

Chalcogen Bonding Hot Paper

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Supramolecular Capsules: Strong versus Weak Chalcogen Bonding

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Dedicated to Professor Jean-Marie Lehn on the occasion of his 80th birthday

Abstract: Resorcin[4] arene cavitands containing either 2,1,3benzotelluradiazole or 2,1,3-benzothiadiazole motifs were dimerized to supramolecular capsules by chalcogen bonding. Their respective behavior varied depending on the interaction strength of the chalcogen bonds with Te forming strong interactions and S weak interactions. The tremendous strength of multiple 2Te-2N square interactions led to formation of a chalcogen-bonded dimeric capsule in all solvents, as shown by X-ray crystal structures with 16 short Te-N distances (<2.9 Å) and confirmed by native electrospray ionization mass spectrometry (ESI-MS). With the S cavitand, solventdependent crystallization resulted in different arrangements: either a shifted 2S-2N square-bonded capsule or an interlocked 1D polymer with an infinite π - π stacking array. The association constant to form the dimeric capsule in $[D_8]THF$ at 283 K, solely based on weak 2S-2N square interactions, was determined as $K_a = 786 \,\mathrm{M}^{-1}$.

Chalcogen bonding, the equivalent to halogen bonding^[1] but comprising Group VI elements (S, Se, Te) has become a frequent topic in recent literature.^[2-8] For years, noncovalent contacts with sulfur in biological molecules have been reported.^[9,10] But only recently, widening the scope from sulfur to other Group VI elements, such as selenium or tellurium, revealed the application potential of chalcogen bonding in various fields, such as supramolecular chemistry,^[3,4] medicinal chemistry,^[5] catalysis,^[6] crystallography,^[7] and computational studies.^[8] In particular, the benzochalcogenadiazole motif received considerable attention in the last decades for its tendency to form chalcogen (Z)-bonded 2Z-2N square assemblies.^[7a-d, 8d, 11] Its ability to dimerize in the solid state is discussed in numerous publications (Figure 1, top). Nevertheless, only few experimental studies address the investigation of intermolecular chalcogen-bonding interactions in solution.^[3] In 2015, Taylor and co-workers presented a quantitative study employing 2,1,3-benzochalcogenadiazoles.^[3a] They observed strong complexation of 2,1,3-benzotelluradiazole derivatives with association constants (K_a) at 298 K up to 96 m^{-1} with neutral Lewis bases and up to

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2,1,3-Benzochalcogenadiazole motif: $\begin{array}{c}
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Figure 1. Schematic representation of dimerization with the 2,1,3benzochalcogenadiazole motif for small molecules (top) and applied in a capsular assembly (bottom). Chalcogen-bonding interactions are indicated by red, dashed lines. In perfect capsules, 16 such interactions (8 2Z–2N squares) are established.

 $130\,000\,\text{m}^{-1}$ with anionic Lewis bases. However, no association was observed with the corresponding sulfur and selenium analogues, showcasing the decreased ability of S and Se to establish chalcogen bonds.

Herein, we incorporate the well-established 2,1,3-benzotelluradiazole and 2,1,3-benzothiadiazole motifs in top-rimfunctionalized resorcin[4]arene based cavitands,^[12] and utilized their ability to self-assemble by forming supramolecular capsules (Figure 1, bottom).^[13] Employing the 2,1,3-benzotelluradiazole cavitand (Te cavitand) **1** and its sulfur-containing analogue (S cavitand) **2**, we report for the first time multidentate dimeric capsular assemblies solely based on chalcogen-bonding interactions. We contrast strong Te…N in **1** and weak S…N interactions in **2** and highlight the differences in behavior in the solid state and in solution dependent on the association strength.

The synthesis of target cavitands **1** and **2** is shown in Scheme 1. As precursor, octanitro cavitand **3** was prepared following reported procedures (see Section S1 in the Supporting Information for details).^[14] Tin-mediated reduction of **3** gave an air-sensitive octamino cavitand, which was directly treated with TeCl₄ or *N*-thionylaniline (PhNSO) to give 2,1,3benzotelluradiazole cavitand **1** or 2,1,3-benzothiadiazole cavitand **2**, respectively (see Section S1.3). Longer side chains (C₁₁) were installed for increased solubility in solution studies, while shorter side chains (C₆) were intended for improving the crystallization process.

