Self-assembly of Tetramethylated Resorcin[4]arene to Form Molecular Capsules Incorporating Methanol, Ethanol, and Imidazole: A Comparison with the Unsubstituted Resorcin[4]arene System

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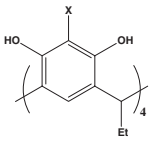
Tetramethylated resorcin[4]arene (MRCT) forms 'head-to-head' arranged self-dimers incorporating neutral guest molecules methanol, ethanol, and imidazole within the cavity, with the MRCT:guest composition of 2:2, while unsubstituted resorcin[4]arene forms 1:1 monomers, showing the significance of the methyl substituents of the MRCT rings in the capsule formation through methyl···methyl hydrophobic interactions between the facing substructures, as evidenced by X-ray diffraction.

Resorcin[4]arene (resorcinol cyclic tetramer: RCT, **1**) is useful as a building block of self-assembled supramolecules, through conventional O–H···O hydrogen bonds. These include a hexamer[1] and dimers:[2–4,6] the hexamer[1] forms a shell-like molecular capsule held by water bridges in addition to direct O–H···O hydrogen bonds between substructures; the dimers form molecular capsules held by alcohol bridges,[2] water bridges,[3,4] alcohol and water-mixed[5] bridges, and alcohol and halide ion-mixed[6] bridges. Similar hexameric[7] and dimeric[8] capsules are reported for tetrahydroxylated resorcin[4]arene (pyrrogallol cyclic tetramer: PCT), in which its additional hydroxy groups offer the expanded hydrogen bonding patterns for self-assembly. In the previous reports,[3,9] we have presented a guest-driven capsule formation mechanism in which a tetraethylammonium guest cation might lead the formation of a 'head-to-head' arranged RCT dimer through cation-π interaction. We have now extended this study to the tetramethylated resorcin[4]arene[10] (2-methylresorcinol cyclic tetramer: MRCT, **2**) system in order to further address the capsule formation mechanism for quaternary alkylammonium ions by comparing structures of molecular complexes formed between MRCT and alkylammonium ions with those formed between MRCT and neutral molecules, expecting that MRCT forms a molecular capsule incorporating an alkylammonium ion while it forms 1:1 (MRCT:guest) monomers for neutral guest molecules. We report here the unexpected capsule formation of 'head-to-head' arranged MRCT dimers incorporating neutral molecules methanol, ethanol or imidazole, possibly due to hydrophobic interactions between the methyl substituents from two facing substructures.[11]



X=H: RCT(1)
X=OH: PCT
X=CH_3: MRCT(2)

Tetramethylated tetraethylresorcin[4]arene[10] (MRCT, **2**) was synthesized, by an analogous method[12] for tetraethylresorcin[4]arene (RCT, **1**), from 2-methylresorcinol and propionaldehyde. Molecular complexes[13] of 2(**2**)·2MeOH·$4H_2O$ (dark-yellow) and 2(**2**)·3.4EtOH·$0.6H_2O$ (brown) were crystallized from MRCT (0.1 mmol) dissolved in MeOH or EtOH solution (10 mL) by slowly evaporating the solution (pH 5) with the yield of 50 and 40%, respectively. Molecular complex[13] of 2(**2**)·2(imidazole)·$3H_2O$ was prepared by dissolving MRCT (0.1 mmol) and imidazole (1 mmol) in ethanol (10 mL)–water (4 mL), followed by slow evaporation of the solution (pH 5) to yield brown crystals with the yield of 30%. Crystal structures of these compounds were determined by X-ray diffraction.[14]

The methanol and ethanol complexes of MRCT, 2(**2**)·2MeOH·$4H_2O$ and 2(**2**)·2EtOH·1.4EtOH·$0.6H_2O$, are isostructual to each other. Figure 1 shows the molecular structure of the methanol complex, which forms an irregularly shaped 'head-to-head' dimer across a crystallographic inversion center. A pair of MeOH or EtOH molecules are captured in the cavity, where its hydroxyl and alkyl groups locate near the phenyl rings of a MRCT substructure through O(9)–H (alcohol)···π (ring A) and CH_3 (MeOH)··· or CH_2CH_3 (EtOH)···π (rings C and D for MeOH or rings B, C, and D for EtOH) interactions and, in addition, its hydroxy head forms a hydrogen bond with the phenolic hydroxy group of the pairing substructure, O(5*)–H (MRCT)···O(9) (alcohol). The methyl substituents on the MRCT rings make hydrophobic close contacts with themselves between the facing resorcinarenes, forming a pair of methyl-zippers, C(29)···C(31*)···C(30)···C(32*) and C(29*)···C(31)···C(30*)···C(32), in the MeOH complex while two pairs of methyl···methyl contacts, C(29)···C(31*) and C(29*)···C(31) and C(30)···C(32*) and C(30*)···C(32), in the EtOH complex. The capsule structure is furthermore stabilized by a pair of water

