Molecular Recognition at the Electrode–Solution Interface. Design, Self-Assembly, and Interfacial Binding Properties of a Molecular Sensor

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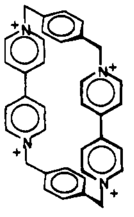
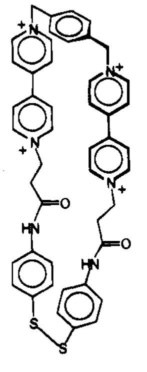
The advent of self-assembled monolayers[1] (SAMs) formed by organosulfur compounds on gold and other surfaces is opening the possibility of designing the molecular architecture of the electrode–solution interface. One of the primary goals of this research area is to control the reactivity of the electrode so that it becomes selectively responsive to a given species. Accomplishing this goal requires the preparation of supported monolayer (or multilayer) films containing selective binding sites for the target molecules.[2–6] In addition, a mechanism for the detection of the bound species should be devised. In this letter, we report the design and synthesis of a novel redox-active molecular receptor that chemisorbs readily on gold surfaces and forms mixed monolayer assemblies with decanethiol ($C_{10}H_{21}SH$). The voltammetric response of electrodes derivatized with these mixed monolayers is sensitive to the presence and concentration of compounds possessing electron-rich aromatic rings, such as the biologically relevant catechol and indole. These guests bind to the electron acceptor cavities of the chemisorbed host structures, inducing well-defined shifts in the formal potential of the host's reducible groups.

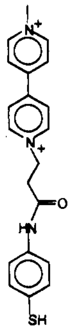
The interfacial receptor reported here is based on the well-known host cyclobis(paraquat-*p*-phenylene)[7] ($\mathbf{1}^{4+}$), which forms stable inclusion complexes with π-donor guests in aqueous and nonaqueous media. The stability of these complexes results, at least partially, from the charge transfer interactions between the included π-donor guest and the two electron acceptor bipyridinium (paraquat) groups which line the receptor's cavity.[8] The inclusion of an electron-rich guest inside $\mathbf{1}^{4+}$ typically shifts the host's first reduction potential (corresponding to the simultaneous monoelectronic reduction of both paraquat groups) to more negative values[9] due to the preferential stabilization of the 2+ state of the paraquat groups. We have employed these potential shifts to detect catechol and indole[10] using electrodes covered with a polymeric layer incorporating receptor $\mathbf{1}^{4+}$. However, the dynamic range and the analytical sensitivity of this system were hampered by the use of the relatively thick polymeric layer. Therefore, we decided to attempt similar experiments while limiting the derivatization of the electrode surface to monolayer thickness.



$\mathbf{1}^{4+}$



$\mathbf{2}^{4+}$



$\mathbf{3}^{2+}$

In the design of an interfacial analog of host $\mathbf{1}^{4+}$, we attempted to meet two main criteria: (i) to maintain the well-defined cavity of $\mathbf{1}^{4+}$ (lined by two redox-active paraquat groups) and (ii) to incorporate thiol or disulfide functionalities that will drive the receptor's chemisorption on the electrode surface. A combination of these ideas and considerations of synthetic accessibility led us to receptor $\mathbf{2}^{4+}$. The synthetic procedure is shown in Scheme 1. The final product was isolated in the tetrachloride form and characterized by ^{1}H NMR spectroscopy, FAB-MS, and combustion analysis.[11]

The immersion of a clean gold bead electrode in a solution of $\mathbf{2}^{4+}$ (1.0 mM in a 25:75 v/v mixture of methanol/ethanol, 18 h), followed by immersion in a solution containing 1.0 mM concentrations of both $\mathbf{2}^{4+}$ and $C_{10}H_{21}SH$ in the same solvent system (15 h), resulted in the formation of a mixed monolayer of these two compounds, which chemisorb on the gold surface *via* thiolate–Au bonds. After extensive rinsing of the electrode, the voltammetric response in pure 0.1 M phosphate buffer (pH = 7) solution clearly exhibited the cathodic and anodic waves characteristic of the reversible one-electron reduction of the immobilized host's paraquat groups (see Figure 1). The formal potential for the reduction process was −0.44 V vs SSCE. The potential difference between the cathodic and anodic peaks was 25 mV or less at moderate scan rates (<200 mV/s), and the cathodic peak current increased linearly with the scan rate (see inset in Figure 1). These two voltammetric features unequivocally indicate the surface-confined nature of the electroactive paraquat groups. Integration of the current under the cathodic wave yielded a host surface coverage of 2.8×10^{-11} mol/cm^2 (taking two electrons per molecule of $\mathbf{2}^{4+}$). The interfacial capacitance of the monolayer-covered electrode was found to be about 3 μF/cm^2, which is consistent with the value of 2 μF/cm^2 that Chidsey and Loiacono determined for a monolayer of pure decanethiol on gold.[12]