Suitable crystals for X-ray analysis were obtained from various solvents for both the Te cavitand $\mathbf{1}_{C6}$ and the S

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Figure 2. a) X-ray crystal structure 1_{c6} ... 1_{c6} (left, CCDC: 1873512) obtained from a benzene solution revealing a linear capsule and X-ray crystal structure 2_{c6} ... 2_{c6} (right, CCDC: 1873519) obtained from a toluene solution revealing a shifted capsule. b) Schematic representation of the capsular assembly 1_{c6} ... 1_{c6} with a circular array of 16 Te...N interactions (left) and 2_{c6} ... 2_{c6} with two lines of 6 S...N interactions each (right). Black and gray dots indicate benzochalcogenadiazole moieties. Chalcogen bonds are shown as red dashed lines. c) Top view of 1_{c6} (left) encapsulating a benzene molecule and of 2_{c6} (right) encapsulating a toluene molecule. Gray $C_{cavitand}$, green $C_{solvent}$, blue N, red O, orange Te, yellow S. Distances are given in Å. Hydrogen

atoms are omitted for clarity.[15]

for toluene in Figure 2a, right). Compared to $\mathbf{1}_{C6}\cdots\mathbf{1}_{C6}$, the chalcogen-bonding interactions are not arranged in a circular array but rather in two lines on the elongated sides of the rectangularly shaped capsule (Figure 2b). As observed for $\mathbf{1}_{C6}\cdots\mathbf{1}_{C6}$, a solvent molecule is encapsulated in each hemisphere (Figure 2c). However, the rectangular structure of the $\mathbf{2}_{C6}\cdots\mathbf{2}_{C6}$ cavity binds the guest more tightly reducing the



Scheme 1. Synthesis of cavitands 1, 1_{c6} , 2, and 2_{c6} . Reagents and conditions: i) SnCl₂·H₂O, EtOH/conc. HCl (3:1), 95 °C, 16 h; ii) TeCl₄, NEt₃, toluene, 22 °C, 16 h (1 24% over 2 steps, 1_{c6} 17% over 2 steps); iii) *N*-thionylaniline, NEt₃, toluene, 100 °C, 16 h (2 43% over 2 steps, 2_{c6} 47% over 2 steps).

cavitands **2** and **2**_{C6} (Section S4).^[15] The vast difference in association strength between Te···N and S···N interactions caused remarkable differences in the solid-state structures.

The crystal structures obtained from a solution of Te cavitand $\mathbf{1}_{C6}$ in benzene revealed a perfect linear capsular assembly $\mathbf{1}_{C6}$... $\mathbf{1}_{C6}$ (Figure 2, left). Two head-to-head arranged cavitands form a circular array of 16 strong Te...N interactions in eight 2Te-2N squares with short distances between 2.9 and 2.6 Å (20–28% below the sum of the van der Waals radii,^[16] Figures 2 a,b, left). Each hemisphere encapsulates a benzene molecule deep inside the cavity which establishes moderately strong aromatic interactions with the cavitand walls (Figure 2c, left). Flexibility and rotation of the bound guest resulted in disorder in the crystal structure. Analysis of the crystal packing showed several additional solvent molecules outside the capsule complying with the necessary high packing density in crystals. It was found that the crystals lose the outer solvent molecules after being exposed to air for several days, though maintaining the capsular assembly (see Section S4.3). Notably, an analogous structure displaying a chalcogen-bonded dimeric capsule $\mathbf{1}_{C6} \cdots \mathbf{1}_{C6}$ was obtained from a solution in CHCl₃, though solvent molecules within the cavity were unresolvable owing to fast rotation or small energetic discrimination of different orientations during the crystallization process (Section S4.4).

In contrast to the consistent capsular packing of 1_{C6} , crystallization of S cavitands 2_{C6} proved to be solvent-dependent and resulted in two distinct structures.

