactional complementarity, i.e. presence of complementary binding sites (electrostatic such as positive/negative, charge/dipole, dipole/dipole, hydrogen bond donor/acceptor, etc.) in the correct disposition on receptor and substrate so as to achieve complementary electronic and nuclear distribution (electrostatic, H-bonding and van der Waals) map;
- 3) large contact areas between receptor and substrate so as to contain multiple interaction sites, since non-covalent interactions are rather weak compared to covalent bonds;
- 4) strong overall binding; although high stability does in principle not necessarily imply high selectivity, this is usually the case; indeed, the differences in free energy of binding are likely to be larger when the binding is strong; high binding efficiency (i.e., high fraction of bound with respect to free substrate) requires strong interaction; thus, in order to achieve efficient recognition, i.e., both high stability and high selectivity, strong binding of substrate by receptor is required.

1.3 Calix[4]arenes

Calix[n]arenes are oligophenols readily accessible by simple condensation of para-substituted phenols with formaldehyde under basic catalysts, Figure 1.2.

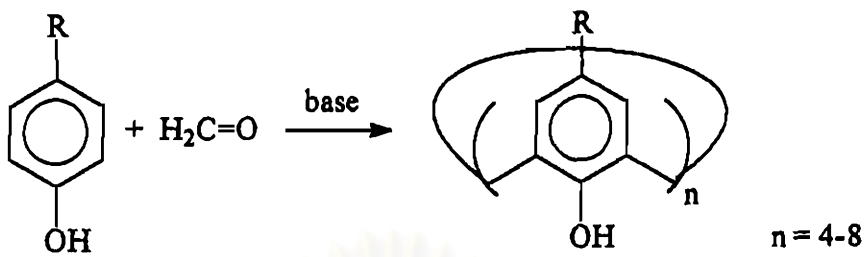


Figure 1.2 Preparation of calix[n]arenes.

The name “calixarene” has been given by Gutsche⁽¹⁾ because of the resemblance of the four-membered ring with a chalice (in Greek : calix). The suffix “arene” indicates the represent of aryl rings in the molecular framework.

Calix[n]arenes can be selectively prepared in different conditions. The calix[n]arene containing an even number of phenolic units such as calix[4]arene and calix[8]arene can be synthesized by simple techniques in satisfying yields. On the other hand, calixarenes that contain an odd member of [n] are more difficult to prepare. Calix[n]arene and their derivatives can be used as host molecules to form complexes with target ions and/or neutral molecules. They can also be developed and modified for the construction of new types of molecular devices for various industrial applications. Calix[4]arene is surely the most significant member of the calix[n]arene family, and its chemistry is by far most advanced. This molecule represents a well-preorganized cavity, the shape of which is tunable by suitable substitution of hydroxy groups (substitution on the “lower rim”).

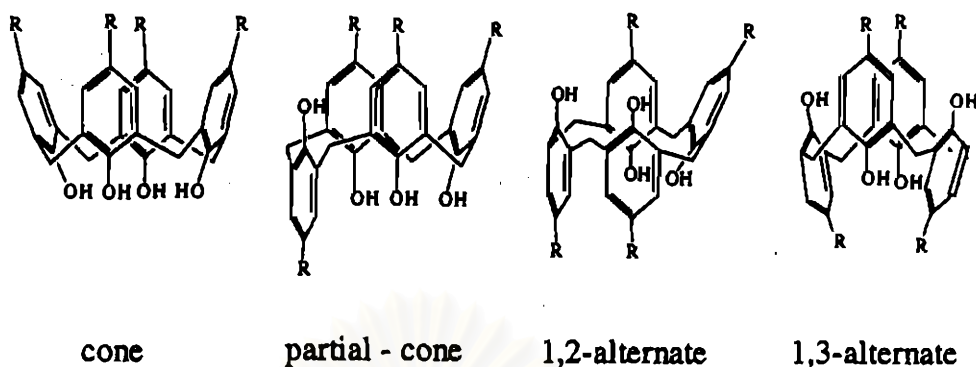


Figure 1.3 Possible conformers of calix[4]arene.

Figure 1.3 shows four basic conformers (isomers) which can be prepared from calix[4]arene: cone, partial cone, 1,2-alternate and 1,3-alternate. Each of them has its own specific properties and characteristic utilization in host-guest chemistry. This makes calix[4]arene a very attractive compound that can be used as a starting platform for designing more sophisticated structures for binding ions and neutral molecules.

