CrystEngComm

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/crystengcomm

Journal Name RSCPublishing

ARTICLE

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Encapsulation of secondary and tertiary ammonium salts by resorcinarenes and pyrogallarenes: The effect of size and charge concentration

N. K. Beyeh,*[a] F. Pan,[a] A. Valkonen[a,b] and K. Rissanen*[a]

The binding of different categories of alkyl ammonium (secondary and tertiary mono- and di-ammonium) salts by resorcinarenes and a pyrogallarene through weak interactions were analysed in all phases. ^{1}H NMR spectroscopy and electrospray ionisation mass spectrometry were utilized in analysing the complexes in solution and in the gas phase respectively. The ^{1}H NMR titration studies in methanol-d_4 reveal the association constants for the 1:1 complexes to vary according to the electronic properties of hosts as well as the size, geometric orientation and charge concentration of the guest cations with binding constants of up to 950 M^{-1} in some cases. Mass spectrometry reveals 1:1 monomeric and 1:2 dimeric complexes in the gas phase. Six co-crystals, three of which are dimeric host-guest capsular assemblies, two open inclusion complexes and a pseudocapsular methanol solvate were analysed in the solid state through single-crystal X-ray diffraction. The crystal structures confirm the complexes to be held together by multiple cation···π, CH···π and hydrogen bond interactions.

Introduction

The discovery of new receptors with new properties such as high selectivity or versatility is a continuous quest for supramolecular researchers.[1-3] Modifying known receptors in most cases increases their binding efficiency and in some cases increases the variety of guests.[2] Resorcinarenes and pyrogallarenes constitute a class of phenolic macrocyclic receptors.[4-7] The bowl-shaped electron rich cavity of the C_{4v} of resorcinarenes and pyrogallarenes has been vastly explored in the binding of a variety of different guests through multiple weak interactions.[8-12] The eight and twelve hydroxyl groups on the upper rim of the resorcinarenes and pyrogallarenes respectively, play a key role in maintaining their conformation.[13] These hydroxyl groups also aid the formation of the many supramolecular assemblies and in co-crystallization studies.[5,14] The electron rich interior are particularly suitable to bind guests through cation···π and CH···π interactions with a distinct preference for size and orientation of the guests.[5,15] Host-guest complexes of unfunctionalized resorcinarenes with a variety of guests have resulted in supramolecular assemblies such as 1:1 open inclusion complexes,[16,17] dimeric[5,14,17-21] and hexameric[22-24] capsular as well as tubular assemblies.[25,26]

The ammonium group is particularly important in biotechnology since it constitutes part of many active pharmaceutical compounds.[27-29] A recent trend is the co-crystallization of some pharmaceutical compounds with receptors like resorcinarenes and pyrogallarenes with the hope of improving their pharmaceutical properties[30,31] making Crystal engineering[32] a useful tool in analysing supramolecular assemblies. A recent example is the co-crystallization of the pharmaceutical gabapentin, a primary amine, widely used for the treatment of epilepsy and neuropathic pain,[33,34] with pyrogallarenes by Atwood *et al*.[30]

Secondary and tertiary ammonium salts possess hydrogen bond donating groups -NH_2 and -NH respectively and these can further enhance their complexation through intermolecular hydrogen bonds. Rissanen *et al.*[35] reported one example of this type of complex whereby a dimeric capsule is formed between resorcinarene and triethylammonium chloride. In this complex, the –NH group is hydrogen bonded to a water molecule and this mini-assembly acts as a template for the larger dimeric capsule.[35]

The ability of resorcinarenes to bind both symmetrical and unsymmetrical quaternary ammonium salts is well reported.[5-21] Tetramethyl ammonium (TMA) cation is of optimum size and orientation to template dimeric capsular assemblies.[5,8,10,17-19] Complexes of resorcinarenes and diquaternary ammonium [*N*,*N*-dialkyl-1,4-diazabicyclo[2.2.2]octane (alkyl$_2$-DABCO)] dications show higher binding constant in alcoholic solvents than the quaternary ammonium analogues[14] due to the higher charge concentration of the diquaternary ammonium cations.

The orientation of the alkyl$_2$-DABCO dication in the cavity of the resorcinarene influences the final structure of the complex as seen in several X-ray crystallographic studies.[14,17,19,25,26] The alkyl$_2$-DABCO dication has templated several structures with resorcinarenes such as 1:1 inclusion complexes,[14] dimeric capsular assemblies and nanotubes.[25] Dimethylpiperazine has been shown to deprotonate resorcinarenes and templates a directly hydrogen bonded assembly.[36] In this assembly, the protonated -NH is directly hydrogen bonded to the hydroxyl groups of the resorcinarenes (NH···O) leading to a pseudocapsular dimeric assembly.[36]

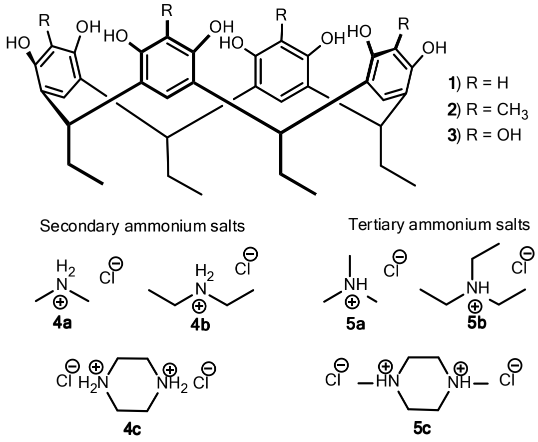


Fig. 1 Resorcinarene and pyrogallarene hosts **1**-**3**, secondary **4a**-**c** and tertiary **5a**-**c** ammonium salts.