Crystallization from aromatic solvents, such as benzene or toluene, yielded a shifted capsular assembly 2_{C6} ... 2_{C6} , bound together by only 12 S...N contacts in 6 2S–2N squares (3.0–3.5 Å, 90–105 % of the sum of the van der Waals radii, shown

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flexibility and establishing more favorable aromatic interactions inside the deep resorcin[4]arene framework.

Intriguingly, crystal structures of 2 obtained from dichloromethane do not display a capsular assembly nor chalcogen-bonding interactions.^[17] Instead, they reveal an interlocked one-dimensional (1D) supramolecular polymeric arrangement with a linear π - π stacking array, where two cavitand walls are incorporated into the cavity of a third hemisphere (Figure 3). To our knowledge, this structure presents the first example in which one resorcin[4]arenebased cavitand encapsulates two aromatic guests in the solid state.^[18] This exception entails a widening of the cavity which is stabilized by the encapsulated 2,1,3-benzothiadiazole moieties undergoing antiparallel π - π stacking with two opposite lying walls (3.4 Å) and edge-to-face interactions with the remaining two walls (center-to-center distances between 4.7–5.3 Å, Figures 3a,b). The crystal packing reveals a membrane-like structure where a hydrophobic layer of intertwining alkyl legs is alternated with an infinite arrangement of interlocked cavitands (Figure 3c).^[19] The alkyl chains pack very tightly, leaving no space for solvent inclusion.

Investigations in solution showed a solvent-dependent conformational switching of 2,1,3-benzothiadiazole cavitand 2, consistent with other resorcin[4]arene-based cavitands in the literature.^[20] In chlorinated solvents (such as CH₂Cl₂, see Figure S9a), the flat kite conformation with equatorially oriented walls dominates, indicated by an upfield shifted methine resonance frequency at 4.2 ppm. The deep vase conformation with axially standing walls on the other hand is stabilized by small aprotic solvent molecules with the ability to solvate the inner cavity (e.g. THF and benzene in Figures S9b,c). There, the methine protons encounter deshielding from the axially oriented walls, resulting in a chemical shift above 5.5 ppm. Note that exclusively the vase conformation was observed for 2,1,3-benzotelluradiazole cavitand 1 and 1_{C6} in all solvents screened, indicated by a methine ¹H chemical shift in the downfield region above 5.5 ppm (Figure S10).

These observations support our findings in the solid state. The crystal structure obtained for Te cavitand $\mathbf{1}_{C6}$... $\mathbf{1}_{C6}$ shows a supramolecular dimeric capsule with 16 short Te-N contacts suggesting exceptionally strong interactions. In all solvents, regardless of solvation of the deep cavity, strong Te---N interactions favor the supramolecular capsule with both hemispheres in the vase conformation. Crystallized in aromatic solvents, S cavitand 2_{C6} in the vase conformation forms a shifted dimeric capsule assembled by S…N chalcogen bonds. It can be reasoned that these weak S…N interactions in solution allow for a dynamic process of forming and breaking the contacts between two hemispheres, resulting in a shifted capsular assembly in the solid state, additionally stabilized by packing effects. In dichloromethane, the kite conformation of 2 and 2_{C6} dominates owing to the lack of proper solvation of the deep cavity. To enable a high packing density upon crystallization, the cavitands are forced into a vase conformation with adjacent cavitand walls stabilizing the thereby formed cavity. Furthermore, the absence of S…N chalcogenbonding interaction in this crystal structure demonstrate the significance of preorganization. Only if ideal geometric



Figure 3. a) X-ray crystal structure **2** obtained from a dichloromethane solution revealing a polymeric arrangement with an infinite π - π stacking array between cavitand walls (CCDC: 1873516). b) Top view of **2**: encapsulation of two 2,1,3-benzothiadiazole scaffolds leads to widening of the cavity. c) Crystal packing shows membrane-like layers of entangled alkyl legs (ca. 13–14 Å width) and stacked cavitands, indicated by gray dashed lines. Gray C, blue N, red O, yellow S. Distances are given in Å. Hydrogen atoms are omitted for clarity.^[15]

requirements for capsule formation in solution are provided by prevalence of the vase conformation, the system is able to establish weak S…N contacts between two hemispheres.

