Journal of Inclusion Phenomena and Macrocyclic Chemistry **39:** 47–53, 2001.

Recognition Studies of a Pyridine-Pendant Calix[4]arene with Neutral Molecules: Effects of Non-covalent Interactions on Supramolecular Structures and Stabilities

THAWATCHAI TUNTULANI*, GAMOLWAN TUMCHARERN and VITHAYA RUANGPORNVISUTI

Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand

(Received: 25 October 1999; in final form: 1 June 2000)

Key words: pyridine-pendant, *p-tert*-butylcalix[4]arene, neutral molecule recognition, NMR titrations, NOESY, supramolecular framework

Abstract

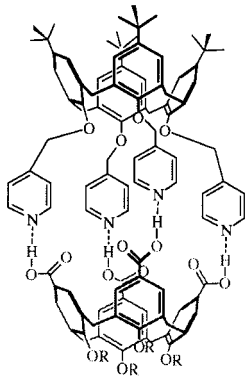
A new calix[4]arene derivative containing hydrogen bond acceptors, 5,11,17,23-tetra-*tert*-butyl-25,27-bis[(4-pyridylmethyl)oxy]-26,28-dihydroxycalix[4]arene (**L**), has been synthesized. ^{1}H-NMR titrations in chloroform-*d* were carried out to investigate the host–guest chemistry of **L** towards neutral molecules containing a wide variety of hydrogen bond donor groups such as aldehyde derivatives of *p-tert*-butylcalix[4]arenes (compounds **3** and **4**), acetylacetone, 1,2-diaminoethane, 2,6-diaminopyridine, catechol, resorcinol, hydroquinone, phthalic acid, isophthalic acid and terephthalic acid. **L** can form complexes with resorcinol, phthalic acid and catechol in 1 : 1 (log K = 3.13), 1 : 1 (log K = 5.41) and polymeric fashions, respectively. In addition, the solution structures of these complexes have been revealed by NOESY experiments. **L** forms a 1 : 1 complex with resorcinol by hydrogen bonding and van der Waals interactions resulting in a supramolecular framework. The phthalic acid molecule interacts with **L** via hydrogen bonding and is included into the lower rim cavity of **L**.

Introduction

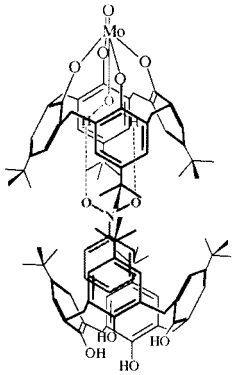
The assembly of organic supramolecular species incorporates non-covalent interactions such as van der Waals effects and hydrogen bonding to produce specific structural and functional properties [1]. Examples are liquid crystals [2] and molecular devices such as molecular cages and capsules [3, 4]. Calix[4]arenes, one of the most versatile building blocks in supramolecular chemistry, were derivatized and their self-assembly interactions investigated. Shimizu *et al.* have demonstrated the use of self-complementary hydrogen bonding to construct molecular capsules from calix[4]arene derivatives containing urea moieties at the upper rim [5]. This type of molecule can bind several polycyclic compounds such as nopinone, myrtenal, camphor and tricyclene to a different extent depending on the orientation of the guest molecules [6]. Böhmer and coworkers have also demonstrated the use of ^{1}H NMR spectroscopy to unambiguously determine the structures of tetraurea calix[4]arenes and also the exchange rates for four sets of protons by NOESY experiments [7]. Scheerder *et al.* [8] showed that the bis(ureido)calix[4]arenes gave a hydrogen-bonded dimer in a pinched cone conformation.

Several assemblies of calix[4]arene derivatives towards neutral molecules were also investigated [9–11]. Calix[4]arenes containing pyridone moieties at the upper rim can bind urea derivatives such as imidazolidone in a 1 : 1 fashion [9]. A calix[4]arene substituted with four carboxylic groups at the upper rim interacted with a calix[4]arene containing pyridine moieties at the lower rim to form a 1 : 1 complex, **1**, via hydrogen bonding interactions [10]. Corazza *et al.* have synthesized an interesting oxo-molybdenum calix[4]arene in which oxo-molybdenum binds four oxygen atoms from the phenolic O-atoms of a calix[4]arene [11]. The oxo-molybdenum calix[4]arene reacted with calix[4]arene to give a product, **2**, which could be crystallized in nitrobenzene. The crystal structure of the product shows that nitrobenzene is probably stabilized in the structure by both hydrogen bonding with a H_2O molecule and van der Waals interactions of the arene rings. Thus far, the understanding of how interactions between hosts and guests affected the structures of the assembled molecules is still unclear and, thus, should be a subject to pursue.

* Author for correspondence.



1



2

Besides the work of van Loon *et al.* [9], other pyridinocalixarenes have been reported in the literature [12–14]. Shinkai and colleagues synthesized (2-pyridylmethoxy)calix[n]arenes (n = 6 and 8) and found that they were efficient extractants for UO_2 at 100 °C [12]. Pappalardo *et al.* [13] synthesized nine conformers of [2-pyridylmethyl)oxy]calix[4]arenes by alkylation of calix[4]arenes with 2-(chloromethyl)pyridine in the presence of various bases. Later, they studied the extractive ability of tetrapyridinocalix[4]arene towards alkali cations and found that the selectivity followed the order $Na^+ > K^+ > Rb^+ > Cs^+ > Li^+$ [14].

