

The Effect of Steric Hindrance on Rate Constant of a Diels-Alder Reaction on the Hydroquinone-Terminated Self-Assembled Monolayer

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The self-assembled monolayers (SAMs)^{1,2} of alkanethiolates on gold have been used as a powerful method to prepare a chemical interface which is stable and structurally well-defined monolayer with a controllable thickness and desirable chemical functionality. These characteristics of SAMs based on Au-sulfur interactions make them ideal model systems to study fundamental issues such as adsorption, wetting, lubrication, chemical sensing, biocompatibility, lithography, and electron transfer. Since Hubbard, Soriaga and co-workers^{3,4} investigated the electrochemical behavior of quinone and mercaptohydroquinone adsorbed on metal surfaces because of their important biological activities,⁵ Sato *et al.*⁶ reported potential dependent spectroscopic properties of hydroquinone-terminated self-assembled monolayer on gold. We also reported that the long-range electron transfer rate constant in 2-(*n*-mercaptoalkyl)-hydroquinone SAM is exponentially decreased to the length of an alkyl chain spacer between hydroquinone (H₂Q) and Au electrode surface.⁷⁻⁹ In recent, Mrksich *et al.*¹⁰ studied Diels-Alder reaction of cyclopentadiene (Cp) in the electrolyte solution with a mixed SAM, which is prepared from benzoquinone (BQ)-terminated alkylthiol and ω -hydroxy-alkylthiol. They first monitored that the redox peak current of BQ is gradually decreased due to the formation of an electroinactive cycloaddition adduct from the Diels-Alder (D-A) reaction. From the current measurements, they estimated the rate of interfacial D-A reaction and reported that it could be dependent upon the geometry of monolayer structure surrounding BQ attached to the SAM.¹¹ However, it should be noted that Cp molecule they used is relatively small enough to be easily accessible to BQ at the interface. In this situation, it is expected that the effect of geometric structure on the rate might be small.

In this work, we present a kinetic characterization for the D-A reaction of cyclopentadienylethylferrocene (CpEF), which has been synthesized first in our lab. on a mixed SAM containing 2-(*n*-mercaptododecyl)hydroquinone (MDH₂Q). The choice of CpEF molecule has two advantages. First, we can measure D-A reaction rate that is dependent upon the difficulty of access due to bulkiness of CpEF. Second, it makes much easier to study the amount of D-A interfacial reaction based on the surface density by monitoring changes

in the redox activity of CpEF reactant. Using these advantages of CpEF, the effect of structural environment surrounding the immobilized MDH₂Q on the kinetics of interfacial D-A reaction will be more carefully understood in view of a reaction rate constant.

Experimental Section

Synthesis of CpEF. 1 M BH₃·THF (8 mL, 8 mmole) was added dropwise to 10 mL of dry THF solution of ferroceneacetic acid (0.49 g, 2 mmol) in a flask cooled in an ice bath and the reaction was allowed to warm to room temperature. After 6 h, cold water was added and the resultant solution was extracted three times with methylene chloride (MC). The organic layer was washed with brine, dried with anhydrous MgSO₄, and then concentrated under vacuum. After column separation using mixture solvent of MC and ethyl acetate (v/v, 3 : 1), red crystalline of ferroceneethanol was obtained (yield 82%) and identified with nmr. To 10 mL MC solution of ferroceneethanol (0.38 g, 1.65 mmol) and triethylamine (0.46 mL, 3.3 mmol) at 0 °C was added methanesulfonyl chloride (0.16 mL, 1.98 mmol) dropwise. After 30 min mixing, the reaction mixture was concentrated under vacuum and extracted with water and MC. The organic layer was dried with anhydrous MgSO₄, concentrated under vacuum. After column separation with MC, the crude red oil obtained was identified as ferroceneethyl mesylate. Sodium cyclopentadienylide (1.53 mL, 2 M solution in THF) was slowly added to 15 mL of dry THF solution of ferroceneethyl mesylate (0.47 g, 1.53 mmol) and the reaction temperature was slowly increased to room temperature. After 6 h, an ice water was added and extracted with MC. The resultant organic solution was dried with anhydrous MgSO₄ and concentrated under vacuum. The crude product was purified by chromatography (silica gel, 230-400 mesh) and gave red colored liquid of CpEF (C₅H₅FeC₃H₄(CH₂)₂C₃H₄) as a final product. CpEF was identified by ¹H NMR (200 MHz, CDCl₃): 2.54 (s, 4H), 2.89 (dd, 2H), 4.02-4.08 (m, 9H), 6.02-6.17 (m, 1H), 6.23-6.26 (m, 1H), 6.40-6.44 (m, 1H).