Consequently, we decided to use [D₈]THF in quantitative ¹H NMR studies to provide the necessary geometrical requirements to form a supramolecular capsule while ensur-

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ing sufficient solubility. Dimerization of cavitands 1 and 2 was investigated by a ¹H NMR dilution study at 283 K (see Section S3.2). A highly concentrated solution of 2 at 16.2 mm was diluted stepwise to 0.1 mm. At high concentration, dimerization forces both hemispheres into a more rigid structure. Upon dilution, the capsular assembly dissociates resulting in a more flexible vase conformation, indicated by a clear upfield shift of the methine resonance frequency and all aromatic signals. The association constant could be determined by non-linear curve fitting of the dimerizationinduced chemical shift as a function of concentration. The multitude of weak S…N interactions forming a dimeric capsule 2...2 resulted in an association constant of $K_a =$ $786 \,\mathrm{M}^{-1}$.^[21,22] Dimerization of **2** was further confirmed by determination of the diffusion coefficient through ¹H diffusion ordered spectroscopy (DOSY).^[23] With increasing concentration the diffusion coefficient decreased, indicating a doubling of volume and thus, corroborating dimerization of S cavitand 2 to a chalcogen-bonded capsule 2...2 (see Section S3.4.1).

As expected, the ¹H NMR spectra of Te cavitand **1** in $[D_8]$ THF did not display a change in chemical shift upon dilution (Figure S12). We concluded that strong chalcogenbonding interactions favor formation of a supramolecular structure at all concentrations measured. Hence, a dimeric assembly **1**...**1** could be detected exclusively within the NMR detection limit, never the monomeric cavitand **1**.

The Te capsule $1 \cdots 1$ (and analogously $1_{C6} \cdots 1_{C6}$) displayed a time-dependent transformation in solution from an initial species $(1 \cdots 1)_a$ to a second species $(1 \cdots 1)_b$, noticeable by a doubling and shifting of NMR signals (see Section S3.3). The pace of this transformation was dependent on solvent and concentration ranging from full conversion within one day (e.g. in CDCl₃, 1 mM) to more than one week (e.g. in [D₈]toluene, 10 mm). The equilibrium could be shifted in favor of the second species by heating to $85 \,^{\circ}$ C in [D₈]toluene, as shown for $\mathbf{1}_{C6}$... $\mathbf{1}_{C6}$ in Figure 4. The transformation proves irreversible upon cooling as the second species $(1_{c6} - 1_{c6})_{b}$ continues to prevail. Considering that crystals of the Te capsule 1_{C6} were grown over several days, the second species formed is more likely to crystallize. Indeed, a ¹H NMR investigation of the redissolved crystals verified the sole presence of the second species $(1_{C6} - 1_{C6})_{b}$. The tremendous strength of 16 Te···N interactions in 8 2Te-2N squares leads to the kinetically inert, thermodynamically most stable capsule $(\mathbf{1}_{C6}\cdots\mathbf{1}_{C6})_{b}$. This perfect capsule with 16 Te···N interactions forms very slowly from an initial less symmetrical, less stable capsular assembly with a lower number of Te-N interactions. Fujita and co-workers reported a similar observation for the self-assembly of Pd^{II}- or Pt^{II}-linked macrocycles with 4,4'-bipyridine (bpy).^[24] While the thermodynamically most stable cyclic tetramer was immediately formed with weak Pd…N interactions, strong Pt…N interactions led first to formation of a mixture of oligomers which eventually, after heating to 100 °C for several weeks, resulted in the thermodynamically stable cyclic tetramer after all. However, in the case of our Te cavitand 1, oligomerization could be excluded on taking into account that ¹H DOSY experiments in C_6D_6 gave an equal diffusion coefficient for



Figure 4. Variable temperature (VT) study of 1_{c6} in $[D_8]$ toluene (10 mM, ¹H NMR, 500 MHz). The region of the methine and aromatic signals is displayed. Signals corresponding to species (1_{c6} ··· 1_{c6})_a are indicated in red, to species (1_{c6} ··· 1_{c6})_b in blue. The equilibrium is shifted upon heating from 20 to 85 °C in less than one hour.

both species $(D_{(1\cdots 1)_a} = 2.99 \times 10^{-10} \text{ m}^2 \text{s}^{-1}, D_{(1\cdots 1)_b} = 2.83 \times 10^{-10} \text{ m}^2 \text{s}^{-1}$, see Section S3.4.2), suggesting a comparable volume of $(1\cdots 1)_a$ and $(1\cdots 1)_b$. Furthermore, mass spectrometry showed signals of the singly charged homodimer and monomer but not of oligomeric assemblies (Section S5).

