Hydrogen-bonded dimers of tetraurea calix[4]arenes: unambiguous proof by single crystal X-ray analysis

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Self-assembly of calix[4]arenes substituted by four urea residues at the wider rim leads to hydrogen-bonded dimers; the first single crystal X-ray analysis of such a dimer is reported.

Calix[4]arenes bearing urea functions at the 'wider rim' such as **1** form dimers in apolar solvents (and in the absence of other hydrogen bond acceptors) which are held together by 16 hydrogen bonds between the NH and C=O functions.[1,2] We have recently demonstrated by ^{1}H NMR spectroscopy the existence of heterodimers in addition to the two possible homodimers in a solution containing a mixture of two urea derivatives.[3] We report here the single crystal X-ray structure† of **1** which not only confirms unambiguously the existence of such hydrogen-bonded dimers in the crystalline state, but also provides an exact description of their geometry for the first time.[4]

The dimer is composed of two crystallographically independent calix[4]arenes with slightly different shape which are entangled *via* their urea residues. Both molecules lie on a four-fold crystallographic axis turned by 43° with respect to each other. Therefore, all analogous atoms of the four phenolic units are situated at the corners of regular squares, some typical distances of which (diagonals) are shown in Table 1. The inclination of the phenolic units with respect to the crystallographic axis is 27.6 and 25.9° respectively. The diarylurea units form a stiff and nearly planar system with an interplanar angle of 12.4/22.0° between the rings I (phenolic unit of the calixarene) and II (tolyl residue of the urea). The ether–ester residues attached to the phenolic oxygens are also nearly planar and these O–CH$_2$–CO–CH$_2$ planes, containing the ester groups in a *trans*-arrangement, are inclined by 45.0/53.4° with respect to the axis, thus forming a funnel-shaped cavity. The distance between the planes through the methylene carbon atoms is 9.78 Å and for the 'inner' cavity formed by the two calixarenes a volume of 202 Å^3 can be estimated.

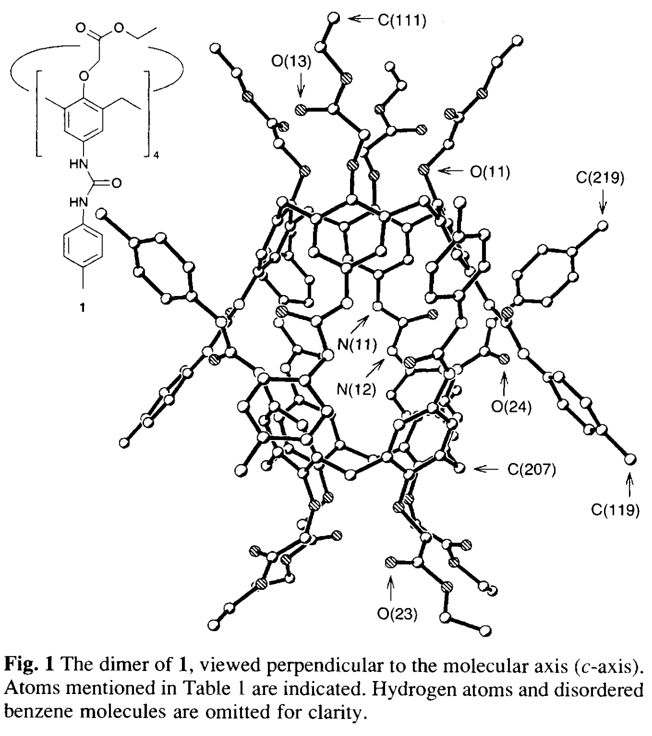

Fig. 1 The dimer of **1**, viewed perpendicular to the molecular axis (*c*-axis). Atoms mentioned in Table 1 are indicated. Hydrogen atoms and disordered benzene molecules are omitted for clarity.

Fig. 2 shows the belt of amide functions forming the hydrogen-bonding system which holds together the dimer. The urea units connected *via* hydrogen bonds are nearly perpendicular to each other (the dihedral angle of the N–CO–N planes is 73.8/83.7°). The distance $N_{n1}\cdots O{=}C$ (3.16/3.10 Å) is more than 0.2 Å longer than the distance $N_{n2}\cdots O{=}C$ (2.85/2.84 Å) showing that both hydrogen bonds are quite different in strength.

