

## Sr<sup>2+</sup> Ion Selective *p*-*tert*-Butylthiacalix[4]arene Bearing Two Distal Amide Units

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A new thiacalix[4]arene diamide (**TCAm**) has been prepared and its electrochemical property and complexation behavior toward various metal ions have been investigated by voltammetry. *p*-*tert*-Butylthiacalix[4]arene diamide (**TCAm**) exhibited selectivity toward Sr<sup>2+</sup> ion over alkali, alkaline earth and transition metal ions while conventional calix[4]arene diamides showed selective binding property with Ca<sup>2+</sup> ion. This is probably due to the bigger size of thiacalix[4]arene than those of calix[4]arene.

**Key Words** : Calixarene, Thiacalixarene, Strontium, Voltammetry, Ion recognition

### Introduction

Since the conventional calix[4]arenes have poor coordination ability to metal ions due to their intrinsic hydrogen bonding of phenols in the lower rim, it has been a common practice to design and synthesize calix-type ligands by introducing functional groups having metal-ligating ability.<sup>1-3</sup>

Thiacalixarene-based synthetic receptor can also be obtained by introduction of appropriate functional groups,<sup>4</sup> although thiacalix[4]arenes have transition metal ion binding ability. Such modification may involve the upper and lower rims of the molecule, as well as the bridging sulfur atoms. Alkylation of hydroxyl groups of tetrahydroxythiacalixarenes in the lower rim has been used to limit the macrocycle conformation and thereby tune complexation properties.<sup>5</sup>

Various functional groups can be introduced at the hydroxyl groups by simple base-catalyzed etherification.<sup>1</sup> Along this line, various thiacalix[4]arene-based ligands have been prepared by introducing functional groups such as ether,<sup>6</sup> ester,<sup>7</sup> ketone,<sup>8</sup> carboxylic acid,<sup>9</sup> phosphine oxide,<sup>10</sup> amide,<sup>11</sup> and so on. Especially, thiacalix[4]arene with amide functional groups showed good extraction ability for various metal ion picrates in solvent extraction study.<sup>8</sup> Generally, the coordination ability of these thiacalix[4]arenes was investigated by solvent extraction study. Compared to solvent extraction method, voltammetric determination is very promising because of its high sensitivity, very small amount of sample needed and applicability for *in situ* monitoring. Previously we reported the electrochemical behaviors of thiacalix[4]arene and *p*-*tert*-butylthiacalix[4]arene.<sup>12</sup> To the best of our knowledge, however, electrochemistry of thiacalix[4]arene bearing amide units has never been reported yet. Thus, we herein discuss the complexation behavior of 1,3-distally substituted thiacalix[4]arene diamide (**TCAm**, Figure 1).

### Experimental Section

#### Synthesis.

**Preparation of TCAm:** Under nitrogen, a mixture of *p*-

*tert*-butylthiacalix[4]arene<sup>4</sup> (1.0 g, 1.38 mmol), *N,N*-dibutylchloroacetamide (2.85 g, 13.8 mmol), K<sub>2</sub>CO<sub>3</sub> (0.2 g, 1.38 mmol) and a catalytic amount of NaI in dry acetone (80 mL) was heated at reflux. After refluxing for 24 h, the mixture was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) and treated with dilute HCl. The organic layer was washed with water (300 mL), dried over anhydrous MgSO<sub>4</sub> and filtered. Recrystallization from diethyl ether produced 0.51 g (35%) of **TCAm** as a yellow solid. IR (KBr pellet, cm<sup>-1</sup>): 3365, 1664. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ 9.78 (2H, s, OH), 7.63-7.26 (8H, m, ArH), 5.31 (4H, s, CH<sub>2</sub>CON), 3.68-3.37 (4H, m, CONCH<sub>2</sub>), 1.58 (4H, m, CONCH<sub>2</sub>), 1.38-1.31 (16H, m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.22 (36H, s, C(CH<sub>3</sub>)<sub>3</sub>), 1.08 (8H, m, CH<sub>2</sub>CH<sub>2</sub>-CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.05-0.87 (12H, m, CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz): 164.5, 162.5, 142.0, 136.0, 120.0, 60.0, 52.3, 41.1, 38.1, 30.2, 19.8, 13.8 ppm. FAB MS *m/z* (M<sup>+</sup>): calcd, 1106.8. Found, 1106.2; Anal. Calcd. for C<sub>64</sub>H<sub>88</sub>N<sub>2</sub>O<sub>8</sub>S<sub>4</sub>: C, 69.43; H, 7.77. Found: C, 69.45; H, 7.80.

