

## Syntheses of Tetrasulfonylcalix[4]biscrown-6 and Crystal Structures

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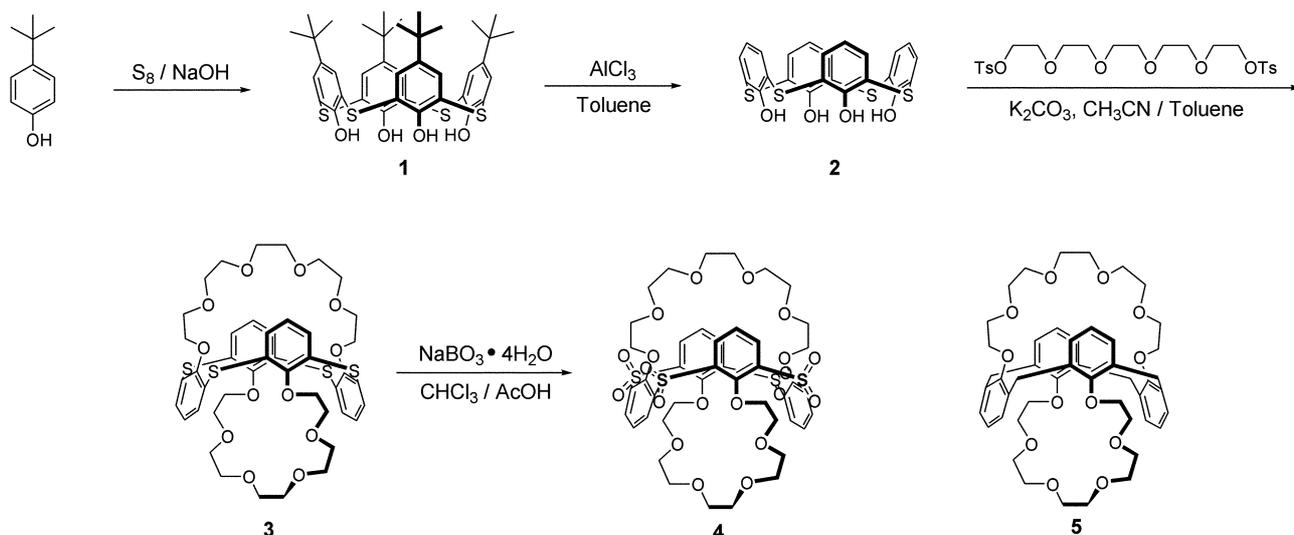
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Since Kumakai *et al.*<sup>1</sup> reported viable synthetic routes on *p*-*tert*-butylthiacalixarenes in 1997, this class of macrocyclic ligand has attracted considerable interest as an alternative to 'classic' calixarenes<sup>2</sup> by providing sites for functionalization not only on the aromatic rings but also on the bridging sulfur atoms. Thiacalixarenes possess additional coordination sites and the cavity dimensions are increased compared with analogous calixarenes. Unlike calix[4]arenes, thiacalix[4]arenes show affinity for transition metal ions because the sulfur atoms in the calixarene framework take part in the metal ion complexation.<sup>3</sup> For this concern, syntheses of several 1,3-thiacalix[4]biscrown derivatives, the first representatives of crown ether-bridged compounds in the thiacalixarene series were reported.<sup>4</sup> Investigation of their complexing abilities towards alkali metal cations (Na<sup>+</sup>, K<sup>+</sup>, Rb<sup>+</sup>, and Cs<sup>+</sup>) showed lower extraction efficiencies than those for related 1,3-calix[4]biscrown-5 and crown-6. This behavior was attributed to a larger (about 0.5 Å) thiacalix[4]arene cavity as determined from X-ray crystal diffraction.<sup>5</sup> Molecular modeling indicated that the Cs<sup>+</sup> ion is located close to the thiacalix[4]arene cavity, but does not interact

