Heterocalixarene Inclusion Chemistry. Structure of a Crystalline Host–Guest Complex Including endo-Calix Ethyl Acetate and exo-Calix Clustering of Water

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Abstract. The X-ray crystal structure of the solvent inclusion compound formed between heterocalix[8]arene **1**, ethyl acetate and water $(1 : 1 : 4.5)$ has been studied. The compound crystallized in tetragonal space group $I4_1/a$, $a = b = 21.278(3)$, $c = 31.290(4)$ Å, $V = 14167(4)$ Å^3, $Z = 8$. The host molecule, incorporating benzimidazol-2-one and 2,5-dimethoxy-1,3-phenylene subunits in an alternate cyclic arrangement, forms an almost perfectly closed cavity which encapsulates one solvent ethyl acetate guest molecule. Water molecules being entrapped in the lattice cages in the form of cyclic and linear clusters bind the bulky inclusion complexes via H-bonds in infinite layers. Two symmetry center related benzimidazole-2-one moieties of two hosts from neighbouring layers in the crystal lattice are arranged such that they partially overlap exhibiting stacking interaction.

1. Introduction

Calixarenes have emerged as a central class of compounds in supramolecular chemistry [1]. In the original sense, they are cyclic oligomers produced by condensation of *p*-substituted phenols with formaldehyde, but appear now as an enormous variety of such compounds with different ring sizes and substituents [2]. Nevertheless, calixarenes made of heterocycles instead of the conventional phenol moiety are still in their infancy [3], although a series of such heterocalixarenes comprising the benzimidazol-2-one characteristic building unit and the 1,3-phenylene com-

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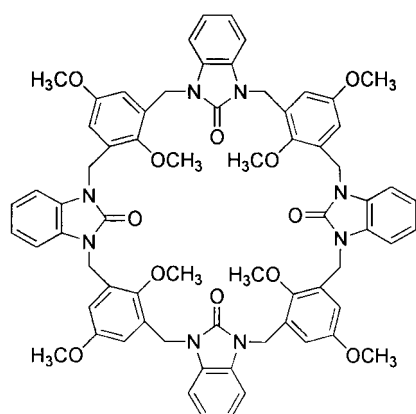
Scheme 1.

ponent in an alternate cyclic arrangement have recently been described by us [4]. One of these interesting compounds refers to the heterocalix[8]arene **1** (Scheme 1).

While analogues of this macroring topology have been shown to encage a number of different guest solvents in the crystalline state [4a], **1** appears to be very selective in this respect yielding only a crystalline complex with ethyl acetate, even when crystallized from mixtures of ethyl acetate with other solvents such as picolines and pyrazoles. This complex proved to contain **1**, ethyl acetate and water in stoichiometric ratio $1:1:4.5$. In order to understand the motive behind this remarkable behaviour demonstrating the selectivity of **1**, the crystal structure of the respective inclusion compound was studied and is presented here.

2. Experimental

2.1. SYNTHESIS AND SAMPLE PREPARATION

The heterocalixarene host **1** was synthesized by a two-step fragment condensation between benzimidazol-2-one and 2,6-bis(bromomethyl)-1,4-dimethoxybenzene building elements using blocking/deblocking, high dilution and template (Cs_2CO_3) techniques [4a]. Crystals of the inclusion compound [**1**·ethyl acetate·H_2O $(1:1:4.5)$] suitable for X-ray diffraction studies were obtained by dissolving the host in ethyl acetate at 77 °C and slow solvent evaporation. The crystals were clear, colorless, well defined with a square bipyramid habit.