Due to the versatile donor abilities of pyridinocalix[4]-arenes, we are interested in synthesizing a pyridinocalix[4]arene and studying its interactions with neutral molecules containing hydrogen bond donor groups such as aldehydes, ketones, amines, alcohols and carboxylic acids. The complexation studies are carried out by ^{1}H-NMR titrations, and the solution structures of the complexes are determined by 2D-NMR spectroscopy. The results lead to the understanding of the relationship between size, shape, interactions between host/guest and structures of aggregated molecules.

Experimental

Materials

Unless otherwise stated, all materials and solvents were standard analytical grade, purchased from Fluka, J. T. Baker or Merck, and used without further purification. Commercial grade solvents such as acetone, dichloromethane and methanol were distilled and stored over 4 Å molecular sieves. Chromatographic separations were performed on silica gel columns (kieselgel 60, 0.063–0.200 mm, Merck). Deuterated solvents (chloroform-*d*, methanol-d_4 and DMSO-d_6) were stored over 3 Å molecular sieves. *p-tert*-Butylcalix[4]arene [15] and its derivatives, **3** [16] and **4** [17], were prepared as previously described. 1,2-Dihydroxybenzene (catechol), 1,3-dihydroxybenzene (resorcinol) and 1,4-dihydroxybenzene (hydroquinone) were purified by standard procedures [18]. Benzene-1,3-dicarboxylic acid (isophthalic acid) was synthesized according to the procedure described in the literature [19].

Analytical procedures

Elemental analysis was performed on a Perkin Elmer CHON/S analyzer (PE2400 series II). MALDI-TOF mass spectra were recorded on a Bruker MALDI-TOF mass spectrometer (BIFEX) using α-cyanocinnamic acid as matrix. The melting point measurement was carried out on an Electrothermal 9100 apparatus. ^{1}H NMR titration and ^{13}C NMR experiments were conducted on a Bruker ACF 200 MHz nuclear magnetic resonance spectrometer. Two dimentional NMR spectra were recorded on a Jeol 500 MHz nuclear magnetic resonance spectrometer. Typically, samples were dissolved in deuterated chloroform and chemical shifts were recorded using a residual chloroform signal as internal reference. All NMR experiments were carried out at room temperature (25 °C).

Synthetic procedures

*Preparation of 5,11,17,23-tetra-tert-butyl-25,27-bis[(4-pyridylmethyl)oxy]-26,28-dihydroxycalix[4]arene (***L***)*

The following procedure was adapted from the method used for synthesizing 5,11,17,23-tetra-*tert*-butyl-25,27-bis[(2-pyridylmethyl)oxy]-26,28-dihydroxycalix[4]arene [13]. A suspension of calix[4]arene (2.00 g, 3.08 mmol) and potassium carbonate (4.25 g, 30.8 mmol) in the presence of NaI (2.30 g, 15.3 mmol) in acetonitrile (200 mL) was heated to reflux under nitrogen for 30 minutes. The methanolic solution (50 mL) of 4-(chloromethyl)pyridine hydrochloride (1.05 g, 6.40 mmol) was subsequently added dropwise to the reaction mixture over a 15 minute period. The dark brown slurry was refluxed for an additional 24 hours. The solvent was then removed by a rotary evaporator to obtain a dark brown solid. The solid was dissolved in CH_2Cl_2 (100 mL) and subsequently washed with 0.5 M HCl (150 mL) and 1 M $NaHCO_3$ (150 mL). The organic layer was then separated, dried over anhydrous sodium sulfate and solvent was removed under reduced pressure to afford a red brown solid. The solid was dissolved in a minimum amount of dichloromethane and placed on a silica gel column. Unreacted reagents were eluted with 2% acetone/dichloromethane. The desired product was eluted with 10% acetone/dichloromethane and was purified by adding diethylether to precipitate a white solid (1.13 g, 44%).

Characterization for **L**:^{1}H NMR (δ in $CDCl_3$): 8.60 (d, 4H, J_{H-H} = 6.1 Hz, Py-2-proton); 7.64 (d, 4H, J_{H-H} = 5.9 Hz, Py-3-proton); 7.05 (s, 4H, HOAr*H*); 6.99 (s, 2H, ArO*H*); 6.77 (s, 4H, ROAr*H*); 5.05 (s, 4H, OCH_2Py); 4.23, 3.31 (dd (AB system), 8H, J_{H-H} = 13.1 Hz, $ArCH_AH_BAr$); 1.28 (s, 18H, HOAr-*t*-C_4H_9); 0.91 (s, 18H, ROAr-*t*-C_4H_9). ^{13}C NMR (δ in $CDCl_3$): 30.93, 31.55, 31.68, 33.84, 33.94, 75.93, 121.33, 125.13, 125.71, 127.52, 132.23, 141.85, 146.13, 147.57, 149.36, 150.11, 150.47. MALDI-TOF MS (M^+, m/z): 830.3. *Anal Calcd.* for $C_{56}H_{66}O_4N_2$: C, 80.93; H, 8.00; N, 3.37. *Found*: C, 80.60; H, 7.92; N, 3.21. Melting Point: 107 °C.

