# Calix[n]arenes Provided with Thiols for Modified Electrode Applications; Ring-size Dependent Voltammetric Behavior toward Ferrocene Derivatives

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Calix[*n*]arenes (*n* = 4, 6) adlayers formed by thiol-aided self-assembly showed calixarene ring-size distinctive voltammetric behavior to water-soluble ferrocene derivatives. Computer simulations of the cyclic voltammetric *i-E* responses were made and parameters for the electrode reaction were discussed.

Chemically modified electrodes (CMEs) provide unique opportunities of bringing higher selectivity and sensitivity in electroanalysis.[1] By deliberately attaching a chemical reagent to an electrode surface, it would take on the chemical property of the attached reagent leading to reagent-based control of a rate of an electrode reaction. For the successful development of CMEs, rational attachment of selected types of molecules onto an electrode surface is an essential key and one of the recent work in this area has focused on molecular self-assemblies through metal-sulfur interactions.[2,3] In the present study, calix[*n*]arenes (*n* = 4, 6) provided with thiols were used for modified electrode preparations and monolayer functions of the calixarene adlayers were studied with using cyclic voltammetry.

Calix[*n*]arene derivatives were synthesized according to the literature.[4] The hexamer (**CA6S**) was dissolved into chloroform to give a 1 mM (1 M = 1 mol dm$^{-3}$) solution. For the tetramer (**CA4S**), tetrahydrofuran was used as solvent (1 mM). A freshly evaporated gold substrates was immersed into the calixarene solution for 24 hr at room temperature. Then, the substrate was thoroughly washed with the adsorbate-free solvent, dried under vacuum. The substrate thus prepared was used immediately for reflection-absorption Fourier-transform infrared spectroscopy (FT-IRRAS).



n = 6  (**CA6S**)
n = 4  (**CA4S**)
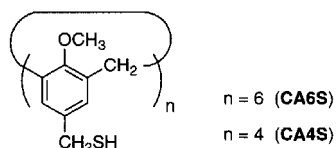
The FT-IRRAS spectrum of the substrates treated with **CA6S** showed a spectrum fundamentally similar to the transmittance spectrum of **CA6S** in its isotropic sample; it showed phenyl vibrations (1610 - 1430 cm$^{-1}$) and two peaks at 1223 cm$^{-1}$ and 1137 cm$^{-1}$ due to the asymmetric and the symmetric vibrations for the ether linkage. These characteristics in FT-IRRAS spectra were also confirmed for the case of **CA4S** modifications and there was almost no noticeable sprectral difference from the **CA6S**-modified Au substrates. These data suggest that calixarenes studied in the present study also adsorb onto gold surfaces like alkanethiols.

Next, monolayer functions of the calixarene adlayer were examined based on cyclic voltammetric (CV) measurements. Ferrocenemethanol (**FcOH**), ammonium ferrocenesulfonate (**FcS**), and ferrocenylmethyl-trimethylammonium bromide (**FcN**) were used as redox species since they represent an electrochemically reversible, one-electron redox reaction with moderate formal potential. A gold electrode ($\phi$ 1.6 mm) was polished to mirror finish with alumina slurry and was used as working electrode through out the CV measurements. Treatment of the electrode surface with the calixarene solution was made by the same procedure described above.

Steady-state CVs for **FcOH** on the bare and the modified electrodes are shown in Figure 1. The peak currents due to the reversible electrode reaction of the ferrocene/ferricinium redox couple are significantly suppressed by **CA4S** treatment. The voltammogram is also characterized by its large peak separation which means a sluggish electrode reaction. Formation of the calixarene adlayer which is intrinsically insulating, limits the effective surface area resulting in suppression of the magnitude of the voltammetric peak currents. In the same time, the adlayer restricts the closest approach of redox molecules to the electrode surface, decreasing the rate of electron transfer. As can be seen in this figure, the **CA6S** adlayer also suppresses the redox reaction but only slightly. Measurements with **FcS** and **FcN** also gave similar results (data are not shown).

We made mathematical simulations of CVs (DigiSim 2.0, BAS Co.) to estimate electrode reaction parameters. Here, we assumed one-electron transfer reaction with semi-infinite diffusion of the solution species.[5] For the sake of convenience, the diffusion coefficients for the oxidized and the reduced species were approximated to be identical each other. Simulations were first made for the case of the electrode reaction on the bare Au electrode with varying the magnitudes of the heterogeneous electron transfer rate constant ($k_s$) and the apparent diffusion coefficient ($D$) of the corresponding solution species to give the best-fitted *i-E* response. Concerning that procedure, the formal potential ($E°'$) of the redox couple was experimentally determined from its CVs and the transfer coefficient ($\alpha$) was fixed to be 0.5 for the most cases of simulations. The surface area ($A$) was approximated to be 0.02 cm$^2$ which was the geometric value of the electrode used here.

