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Halogen-Bonded Solvates of Tetrahaloethynyl Cavitands

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The formation and structures of the halogen-bonded solvates of three different tetrahaloethynyl cavitands with acetone, chloroform, acetonitrile, DMF and DMSO, were prepared and investigated. The inclusion and host-guest behaviour of the resorcinarene cavitands was found to be highly dependent on the flexibility of the ethylene-bridging unit.

Halogen bonding (XB) has been receiving considerable increasing attention as it provides a complementary interaction to hydrogen bonding (HB).1,2 XB has proven to play crucial roles in supramolecular chemistry,3,4 nanoscience,5 biosystems,6 and functional materials.5 The directionality and tunability makes XB an important non-covalent interaction, geometrically and thermodynamically, similar to HB; however, its allowance for hydrophobicity makes it a complementary force to the hydrophobic HB.7 To exploit this interaction, many macrocyclic host molecules, functionalized with classical XB donors/acceptors pairs, have been designed.8–13 Resorcinarenes, a subclass of the calixarene family, result from the condensation reaction of resorcinol and an aldehyde.14 These easily functionalizable derivatives have been extensively studied due to their tuneable cavity size, solubility profile, and ligand specificity.10–13 Recently, we reported a series of preorganized resorcinarene cavitands functionalized with four halo-ethynyl moieties.15 As part of our program to construct halogen bonded capsules, we first investigated their XB donor ability using standard XB acceptors: the oxygen in 1,4-dioxane, the sp2 nitrogen in pyridine, and the bromide anion of tetrpropyl ammonium bromide.16 The results provided some insight into the specific features of these resorcinarene cavitand XB receptors, not only of their XB related behaviour, but also of their structural features in the solid-state.

To rationally design and selectively assemble a halogen-bonded capsule, it is necessary to understand the binding preferences of these macrocyclic XB donors with different solvents. As each solvent has unique polarity, acidity, hydrophobicity and nucleophilicity properties, the halogen-bonding interactions between the XB donor and the solvent molecules have been found to be very sensitive to the nature of the solvent.15 Studying different resorcinarene cavitand XB donors in various solvents can shed light on the efficiency of halogen bonding. This allows us to extract, from the resulting crystal structures, an understanding of the basic factors that influence the formation and properties of the different solvates. The role of the solvent in the halogen bonding is often unpredictable and one cannot foresee if the solvent acts as an XB acceptor or just a passive solvent. In the current contribution, we present a detailed study of the crystallization of three tetrahaloethynyl cavitands (the rigid methylene-bridged bromo- and iodoethynyl cavitands 1 and 2; and the more flexible ethylene-bridged iodoethynyl, 3, Figure 1) from several different solvents.

Figure 1. The chemical structures of the tetrahaloethynyl cavitands 1 – 3.

Crystalization of the three tetrahaloethynyl cavitands was done from acetone, chloroform, acetonitrile, a methanol-acetone mixture, a methanol-DMF mixture, and a methanol-DMSO mixture. A total of seven crystalline solvates were obtained from these experiments: 1-acetone, 1-CHCl3, 2-MeCN, 2-DMF, 3-DMF, 3-DMSO, and 3-acetone.
Bromoethynyl-functionalized resorcinarene cavitand 1 provided three solvates, 1 CHCl₃, 1 acetone, and 2 MeCN, which all are, surprisingly, isostructural, crystallizing in the monoclinic space group P2₁/n (Figure 2) with very similar unit cell parameters. In each case, the asymmetric unit contains one tetrahaloethynyl cavitand, and one solvent molecule enclosed in the concave space between the lower rim hexyl tails. The cavitand-solvent unit appears in the crystal lattice as a self-included dimer (see below). Only very weak C-H-O/N/Cl hydrogen bonds were observed between the α-carbon hydrogen of the lower rim hexyl chains and the solvent. The flexibility of the hexyl chains induces a slight disorder of the enclosed solvent. The self-inclusion behaviour of these tetrahaloethylcavitand is similar to that of our previously reported tetraidoethynyl cavitand structures.¹⁴

![Figure 2](image.png)

**Figure 2.** Isostructural solvates of (a) 1 CHCl₃, (b) 1 acetone, and (c) 2 MeCN. The ORTEP were drawn at 50 % probability level.