2.2. CRYSTALLOGRAPHY

Crystal and data collection details together with structure refinement are summarized in Table I. Data were collected on a KUMA diffractometer equipped with graphite-monochromated CuK_α radiation and corrected for Lorentz and polarization effects. Crystals could only be exposed at room temperature; they decomposed

Table I. Crystal data and structure refinement details

Empirical formula	$C_{68}H_{64}N_8O_{12} \cdot C_4H_8O_2 \cdot 4.5H_2O$
Formula weight	1354.45
Temperature/K	293(2)
Radation, $\lambda/\text{Å}$	1.54178
Crystal system	Tetragonal
Space group	$I4_1/a$
Unit cell dimensions	
$a/\text{Å}$	21.278(3)
$b/\text{Å}$	21.278(4)
$c/\text{Å}$	31.290(4)
$V/\text{Å}^3$	14167(4)
Z	8
$D_{calc}/\text{g cm}^{-3}$	1.270
μ/cm^{-1}	7.64
$F(000)$	5736
Crystal size/mm	$0.60 \times 0.35 \times 0.25$
Θ range for data collection/°	2.51–65.56
Index ranges	$0 < h < 24, -24 < k < 0, 0 < l < 36$
Reflections collected	6170
Independent reflections	5807 [$R(\text{int}) = 0.0479$]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4490/23/444
Goodness-of-fit on F^2	1.009
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0700$, $wR^2 = 0.1990$
R indices (all data)	$R_1 = 0.2124$, $wR^2 = 0.3226$
Largest diff. Peak and hole/e Å^{-3}	0.466 and −0.176

Weighting scheme: $w = 1/[\sigma^2(F_0^2) + (0.1533P)^2]$, where $P = (F_0^2 + 2F_c^2)/3'$.

at any attempt of cooling. Lattice constants and orientation matrices were refined by least-squares fits of 45 reflections in the Θ range 14.6–22.5 °. Three standard reflections were measured after every 200 reflections showing no decay of the crystal during the data collection.

The structure was solved by using the direct method [5] and difference Fourier synthesis and refined by full-matrix least squares [6]. The asymmetric ethyl acetate guest molecule resides close to the two-fold component of inversion axis 4 bar and occupies two positions with equal probability (static disorder). This guest molecule location was refined with fixed s.o.f. 0.5 and individual isotropic thermal parameters for their atoms, using geometrical restraints for covalent distances of a similar ideal molecule [7] as a target. Two of the methoxy groups in the upper rim of the heterocalixarene have also exhibited disorder. The procedure of their

refinement shows that the methyl atoms in each of these groups occupied two positions with equal probability. The presence of the disordered water molecules of partial occupancy was noted towards the latter stages of refinement, in contrast to the ordered one, which has been determined in the first stage of structure solution. A model for this area of strong disordered water molecules with high thermal motion was constrained using crystal chemical estimation. The positional and isotopic thermal parameters for these disordered water molecules (about 2.5 per one heterocalixarene molecule) were included in the further refinement cycles and improved the R-factor from 0.084 to 0.072. Correction for diffuse solvent [8] was also applied. The anisotropic thermal parameters were used for all non-H atoms of the heterocalixarene and the solvent water with full occupancy. The H-atoms of nondisordered H_2O were found on a differential Fourier map and refined in a "ride" mode. The position of most of the other hydrogen atoms was also at first located from difference maps. Then the hydrogen atoms of the CH_3 groups were refined assuming their trigonal pyramidal geometry by rotation around the corresponding O—CH_3 bond. The residual hydrogens on carbon atoms were included in the model in calculated position and were refined as constrained to bonding atoms. For all H-atoms not being refined $U(H) = 1.2U_{eq}$ (attached atom). The positions of hydrogen atoms on disordered atoms did not appear from difference Fourier synthesis and were not considered in the model. Scattering factors were taken from the usual source [9]. The final atomic coordinates with equivalent isotropic displacement parameters for the nonhydrogen atoms are given in Table II.

3. Results and Discussion

3.1. MOLECULAR STRUCTURE

The heterocalix[8]arene host molecule **1** resides around the two-fold component of the inversion axis 4 bar thus having C_2 symmetry (Figure 1). The transannular distances between equivalent two-fold related, bridging carbon atoms indicate an oval molecular shape. The sphericity aberration parameter which is determined on the basis of transannular distances $\Delta sp = d_{max} - d_{min}$ equal 2.581 Å (Table III). The p-methoxyphenyl (A and C) and benzimidazol-2-one (B and D) moieties adopt alternating positions and show a helical arrangement around the macroring with mutual dihedral angles close to 90 °: A/B 88.33(13), B/C 85.30(11), C/D 89.12(15) and D/A$'$ 84.47(13) ° (A$'$ corresponds to symmetry equivalent residue A). The symbolic representation of the molecular conformation on the basis of torsion angles about the methylene bridges (Table IV) (according to the system of Ugozzoli and Andreetti [10] developed for calix[n]arenes) may be easily transferred to the heterocalixarene. The conformation of the present host can be described by the notation "C2−−++−−++" corresponding to alternate cone (Figure 2). The host conformation can also be characterized by the dihedral angles δ between the flat fragments and the mean plane (M) of the eight methylene bridging carbon atoms. The Rms deviation of fitted atoms forming this references plane is 0.252 Å, with