Despite the multitude of reported structures involving quaternary ammonium salts and unfunctionalized resorcinarenes and pyrogallarenes, there are limited reports of host-guest complexes with primary[30] and tertiary[35,37-39] ammonium cations. Host-guest complexes between unfunctionalized resorcinarenes and secondary ammonium cations are very poorly studied. Only one co-crystal structure of a secondary ammonium salt *viz.* proline is reported by Aoki *et al.*[40]

In this contribution, we report several supramolecular co-crystals between two resorcinarenes **1**-**2**, pyrogallarene **3** as the receptors and a series of secondary and tertiary mono- and di-ammonium salts (Fig 1) in the solid state via single crystal X-ray diffraction analyses. These assemblies were studied in solution through ^{1}H NMR titration analyses and in the gas phase via electrospray ionization mass spectrometry (ESI-MS). The ammonium salts all possess a hydrogen bond donating NH/NH$_2$ group and are of different sizes and orientations compared to quaternary TMA and diquaternary alkyl$_2$-DABCO cations. The interactions and template effects of these salts in the final assemblies are analysed.

Results and discussion

Solid State Analyses

Single crystals were obtained from several host-guest systems and structurally characterized as the pseudo-capsular solvate **2MeOH@2**$_2$, the dimeric host-guest capsules **5a@2**$_2$, **5b@2**$_2$, **5b@3**$_2$, and the host-guest inclusion complexes **4a@2** and **5c@1**.

2MeOH@2$_2$ is the crystallization product of **2** in methanol by slow evaporation. Despite the absence of an ammonium ion template, the solvate forms a pseudo capsule with two MeOH solvent molecules in the cavity and another two MeOH molecules outside the cavity. The role of the methanol in the formation of the pseudocapsule is crucial. The two in-cavity MeOH interact with one of the resorcinarene molecules in the pseudo capsule via OH···π interaction and through O···HO hydrogen bond (donated by host -OH) with the second resorcinarene molecule (Figure 2A and B), while the two out-of-cavity MeOH act as hydrogen bond donor and acceptor bridging adjacent resorcinarene pseudo capsules (Fig 2C). In addition, along the crystallographic *b* direction, the pseudo capsules hydrogen bond with each other by O···HO interactions, thus, extending the structure to a two dimensional network (Fig 2C).

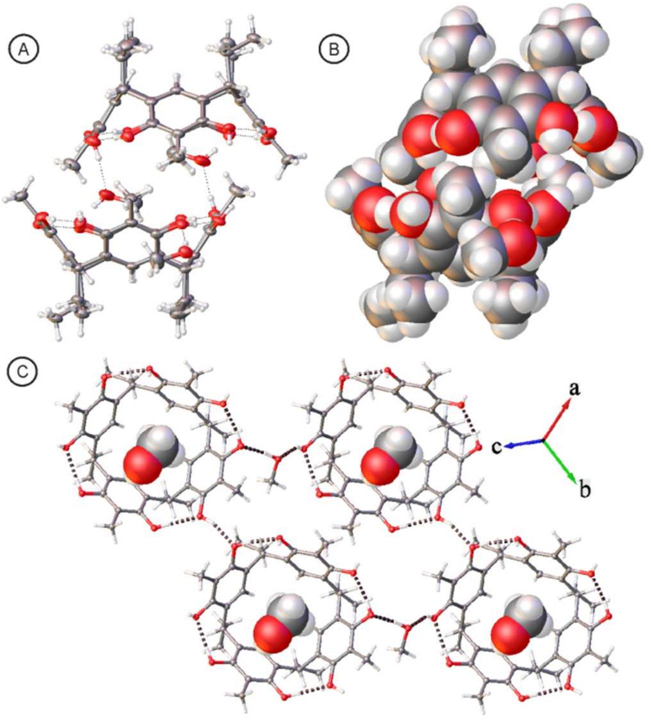


Fig. 2 Views of the pseudocapsular structure of the solvate **2MeOH@2**$_2$. A) the 30% thermal ellipsoids to show the capsule; B) the space filling model; C) the hydrogen bonding extended 2-D network.

Structures of **5a@2**$_2$, **5b@2**$_2$ and **5b@3**$_2$ are observed in the solid state as dimeric capsules with the ammonium cation sitting in each capsular assembly (Fig. 3). Among them, both **5a@2**$_2$ and **5b@2**$_2$ crystallize in orthorhombic space group *Pnnn*, where the guest cations are located around the intersection of three 2-fold axes. However, **5b@3**$_2$ crystallizes in triclinic space group $P\bar{1}$, with the N$_{TEA}$ atom lying exactly on the centre of inversion. The symmetries of the ammonium cations are lower than those of the cavities in all the cases and are accordingly disordered in the cavities. The sizes of the cavities and the ammonium cations also reflect the disorders. The volumes of the cavities in **5a@2**$_2$, **5b@2**$_2$ and **5b@3**$_2$ are approximate 200, 212 and 274 Å^3, respectively, calculated by PLATON,[41] whereas the corresponding ammoniums are much smaller. In the structures of **5a@2**$_2$ and **5b@2**$_2$, the Cl$^-$ anions generally prefer to sit in the middle of the lower rim of the ethyl chains stabilized by weak CH···Cl$^-$ interactions (the mean C$_{methylene}$···Cl$^-$ distances are 3.835 in **5a@2**$_2$ and 3.743 in **5b@2**$_2$) similar to structures with quaternary salts.[5,14] However, hydroxyl groups of the resorcinarenes also compete for the Cl$^-$ anions, therefore, part of the chloride anions are located beside the OH groups participating in the capsule formation. The competition of the hydroxyls is overwhelming in the case of pyrogallarene whereby all the Cl$^-$ form OH···Cl$^-$ hydrogen bonds with no Cl$^-$ anion located between the lower rim of the ethyl chains.

