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Structures and C–H···π interactions in DMF inclusion complexes of homoazacalix[4]arenes

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Abstract—The molecular packing modes of DMF inclusion complexes of three homoazacalix[4]arenes were significantly changed by altering the substituents on the azacalixarene skeleton. As for *N*-methyl-*p*-*tert*-butyl-homoazacalix[4]arene, one of the phenolic OH protons transferred to the nitrogen atom was being accompanied by the inclusion of a DMF molecule. The DMF molecule in the cavity of each azacalixarenes is stabilized by C–H···π interaction.
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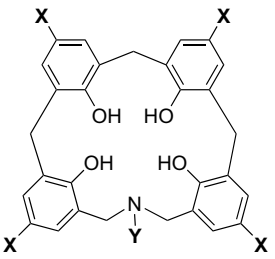
The C–H···π interaction is becoming more and more emphasized in modern chemistry, especially, in the field of biochemistry, and it is considered as an important interaction in the construction of a higher structure of protein.[1] Also in the field of supramolecular chemistry and host–guest chemistry, C–H···π interaction is one of the factors for the structure determination.[2] During the course of our continuous investigation of azacalixarene studies, we found C–H···π interaction plays an important role in the inclusion phenomena of homoazacalix[4]arenes system with a simple molecule, DMF.

In a previous report, we showed that *N*-benzyl-*p*-*tert*-butyl-homoazacalix[4]arene **3** generated a 1:1 complex with a DMF molecule from a mixed solvent (DMSO/DMF).[3] The crystallographic analysis revealed that it was a clathrate complex and the DMF molecule is situated in the crystal lattice. On the other hand, an inclusion complex was obtained from a CH_2Cl_2/DMF solution. Slow evaporation of CH_2Cl_2 and absorption of moisture from air into the DMF formed crystals suitable for crystallographic analysis. Analogous azacalixarene, *N*-benzyl-*p*-methyl-homoazacalix[4]arene **2**, in which the *para* position to phenolic OH group is a methyl group, formed a capsule inclusion complex with two DMF molecules.[4] Such a difference in the inclusion pattern caused by the change in the substituents was noted, and thus, a *tert*-butyl group *para* to the phenolic OH and methyl group on the nitrogen atom was introduced (compound **1** in Fig. 1).

The synthesis of the *N*-methyl-*p*-*tert*-butyl-homoazacalix[4]arene **1** was achieved by a simple one-pot reaction of *p*-*tert*-butylphenol, aq methylamine, and formalin in satisfactory yield (29.3%).[5] A yellow prism suitable for crystallographic analysis was obtained by a method similar to that of the DMF ⊂ **3** complex. Very interestingly, the crystallographic analysis revealed that the crystal packing modes of the DMF complexes of **1**, **2**, and **3** are fairly different from each other (Fig. 2).[6] Another interest is the self-deprotonation–protonation in the cavity of **1**. This is a specific phenomenon to the complex, DMF ⊂ **1**. One of the four phenolic OH protons was transferred to nitrogen atom and formed betaine structure (Fig. 3). A cyclic hydrogen bond pattern is formed



	X	Y
1	*tert*-Bu	Me
2	Me	Benzyl
3	*tert*-Bu	Benzyl

Figure 1. Structures of azacalixarenes **1**, **2**, and **3**.

