



Review Article

Inclusion of Organic Cations by Calix[n]arenes

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Abstract

Calix[n]arenes represent an interesting class of preorganized aromatic hosts exhibiting an enhanced ability for cation- π interaction. Recent results obtained with the complexation of various calix[n]arenes and five structural types of organic cations, namely ammonium ions, quaternary ammonium ions, phosphonium ions, iminium ions and tropylium ions are reviewed. The influence of both the guest structure and the shape and flexibility of the hosts on the complex stability in the gas phase and (mainly) in solution is considered.

Introduction

Among the weak non-covalent attraction forces such as hydrogen bonding, ionic and hydrophobic interactions, those enabling the formation of host-guest-complexes, cation- π interactions, have only been recognized in the last decade [1, 2]. In contrast the cation- π interaction has been known to be a prominent force in the gas phase for 20 years [3], and in the condensed phase it was demonstrated to be important in the formation of artificial cyclophane receptors in the late 1980s [4]. In many biological systems, metal cation- π interactions play an important role in molecular recognition [1]. However, since the determination of the acetylcholine esterase structure, which demonstrates the contact of the ammonium subunit of acetylcholine with the tryptophan side chain [5], interest has focused on the interaction between organic cations in both natural and synthetic receptors. Systematic studies of a series of related structures of artificial receptor molecules have revealed the role played by cation- π interactions.

Calixarenes and related skeletons are a widely used platform in order to study cation- π interactions [6]. The calixarene complexation of cations including ammonium ions was reviewed by Gutsche in 1989 when the cation- π interaction was not so topical [7]; in addition, Lhotak and Shinkai also published a 1997 review concerning calix[n]arene complexes with cations, outlining the importance of cation- π interactions [8]. It is the results obtained since 1990 with respect to organic cations which were not included in the review of Lhotak and Shinkai that are the focus of this current review. The importance of the interaction of the cations with the aromatic π -basic cavity of the host was not evidenced in each case. However, because of the structural environment of the macrocycles considered the cation- π interaction that can be concluded from crystal structures may hold also for other calixarene complexes in solution.

Host-guest complexes with organic cations

The host molecules can be divided into three structure types: calix[n]arenes, resorcinarenes and homooxacalixarenes such as **I**, **II** and **III** (Chart 1).

This review is organized according to the type of cation complexed by the various host molecules. Organic cations used as guests can be divided into 5 structural types: ammonium ions **IV**, quaternary ammonium ions **V**, phosphonium ions **VI**, iminium ions **VII** and tropylium ions **VIII** (see Chart 2).

The strength of the cation- π interaction will depend on: (1) the organic cation type. (2) the cavity size and the conformation of the macrocycles. (3) substituents on the upper and lower rim of the calixarenes which influence the cavity size, the conformation and the flexibility of the host molecule and (4) the solvent and the anion.

Because in any binding event several weak attraction forces may contribute to the molecular recognition, the selection of the cation- π interaction is difficult. However, by comparing related guests with and without positive charges (for example pyridine and pyridinium), the role of the charge can be elucidated. In particular, it is useful to know the crystal structures of the host-guest complexes; this allows us to classify the cation- π interaction according to the distances between the charged molecule and the aromatic units of the host.

Crystal structure

Unfortunately, the crystal structures of calixarene hosts including organic cations are rarely known.

Atwood *et al.* have demonstrated that the tetramethylammonium ion is embedded in the cavity of *p*-sulfonatocalix[4]arene [9]. Two tetramethylammonium ions are included in the cone-like cavity of [*p*-tert-

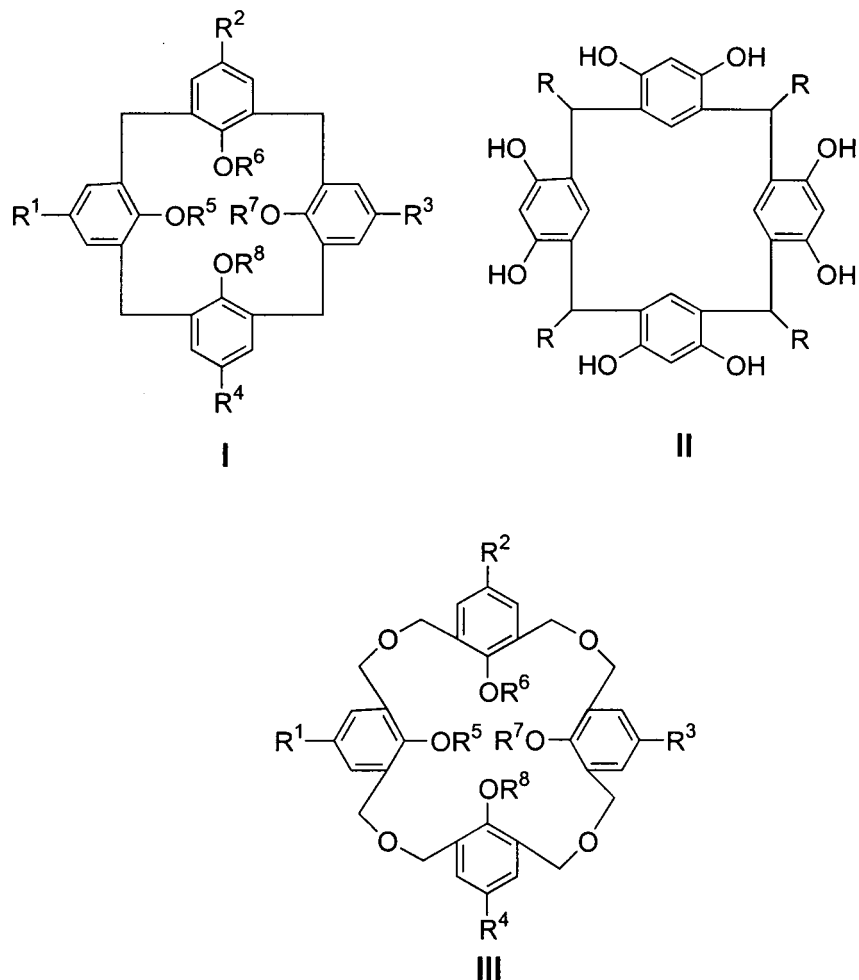


Chart 1.

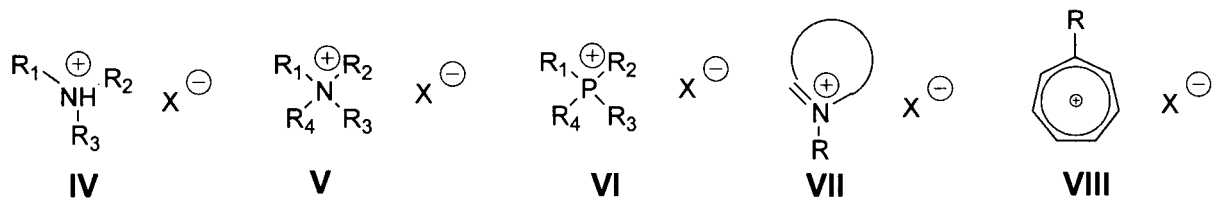
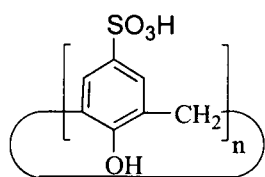


Chart 2.