Host–guest chemistry studies

Host–guest studies of **L** *with ketones, aldehydes and amines*

Typically, a solution of **L** (0.1039 g, 0.125 mmol) in $CDCl_3$ (2.5 mL) was prepared. To each NMR tube containing 0.2 mL of the **L** solution was added 0–4 equivalents of a guest (0.250 mmol) in $CDCl_3$ (2.5 mL). The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements. NMR spectra were then recorded. The chemical shifts of the signals were followed and plotted against the equivalents of the added guest.

Host–guest studies of **L** *with catechol*

A solution of **L** (0.1039 g, 0.125 mmol) in $CDCl_3$ (2.5 mL) and a solution of catechol (0.0275 g, 0 250 mmol) in $CDCl_3$ (2.5 mL) were prepared. To each NMR tube containing 0.2 mL of the **L** solution was added 0-4 equivalents of catechol. In the case of 5–10 equivalents, a solution of **L** (0.0623 g, 0.0750 mmol) in $CDCl_3$ (1.5 mL) was prepared. Solid 1,2-Dihydroxybenzene (0–4 equivalents) was added to each NMR tube containing 0.2 mL of the **L** solution. The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements.

Host–guest studies of **L** *with resorcinol, hydroquinone and benzene dicarboxylic acids*

Typically, a solution of **L** (0.0707 g, 0.0851 mmol) in $CDCl_3$ (1.7 mL) was prepared. Solid guest compounds (0-4 equivalents) were added to each NMR tube containing 0.2 mL of the **L** solution. The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements. Association constants were determined using a curve fitting method [20, 21].

Competitive study between catechol and resorcinol

A solution of **L** (0.0707 g, 0.0851 mmol) and a solution of catechol (0.0275 g, 0.250 mmol) in $CDCl_3$ (1.7 and 2.5 mL, respectively) were prepared. In each NMR tube, 0.2 mL of the prepared **L** solution was mixed with the prepared solution of catechol (0–4 equiv.), and the mixture was subsequently transferred to an NMR tube containing 0–4 equiv. of solid resorcinol. The solution in each NMR tube was adjusted by adding $CDCl_3$ to the same volume before the NMR measurements. Chemical shifts of the mixture were compared to the known chemical shifts of **L**·catechol and **L**·resorcinol.

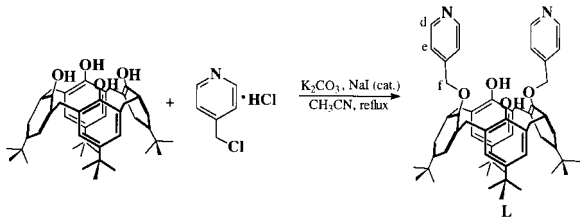
Theoretical calculations

Quantum calculations using a molecular mechanics method (MM+) were performed to obtain a gas phase structure of **L** [22]. An empirical method, PM3, was used to calculate the structures of benzene dialcohols and benzene dicarboxylic acids [23, 24].

Results and discussion

Synthesis and characterization

A *p-tert*-butylcalix[4]arene derivative, 5,11,17,23-tetra-*tert*-butyl-25,27-bis[(4-pyridyl methyl)oxy]-26,28-dihydroxycalix[4]arene (**L**) was synthesized by alkylating calix[4]arene with 2 equivalents of 4-(chloromethyl)pyridine hydrochloride in acetonitrile in the presence of K_2CO_3 as base and NaI (5 equivalents) as catalyst (Equation (1)). Separation of the products by column chromatography (SiO_2) using 10% acetone in dichloromethane as eluent gave **L** in 44% yield. Compared to other pyridylmethoxy derivatives such as *ortho* [13] and *meta* [14] derivatives, the *para* derivative (**L**) was obtained in lower yield because the N-donor in a *para* position could not chelate the K^+ ion to form a template framework that may facilitate the nucleophilic substitution reaction. A ^{1}H-NMR spectrum of **L** composed of a singlet signal of Ar-OC*H*$_2$-Py (f) at 5.05 ppm and two doublets of the aromatic protons on the pyridine moieties at 8.60 (d) and 7.64 ppm (e) as well as the signals of the *p-tert*-butyl calix[4]arene unit which showed a doublet of doublet signal at 4.23 and 3.31 ppm (designating the cone conformation). Furthermore, elemental analysis and MALDI-TOF MS results agree well with the proposed structure.



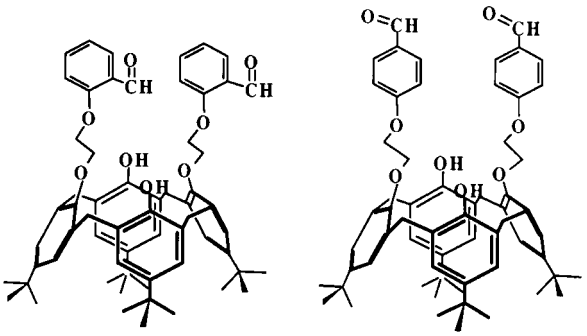
(1)

The compound **L** can possibly form a dimeric structure in a similar fashion with the bis(ureido)calix[4]arene as reported by Reinhoudt and colleagues [8]. However, the NOESY spectrum of **L** in $CDCl_3$ showed no NOE connectivity between the proton d and the proton f, methylene bridge and –O*H* protons, *vide infra*. This evidence suggests that **L** remains a single molecule in the solution.