with the crown ether unit leading to less efficient binding.<sup>5</sup>

Previously we reported on synthesis and metal ion oscillation behavior of a series of thiacalix[4]monocrowns and thiacalix[4]biscrowns.<sup>5b</sup> The cesium ion was more rapidly oscillated in thiacalix[4]crowns than in the conventional calix[4]biscrowns because the former has weaker electrostatic interactions of the polyether ring oxygen atoms with the metal ions and diminished *p*-metal ion interactions between the metal ions and the aromatic rings of the thiacalix[4]crowns. With keeping the metal ion binding behavior of the thiacalixcrown compounds in mind, we tried to prepare a tetrasulfonylcalix[4]crown by oxidation of the thiacalix[4]crown molecule.

Our synthesis began with *para*-*tert*-butylphenol which was cyclized with sulfur molecule (S<sub>8</sub>) to give a *para*-*tert*-butylthiacalix[4]arene (**1**)<sup>3</sup> as shown in Scheme 1. Dealkylation using AlCl<sub>3</sub> in phenol provided a thiacalix[4]arene (**2**) in moderate yield. Subsequently, 1,3-alternate thiacalix[4]biscrown-6 (**3**) was synthesized from the reaction of the thiacalix[4]arene (**2**) with ditosylate of tetraethyleneglycol in the presence of K<sub>2</sub>CO<sub>3</sub>.<sup>5</sup> Oxidation of **3** with 5 equiv of



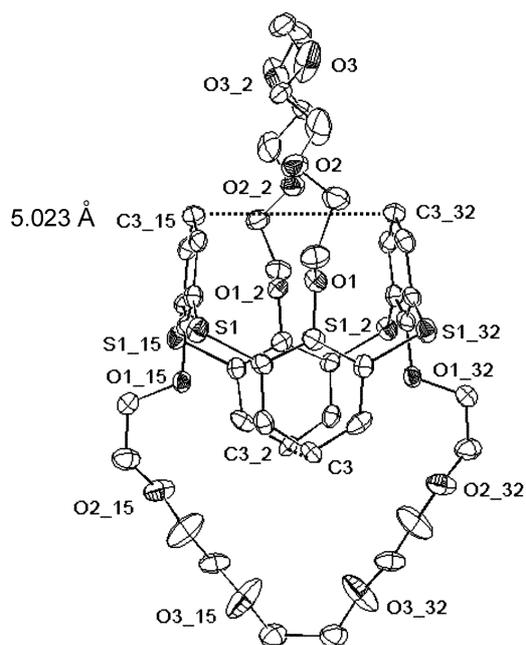
**Scheme 1.** Synthesis of tetrasulfonylcalix[4]-bis-crown-6.

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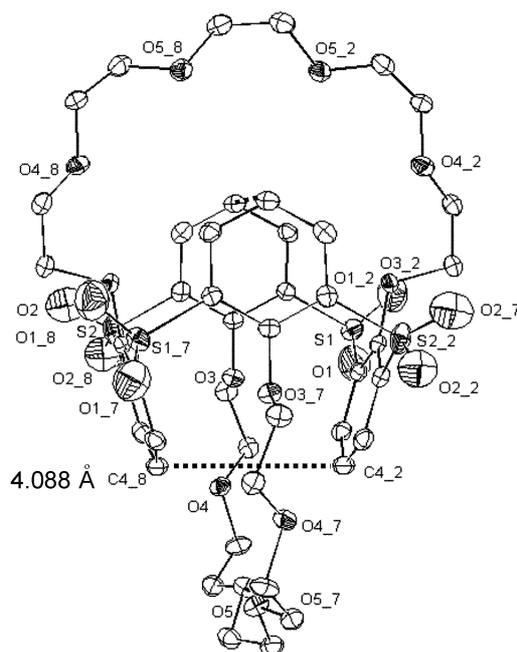
NaBO<sub>3</sub>/AcOH produced tetrasulfonylcalix[4]biscrown-6 (**4**) in 33% yield. The conformation of **3** and **4** were confirmed by X-ray diffraction (Figures 1 and 2).