1.4 Modified Calix[4]arenes as Selective Complexants for Heavy Metal Ions

The complexation studies of heavy metals have attracted inorganic chemists for an extended period of time. The reason for this growing interest is the use of ligands as complexants for the selective extraction of metals in purification procedures. Among the most widely used ligands are chelates and macrocycles. These types of ligands are particularly attractive because they can be designed to have very high stability constants for particular metal ions due to judicious choices of ligating atoms and ring sizes.

Use of calixarenes as complexants for metal ions is a much more recent development. Calixarenes are akin to macrocycles in that they have a lower rim of

oxygens in a cyclic arrangement that can be used to coordinate metal ions. Chemically modified calixarenes are used where both the lower rim oxygens and the functional groups appended as substituents coordinate to the metals. These chemically modified calixarenes can therefore be considered to have a combination of both a chelating and a macrocyclic portion.

Since Alfieri et al.⁽¹²⁾ reported on the synthesis of the first member of a new class of macrocyclic crown compounds with two opposite OH group of *p-tert*-butylcalix[4]arenes bridged by a pentaethylene glycol chain, extensive work has been devoted to the synthesis of 1,3-bridged calix[4]arenes as preorganized ligands. Calix[4]arenes are easily modified at the 1,3-difunctional hydroxyl groups (two opposite OH) at lower rim (Figure 1.4). This form is the most appropriate form for preorganization of potential binding sites, making possible the synthesis of several mixed ligand receptors.

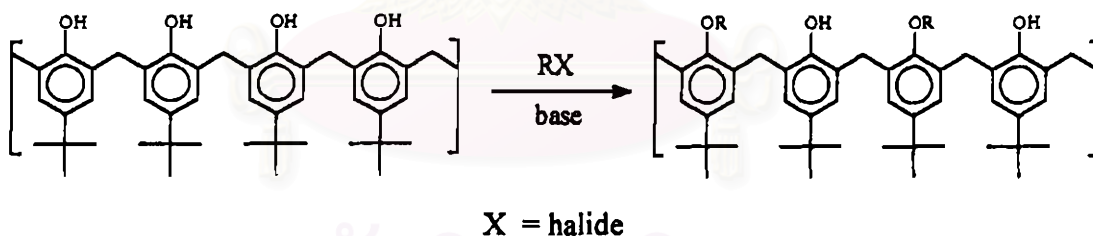


Figure 1.4 Chemical modification of 1,3-dihydroxyl groups of calix[4]arene at the lower-rim.

Diaza-benzo crown ether-*p-tert*-butylcalix[4]arene^(13,14) (Figure 1.5) were synthesized and studied complexation with Zn^{2+} , where the counter anions are Cl^- , Br^- , I^- , ClO_4^- , NO_3^- by 1H NMR spectroscopy. This study showed that this ligand could bind Zn^{2+} to a different extent depending on the counter anions and the cavity

size of the ligands. The stability of Zn^{2+} complexes of this ligand varied as follow : $NO_3^- > ClO_4^- > I^- > Br^- > Cl^-$. Recently, the protonation of this ligand and its complexation with $Zn(ClO_4)_2$ were studied by potentiometric and ultraviolet spectroscopy titrations⁽¹⁵⁾.

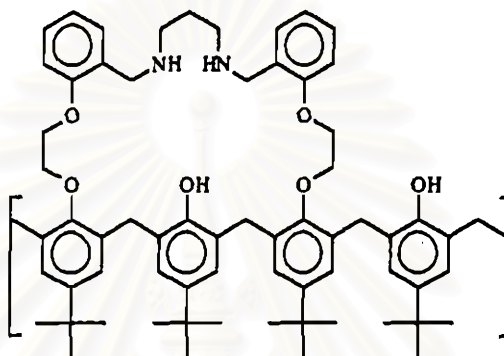


Figure 1.5 Diaza-benzo crown ether-*p-tert*-butylcalix[4]arene.

In 1994, Schiff base *p-tert*-butylcalix[4]arenes⁽¹⁶⁾, (Figure 1.6) were synthesized. Alkali and alkaline earth cations were very poorly extracted by the ligands (I-III). However, the better extraction of Li^+ and Na^+ with ligand (III) may be explained by greater flexibility of its bridge which was due to an additional carbon that allows the chain to adopt a more suitable geometry for complexation. In the transition metal series, Fe^{2+} and Cu^{2+} were extracted more efficiently. Heavy metal cations were extracted with ligand (II) and (III), with higher preference for Pb^{2+} . For lanthanide series, there was an extraction selectivity for Nd^{3+} and Eu^{3+} with (II) and for Eu^{3+} with (III).

