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Crystal structure and inclusion property of *p*-*tert*-butylthiacalix[6]arene

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Abstract

Although the reaction of *p*-*tert*-butylphenol with elemental sulfur in the presence of CsOH as a base catalyst yielded a complex mixture comprised of sulfur-bridged phenol oligomers, *p*-*tert*-butylthiacalix[6]arene (TC6A) could be isolated in an appreciable yield (0.8%). The X-ray analysis revealed that TC6A adopted a distorted cone conformation stabilized by two sets of hydrogen bondings comprising three phenolic OH groups. The recrystallization from various solvents showed that TC6A had higher inclusion ability toward more guests than TC4A did, suggesting that the expanded central cavity and/or the crystal lattice of the former allowed a more comfortable accommodation of the guest molecules.

Keywords: calixarenes; sulfurization; X-ray crystal structures; inclusion.

In the last decade, calix[*n*]arenes have attracted much attention as versatile host molecules owing to the ready availability of a wide range of [*n*]arenes (n=4∼8) and the ease in the chemical modification at the lower rim (phenolic OH groups) and/or the upper rim (the *p*-position).[1,2] By contrast, replacement of the bridging methylene groups by hetero atoms had long been an almost unexplored strategy because of the synthetic difficulty. For example, Sone et al. first reported the synthesis of *p*-*tert*-butylthiacalix[4]arene (TC4A, Scheme 1) by stepwise joining of the phenol unit by epithio linkage followed by acid-catalyzed cyclization of the acyclic tetramer, but the tedious procedure with low yield apparently prevented its utilization as a host molecule.

Since we reported the facile synthesis of TC4A,[3,4] its ready availability led us to develop its functions in a wide variety of ways, including metal-ion recognition, inclusion of halomethanes, and chiral discrimination.[5] It should be noted that most of these functions are ascribed to the intrinsic properties of

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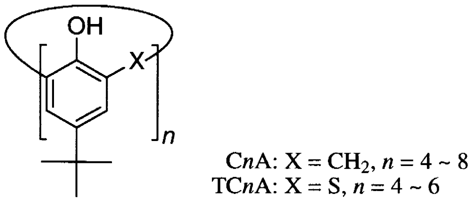

Scheme 1. The structure and abbreviations of *p*-*tert*-butylcalix[*n*]arene (C*n*A) and *p*-*tert*-butylthiacalix[*n*]arene (TC*n*A)

sulfur such as coordination ability to metal ions, oxidizability to sulfoxide and sulfone, the larger size and increased fluxionality than those of the methylene-bridged calix[4]arene skeleton, which have invoked the recent growing interest in the chemistry of TC4A.[6]

Now it is obvious that the extension of the number of the phenol units of the TC*n*A (Scheme 1) from *n*=4 to larger numbers is not only highly interesting but also of great importance, as it would enlarge the potentials of TC*n*As as synthetic receptors. As the first success in our efforts in this line, herein we report the isolation of a small, but appreciable amount of TC6A sufficient for study of its crystal structure and inclusion property.

In previous papers, we reported the synthesis of TC4A by simply heating a mixture of *p*-*tert*-butylphenol with elemental sulfur in tetraethylene glycol dimethyl ether in the presence of NaOH as a base catalyst at 230°C to afford TC4A in a satisfactory yield (54%).[3,4] Also isolated from the reaction mixture were TC5A and TC6A, though only in poor yields (trace and 0.03%, respectively). The almost exclusive formation of TC4A among TC*n*As (*n*=4~6) suggests the highest thermodynamic stability of TC4A and/or template effect of Na^+ to stabilize the reaction intermediate or the product. It has been reported that a template effect operates in the synthesis of *p*-*tert*-butylcalix[*n*]arenes (C*n*As, Scheme 1) by the base-catalyzed condensation of *p*-*tert*-butylphenol with formaldehyde since a larger metal ion such as Cs^+ tends to incorporate more of the phenols (typically *n*=6) to give C*n*As.[7] Expecting the same template effect of the base catalyst for the TC*n*A synthesis, we replaced CsOH for NaOH and found that the major products were a complex mixture of the acyclic oligomers in which TC4A was hardly found by HPLC analysis. Gratifyingly, however, we were able to secure a sample of pure TC6A in poor but appreciable yield (0.8%).[8]