Host–guest chemistry studies

^{1}H-NMR titrations have been carried out to investigate the host–guest chemistry of **L** towards neutral molecules. A series of compounds containing different types of hydrogen bond donor groups such as 1,3-bis(ethoxybenzaldehyde)-*p-tert*-butylcalix[4]arenes (**3** and **4**), 1,2-diaminoethane, 2,6-diaminopyridine, 1,2-dihydroxybenzene (catechol), 1,3-dihydroxybenzene (resorcinol), 1,4-dihydroxybenzene (hydroquinone), benzene-1,2-dicarboxylic acid (phthalic acid), benzene-1,3-dicarboxylic acid (isophthalic acid) and benzene-1,4-dicarboxylic acid (terephthalic acid) has been used in the investigation. In addition, a host–guest chemistry study between **L** and 2,4-pentanedione or acetylacetone has also been conducted. Generally, acetylacetone occurs in solution as an equilibrium mixture of 87% enol and 13% diketone [25]. The keto form contains acidic methylene

protons which may be suitable for hydrogen bonding with **L**. The change in the keto:enol proportion due to hydrogen bonding interactions is anticipated.



3 **4**

^{1}H-NMR titrations of **L** with various hydrogen bond donors were performed in $CDCl_3$ solution at 25 °C. The results showed that the proton on the *ortho* and *meta* positions of the pyridine pendant groups (d and e) only slightly shifted upon addition of ligands **3** and **4**, 1,2-diaminoethane, 2,6-diaminopyridine and acetylacetone and suggested that **L** had no recognition towards such compounds. In the case of compounds **3** and **4**, the hydrogen bonding interactions may be too weak to be observed by NMR spectroscopy. For moderate hydrogen bond donors, 1,2-diaminoethane and 2,6-diaminopyridine, the absence of hydrogen bonding interaction with **L** may stem from the electron repulsion between *N*-amine and *N*-pyridine. It was surprising that no hydrogen bonding interaction between **L** and acetylacetone was observed. The intramolecular hydrogen bonding between –OH and O=C– in the enol form of acetylacetone must be very strong and prevents the intermolecular hydrogen bonding to occur.

In the light of the fascinating molecular structures of **1** and **2** which showed molecular assemblies by hydrogen bonding and van der Waals interactions, host–guest studies of **L** towards dihydroxybenzenes and benzene dicarboxylic acids containing two hydrogen bond donor groups at different positions are the subject of our interest. A relationship between the positions or orientations of the hydrogen bond donors and the structures/stabilities of the complexes is expected. Host–guest studies between dihydroxybenzenes and **L** were performed by adding various amounts of the guests into a deuterated chloroform solution of the host (**L**), and interactions of host and guest molecules were investigated by ^{1}H-NMR spectroscopy. Due to the insolubility of dihydroxybenzenes except catechol, they were added directly as solid into NMR tubes. Dissolution of the solids into the solution of **L** indicates that the alcohols have interacted with or formed complexes with **L**. It was found that the solution of **L** could not dissolve hydroquinone, and the Py-2-proton and Py-3-proton (d and e) were only slightly shifted. Therefore, **L** did not form a complex with hydroquinone. For catechol and resorcinol, each ^{1}H-NMR spectrum of the complexes with **L** possessed a doublet of doublet signal at approximately 3.34 and 4.23 ppm (J $\sim$ 13 Hz) suggesting that **L** retained the cone conformation of calix[4]arene upon complexation.

Addition of resorcinol into the deuterated chloroform solution of **L** led to the evolution of a new set of proton resonances at 7.13 (t), 6.59 (d) and 6.46 (dd) ppm. All signals except the one for proton d shifted continuously downfield until 1 equivalent of the guest was added. A plot of chemical induced shift (CIS) against the equivalent of resorcinol is displayed in Figure 1a. The plot suggests that **L** forms a complex with resorcinol in a 1 : 1 fashion. The stability or complex formation constant of **L** towards resorcinol has been estimated using a curve-fitting program to be log K = 3.13 [20, 21].

The complexation of **L** and resorcinol was also studied in methanol-d_4 and DMSO-d_6. Unfortunately, the results showed that **L** did not complex resorcinol in these solvents. In deuterated methanol, the complexation of **L** and resorcinol may be disrupted and replaced by the stronger hydrogen bonding interactions of methanol towards **L** and resorcinol because the hydroxy group of methanol acted as both hydrogen bond donors and hydrogen bond acceptors. In the case of tetrapyridinocalix[4]arene, the crystal structure of the compound showed that a methanol of solvation was hydrogen bonded to one pyridine N atom [13]. Either the hydrogen bond donor character of the O-atom or the presence of H_2O in deuterated DMSO accounted for the absence of an interaction between **L** and resorcinol in this solvent.