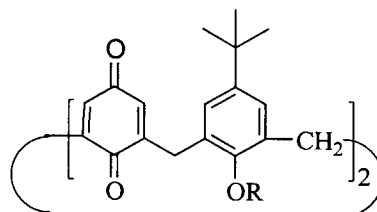
butylcalix[6]arene-2H) formed by three phenyl rings. One of the cations is included in the cavity and another is associated but not included [10]. The included ammonium ion also has access to the negative array of three oxygen atoms on the other half of the calix[6]arene. Therefore, both the cation-anion attraction and cation- π interaction may contribute to the binding mode. In contrast, Aoki and Murayama [11] have shown that the ammonium part of the neurotransmitter acetylcholine preferably associates with the aromatic rings of a resorcin[4]arene (**III**; $R^5 - R^8 = H$; $R^1 - R^4 = Et$). The conclusion drawn from the solid state structure may not hold true for the fluid phase. However, the methylprotons of acetylcholine in complex with the resorcinarene are upfield shifted by more than 1 ppm in solution [11] indicating that the complex is strongly related to the solid state structure.

Gas phase

In the last ten years, host-guest chemistry in the gas phase has been studied by mass spectroscopy [12], and it turns out that the ionization mode determines whether the results obtained by mass spectroscopy reflect those of solution chemistry. The complexation of alkylammonium ions by resorcin[4]arene in the gas phase has been determined by electrospray ionisation (ESI) [13]. Shinkai *et al.* [14] have studied type **V** and **VII** organic cation complexes with several calix[n]arenes of differing conformation and ring size by the use of positive secondary ion mass spectrometry (SIMS) using *m*-nitrobenzyl alcohol as a matrix. Relative peak intensities have been shown to reflect the complex stability in the gas phase but the selectivity of the complexation with respect to the size of both the host and the guest differs greatly from that observed in solution. Whereas the conformation

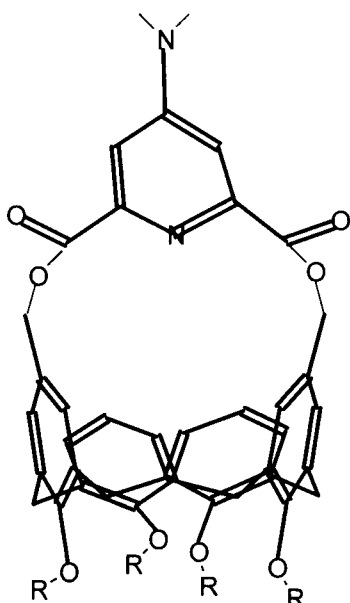


I-3: $n = 4$; **I-4:** $n = 5$; **I-5:** $n = 6$; **I-6:** $n = 8$

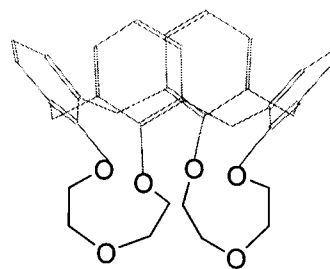


I-7

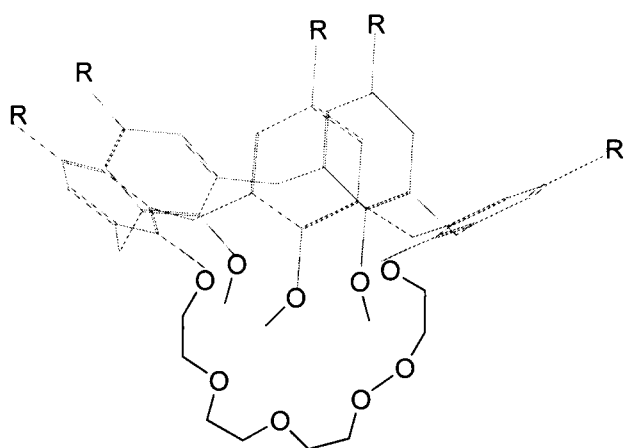
$R = \text{CH}_3, \text{CH}_2\text{COOEt}, \text{CH}_2\text{CONEt}_2, (\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{CH}_2$



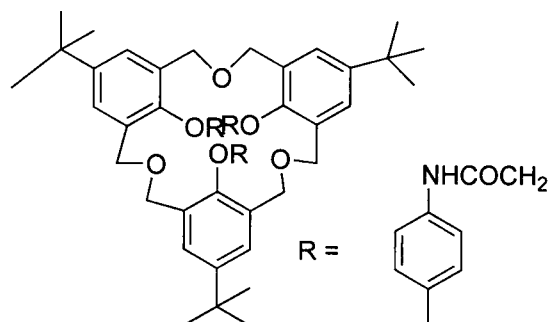
I-8: $R = \text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_3$



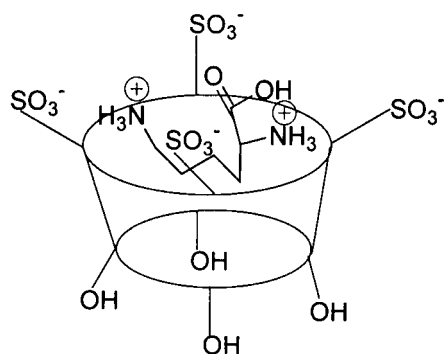
I-9



I-10 $R = \textit{tert}$ -butyl



III-1



Scheme 1. Schematic representation of the complex of **I-3** and lysine.

complexes, ionic interactions may dominate the inclusion properties.

For example, a salt is precipitated by the addition of ethylenediamine to **I-3**. According to the crystal structure, the ammonium groups are directed towards the sulfonate anionic groups, forming hydrogen bonds [18]. In the case of the mono-cation of ethylenediamine, the positively charged group points towards the exterior of the aromatic cavity whilst the amino group is embedded in the cavity and interacts with the aromatic surface by weak N–H... π hydrogen bonds.

The electrostatic attraction between the negative sulfonate groups of **I-5** on the upper rim and the positive charge carried by polyallylaminhydrochloride has been reported to yield insoluble complexes [19]. The interaction of alkylammonium ions with **I-3**, is charge assisted. At pH = 2 and pH = 7.1, these ions are located near the negatively charged sulfonate groups [20, 21]. It is noteworthy that in contrast to metal ions, the complexation of alkylammonium ions by the sulfonate calix[4]arene is enthalpy-driven and that the binding of alkylammonium ions is weaker than that of quaternary ammonium ions [19]. On the other hand, alkane diammonium ions bind more strongly than monoammonium ions, however, the binding mode has not been completely determined [22].