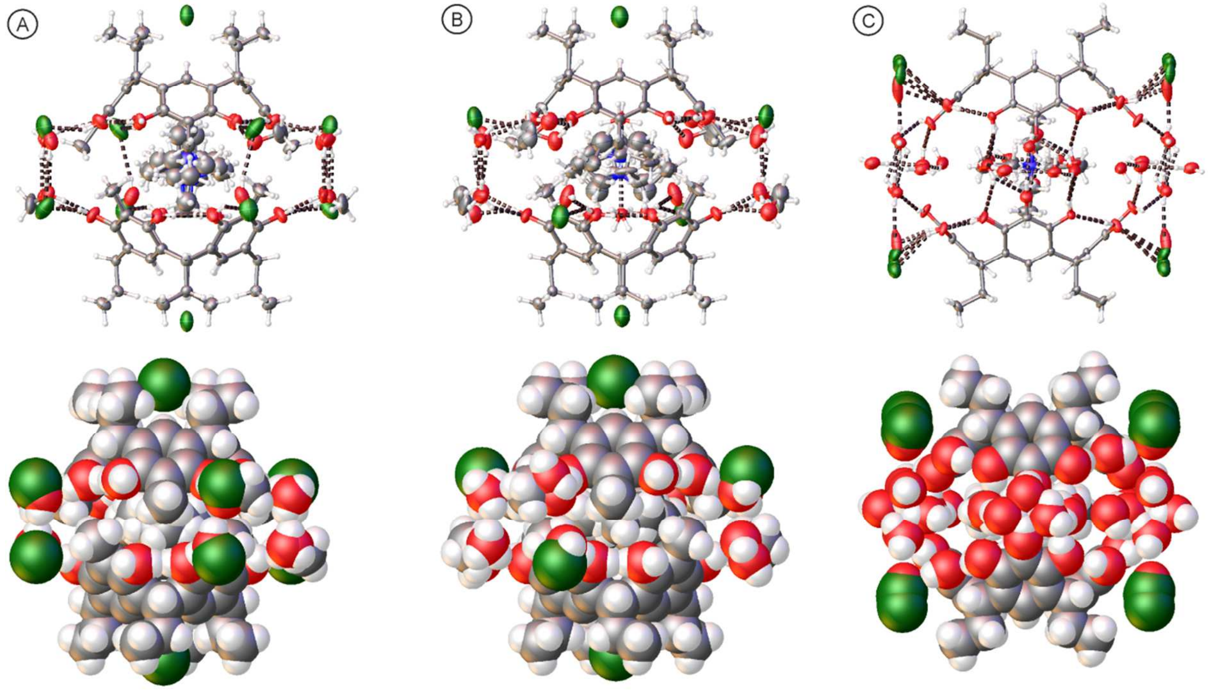


Fig. 3 Dimeric capsules formed via multiple cation···π, CH···π and hydrogen bond interactions with ammonium cations in the cavities: (A) **5a@2**$_2$, (B) **5b@2**$_2$, (C) **5b@3**$_2$.

In the two host-guest complexes **5a@2**$_2$ and **5b@2**$_2$, four OH···O intramolecular hydrogen bond interactions support the C_{4v} conformation of the resorcinarene while the other four OH groups interacts with either the guest water, MeOH or Cl$^-$ anions. The guests link each half of the dimeric capsule equally, thus templates the capsule formation. The two resorcinarene molecules in the capsule are arranged in a staggered orientation. Such an arrangement further stabilizes the capsule through weak CH···O interactions. In the capsule **5b@3**$_2$, the four central OH groups breaks the staggered arrangement due to the direct OH···O intermolecular hydrogen bond interactions between the two pyrogallarene molecules. As a result of two such intermolecular hydrogen bonds, the two pyrogallarene molecules are pushed further away from each other with a bottom-to-bottom distance of 11.964 Å compared to 10.382 Å in **5a@2**$_2$ and 10.441 Å in **5b@2**$_2$ (the bottom centres are defined by the centroid of the four H atoms attached to the aromatic rings). The other two central hydroxyl groups of the first pyrogallarene are indirectly connected via H$_2$O molecules to the hydroxyl groups of the second one within the capsule.

Fig. 4A illustrates the packing of the capsules in **5a@2**$_2$, viewed from crystallographic *c* direction. Direct OH···O hydrogen bonds between resorcinarene groups connects the dimeric capsule along the *a* axis, whereas along *b* axis direction, two water molecules bridge the adjacent capsules by OH···O hydrogen bond interactions. Four neighbouring capsules in the same layer are further joined by hydrogen bonds with disordered water, MeOH and Cl$^-$ molecules. The packing of the capsules in **5a@2**$_2$ and **5b@2**$_2$ is quite similar contrary to **5b@3**$_2$. Fig. 4B displays the arrangement of **5b@3**$_2$ in *ab* plane. Intermolecular OH···O hydrogen bond interactions between adjacent capsules extend the structure along *a* and *b* directions to two-dimensional layers. Solvent water molecules and chloride anions squeeze into the interspace and further glue the capsules through hydrogen bonds.

In the structure of **4a@2**, due to the small volume of dimethyl ammonium chloride, the salt is entirely captured by one resorcinarene. In addition to the NH···Cl$^-$ hydrogen bonds, cation···π interaction and in-cavity OH···Cl$^-$ hydrogen bond between the Cl$^-$ and resorcinarene are also observed (Fig. 5A).

