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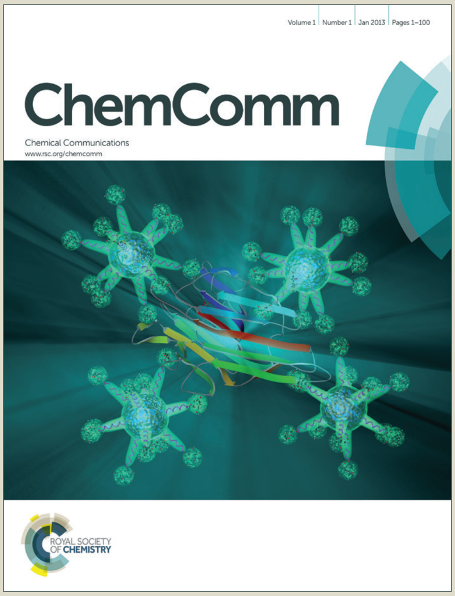

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Tetraiodoethynyl resorcinarene cavitands as multivalent halogen bond donors

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The syntheses and halogen bonded (XB) complexes of tetrahalogenated ethynyl cavitands are presented. These cavitands act as quite rigid 3D multivalent halogen bond donors and show strong XB with oxygen, nitrogen and bromide XB acceptors.

Resorcinarenes are synthetic concave macrocyclic compounds with suitable cavity to complex small organic compounds or cations.[1] Covalent bridging of the adjacent hydroxyl groups in the resorcinarene core results in a more rigid analogues of resorcinarenes, called cavitands.[2] Cavitands are especially attractive family of host molecules because the size, shape and rigidity of the cavity can be varied by using different types of bridging groups.[3] Similarly as for resorcinarenes, functional groups can be introduced at different positions on the cavitand, at the 2-position of the phenyl ring, the lower rim of the connecting bridge.[1,3] Cavitands have been used as the recognition unit or core structural component in various molecular receptor or building block for large supramolecular assemblies.[2,3] The cavity of cavitands can be extended further through the formation of a second cavitand seam leading to the formation of deep cavity cavitands.[4] Deep cavity cavitands possess a more elongated deeper cavity and can bind a variety of larger and/or elongated guests.[5]

Halogen bonding (XB) has been recently defined[6] and extensively reviewed[7] to be an interaction between an electrophilic region associated with a halogen atom (XB donor) in a molecular entity and a nucleophilic region (XB acceptor) in another, or the same, molecular entity. The perfluorohalocarbons (PFHC) are by far the most studied halogen bond donors and can be considered to be 'iconic' halogen bond donors.[8] Though other XB donor systems exists,[9] haloethynyl XB systems have arguably received the least attention. These systems have been elegantly used as XB donors by Goroff[10] and Fourmigué[11], mainly in the solid state. Recently, Diederich *et al.* reported[12] solution studies of XB between (iodoethynyl)benzene donors and quinuclidine.

The most commonly used XB acceptors giving strong XB complexes are the sp^3- and sp^2-hybridized nitrogen atoms and halide anions.[7-9] Yet the substantially less investigated oxygen, sulphur and selenium acceptors can also form strong XB complexes.[7-9] The interaction ratio R_{XB} ($R_{XB}=d_{XB}/(X_{vdw}+B_{vdw})$) can be used as a rough measure of the strength of the halogen bond.[13]