**Electrochemistry.** Electrochemical measurements were carried out with a Model 660 electrochemical workstation (CH Instruments, Austin, TX, USA). The three-electrode system consists of a glassy carbon working electrode, an Ag/Ag<sup>-</sup> (0.1 M) reference electrode and a Pt wire counter electrode. The surface of the working electrode was polished

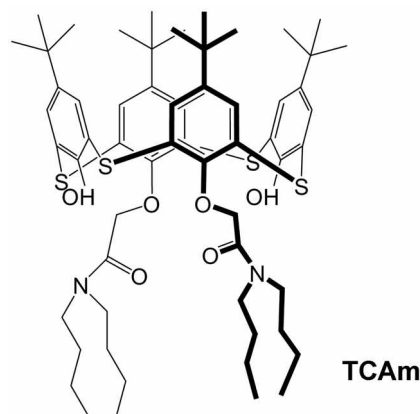


Figure 1. Structure of thiacalix[4]arene diamide (**TCAm**).

with 0.3  $\mu\text{m}$  alumina (Buehler, Lake Bluff, MN) and rinsed with deionized water. Residual alumina particles were thoroughly removed by positioning the electrode in an ultrasonic cleaner for 15 min. Then, the electrode was dried and washed with pure acetonitrile before use. The supporting electrolyte in organic solution was 0.1 M tetrabutylammonium perchlorate (TBAP) in acetonitrile.

## Results and Discussion

**Electrochemical Behavior.** Figure 2 shows a cyclic voltammogram (CV) of 0.032 mM **TCAm** in 0.1 M TBAP/acetonitrile solution. Irreversible redox peaks are observed at 0.83 V, 0.97 V and 1.17 V as in the oxidation behavior of parent thiacalix[4]arenes.<sup>12</sup> Compared to parent thiacalix[4]arenes,<sup>12</sup> however, oxidation waves are not clear and resolution is poor due to the solubility problem of **TCAm**, of which concentration is 0.032 mM in acetonitrile, while those of parent thiacalix[4]arenes are 1 mM. Differential pulse voltammetry (DPV) was carried out in order to get a better resolution of waves. Figure 3 shows DPV of **TCAm** obtained from the same solution as for the corresponding CV shown in Figure 2. Differently from parent thiacalix[4]arenes,<sup>12</sup> two peaks and a shoulder in the oxidation were observed at 0.84 V, 1.07 V and 0.73 V, respectively, in **TCAm**. Firstly, ill-defined peaks of **TCAm** are probably due to the peripheral sulfur bridge, the sulfide group in **TCAm** which is able to destabilize the radical cation as an electron accepting group.<sup>13</sup> Secondly, the two peaks are thought to be due to intramolecular hydrogen bonding of two phenols in **TCAm**. In the case of parent thiacalix[4]arenes,<sup>12</sup> the four phenols in the lower rim form cyclic array through intramolecular hydrogen bonding. Thus all phenols of parent thiacalix[4]arenes are identical and their electrochemical behavior must be the all the same. The two phenols of **TCAm** are also essentially equivalent, but the first-electron transfer needs less energy while the second-electron transfer requires more because of the intramolecular hydrogen bonding between phenoxide ion and second phenol caused by cone conformation.

