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Self-assembled dimers with supramolecular chirality

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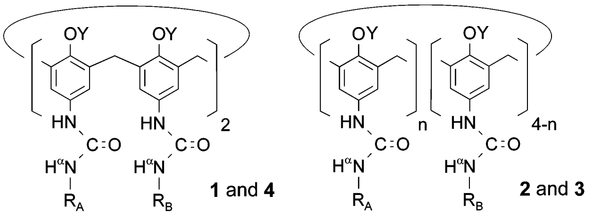
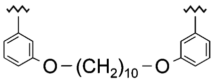
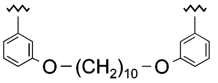
The possibilities to form dimeric capsules with supramolecular chirality from tetraurea calix[4]arenes composed of two different phenolic urea units are discussed in general and demonstrated experimentally for various selected examples.



	n	Y	R_A	R_B
1	-	C_5H_{11}	R	R
2a	1	$C_{10}H_{21}$	Tolyl	*t*-Butyl
3a	2	C_5H_{11}		$C_{12}H_{25}$
3b	2	C_5H_{11}		Tolyl
3c	2	C_5H_{11}	Tolyl	n-Hexyl
3d	2	C_5H_{11}	Tolyl	Adamantyl
4a	-	C_5H_{11}	Tolyl	Adamantyl

Tetraethers of calix[4]arenes, substituted at their wide rim by four urea residues (general formula **1**), form dimeric capsules in non-polar solvents which are held together by a seam of hydrogen bonds between N–H and O=C functions.[1] This dimerisation occurs with the inclusion of a suitable guest molecule, often the solvent itself.

As illustrated in Fig. 1 the two calix[4]arene parts of the capsule are turned by (time averaged) 45° around their common axis with respect to each other. Due to the directionality of the hydrogen bonded belt, the symmetry of a capsule is S_8, since two enantiomeric C_4-symmetrical calix[4]arenes† are combined.

Consequently a heterodimer, composed of two different calix[4]arene tetraureas[2] is chiral (C_4-symmetry), but this chirality[3] is caused by the directionality of the hydrogen bonded belt (Fig 2a). In other words, changing this directionality creates the other enantiomer. If this process occurs fast on the NMR time-scale within a capsule, as we recently showed for capsules with included ammonium cations,[4] racemisation takes place much faster, than dissociation/recombination.[5] Due to their geometry dimeric capsules offer further possibilities to achieve chirality, if we consider tetraurea calix[4]arenes composed by different phenolic units A and B. This difference may be expressed by different residues Y or R or both. Although the single calixarene ABBB (**2**, C_S), AABB (**3**, C_S), and ABAB (**4**, C_{2v}) is achiral, its incorporation into a homodimer makes the assembly chiral, as illustrated in Fig. 2b. This ***supramolecular chirality***[6] is due ***only*** to the mutual arrangement of the two calixarenes in the dimer! The directionality of the hydrogen bonded belt does not create additional stereoisomers, it just decreases the symmetry of the capsule. It may be anticipated that this supramolecular chirality is more pronounced for different residues R_A/R_B than for different ether residues Y_A/Y_B.

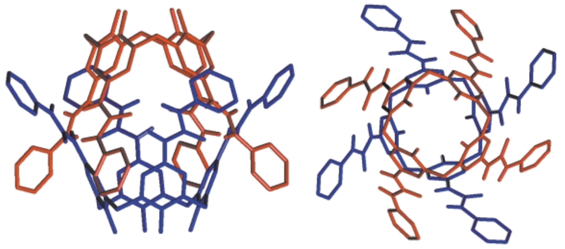


Fig. 1 Molecular shape of a dimeric capsule $\mathbf{1}_2$.