In these mixed monolayers, owing to the dissimilar lengths of the two components (the receptor spans ~23 Å and decanethiol ~17 Å), the bis(paraquat) cavities of the receptors protrude from the hydrophobic monolayer core into the monolayer–solution interface (see Scheme 2). Exposure of these Au/$\mathbf{2}^{4+}$ + $C_{10}H_{21}SH$ derivatized electrodes to solutions containing variable concentrations of indole induced cathodic shifts in the apparent formal potential for the reduction of the receptor's paraquat groups, as shown in Figure 2A. Similar concentration-dependent potential shifts were found with catechol in the solution (Figure 2B). Both catechol and indole are strong π-donors.

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(11) ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.1 (s, 2H), 9.8 (d, 4H), 9.5 (d, 4H), 8.8 (d, 4H), 8.7 (d, 4H), 7.9 (s, 4H), 7.6 (d, 4H), 7.3 (d, 4H), 6.1 (s, 4H), 5.0 (t, 4H), 3.15 (t, 4H). FAB-MS after counterion exchange to the tetra(hexafluorophosphate) form: *m/z* 1210 $(M - PF_6)^+$, 1065 $(M - 2PF_6)^+$, and 920 $(M - 3PF_6)^+$ in 3-mercapto-1,2-propanediol matrix. Anal. Calcd for $C_{46}H_{42}N_6S_2O_2Cl_4 \cdot 7H_2O$: C, 52.98; H, 5.41; N, 8.06. Found: C, 52.97; H, 5.47; N, 8.02.

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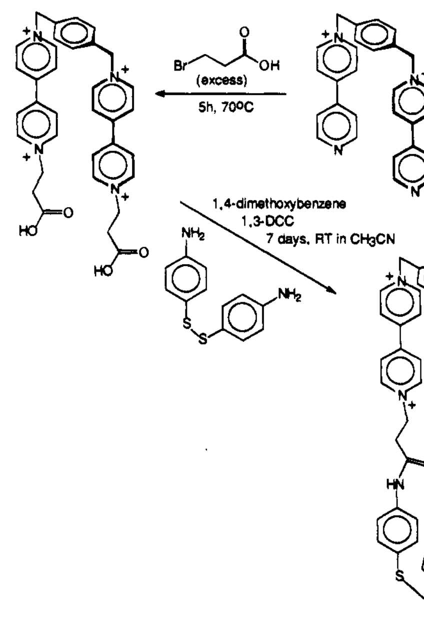
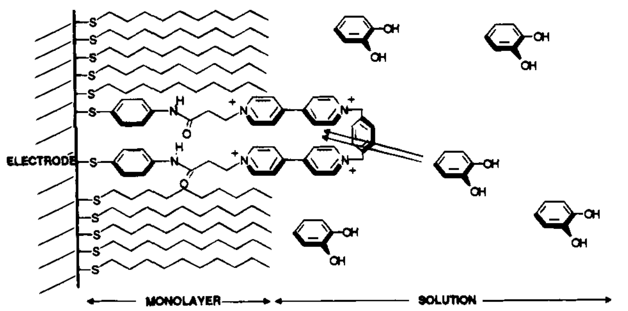
Scheme 1. Synthesis of Receptor 2^{4+}



Scheme 2. Idealized Representation of an Interfacial Binding Event



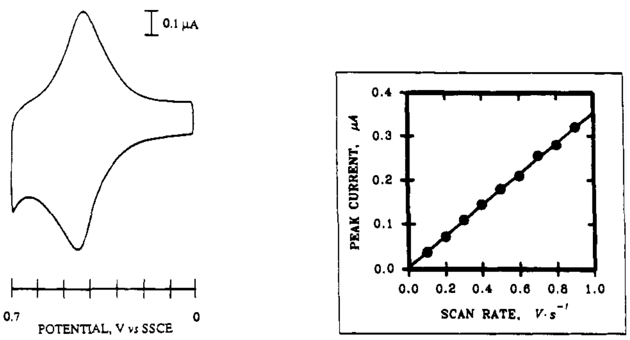


Figure 1. Voltammetric response of a Au/2^{4+} + $C_{10}H_{21}SH$ electrode in 0.1 M phosphate buffer (pH = 7). Scan rate, 0.3 V·s^{-1}. Inset: Scan rate dependence of the cathodic peak current.