Slow diffusion of CH_3CN into a solution of TC6A in CH_2Cl_2 afforded single crystals suitable for X-ray structure analysis.[9] It can be seen that TC6A adopts a distorted cone conformation, which has two cavities comprising BAB′ and CDC′ rings (Fig. 1). The conformation seems to be stabilized by two sets of strong hydrogen bondings comprising three OH groups as suggested by the phenolic O–O distances; 2.762(8), 2.822(7) and 2.774(7) Å for A/B, B/C, and C/D, respectively. The dihedral angles between the phenyl rings A/D, B/B′ and C/C′ are 127.7°, 88.9° and 91.1°, respectively. The similarity of O–O distances and dihedral angles for A/D and B/C rings indicates that the molecule has approximately C_{2v} symmetry, including one crystallographic mirror plane. Ungaro et al. reported the X-ray analysis of a single crystal of C6A, which showed a very similar structure to that of TC6A.[10] Comparison of these crystal data suggests that the two crystals of TC6A and C6A are isomorphous with the same crystal packing.[11] It should be noted, however, that TC6A bears one CH_2Cl_2 molecule which is disordered in four situations to form, as a whole, a spherical shape included exclusively in the cavity comprising CDC′.

Table 1 lists the inclusion behavior of TC6A as well as that of TC4A[4] studied by recrystallization from various solvents. It can be seen that TC6A forms inclusion complexes with more discrete compositions than those of TC4A, the guests being included mostly in a 1:1 manner regardless of their sizes. It is noteworthy that benzene, aniline, *n*-octane, and *o*-, *m*- and *p*-xylenes formed inclusion complexes with TC6A but not sufficiently with TC4A. Although direct evidence such as X-ray crystal structure

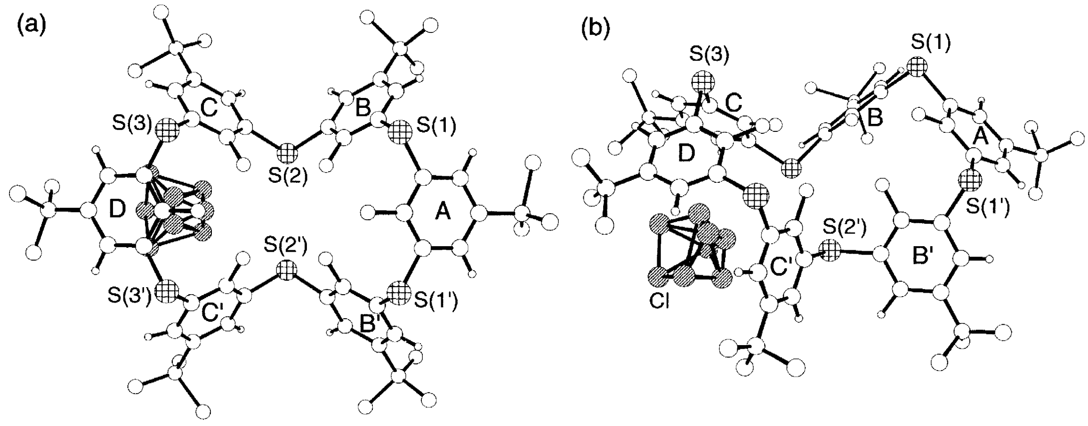

Fig. 1. Molecular structure of TC6A·CH_2Cl_2. (a) Top view, (b) side view. Atoms and benzene rings denoted prime are related to their counterparts by the symmetry operator: *x*, 1/2–*y*, *z*

of the complexes should be awaited, the improved inclusion properties of TC6A compared to those of TC4A may be explained by the expanded inner cavity of TC6A to form inclusion complexes, and/or, enlargement of the crystal lattice to accommodate such larger guest molecules to form clathrates.

It is interesting that aniline was included in such high content as to form the crystal in a 1:3 (host:guest) manner. This may suggest that inclusion of aniline is promoted by a strong interaction such as hydrogen bonding between $PhH_2N\cdots\cdot HO–$ or electrostatic interaction between $PhNH_3^+$ and phenolate O^- of TC6A.