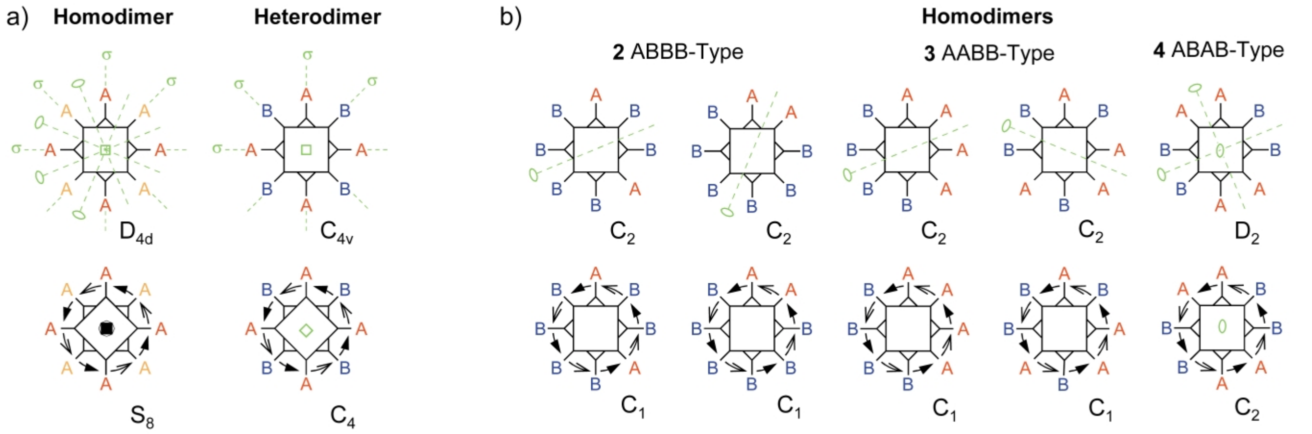


Fig. 2 Schematic representation of the symmetry properties of a) homo- and heterodimer of calixarenes **1** consisting of the same phenolic units (AAAA or BBBB) and b) homodimers of calixarenes consisting of different phenolic units (**2**, ABBB; **3**, AABB; **4**, ABAB); the symmetry class is indicated with and without directionality of the hydrogen bonded belt (symbolised by arrows); □, 0: C_4, C_2 axes; σ: symmetry plane.

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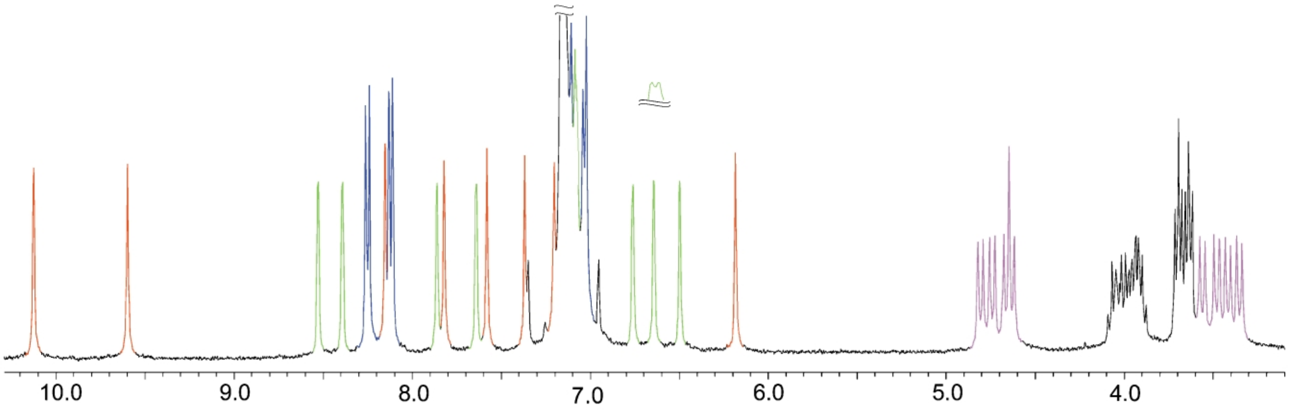

Fig. 5 Section of the ^1H NMR-spectrum 400 MHz of $\mathbf{4a_2}$ in benzene (NH in red, Ar–H_{calix} in green, Ar–H_{tolyl} in blue, Ar–CH_2–Ar in violet).

Calixarenes **2** and **3**, differing in their urea residues R_A and R_B are easily prepared, using protection strategies described earlier.[7] As shown in Fig. 2b, **2** and **3** are expected to form two regioisomeric capsules upon dimerisation.[8] This is demonstrated by the NMR-spectra of $\mathbf{2a_2}$, $\mathbf{3c_2}$ and $\mathbf{3d_2}$ (Fig. 3). The ratio of the two regioisomers can be influenced not only by the residues R (and eventually Y) but for a given compound also by the solvent (= guest). Replacement of R_B = n-hexyl (**3c**) by R_B = adamantyl (**3d**), for instance, changes the ratio from 1:1 to 2:1. The two regioisomers of **2a** are formed in 1:1 ratio in $CDCl_3$, but in a ratio of 1:6 in C_6D_{12}, an interesting effect from the viewpoint of supramolecular chemistry.

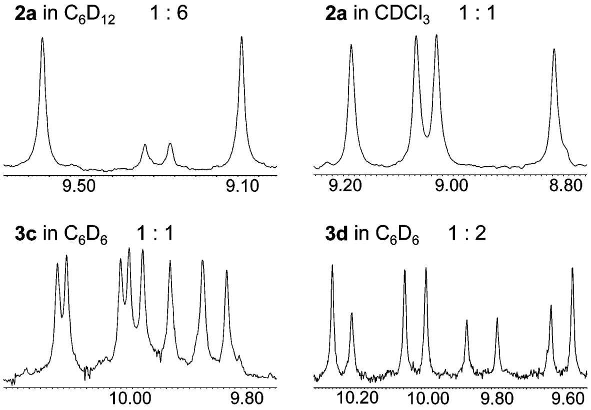

Fig. 3 Section of the ^1H NMR-spectra (Aryl-NH$^\alpha$) of $\mathbf{2a_2}$, $\mathbf{3c_2}$, $\mathbf{3d_2}$ proving the formation of two regioisomeric capsules in the indicated ratio.