Table II. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{Å}^2 \times 10^3$) for **1** · ethyl acetate · H_2O (1 : 1 : 4.5)

Atom	x	y	z	U_{eq}
O(1)	2264(2)	978(2)	310(2)	82(1)
C(1O1)	1820(3)	478(3)	316(2)	108(2)
O(2)	3216(3)	1681(2)	1870(2)	117(2)
C(1O2)	2821(7)	2157(7)	2093(5)	113(5)
C(2O2)	3862(9)	1522(12)	2019(7)	201(10)
O(3)	4270(2)	−452(2)	1062(1)	95(1)
O(4)	6827(2)	−131(2)	517(1)	68(1)
C(1O4)	7017(3)	−746(3)	659(2)	87(2)
O(5)	6220(4)	1470(3)	1836(2)	176(3)
C(1O5)	5748(13)	1445(14)	2117(9)	195(13)
C(2O5)	5564(8)	1505(11)	1941(8)	151(9)
O(6)	8462(2)	1773(2)	1189(2)	128(2)
N(1)	3996(2)	367(2)	610(2)	73(1)
N(2)	4998(2)	135(2)	683(1)	71(1)
N(3)	7859(2)	1344(2)	648(2)	88(2)
N(4)	8096(2)	2348(2)	609(2)	87(2)
C(1)	2222(2)	1647(3)	924(2)	82(2)
C(2)	2495(3)	1145(3)	714(2)	74(2)
C(3)	3014(3)	835(2)	867(2)	69(2)
C(4)	3259(3)	1035(3)	1257(2)	84(2)
C(5)	2986(4)	1514(3)	1488(2)	91(2)
C(6)	2473(3)	1829(3)	1312(3)	91(2)
C(7)	3323(3)	307(3)	627(2)	79(2)
C(8)	4414(3)	−33(3)	805(2)	73(2)
C(9)	4954(3)	637(3)	386(2)	72(2)
C(10)	5411(3)	943(3)	151(2)	80(2)
C(11)	5207(4)	1419(3)	−110(2)	92(2)
C(12)	4585(4)	1578(3)	−133(2)	92(2)
C(13)	4125(3)	1260(3)	91(2)	81(2)
C(14)	4334(3)	779(3)	346(2)	67(2)
C(15)	5567(3)	−184(3)	809(2)	74(2)
C(16)	6049(3)	245(2)	1005(2)	69(2)
C(17)	6656(3)	256(2)	851(2)	65(1)
C(18)	7102(3)	674(3)	1012(2)	79(2)
C(19)	6928(4)	1075(3)	1342(3)	101(2)
C(20)	6335(5)	1048(3)	1503(2)	110(2)
C(21)	5894(4)	649(3)	1337(2)	89(2)
C(22)	7754(3)	724(3)	834(2)	88(2)
C(23)	8173(3)	1818(3)	853(3)	102(2)