**TCAm** has the stable cone structure by the strong hydro-

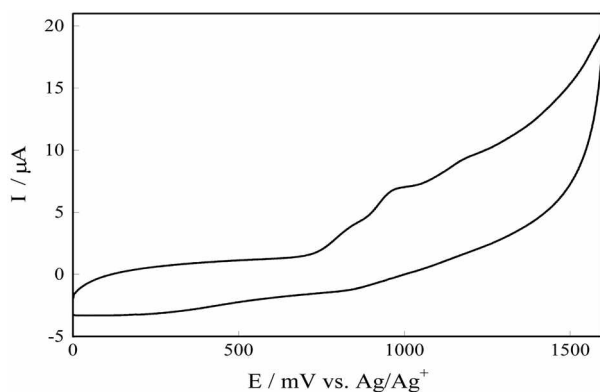


Figure 2. Cyclic voltammogram (CV) of 0.032 mM **TCAm** in 0.1 M TBAP/acetonitrile solution. Scan rate 50 mV.

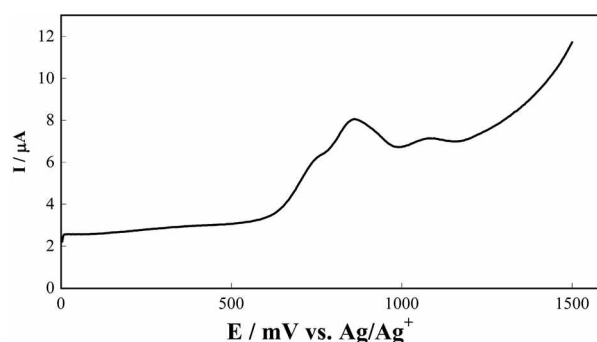


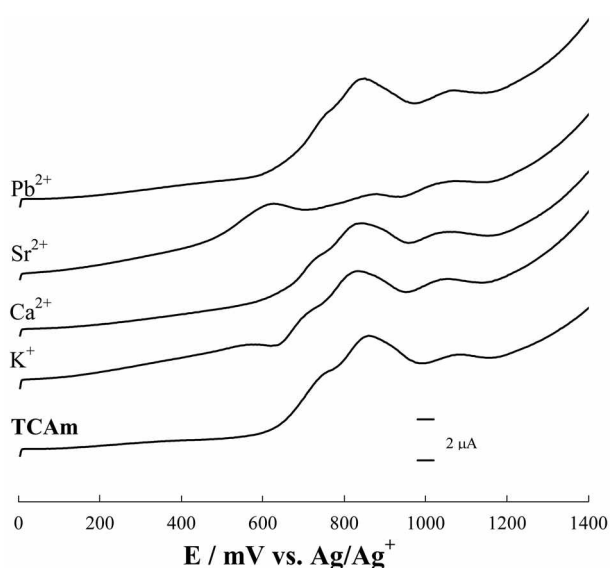
Figure 3. Differential pulse voltammogram (DPV) of 0.032 mM **TCAm** in 0.1 M TBAP/acetonitrile solution. Pulse amplitude: 50 mV.

gen bonds between phenolic OH groups.<sup>14</sup> The oxidation mechanism of phenol involves successive two one-proton transfers, in which both  $-\text{e}^{-}\text{H}^{+}\text{e}^{-}$  and  $-\text{e}^{-}\text{H}^{-}\text{e}^{-}$  mechanisms are possible but the final product is the same.<sup>15</sup> These proton-coupled mechanisms imply that hydrogen bond to phenol group can influence strongly on the electrochemical behavior of phenol. In **TCAm**, the proton of one phenol moiety is located between two phenols because of the intramolecular hydrogen bonding. Thus, the elimination of this proton in the oxidation process becomes easier and the oxidation peak appears at a less positive potential; whereas, the proton transfer from the second phenol moiety becomes difficult and the oxidation peak appears at a more positive potential.