Keywords: C–H···π interaction; Azacalixarene; Host–guest chemistry; Proton transfer.
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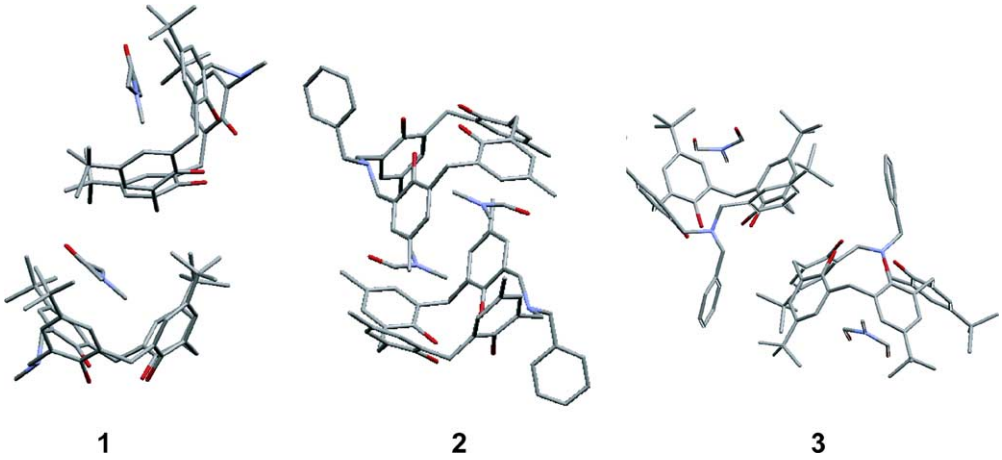

Figure 2. Molecular packing modes in the crystals of the DMF inclusion complexes. Only two molecules are shown for clarity.

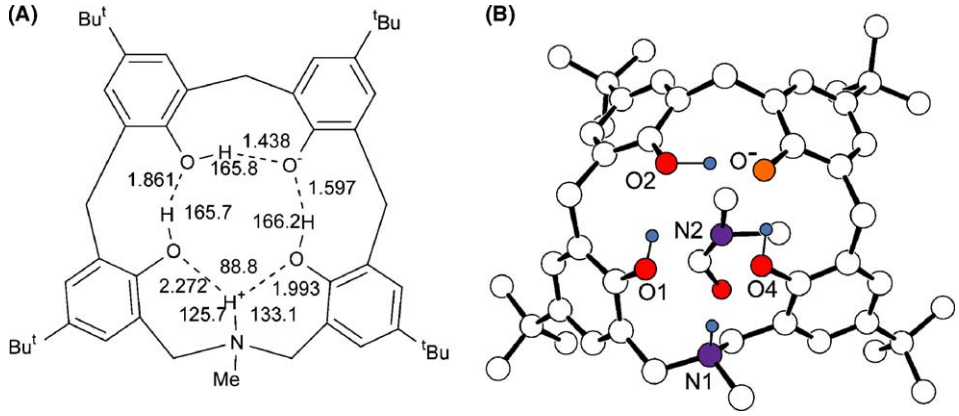

Figure 3. Structure of DMF ⊂ **1**. (A) Schematic representation. The DMF molecule is omitted for clarity. (B) bottom view. Red, oxygen; orange, phenolate oxygen; blue, hydrogen; purple, nitrogen.

along with a bifurcated hydrogen bond, O···N–H$^+$···O. Furthermore, unexpectedly, the proton comes not from neighboring OH but from opposite OH group. This phenomenon apparently reflects to O–H···O bond distances, that is, two O–H···O$^-$···H–O bonds are significantly short (1.438 and 1.597 Å, respectively) but another HO···H–O bond (1.861 Å) is long (Fig. 3, (A)). The O–H···O angles are almost the same (166°) and near to linear, but another O–H–O angle of the bifurcated hydrogen bond O···N–H$^+$···O is almost at right angles (88.8°). Similar proton transfer phenomena were observed in azacalixarene system. Previously, we reported that the *N*,*N*,*N*′,*N*′-tetramethyl-tetrahomodiazacalix[4]arene formed betaine structure by action of a weak base.[7] We also reported that a similar proton transfer occurred by uranyl and lanthanides complex formation of triazacalix[3]- and diazacalix[4]arenes.[8] In this case, proton transfer occurred by coordination of metal ions to O atoms.