Therefore, we propose for initial species $(1\cdots 1)_a$ a dimeric assembly, similar to the crystal structure obtained for $2_{C6}\cdots 2_{C6}$ (Figure 2 a, right) displaying a shifted supramolecular capsule based on chalcogen bonding.^[25] In a shifted capsule, fewer Te…N interactions than the maximum of 16 in a linear capsule with 8 2Te–2N squares would make this structure more easily accessible but less stable.

Finally, a native electrospray ionization mass spectrometry (ESI-MS)^[26] titration was performed to determine the association constant of the dimerization of Te cavitand 1 to a supramolecular capsule (Section S5). To ensure the presence of the vase conformation of 1 at low concentration while maintaining an environment suitable for ESI experiments, a solvent mixture of DMSO/toluene/MeOH 10:6:1 (v/v/v) was used. Comprising DMSO and protic MeOH, this solvent system allows competitive interactions to chalcogen bonding, possibly weakening the association. Furthermore, the optimized conditions resulted in precipitation after one day, which is why presumably only the association of species $(1 \cdot \cdot \cdot 1)_a$ could be determined. Figure 5 shows an increasing intensity for the singly charged dimer at concentrations going from 9.5 µm to 380 µm while the singly charged monomer signal substantially decreases. This concentration-dependent change in intensity allowed determination of a high association constant of $K_{a,(1\dots 1)_a} = 2.9 \pm 0.4 \times 10^7 \,\mathrm{m}^{-1}$, caused by the cooperativity of several strong Te-N interactions. For the thermodynamic species $(1 - 1)_{b}$ under optimal conditions, without competitive solvent effects and a linear arrangement with 16 Te…N interactions in 8 2Te-2N squares, an even much larger association constant can be expected.

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In summary, we present the first purely chalcogen-bonded supramolecular capsules formed by dimerization of either 2,1,3-benzotelluradiazole or 2,1,3-benzothiadiazole cavitands. Crystal structures of Te cavitand $\mathbf{1}_{C6}$ revealed a highly organized linear capsule with 16 short Te-N chalcogen bonds (2.6–2.9 Å) hosting a benzene molecule in each hemisphere. In solution, the kinetic inertness of multiple strong Te...N bonds resulted in a time-dependent conversion from an initial $(1 \cdots 1)_a$ into the thermodynamically more stable linear capsular assembly $(1 \cdots 1)_{b}$. This species is seen in the crystal structures. The association constant of the initial species was determined by a native ESI-MS titration study in DMSO/ toluene/MeOH ($K_{\rm a,(1\cdots1)_a} = 2.9 \pm 0.4 \times 10^7 \,{\rm m}^{-1}$). In the case of S cavitand 2, solvents stabilizing the vase conformation of hemisphere 2 enabled dimerization to a supramolecular capsule 2...2 based on 12 weaker S...N interactions ($K_a =$ 786 m⁻¹ in [D₈]THF).^[27] In solvents favoring the kite conformation however, no capsular assembly was observed. Instead, crystallization resulted in a 1D supramolecular polymeric arrangement of interlocked cavitands 2. Only vase hemispheres, stabilized by solvent inclusion, provide the crucial preorganization to establish weak S...N interactions in a capsular assembly.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: chalcogen bonding · mass spectrometry · self-assembly · supramolecular capsules · X-ray diffraction