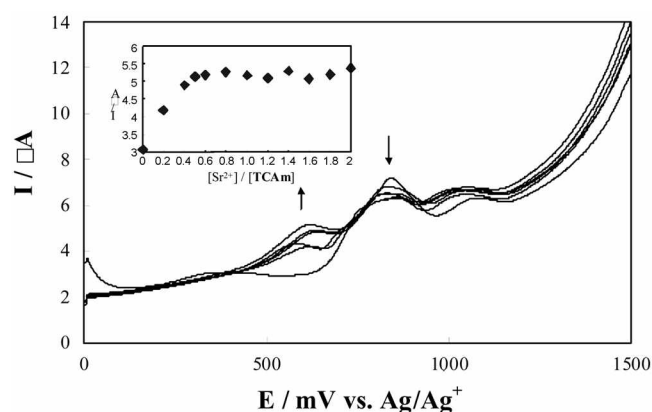
**Selective Recognition of Sr<sup>2+</sup>.** For the calix[4]arene in which two phenol groups are modified with diamide in the lower rim, Ca<sup>2+</sup> ion fits best into the pore so that very high selectivity over other metal ions as well as the formation of a remarkably stable complex has been discovered.<sup>16-18</sup> Among carbonyl compounds, amide compounds have high dipole moment and tautomerize at high concentration of mineral acid.<sup>19,20</sup> They have a preorganized conformation for metal cation binding in which carbonyl and etheral oxygens of calix[4]arene diamide form a ligand proximity toward metal ion. And also strong dipole moment of amide can facilitate to interact with metal ion.

Of primary importance is the electrostatic interaction of metal cations with two phenol moieties as well as the ion-dipole interaction with the binding site lined with two pairs of ether amide carbonyl moieties.

Figure 4 shows the effect of various metal ions on the redox behavior of **TCAm**. The addition of K<sup>+</sup>, Ca<sup>2+</sup>, and Pb<sup>2+</sup> to free **TCAm** solution leads no significant change in DPVs of **TCAm**. But the presence of Sr<sup>2+</sup> alters anodic peak potential and current. And the addition of other metal ions such as other alkali metal ions, Mg<sup>2+</sup>, Ba<sup>2+</sup>, and other transition metal ions also show the same electrochemical behaviors with free **TCAm**. With respect to the electrochemical behavior, the oxidation peak of free **TCAm** at 0.84 V diminishes and new peak at 0.62 V is observed by the addition of Sr<sup>2+</sup>. This indicates that **TCAm** exhibits selectivity toward Sr<sup>2+</sup> ion, and it suggests possible applications as a



**Figure 4.** DPVs of 0.032 mM TCAM in the absence and presence of 0.032 mM various metal ions in CH<sub>3</sub>CN. Pulse amplitude: 50 mV.



**Figure 5.** DPVs of TCAM in CH<sub>3</sub>CN in the presence of increasing amount of Sr<sup>2+</sup>. Inset is the amperometric titration curve at a new peak potential (0.62 V).

new electroactive ionophore for a sensing material useful for Sr<sup>2+</sup> ion. This result could be explained by the Corey-Pauling-Koltun space filling molecular model (CPK model). According to CPK model, the geometry of the binding site of the host, bearing the two amide phenol ethers and two phenol units, seems to be ideal in terms of size and arrangement for the recognition of doubly charged metal cation.<sup>16</sup> The size of TCAM could explain the selectivity for Sr<sup>2+</sup> compared to Ca<sup>2+</sup> selective calix[4]arene diamide which has a smaller cavity than thiacalix[4]arene diamide TCAM.<sup>14</sup>

In order to gain insight into the complexation behavior between TCAM and Sr<sup>2+</sup>, we carried out voltammetric titration experiments. Figure 5 shows the effect of the concen-

tration of Sr<sup>2+</sup> ion. Upon interacting with Sr<sup>2+</sup> ion, TCAM solution experienced a marked positive shift in its peak potential. The oxidation peak at 0.84 V shifts to 0.62 V and grows largely at the expense of the oxidation peak at 0.84 V. The peak current (I<sub>p</sub>) quantitatively increases as the concentration of the Sr<sup>2+</sup> ion increases. But it gradually reaches a maximum value around 1 equivalent.

In conclusion, 1,3-distally substituted thiacalix[4]arene diamide (TCAM) has been newly synthesized, and its electrochemical behavior and complexation behavior toward various metal ions have been also investigated. This new thiacalix[4]arene diamide shows selectivity for Sr<sup>2+</sup> ion over alkali, transition and other alkaline earth metal ions in acetonitrile solution.

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