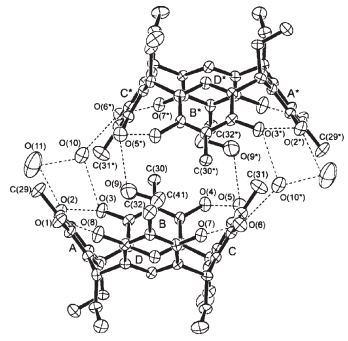


Figure 1. Molecular structure of 2(**2**)·2MeOH·$4H_2O$. Atoms designated by asterisk (*) are related to their parent atoms by a center of symmetry. Close contacts (Å): O(9)···ring A (perpendicular distance) = 3.23; C(41)···ring C = 3.60; C(41)···ring D = 3.75; O(5*)···O(9) (hydrogen bond) = 2.63(2); C(29)···C(31*) = 3.92(2); C(31*)···C(30) = 4.25(2); C(30)···C(32*) = 4.03(2); C(30)···O(6*) = 3.51(2); C(30)···O(7*) = 3.52(2); C(31)···O(2*) = 3.27(2); C(31)···O(3*) = 3.56(2).

bridges, O(3)···O(10) (water)···O(6*) and O(3*)···O(10*)···O(6), in the MeOH complex while by a pair of EtOH bridges O(3)···O(10) (EtOH)···O(6*) and O(3*)···O(10*)···O(6) in the EtOH complex.

Figure 2 shows the molecular structure of the imidazole complex, 2(**2**)·2(imidazole)·3H_2O, where two MRCT molecules related by a crystallographic center of symmetry form a 'head-to-head' arranged molecular capsule which captures a pair of imidazole substrates within the cavity. The imidazole ligand is oriented in such a way that the successive C–H and the N–H groups of the lower part of the ring make close contacts with the phenyl rings of a MRCT substructure, C(42)–H···ring B and N(2)–H···ring D in Figure 2, through, we suggest, C–H··· and N–H···π interactions, respectively, and the remaining ring-nitrogen atom is directed toward the phenolic O–H group of the pairing substructure to form a hydrogen bond, O(5*)–H···N(1). The two substructures are slightly shifted to each other to make close contacts between methyl substituents from the facing resorcinarenes, forming two pairs of methyl···methyl close contacts, C(29)···C(31*) and C(29*)···C(31) and C(30)···C(32*) and C(30*)···C(32). A pair of water-bridges between the facing resorcinarenes, O(3)···O(9*)···O(6*) and O(3*)···O(9)···O(6), further stabilize the capsule structure.

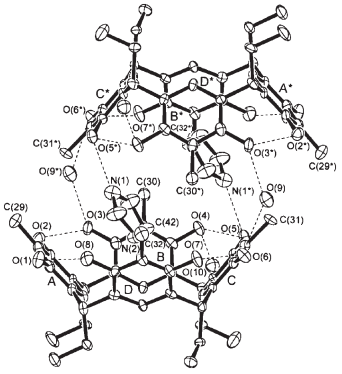


Figure 2. Molecular structure of 2(**2**)·2(imidazole)·3H_2O. Atoms designated by asterisk (*) are related to their parent atoms by a center of symmetry. Close contacts (Å): C(42)···ring B (perpendicular distance) = 3.30; N(2)···ring D = 3.05; O(5*)···N(1) (hydrogen bond) = 2.55(2); C(29)···C(31*) = 4.14(2); C(30)···C(32*) = 3.96(2); C(30)···O(6*) = 3.98(2); C(30)···O(7*) = 3.62(2); C(31)···O(2*) = 3.81(2); C(31)···O(3*) = 3.90(2).

Crystallization of RCT (**1**) from MeOH–H_2O or EtOH–H_2O gave compounds **1**·2MeOH·H_2O or **1**·EtOH·3H_2O, respectively, and their X-ray analyses[15] have shown that they form a monomeric adduct in which a MeOH or an EtOH molecule is incorporated in the cavity of a bowl-shaped RCT molecule in a similar manner to that in the present MRCT–MeOH or –EtOH complexes, that is, the CH_3 (MeOH) or CH_2OH (EtOH) groups locate in the vicinity of the aromatic rings through C–H··· and O–H···π interactions. Unlike the MRCT complexes, however, its O–H head is capped by solvent molecules, a methanol and a water, through hydrogen bonds in the MeOH compound or covered by a phenolic OH group of the neighboring RCT molecule through a hydrogen bond in the EtOH compound. In another EtOH compound,[16] **1**·3EtOH, a bowl-shaped RCT molecule forms a monomeric structure which captures an ethanol molecule with its OH group facing the phenyl ring of RCT, possibly through O–H···π interaction. Similarly, RCT gave a 1:1 monomeric adduct with imidazole, **1**·imidazole·propan-2-ol,[15] whose crystal structure has revealed that an imidazole ligand is embedded in the cavity of a bowl-shaped RCT molecule with its upper side capped by a propan-2-ol solvation through an O–H (propan-2-ol)···N (imidazole ring nitrogen) hydrogen bond. These observations indicate that the dimer formation is characteristic of the MRCT host system and this might be due to methyl···methyl hydrophobic interactions between the facing MRCT molecules, coupled with the formation of host–guest direct hydrogen bonds.