The Cl^- further bridges two more host molecules by two out-of-cavity OH···Cl^- hydrogen bonds. Solvent molecules are not crystallized in the lattice, thus adjacent resorcinarene molecules interact with each other via OH···O hydrogen bonds along the *b* direction (Fig. 5C).

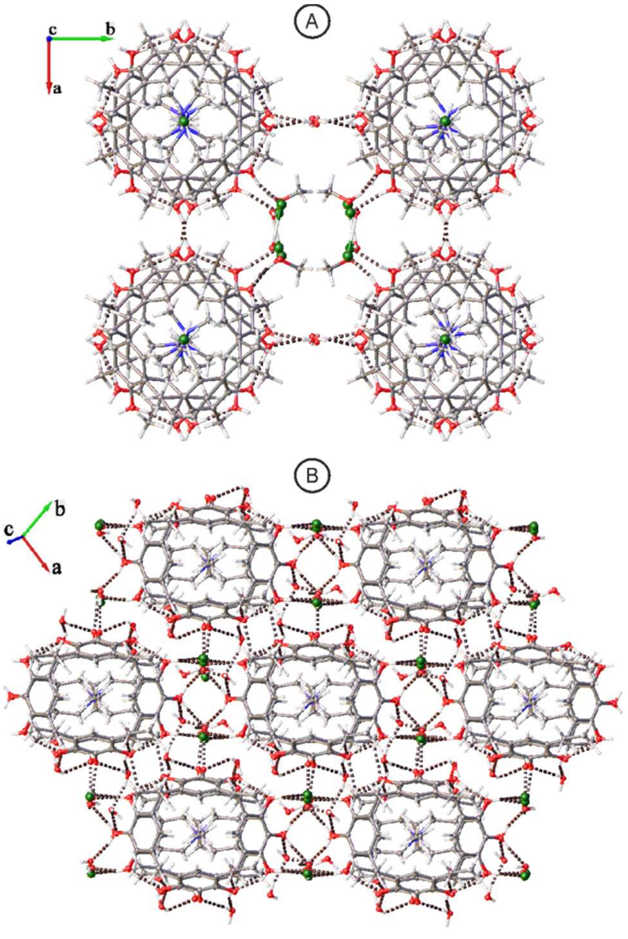


Fig. 4 Packing of the capsules in the crystals of **5a@2**$_2$ (A) and **5b@3**$_2$ (B). The packing in **5b@2**$_2$ is the same as that in **5a@2**$_2$.

In the complex **5c@1**, despite the dication **5c** connecting two resorcinarenes **1** via cation···π interactions (the average distance between C_{methyl} and aromatic centre is 3.425 Å), two cations share the same resorcinarene cavity (Fig. 5B). The ratio of the host and guest in **5c@1** is therefore 1:1. One of the two chlorides, Cl1, is captured by the positive nitrogen through electrostatic interaction while the other chloride, Cl2, is involved in linking two adjacent resorcinarene molecules. In such way, a 2-D hydrogen bond network is formed in **5c@1** (Fig. 5D).

Solution Studies

A series of ^1H NMR titration studies were performed to probe the binding capabilities of the different hosts **1-3** and the ammonium guests **4a-5c**. The presence of the NH and NH_2 groups on the guests has the potential of adding a direct hydrogen bond motif between the hosts and the guests. The ^1H NMR titration experiments between the hosts **1-3** and the guests **4a-5c** were done in methanol-d_4 at 303 K. In the experiment, increasing amounts of the ammoniums salts (50 mM) were added to a solution of each of the hosts **1-3** (5 mM). Complexation induced shifts of the ^1H NMR resonances of the guest protons were observed (Fig. 6). This results from the shielding effects of the aromatic rings of the bowl-shaped host cavity upon addition of the guests. This phenomenon clearly points to a guest exchange fast on the NMR time scale.

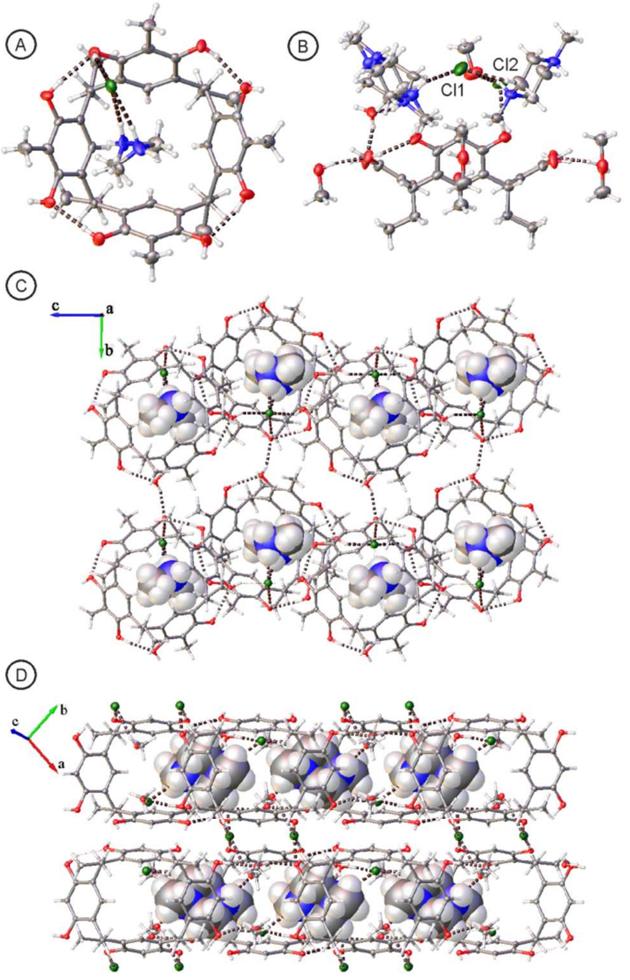


Fig. 5 Projections to show the structures in **4a@2** (A and C) and **5c@1** (B and D). A and B, the unit structures with 30% of the thermal ellipsoids; C and D, the 2-D layers by the intermolecular interactions.

