Guest exchange in dimeric capsules of a tetraurea calix[4]arene in the solid state†‡

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A solid powder of hydrogen bonded dimers of a tetraurea calix[4]arene is able to exchange the encapsulated guest in contact with the vapor of a second guest. The molecules of a guest-free powder obtained from a polar solvent cannot rearrange in the solid phase to form new guest-filled capsules under these conditions.

The molecular encapsulation of guests in self-assembled molecular containers is one of the present topics in supramolecular chemistry. Potential applications are seen in various areas, such as separation, molecular recognition in sensors, and transport in nonpolar media.

Numerous examples of dimeric molecular capsules have been described since the first examples were reported by Rebek, de Mendoza et al.[1] Especially cone-shaped molecules such as calix[4]arenes, resorcarenes or resorcarene derived cavitands are suitable building blocks. Their interaction occurs via hydrogen bonding,[2] via electrostatic forces[3] or via metal coordination.[4]

Hydrogen bonded dimeric capsules of calix[4]arenes substituted by urea functions at the wide (1) rim present a special case, since
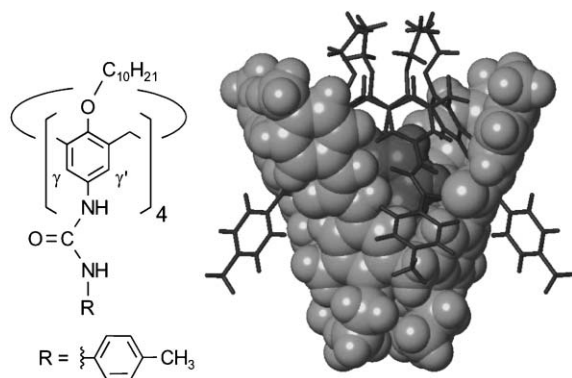

Fig. 1 Tetraurea calix[4]arene 1 and a spherical representation of its dimeric capsule with benzene as included guest (ether residues are shown as ethyl groups). The aryl protons γ, γ' of the calixarene are different within the dimer.

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[b]Fachbereich Chemie, Pharmazie und Geowissenschaften, Abteilung Lehramt Chemie, Johannes Gutenberg-Universität, Duesbergweg 10-14, D-55099 Mainz, Germany. E-mail: vboehmer@mail.uni-mainz.de
† Electronic supplementary information (ESI) available: vapor sorption isotherm of benzene on C at 298 K. See DOI: 10.1039/b607568a
‡ The HTML version of this article has been enhanced with colour images.

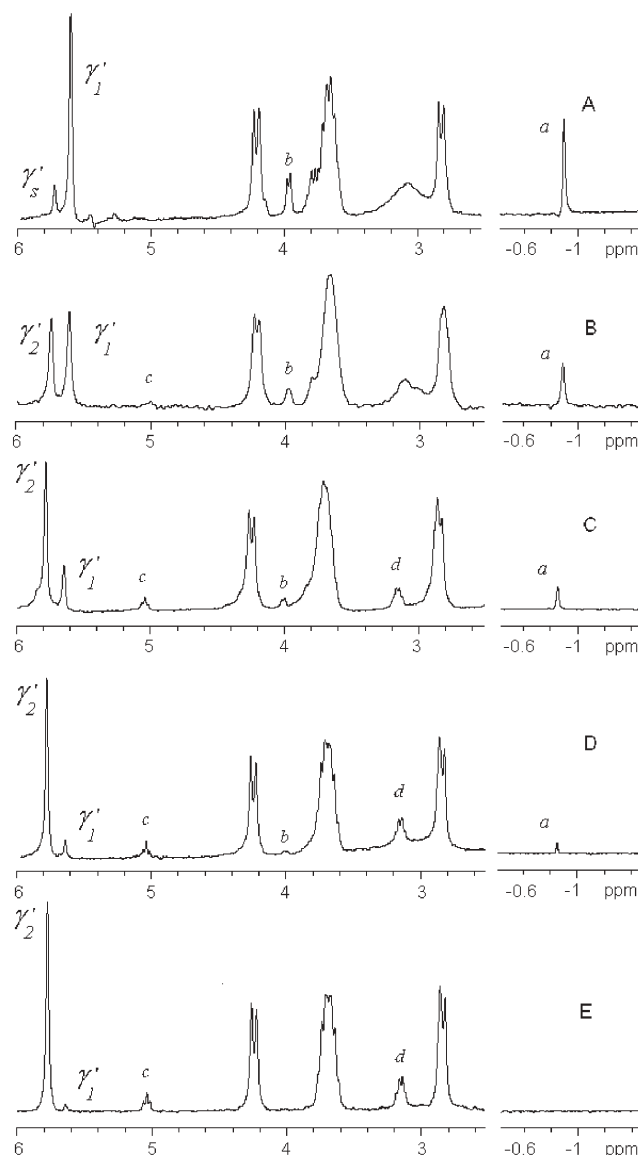**Fig. 2** ^{1}H NMR spectra (C$_6$D$_{12}$, 300 MHz, 295 K) of the initial 1·toluene·1 complex (A) and samples obtained by saturation of 1·toluene·1 powder with fluorobenzene vapor for 3 h (B), 5 h (C), 20 h (D), and 7 days (F); a (δ_H = −0.85 ppm, 3H) and b (3.99, 2H) are the signals of encapsulated toluene; c (5.03, 1H) and d (3.16, 2) are the signals of encapsulated fluorobenzene; γ'_1 (5.64), γ'_2 (5.78) and γ'_s (5.76) are the signals of γ' protons in dimers of 1 with toluene, fluorobenzene and cyclohexane, respectively.