Materials. 2-(*n*-mercaptododecyl)hydroquinone (MDH₂Q) was synthesized according to the procedure described in our previous reports.^{7,9} Hexanethiol, octanethiol, decanethiol, dodecanethiol, hexadecanethiol, and octadecanethiol were used as received from Aldrich.

Apparatus and monolayer preparation. Using a com-

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mercial BAS 100B/W Potentiostat, all voltammetric measurements were carried out in a single compartment cell with home-made Au bead electrode as working electrode, platinum counter electrode, and a Ag/AgCl reference electrode. The electrolyte solutions were prepared with deionized water purified to a resistivity of 18 M/cm with UHQ II system (Elga) and deaerated by purging with nitrogen. The gold bead electrodes (*ca.* 2.5–2.9 mm diameter) were made by annealing the tip of a gold wire (99.999%, 0.5 mm diameter) in a gas-oxygen flame. The gold bead electrode was cleaned by immersion for 10 min in a "piranha" solution (3 : 1 mixture of concentrated H₂SO₄ and 30% H₂O₂) prior to use. After rinsing with deionized water, ethanol and drying with nitrogen gas blowing, the electrode was immersed in the ethanol mixture solution containing MDH₂Q and n-alkanethiol for 2–5 h. For the electrochemical measurements, the surface coverage of MDH₂Q of mixed SAM on gold was maintained to be *ca.* 0.2 by varying mole fraction of MDH₂Q in coating solution. The electrode was rinsed with fresh ethanol and deionized water and then used for voltammetric studies.

Results and Discussion

Figure 1 shows the model substrate of a mixed SAM on which a Diels-Alder reaction takes place. Benzoquinone (BQ) produced in the reversible electrochemical oxidation of the immobilized MDH₂Q reacts with a CpEF molecule in the electrolyte to give cycloaddition adduct. However, the D-A reaction stops on the reduction process of the immobilized BQ because H₂Q moiety, a reduced form of BQ, does not react with a CpEF molecule. Therefore, the D-A reaction on a mixed SAM is only triggered by the reversible oxidation reaction of MDH₂Q. Using this feature, the D-A reaction progress can be easily monitored by a decrease in the reduction current of BQ at the solid-liquid interface. We used cyclic voltammetry to investigate the current decrease due to the formation of cycloaddition product in the D-A reaction. In this mixed monolayer, simple n-alkanethiol molecule were used as a diluent, which isolates MDH₂Q molecule from one another at the interface. Another important reason for using n-alkanethiol with a

different alkyl chain length (*n* = 6, 8, 10, 12, 16, and 18) is to be able to modify the surrounding environment around MDH₂Q immobilized to a mixed SAM on gold electrode. Figure 2a shows typical cyclic voltammogram (CV) of a mixed SAM of MDH₂Q and n-decanethiol on gold in the mixture solution of 1 : 1 tetrahydrofuran : aqueous buffer containing sodium chloride (154 mM) and sodium phosphate (3 mM). A pair of surface waves was observed due to the oxidation and reduction of H₂Q group in the mixed SAM which follows a 2e⁻, 2H⁺ transfer reaction mechanism. The faradaic charges estimated by the integration of the redox peak area for the mixed monolayer yields a surface coverage value of 1.2×10^{-10} mole cm⁻², which is *ca.* 20% of a full monolayer coverage. These redox peaks are not changed during continuous potential cycling over 2 h, demonstrating that H₂Q-terminating monolayer are stable. However, an adding of 0.70 mM CpEF to the electrolyte solution as described above results in remarkable change in shape of CVs (shown in Figure 2b). For the continuous potential cycling from -0.45 V to 0.60 V, two pairs of redox waves are gradually increasing in their peak currents as a number of potential cycle increases. One pair of redox peaks observed at 0.39 V and 0.32 V is due to the diffusional access of CpEF molecule through some structural defects in the mixed SAM, showing *ca.* 70 mV of peak-to-peak separation. However, the large diffusional current is mainly due to the space-through electron transfer of CpEF in solution because the thickness of the mixed SAM is not large enough to block the heterogeneous electron transfer of diffusing solution species. In addition, we could observe the other pair of redox waves slowly growing around 0.47 V which is due to a surface-confined ferrocene group of CpEF via cycloaddition adduct formed as a result of interfacial D-A reaction. After 50 potential scans, this electrode shows a fully grown surface redox wave of CpEF immobilized to the mixed SAM (shown in Figure 2c) in the mixed electrolyte solution. The symmetric surface wave observed at 0.47 V seems to be fairly ideal due to fast electron transfer of a ferrocene group because the peak-to-peak separation value was *ca.* 15 mV and the redox current ratio was unity. However, ΔE_{whm} is only 48 mV, which is only a half of the theoretical value of