As noted in the previous section, formation of the calixarene adlayer is expected to decrease the effective electrode surface area and the magnitude of the electron transfer rate constant of the solution species. In contrast, the mass-transfer process of the solution species should be independent since the expected thickness of the calixarene adlayer is much smaller than that of the diffusion layer. From these viewpoint, we made mathematical simulations for reactions on the calixarene-modified electrode with varying the magnitudes of $k_s$ and $A$
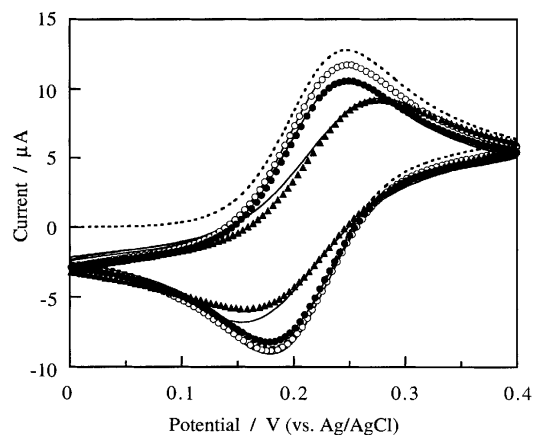
**Figure 1.** Steady-state and simulated cyclic voltammograms for ferrocenemethanol on the bare ( ○ ), **CA6S**-modified ( ● ), and **CA4S**-modified ( ▲ ) Au electrodes.
Each solid curve represents a simulated voltammogram and for the reaction on the bare Au, the trace for the first sweep is also indicated (broken curve). Conditions, 5 mM ferrocenemethanol (0.1 M KCl), 25 mV/s, 25 °C

**Table 1.** Estimated CV parameters for the redox reaction of ferrocene derivatives on the bare and the modified Au electrodes

| | $E^{\circ\prime}$ / mV | $A$ / cm$^2$ | $k_s$ / $10^{-2}$ cm s$^{-1}$ | $\alpha$ | $D$ / $10^{-5}$ cm$^2$ s$^{-1}$ |
|---|---|---|---|---|---|
| **FcOH** | | | | | |
| **bare** | 213 | 0.020 | 2.0 | 0.5 | 0.93 |
| **CA6S** | 213 | 0.018 | 2.0 | 0.5 | 0.93 |
| **CA4S** | 213 | 0.018 | 0.18 | 0.5 | 0.93 |
| **FcS** | | | | | |
| **bare** | 405 | 0.020 | 1.5 | 0.5 | 0.65 |
| **CA6S** | 405 | 0.018 | 0.80 | 0.5 | 0.65 |
| **CA4S** | 405 | 0.014 | 0.080 | 0.5 | 0.65 |
| **FcN** | | | | | |
| **bare** | 413 | 0.020 | 2.5 | 0.1 | 0.64 |
| **CA6S** | 413 | 0.018 | 2.5 | 0.1 | 0.64 |
| **CA4S** | 413 | 0.016 | 0.090 | 0.2 | 0.64 |

Solution resistance of 100 Ω cm$^{-2}$ and double layer capacitance of 0.4 μF cm$^{-2}$ are commonly used for these simulations. Note that these equivalent parameters are normalized to the electrode geometric area. Other conditions are the same as Figure 1.

while the values of $E^{\circ\prime}$, $\alpha$ and $D$ were kept constant as those obtained for the case of the bare Au electrode.

In Figure 1, each solid line represents the simulated $i$-$E$ response. Mathematical simulations satisfactorily reproduced the experimentally obtained CVs for reactions on the bare and the **CA6S**-modified electrodes. For the case of the **CA4S**-modified electrode, the simulated data for the reversed (negative) scan suffer with deviation from the experimental ones. This is probably due to the quasi-reversible nature of the electrode reaction; the ferricinium ion formed in the forward scan diffuses into bulk solution leading to a reverse peak of smaller magnitude than the forward peak. Mathematical simulations for the **FcS** reactions on the bare and the modified electrodes gave similar results. On the other hand, results for the case of **FcN** were unsatisfactory; the experimentally obtained CV was characterized by its considerably smaller size of the reversed peak relative to the forward peak and one needed to assume an extraordinary smaller $\alpha$ value. At present reasons account for the observation are unclear and will be discussed in the near future.

Table 1 summarizes the electrochemical parameters which satisfactorily reproduce the experimental $i$-$E$ response of the corresponding electrochemical system. Due to the limited number of the experimental data in the past, it was difficult to confirm the validity of these kinetic parameters. However, judging from commonly available data,[6,7] a $k_s$ about $10^{-2}$ cm s$^{-1}$ and a $D$ about $10^{-5}$ cm$^2$ s$^{-1}$ for the present system seem to be reasonable. For cases of the **FcOH** electrode reaction, surface adlayer formation by **CA6S** leads to a 10% of decrease in $A$ while $k_s$ remains constant. On the other hand, suppression of $k_s$ at about one-tenth is associated with surface modification by **CA4S** which possesses a more compact inner pore. For the more bulky solution species, **FcS**, both of $A$ and $k_s$ decrease upon surface adlayer formation of **CA6S** as well as **CA4S** treatment.

We think these behavior should be explained based on the unique character for macrocyclic compounds; calixarene molecules absorbed on the electrode surface provide a cavity which has specific dimension according to their ring size. The cavity may allow the solution species to access to the underlying Au electrode as reported by Umezawa *et al.* in a comprehensive study on a voltammetric ion-channel sensor using a Langmuir-Blodgett membrane from a cyclodextrin derivative having long alkyl chains.[8] Of course there is a possibility that electrode reactions occur at the bare, defect site residing on the electrode surface.[9] However, recent studies on molecular recognition by self-assembled monolayers from cavitand receptors based on mass changes with a quartz microbalance[10] and surface-confined voltammetric behavior of a solution species (ferrocene) observed on a gold electrode modified with per-6-thio-β-cyclodextrin[11] also suggest the possibility of an electrode reaction in a size-dependent fashion.

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