ORGANIC
LETTERS

2011
Vol. 13, No. 13
3392–3395

Selective Binding of Carbamate Pesticides by Self-Assembled Monolayers of Calix[4]arene Lipoic Acid: Wettability and Impedance Dual-signal Response

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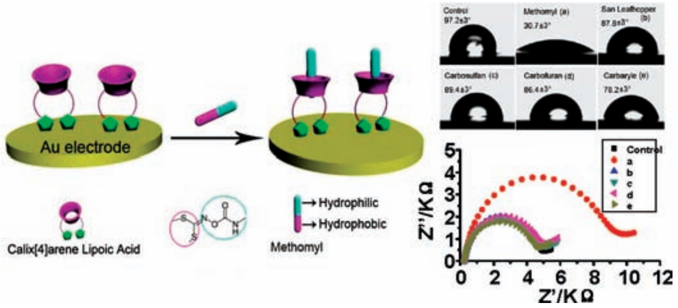
Received April 29, 2011

ABSTRACT



A calix[4]arene lipoic acid (C4LA) was synthesized by click chemistry in 62% yield. It was immobilized on Au surfaces via self-assembly to offer C4LA Self-Assembled Monolayers (SAMs). The SAMs show wettability and electrochemical impedance dual-signal response for methomyl with highly sensitivity and selectivity.

Self-assembly monolayers (SAMs) are an important direction of smart-functional interfaces.[1] Many functional supramolecular systems, including crown ethers,[2] cyclodextrin derivatives[3] and calixarenes,[4] can be immobilized on substrate surfaces to form self-assembled monolayers (SAMs). These studies have the common goal of demonstrating molecular recognition through host–guest interactions. Echegoyen and co-workers have demonstrated that the SAMs of crown ethers were employed to selectively bind K^+ in aqueous solutions.[2a] The Kaifer[3a] and Park groups[3b] have used β-cyclodextrin SAMs to study the inclusion of electrochemically active guests such as ferrocene and quinone derivatives, respectively. Calixarenes are a family of cavity-shaped cyclic molecules with outstanding complex activity toward

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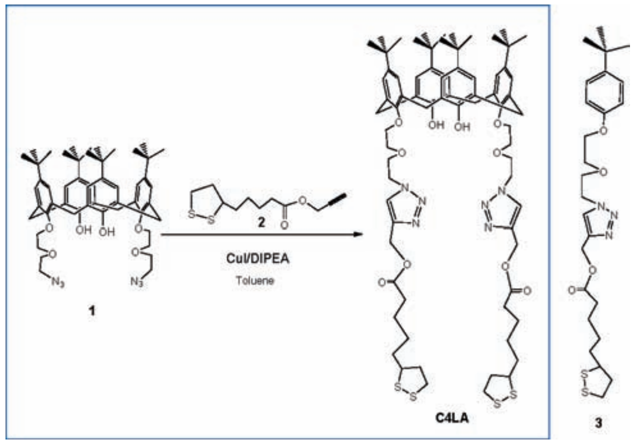
10.1021/ol201143z

neutral molecules, including pesticides and other biologically important molecules such as amino acids and peptides.[5] The potential of calix[*n*]arenes applied to form SAMs for neutral molecules has been given considerable attention. The SAMs of calix[4, 6, 8]arenes derivatives exhibited selective binding of polyamines,[4d] aromatic amines[4b] and fullerenes,[4c] respectively.

In general, molecular recognition of SAMs focuses on electrochemistry, while the wettability is an important property of functional interface.[6] The control of the hydrophilic/hydrophobic properties of surfaces attracts growing interest due to its implementation in practical applications in antiadhesive coatings, biosensors, and so forth.[7] However, by applying wettability to realize molecular recognition of SAMs and switch the transition between hydrophobicity and hydrophilicity has seldom been reported. In this article, SAMs of calix[4]arene lipoic acid (**C4LA**), which is synthesized by click chemistry, was constructed. The C4LA SAMs show wettability and impedance dual-signal response for methomyl with excellent selectivity and sensitivity, which may be developed as pesticide-detecting chips.