Close observation of the chemical shifts reveals the pyrogallarene **3** shields the guests better than the methylresorcinarene **2** and the resorcinarene **1** (Fig. 6, SI) respectively. The presence of the extra hydroxyl group on the pyrogallarene **3** and the methyl group on resorcinarene **2** can explain this observation since they enhance the electron density of the host cavity by electron donation. Job plot[42,43] experiments reveal mainly 1:1 binding stoichiometry (see SI). In the case of **5c**, the job plots showed the possible formation of 2:1 species (see SI). Signals from the guests were successfully followed and the binding constants were obtained by non-linear least square titration curve fit of the respective titration data based on a 1:1 and 2:1 (for **5c**) host-guest binding mode using the winEQNMR2 computer program.[44] The binding constants and the signals followed are presented in table 1.

Significantly higher binding constant K_1 for the tertiary di-ammonium salt **5c** as compared to the tertiary mono-ammonium salts **5a-b** as well as the secondary mono-ammonium salts **4a-b** were observed. The high affinity of the hosts towards the di-tertiary ammonium salt **5c** could be explained by the high charge concentration and a suitable size of the guest **5c**. The second binding constant K_2 was much lower in all cases with **5c**, highlighting the well known[14,16,20] interference of the bulk methanol. Titration study was not possible for the dication **4c** due to its extremely low solubility in methanol. The binding constant K_1 of the dication **5c** is equally higher than the values reported for its diquaternary Me_2-DABCO analogue (145 M^{-1} at 288 K and 105 M^{-1} at 313 K for host **1**).[14] The high binding constant K_1 can be explained by the presence of the -NH groups on **5c**. The crystal structure of the host-guest complex **5c@1** (Fig. 5b) shows the guest ion-pair to be located in the cavity of the resorcinarene held together by NH···Cl hydrogen bond. This complex process is believed to be responsible for the increase in the binding affinity of **5c**.

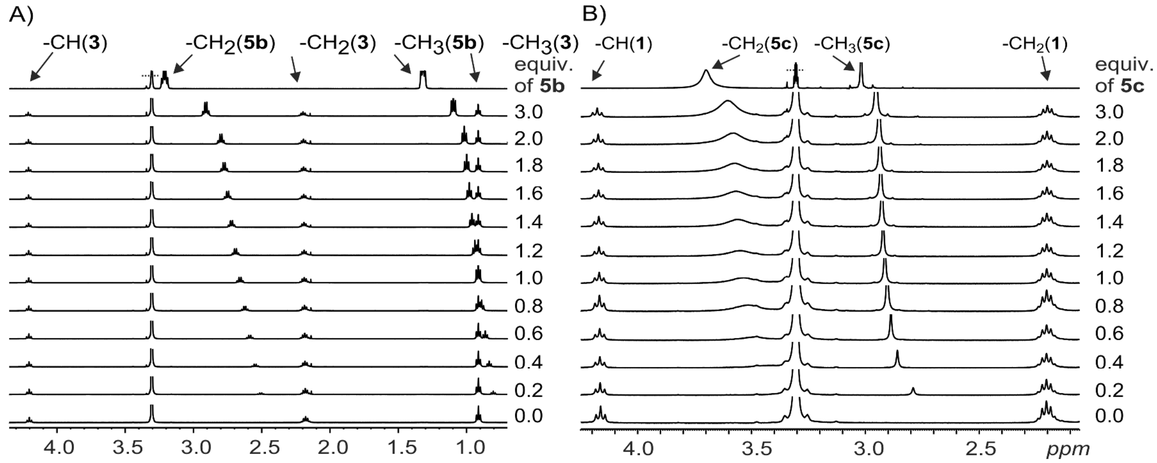


Fig. 6 A) ^1H NMR spectral changes observed (A) upon the addition of **5b** (50 mM) to Pyrogallarene **3** (5 mM) and (B) upon the addition of **5c** (50 mM) to resorcinarene **1** (5 mM). Measurements were done in CD_3OD at 303 K.

Table 1 Binding constant K_1 [M^{-1}]^a and K_2 [M^{-2}]^a for host **1-3** with guests **4a-5c** in CD_3OD at 303K.

	K_1 M^{-1}		K_1 M^{-1}		K_1 M^{-1}	K_2 M^{-2}
			Secondary Ammonium Salts			
1:1		1:1				
4a@1	45±1.3	**4b@1**	23±2.7	**4c@1**	-^{b}	
4a@2	51±1.6	**4b@2**	19±3.5	**4c@2**	-^{b}	
4a@3	59±8.2	**4b@3**	25±2.7	**4c@3**	-^{b}	
			Tertiary Ammonium Salts			
1:1		1:1		2:1		
5a@1	65±11	**5b@1**	23±1.7	**5c@1**	667±22	317±52
5a@2	23±4.3	**5b@2**	37±2.0	**5c@2**	778±35	327±48
5a@3	48±3.0	**5b@3**	24±1.3	**5c@3**	413±96	340±95

^{a} Obtained from monitoring the guests CH_3 signals. ^{b} K could not be determined due to low solubility of **4c** in methanol

Comparatively, the binding constant of the secondary **4a-4b** and tertiary **5a-5b** ammonium cations are lower than the values reported for the quaternary TMA analogue (195 M^{-1} at 288 K, 93 M^{-1} at 298 K and 170 M^{-1} at 303 K for host **1**, 121 M^{-1} at 303 K for host **2** and 478 M^{-1} at 303 K for host **3**).[7,14,16] The dimethyl **4a** and trimethyl **5a** cationic analogues are relatively smaller and tumbles freely within the cavity of the resorcinarenes and pyrogallarene hosts resulting in lower binding constants as compared to the quaternary TMA analogue. The small size of **4a** for example was highlighted in the crystal structure **4a@2** where the entire ion pair was bound in the cavity of the resorcinarene (Fig. 5a). The ethyl groups of the diethyl **4b** and triethyl **5b** ammonium cations are slightly longer as compared to quaternary TMA thus resulting in lower binding constants.