- a) L. C. Gilday, S. W. Robinson, T. A. Barendt, M. J. Langton, B. R. Mullaney, P. D. Beer, *Chem. Rev.* **2015**, *115*, 7118–7195;
 b) G. Cavallo, P. Metrangolo, R. Milani, T. Pilati, A. Priimagi, G. Resnati, G. Terraneo, *Chem. Rev.* **2016**, *116*, 2478–2601.
- [2] K. T. Mahmudov, M. N. Kopylovich, M. F. C. Guedes da Silva, A. J. L. Pombeiro, *Dalton Trans.* 2017, 46, 10121–10138.
- [3] a) G. E. Garrett, G. L. Gibson, R. N. Straus, D. S. Seferos, M. S. Taylor, J. Am. Chem. Soc. 2015, 137, 4126-4133; b) J. Y. C. Lim, I. Marques, A. L. Thompson, K. E. Christensen, V. Félix, P. D. Beer, J. Am. Chem. Soc. 2017, 139, 3122-3133; c) Y. Geboes, F. De Vleeschouwer, F. De Proft, W. A. Herrebout, Chem. Eur. J. 2017, 23, 17384-17392; d) L. Chen, J. Xiang, Y. Zhao, Q. Yan, J. Am. Chem. Soc. 2018, 140, 7079-7082; e) J. Y. C. Lim, I. Marques, V. Félix, P. D. Beer, Chem. Commun. 2018, 54, 10851-10854; f) N. Biot, D. Bonifazi, Chem. Eur. J. 2018, 24, 5439-5443.
- [4] D. J. Pascoe, K. B. Ling, S. L. Cockroft, J. Am. Chem. Soc. 2017, 139, 15160-15167.
- [5] a) B. R. Beno, K.-S. Yeung, M. D. Bartberger, L. D. Pennington, N. A. Meanwell, J. Med. Chem. 2015, 58, 4383-4438; b) A. Lange, M. Günther, F. M. Büttner, M. O. Zimmermann, J. Heidrich, S. Hennig, S. Zahn, C. Schall, A. Sievers-Engler, F. Ansideri, P. Koch, M. Laemmerhofer, T. Stehle, S. A. Laufer, F. M. Boeckler, J. Am. Chem. Soc. 2015, 137, 14640-14652; c) M. Giroud, J. Ivkovic, M. Martignoni, M. Fleuti, N. Trapp, W. Haap, A. Kuglstatter, J. Benz, B. Kuhn, T. Schirmeister, F. Diederich, ChemMedChem 2017, 12, 257-270.
- [6] a) P. Wonner, L. Vogel, M. Düser, L. Gomes, F. Kniep, B. Mallick, D. B. Werz, S. M. Huber, Angew. Chem. Int. Ed. 2017, 56, 12009–12012; Angew. Chem. 2017, 129, 12172–12176; b) S. Benz, J. López-Andarias, J. Mareda, N. Sakai, S. Matile, Angew. Chem. Int. Ed. 2017, 56, 812–815; Angew. Chem. 2017, 129, 830–833; c) S. Benz, A. I. Poblador-Bahamonde, N. Low-Ders, S. Matile, Angew. Chem. Int. Ed. 2018, 57, 5408–5412; Angew. Chem. 2018, 130, 5506–5510.
- [7] a) A. F. Cozzolino, I. Vargas-Baca, S. Mansour, A. H. Mahmoudkhani, J. Am. Chem. Soc. 2005, 127, 3184-3190; b) A. F. Cozzolino, J. F. Britten, I. Vargas-Baca, Cryst. Growth Des. 2006, 6, 181-186; c) A. F. Cozzolino, P. S. Whitfield, I. Vargas-Baca, J. Am. Chem. Soc. 2010, 132, 17265-17270; d) A. F. Cozzolino, Q. Yang, I. Vargas-Baca, Cryst. Growth Des. 2010, 10, 4959-4964; e) H. Wang, J. Liu, W. Wang, Phys. Chem. Chem. Phys. 2018, 20, 5227-5234; f) O. Jeannin, H.-T. Huynh, A. M. S. Riel, M. Fourmigué, New J. Chem. 2018, 42, 10502-10509.
- [8] a) J. S. Murray, P. Lane, T. Clark, P. Politzer, J. Mol. Model. 2007, 13, 1033–1038; b) J. George, V. L. Deringer, R. Dronskowski, J. Phys. Chem. A 2014, 118, 3193–3200; c) K. Kříž, J. Fanfrlík, M. Lepšík, ChemPhysChem 2018, 19, 2540–2548; d) F. De Vleeschouwer, M. Denayer, B. Pinter, P. Geerlings, F. De Proft, J. Comput. Chem. 2018, 39, 557–572.