By taking into account the results obtained with alkylammonium ions, it is not surprising that amino acids also form complexes with hosts **I-3–I-6** in acidic aqueous solution [23]. The inclusion of basic amino acids such as lysine and arginine have been studied with the aid of microcalorimetry. Both amino acids form relatively strong complexes with arginine binding more strongly than lysine. The complexation process is enthalpy-driven; in addition, the complexation is attributed to the electrostatic attraction between the opposite charged groups, the charged groups of the amino acids point to the exterior whilst those of the alkyl chain point within the host cavity (see Scheme 1).

For **I-3** and **I-4**, 1:1 complexes were formed according to the microcalorimetric data, whilst a 1:2 host–guest complex for **I-6** and the amino acids is proposed.

Bridged calix[4]arenes such as **I-8** exhibit selectivity in the complexation of alkylammonium tosylates as only the mono-methylammonium salt binds with a stability constant of 10^3 M^{-1} [24]. The selectivity has been ascribed to the size of the cavity of the rigid calix[4]arene **I-8**, it being only

large enough to accommodate the mono-methylammonium ion and not the larger di-, tri- and tetramethylammonium ions. Similarly, the rigid calix[4]arene-biscrown-3 derivative **I-9** is also able to complex ammonium ions with a preference for the methylammonium ion. According to ^1H NMR data, methylammonium tosylate is complexed as a tight ion pair with the methyl group of the cation penetrating inside the π -donor cavity of the host. Calixarenes having substituents such as R = *tert*-butyl and R = cyclohexyl (see Chart 4) do not bind ammonium ions due to steric reasons [25]. In contrast, the (1,3)-*p-tert*-butylcalix[5]crownethers **I-10** are able to form endo-complexes with linear alkylammonium cations [26]. Hexahomotrioxacalix[3]arene triamide derivatives such as **III-1** enclose the *n*-butylammonium ion and the charged part is located deep in the cavity of the cone-like conformation of **III-1** [27].

Calix[4]arene based α -aminophosphonates have been reported to be able to carry zwitterionic amino acids through a supported liquid membrane [28]. The complexation of the protonated 2-phenylethylamine by *p-tert*-butylcalix[6]arene hexa-ethoxycarbonylmethyl ester incorporated into PVC membrane containing a fluorescent dye can be used as an optode, responding to this amine [29].

Quaternary ammonium ions (V)

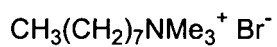
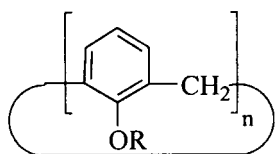
Calix[4]arenes and calix[5]arenes. The contribution to the binding energy due to the cation- π interaction has been estimated to be of the order of 1–1.3 kcal mol $^{-1}$ per aromatic ring in aqueous solution [30]. However, solvophobic effects may mask the cation- π interaction in this solvent, therefore, binding studies performed in lipophilic, mostly halogenated solvents will be discussed in this section. These similar solvents stimulate a discussion regarding the influence of a number of parameters on the strength of the cation- π interaction. These include:

- the structure and flexibility of the host,
- the cation type, and
- the nature of the anion.

Because of the low solubility of tetramethylammonium salts in deuteriochloroform and CD $_2$ Cl $_2$, complexation studies are rather rare. The association constants reported so far are collected in Table 1.

Shinkai *et al.* have determined the association constants of **V-4** (Chart 5) with simple hosts **I-11–I-13** in CDCl $_3$:CD $_3$ CN=10:2 [31]. Two of their findings are remarkable; firstly there is no significant hole-size-selectivity from **I-11** to **I-13** and secondly the flexible methylether, which exhibits interconversion between different conformers (cone, partial cone, 1,3-alternate), binds the guest **V-4** whilst the fixed cone **I-11** (R = Pr) does not (see Chart 5).

It is usually expected that the more rigid host results in the more stable complexes. Therefore, efforts were made to make the cone-conformation more rigid. Cone tetraalkoxycalix[4]arenes experience residual conformational mobility between two flattened cone structures [25], however, the attachment of short diethyleneglycol bridges in proximal positions at the lower rim (**I-9** in Chart 4) results in association constants of only 80 M $^{-1}$ for **V-3** in CDCl $_3$ solution [25].

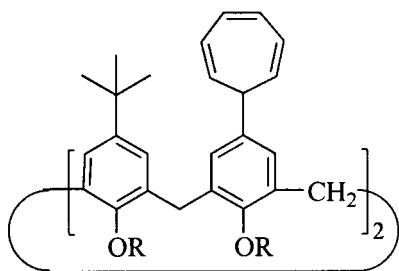


V-4

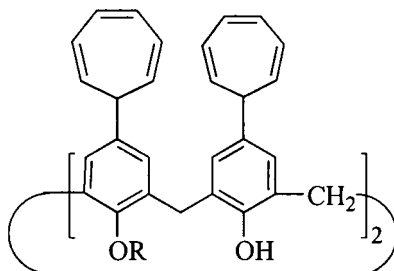
I-11: $n = 4$; $R = \text{Me}$

I-12: $n = 6$; $R = \text{Me}$

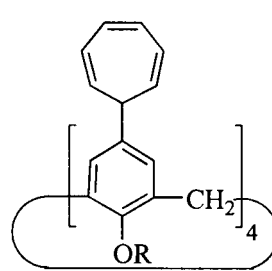
I-13: $n = 8$; $R = \text{Me}$



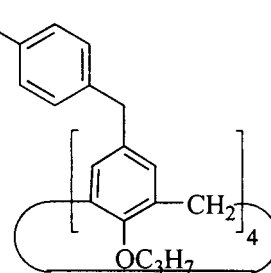
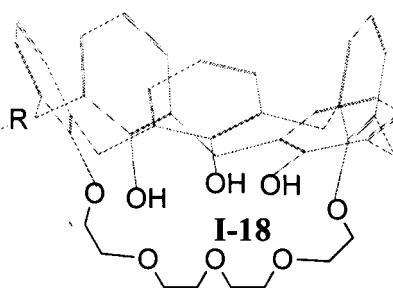
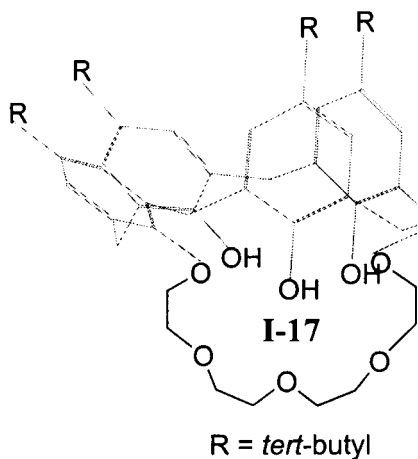
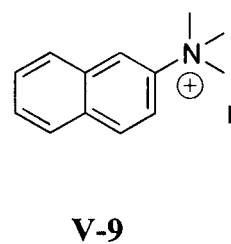
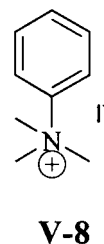
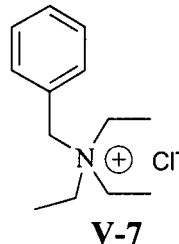
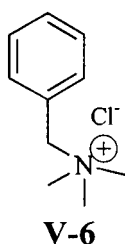
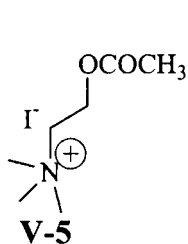
I-14: $R = \text{CH}_2\text{COO}t\text{-Bu}$



I-15: $R = \text{Bzl}, \text{CH}_2\text{COO}t\text{-Bu}$



I-16: $R = \text{Bzl}, \text{CH}_2\text{COO}t\text{-Bu}$



I-19

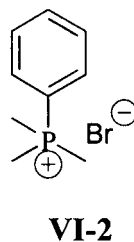
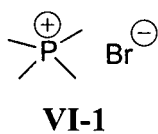


Chart 5.