Gas phase analyses

The complexation of the ammonium guests **4a**–**5c** by the hosts **1-3** was investigated in the gas phase via electrospray ionization Mass Spectrometry ESI-MS.[45-47] Using methanol as the spray solvent in the positive ion mode, the complexes can be observed in the gas phase. Samples containing combinations of the hosts **1-3** and the ammonium guests **4a-5c** were prepared and analysed.

Taking a mixture of secondary mono-ammonium guest **4a** and pyrogallarene host **3** as an example in the positive ion mode, signal corresponding to 1:1 monomeric assembly **4a@3** (m/z 710) was observed as the main species with the dimeric assembly **4a@3**$_2$ (m/z 1374) observed as the secondary species (Fig. 7). The complexation of the dications **4c** and **5c** by the resorcinarenes were also investigated in the gas phase. Taking the combination of the tertiary di-ammonium guest **5c** and resorcinarene host **1** as an example in the positive ion mode, singly charged species were observed. The singly charged species were observed as a result of the dication losing a hydrogen atom in the process. The monomeric 1:1 complex **5c**-H@**1** (m/z 715) was observed as the main species with the dimeric assembly **5c**-H@$\mathbf{1}_2$ (m/z 1315) observed as the secondary species. In all cases, the isotope patterns obtained by experiment agree with those simulated on the basis of natural abundances. Samples containing combinations of all the hosts **1-3** and the guests **4a-5c** were measured and analysed with results showing similar patterns as observed in figure 7 (see SI).

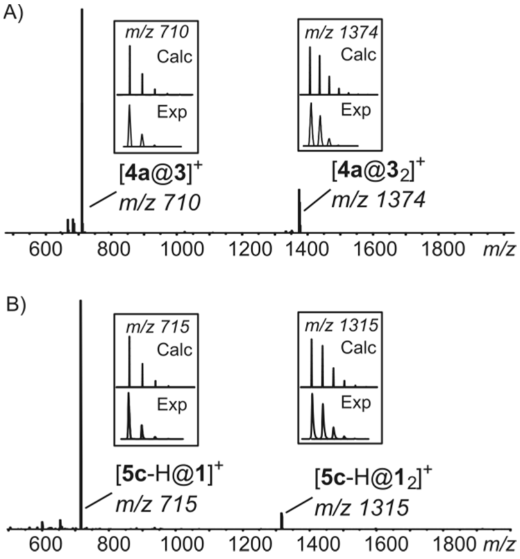


Fig. 7 ESI mass spectra of a mixture of the secondary mono-ammonium salts **4a** and Pyrogallarene **3** showing the 1:1 monomeric $[\mathbf{4a}@\mathbf{3}]^+$ and 1:2 dimeric $[\mathbf{4a}@\mathbf{3}_2]^+$ complexes (A); a mixture of the tertiary di-ammonium salts **5c** and resorcinarene **1** showing the 1:1 monomeric $[\mathbf{5c}\text{-H}@\mathbf{1}]^+$ and 1:2 dimeric $[\mathbf{5c}\text{-H}@\mathbf{1}_2]^+$ complexes (B). Insets: experimental and calculated isotope patterns of the monomeric and dimeric complexes.

Conclusions

This study reports the complexation of several secondary and tertiary mono- and di-ammonium salts **4a-5c** by resorcinarenes and pyrogallarenes **1-3** in the solid state, in solution and in the gas phase. Co-crystals of several host-guest assemblies were analysed in the solid state via single crystal X-ray diffraction studies. Three dimeric host-guest capsular assemblies (**5a**@$\mathbf{2}_2$, **5b**@$\mathbf{2}_2$, **5b**@$\mathbf{3}_2$) two open inclusion complexes (**4a**@**2**, **5c**@**1**) and a pseudocapsular methanol solvate (**2MeOH**@$\mathbf{2}_2$) were all analysed. The cations act as templates in the construction of the assemblies. The complexes are held together by multiple cation···π, CH···π and hydrogen bond interactions. The anions in some cases assist the capsular formation and together with solvent molecules connect the complexes resulting in complex three-Dimensional architectures. The size and electronic properties of the alkyl groups of the guests had a direct effect on the binding strength of the assembly as shown by ^{1}H NMR titration studies. Due to a higher charge concentration and a better fit, the guest **5c** showed the strongest binding in solution. The other ammonium salts that were either too small or slightly larger and unsymmetrical as compared to TMA showed lower binding constants. The substituent on the 2-position of the benzene ring also had an influence in the shielding effects of the guest with the most shielding observed with pyrogallarene **3**. Positive-ion mass spectrometric studies also confirmed the 1:1 monomeric and 1:2 dimeric complexes to prevail in the gas phase. This work adds substantial information on the recognition abilities of resorcinarenes to secondary and tertiary mono- and di-ammonium salts in all phases. It supplements the literature on the binding of quaternary ammonium salts and also contributes to our understanding of non-covalent interactions, which are very important in supramolecular chemistry and can be applied in other areas of chemistry.