Interestingly, addition of up to 10 equivalents of catechol produced continuous shifts of all proton signals of **L** (Figure 1b) except Py-3-proton (e). It should also be noted that catechol was completely dissolved in the solution of **L** in spite of the low solubility of catechol (>10 equivalents of catechol were added). The CIS of the protons and the evidence from the increasing solubility of catechol suggested that the interactions between the aromatic protons of catechol and the aromatic protons of **L** may be in a polymeric manner. Therefore, the stability constant was not able to be calculated using our curve-fitting program.

The abilities of **L** to form complexes with benzene dicarboxylic acids such as phthalic acid, isophthalic acid and terephthalic acid have been studied by ^{1}H-NMR titrations which were carried out by direct addition of the acid as solid into $CDCl_3$ solutions of **L**. It was found that isophthalic acid and terephthalic acid did not dissolve in the solution of **L** and, thus, did not form complexes with **L**. Only phthalic acid dissolved in a solution ($CDCl_3$) of **L** and a complex formation constant was able to be estimated by ^{1}H-NMR spectroscopy. In addition, each ^{1}H NMR spectrum contained a pair of doublet signals (J $\sim$ 13 Hz) due to the methylene bridge protons (ArCH_2Ar) signifying a cone conformation of calix[4]arene. The titration results shown in Figure 1c suggested a 1 : 1 stoichiometry of the **L**·phthalic acid complex. The protons d, e and ArO*H* were used for determining a stability constant of **L**·phthalic acid which was estimated to be log K = 5.41.

Although the stability constant of the **L**·catechol complex could not be determined, the comparative binding ability of catechol and resorcinol was conducted. Addition

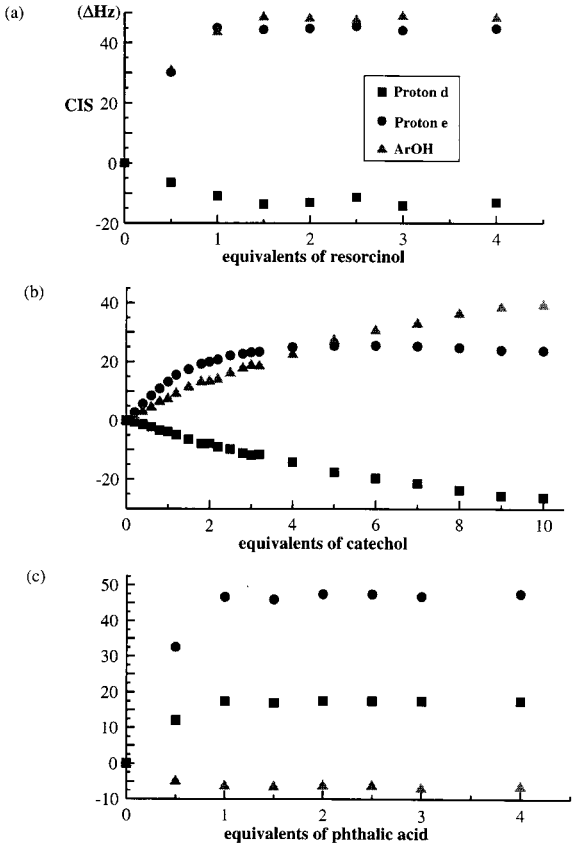


Figure 1. Titration curves for (a) resorcinol (b) catechol (c) phthalic acid (1equivalent of **L** present in the solutions). The negative ΔHz denotes the upfield shift of the signal.

of various stoichiometries of **L**·catechol in $CDCl_3$into the same various ratios of resorcinol resulted in the shifting of proton signals which was similar to the chemical shifts of **L**·resorcinol. The result signified that **L** formed a more stable complex with resorcinol.

Solution structures of complexes

In order to understand the factors that control the stability of the complexes, the solution structures of the host–guest complexes must be determined. Thus, NOESY experiments for **L** and the mixture of **L** and guests in $CDCl_3$ have been carried out. It can be clearly seen from the NOESY spectra of **L** that the proton e on the pyridine pendant groups has interacted with ArO*H* and the methylene bridge protons (g) on the calix[4]arene unit. We have calculated a structure of **L** by MM+ and found that the pyridine pendant arms organize themselves by bending towards the calix[4]arene unit. This is pertinent to the connectivity of the protons observed in NOESY. The distance between N_{py}–N_{py} of the pyridine groups was 6.34 Å. Figure 2 displays connectivities among protons of **L** as deduced from the NOESY spectra and the calculated structure of **L** which shows the preorganized cavity of the ligand.

Certain regions of the NOESY spectra of the mixture of **L** and resorcinol in a 1 : 1 stoichiometry are shown in Figures 3a and 3b. The proton H_c of resorcinol is found to have a connectivity with the proton d while the protons

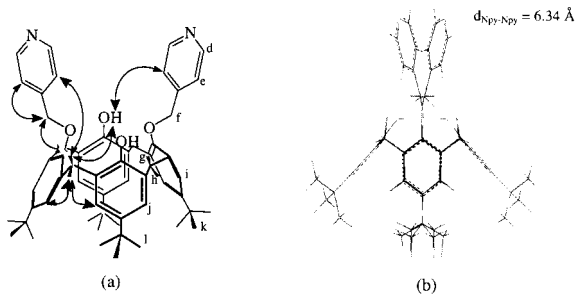


Figure 2. (a) NOE connectivities of **L**, (b) calculated struture of **L**.

