Resorcin[4]arene dimer linked by eight water molecules and incorporating a tetraethylammonium ion: guest-driven capsule formation *via* cation–π interactions

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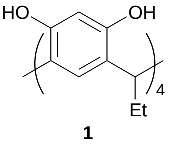
X-Ray analysis of the co-crystallization compound formed between tetraethylresorcin[4]arene 1 and tetraethylammonium ion, $Et_4N^+\cdot1\cdot1^-\cdot8H_2O\cdot2EtOH$, has shown that the two 'head-to-head' arranged resorcinarenes are linked by eight water molecules and encapsulate a tetraethylammonium ion within the cavity *via* cation–π interactions.

Molecular containers,[1–7] which have the ability to encapsulate substrates, have attracted much attention in supramolecular chemistry because of their numerous applications: the design of artificial receptors, transport and storage of small organic guests, design of chemical sensor devices, removal of pollutants from water, and use as reaction chambers. A variety of container compounds whose interior cavities are constructed by covalently linked structures, typically involving carcerands,[1,2] cryptophanes[3] or cucurbiturils,[4] have been synthesized and well characterized. More recently, self-assembly through non-covalent interactions such as hydrogen bonding has proved to give novel types of molecular containers, which we here tentatively call 'molecular capsules', the still-limited examples being glycolurils,[5] urea-substituted calix[4]arenes[6] and tetrols.[7] Most recently, MacGillivray and Atwood have reported[8] a self-assembled resorcin[4]arene hexamer, forming a shell-like molecular capsule, held together by eight water bridges in addition to direct hydrogen bonds between the substructures. We report here the preparation and crystal structure of a dimeric resorcin[4]arene molecular capsule, linked by eight water bridges and incorporating a tetraethylammonium ion inside the cavity. The formation of the capsule might be guest-driven through the cation–π interaction, an important mechanism for molecular recognition that is not yet sufficiently explored.[9]

Tetraethylresorcin[4]arene **1**‡ (0.1 mmol) and tetraethylammonium perchlorate (1 mmol) were dissolved in EtOH–H_2O (5 : 3, 8 ml). The mixture (pH 5) was allowed to stand at room temperature for three weeks to give colourless crystals with a yield of 60%,§ the structure of which has been determined.¶



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The molecular structure of the compound with the composition of $Et_4N^+\cdot\mathbf{1}\cdot\mathbf{1}^-\cdot8H_2O\cdot2EtOH$‖ is shown in Fig. 1, where, coinciding with crystallographic symmetries, each macrocyclic resorcinol tetramer **1** has four-fold symmetry and the two macrocycles are related to each other by a mirror plane. The resorcinarene molecule adopts a bowl-shaped conformation with the usually observed intramolecular hydrogen bonds between neighbouring hydroxy groups: the crystallographically independent hydrogen bond O(1)···O(2′) = 2.767(9) Å. The most interesting structural feature is the formation of a molecular capsule constructed of two 'head-to-head' arranged substructures which captures a tetraethylammonium ion within the cavity.** The Et_4N^+ nitrogen atom is located at a crystallographic centre of symmetry, the point that the four-fold axis and the mirror plane intersect, and thus the ethyl groups of the cation are disordered over two sets of sites related by the mirror plane on which the central nitrogen and terminal carbon atoms ride. The architecture of the capsule structure is unique in that the two substructures are not directly but indirectly connected to each other *via* eight water bridges, because in so far reported molecular capsules[5–7] the two substructures are directly hydrogen-bonded to each other *via* functional groups, *e.g.* urea-substituents,[6] that are designed to form complementary hydrogen bonds. Thus each water molecule, which lies on the mirror plane noted above, is hydrogen-bonded to two hydroxy groups, one from each substructure, summing to a total of 16 hydrogen bonds in the capsule unit: the crystallographically independent hydrogen bonds O(3)···O(1) = 2.76(1) and O(4)···O(2) = 2.753(10) Å. The water linking is engaged also in the assembly of the tetramethylresorcin[4]arene hexamer,[8] in addition to, in this case, direct hydrogen bonds between the hydroxy groups of the 'head-to-head' arranged resorcinarenes. As shown in Fig. 2, the Et_4N^+ ion is arranged in such a way that its ethyl groups project toward the bridging C(7) carbons of **1**, where each ethyl group makes close contacts with the phenyl rings through, we suggest, multiple cation–π interactions. Since the capsule unit is negatively (monovalently) charged, the presence of the cation–π interactions between the quaternary cationic Et_4N^+ group and the aromatic rings of **1** is