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These are not the final page numbers!

- [9] R. E. Rosenfield, Jr., R. Parthasarathy, J. D. Dunitz, J. Am. Chem. Soc. 1977, 99, 4860–4862.
- [10] M. Iwaoka, S. Takemoto, S. Tomoda, J. Am. Chem. Soc. 2002, 124, 10613-10620.
- [11] a) K. Ono, S. Tanaka, Y. Yamashita, Angew. Chem. Int. Ed. Engl. 1994, 33, 1977–1979; Angew. Chem. 1994, 106, 2030–2032; b) T. Chivers, X. Gao, M. Parvez, Inorg. Chem. 1996, 35, 9–15; c) Y. Yamashita, K. Ono, M. Tomura, S. Tanaka, Tetrahedron 1997, 53, 10169–10178; d) M. Velusamy, K. R. J. Thomas, J. T. Lin, Y. S. Wen, Tetrahedron Lett. 2005, 46, 7647–7651; e) A. Boudebous, E. C. Constable, C. E. Housecroft, M. Neuburger, S. Schaffner, Aust. J. Chem. 2008, 61, 755–757; f) B. D. Lindner, B. A. Coombs, M. Schaffroth, J. U. Engelhart, O. Tverskoy, F. Rominger, M. Hamburger, U. H. F. Bunz, Org. Lett. 2013, 15, 666–669; g) S. Langis-Barsetti, T. Maris, J. D. Wuest, J. Org. Chem. 2017, 82, 5034–5045; h) S. Ito, T. Taguchi, T. Yamada, T. Ubukata, Y. Yamaguchi, M. Asami, RSC Adv. 2017, 7, 16953– 16962.
- [12] For a recent Review, see: C. Gropp, B. L. Quigley, F. Diederich, J. Am. Chem. Soc. 2018, 140, 2705–2717.
- [13] For other examples of supramolecular capsule formation by self-assembly of resorcin[4]arene based cavitands, see: a) D. Rechavi, A. Scarso, J. Rebek, Jr., J. Am. Chem. Soc. 2004, 126, 7738-7739; b) A. Asadi, D. Ajami, J. Rebek, Jr., J. Am. Chem. Soc. 2011, 133, 10682-10684; c) D. Ajami, J. Rebek, Jr., Acc. Chem. Res. 2013, 46, 990-999; d) N. K. Beyeh, F. Pan, K. Rissanen, Angew. Chem. Int. Ed. 2015, 54, 7303-7307; Angew. Chem. 2015, 127, 7411-7415; e) O. Dumele, N. Trapp, F. Diederich, Angew. Chem. Int. Ed. 2015, 54, 12339-12344; Angew. Chem. 2015, 127, 12516-12521; f) O. Dumele, B. Schreib, U. Warzok, N. Trapp, C. A. Schalley, F. Diederich, Angew. Chem. Int. Ed. 2017, 56, 1152-1157; Angew. Chem. 2017, 129, 1172-1177.
- [14] S. Mosca, Y. Yu, J. Rebek, Jr., Nat. Prot. 2016, 11, 1371-1387.
- [15] CCDC 1873512, 1873513, 1873514, 1873515, 1873516, 1873517, 1873518, 1873519, 1873520 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
- [16] A. Bondi, J. Phys. Chem. 1964, 68, 441-451.
- [17] Similar crystal structures were obtained from a dichloromethane solution for 2_{C6} and even for 2 which has long undecyl legs. Details are shown in Sections S4.5 and S4.6.
- [18] More examples of single self-inclusion of resorcin[4]arene cavitands are in the literature: a) C. von dem Bussche-Hünnefeld, R. C. Helgeson, D. Bühring, C. B. Knobler, D. J. Cram, *Croat. Chem. Acta* **1996**, *69*, 447–458; b) A. R. Renslo, F. C. Tucci, D. M. Rudkevich, J. Rebek, Jr., J. Am. Chem. Soc. **2000**, *122*, 4573–4582; c) B. Dubessy, S. Harthong, C. Aronica, D.