Table II. Continued

Atom	x	y	z	U_{eq}
C(24)	7710(3)	2216(3)	259(2)	76(2)
C(25)	7484(3)	2588(3)	−63(2)	88(2)
C(26)	7090(3)	2293(4)	−362(2)	94(2)
C(27)	6957(3)	1672(4)	−334(2)	89(2)
C(28)	7192(3)	1291(3)	−12(12)	84(2)
C(29)	7564(3)	1584(3)	285(2)	78(2)
C(30)	8316(3)	2975(3)	733(2)	88(2)
O(1W)	4665(3)	−1652(2)	1333(2)	140(2)
O(2W)	9395(13)	2568(14)	1728(11)	353(14)
O(3W)	8864(12)	2477(12)	1910(8)	288(11)
O(4W)	10000	2500	2199(12)	316(17)
O(1G)	4580(8)	1948(9)	1203(6)	217(7)
O(2G)	5038(8)	2706(6)	833(3)	151(4)
C(1G)	3924(12)	2600(15)	832(9)	156(15)
C(2G)	4458(10)	2374(11)	1008(6)	119(6)
C(3G)	5588(15)	2255(16)	994(10)	209(13)
C(4G)	6090(9)	2361(11)	708(8)	110(9)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

maximum deviation being −0.388 Å for the C(7) atom (Table III). Dihedral angles δ equal M/A 118.10(3), M/B 139.18(5), M/C 131.73(13) and M/D 122.81(6)° for residues A, B, C and D, respectively, giving a mean value δ of 128 ° (cf. the mean value of $\delta = 124(2)°$ for calix[4]arenes [2b]). Even though this heterocalixarene host reveals the most elliptical molecular shape among related host molecules [4] (cf. Δsp in the range 0.52–2.123 Å) the similar values of the heterogeneous dihedral and torsion angles indicate a stress-free molecular conformation.

3.2. SUPRAMOLECULAR ASSEMBLY AND PACKING STRUCTURE

The mutual arrangement of the flat aromatic moieties of the host molecule forms an almost perfectly closed cavity which encapsulates one molecule of ethyl acetate. This guest in the middle of the calix cavity lies close to the bridging carbon atoms mean plane (Figure 2). Guest atom distances to this plane range from −0.13(3) [C(4g)] to 1.42(3) Å [O(1g)] and the guest molecule as a whole elongates roughly parallel to the C(30)···C(30′) diameter which is determined as the biggest transannular distance (Table III). As a consequence of two-fold crystallographic symmetry, the guest molecule occupies two positions with equal probability (static disorder). To avoid the short interatomic contacts between guest and host, methoxy
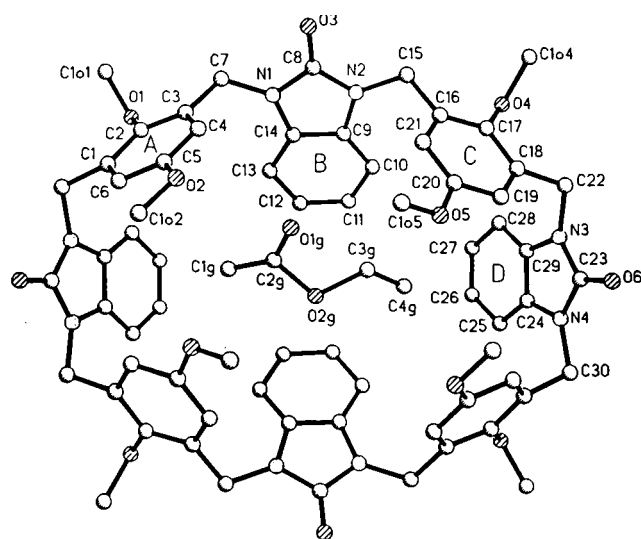
Figure 1. Top-view of the heterocalix[8]arene (**1**) · ethyl acetate · water 1 : 1 : 4.5 molecular associate including partial atomic numbering scheme. Only one location of the disordered guest and the methoxy groups is shown; water molecules and H-atoms are omitted for the sake of clarity.

Table III. Transannular distances d (Å) between equivalent bridging carbon methylene atoms $C \cdots C(1 - x, 1/2 - y, z)$ and the deviations Δ of these atoms from the mean least-squares plane (M) with their esd's (Å)

Atom	d (Å)	Δ (Å)
C(7)	11.750(12)	−0.388(6)
C(15)	11.676(11)	0.181(5)
C(22)	13.945(12)	0.261(6)
C(30)	14.257(12)	−0.055(6)

Table IV. Methylene bridge torsion angles ω (°)