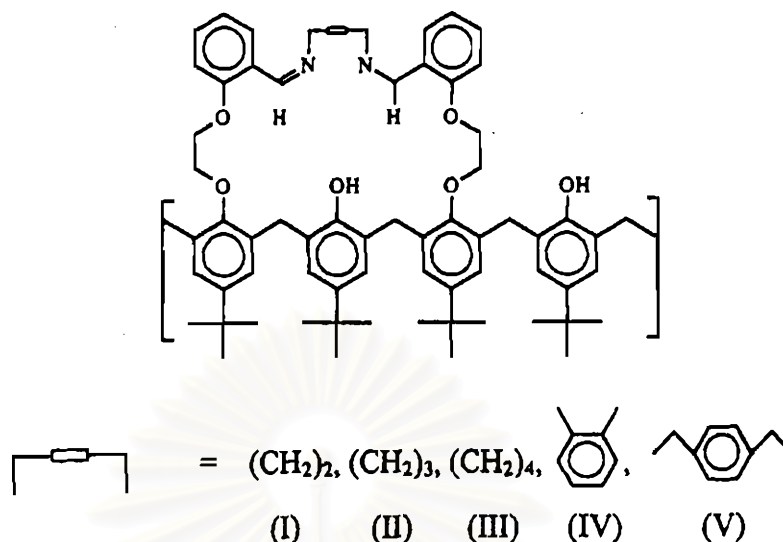


Figure 1.6 Schiff base *p*-*tert*-butylcalix[4]arenes.

The complexation work to date with calixarenes has primarily focused on metals of Group I or II, or on other oxophilic metal centers such as UO_2^{2+} . Calixarene based ligands with functionalities binding *via* their oxygen or nitrogen sites have been widely employed as selective complexants for both Group I and II metal ions. Nevertheless, little has been published on the preparation of calixarene derivatives which coordinate to the metal center *via* other heteroatoms. Such compounds are important if selective complexants for heavy metals are to be developed. Specific ligands need to be designed for these particular metals because they form stable complexes with “soft” rather than with “hard” donor ligands. For example, Cu^+ , Ag^+ , Au^+ , Cd^{2+} and Hg^{2+} are soft acids which can show soft-soft interactions with soft bases such as R_2S , RSH or RS^- .

In 1993, Gutsche et al.⁽¹⁷⁾ reported the synthesis of *p*-*tert*-butyltetramercaptocalix[4]arene which is a $-\text{SH}$ containing calix[4]arene. The $-\text{SH}$ groups substituted at all $-\text{OH}$ groups in calix[4]arene molecules, Figure 1.7.

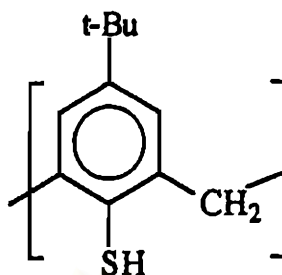


Figure 1.7 *p*-tert-Butyltetramercaptocalix[4]arene.

Hosseini et al.^(18,19) reported the synthesis of *p*-tert-butyltetramercaptocalix[4]arene from *p*-tert-butylcalix[4]arene. The ligand forms a binuclear complex with two mercury ions. These two ions are linearly coordinated to two arenethiolate groups that rearranged in a 1,3-alternate conformation, Figure 1.8.

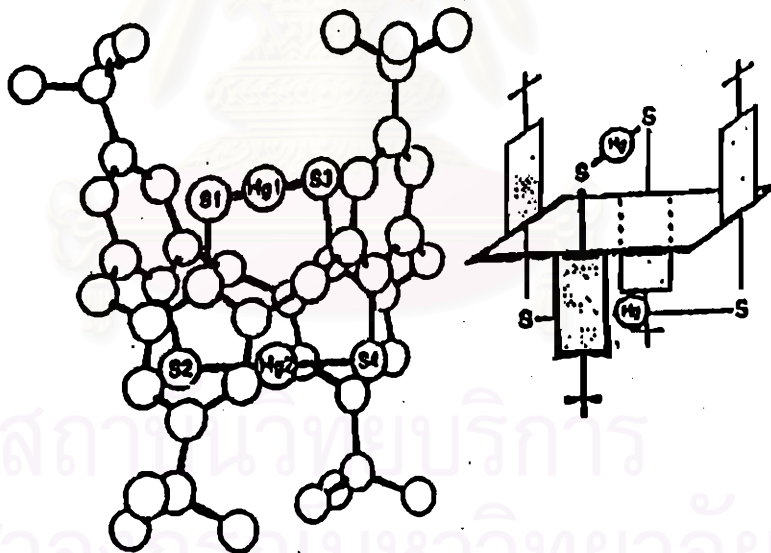


Figure 1.8 Binuclear complex of *p*-tert-butyltetramercaptocalix[4]arene with Hg^{2+} ions.