their interaction does not occur between functions placed directly at the rim.[5] The urea groups form a hydrogen bonded belt somewhere in the middle of the interdigitating *para*-substituents which are pointing alternatively in opposite directions (see Fig. 1). Bulky urea substituents R thus lead to lower rates for the guest exchange,[6] which according to early NMR-studies occurs (mainly) *via* dissociation/recombination.[7] The rate of the exchange of an included guest molecule against a solvent molecule is especially low in apolar solvents such as cyclohexane where half-life times between several hours and several months have been observed.[8]

Evaporation of a solution of **1** in toluene leads to a dry powder **A** consisting of dimeric capsules with toluene as guest. This can be easily demonstrated since a solution of **A** in cyclohexane-d_{12} shows the ^{1}H NMR signals for included toluene (*e.g.* $\delta_H = -0.85$ ppm for the methyl group) at the expected intensity.§

If this material is equilibrated (*via* the gas phase) at 298 K in hermetically closed vials with liquid samples of potential guests such as benzene, fluorobenzene, chlorobenzene, bromobenzene, cyclohexane, methylcyclohexane, 1,4-difluorobenzene or tetra-chloromethane in the presence of vapor drying agents (KOH and P_4O_{10}) using a previously described technique,[9] powder **B** is obtained, in which the encapsulated guest is (partly) exchanged.[10] This is unambiguously proved again by the ^{1}H NMR spectra of samples dissolved in C_6D_{12}. Fig. 2 shows a series of experiments for the exchange of toluene against fluorobenzene. Each spectrum was determined for a separately equilibrated sample in the system "guest vapor–solid capsules". The guest exchange is indicated by the methyl signals of the originally included toluene and by the signals of the γ' protons of the host **1** ($\delta_H = 5.64$ for toluene and 5.78 for fluorobenzene as guest).

In a control experiment **1**·toluene·**1** capsules were dissolved in C_6D_{12} containing 0.2 vol% of fluorobenzene. The spectrum of this solution does not show any traces of fluorobenzene capsules, although the concentration of free fluorobenzene is at least 5 times higher than the total concentration of this guest in a C_6D_{12} solution of powder **B**. This proves unambiguously that the encapsulation of fluorobenzene occurred before the dissolution.

The spectra in Fig. 2 indicate that the encapsulated toluene is half-replaced by fluorobenzene during the first 3 h (Fig. 2B), and that this process is practically finished after the first 20 h (Fig. 2D). No traces of initially encapsulated toluene were found (above the signal/noise level) if **1**·toluene·**1** powder was treated with vapors of fluorobenzene for 7 days (Fig. 2E). The same was observed for the solid-phase exchange of toluene-filled capsules with benzene, cyclohexane, methylcyclohexane, 1,4-difluorobenzene and tetra-chloromethane vapors. After one week the products of this exchange¶ showed ^{1}H NMR spectra in cyclohexane-d_{12} identical to those of capsules formed directly in the respective solvent.[8]

The solid-phase exchange with fluorobenzene was additionally proved using ^{19}F NMR spectroscopy. In capsules treated with fluorobenzene vapor, dried and dissolved in C_6D_{12}, signals for free ($\delta_F = -114.52$ ppm) and encapsulated ($\delta_F = -117.52$ ppm) fluorobenzene were found. The CIS value of -3 ppm is in line with the CIS = -5.4 ppm for the same guest encapsulated in similar dimers of tetraphenylureacalix[4]arene with four benzyloxy substituents on the lower rim.[11]