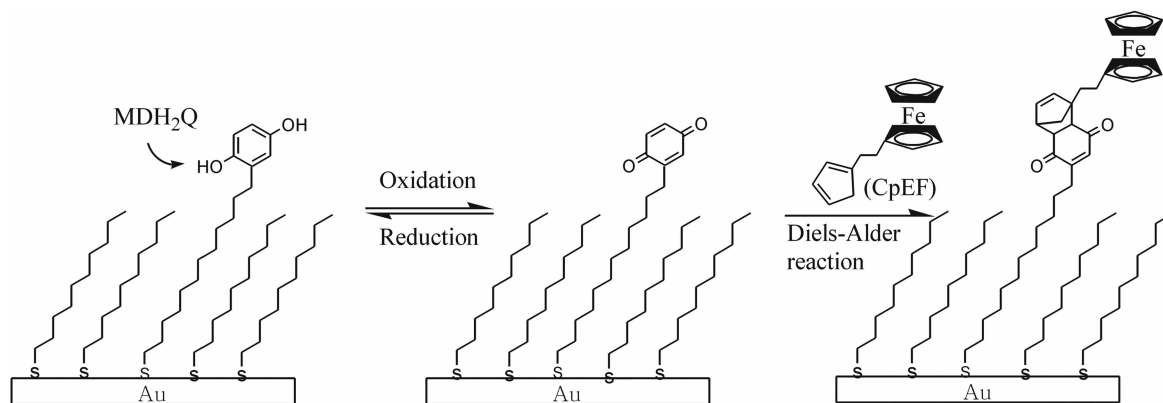


Figure 1. Electrochemical reaction of ω -mercaptododecylhydroquinone (MDH₂Q) in a mixed SAM. Benzoquinone (BQ) group produced in the oxidation step reacts with cyclopentadienylethylferrocene (CpEF) to give the Diels-Alder cycloaddition reaction adduct on the SAM surface.