Table 1. Association constants (M^{-1}) of the complexes between various hosts and ammonium ions V

Host	Guest								
	V-1	V-2	V-3	V-4	V-5	V-6	V-7	V-8	V-9
I-9			80 [40]						
I-11				871 [31]					
I-12				871 [31]					
I-13				646 [31]					
I-15					52 [33]	3 [33]	27 [33]	28 [33]	
I-17					47 [34]	21 [34]		71 [34]	
I-18					210 [34]			210	
I-19	3526 [36]								
I-20		10^3-10^5 [38]							
I-23	191 [40]		340 [40]						
I-24			1407 [40]						
I-25			54 [40]						
I-26			750 [42]						
I-27						50 [48]		158 [48]	
I-28						1995 [48]		1995 [48]	
I-29								8042 [51]	3134 [51]
III-2			450 [41]						
III-3			470 [41]						

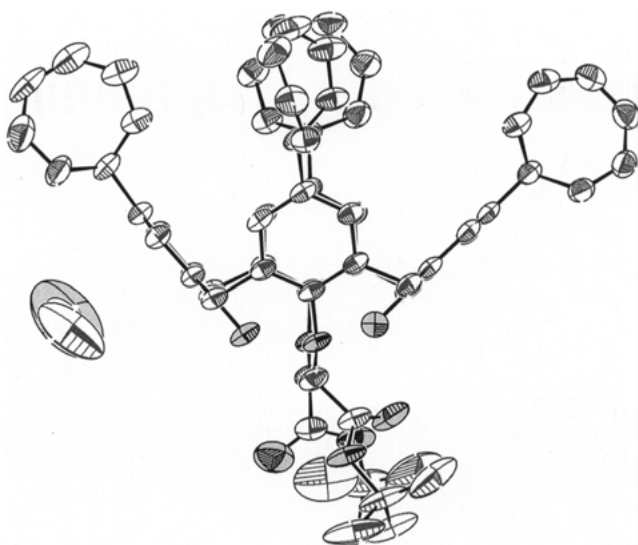


Figure 1. Molecular structure of the host I-15.

Comparable effects can be obtained by strengthening the cone structure with two nonbridging substituents at the lower rim. Hydrogen bonds between the two remaining OH-groups and the neighboring oxygen atoms lower the cone mobility. These hydrogen bonds are revealed by the crystal structure of the host I-15 (Figure 1, R = $\text{CH}_2\text{COO}t\text{-butyl}$) [32].

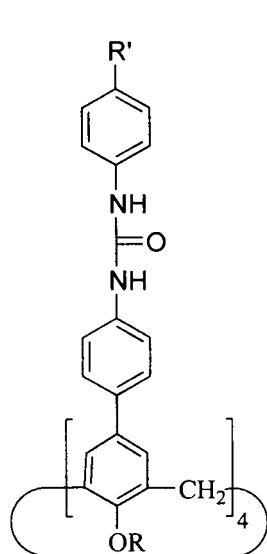
The calix[4]arenes I-14–I-16 bearing cycloheptatrienyl groups at the upper rim were tested for their binding properties with V-5–V-8 as guests [33]. Only I-15 was able to bind the ammonium ions V-5–V-8 with a relatively low complex stability. It seems that the flexibility due to the interconversion between two flattened cone conformations hinders the complexation. Interestingly, among the ammonium ions, choline V-5 is more strongly bound than the other ones

(see Table 1). Similar results were obtained by Böhmer and coworkers [34] by studying the binding properties of the 1,3-bridged calix[5]crowns I-17 and I-18 (Chart 5) with a number of quaternary ammonium ions such as V-5 and V-8 and, additionally, with the phosphonium salts VI-1 and VI-2 (see Chart 5). Whereas VI-1 was found to be bound by I-17 with a higher association constant than V-5, the arylphosphonium salt VI-2 only forms a very weak complex. Complexes of the host I-18 have a higher stability than that of I-17. The calix[5]arene without a crown bridge forms very weak complexes with ammonium ions.

Three conclusions related to the host structure can be drawn:

1. The different size of the cavity of calix[4]- and calix[5]arene does not strongly influence the binding properties.
2. *p*-*tert*-butyl groups at the upper rim hinder the complexation due to steric interference of guest inclusion [35].
3. The conformational mobility of the hosts has to be restricted in order to increase complex stability. The mobility of the tetraalkyl-calix[4]arenes is too high to allow high complex stability.

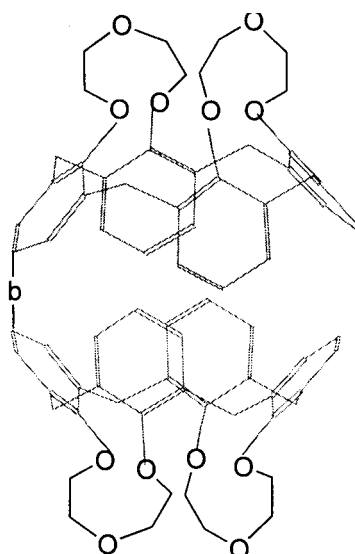
The mobility exhibited by tetraalkylated calix[4]arenes can not only be restricted by hydrogen bonds formed at the lower rim but also by hydrogen bonds formed on the upper rim. Recently, Pochini and coworkers have reported that the anion of the tetramethylammonium ion increases the complex stability of the host I-19 due to an allosteric effect in the recognition of tetramethylammonium salts [36]. The anion was hypothesized to be acting as hydrogen bond acceptor towards the OH-groups of the benzylic substituents at the upper rim, thus preorganizing the extended cavity of the host for cation binding. The complex stability is increased by one