On the other hand, proton transfer of **1** was induced by inclusion of a DMF molecule, although analogs **2** and **3** formed DMF inclusion complexes without proton transfer. The driving force of the proton transfer by the DMF molecule inclusion of **1** is not clearly understood, but one of the reasons should be attributed to the basicity of the amine moiety of **1**, **2**, and **3**, viz., tribenzylamine is reported to be a weaker base than dibenzylamine.[9] Origin of yellow color of the DMF ⊂ **1** can be speculated as a result of intramolecular charge-transfer caused by the phenolate formation.

In each DMF inclusion complex, CH–π interaction between an *N*-Me group of DMF and benzene ring was clearly observed. As shown in Figure 4, one of the *N*-Me group of the DMF closes to two of the four aromatic rings. Table 1 summarizes short contacts between *N*-Me carbons (protons) and two aromatic rings. Interestingly, the DMF molecule went into the cavity from the side of the more bulky *N*,*N*-dimethyl group (not from the CHO group).

The C–H···π interaction is a kind of weak hydrogen bond between C–H and π electron, and several examples have been shown in calixarene inclusion complexes.[10] The average non-bonding distance of C–H···π was estimated to be 2.91 Å by CSD crystallographic database search.[1a–c] Furthermore, a protein data bank analysis estimated that the most frequently occurred distance between C and π plane is 3.7–3.8 Å.[1h] Therefore, by the comparison of these values with C–H···π distances of DMF ⊂ **1**, **2**, and **3**, it is obvious that each *N*-Me group

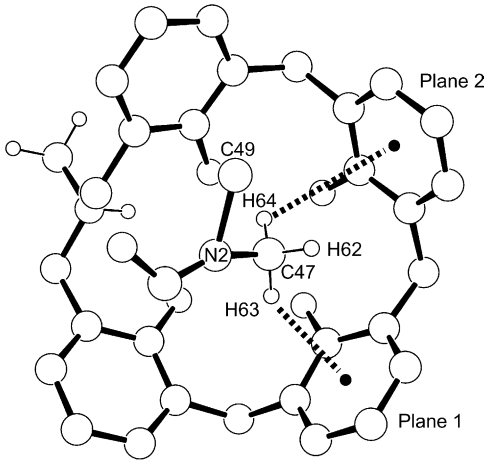

Figure 4. CH···π interaction in the inclusion compound, DMF ⊂ **1**. Protons except H62, H63, H64, and NH^{+}–CH_3 were omitted for clarity.

Table 1. Distances between *N*-Me carbon (proton) and benzene rings (Å), which are shown to two decimal places and rounded off to three decimal places

	CH_3 (DMF)···π plane 1		CH_3 (DMF)···π plane 2	
DMF ⊂ **1**	C (47)	3.44	C (47)	3.53
	H (63)	2.67	H (64)	2.90
DMF ⊂ **2**	C (161)	3.37	C (161)	3.62
	H (150)	2.52	H (151)	3.08
DMF ⊂ **3**	C (53)	3.32	C (53)	3.46
	H (65)	2.60	H (66)	2.83

Plane 1 of DMF ⊂ **1**: C(9)–C(10)–C(11)–C(12)–C(13)–C(14).
Plane 2 of DMF ⊂ **1**: C(16)–C(17)–C(18)–C(19)–C(20)–C(21).
Plane 1 of DMF ⊂ **2**: C(2)–C(3)–C(4)–C(5)–C(6)–C(7).
Plane 2 of DMF ⊂ **2**: C(26)–C(27)–C(28)–C(29)–C(30)–C(31).
Plane 1 of DMF ⊂ **3**: C(24)–C(25)–C(26)–C(27)–C(28)–C(29).
Plane 2 of DMF ⊂ **3**: C(13)–C(14)–C(15)–C(16)–C(17)–C(18).

showed relatively short contact. Charge transfer interaction is another candidate of driving force of the DMF inclusion, but by looking at these inclusion structures, the major driving force should be attributed to C–H···π interaction.