The seminal work of Laurence *et al.*[14] shows iodoethynylarenes through IR studies to be suitable XB donors. Simple iodoethynylalkanes and iodoethynylarenes have thus been utilized in the construction of expanded XB anion organic networks such as hexagonal lattices and interpenetrated networks.[11] The haloethynyl moiety shows quite strong XB donor power, R_{XB} values being on average ca. 0.80, as observed in some of the X-ray structures of such systems.[11,15] The iodoethynyl derivatives by Fourmigué[11] show R_{XB} values between 0.85 – 0.90 for the $R{-}C{\equiv}C{-}I\cdots I^-$ (iodide) and 0.78 and 0.79 for the $R{-}C{\equiv}C{-}I\cdots O$ (DMSO) motif, with the $R{-}C{\equiv}C{-}I\cdots XB$ acceptor angle > 175°. The interaction between $R{-}C{\equiv}C{-}I\cdots Br^-$ and $R{-}C{\equiv}C{-}I\cdots N$ (pyridine) moieties are of similar strength, the R_{XB} for iodine-to-bromide being 0.82 in the crystal structure of tris(bis(ethylenedithio)tetrathiafulvalene 2,3,5,6-tatrafluoro-1,4-bis(iodoethynyl)benzene bromide,[15a] while the iodine-to-nitrogen interaction distance is shorter in the 1-iodo-4-(iodoethynyl)benzene 4-phenylpyridine,[15b] where the R_{XB} is 0.77.

Halogen bonded assemblies involving rigid 3D container compounds, either as XB donors or XB acceptors are rare. A recent example is the dimeric pseudo-capsular XB complex between a rigid tetra(3-pyridyl) cavitand and a flexible tetra(4-iodotetrafluorophenyl)calix[4]arene.[16] We recently reported the utilization of *N*-alkyl ammonium resorcinarene salts as XB acceptors to construct XB analogues of deep cavity cavitands with suitable cavities for guest encapsulation.[17]

Herein, we present the synthesis of preorganized methylene and ethylene connected resorcinarene cavitands with four bromo- and four iodoethynyl groups (Figure 1). Solid state structural analyses of the XB complexes manifesting strong interactions between the polarized iodine XB donor atoms of the cavitands and three different XB acceptors, namely oxygen in 1,4-dioxane, nitrogen in pyridine, and bromide anion in tetrapropyl ammonium bromide (TPABr) are presented.

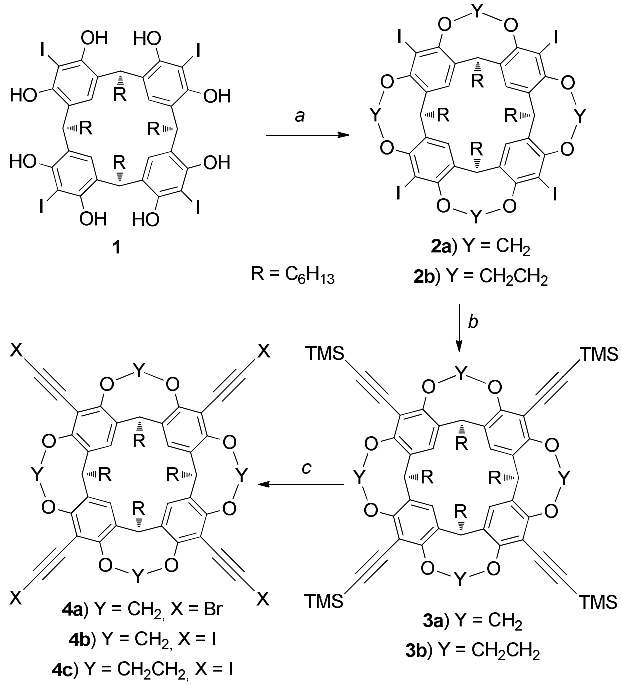

Figure 1. Synthesis of tetrahaloethynyl cavitands. (a) K_2CO_3, DMF, Bromochloromethyl/ethyl, 40-80°C; (b) ethynyltrimethylsilane, CuI, TEA, $[Pd(PPh_3)_4]/[Pd(PPh_3)_2Cl_2]$, 98°C; (c) NBS/NIS, AgF, acetonitrile, room temperature.