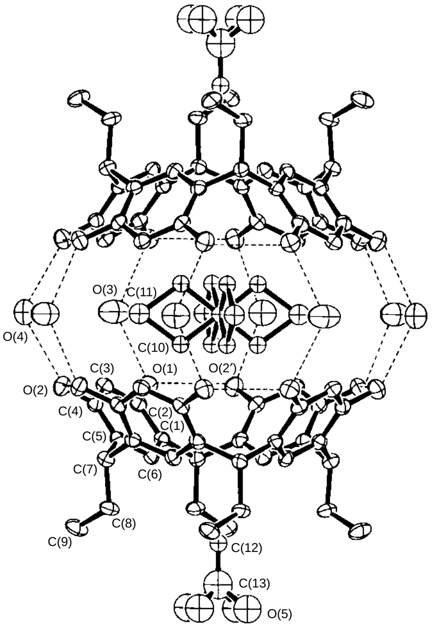

Fig. 1 Molecular structure of the capsule molecule [the ethanol solvate is disordered at four positions due to the four-fold axis passing through it, where the thermal ellipsoid of the C(12) atom is given at arbitrary scale for clarity]. O(2′) is related to O(2) by four-fold symmetry. Broken lines denote hydrogen bonds.

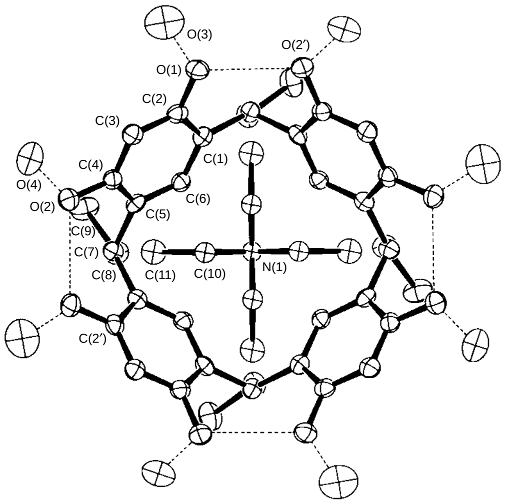

Fig. 2 A top view of the capsule molecule along the four-fold axis, showing the disposition of the Et_4N^+ ion within the cavity. Close contacts: C(2′)···C(10) = 3.58(2), C(2′)···C(11) = 3.59(1), C(4)···C(10) = 3.59(2), and C(4)···C(11) = 3.59(1) Å. O(2′) and C(2′) are related to O(2) and C(2), respectively, by four-fold symmetry. Broken lines denote hydrogen bonds.

not self-evident. However, X-ray evidence for such an interaction between the Me_3N^+ group of acetylcholine and the π-rings of the *neutral* resorcin[4]arene is available.[10] The bond lengths and angles of the resorcin[4]arene molecule are in good agreement with those in the literature.[10]

Crystallization of **1**, in the absence of tetraethylammonium ion, from EtOH–H_2O or EtOH–acetone–H_2O gave compounds, 2(**1**)·2EtOH·10H_2O or **1**·Me_2CO·EtOH·2H_2O, respectively, and their X-ray analyses have shown that in both compounds no molecular capsule is formed.[11] The lack of formation of a molecular capsule for *neutral* substrates in these two and, to the best of our knowledge, six other cases such as MeCN–H_2O,[12] acetone–EtOH–H_2O,[12] ethyl methyl ketone,[13] EtOH,[14] pyridine,[15] and MeCN–4,4′-bipyridine[15] may give circumstantial evidence for the important role of the cation–π interaction in the formation of the present resorcinarene molecular capsule, suggesting that capsule formation might be guest-driven through cation–π interactions. This is in contrast to the usually observed[5–7] host-driven capsule formation by direct hydrogen bonding between two substructures that are predesigned to form self-complementary hydrogen bonds.