Bouchu, M. Busi, E. Dalcanale, J.-P. Dutasta, J. Org. Chem. 2009, 74, 3923–3926.

- [19] All X-ray structures obtained in this study display a membranelike arrangement in the packing where the C_6 or C_{11} alkyl residues form a hydrophobic layer. More details are presented in Section S4.
- [20] For detailed information on the conformational behavior and the vase-kite equilibrium of resorcin[4]arene based cavitands see: a) J. R. Moran, J. L. Ericson, E. Dalcanale, J. A. Bryant, C. B. Knobler, D. J. Cram, J. Am. Chem. Soc. 1991, 113, 5707–5714; b) D. J. Cram, H.-J. Choi, J. A. Bryant, C. B. Knobler, J. Am. Chem. Soc. 1992, 114, 7748–7765; c) V. A. Azov, B. Jaun, F. Diederich, Helv. Chim. Acta 2004, 87, 449–462; d) P. Roncucci, L. Pirondini, G. Paderni, C. Massera, E. Dalcanale, V. A. Azov, F. Diederich, Chem. Eur. J. 2006, 12, 4775–4784; e) I. Pochorovski, C. Boudon, J.-P. Gisselbrecht, M.-O. Ebert, W. B. Schweizer, F. Diederich, Angew. Chem. Int. Ed. 2012, 51, 262–266; Angew. Chem. 2012, 124, 269–273.
- [21] The given value $K_a = 786 \,\mathrm{m}^{-1}$ is an average of two independent measurements. The estimated uncertainty in K_a is $\pm 20\%$. Details are described in Section S3.2.
- [22] From the literature it is known that suitably sized heteroalicycles form very stable complexes with resorcin[4]arene cavitands based on polar interactions in addition to dispersion interactions: J. Hornung, D. Fankhauser, L. D. Shirtcliff, A. Praetorius, W. B. Schweizer, F. Diederich, *Chem. Eur. J.* 2011, *17*, 12362– 12371. Indeed, performing a dilution study with S cavitand 2 in a solvent mixture of $[D_8]$ THF/C₆D₆ 6:4 resulted in a decreased association constant ($K_a = 146 \pm 3 \text{ M}^{-1}$).
- [23] Y. Cohen, L. Avram, L. Frish, Angew. Chem. Int. Ed. 2005, 44, 520-554; Angew. Chem. 2005, 117, 524-560.
- [24] a) M. Fujita, J. Yazaki, K. Ogura, J. Am. Chem. Soc. 1990, 112, 5645-5647; b) M. Fujita, J. Yazaki, K. Ogura, Chem. Lett. 1991, 20, 1031-1032; c) M. Fujita, Chem. Soc. Rev. 1998, 27, 417-425.
- [25] If the initial species $(1\cdots 1)_a$ undergoes dynamic motion in solution, a shifted capsular assembly similar to the crystal structure of $2_{c6}\cdots 2_{c6}$ (in Figure 2a, right) can tentatively be assumed.
- [26] a) R. H. H. van den Heuvel, A. J. R. Heck, *Curr. Opin. Chem. Biol.* 2004, 8, 519–526; b) A. C. Leney, A. J. R. Heck, *J. Am. Soc. Mass Spectrom.* 2017, 28, 5–13.
- [27] The self-assembly of 2,1,3-benzothiadiazoles in the solid state has been comprehensively studied, see: M. R. Ams, N. Trapp, A. Schwab, J. V. Milić, F. Diederich, *Chem. Eur. J.* 10.1002/ chem.201804261.

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Communications

Chalcogen Bonding

L.-J. Riwar, N. Trapp, K. Root, R. Zenobi, F. Diederich* _____

Supramolecular Capsules: Strong versus Weak Chalcogen Bonding





Strengths and weaknesses: Dimeric chalcogen-bonding capsules display a distinct behavior depending on the association strength, as shown by X-ray structures and confirmed by NMR spectroscopy solution studies. While capsules based on weak S…N interactions rely on solvation and the associated hemisphere preorganization, capsular assemblies formed by strong Te…N interactions are beyond external influences.