Iodinated resorcinarene **1** was prepared according to literature procedures.[18] Treatment of the iodinated resorcinarene **1** with either bromochloromethane or 1-bromo-2-chloroethane in the presence of K_2CO_3 as base gave the methylene and ethylene bridged cavitands **2a,b**.[18] Sonogashira cross-coupling reaction[11,19] between the cavitand **2a,b** and ethynyltrimethylsilane gave the tetra[(trimethylsilyl)ethynyl] cavitands **3a,b**. The cavitands **3a,b** were treated with either *N*-bromosuccinimide (NBS) or *N*-iodosuccinimide (NIS) in the presence of silver fluoride in acetonitrile to give the tetrabromoethynyl and the tetraiodoethynyl cavitands **4a-c**.[20] The ^1H NMR spectra of the cavitands **4a-c** show the compounds to be relatively symmetrical in solution as seen from the relatively simple NMR spectrum in accordance with a C_{4v} symmetrical structure. The diastereotopic protons of the ethylene bridge of the cavitand **4c** are easily identified as two sets of multiplets at 3.7 and 4.4 ppm (SI).

Iodoethynylarenes are known to be good XB donors and have been shown to form interesting architectures[10,11,14,15] with suitable XB acceptors. The halogenated ethynyl cavitands **4a-c** has four XB donor moieties pointing at the same direction from the upper rim of the cavitand. Though the cavitand has a preorganized cavity, the methylene and ethylene bridges connecting the adjacent hydroxyl offer some degree of flexibility. Also the iodoethynyl groups are known to deviate from the expected linearity.[11] The crystal structures of the tetraiodoethynyl methyl cavitand **4b** and the tetraiodoethynyl ethyl cavitand **4c** confirm the XB complexes with 1,4-dioxane, pyridine and Br^- anion in TPABr (Figure 2).

Crystallization of the methylene-bridged cavitand **4b** in 1,4-dioxane resulted in single crystals of the XB complex [**4b**•3.7(1,4-dioxane)•0.3(H_2O)]. Only three iodine atoms act as XB donors toward the oxygen atom of the 1,4-dioxane due to self-inclusion behaviour of the methylene-bridged cavitand (Figure 2b). The non-XB iodine is complexed/embedded into the cavity of the second cavitand resulting in a self-included dimer (Figure 2b). The I···O halogen bonds are relatively short (2.76 – 2.86 Å) resulting in the XB ratio $R_{XB} = 0.78 - 0.82$ (Fig. 2a-c) thus demonstrating the strong XB donor character of the iodoethynyl groups. The C–I···O angles varies between 165 - 168° (Table 1).

Table 1. The XB interaction parameters in the studied complexes.[a]

	I···X	R_{XB}	Distance (Å)	C–I···X angle (°)
4b•1,4-Dioxane	I2···O13	0.80	2.785	165.3
	I3···O14	0.79	2.756	168.1
	I4···O10	0.82	2.856	167.6
4c•Pyridine	I1···N2	0.79	2.781	170.6
	I2···N1	0.78	2.751	175.6
	I1···N2[b]	0.79	2.781	170.6
	I2···N1[b]	0.78	2.751	175.6
4c•BrTPA	I2···Br1	0.83	3.160	177.6
	I3···Br2	0.83	3.164	177.8
	I1···Br1[c]	0.83	3.179	175.5
	I4···Br2[d]	0.82	3.154	174.2

[a] The XB ratio R_{XB} is calculated relative to the sum of the van der Waals radii. [b] 2-x, y, ½-z, [c] 2-x, 2-y, 2-z, [d] 1-x, 2-y, 1-z.

Crystallization of the more flexible ethylene-bridged cavitand **4c** in pyridine resulted in single crystals of the XB complex [**4c**•7(Pyridine)]. The ethylene-bridged cavitand has much weaker self-inclusion tendency and thus all four iodine atoms are free to act as XB donor. The XB distances between nitrogen atom of the pyridine molecule and the iodine atom are 2.75 - 2.78 Å and the XB ratio R_{XB} = 0.78 - 0.79 (Figure 2d, Table 1).