Reaction of mercury(II)acetate with *p*-tert-butyl-1,3-dihydroxy-2,4-disulfanylcalix[4]arene, obtained by a highly efficient synthesis starting from *p*-tert-butylcalix[4]arene,

leads to a mononuclear complex in which the Hg^{2+} ion is coordinated linearly to two arenethiolate groups, Figure 1.9.

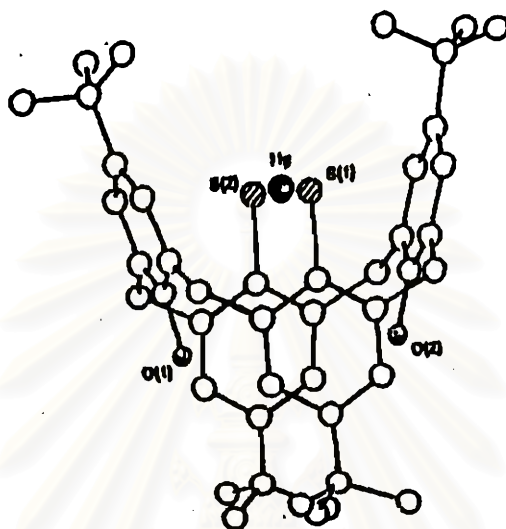


Figure 1.9 Mononuclear complex of *p*-*tert*-butyl-1,3-dihydroxy-2,4-disulfaxylcalix[4]arene with Hg^{2+} ion.

Roundhill et al.^(20,21) reported the preparation of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(2-bromoethoxy)calix[4]arene, (a), and its derivatives, Figure 1.10. They found that two lower rim functionalized calixarene, 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetra(2-*N,N*-dimethyldithiocarbamoylethoxy)calix[4]arene, (b), and 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetra(2-mercaptoethoxy)calix[4]arene, (c), were effective extractants for Hg^{2+} , Hg_2^{2+} , Ag^+ and Au^{3+} , but not for Pb^{2+} , Cd^{2+} , Ni^{2+} and Pt^{2+} . For MeHg^+ the later was an effective extractant, but the former was relatively ineffective. Generally, it can be concluded that the aforementioned mercepto-containing calix[4]arenes are look of selectivity towards specified heavy metal ions due to their open ring characters.

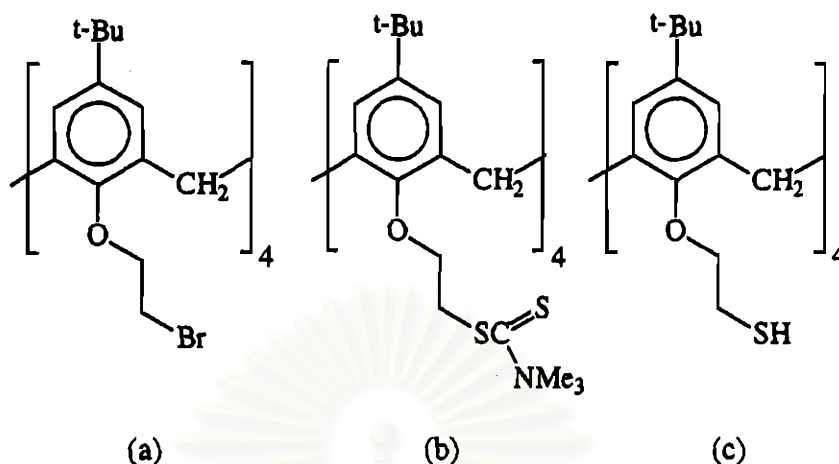


Figure 1.10 Structures of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis(2-bromoethoxy)calix[4]arene, (a), 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetra(2-*N,N*-dimethyldithiocarbamoyloxy)calix[4]arene, (b), and 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetra(2-mercaptoethoxy)calix[4]arene, (c).

1.7 Objective and Scope of the Research

To address the selectivity toward a specified heavy metal ion, new closing ring diazadithiol *p-tert*-butylcalix[4]arenes (Figure 1.11) are synthesized by reactions of dialdehyde-*p-tert*-butylcalix[4]arene derivatives and sulfur containing amines, 1,9-diaza-3,7-dithianonane and 1,8-diaza-3,6-dithiooctane. The protonation and complexation studies of these compounds with some heavy metal ions such as Hg^{2+} and Cd^{2+} by potentiometric titrations are, therefore, subjected to investigate. The results of this research should lead to understanding of ligands complexing ability towards target heavy metal ions. The species distribution of the ligands and their complexes with heavy metal ions over the varied pH values will also be obtained. In addition, the knowledge of this research may lead to application of these ligands for heavy metal ion separation from environment in the future.