Acknowledgements

Esa Haapaniemi (JYU Jyväskylä) is acknowledged for help with NMR experiments. Prof. Dr. Keiji Hirose is acknowledged for providing the spreadsheet software for calculating the binding constants. We gratefully acknowledge the Academy of Finland (K.R.: grant no. 265328 and 263256; N.K.B.: grant no. 258653), the University of Jyväskylä and the Tampere University of Technology for financial support.

Notes and references

[a] Department of Chemistry, Nanoscience Center, P. O. Box 35, 40014 University of Jyväskylä, Finland.

[b] Department of Chemistry and Bioengineering, Tampere University of Technology, P. O. Box 541, 33101 Tampere, Finland.

† The resorcinarene and pyrogallarene hosts **1-3**, were synthesized according to reported procedures.[13] The ammonium salts **4a**, **4b** **5a** and **5b** were commercially available. The ammonium salts **4c** and **5c** were obtained from the corresponding piperazine and 1,4-dimethylpiperazine through protonation with HCl. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX 500 (500 MHz for ^{1}H and 126 MHz for ^{13}C) and a Bruker Avance DRX 400 (400 MHz for ^{1}H and 100 MHz for ^{13}C) spectrometers. The mass spectrometric studies were performed with a QSTAR Elite ESI-Q-TOF mass spectrometer equipped with an API 200 TurboIonSpray ESI source from AB Sciex (former MDS Sciex) in Concord, Ontario (Canada). All experiments were performed on positive polarization. The parameters of the ion source, ion optics and quadrupole were optimized to get maximum abundance of the ions under study. Single crystals X-ray diffractions for **2MeOH**@$\mathbf{2}_2$, **5a**@$\mathbf{2}_2$, **5b**@$\mathbf{3}_2$ and **4a**@**2** were conducted at 173 K on an Agilent Super-Nova diffractometer using mirror-monochromatized Mo-*K*α (λ = 0.71073 Å) radiation. The single crystal data for **5b**@$\mathbf{2}_2$ and **5c**@**1** were collected at 123K using an Agilent SuperNova dual wavelength diffractometer with a micro-focus X-ray source and multilayer optics monochromatized Cu-*K*α (λ = 1.54184 Å) radiation. All the data collection and reduction were performed using the program *CrysAlisPro*.[48]

Electronic Supplementary Information (ESI) available: [X-ray crystallographic, NMR spectroscopic and mass spectrometric data]. See DOI: 10.1039/b000000x/

1 J-M Lehn, *Pure Appl. Chem.*, 1994, **66**, 1961-1966.

2 J-M Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, 1995.

3 M. M. Conn and J. J. Rebek, *Chem. Rev.,* 1997, **97**, 1647-1668.

4 M. Nissinen, E. Wegelius, D. Falabu and K. Rissanen, *CrystEngComm,* 2000, **28**, 1-3.

5 H. Mansikkamäki, M. Nissinen, C. A. Schalley and K. Rissanen, *New J. Chem.,* 2003, **27**, 88-97.

6 K. Rissanen, *Angew. Chem., Int. Ed.,* 2005, **44**, 3652-3654.

7 J. L. Atwood and A. Szumna, *Supramol. Chem.,* 2002, **2**, 479-482.

8 A. Åhman, M. Luostarinen, K. Rissanen and M. Nissinen, *New J. Chem.,* 2007, **31**, 169-177.

9 N. K. Beyeh, A. Valkonen and K. Rissanen, *Supramol. Chem.,* 2009, **21**, 142-148.

10 S. Busi, H. Saxell, R. Fröhlich and K. Rissanen, *CrystEngComm,* 2008, **10**, 1803-1809.

11 K. Murayama and K. Aoki, *Chem. Commun.,* 1997, 119-120.

12 K. Murayama, *Chem. Commun.,* 1998, 607-608.

13 P. Timmerman, W. Verboom and D. N. Reinhoudt, *Tetrahedron,* 1996, **52**, 2663-2704.

14 H. Mansikkamäki, C. A. Schalley, M. Nissinen and K. Rissanen, *New J. Chem.,* 2005, **29**, 116-127.

15 K. Murayama and K. Aoki, *Chem. Lett.,* 1998, **27**, 301-302.

16 N. K. Beyeh, D. P. Weimann, L. Kaufmann, C. A. Schalley and K. Rissanen, *Chem. Eur. J.,* 2012, **18**, 5552-5557.

17 H. Mansikkamäki, M. Nissinen and K. Rissanen, *CrystEngComm*, 2005, **7**, 519-526.

18 M. Luostarinen, A. Åhman, M. Nissinen and K. Rissanen, *Supramol. Chem.,* 2004, **16**, 505-512.

19 H. Mansikkamäki, M. Nissinen and K. Rissanen, *Chem. Commun.,* 2002, 1902-1903.

20 N. K. Beyeh, M. Göth, L. Kaufmann, C. A. Schalley and K. Rissanen, *Eur. J. Org. Chem.,* 2014, **2014**, 80-85.

21 N. K. Beyeh and K. Rissanen, *Isr. J. Chem.,* 2011, **51**, 769-780.

22 L. R. MacGillivray and J. L. Atwood, *Nature,* 1997, **389**, 469-472.

23 T. Gerkensmeier, W. Iwanek, C. Agena, R. Fröhlich, S. Kotila, C. Näther and J. Mattay, *Eur. J. Org. Chem.,* 1999, **1999**, 2257-2262.