Both **3** and **4** were crystallized in the tetragonal and their space group are *I*<sub>4</sub> and *P*4<sub>2</sub>2<sub>1</sub>2, respectively. The thiacalix[4]arene platform in both A and B molecules is in the 1,3-*alternate* conformation. Except for the sulfonyl oxygen atoms, both compounds are isostructural and have a pseudo 4-fold rotation-reflection (*S*<sub>4</sub>) axis. Consistent with this symmetry, the facing benzene rings are relatively parallel to each other and the adjacent benzene rings lie above and below the plane defined by the four sulfur atoms. The pseudo *S*<sub>4</sub> symmetry also reasonably depicts the overall perpendicular orientation of two cyclic ether moieties above and below the sulfur planes. Regarding the distance between two facing benzenes, which is quite related to the  $\pi$ -cesium complexation, tetra-*sulfonyl*-thiacalix[4]biscrown-6 (**4**) was of shorter distance with 4.088 Å than the thiacalix[4]biscrown-6 (**3**) (5.023 Å) as shown in Figure 1 and 2.

Extractabilities (*E* %) of **3** and **4** toward Na<sup>+</sup>, K<sup>+</sup>, Rb<sup>+</sup>, Cs<sup>+</sup>, NH<sub>4</sub><sup>+</sup>, Ag<sup>+</sup>, Sr<sup>2+</sup>, Ba<sup>2+</sup>, and Pb<sup>2+</sup> were determined by two-phase picrate extraction and the results are summarized in Table 1. Both compounds gave lower extractabilities than the conventional 1,3-calix[4]biscrowns.<sup>6</sup> For tested cations, compound **3** shows a cesium ion selectivity, probably because the crown-6 ring and two aromatic benzene rings ( $\pi$ -metal complexation) participated in the metal ion complexation. For **4**, however, the binding ability for cesium ion diminished. Lower extractability of tetrasulfonyl-calix[4]biscrown-6 toward Cs<sup>+</sup> ion is due to the fact that a distance between two facing benzene rings of the tetrasulfonylcalix[4]biscrown-6 (C4-2 to C4-8 = 4.088 Å) was shorter than that of thiacalix[4]biscrown-6 (C3 to C3-2 =



**Figure 1.** ORTEP drawing of **3** with 50% probability thermal ellipsoids.



**Figure 2.** ORTEP drawing of **4** with 50% probability thermal ellipsoids.

**Table 1.** Extractability (*E* %) of cation picrates by ligands

Ligand	Extractability (%)								
	Na <sup>+</sup>	K <sup>+</sup>	Rb <sup>+</sup>	Cs <sup>+</sup>	NH <sub>4</sub> <sup>+</sup>	Ag <sup>+</sup>	Sr <sup>2+</sup>	Ba <sup>2+</sup>	Pb <sup>2+</sup>
<b>3</b>	0	0	8.5	<b>27.2</b>	1	0.9	0.7	3.9	0
<b>4</b>	1.8	0.8	0	1.5	1.2	2	1.2	1.3	0

5.023 Å) to give an insufficient space to the  $\pi$ -Cs<sup>+</sup> ion complexation (see Figures 1 and 2).