I-20: R = CH₂C(O)NEt₂, R' = Me

I-21: R = C₅H₁₁, R' = C₆H₁₃

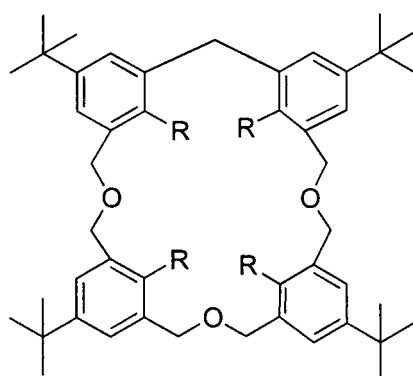
I-22: R = CH₂C(O)OEt, R' = Me



I-23: b = CH₂

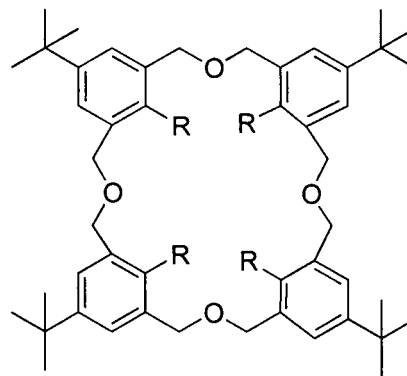
I-24: b = C≡C

I-25: b = N=N

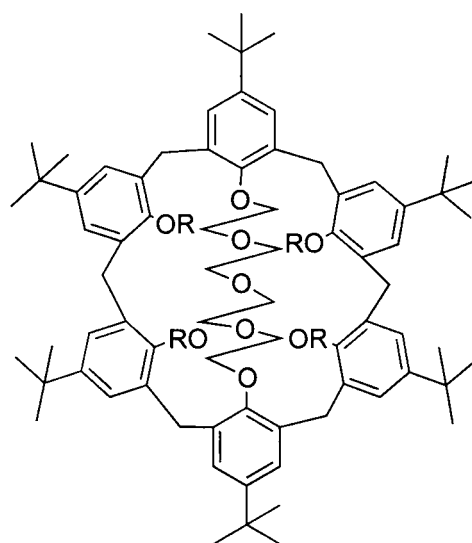


III-2

R = OMe



III-3

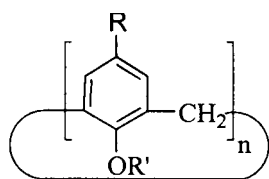


I-26: R = CH₂CONEt₂

Chart 6.

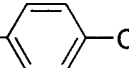
Table 2. Association constants (M^{-1}) of the complexes between various hosts and iminium ions **VII**

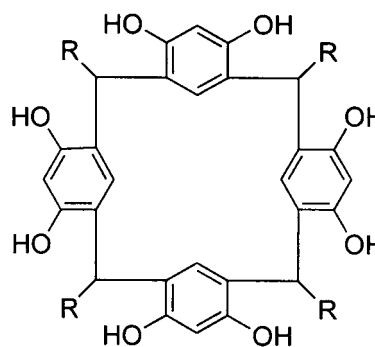
Guest	Host								
	I-3	I-5	I-6	I-11	I-15	I-16	I-18	III-2	III-3
VII-1					82 [33]	no compl. [33]		190 [41]	190 [41]
VII-7	9780 [57]	12500 [57]	15800 [57]						
VII-8	22700 [57]	20000 [57]	18600 [57]	252 [14]					
VII-9				372 [14]	190 [33]	no compl. [33]	200 [34]		
VII-10				2340 [14]					
VII-11					93 [33]				
VII-12		220 [58]							
VII-15		1600 [58]							
VII-16		1900 [58]							



I-27: R = H; R' = CH₂COOH

I-28: R = SO₃H; R' = CH₂COOH

I-29: R = N=N--COOH; R' = H



II-1: R = (CH₂)₂SO₃Na

Chart 7.

order of magnitude as a result ($K = 3526 M^{-1}$, anion Cl^{-} , $CDCl_3$).

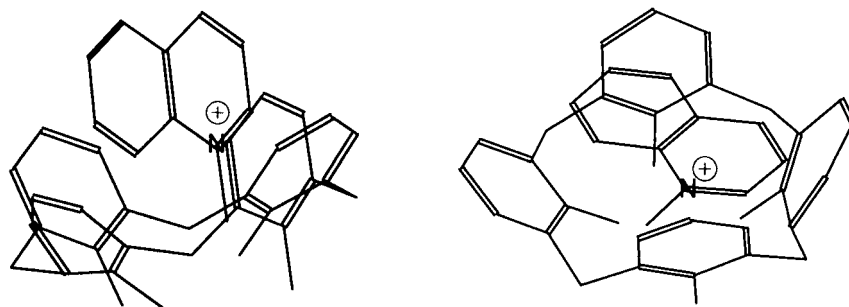
Expanded calixarene cavities. Calix[4]arene tetraureas are able to form dimeric assemblies held together by a seam of intermolecular hydrogen bonds [37]. Such capsules formed by **I-20** (Chart 6) allow the inclusion of ammonium ions such as **V-2** with high association constants in the range of 10^4 – $10^5 M^{-1}$ (see Table 2) [38].

Böhmer's group has observed that the directionality of the hydrogen bonds of capsules formed by **I-21** and **I-22** (homo- and heterodimers, respectively) are inverted within the complex of the dimeric capsule with **V-1** (Chart 3) [39]. Two ethyl groups of the guest are assumed to be oriented towards the poles of the capsule, the other two are arranged within the equatorial plane.

The covalent bridging of the two fixed cone conformations of calix[4]arene realized in **I-23**–**I-25** also leads to a

significant improvement in the binding properties. The association constants of 1:1 complexes with **V-1** and **V-3** are increased by one order of magnitude compared to the host **I-9** (for instance from $33 M^{-1}$ of **I-9/V-3** to $1407 M^{-1}$ of **I-24/V-3**, X = tosylate, $CDCl_3$) [40]. The binding properties can be changed by modifying the bridge length and rigidity.

Homooxacalix[4]arenes, in which the cavity size can be modulated by the number of the CH_2OCH_2 -bridges such as in **III-2** and **III-3** (Chart 6), appear not to be well preorganized. Nevertheless, fairly strong complexation of **V-3** in $(CDCl_2)_2$ solution occurs (see Table 1) [41]. This means that several of the expected entropic and enthalpic handicaps can be overcome; an additional electrostatic interaction between the cation and the oxygen atoms may play a role in these cases. These kinds of interaction are also assumed in the case of the bridged calix[6]arene **I-26**. According to chemical induced shifts caused by complexation, **V-3** is interacting



Scheme 2. Schematic representation of the binding mode of a quinolinium ion within a calixarene cavity.