In summary, three different types of packing modes of inclusion complexes took place by altering the combination of substituents of azacalix[4]arene on the *para* position of the aromatic ring and on nitrogen atom. This information will be useful to further design the supramolecular system based on azacalixarenes. Azacalixarene **1** formed a specific structure possessing + and − charges in the molecule as a result of intramolecular proton transfer. Furthermore, it was revealed that the major driving force of the inclusion of DMF molecule is C–H···π interaction.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.07.144.

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5. A mixture of *p-tert*-butylphenol (100 g, 0.67 mol) and 40% formalin (110.0 mL, 1.36 mol) was cooled in an ice bath. To this solution, 40 % aq methylamine (110 mL, 1.27 mol) was added in a small portion. Potassium hydroxide (4.3 g, 0.095 mol) was added to this mixture and heated at 60 °C with continuous stirring. The yellow sticky mass was separated after 24 h, which was collected by decantation and 500 mL of xylene was added. The mixture was heated under reflux for 72 h. The solvent was removed under reduced pressure and the resultant material was chromatographed on silica gel with CH_2Cl_2–MeOH (95/5, v/v) as an eluent. The obtained crude compound **1** was recrystallized from cyclohexane. Cyclohexane adduct, **1**·3/2C_6H_{12} was obtained as pale yellow powder. 39.9 g (29.3 %). The spectral and analytical data were reported previously (see Ref. 4).
6. Crystal data for DMF ⊂ **1**: $C_{49}H_{68}N_2O_5$, Mr = 765.09 g mol^{-1}, colorless block (grown from CH_2Cl_2–DMF), size 0.60 × 0.50 × 0.10 mm, monoclinic, space group $P2_1/n$ (#14), $a = 13.1531(5)$, $b = 12.8871(5)$, $c = 26.5381(9)$ Å, $\beta = 94.0196(5)°$, $V = 4487.3(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.13$ g cm^{-3}, μ(Mo Kα) = 0.72 cm^{-1}, $F(000) = 1664.00$, $T = 160.0 \pm 1$ °C using the $\omega - 2\theta$ scan technique to a maximum 2θ value of 55.0°. A total of 37,419 reflections were collected. The final cycle of the full-matrix least-squares refinement was based on 6316 observed reflections ($I > 3.00\sigma(I)$) and 523 variable parameters and converged with unweighted and weighted agreement factors of $R = 0.062$, $Rw = 0.095$, and GOF = 1.27. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.67 and −0.24 e$^-$/Å^3, respectively.
Crystal data for DMF ⊂ **3**: $C_{55}H_{65}N_2O_5$, Mr = 834.13 g mol^{-1}, yellow block (grown from CH_2Cl_2–DMF), size 0.29 × 0.17 × 0.22 mm, monoclinic, space group $P2_1/c$ (#14), $a = 9.9662(3)$, $b = 16.7535(4)$, $c = 29.6474(6)$ Å. $\beta = 93.1734(6)°$, $V = 4942.6(2)$ Å^3,

$Z = 4$, $\rho_{calcd} = 1.12$ g cm^{-3}, μ(Mo Kα) = 0.71 cm^{-1}, $F(000) = 1796.00$, $T = -160.0 \pm 1$ °C using the $\omega - 2\theta$ scan technique to a maximum 2θ value of 55.0°. A total of 42,460 reflections were collected. The final cycle of the full-matrix least-squares refinement was based on 4775 observed reflections ($I > 2.00\sigma(I)$) and 568 variable parameters and converged with unweighted and weighted agreement factors of $R = 0.076$, $Rw = 0.226$, and GOF = 1.21. The maximum and minimum peaks on the final difference Fourier map corresponded to 1.13 and -0.71 e$^-$/Å^3, respectively.

Crystallographic data (excluding structure factor) for structures of DMF ⊂ **1** and DMF ⊂ **3** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-213847 and CCDC-230864. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 1223 33603; e-mail: deposit@ ccdc.cam.ac.uk).

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