The synthetic procedure to prepare the target compound **C4LA** is depicted in Scheme 1. Azide-functionalized calix[4]arene **1** was synthesized according to the literature.[8] Then, treatment of thioctic acid with propargyl alcohol in the presence of DCC and DMAP in dry dichloromethane afforded thioctic-propyne **2**. Further reactions of **2** with **1** were carried out in refluxing toluene using CuI as catalyst for 24 h to afford calix[4]arene lipoic acid **C4LA** in 62% yield.[9] Reference compound **3** was synthesized in 69% yield using a method similar to that of **C4LA**. The structure and conformation of **C4LA** were confirmed by EI(+)MS spectra, elemental analyses, and NMR studies. The ^{1}H NMR spectrum shows two single peaks for the aromatic protons, two doublets for the bridging methylene groups and two singlets for the *tert*-butyl groups indicating a cone conformation. The ^{13}C NMR spectrum data further corroborated the cone conformation by the presence of a peak for the methylene resonances.[10]

Scheme 1. Synthesis of the **C4LA** and Reference Compound **3** via Click Chemistry



C4LA SAMs were constructed according to ref 11. The SAMs were characterized by X-ray photoelectron spectra (XPS), contact angle (CA), and impedance spectroscopy. XPS of **C4LA** modified Au electrode is shown in Figure S1 (see Support Information). A characteristic peak of S (2p) appeared at 170.7 eV due to the S atoms in the **C4LA**, which confirmed the presence of **C4LA** on the electrode. The properties of functional interface were studied by CA and impedance spectroscopy. As shown in Figure 1, the CA of C4LA SAMs was 97.2 ± 3°, which was comparatively hydrophobic in comparison with bare Au surface (52.6 ± 3°). Also, impedance spectroscopy of C4LA SAMs (4.97 KΩ) was greatly increased compared to the bare Au electrode (0.21 KΩ). The results indicated that the calix[4]arene lipoic acid was modified on the gold surface successfully.

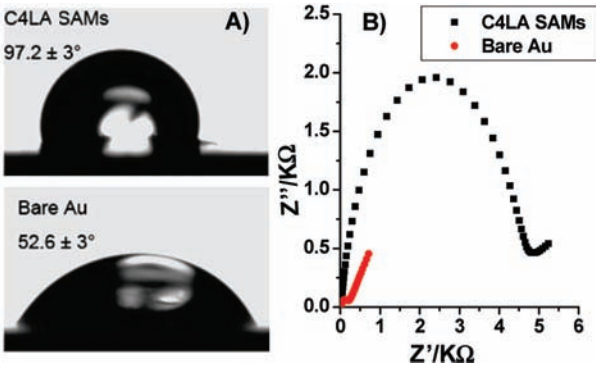


Figure 1. (A) Water-drop profiles on bare Au surface and C4LA/SAMs. (B) Impedance spectroscopy of 5.0 mM Fe(CN)$_6^{3-/4-}$ in 0.10 M KNO$_3$ aqueous solution on bare Au and C4LA SAMs electrode with the frequency ranging from 10 kHz to 1.0 kHz, scan rate: 0.10 v/s, indicating that **C4LA** successfully modified on gold surface.

Considering the special structure of **C4LA**, the carbamate pesticides (methomyl, san leafhopper, carbosulfan, carbofuran and carbaryl) were selected as guest molecules. The wettability and impedance of C4LA SAMs toward carbamates were investigated. As shown in Figure 2, after adding

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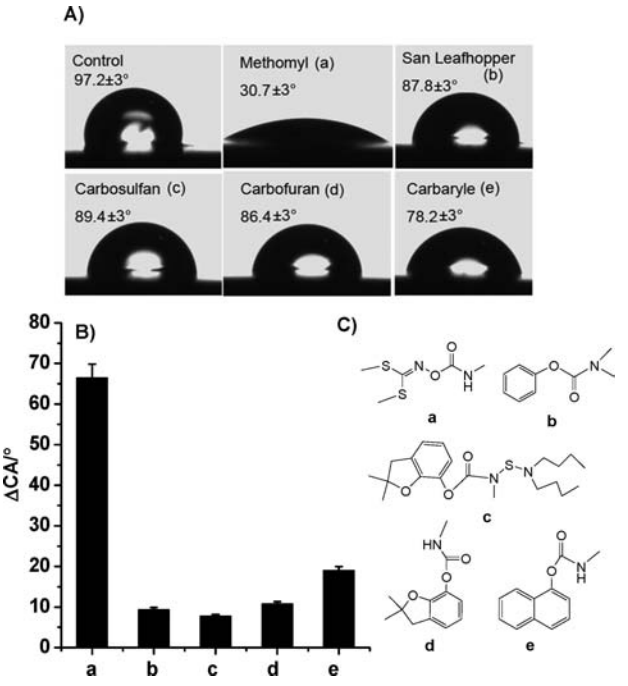