H_a and H_b do not show any connectivities with the proton d. In addition, there is no connectivity between H_a/H_b and the proton e. The resorcinol molecule must arrange its H_c into the cavity of the pyridine pendant arms and pointing H_b and H_a outwards. This orientation should be stabilized by hydrogen bonding interactions between resorcinol-O*H* and *N*-pyridine of **L**. Unexpectedly, connectivities of the proton H_b with ROAr*H* (i) and HOAr*H* (j) of the calix[4]arene framework are detected. Furthermore, the NOESY spectrum in Figure 3b shows that the proton H_c has a connectivity with *t*-butyl protons (l) of the ArOH rings. These connectivities cannot result from through space interactions within a single aggregate because these protons are too far from each other. They must arise from interactions with hydrogens of another molecule. The interactions summarized in Figure 3c imply that a resorcinol molecule must also be included into the hydrophobic upper rim cavity of another calix[4]arene unit of **L**. Recently, Hosseini and coworkers have demonstrated use of the double fusion of two calix[4]arenes and *p*-xylene to form a unidirectional supermolecule in the solid state [26]. The possible solution structure of **L**·resorcinol is thus proposed in Figure 3d accounting for the 1:1 stoichiometry of **L**·resorcinol suggested by the titration results. The structure also corresponds with the upfield shifts of the proton d and all protons of resorcinol due to the diamagnetic anisotropy of the neighboring ring currents.

NOESY experiments of the 1 : 1 mixture of **L** and phthalic acid have also been performed in $CDCl_3$ and a spectrum is depicted in Figure 4a. The signal due to H_a on phthalic acid is superimposed on the signal of the proton e. Therefore, some interactions related to these two protons cannot be distinguished. From Figure 4a, only the connectivity between H_b of phthalic acid and the proton j of **L** can be unambiguously assigned. In addition, an interaction of the proton b towards *H*OArH can also be observed (Figure 4b). However, no intermolecular NOE connectivity encountered in **L**·resorcinol has been detected in the phthalic acid case. The results imply that phthalic acid resides within the cavity of **L** close to the lower rim ArO*H* and HOAr*H*. The possible solution structure of the **L**·phthalic acid complex can be drawn as shown in Figure 4c. The structure also agrees with the fact from titrations that ArO*H* shifted upfield (due to the anisotropic effect of the phthalic ring current).

NOESY spectra of the mixture of **L** and catechol have also been obtained. We observed that a proton of catechol had connectivities with protons d, e, f and g of **L**. However,

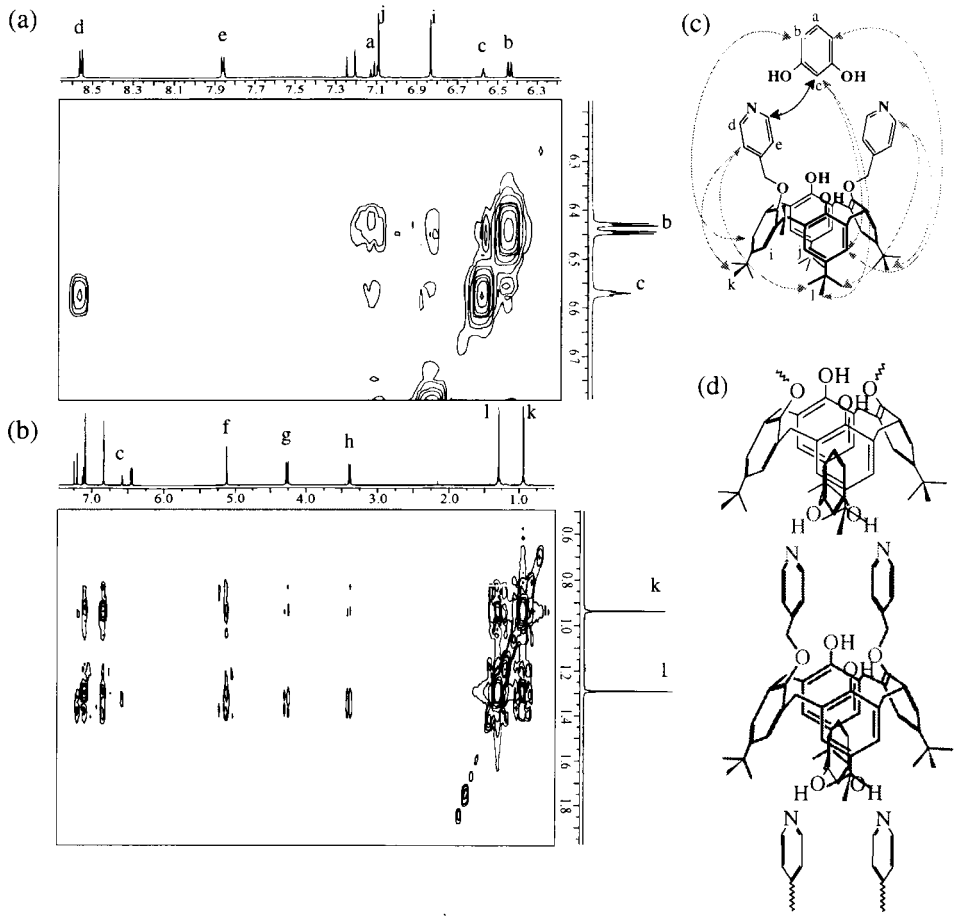


Figure 3. (a), (b) NOESY spectra of **L**·resorcinol in $CDCl_3$ (c) summary of interactions deduced from NOESY spectra, (d) possible solution structure of **L**·resorcinol.