Atoms	ω (°)	Atoms[a]	ω (°)
C(4)—C(3)—C(7)—N(1)	−45.2(7)	C(3)—C(7)—N(1)—C(14)	−76.3
C(9)—N(2)—C(15)—C(16)	59.2(7)	N(2)—C(15)—C(16)—C(21)	51.0(7)
C(19)—C(18)—C(22)—N(3)	−61.8(8)	C(18)—C(22)—N(3)—C(29)	−66.9(8)
C(24)—N(4)—C(30)—C(1)	72.6(8)	N(4)—C(30)—C(1)′—C(6)′	67.7(7)

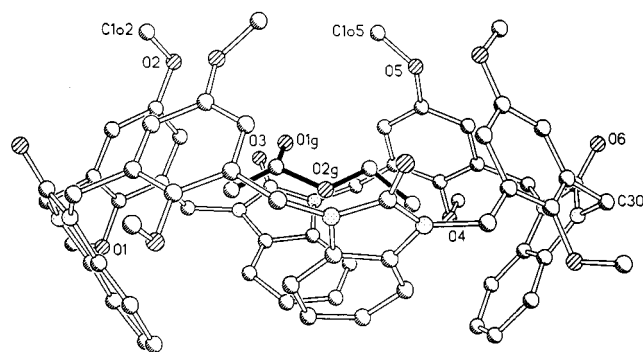[a] Quotation-marks indicate equivalent position $1 - x, 1/2 - y, z$.

Figure 2. Side-view of the host-guest associate showing the cavitate mode of inclusion.
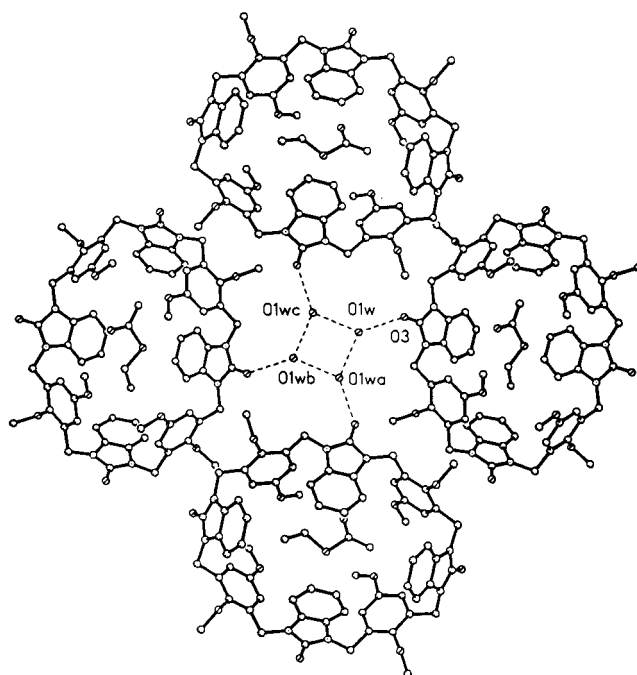

Figure 3. Fragment of the crystal packing in the layer around the regular four-membered water cluster.

groups in the upper rim also occupy two positions with equal probability (the short contacts $O(1g)\cdots C(1O2) = 3.11(3)$ and $O(1g)\cdots C(1O5) = 3.26(3)$ Å are formally observed for one mutual orientation of the guest and the methoxy groups). The methoxy group $O(2)$—$C(1O2)$ is oriented clockwise or anti-clockwise along the macroring in accordance with the guest position. The distinction in these two positions can be described by rotation of the corresponding methoxy group around the $C(5)$—$O(2)$ bond to 162.2°. The second methoxy group in the upper rim [$O(5)$—$C(1O5)$] is also disordered and occupies two positions related by a rotation of 28.2°
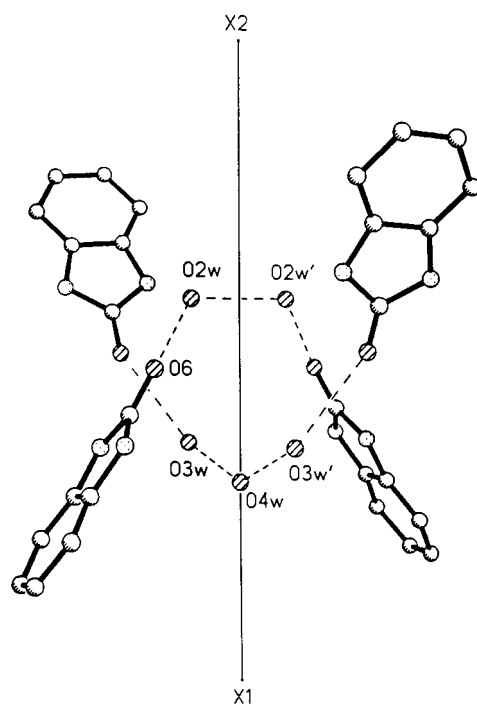
Figure 4. Fragment of the crystal packing showing a plausible location of the disordered linear water clusters and their interaction with the host matrix. Only one cluster (two or three membered) is presented in the unique cavity. The X1–X2 line depicts a part of inversion axis 4 bar.