Similarly the cavitand **4c** and TPABr bromide crystallized from a mixture of acetone and $CHCl_3$ gave the XB complex **4c**•2($C_{12}H_{28}N$)•2Br. All four iodine atoms form XB with the bromide anions with distances of 3.15 - 3.18 Å with XB ratios 0.82 - 0.83 (Figure 2a, Table 1).

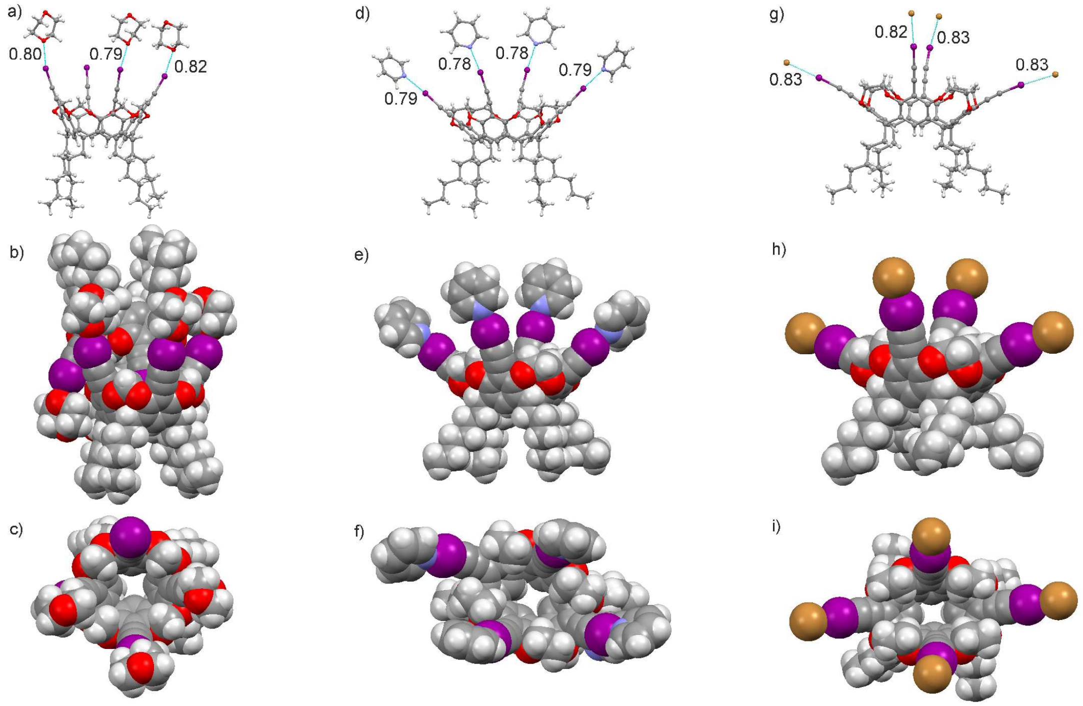

Figure 2. The X-ray structures of (a,b,c) The ball-and-stick and CPK, side view (self-included dimer) and top view (showing the interior cavity) of **4b**•1,4-Dioxane. The ball-and-stick and CPK, side and top view of **4c**•Pyridine (d,e,f) and **4c**•TPABr (g,h,i). The guest solvent molecules, counter cations and hydrogen bond connected solvent molecules are omitted. The XB interactions are highlighted with turquoise colour.