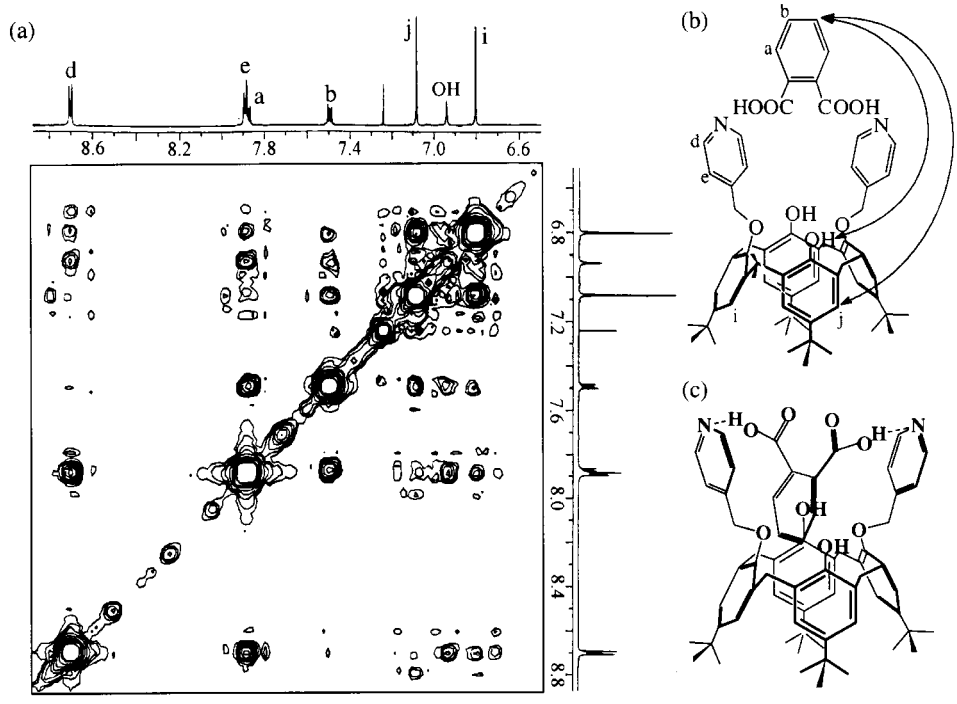


Figure 4. (a) NOESY spectrum of **L**·phthalic acid (b) NOE connectivities, (c) possible solutions structure of **L**·phthalic acid.

the NMR titration results indicated the polymeric structure of the complex. The data obtained from NOESY are, therefore, not conclusive enough for deducing the solution structure of **L**·catechol.

Effects of size, shape and interaction between host/guest towards aggregated molecules

The structures of dicarboxylic acids and benzene dialcohols used in these studies were calculated by the PM3 method. The results show that the **H**–**H** distances of **H**O–Ar–O**H** in catechol, resorcinol and hydroquinone are 3.29, 4.58 and 6.39 Å, respectively. For the acids, the **H**–**H** distances of **H**O–(C=O)–Ar–(C=O)–O**H** in phthalic acid, isophthalic acid and terephthalic acid are 5.82, 8.68 and 9.13 Å, respectively. Our results show that catechol, resorcinol and phthalic acid can form complexes with **L**. The size and dimensionality of hydroquinone, isophthalic acid and terephthalic acid may be unsuitable to form hydrogen bonding with **L** or fit into the cavity of **L**. Phthalic acid may have a suitable geometry for its hydroxy groups to form hydrogen bonding with *N*-pyridine of **L** and simultaneously be included into the lower rim cavity of **L**. The combination of hydrogen bonding and the preorganized structure of **L** for inclusion of phthalic acid may account for the high stablity constant of the **L**·phthalic acid complex. In contrast, the geometry of catechol and resorcinol are probably too constrained to organize such an alignment in the phthalic acid case. Nevertheless, the dimensionality of resorcinol must be appropriate for the inclusion into an upper rim cavity of calix[4]arene. In this case **L** requires a dramatic disturbance of the calix[4]arene compartment and this may result in the lower stability constant of the **L**·resorcinol complex. In the case of catechol, the polymeric structure of **L**·catechol may stem from the versatility of catechol to form both homonuclear hydrogen bonding (catechol-catechol) and heteronuclear hydrogen bonding (catechol-**L**). The structure of the catechol complex cannot be deduced from the present data. More experiments will be carried out in due course to elucidate its solution structure.