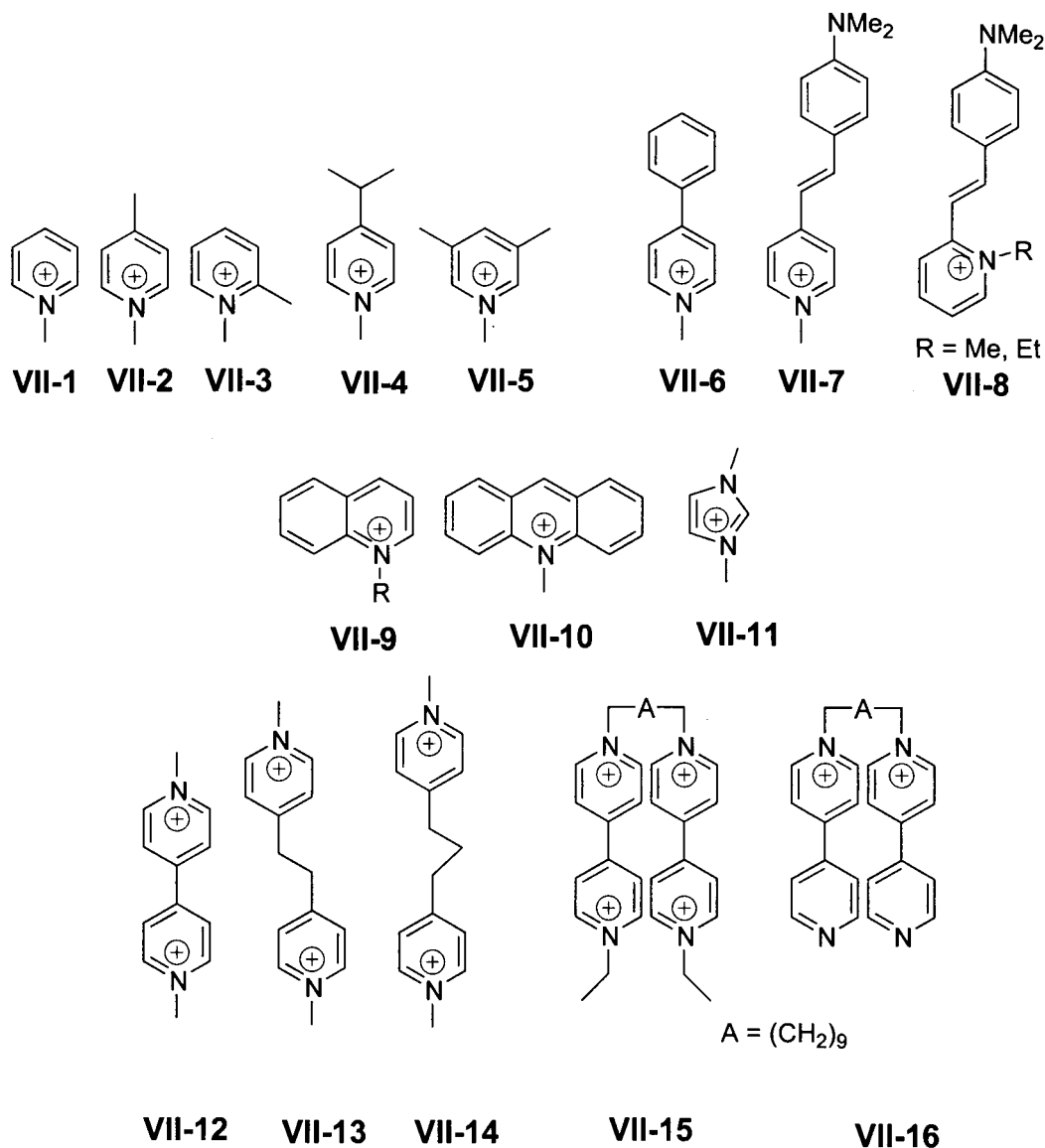


Chart 8.

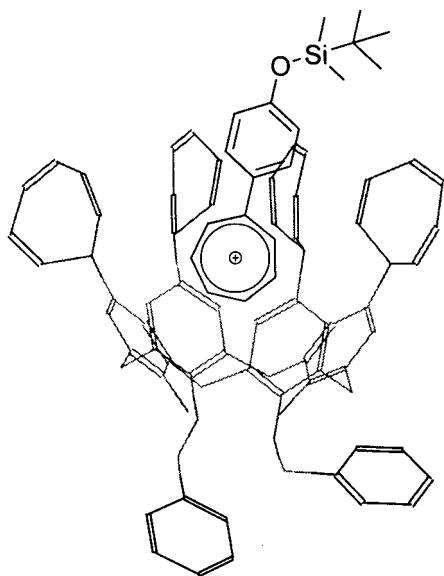
more strongly with the oxygen containing chain at the lower rim of the calix than with the π -basic cavity [42].

Anion influence. The binding of organic cations by neutral receptors in lipophilic solvents may be strongly affected by ion pairing [43]. Apart from an increase in binding as mentioned above, in special cases, a binding inhibition can be

observed particularly with anions such as iodide or tosylate [40]. The stability order picrate > trifluoroacetate > I > Br > Cl > tosylate has been confirmed by Böhmer and coworkers looking at the complexation of **V-3** by the calixarene **I-10** [44]. The calixarene itself may serve as the anion of **V-3**. Even in the salt of the tetramethylammonium cation with the deprotonated unsubstituted calix[4]arene (**I**; R¹ – R⁸ = H) in

Table 3. Association constants (M^{-1}) of the complexes between hosts forming capsules and iminium ions VII

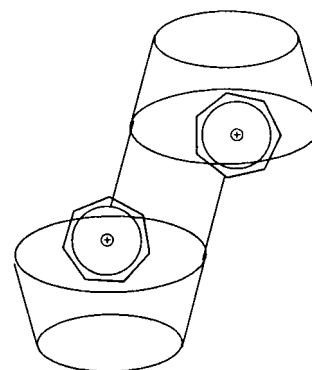
Guest	Host						
	I-21	I-23	I-24	I-25	I-30	I-31	I-32
VII-1		>10000 [40]	7260 [40]	797 [40]	480 [53]	3310 [54]	
VII-2		1935 [40]	1632 [40]	2450 [40]	36 [53]	166 [54]	
VII-3		1167 [40]	5713 [40]	3693 [40]			
VII-4	22000 [38]						
VII-5					2 [53]	no compl. [54]	
VII-6	5600	[38]					
VII-7	190000 [38]					no compl. [54]	
VII-9					97 [53]		
VII-12							320 [56]
VII-13							154 [56]
VII-14							124 [56]



Scheme 3. Schematic representation of the inclusion of a tropylium ion in a calix[4]arene.

the crystal, one cation moiety is included in the cavity of a neutral host molecule whilst another entity is encapsulated by a facing pair of calixarene anions [45].

Water-soluble calixarene hosts. Water soluble calixarenes usually contain sulfonate groups such as **I-3**–**I-6** at the upper rim (Chart 4) or carboxylate groups such as **I-27** at the lower rim (Chart 7) and are used as salts. The inclusion of tetraalkylammonium ions in the calixarene cavity is therefore supported by the electrostatic attraction of the two oppositely charged ions.



Scheme 4. Schematic representation of the inclusion of a tropylium ion in a calix[4]arene **I-35**.