Fig. 3 shows that dimers with identical orientation of the carbonyl groups are aligned in the crystal lattice to infinite 'channels'. Their narrowest part is given by the ring of the phenolic oxygens. The funnels formed by the ester groups are opposed to form additional cavities in the crystal lattice with a

Table 1 Diagonal distances (Å) of selected atoms in both calix[4]arene molecules (n = 1, 2) of the dimer of **1c** in the crystal and in the energy minimized structure

	Crystal structure		Energy minimized structure		
Atom	Calixarene 1	Calixarene 2	Without	1 Benzene	2 Benzene
Cn11	13.217	11.187	5.68	5.68	5.68
On3	8.159	7.698	5.92	5.93	5.89
On1	4.375	4.469	4.30	4.29	4.28
Cn07	7.223	7.212	7.20	7.20	7.20
Nn1	9.479	9.300	9.08	9.05	9.22
On4	11.212	11.641	10.43	10.43	10.35
Nn2	12.011	11.934	11.31	11.29	11.32
Cn19	19.447	20.141	17.82	17.83	17.54

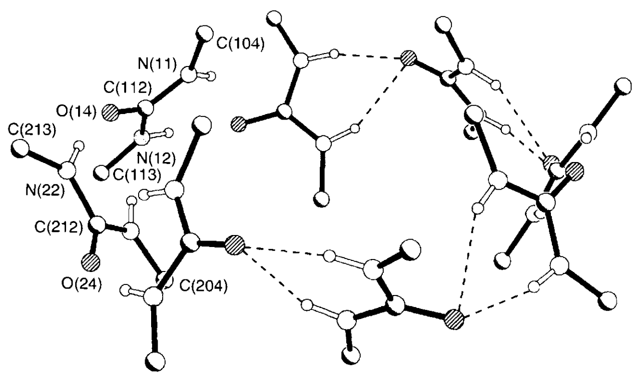

Fig. 2 Ring of the eight urea structures, which are connected alternatingly to the two calix[4]arenes of the dimer. Hydrogen bonds are partly indicated by dashed lines.

size comparable to the 'inner' cavities of the dimers (estimated $V = 225$ Å^3, distance of the planes through the phenolic oxygens in adjacent dimers 8.99 Å, for distances perpendicular to the axis see Table 1). Both cavities and further voids of the crystal lattice contain completely disordered benzene molecules, for which only maxima of the electron density are found. Per dimer the following values can be estimated: 1.06 benzene molecules in the 'inner' cavity, 0.81 benzene molecules in the 'outer' cavity and 5.8 benzene molecules in further voids of the crystal lattice.

The dimer found in the crystalline state entirely confirms the predictions of molecular mechanic calculations.‡ A quantitative comparison shows a nearly perfect agreement for the calixarene part. An rms-value of 0.12 Å results for the eight aromatic rings, the methylene carbons and the phenolic oxygens. Strong deviations are found for the ester groups and for parts of the urea functions (compare Table 1).

The calculations give, in very good agreement with the crystal structure analysis, an estimated volume of 190 Å^3 for the inner cavity,‡ which would be large enough to include even two benzene molecules ($V = 73.5$ Å^3). The interaction energies for the energy minimized complexes are -20.2 kcal mol^{-1} for one included benzene and -40.0 kcal mol^{-1} for a complex with two benzene molecules. Molecular dynamic simulations show for both cases that the complex remains intact during the simulation time (200 ps). A comparison of the minimized structures with and without guest molecules shows that the included benzene has no significant influence on the geometry of the dimer (Table 1).

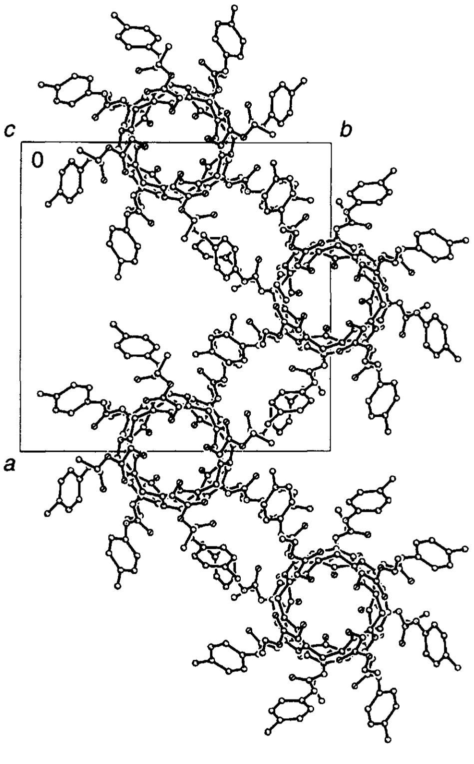

Fig. 3 Arrangement of the dimers in the crystal lattice viewed along the *c*-axis. Hydrogen atoms and benzene molecules omitted.