The packing of the complexes in the lattice of **4b**•1,4-dioxane structure shows that the self-included dimers are connecting to two adjacent dimers via 1,4-dioxane induced XB interactions (Figure 3a). The wider upper rim of the ethylene-bridged cavitand leads to a different packing motif of the **4c**•Pyridine complex. The lower rim of the cavitand **4c** is encapsulated into the deep upper rim cavity, formed by the four XB complex pyridines. Thus the **4c**•pyridine XB complexes pack into a polymeric herringbone or cup-pile arrangement with one non-XB pyridine sitting between the hexyl groups of the lower rim (Figure 3b). The remaining two non-XB pyridines fill up the voids outside the cavitand. The XB interactions in the crystal lattice of **4c**•TPABr are clearly different since each bromide anion is halogen bonded to two iodide atoms of the adjacent cavitand and hydrogen bonded to the TPA cation and one water molecule. The two bromide anions connect the two iodoethynyl groups of the same cavitand into a 1D zig-zag polymeric ribbon along crystallography [101] direction. One $CHCl_3$ molecule is encapsulated in the cavity of the cavitand (Figure 3c).

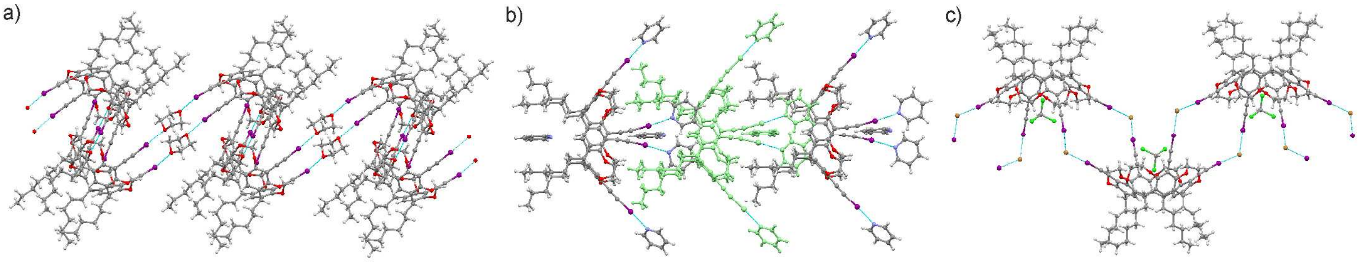

Figure 3. a) The partial packing plot of the self-inclusion complex **4b**•1,4-Dioxane showing the 1,4-dioxane molecules connecting the self-included dimers into a polymeric chain. b) Head-to-tail presentation of the complex **4c**•Pyridine. The upper cavity of the **4c**•Pyridine complex acts as host for the lower rim of the next complex. c) The partial view of the 3D-network of the complex **4c**•TPABr with included $CHCl_3$ shown in each cavitand cavity.

Conclusions

In conclusion, four (iodoethynyl) groups were successfully attached into a rigid or semi-rigid cavitand skeleton as spatially oriented XB donor groups. The XB complexes were successfully formed with three different XB acceptors, *viz.* oxygen in 1,4-dioxane, nitrogen in pyridine and bromide anion in TPABr salt. The more rigid methylene-bridged cavitand **4b** shows strong self-inclusion behaviour, forming a dimer and thus blocking one of the iodoethynyl groups in each cavitand from halogen bonding interaction. The self-included dimer $\mathbf{4b}_2$ then acts as hexavalent XB donor, with XB interaction ratio $R_{XB} = 0.80$ between the oxygen and iodine atoms. The more flexible ethylene-bridged cavitand **4c** does not show similar self-inclusion behaviour and thus acts as tetravalent XB donor for XB acceptors, here nitrogen and bromide anion. The XB interaction distance is shorter to the pyridine nitrogen (R_{XB} = 0.78) than to the bromide anion (R_{XB} = 0.83). These results demonstrate the usefulness of the resorcinarene skeleton to act as a platform for the construction of new 3-D cavitand based halogen bonded supramolecular assemblies. The (iodoethynyl) groups do act as strong XB donors. Up to date we have not yet found suitable conditions and guests to promote the evident dimeric capsular assembly using these concave building blocks. Structurally similar cavitands have been used in the construction of dimeric capsules via hydrogen bonding and metal ion coordination and we are currently pursuing towards the first halogen bonded dimeric capsules using these tetraiodoethynyl resorcinarene cavitands.

Notes and references

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