around the corresponding C(20)—O(5) bond. As mentioned above, the disorder perhaps slightly infringes an ideal C_2-symmetry of the host molecule. Certainly in the unique complex the guest molecule occupies one location, thus the unique complex does not have exact C_2-symmetry. The interatomic contacts between the guest and the macroring interior correspond to or exceed the sum of van der Waals radii. The shortest O...C distances are: $O(1g) \cdots C(4) = 3.42(2)$, $O(5) \cdots C(3g) = 3.40(3)$ Å; the shortest $C \cdots C$ is $C(20) \cdots C(3g) = 3.42(3)$ Å. These distances together with the stress-free molecular conformation of the host in the presence of the asymmetrical guest inside indicates that the hollow shape of the host cavity is roughly complementary to the guest van der Waals surface. Nevertheless, the rather high thermal motion of the guest molecule atoms $[0.119(6) < U_{iso} < 0.217(7)]$ involve relative freedom of guest location in the cavity.

Of particular interest in this crystal is the fact of entrapping of water molecules in the lattice in the form of cyclic and linear clusters. The bulky inclusion complexes pack in such a way that large interstitial lattice voids arise around special positions of inversion axis 4 bar. The four water molecules related by this axis in one such cage (around positions 1/2, 1/4, 1/8, e.g.) form a well organized cyclic cluster *via* H-bonds involving both H-atoms and lone pairs in coopera-

tion [O(1w)$\cdots$O(1w$'$) = 2.792(7), H(1)$\cdots$O(1w$'$) = 1.965, O(1w)—H(1)$\cdots$O(1w$'$) = 161.8°]. These united water molecules bind the four neighbouring complexes by a H-bond to the O(3) carbonyl oxygen atom of the benzimidazol-2-one moiety [O(1w)$\cdots$O(3) = 2.819(6), H(2)$\cdots$O(3) = 1.972 Å, O(1w)—H(2)$\cdots$O(3) = 140.2(2)°] (Figure 3). Five water molecules of partial occupancy (0.5) fill the other intercomplex void around the second special position of inversion axis 4 bar (1, 1/4, 1/8, e.g.). One could propose the model of two [O(2w)$\cdots$O(2w$'$)] and three [O(3w), O(4w)$\cdots$O(3w$'$)] membered water clusters. Such clusters with probability 0.5 (static disorder) occupy this void in turn. The atoms in each cluster related by a two-fold component of the 4 bar axis probably bind the neighbouring two-fold related complex by a H-bond to the O(6) atoms of the benzimidazol-2-one moiety, which point inside this interstitial void (Figure 4). The corresponding distances are: [O(2w)$\cdots$O(2w$'$) = 2.59(6), O(2w)$\cdots$O(6) = 3.11(6), O(3w)$\cdots$O(4w) = 2.58(3) and O(3w)$\cdots$O(6) = 2.84(3) Å].