The steric fit of the iodoethynyl group into the cavity of the adjacent cavitand is reinforced by several weak C-H-C≡C triple bond interactions that drive the formation of the self-included dimer. This can be visualized using the Hirshfeld surface analysis of the interactions between the cavitand bridging methylene group hydrogen to the triple bond of the self-included dimer pair, shown by green broken lines in Figure 3b. The large white surface at the molecular interface between the dimer indicates the existence of significant van der Waals interactions, explaining the close packing of adjacent dimers observed by X-ray. Along the self-inclusion axis (the crystallographic c-axis), weak intermolecular Br···O XB pairs link adjacent dimers into a one dimensional (1D) chain (Figures 4 and S1A). Two additional symmetric Br···O halogen bonds (resulting from definitive σ-holes, Figure S1A) bridge the adjacent self-included dimers and have quite short interaction ratios (Rₛₒᵥ = dₛₒᵥ/(Xₛₒᵥ + Bₒᵥ))¹⁷ Rₛₒᵥ = 0.97 in 1 acetone, 0.97 in 1 CHCl₃ and 0.95 in 2 MeCN. Along the crystallographic σ-axis, the arrangement of the molecules indicates a weak Br···π contact, with a Br···C (closest phenyl carbon atom) distance of 3.429 Å for 1 acetone (Figure S1B), 3.594 Å for 1 CHCl₃, and 3.393 Å for 2 MeCN. These halogen bonding interactions are visible from the Hirshfeld surface plots. Although weak these XB are clearly essential for the crystal packing. The Hirshfeld surface analysis also allows for a statistical evaluation of the packing interactions. For example, in the case of 2 MeCN, the H···H contacts comprise almost 38.8 % of all non-covalent interactions, while the C···H contacts provide an additional 17.1 % of all intermolecular interactions. We were not successful in getting crystals of DMF and DMSO solvates using bromoethynyl 1, but managed to obtain them using iodoethylene cavitand 2 and 3.

![Figure 4](image.png)

**Figure 4.** A visualization of the self-assembly of 2 MeCN into 2-dimensional sheets. This secondary bonding between adjacent resorcinarene cavitands along the crystallographic b- (cyan for Br···π) and c-axes (blue for Br···O) is organized through intermolecular halogen bonds.
The O-atom in the DMF molecule can be a good XB acceptor, particularly when iodine is the XB donor. Suitable crystals of tetraiodoethynyl cavitand 2 were grown in chloroform containing a few drops of DMF to provide the 2•DMF solvate. In this crystal, three of the four 2•DMF iodoethynyl groups participate in XBs with the oxygen atoms of three different DMF (Figure 5a), while the fourth iodoethynyl group is embedded into the cavity of a second cavitand to form a self-included dimer, and is better described as a 2:6 complex (2 cavitands with six DMF molecules). These moderately strong XBs lead to smaller $R_{XB}$ values (0.8 in average) than were observed for the bromoethynyl 1 and are in line with those reported previously for the 2•dioxane structure.14 Unlike the 1•solvates (which used XB interactions), the structure extends along the crystallographic c-axis through π···π interactions between the phenyl groups from two cavitands (Figure 5b). It is worth mentioning that only one side of the cavitand is involved in the π···π interactions due to the lattice symmetry.

Figure 5. Halogen-bonded 2•DMF: (a) ORTEP drawn at 30 % probability level, (b) π···π interaction between adjacent cavitands that induces dimer formation, (c) an extension of this self-assembly pattern through the (-1 0 1) plane.

The CPK mode plots to show the geometry difference between the methylene (2) and ethylene (3) bridged resorcinarene cavitands.

Figure 6. The CPK-mode plots to show the geometry difference between the methylene (2) and ethylene (3) bridged resorcinarene cavitands.

Figure 7. Projections of 3•DMF to show: (a) the off-axis self-inclusion dimer; (b) the I···O XB connection between the neighbouring dimers, and (c) the π···π interactions (3.701 Å) along the crystallographic c directions.

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In addition to the halogen-bonded DMF molecule in the 2·DMF solvate, a symmetry-induced disordered second DMF occupies the cavity of the resorcinarene cavitand. Likewise, a third DMF molecule is located between the lower rims of the cavitand instead of the regular solvent molecules seen in the cavitand 1 structures. The disordered cavity-based DMF with its oxygen atom pointing upwards, forms an XB with the iodine of a vertically adjacent cavitand, extending the interactions into 1D-chains along the (-1 0 1) plane (Figure 5c).