Conclusion

The compound 25,27-di-(4-pyridylmethoxy)-*p*-*tert*-butylcalix[4]arene (**L**) has been synthesized and found by NMR studies to interact with some dialcohols and diacids. The recognition of **L** towards dialcohols and diacids is as follows: phthalic acid (log K = 5.41) > resorcinol (log K = 3.13) > catechol. **L** selectively binds resorcinol in a 1 : 1 fashion by hydrogen bonding and van der Waals interactions to form a supramolecular structure. **L** also forms a 1 : 1 complex with phthalic acid. The phthalic acid molecule was included into the lower rim cavity of **L**, and the complex was stabilized by hydrogen bonding. Catechol was also found to form a complex with **L** in a polymeric manner *via* hydrogen bonding interactions. We have demonstrated thus far that a combination of hydrogen bonding and van der Waals interactions between **L** and certain neutral guests can result in interesting supramolecular structures.

Acknowledgements

We thank the Thailand Research Fund for financial support (Grant No. PDF4080055) and the Bio-Technology Institute, Chulalongkorn University for MALDI-TOF mass spectrometry results. Mrs. Wanna Sririnnuth of the Scientific and Technological Research Equipment Center, Chulalongkorn University is gratefully acknowledged for her help in 2D NMR experiments. We appreciate Dr. Mongkol Sukwattanasinitt for helpful discussion on the NMR analyses. G.T. is a student under support of the Development and Promotion of Science and Technology Talent project. Finally, we are indebted to the referees of this article for their valuable suggestions.

References

1. J.-M. Lehn: *Supramolecular Chemistry: Concepts and Perspectives*, VCH Publishers, Weinheim, pp. 161–180 (1995).
2. F. Vögtle: *Supramolecular Chemistry*, John Wiley & Sons, New York, pp. 231–281 (1991).
3. J. Rebek, Jr.: *Chem. Soc. Rev.* 255 (1996).
4. R.G. Chapman and J.C. Sherman: *Tetrahedron* **53**, 15911 (1997).
5. K.D. Shimizu and J. Rebek, Jr.: *Proc. Natl. Acad. Sci. U.S.A.* **92**, 12403 (1995).
6. R.K. Castellano, B.H. Kim and J. Rebek, Jr.: *J. Am. Chem. Soc.* **119**, 12671 (1997).
7. O. Mogck, M. Pons, V. Böhmer and W. Vogt: *J. Am. Chem. Soc.* **119**, 5706 (1997).
8. J. Scheerder, R.H. Vreekamp, J.F.J. Engbersen, W. Verboom, J.P.M. van Duynhoven and D.N. Reinhoudt: *J. Org. Chem.* **61**, 3476 (1996).
9. J.-D. van Loon, R.G. Janssen, W. Verboom and D.N. Reinhoudt: *Tetrahedron Lett.* **33**, 5125 (1992).
10. R.H. Vreekamp, W. Verboom and D.N. Reinhoudt: *J. Org. Chem.* **61**, 4282 (1996).
11. F. Corazza, C. Floriani, A. Chiesi-Villa and C. Guastini: *J. Chem. Soc., Chem. Commun.* 640 (1990).
12. S. Shinkai, T. Otsuka, K. Araki and T. Matsuda: *Bull. Chem. Soc. Jpn.* **62**, 4055 (1989).
13. S. Pappalardo, L. Giunta, M. Foti, G. Ferguson, J.F. Gallagher and B. Kaitner: *J. Org. Chem*. **57**, 2611 (1992).
14. S. Pappalardo, G. Ferguson, P. Neri and C. Rocco: *J. Org. Chem.* **60**, 4576 (1995).
15. C.D. Gutsche and M. Iqbal: *Org. Synth.* **68**, 234 (1989).
16. R. Seangprasertkij, Z. Asfari, F. Arnaud, J. Weiss and J. Vicens: *J. Incl. Phenom.* **14**, 141 (1992).
17. K. Navakhun, T. Tuntulani and V. Ruangpornvisuti: *J. Incl. Phenom*. **38**, 113 (2000).
18. D.D. Perrin and W.L.F. Armarego: *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, p. 117, 196, 272 and 391 (1988).
19. H.T. Clarke and E.R. Taylor: *Org. Synth*. **22**, 135 (1943).
20. T. Pothsree, R. Seangprasertkij-Magee and T. Tuntulani: *J. Incl. Phenom.* **29**, 99 (1997).
21. T. Rojsajjakul, S. Veravong, G. Tumcharern, R. Seangprasertkij-Magee and T. Tuntulani: *Tetrahedron* **53**, 4669 (1997).
22. A. R. Leach: *Molecular Modelling: Principles and Applications*, *Longman*, London, pp. 131–206 (1996).
23. J.J.P. Stewart: *J. Comput. Chem*. **10**, 209 (1989).
24. J.J.P. Stewart: *J. Comput. Chem*. **10**, 221 (1989).
25. E. Breitmaier: *Structure Elucidation by NMR in Organic Chemistry: A Practical Guide*, John Wiley & Sons, New York, pp. 9–10 (1993).
26. F. Hajek, M.W. Hosseini, E. Graf, A.D. Cian and J. Fisher: *Angew. Chem. Int. Ed. Engl*. **36**, 1760 (1997).