## Experimental Section

**Synthesis.** Compounds **1-3** were prepared following procedures reported in literature.<sup>5</sup>

**2,8,14,20-Tetrasulfonylcalix[4]-bis-crown-6 (**4**).** A solution of (0.50 g, 0.55 mmol) of thiacalix[4]biscrown-6 (**3**) and sodium perborate tetrahydrate (0.42 g, 2.72 mmol) in chloroform (50 mL) and acetic acid (80 mL) was stirred at room temperature for 10 h. To the reaction solution were added 100 mL of CHCl<sub>3</sub> and 100 mL of 10% aqueous NaHCO<sub>3</sub> solution. The organic layer was separated and dried over MgSO<sub>4</sub>. Removal of the organic solvent *in vacuo* gave a white solid. Purification by column chromatography using ethyl acetate/hexane (1 : 1) as eluents gave **4** as a white solid. Yield 33%. Mp 289.4-293.5 °C: IR (KBr pellet, cm<sup>-1</sup>): 2872, 1567, 1436, 1359, 1306, 1235, 1135, 1050; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  8.16-7.15 (m, 8H, Ar-*H*<sub>m</sub>); 4H, Ar-*H*<sub>p</sub>), 4.85-3.81 (m, 40H, -OCH<sub>2</sub>CH<sub>2</sub>O-); FAB MS, *m/z* (M<sup>+</sup>) calcd 1029.14, found: 1029.15.

**Two-phase extraction.** All solvents and inorganic compounds were purchased from Aldrich Chemical and Prolabo. Metal picrates were prepared by reaction of picric acid with the appropriate metal carbonate.<sup>6</sup> Liquid-liquid

**Table 2.** Crystallographic Data and Structure Refinement Parameters for **3** and **4**

Parameter	<b>3</b>	<b>4</b>
Empirical formula	C <sub>44</sub> H <sub>52</sub> O <sub>12</sub> S <sub>4</sub>	C <sub>44</sub> H <sub>52</sub> O <sub>20</sub> S <sub>4</sub>
Formula weight	901.1	1029.1
Temperature (K)	293(2)	295(2)
Crystal system	Tetragonal	Tetragonal
space group	I 41/a c d	P4 <sub>2</sub> 2 <sub>1</sub> 2
Unit cell dimensions	a = 14.817 Å $\alpha = 90^\circ$ b = 14.817 Å $\beta = 90^\circ$ c = 40.848 Å $\gamma = 90^\circ$	a = 12.786(2) Å c = 14.155(2) Å
Volume	8968(4) Å <sup>3</sup>	2314.1(5) Å <sup>3</sup>
Z	8	2
Density (calculated)	1.335 g/cm <sup>3</sup>	1.477 g/cm <sup>3</sup>
Absorption coefficient	0.273 mm <sup>-1</sup>	0.287 mm <sup>-1</sup>
F(000)	3808	1080
Crystal size	0.5 × 0.1 × 0.5 mm	0.50 × 0.44 × 0.40 mm
2 $\theta$ data collection	11.709 to 18.490°	3.5 to 50°
Independent reflections	1977	1204
Goodness-of-fit on F <sup>2</sup>	1.188	1.067
R indices (all data)	R1 = 0.1518 wR2 = 0.4448	R1 = 0.0815 wR2 = 0.1844
Largest diff. peak and hole	0.535 and -0.853 e.Å <sup>-3</sup>	0.237 and -0.395 e.Å <sup>-3</sup>

solvent extraction experiments were performed by contacting an aqueous solution (2.0 mL) containing the metal picrate (0.20 mM) and a chloroform solution (2.0 mL) of the ligand (0.10 mM) with shaking for 30 min at 25 °C. The concentration of picrate anion extracted from the aqueous phase into the organic layer was determined by UV spectrophotometry ( $\lambda_{\text{max}}=373$  nm). Three independent experiments were carried out for each combination of ligand and metal picrate.

**Solid-state determination.** Both single crystals of **3** and **4** were obtained by slow evaporation of CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub> (1 : 9). All X-ray data were collected with the use of a Siemens P4 diffractometer equipped with a Mo X-ray tube and a graphite monochromator. The orientation matrix and unit-cell parameters were determined by the least-squares analyses of the setting angles of 28 reflections in the range  $10.0^\circ < 2\theta < 25.0^\circ$ . Three check-reflections were measured every 100 reflections throughout data collection. Intensity data were empirically corrected for absorption with  $\psi$ -scan data. All calculations were carried out with the use of SHELXTL programs.<sup>8</sup>

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