The water clusters unite the complexes in infinite layers perpendicular to the c crystallographic axis. The inclusion complexes from two proximal layers close the water filled intermolecular cavity. The edge of the benzimidazol-2-one benzene rings approach the regular quartet cluster from both sides. The space filled by the linear water cluster is also covered by two complexes from neighbouring layers but in this case the disordered methoxy groups approach this region. Since the thermal motion of the disordered water [0.29(1) $< U_{\text{iso}} <$ 0.35(1)] and the methoxy groups atoms [0.113(5) $< U_{\text{iso}} <$ 0.20(1)] is very high and these atoms have partial occupancies, this area can be considered as a liquid-like state.

In summary, the structural study showed that in the present crystalline inclusion compound of heterocalix[8]arene (**1**) with ethyl acetate and water both an *endo*-calix and an *exo*-calix complex, i.e., a cavitate and a clathrate mode of supramolecular relationship [11] with a conceived 1 : 1 : 4.5 host · ethyl acetate · H$_2$O stoichiometry is involved. Moreover, two symmetry centre related benzimidazol-2-one units of the host macroring from neighbouring layers of the crystal lattice are placed such that they partially overlap to give an interplanar distance 3.519(7) Å which may be designated a common characteristic feature of this series of basket like hosts [4].

References

1. (a) J. L. Atwood, J. E. D. Davies, D. D. MacNicol, and F. Vögtle (eds): *Comprehensive Supramolecular Chemistry*, Vols 1–10, Elsevier, Oxford (1996). (b) E. Weber: in J. I. Kroschwitz (ed.), *Kirk–Othmer Encyclopedia of Chemical Technology*, 4th edn, Vol. 14, Wiley, New York, p. 122 (1995).

2. (a) C. D. Gutsche: *Calixarenes (Monographs in Supramolecular Chemistry)*, Vol. 1, The Royal Society of Chemistry, Cambridge (1989). (b) J. Vicens and V. Böhmer: *Calixarenes: A Versatile Class of Macrocyclic Compounds (Topics in Inclusion Science)*, Vol. 3, Kluwer, Dordrecht (1991). (c) V. Böhmer: *Angew. Chem.* **107**, 785 (1995); *Angew. Chem. Int. Ed. Engl.* **34**, 713 (1995). (d) V. Böhmer: *Liebigs Ann./Recueil* 2019 (1997) (e) A. Ikeda and S. Shinkai: *Chem. Rev.* **97**, 1713 (1997).

3. (a) G. R. Newkome, Y. J. Joo, and F. R. Fronczek: *J. Chem. Soc., Chem. Commun.* 854 (1987). (b) J. A. E. Pratt, I. O. Sutherland, and R. F. Newton: *J. Chem. Soc., Perkin Trans. 1*, 13 (1988).

4. (a) E. Weber, J. Trepte, K. Gloe, M. Piel, M. Czugler, V. Ch. Kravtsov, Y. A.Simonov, J. Lipkowski, and E. V. Ganin: *J. Chem. Soc., Perkin Trans. 2*, 2359 (1996). (b) J. Trepte, M. Czugler, K. Gloe, and E. Weber: *J. Chem. Soc., Chem. Commun.*, 1461 (1997).

5. G. M. Sheldrick: SHELXS-86, Program for crystal structure solution, University of Göttingen, Germany (1993).

6. G. M. Sheldrick: SHELXL-93, Program for crystal structure refinement, University of Göttingen, Germany (1993).

7. W. B. Schweizer and J. D. Dunitz: *Helv. Chim. Acta* **65**, 1547 (1982).

8. (a) R. Langridge, D. A. Marvin, W. E. Seeds, H. R. Wilson, C. W. Hooper, M. H. F. Wilkins, and L. D. Hamilton: *J. Mol. Biol.* **2**, 38 (1960). (b) H. Driessen, M. I. J. Haneef, G. W. Harris, B. Howlin, G. Khan, and D. S. Moss: *J. Appl. Crystallogr.* **22**, 510 (1989).

9. A. J. C. Wilson: *International Tables for Crystallography*, Vol. C, Kluwer, Dordrecht (1992), Tables 6.1.1.4 (pp. 500–502) and 4.2.6.8 (pp. 219–222).

10. F. Ugozzoli and G. D. Andreetti: *J. Incl. Phenom.* **13**, 337 (1992).

11. E. Weber and H.-P. Josel: *J. Incl. Phenom.* **1**, 79 (1983).