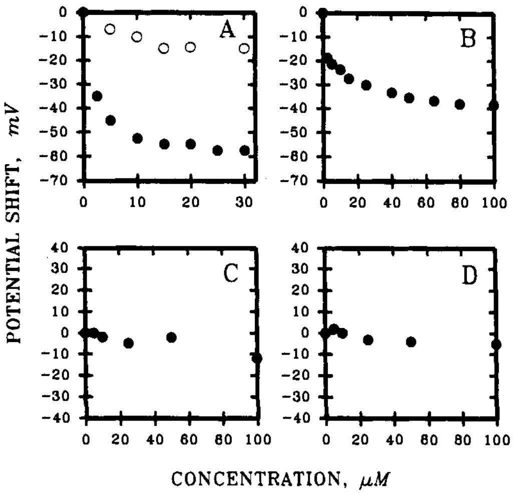


Figure 2. Observed shifts in the formal potential for the monoelectronic reduction of the surface-confined paraquat groups of Au/2^{4+} + $C_{10}H_{21}SH$ electrodes immersed in 0.1 M phosphate buffer (pH = 7) solutions also containing variable concentrations of (A) indole, (B) catechol, (C) benzonitrile, and (D) nitrobenzene. For comparison purposes, graph A also shows similar data obtained with a Au/3^{2+} + $C_{10}H_{21}SH$ electrode (open circles).

However, aromatic compounds with π-acceptor character, such as benzonitrile or nitrobenzene, fail to induce any significant potential shifts (Figure 2C,D) at similar concentrations.

Control experiments with electrodes derivatized with a mixed monolayer of $C_{10}H_{21}SH$ and the thiolated paraquat derivative 3^{2+} (see Figure 2A) indicate that the potential shifts observed with monolayers containing receptor 2^{4+} cannot be ascribed to the formation of simple charge transfer complexes between the solution π-donor guest and the monolayer-anchored paraquat groups. Our data clearly suggest that the cavity of the receptor, lined by the two paraquat groups, is crucial for the observation of substantial potential shifts at micromolar concentration levels of the guests indole and catechol. Furthermore, the shape of the plots for the concentration dependence of the potential shifts is consistent with guest binding in the monolayer cavities. The experimental data can be rationalized by a simple model in which the observed formal reduction potential—at a given concentration of guest—would result from the weighted contributions of two types of monolayer redox sites: bound and unbound. Fitting the experimental values to this model allowed us to determine the fraction of bound receptor molecules as a function of guest concentration in the contacting solution. Application of the Langmuir adsorption isotherm[13] to these values yields the maximum surface coverage of bound guest molecules (Γ_{max}) and the equilibrium constant (K) for the guest adsorption (binding by monolayer-anchored receptor) process. For indole, we found $\Gamma_{max} = 3.2 \times 10^{-11}$ mol/cm^2 and $K = 2.7 \times 10^5$ M^{-1}, while for catechol, $\Gamma_{max} = 2.9 \times 10^{-11}$ mol/cm^2 and $K = 1.0 \times 10^5$ M^{-1}. Both Γ_{max} values are in very good agreement with the experimentally obtained coverage of immobilized receptor molecules (2.8×10^{-11} mol/cm^2). The equilibrium constant for indole is larger than that for catechol, as anticipated from the binding constant values measured in solution[10] for complexation of these guests by host 1^{4+}. However, the absolute values of the binding constants determined here are substantially higher than the corresponding solution values. The reasons behind this finding are unclear at this point, but we have found a similar discrepancy in an unrelated interfacial host–guest system.[6a]

In conclusion, we have designed and synthesized a redox-active receptor that chemisorbs on gold electrode surfaces, where it binds electron-rich aromatic guests, such as the biologically relevant compounds catechol and indole, allowing their voltammetric detection at micromolar concentration levels. This work demonstrates the feasibility of designing molecular receptors for interfacial use as components of self-assembled monolayers. The challenge now is to increase the selectivity of these systems to make their use as sensors possible.

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[13] We used the following equation derived from the Langmuir isotherm: $C\Gamma^{-1} = (K\Gamma_{max})^{-1} + C(\Gamma_{max})^{-1}$, where C is the solution concentration of the guest and Γ is the observed surface coverage at that concentration. Plots of C/Γ vs C were linear and allowed the determination of K and Γ_{max} values (see text for definitions).