Figure 2. (A) CAs relationship images of C4LA SAMs with different guests: methomyl, san leafhopper, carbosulfan, carbofuran, carbaryl. (B) Contact angle variation ($\Delta CA = CA_{control} - CA$) histogram of C4LA SAMs in the presence of different carbamates, indicating that the selectively wettability responsive of **C4LA** toward methomyl. (C) Structure of the five guests.

mehtomyl solution, CA of C4LA SAMs was 30.7 ± 3°, which was greatly decreased compared to that of C4LA SAMs (97.2 ± 3°). However, the other four carbamates including san leafhopper, carbosulfan, carbofuran, and carbaryl did not show any distinct CA change, indicating that the excellent wettability was responsive for **C4LA** toward methomyl.

Simultaneously, the C4LA SAMs were further investigated by electrochemical impedance spectroscopy. Figure 3 shows impedance response of the redox couple Fe(CN)$_6^{3-/4-}$ in the presence of the five carbamates (0.1 mM). A simple Randles equivalent circuit[12] to describe the impedance consists of a charge-transfer resistance, R_{ct}, in series with a Warburg impedance and in parallel with a total interfacial capacitance. Addition of 0.1 mM methomyl to the electrolyte, R_{ct} value was increased from 4.97 KΩ to 9.82 KΩ while the R_{ct} value was seldom affected by other four carbamates. The results indicated that the C4LA SAMs exhibited a remarkably sensitive response to methomyl due to a host–guest interaction between methomyl and C4LA SAMs.[13] The impedance results were consistent with the selectivity of contact angles which indicated that the SAMs show wettability and electro-chemical impedance dual-signal response for methomyl with high selectivity.

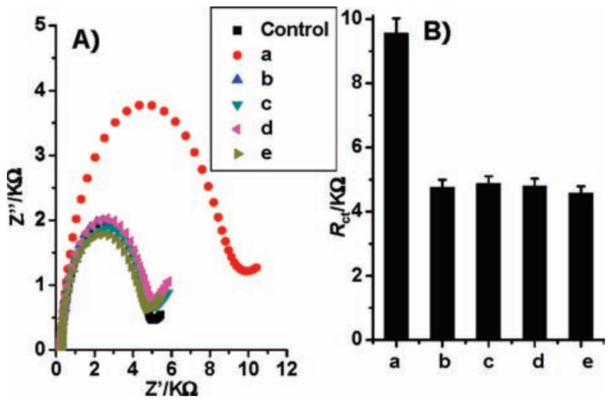

Figure 3. (A) Impendance response of Fe(CV)$_6^{3-/4-}$ at C4LA SAMs electrode in the presence of the five carbamates (1×10^{-4} M), including blank as control, methomyl, san leafhopper, carbosulfan, carbofuran, carbaryl. (B) Histogram showed the impedance value of A.

To substantiate the role of the calix[4]arene platform in the recognition process, the control experiments were carried out. Reference compound **3** without calix[4]arene platform was synthesized and **3** SAMs was also successfully constructed which adopted the same method as **C4LA**. The contact angle of **3** SAMs in the presence of methomyl, san leafhopper, carbosulfan, carbofuran and carbaryl were studied. As can be seen from Figure S2 (Supporting Information), the wettability of **3** SAMs shows only a little change upon addition of the carbamates (< 20°). Moreover, impedance response with no obvious selectivity was observed after the addition of the five carbamates in the redox probe solution (Figure S3, Supporting Information). Thus, the control experiment results indicated that the calix[4]arene cavity played an important role in the efficient recognition process of methomyl.

Compared the wettability and impedance dual-signal responsive results of the reference compound **3** to that of **C4LA** molecules modified the self-assembly monolayer, the C4LA SAMs expressed well selective to methomyl, indicating that the special **C4LA** cavities played a critical role in binding methomyl guest which caused the interface wettability change. The contact angle for C4LA SAMs is 97.2 ± 3°, indicating a hydrophobic surface, which agrees with the fact that calix[4]arene has four hydrophobic *tert*-butyl groups at the upper rim. After methomyl is encapsulated by the C4LA SAMs on the Au substrates, the CA value decreases significantly to 30.7 ± 3°, indicating the transformation from the hydrophobic surface to the hydrophilic surface.