In summary, this study shows the significance of the methyl substituents of the MRCT rings in the self-assembled 'head-to-head' dimer formation via intra-capsular methyl···methyl hydrophobic interactions.

References and Notes

1 L. R. MacGillivray and J. L. Atwood, *Nature*, **389**, 469 (1997).
2 K. N. Rose, L. J. Barbour, G. W. Orr, and J. L. Atwood, *Chem. Commun.*, **1998**, 407.
3 K. Murayama and K. Aoki, *Chem. Commun.*, **1998**, 607.
4 A. Shivanyuk, K. Rissanen, and E. Kolehmainen, *Chem. Commun.*, **2000**, 1107.
5 H. Mansikkamäki, M. Nissinen, and K. Rissanen, *Chem. Commun.*, **2002**, 1902.
6 H. Mansikkamäki, M. Nissinen, C. Schalley, and K. Rissanen, *New J. Chem.*, **2003**, 88.
7 J. L. Atwood, L. J. Barbour, and A. Jerga, *Chem. Commun.*, **2001**, 2376.
8 A. Shivanyuk and J. Rebek, Jr., *Chem. Commun.*, **2001**, 2374.
9 Presented at XIth International Symposium on Supramolecular Chemistry, Fukuoka, July-August 2000, Abstr. No., P-266.
10 2,8,14,20-Tetraethyl-4,6,10,12,16,18,22,24-octahydroxy-5,11,17,23-tetramethylcalix[4]arene.
11 Expectedly, MRCT forms a molecular capsule incorporating a tetraethylammonium ion through cation-π interaction, unpublished result.
12 Y. Aoyama, Y. Tanaka, and S. Sugahara, *J. Am. Chem. Soc.*, **111**, 5397 (1989).
13 Elemental microanalyses of these compounds were not possible due to their rapid decomposition out of solution. The molecular formulae ware determined by X-ray analyses.
14 Crystal data for **2**·MeOH·$(H_2O)_2$: $C_{41}H_{56}O_{11}$, fw = 724.89, triclinic, space group $P-1$, $a = 12.654(7)$, $b = 15.759(13)$, $c = 12.299(8)$ Å, $\alpha = 107.51(5)$, $\beta = 108.83(4)$, $\gamma = 108.91(5)^\circ$, $V = 1958(3)$ Å^3, $Z = 2$, $D_{calcd} = 1.229$ g cm^{-3}, μ(Mo Kα) = 0.88 cm^{-1}, $R = 0.106$ and $R_w = 0.124$ ($I > 3\sigma(I)$). Crystal data for **2**·EtOH·$(EtOH)_{0.7}$·$(H_2O)_{0.3}$: $C_{43.4}H_{58.8}O_{10}$, fw = 740.54, triclinic, space group $P-1$, $a = 12.597(8)$, $b = 14.765(9)$, $c = 12.322(14)$ Å, $\alpha = 102.86(8)$, $\beta = 108.96(8)$, $\gamma = 103.62(5)^\circ$, $V = 1991(3)$ Å^3, $Z = 2$, $D_{calcd} = 1.235$ g cm^{-3}, μ(Mo Kα) = 0.86 cm^{-1}, $R = 0.115$ and $R_w = 0.126$ ($I > 3\sigma(I)$). Crystal data for **2**·(imidazole)·$(H_2O)_{1.5}$: $C_{43}H_{55}N_2O_{9.5}$, fw = 751.92, triclinic, space group $P-1$, $a = 12.488(3)$, $b = 14.975(5)$, $c = 12.319(4)$ Å, $\alpha = 102.13(3)$, $\beta = 109.72(2)$, $\gamma = 103.17(3)^\circ$, $V = 2005(1)$ Å^3, $Z = 2$, $D_{calcd} = 1.245$ g cm^{-3}, μ(Mo Kα) = 0.87 cm^{-1}, $R = 0.097$ and $R_w = 0.108$ ($I > 3\sigma(I)$).
15 K. Aoki, T. Shimizu, T. Nakahara, and R. Matsubara, unpublished results.
16 M. Nissinen, E. Wegelius, D. Falábu, and K. Rissanen, *CrystEngComm*, **28**, 1 (2000).

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