The equilibrium between the two regioisomeric capsules can be shifted entirely to one side for compounds of type **3** by a covalent connection between two adjacent residues (**3a,b**). In fact **3a** and **3b** form only one of the two possible dimers, in which an overlap of the two connecting loops R_A–R_A is avoided. The NMR spectra presented in Fig. 4 give an unambiguous evidence.

Tetraureas of type **4**, on the other hand, form only a single regioisomeric dimer (as a pair of enantiomers).‡ Again this is definitely proved by ^1H NMR spectroscopy. Fig. 5 shows the first example of such C_2-symmetrical dimer with different urea residues R_A and R_B. A complete assignment of all signals with the help of 2D NMR spectra: gs-COSY, gs-NOESY, gs-TOCSY confirms the C_2-symmetry of the capsule: 8 singlets for NH, 8 m-coupled doublets for Ar–H (calix); 4 o-coupled doublets Ar–H (tolyl), 8 doublets (geminal coupling) for Ar–CH_2–Ar.

It could be shown that dimeric capsules with supramolecular chirality are in principle kinetically stable enough[9] for optical resolution by chromatography on chiral stationary phases, although a complete separation of all four stereoisomers of $\mathbf{2_2}$ and $\mathbf{3_2}$ was not possible.[10] Resolution is studied presently for dimers of **3a,b** or **4a** where only a single pair of enantiomers exists.

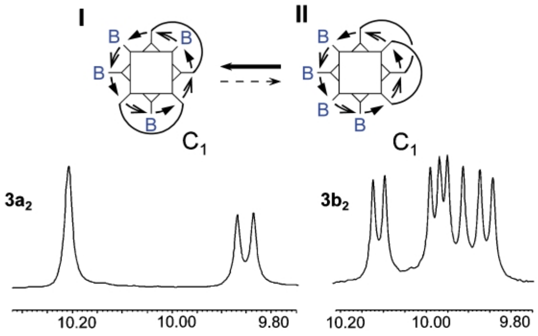

Fig. 4 Schematic representation of the two potential regioisomers **I** and **II** of **3a,b**. Sections of the ^1H NMR-spectra (Aryl-NH$^\alpha$) of $\mathbf{3a_2}$ (4 different protons) and $\mathbf{3b_2}$ (8 different protons) proving the formation of the single capsule **I** with C_1-symmetry.

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Notes and references

† The usual C_{4v}-symmetry of a calixarene in the cone conformation is reduced to C_4 by the directionality of the hydrogen bonded belt.

‡ For an example with different ether residues see ref. 5

1 (*a*) J. Rebek Jr., *Chem. Commun.*, 2000, 637; (*b*) V. Böhmer and M. O. Vysotsky, *Aust. J. Chem.*, 2002, **54**, 671.
2 A stoichiometric mixture of tolyl and tosyl ureas forms exclusively heterodimers: (*a*) R. K. Castellano, B. H. Kim and J. Rebek Jr., *J. Am. Chem. Soc.*, 1997, **119**, 12671; (*b*) R. K. Castellano and J. Rebek Jr., *J. Am. Chem. Soc.*, 1998, **120**, 3657.
3 For chiral capsules formed by tetra ureas with chiral residues R, derived from aminoacids see: R. K. Castellano, C. Nuckolls and J. Rebek Jr., *J. Am. Chem. Soc.*, 1999, **121**, 11156.
4 M. O. Vysotsky, A. Pop, F. Broda, I. Thondorf and V. Böhmer, *Chem. Eur. J.*, 2001, **7**, 4403.
5 Earlier studies with a C_2-symmetrical capsule of type **4** in benzene (present also as guest) suggest a racemisation *via* dissociation/recombination with a half-life time of ~1.5 s: O. Mogck, M. Pons, V. Böhmer and W. Vogt, *J. Am. Chem. Soc.*, 1997, **119**, 5706.
6 For other examples of supramolecular chirality see: (*a*) L. J. Prins, J. Huskens, F. de Jong, P. Timmerman and D. N. Reinhoudt, *Nature*, 1999, **398**, 498; (*b*) L. J. Prins, F. de Jong, P. Timmerman and D. N. Reinhoudt, *Nature*, 2000, **408**, 181.
7 M. Saadioui, A. Shivanyuk, V. Böhmer and W. Vogt, *J. Org. Chem.*, 1999, **64**, 3774.
8 The formation of an unimolecular capsule from a bis-calix[4]arene, covalently connected via one urea function may be considered as a special case of type **2**, see M. S. Brody, C. A. Schalley, D. M. Rudkevich and J. Rebek Jr., *Angew. Chem.*, 1999, **111**, 1738; *Angew. Chem., Int. Ed.*, 1999**, 38**, 1640.
9 M. O. Vysotsky and V. Böhmer, *Org. Lett.*, 2000, **2**, 3571.
10 Y. Okamoto and V. Böhmer *et al.*, unpublished results.