Table 1
The content of solvent and the host versus guest (H:G) ratio in the inclusion complex formed with TC6A and TC4A

Solvent	TC6A		TC4A[a]	
	Content of solv. / mol%[b]	H : G	Content of solv. / mol%[b]	H : G[c]
Acetone	46	1:1	41	3:2
Chloroform	58	2:3	50[d]	1:1
Benzene	52	1:1	53	1:1
1,2-Dichloroethane	50	1:1	64	1:2
Toluene	53	1:1	34	2:1
Ethylbenzene	50	1:1	0	–
Cyclohexane	58	1:1	45	1:1
Aniline	76	1:3	22	+
1,4-Dioxane	52	1:1	51	1:1
n-Octane	38	2:1	7	+
m-Xylene	51	1:1	7	+
o-Xylene	48	1:1	7	+
p-Xylene	66	1:2	6	+
Decalin	50	1:1	48	1:1

a) Data from ref. 4. b) Estimated by ^1H NMR (400 MHz). c) – : inclusion complex does not form. + : host to guest ratio is not clear. d) Estimated by elemental analysis.

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6. Recently, other groups have started to report chemistry related to TC4A. For example, see: Mislin, G.; Graf, E.; Hosseini, M. W.; Bilyk, A.; Hall, A. K.; Harrowfield, J. M.; Skelton, B. W.; White, A. H. *Chem. Commun*. **1999**, 373–374; Lang, J.; Dvoráková, H.; Bartosová, I.; Lhoták, P.; Stibor, I.; Hrabal, R. *Tetrahedron Lett*. **1999**, *40*, 373–376 and references cited therein.
7. See Ref. 1, Chapter 2.
8. A mixture of *p*-*tert*-butylphenol (30.0 g, 0.20 mol), elemental sulfur S_8 (12.8 g, 0.40 mol), and $CsOH{\cdot}H_2O$ (17.7 g, 0.10 mol) in tetraethylene glycol dimethyl ether (9 cm^3) was stirred under nitrogen. The stirred mixture was heated at 190°C for 2 h, 200°C for 2 h, and 230°C for 3.5 h with concomitant removal of the evolving hydrogen sulfide with a slow stream of nitrogen. The resulting dark-red product was cooled to ambient temperature and diluted with toluene. Then 1 M sulfuric acid and diethyl ether were added with stirring. After extraction, the organic layer was concentrated by evaporation, which contained many sulfurized products of the phenol as judged by HPLC analysis. Then, to the residual was added acetone to precipitate a crude product. After dissolving in hot chloroform, the solution was filtered to remove solid residual and the filtrate was evaporated to dryness and dried in vacuo (100°C, 4 h) to give an essentially pure sample of TC6A (0.28 g, 0.78% based on the *p*-*tert*-butylphenol) as confirmed by elemental analysis and spectral data.[4] For HPLC analysis of the reaction mixture, see: Hori, T.; Ueda, S.; Kojima, T.; Kumagai, H. *Sekiyu Gakkaishi* **1991**, *34*, 446–451.
9. Crystal data: $C_{60}H_{72}O_6S_6{\cdot}CH_2Cl_2$, M=1166.52, colorless, sizes=0.3×0.4×0.4 mm, orthorhombic, a=18.3854(9), b=17.4851(9), c=19.9308(8) Å, V=6407.2(5), Mo–Kα radiation (λ=0.71069 Å), space group *P*nma (No. 62), Z=4, D_{calc}=1.209 g/cm^3, T=285 K, μ(Mo–Kα)=3.42 cm^{-1}, data collection using Rigaku/MSC mercury CCD diffractometer, 480 images at 20.0 s, number of measured reflections=40536 ($2\theta<47.7°$), independent reflections=5443 (R_{int}=0.050), a symmetry-related absorption correction, final R=0.068, R_w=0.072 for 2444 observed reflections ($I_o>3\sigma(I_o)$), GOF=2.30. All *tert*-butyl carbons are disordered in two parts. The CH_2Cl_2 molecule is included in the ratio of 1:1 (host:guest) in the crystal, which is disordered in four parts. Further details of the X-ray analysis are available on request from the Director of the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK.
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11. Crystal data of C6A: a=18.344, b=17.079, c=19.945 Å, *P*nma (Z=4).[10]