If calixarene **1** is (re)crystallized from methanol–chloroform and dried, a material (**C**) is obtained, which is practically insoluble in cyclohexane. The ^{1}H NMR spectrum of an extract with C_6D_{12} ($\delta_H = 9.53$ (α), 6.88 (β), 7.72 (γ), 5.76 (γ') ppm) corresponds to capsules with included solvent, which may have been formed through dissolution of "monomeric" **1** and subsequent dimerisation. This material **C** was equilibrated for 7 days with benzene vapors as described above to give material **D**. Benzene was added to be bound with a molar ratio of 5 : 1 guest/host monomer, which was not sufficient to form a liquid solution. This ratio is slightly
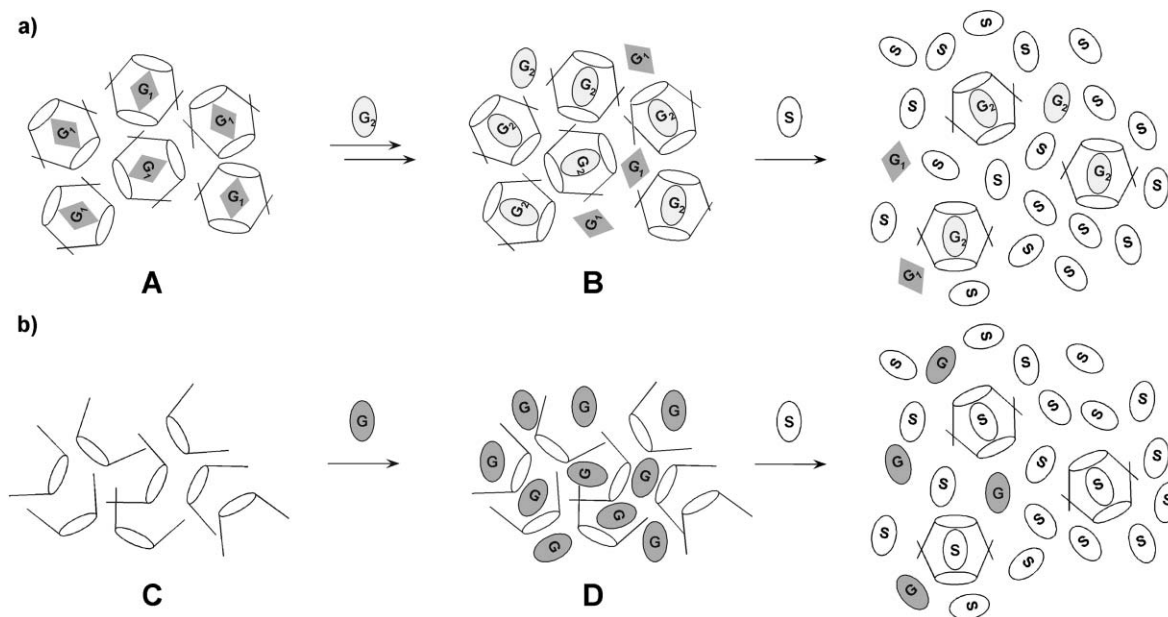

Fig. 3 Schematic representation of the guest exchange: a) A capsular material obtained by evaporation of **1** from toluene exchanges the included toluene against a second guest offered *via* the gas phase. A solution in cyclohexane-d_{12} (S) contains only capsules filled with the second guest. b) Material obtained by crystallization of **1** from chloroform–methanol cannot form capsules with a guest offered *via* the gas phase. An extract with cyclohexane-d_{12} (S) contains only capsules with included S.

higher than the stoichiometry 3.84 : 1 found for a benzene clathrate of a similar tetraureacalix[4]arene derivative.[12] The relative vapor pressure of benzene in the equilibrated systems determined using headspace GC method[13] was 0.70–0.85 (see supporting information†). Hence, the thermodynamic conditions in the solid phase during the preparation of **D** were not far from those of a liquid solution of **1** in benzene, where capsules can be formed. Still, the material **D** showed no better solubility in C_6D_{12} than **C**, and signals of **1**·benzene·**1** capsules were not observed. This experiment shows that the reorganization of calixarene **1** in the solid phase and the formation of soluble dimers with encapsulated benzene is not possible. The same result was obtained when **C** was saturated with toluene vapors under analogous conditions.

To conclude, our experiments and results are summarized in Fig. 3. A dry powder of tetraurea **1** obtained from a polar solvent mixture can absorb a potential guest from the gas phase, but cannot rearrange into dimeric capsules filled by this guest. In contrast, a dry material consisting of dimeric capsules **1**·G_1·**1** containing a first guest G_1 can absorb a second guest G_2 from the gas phase ***and*** exchange it against G_1 to form (quantitatively) capsules **1**·G_2·**1**. This is remarkable, since for the guest exchange the interdigitating *p*-tolylurea residues must be disentangled at least in part.

This behavior contrasts with the properties of van der Waals (vdW) calixarene capsules, which can be formed in the solid phase upon the guest binding.[14] In a recent publication the guest exchange for dimeric capsules of *p*-hexanoylcalix[4]arene is described.[15] Included chloroform was partly replaced by dibenzylketone (DBK), when crystals were kept in a saturated solution of the calixarene in DBK at 70 °C for 3 days without destroying the crystal. However, in this case the capsule is held together by (much weaker) vdW forces and exists only in the crystalline state. A guest exchange is also less astonishing, since no disentanglement of residues has to occur.

Notes and references

§ These signals disappear with a half-life of about 4.2 h since $C_6H_5CH_3$ is replaced by C_6D_{12}.[8]

¶ Although toluene is exchanged nearly completely for chloro- or bromobenzene after 20 h, a residual peak for toluene capsules is still observed after one week ($\delta_H = 5.64$, $\delta_H = -0.85$). This may be due to a lower volatility and a slower diffusion rate of the halogen benzenes, or to their competition with the initially bound toluene for the space inside the capsules.

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