Photochemical Imprint of Molecular Recognition Sites in Monolayers Assembled on Au Electrodes

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Functionalized monolayers assembled on surfaces act as active interfaces for molecular electronic devices, i.e., molecular wires,[1] design of molecular patterns,[2] and signal-triggered surfaces.[3] Tailoring of size and shape specific molecular recognition sites in monolayers represents a novel tailored function of thin film assemblies.[4] Monolayer electrodes with imprinted molecular recognition sites have important implications in future sensor technology, and molecular-imprinted monolayers associated with solid supports are new specific separation materials. Furthermore, specific molecular association of recognition sites imprinted in monolayers mimics fundamental molecular interactions with membranes. Molecular recognition sites were generated in macroscopic polymer matrices by cross-linking of the template-print molecule followed by its physical or chemical exclusion from the polymer.[5] Perforated monolayers that include molecular channels were tailored and molecular components were co-assembled in two-dimensional monolayers.[6] Here we wish to report on a photochemical method to imprint molecular recognition sites in monolayers. We follow the dynamics of molecular association to the sites and address the stability of the resulting lateral supramolecular assemblies.

6-[(4-Carboxymethyl)phenoxy]-5,12-naphthacene quinone,[7] "*trans*"-quinone (**1**), was assembled as a mixed monolayer with 1-tetradecanethiol, $C_{14}H_{29}SH$, as described before,[3c] Scheme 1. The resulting densely packed monolayer includes the "*trans*"-quinone in a rigidified configuration and a surface coverage corresponding to 2×10^{-10} mol·cm^{-2}. The "*trans*"-quinone monolayer exhibits reversible photoisomerizable features[3c] and irradiation of the "*trans*"-quinone monolayer, 320 nm $< \lambda <$ 380 nm, yields the "*ana*"-quinone isomer state, which lacks electrochemical activity. The method of photochemical imprint of the molecular recognition sites in the monolayer array is shown in Scheme 1. The "*ana*"-quinone monolayer reacts with amines,[7d] i.e., butylamine, resulting in the cleavage of the "*ana*"-quinone unit while the phenol residue remains a part of the monolayer assembly, Scheme 1. The 1-tetradecanethiol units ($C_{14}H_{29}SH$) associated with the monolayer provide the supporting element for the imprinted quinone sites while the photochemical detachment of the "*ana*"-quinone units is the chemical route to generate the recognition sites in the monolayer. The number of imprinted holes in the monolayer is estimated to be similar to the surface density of the quinone units in the monolayer.

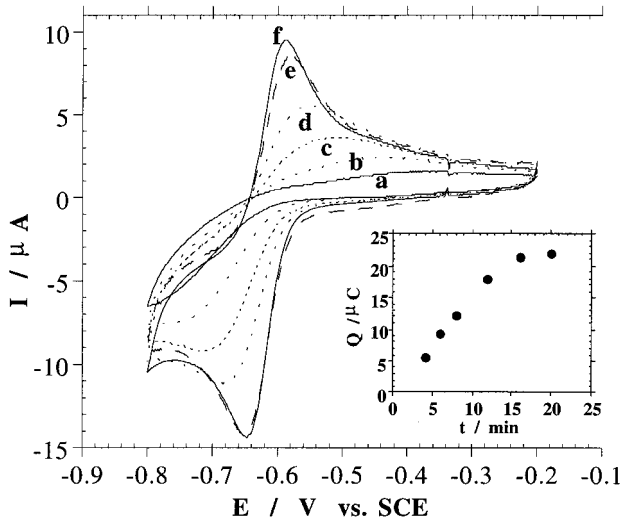

Figure 1. (A) Cyclic voltammograms of the imprinted Au electrode after its incubation with **1**, 1×10^{-4} M, aqueous solution, for (a) 4, (b) 6, (c) 8, (d) 12, (e) 16, and (f) 20 min, respectively, 25 °C. Inset: Dependence of the charge associated with the imprinted **1** on the time of the electrode incubation with **1**. Experiments were performed in a 0.01 M phosphate buffer and 0.1 sodium sulfate solution, pH 7.2. Scan rate 50 mV·s^{-1}.