To further study the binding model and stoichiometry between the **C4LA** host and methomyl guest, UV and NMR spectra in solution were carried out. As shown in Figure S4 (Supporting Information), upon addition of methomyl to the **C4LA** in CH_3CN, a new peak appeared around 360.5 nm while the other four carbamates gave no changes, which indeed indicates the formation of the

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complex between the methomyl and **C4LA**. Simultaneously, the corresponding complex constant (Ks) was evaluated using the Benesi–Hildebrand equation and was found to be $2.58 \times 10^{3}\ \mathrm{M}^{-1}$ (Figure S4). Meanwhile, a Job plot shown in Figure S5 (Supporting Information) has a peak at a molar fraction of 0.5 in 360.5 nm and gave the binding stoichiometry, implying that a 1:1 inclusion complex was formed.

On the basis of the above analysis and for further study, the binding model between the **C4LA** and methomyl, ^{1}H NMR spectra of **C4LA,** methomyl, mixed **C4LA** with methomyl were characterized. As shown in Figure S6 (Supporting Information), protons of SCH_3 groups in methomyl changed significantly from the two doublet peaks and underwent upfield shifting (Ha, −0.139 ppm; Hb, −0.303 ppm); however, the proton of NH in methomyl (Hc) almost had no shifting. The above results indicated that the SCH_3 end of methomyl would interact with the **C4LA** cavities and its upper; the NH end does not associate with the **C4LA**. In summary, the model of inclusion complex between the **C4LA** and methomyl could be constructed in Figure 4, and it also explained the wettability and impedance change before and after C4LA SAMs exposing in methomyl solution well.

It was noted that methomyl was a linear molecular containing the amide groups as the hydrophilic side and two methyl groups as the hydrophobic side. The amide groups were exposed to the outside of **C4LA** cavities and interacted with water through a hydrogen bond interaction, which caused the great changes of wettability from hydrophobic to hydrophilic. At the same time, the impedance of C4LA SAMs dramatically increased due to mutual inclusion interaction between methomyl and **C4LA**.

For quantitative analysis of methomyl, impedance spectroscopies of C4LA SAMs in the presence of different concentrations of methomyl were carried out. A plot of the R_{ct} versus concentrations of methomyl over the range of 1.0×10^{-12} to 1.0×10^{-4} M is shown in Figure S7 (Supporting Information). The linear equation is $R_{ct} = 4835 + 502.7 \times [C]$ with a linearity coefficient of 0.991. The limit of detection (3σ) for methomyl is 1 pM. Meanwhile, a plot of the contact angle (CA) versus concentrations of methomyl over the range of 1.0×10^{-6} to 1.0×10^{-2} M is shown in Figure S8 (Supporting Information). The monolayers show an initially steep decrease in CA as the concentration of methomyl increased. Once the concentration of the methomyl reaches 1.0×10^{-3} M, CA was down to 30.7 ± 3° compared to that of C4LA SAMs (97.2 ± 3°), which suggested the wettability transition from hydrophobicity to hydrophilicity.

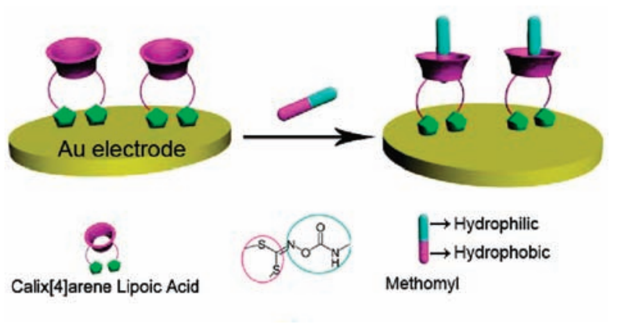

Figure 4. Schematic representation of the possible recognition process for **C4LA** toward methomyl on the surface of a self-assembled calix[4]arene monolayer via host–guest interaction.

In summary, the SAMs of calix[4]arene lipoic acid were successfully constructed and showed remarkable sensitivity for methomyl by a wettability and impedance dual-signal response. The high selectivity and sensitivity with methomyl is attributed to the inclusion complex form between **C4LA** and methomyl through the host and guest inclusion. The dual-signal response for methomyl would develop to a chip or microelectrode and is of potential application.

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China (21072072), Program for Excellent Research Group of Hubei Province (2009CDA048), Self-determined research funds of CCNU from the colleges' basic research, and operation of MOE (CCNU09AO200) and PCSIRT (NO. IRTO953).

Supporting Information Available. Experimental details, NMR spectra of C4LA, XPS, and UV spectra. This material is available free of charge via the Internet at http://pubs.acs.org.