24 N. K. Beyeh, M. Kogej, A. Åhman, K. Rissanen and C. A. Schalley, *Angew. Chem., Int. Ed.,* 2006, **45**, 5214-5218.

25 H. Mansikkamäki, M. Nissinen and K. Rissanen, *Angew. Chem., Int. Ed.,* 2004, **43**, 1243-1246.

26 H. Mansikkamäki, S. Busi, M. Nissinen, A. Åhman and K. Rissanen, *Chem. Eur. J.,* 2006, **12**, 4289-4296.

27 I. Fujisawa, D. Takeuchi, R. Kato, K. Murayama and K. Aoki, *Bull. Chem. Soc. Jp.,* 2011, **84**, 1133-1135.

28 J. G. Shewale and V. K. Sudhakaran, *Enzyme Microb. Technol.,* 1997, **20**, 402-410.

29 T. Yamana, A. Tsuji, E. Miyamoto and E. Kiya, *J. Pharm. Pharmacol.,* 1975, **27**, 283-287.

30 D. A. Fowler, J. Tian, C. Barnes, S. J. Teat and J. L. Atwood, *CrystEngComm,* 2011, **13**, 1446-1449.

31 K. Salorinne, T. Tero, K. Riikonen and M. Nissinen, *Org. Biomol. Chem.,* 2009, **7**, 4211-4217.

32 G. R. Desiraju, *Crystal Engineering: The Design of Organic Solids*, Elsevier, Amsterdam, 1989.

33 B. Rodríguez-Spong, C. P. Price, A. Jayasankar, A. J. Matzger and N. Rodríguez-Hornedo, *Adv. Drug Deliv. Rev.,* 2004, **56**, 241-274.

34 P. Agarwal, A. Griffith, H. R. Costantino and N. Vaish, *Neuropsychiatr. Dis. Treat.,* 2010, **6**, 151-158.

35 A. Shivanyuk, K. Rissanen and E. Kolehmainen, *Chem. Commun.,* 2000, 1107-1108.

36 N. K. Beyeh, A. Valkonen and K. Rissanen, *CrystEngComm,* 2014, **16**, 3758-3764.

37 A. Shivanyuk, E. F. Paulus, K. Rissanen, E. Kolehmainen and V. Böhmer, *Chem. Eur. J.*, 2001, **7**, 1944-1951.

38 A. Shivanyuk, J. C. Friese, S. Döring and J. Rebek, *J. Org. Chem.,* 2003, **68**, 6489-6496.

39 P. Thuery and M. Nierlich, *Supramol. Chem.*, 2000, **11**, 185-190.

40 I. Fujisawa, N. Harima, K. Takagi, S. Hiraoka, M. Shionoya, K. Murayama, S. Itsuno, R. Kato and K. Aoki, *Bull. Chem. Soc. Jp.,* 2012, **85**, 1037-1045.

41 A. L. Spek, *Acta Crystallogr.,* 2009, **D65**, 148-155.

42 K. A. Connors, Binding Constants: The Measurement of Molecular Complex Stability, John Wiley & Sons, Inc., Canada, 1987.

43 K. Hirose, *J. Incl. Phenom. Mac. Chem.,* 2001, **39**, 193-209.

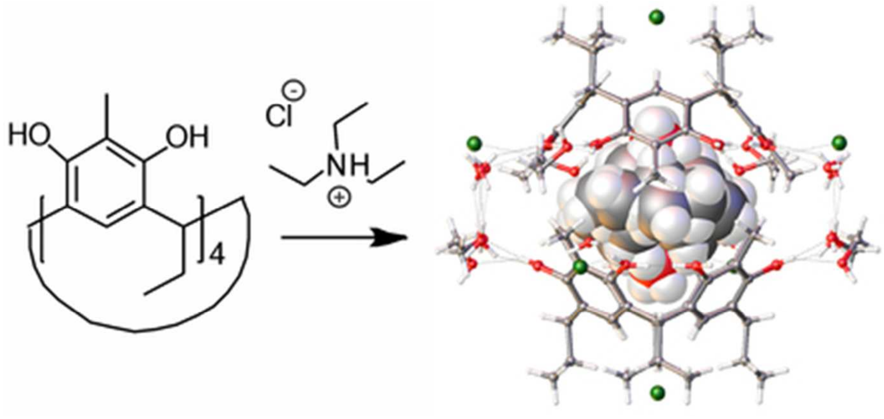
44 M. J. Hynes, *J. Chem. Soc., Dalton Trans.,* 1993, 311-312.

45 M. Przybylski and M. O. Glocker, *Angew. Chem., Int. Ed. Engl.,* 1996, **35**, 806-826.

46 J. S. Brodbelt, *Int. J. Mass Spectrom.,* 2000, **200**, 57-69.

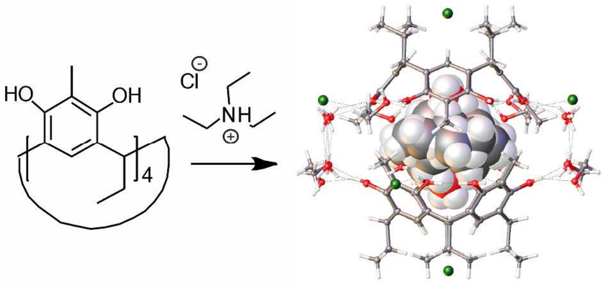
47 C. A. Schalley, *Mass Spectrom. Rev.,* 2001, **20**, 253-309.

48 *CrysAlisPro* 2012, Agilent Technologies. Version 1.171.36.31.



37x17mm (300 x 300 DPI)

Table of Content



Multiple weak interactions are manifested in the complexation of different categories of secondary and tertiary alkyl ammonium salts by resorcinarenes and pyrogallarenes leading to open inclusion and dimeric capsular assemblies with varying binding affinity and analyzed in solid, liquid and gas phases.