In 1988, Shinkai and coworkers reported an association constant of $5600 M^{-1}$ for the complex between **I-3** and **V-8** (as chloride). The host **I-5** forms much weaker complexes and **I-6** is able to bind two anilinium ions [46]. Due to the mobility of **I-3**, the anilinium ion is included with both the phenyl group and the charged part pointing to the interior of the host [47]. In contrast, the calixarene **I-27** ($n = 4$) fixed in the cone conformation, specifically binds the charged head of **V-8** whereas **I-28** ($n = 4$) recognizes only the aromatic ring of the anilinium ion [48]. These findings may be explainable by the electrostatic attraction forces known to be dominant in the binding mode. The presence of the sulfonate groups support the association by favorable enthalpic contribution; such an electrostatic assistance in the complexation of both **V-6** and **V-8** has been confirmed [48]. The additional interaction between the charged groups results in a tenfold higher complex stability compared to hosts without the sulfonate groups, whereby the enthalpic contribution is about 1 kcal mol^{-1} . Surprisingly, the mobile host **I-3** binds

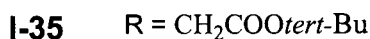
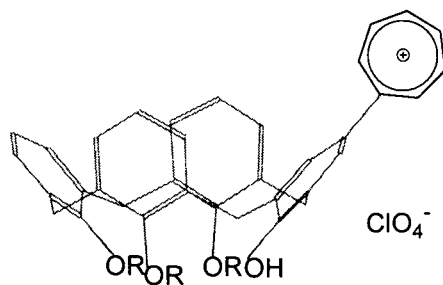
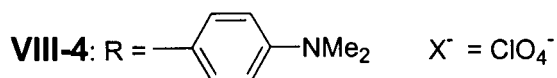
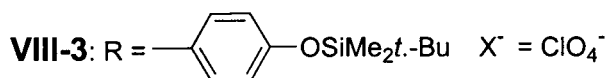
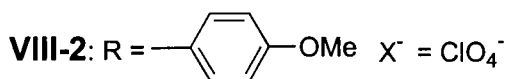
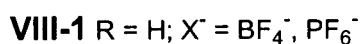
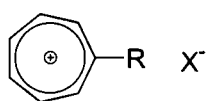
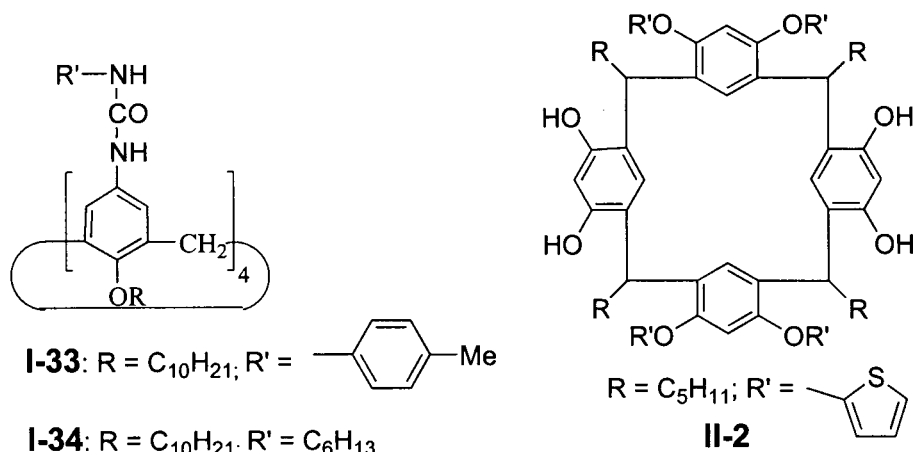


Chart 10.

the case of an edge to face arrangement (B) a downfield shift can be expected as has been found with the interaction of the π -systems of rotaxanes [52]. Pyridinium, bipyridinium, quinolinium, acridinium and imidazolium ions depicted in Chart 8 have been used as guests with a number of different calixarenes where mostly iodide salts were studied in $CDCl_3$ solution. Binding constants are given in Table 2.

In the following guest order **VII-1**, **VII-9** and **VII-10**, the diameter of the iminium cation is considerably increased in one direction. Therefore, the question arises as to whether the cavity of a simple calix[4]arene is sufficiently large to include these cations. Thus, it is somewhat surprising that

the host **I-11** ($R = Pr$) binds **VII-10** ($X^- = I^-$) even better than **VII-8** and **VII-9** (see Table 2) in $CDCl_3/CD_3CN = 8:2$ [14]. In contrast, the larger cavity of **I-18** binds **VII-9** in $CDCl_3$ solution with a lower stability constant of only $200 M^{-1}$ (see Table 2) [34]. Accordingly, the size of the cavity does not seem to determine the complex stability. This is confirmed by the complexation studies of the calixarenes **I-14**–**I-16** with guests **VII-1**, **VII-9** and **VII-11** [33]. As mentioned above, in complexes with quaternary ammonium ions, the number of alkyl groups at the lower rim is decisive in the complex stability. Four alkyl groups prevent complexation, two alkyl groups favor complexation due to the fixed

pinched cone conformation. Among the iminium ions, the quinolinium ion exhibits the highest complex stability and the cycloheptatrienyl groups at the upper rim of **I-15** hinder complexation only very slightly [33].

The *N*-methylpyridinium iodide has also been reported to be bound by the conformationally flexible homoaxalixarenes **III-2** and **III-3**. The association constant is not strongly influenced by the number of the oxamethylene bridges [41], according to the chemical induced shifts of proton resonances of the guest, it seems that the larger the diameter of the host cavity the more the guest is deeply incorporated into the cavity. It is worthwhile noting that with these expanded hosts, the quaternary ammonium ions are more strongly bound than the *N*-methylpyridinium ion.

If the calix[4]arene is able to form a capsule, the cavity is more sensitive towards the size of the iminium ion. The dimeric host **I-30** binds the *N*-methylpyridinium ion **VII-1** with a moderate selectivity compared to the *N*-methylquinolinium ion **VII-9** (Table 3) [53]. However, the second calixarene present in the dimeric calix[4]arene is useless for the binding of the more bulky ions **VII-2** and **VII-5** (see Table 3 and Chart 8).

A similar graduation in the binding capacity has been found with the capsules **I-23–I-25** [40]. Dimeric capsules **I-20–I-22** formed by hydrogen bonds [38] are able to strongly bind iminium ions such as **VII-4**, **VII-6** and **VII-7** in CD₂Cl₂ solution (association constants between 5.6×10^3 and 1.9×10^5 M⁻¹, Table 3). The complexation of the dye **VII-7** can be followed by UV-Vis-spectroscopy.

Two spacers at the upper rim make the capsule formed by two calix[4]arenes more rigid. Therefore, the host **I-31** (see Chart 9) is able to select between the guests **VII-1**, **VII-2**, **VII-5** and **VII-7** by complexing only **VII-1** and **VII-2** in CDCl₃ solution. Attaching one methyl group to the pyridinium ring leads to a decrease in the association constant (Table 3) [54]. At the same time, the closed and restricted space of the host allows only slow exchange of guests.