Figure 1 shows the cyclic voltammograms of the monolayer-hole-imprinted electrode in the presence of the "*trans*"-quinone (**1**) at different numbers of cycles. Initially, no electrical response is observed, implying the lack of electrical communication between **1** and the monolayer-modified electrode. As the experiment proceeds, an electrical response of the quinone is observed (curve b, Figure 1). The signal exhibits initially a large peak-to-peak separation, $\Delta E_p \approx 200$ mV, as a result of nonspecific association of **1** to the monolayer. As time proceeds, the electrical response of **1** turns reversible, $\Delta E_p \approx 60$ mV, and it increases in its intensity. After ca. 90 cycles the cyclic voltammogram of the monolayer electrode levels off to a constant value.[8] Coulometric analysis of the resulting redox wave indicates that the surface density of the quinone units associated with the electrode corresponds to ca. 2×10^{-10} mol·cm^{-2}, a value identical with the value of imprinted holes in the monolayer. The reversible electrical response of **1** suggests that all associated quinone units are aligned in the monolayer array. Control experiments revealed that in the presence of a $C_{14}H_{29}SH$-modified electrode, no electrical response of **1** was observed, and in the presence of a bare Au electrode, **1** exhibits an ill-defined redox process, $\Delta E_p \approx 300$ mV. Thus, the reversible electrical response of **1** associated with the imprinted monolayer clearly indicates the formation of rigidified, aligned, assembly between the "*trans*"-quinone (**1**) and the monolayer-imprinted recognition sites. The time-dependent

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(8) The anodic (or cathodic) peak currents showed linear dependence with the scan rate, implying a surface-confined redox component.

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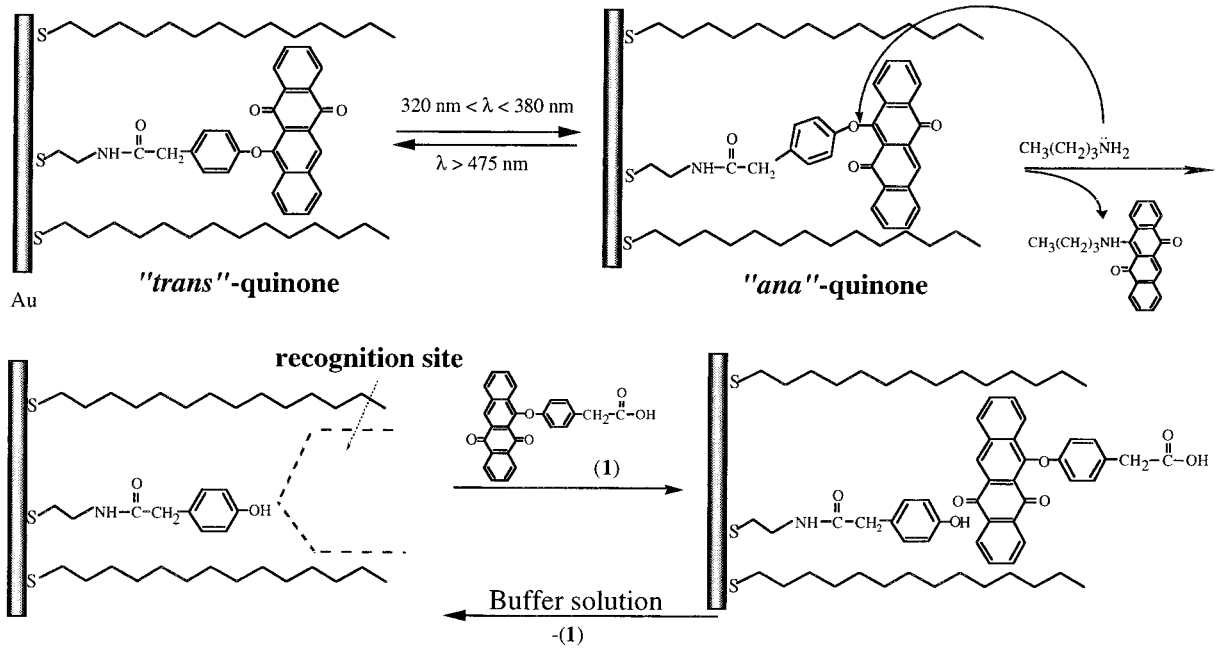
Scheme 1. Preparation of "*trans*"-Quinone/$C_{14}H_{29}SH$ Mixed Monolayer Electrode and the Photoinduced Formation of Molecular Recognition Sites in the Array. Uptake and Release of "*trans*"-Quinone to and from the Sites