Unlike the rigid methylene cavitands 1 and 2, the ethylene bridges increase the internal volume of the cavity and the flexibility of cavitand 3. Thus, the more open cavity has C2v symmetry instead of the pseudo-C4v symmetry of 1 and 2 (Figure 6). In our previous work,14 we reported that the more flexible cavitand 3 has a much weaker tendency to form self-included dimers. This implies that all four iodine atoms will be available as XB donors. In the present work, only one solvate of cavitand 3 demonstrates pure self-inclusion behaviour, viz. 3·DMF. However, in 3·DMF the self-inclusion manifests differently from those of 1 and 2, as the outer side of the iodoethynyl group of 3, whose cavity is occupied by one DMF molecule, faces the inner side of the iodoethynyl group of the second 3 so that the cavity of the second cavitand is filled up by iodoethynyl group of the first cavitand (Figure 7). This arrangement breaks the centre of symmetry, leaving seven XB donor sites free. Interestingly, only five out of these seven iodine atoms are involved in XB s with the oxygen atoms of DMF, leaving two iodine atoms free for additional interactions. The π···π interactions between the phenyl faces of adjacent cavitands is also observed in the lattice of 3·DMF. The π···π interactions extend the molecular arrangement along the crystallographic c-axis (Figure 7c).

The structure of 3·DMSO (Figure 8) is quite different from that of 3·DMF. Instead of a direct self-inclusion dimer as in other cases, one DMSO molecule is encapsulated within the cavity of 3. This resident DMSO is halogen-bonded to one iodine atom of the adjacent cavitand resulting in a 2:2 dimeric assembly (Figure 8a). Of the remaining three iodine atoms of the cavitand, one is halogen-bonded to another DMSO, the second is halogen-bonded with the π-electrons of the ethynyl group of the adjacent cavitand, while the third has no interactions with anything, but sits alone in the void between the cavitands. The two interactions extend the structure into 1D threads along the crystallographic b-axis (Figure 8c). There is

Figure 8. (a) Solvent involved in the self-inclusion dimer in the structure of 3·DMSO; (b) the π···π interaction and (c) the I···π XB s between the dimers; and (d) the packing pattern resulted from the I···π XB s and π···π interactions

Figure 9. Solvent assisted self-inclusion dimer in the structure of 3·acetone (a); and the I···O(cavitand) XB s extending the structure to be 1D (b)
also a face-to-face $\pi \cdots \pi$ interaction between the phenyl groups of two adjacent cavitands (Figure 8b).

The inclusion behaviour of 3 in 3-DMSO emerges also in 3-acetone structure as one acetone molecule is located in the cavity of the cavitand 3 (Figure 9a). The polarized iodine in the iodoethynyl unit of 3 readily forms halogen bonds with the acetone oxygen. Two of the four iodo groups participate in the I–O XBs (Figure 9). In addition, the third iodide is involved in an I–O(cavitand) XB, and $\pi \cdots \pi$ contacts stabilize facing phenyl groups from two adjacent cavitands (Figure 9b).

Conclusions

In conclusion, seven solvates from three tetrahaloethynyl cavitands were successfully crystallized, and their crystal structures analysed. One small (up to five non-H atoms) solvent molecule can be comfortably accommodated in the small space between the lower-rim hexyl chains of the cavitand. Unlike methylene cavitands 1 and 2, all three structures with flexible cavitand 3 show solvent inclusion within the resorcinarene cavity. All solvates demonstrate some common features such as $\pi \cdots \pi$ interactions between the phenyl groups of two adjacent cavitands in the crystal lattice. The oxygen and the $\pi$ system of the cavitands compete with the solvents as potential XB acceptor sites for XB interactions during the crystallization process. Quite surprisingly acetonitrile, which should be a good XB acceptor, does not participate in any XB formation with either bromo-cavitand 1 or iodo-cavitand 2. However, in all cases, the haloethyl groups act as XB donors with the oxygen atoms or the $\pi$ system of the cavitand. When interacting with guest or solvent molecules with stronger XB acceptor ability, such as DMF and DMSO, iodo-cavitand 3 shows prominent I–O halogen bonds. Our results show that the subtle interplay between the XB donor cavitands themselves and with solvent molecules as XB acceptor molecules emerges through complex and many cases unpredictable intermolecular interactions where the fine balance between halogen and hydrogen bonding drives the crystallization process.

Notes and references

# Electrostatic potential surface calculations were carried out using Spartan’14 software18 for the cavitands and solvent molecules in DFT level of theory (B3LYP, 6-311+G** in a vacuum.

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18. SPARTAN ’14; Wavefunction Inc.: Irvine, CA, 2014.