A structure of the **I-31:VII-2** complexes has been proposed as being an arrangement of the guest between the spacer units of the capsule. By replacing the propyl groups in **I-31** by hydrogen, the π -basicity of the aromatic cavity is increased [55], consequently, the association constant with **VII-1** is increased to 5×10^6 M⁻¹.

Two spacers with thiophenimine linkages were used to form the bis-calix[4]arene **I-32** (Chart 9) [56] and the viologens, **VII-12**, **VII-13**, **VII-14**, were complexed in CDCl₃/CD₃CN 2:1, demonstrating association constants between 700 and 100 M⁻¹ (Table 3).

The molecular association of water soluble calixarenes such as **I-3**, **I-5** and **I-6** with the stilbene dyes **VII-7** and **VII-8** has been studied by spectrophotometric and ¹H NMR methods [57]. It was found that independent of the ring size in each case, 1:1 complexes were formed in water solution with association constants of $K = 10^4$ to 10^5 M⁻¹ (Table 2). The largest cavity (**I-6**) bound the dyes with the highest association constant due to a change in the binding mode. Whereas the smaller calixarenes bound only the pyridinium

Table 4. Association constants of complexes of water soluble calixarene hosts with ammonium and iminium ions

Guest	Host				
	I-3	I-5	I-6	I-28	I-29
V-6				1995	
V-8	5600			1995	8042
V-9					3134
VII-7	9780	12500	15800		
VII-8	22700	20000	18600		
VII-15		1600			
VII-16		1900			

Table 5. Association constants of complexes between hosts that are able to form flexible capsules and ammonium and iminium ions

Guest	Host					
	I-19	I-20	I-21	I-23	I-24	I-25
V-2	10 ³ –10 ⁵					
V-3					1407	
VII-1				<10000	7260	797
VII-2				1935	1632	2450
VII-3				1167	5713	3693
VII-4			22000			
VII-6			5600			
VII-7			190000			

part of the dyes the whole molecule is incorporated in the cavity of the larger host (n = 8). Alkylammonium and tetraalkylammonium ions (including surfactants) are able to substitute the dyes, thus indicating the higher stability of ammonium ion complexes compared with iminium ions. This substitution process can easily be followed by UV-Vis-spectroscopy.

The hexaanionic host **I-5** was also used in order to bind dimeric viologen guests such as **VII-15** and **VII-16** [58]. The strongly electrostatically driven association between the iminium part of the guest and the sulfonate groups at the upper rim of the host yielded only slightly higher association constants for the dicationic guest **VII-16** than for the tetracationic guest **VII-15** (Table 2). Together with the binding constant of only 220 M⁻¹ determined for the complex with methylviologen **VII-12**, the conclusion can be drawn that the charge density as well as multiple point interactions are important.

Tropylium ions

There are only a few examples of the complexation of this type of organic cation. The unsubstituted tropylium ion has recently been reported to be able to promote the formation of stable dimeric capsules of the calix[4]arenes **I-33** and **I-34** [59] (Chart 10) as well as the resorcenarene **II-2** [59] in CD₂Cl₂, CDCl₃ and C₂D₄Cl₂ solution of the host and the tropylium salts.

Deep red solutions indicate the formation of a charge transfer complex with absorption bands around 340, 490 [59] and 460 nm [60], respectively. In the ^1H NMR spectra, the proton resonance of the encapsulated tropylium ion is upfield shifted by more than 3 ppm. The formation of heterodimers between **I-33** and **I-34** is induced by the addition of **VIII-1**. The results have shown that the tropylium ion has a much stronger tendency to induce the formation of dimeric capsules than neutral organic guests [59]. The crystal structure of the complex **II-2/VIII-1** reveals the sandwich-like inclusion of the tropylium ion between two aromatic rings of two different resorcinarene species that form the capsule, due to hydrogen bonds the OH-groups of one molecule and the ester group of the other one [60]. The cation- π interaction effective in this arrangement is the origin of the triplex formation. Additional edge-to-face C-H- π interactions of the tropylium ion to the neighboring aromatic rings of the host may also support tropylium ion inclusion.

Whereas the encapsulation of the tropylium ion **VIII-1** between two calixarene species leads to a stable triplex, the arylsubstituted tropylium ions **VIII-2-VIII-4** are included into the π -basic cavity of the hosts **I-15** in CDCl_3 solution, exhibiting a rapid exchange [33]. The charge of the aryl tropylium ion is strongly delocalized between the tropylium moiety and the aryl substituent [61, 62]. Thus the question arises as to whether this delocalization diminishes the complex stability. It turns out that this is not the case. The association constants of **I-15/VII-9** and **I-15/VIII-4** are comparable [33]. Furthermore, the charge transfer from the tropylium moiety to the aryl group is more pronounced with **VIII-4** compared to **VIII-2**. Nevertheless the association constant of the last ion with the host **I-15** ($\text{R} = \text{Bzl}$) is higher (190 M^{-1}) than that of the former one (121 M^{-1}). The extension of the π -basic cavity due to the attachment of cycloheptatrienyl groups at the upper rim, such as in the host **I-15**, supports the inclusion of the tropylium ion **VIII-4** [33]. Chemically induced shifts observed with the protons of the tropylium ions indicate the inclusion of the cations with the tropylium moiety pointing to the interior, thus enabling cation- π interactions [33]. This charged part of the ion is sandwiched between two distal cycloheptatrienylphenyl rings of the host (see Scheme 3) whilst the horizontal rotation of the guest is suppressed within the cavity [33].

In the case of **VIII-4**, the association constant can be determined by the decreased absorption intensity of the intramolecular charge-transfer band of the guest due to complexation by the host **I-15**.

By attaching a tropylium substituent at the upper rim of a calix[4]arene such as in **I-35** (Chart 10), it could be expected that self complexation is achieved.

Indeed, both the resonances of the aromatic hydrogen atoms and of the tropylium group are upfield shifted in the ^1H NMR spectrum with increasing concentration of **I-35** [63]. This finding can be attributed to a complex depicted in Scheme 4.

Conclusions

The present review shows that the cation- π -interaction that is established between aromatic rings of various calixarene hosts and ammonium, iminium and tropylium ions is comparable in their influence on the complex stability (see Tables 1–3). The actual value of the binding strength is relative to a specific anion and solvent. In general the driving force is relatively weak. The type of host has the strongest influence on the complex stability. Two properties can be derived in order to obtain high complex stability:

1. Electrostatic attraction between charged hosts and guests governs the complex stability in D_2O solution. The highest complex stabilities are found within this group as demonstrated in Table 4.
2. Flexible dimeric hosts held together by covalent bonds and by a belt of hydrogen bonds formed in non-polar solvents, respectively, have been shown to exhibit binding efficiencies toward both ammonium and iminium ions much higher than that of comparable rigid capsules and hosts with only one calixarene unit. Therefore, very high complex stability can be obtained within this class of host-guest-complexes (see Table 5).

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