increase of the electrical response of **1** (inset, Figure 1) represents the dynamics of association of the quinone to the imprinted recognition sites. Introduction of the imprinted monolayer electrode with the associated **1** into a pure electrolyte solution results in the slow dissociation of the quinone from the recognition sites (cf. Supporting Information). From the rates of association and dissociation of **1** to and from the imprinted recognition sites at 25 °C, the association constant of **1** to the sites was calculated to be $K_a = 3600 \pm 200\ M^{-1}$. By following the rates of association and dissociation of **1** to and from the imprinted recognition sites at variable temperatures, the activation energies for the two processes were estimated to be $E_a^{as} = 8.7 \pm 0.1$ kcal·mol^{-1} and $E_a^{dis} = 18.0 \pm 0.7$ kcal·mol^{-1}. The binding and dissociation of **1** to and from the imprinted monolayer could be reversibly activated, implying the cyclic operation of the sensing interface.

The association and dissociation of **1** to and from the monolayer-imprinted recognition sites is confirmed by microgravimetric quartz-crystal-microbalance, QCM, analysis. Upon interaction of the imprinted monolayer-functionalized Au/quartz crystal (AT-cut, 9 MHz) with **1**, a frequency decrease of $\Delta f = -12$ Hz was observed. This implies the association of **1** to the electrode at a surface coverage of 1.7×10^{-10} mol·cm^{-2}, consistent with the electrochemical experiments. Upon interaction of the **1**-loaded Au/quartz crystal with a pure buffer solution, the crystal frequency increases and reaches almost the same frequency observed prior to the association of **1** to the monolayer. This indicates that **1** is dissociated from the molecular recognition sites to the bulk buffer solution.

The recognition sites reveal high selectivity for the imprinted "*trans*"-quinone, (**1**). The association of a series of structurally related compounds, i.e., anthraquinone-2-sulfonic acid (**2**), 2-chloro-3-[[2-(dimethylbutylammonium bromide)ethyl]amino]-1,4-naphthoquinone (**3**),[9] *N*,*N*′-dimethyl-4,4′-bipyridinium (**4**), and 2-chloro-3-[amino(4-benzoic acid)]-1,4-naphthaquinone (**5**), to the imprinted monolayer was examined. Microgravimetric, QCM, experiments indicate that no frequency changes of an imprinted Au-quartz monolayer-functionalized crystal occur upon its challenging with **2**−**5** (for structures **2**−**5** see Supporting Information). The selectivity is attributed to the structural fit and complementary hydrophobic interaction, and possible H-bonds between **1** and the imprinted recognition sites.

The formation of specific recognition sites for **1** in the monolayer assembly is further supported by following the temperature effect on the imprinted molecular recognition sites. The densely packed monolayer represents a two-dimensional semicrystalline array that melts at a characteristic temperature.[10] Indeed, heating of the imprinted monolayer up to 60 °C did not influence the imprinted sites and the electrode revealed affinity for **1**. At ca. 65 °C, a sharp deactivation of the electrode toward the association of **1** to the monolayer was observed. Cooling of the electrode after its heating to 65 °C does not restore the recognition sites for **1**. This irreversible destruction of the recognition sites is attributed to the melting of the monolayer, resulting in the exchange of the monolayer components and the destruction of the molecular association sites.

In conclusion, we demonstrated a photochemical method to imprint molecular recognition sites in a monolayer array. The imprinted sites reveal high affinity and specificity for the imprinted molecule. The availability of different photolabile protective groups for different chemical functionalities, e.g. *o*-nitrobenzyl esters, opens the way to generalize the method of photoimprinting of molecular recognition sites in monolayer arrays.

Supporting Information Available: Cyclic voltammograms observed upon the time-dependent dissociation of **1** from the imprinted sites and the kinetics of dissociation of **1** from the sites, the microgravimetric analysis of the association/dissociation of **1** to and from the imprinted sites on an Au/quartz crystal, and the structures of **2**−**5** (PDF). See any current masthead page for Web access instructions.

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