This work was supported by the Deutsche Forschungsgemeinschaft. We thank Professor J. Rebek, Jr, for sending us manuscripts prior to publication.

Footnotes

† *Crystal data* for **1c**: $C_{76}H_{68}N_8O_{16}\cdot 3.84\ C_6H_6$. $M = 1662.0$, tetragonal, space group $P\text{-}42_12$, $Z = 4$, $a = 21.330(1)$, $c = 21.559(1)$ Å, $U = 9808.9(2)$ Å^3, $D_c = 1.125(1)$ g cm^{-3}, dimensions 0.3 × 0.25 × 0.06 mm, Siemens-three circle diffractometer with CCD, Siemens-rotating anode. Mo-Kα radiation (graphite monochromated, $\lambda = 0.7107$ Å), room temperature, $2\Theta_{max} = 51.5°$, 35 072 reflections measured, 8646 independent reflections, which were all used for the structure determination, $R_{int} = 0.058$, $R_0 = 0.044$, $I(hkl)$ of 5385 reflections $> 2\sigma(I)$, LP-correction, no absorption correction was applied ($\mu = 0.08$ mm^{-1}). Direct methods,[5] refinement with full matrix versus F^2 (SHELXL-93),[6] 580 parameter, H-atoms for the calixarene calculated, $wR(F^2) = 0.225$, $R(F)_{4\sigma} = 0.083$, $S = 1.09$, $\Delta\rho_{min} = -0.36$, $\Delta\rho_{max} = 0.38$ eÅ^{-3}. The positions of the benzene molecules could be accounted for only by refining electron density maxima, which could not be completed to benzene molecules. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See information for Authors, Issue No. 1. Any request to the CCDC for the material should quote the full literature citation and the reference nubmer 182/251.

‡ The molecular mechanics calculations and molecular dynamics simulations were performed as described.[7] For the estimation of the cavity volume a closely packed lattice of imaginary carbon atoms was generated that completely filled the interior of the dimer. The size of this lattice was chosen in that way that the lattice atoms were overlapping with the van der Waals radii of the adjoining atoms. Then the volume of the overlapping regions was determined and substracted from the volume of the lattice.

References

1 K. D. Shimizu and J. Rebek, Jr, *Proc. Nat. Acad. Sci. USA*, 1995, **92**, 12 403; B. C. Hamann, K. D. Shimizu and J. Rebek, Jr, *Angew. Chem.*, 1996, **108**, 1425.

2 Dimerisation was also observed for some calix[4]arenes which are substituted by urea functions on two opposite phenolic units: J. Scheerder, R. H. Vreekamp, J. F. J. Engbersen, W. Verboom, J. P. M. van Duynhoven and D. N. Reinhoudt, *J. Org. Chem.*, 1996, **61**, 3476; for similar hydrogen bonded dimers see *e.g.*: C. Valdes, U. P. Spitz, S. W. Kubitz and J. Rebek, Jr, *Angew Chem.*, 1995, **107**, 2031; N. Branda, R. M. Grotzfeld, C. Valdes and J. Rebek Jr, *J. Am. Chem. Soc.*, 1995, **117**, 85; see aslo ref. 6.

3 O. Mogck, V. Böhmer and W. Vogt, *Tetrahedron*, 1996, **52**, 8489.

4 The structure of two similar self-assembled hydrogen bonded pseudospherical capsules could be confirmed by single crystal X-ray analysis: C. Valdes, U. P. Spitz, L. M. Toledo, S. W. Kubik and J. Rebek Jr, *J. Am. Chem. Soc.*, 1995, **117**, 12 733; C. Valdez, L. M. Toledo, U. Spitz and J. Rebek, Jr, *Chem. Eur. J.*, 1996, **2**, 989.

5 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 1990, **46**, 467.

6 G. M. Sheldrick, SHELXL-93, Program for the Refinement of Crystal Structures, Universität Göttingen, Germany, 1993.

7 M. Clark, R. D. Cramer and N. van Opdenbosch, *J. Comput. Chem.*, 1989, **10**, 982; for the modification of some parameters see: I. Thondorf, G. Hillig, W. Brandt, J. Brenn, A. Barth and V. Böhmer, *J. Chem. Soc., Perkin Trans. 2*, 1994, 2259.

Received, 19th August 1996; Com. 6/05744F