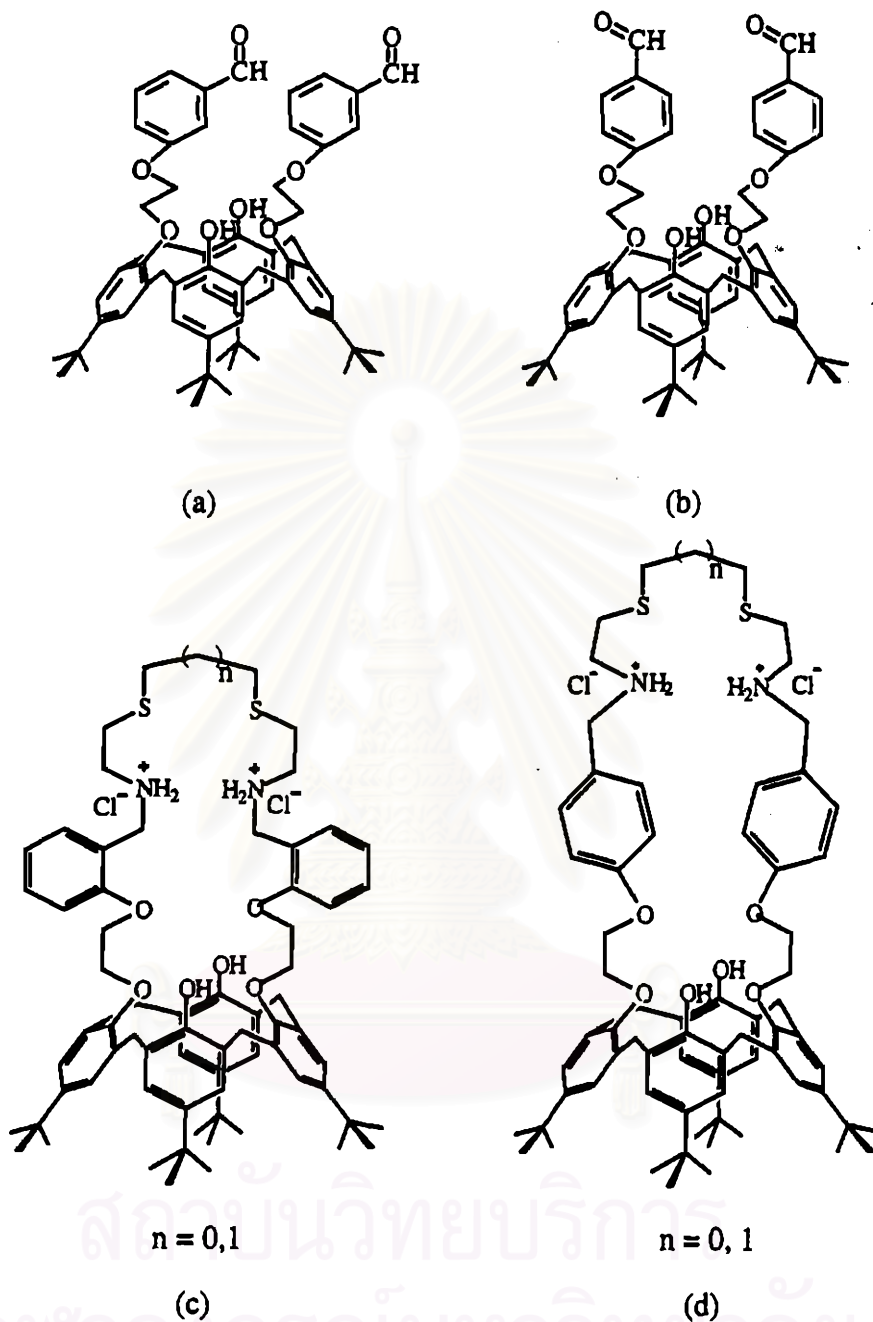


Figure 1.11 Benzo crown-*p*-*tert*-butylcalix[4]arene derivatives (a) 25,27-((2,2'-diethoxy)benzaldehyde)-*p*-*tert*-butylcalix[4]arene, (b) 25,27-((4,4'-diethoxy)benzaldehyde)-*p*-*tert*-butylcalix[4]arene, (c) *ortho* diazadithiol *p*-*tert*-butylcalix[4]arene compounds and (d) *para* diazadithiol *p*-*tert*-butylcalix[4]arene compounds.