The ^1H NMR spectrum (270 MHz, CD_3OD) of the capsule complex (1 mmol dm^{-3}) shows a quartet at δ 3.130 and a triplet at δ 1.173 for the CH_2 and CH_3 protons of Et_4N^+, respectively, whereas the corresponding signals of Et_4N^+ alone appear at δ 3.321 and 1.289. These upfield shifts for the complex are probably due to the shielding effect of the aromatic rings, indicating that the quaternary tetraethylammonium group associates preferentially with the π-rings of **1** in solution.††

In conclusion, the synthesis and isolation of the resorcin[4]arene molecular capsule incorporating an Et_4N^+ ion are straightforward, giving a moderate yield by simply mixing starting materials which are readily available. Unlike other molecular capsules,[5–7] the two substructures are *not directly* hydrogen-bonded but are *indirectly* bonded *via* water bridges. The architecture is simple and elegant: the two hemispherical resorcin[4]arenes are attached *via* their upper rims with eight water molecules to form a spherical capsule having C_{4h} symmetry. The present study provides additional X-ray evidence[10] for cation–π interaction between the quaternary ammonium group and the π-electrons of the aromatic rings, a novel type of binding force that is important in the function of biological systems.[9,16] The cation–π interaction could also play a major role in the process of the capsule formation, by forcing simultaneous interactions between a tetraethylammonium ion and two resorcinarenes. The guest-driven host construction observed here could offer a promising approach for building new supramolecular compounds.

Notes and References

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‡ 2,8,14,20-Tetraethyl-4,6,10,12,16,18,22,24-octahydroxycalix[4]arene **1** was synthesized according to a literature procedure (ref. 17).

§ Elemental microanalysis of the compound was not possible due to its rapid decomposition out of solution. The molecular formula was determined by X-ray analysis.

¶ *Crystal data*: $C_{10.5}H_{15.875}N_{0.125}O_{3.25}$, M = 195.80, colourless columns, tetragonal, space group $P4/mnc$, a = 13.927(2), c = 22.434(2) Å, U = 4351.5(10) Å^3, Z = 16, D_c = 1.195 g cm^{-3}, μ(Mo-Kα) = 0.88 cm^{-1}, T = 293 K, F(000) = 1692. A crystal was sealed in a glass capillary with a drop of mother liquor. Of 2926 unique data in the range $4 < 2\theta < 45°$, 1052 data with $I > 3\sigma(I)$ were used in the refinement. Residuals of R = 0.104 and R_w = 0.115 were obtained after 127 parameters had been refined to convergence, where only the resorcinarene and water atoms were treated anisotropically while all the other atoms were treated isotropically. No attempt was made to locate the H atoms. Extensive disordering of Et_4N^+ and EtOH caused the rather high R values. CCDC 182/753.

‖ The Et_4N^+ : **1** : EtOH composition of 1 : 2 : 2 for the compound formed was consistent with its ^1H NMR spectra. The absence of ClO_4^- was ascertained *via* IR spectroscopy. Any one of the sixteen hydroxy substituents belonging to the two resorcin[4]arenes constituting the capsule could be deprotonated.

** Resorcin[4]arenes as receptors for tetraalkylammonium ions have been demonstrated in alkaline solution (ref. 18), where, however, a tetradeprotonated host anion is assumed to form a 1 : 1 complex with an ammonium cation.

†† A study to clarify the solution structure or structures involved in the capsule formation remains to be carried out.

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Received in Cambridge, UK, 25th November 1997; revised manuscript received 13th January 1998; 8/00340H