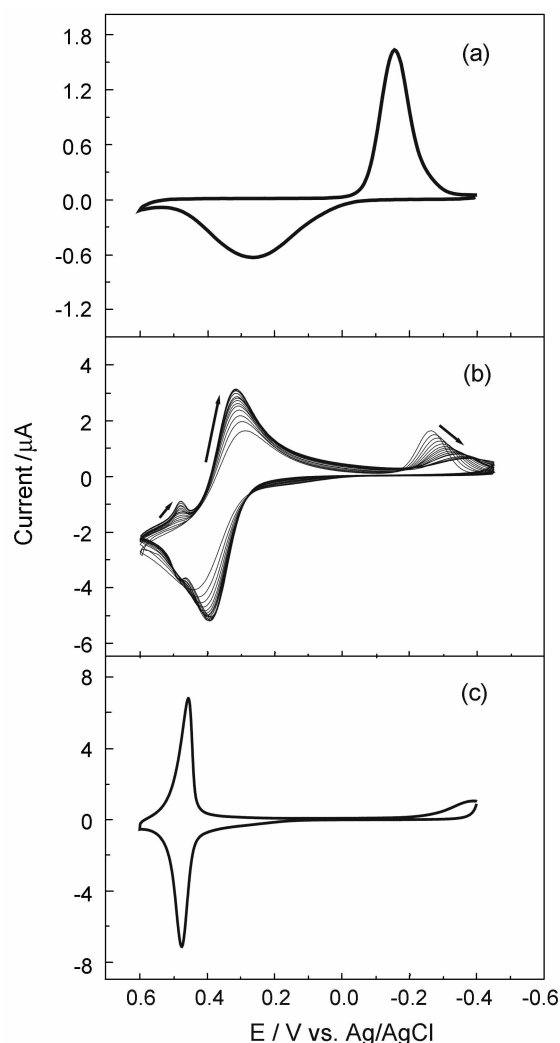


Figure 2. (a) Cyclic voltammogram (CV) of a mixed SAM of MDH₂Q and n-decanethiol on gold at a scan rate of 25 mVs⁻¹ in the mixture solution of volume ratio 1 : 1 tetrahydrofuran : water (154 mM NaCl, 3 mM Na₂HPO₄, pH = 7.8). (b) Consecutive CVs of the mixed SAM in the presence of 0.7 mM CpEF in the same mixture solution. A few CVs shown were partially selected during the time course. (c) CV of CpEF immobilized to SAM surface via D-A cycloaddition in the same solution of (a) at a scan rate of 50 mVs⁻¹.

90.6 mV. We have observed that the magnitude of ΔE_{fwhm} seems to depend on THF composition of electrolyte solution in this experiment. This observation indicates that solvation of hydrophobic CpEF moiety with solvent mixture of THF/water might be a factor to take consideration for a small value of ΔE_{fwhm} . And a relatively small interactions between the adjacent ferrocene groups in the mixed SAM due to a lower surface concentration than one-fifth of the maximum coverage also should be considered.² The integration of charge under the peak gave a CpEF surface coverage value of 1.0×10^{-10} mole/cm². From comparison with a quinone coverage of 1.2×10^{-10} mole/cm², we can estimate that the interfacial D-A reaction was conducted *ca.* 83% to immobilize CpEF on the mixed SAM. In the Figure 2b, the reduction peak current at 0.27 V is continuously decreased due to the decrease in the quinone coverage value because the oxidized

BQ reacts with CpEF molecule in solution phase. The reduction peak potential slowly shifts toward negative direction as the potential is scanned. This might result from the difficulties in the reduction of BQ due to the change in a chemical environment of BQ on the mixed SAM. For a Diels-Alder bimolecular reaction,¹¹ reaction rate (v) is presented by eq. (1):

$$v = k_{\text{DA}} [\text{CpEF}] \Gamma_{\text{BQ}} \quad (1)$$

where k_{DA} is a second-order rate constant, [CpEF] is a molar concentration of CpEF, and Γ_{BQ} is a surface density of the immobilized benzoquinone. Because [CpEF] is much greater than Γ_{BQ} , Eq. (1) can be rewritten into eq. (2):

$$v = k' \Gamma_{\text{BQ}} \quad (2)$$

where k' is a pseudo-first order rate constant in the interfacial D-A reaction. Figure 3 shows a plot for the loss in the peak current for the reduction of benzoquinone versus time for the data shown in Figure 2b. The data could be fit to an exponential decay to obtain a pseudo-first-order rate constant, k' in Eq. (3):

$$I_t = I_f + (I_0 - I_f) \exp(-k' t) \quad (3)$$

Here, I_t is the peak current at time t , I_0 is the initial peak current and I_f is the nonfaradaic residual current¹⁰. A k' value of 1.5×10^{-3} s⁻¹ was obtained from the excellent fit of the experimental data. We repeated the same experiment at different concentrations ranging from 0.5 mM to 1.2 mM of CpEF to obtain a second-order rate constant. In this concentration range, a k_{DA} value of 2.3×10^{-3} M⁻¹s⁻¹ was obtained from an equation $k' = k_{\text{DA}} [\text{CpEF}]$. This value is *ca.* 70 times smaller than that reported by Mrksich *et al.*¹¹ in D-A reaction using cyclopentadiene because k_{DA} depends on the molar concentration of diene molecule used in the reaction. In order to investigate the effect of alkyl chain length of a diluent thiol on rate of the D-A reaction, this set of experiments was repeated for each mixed MDH₂Q-SAM containing different alkyl chain length of n-alkylthiol at different concentrations of CpEF. The pseudo-first-order rate constants

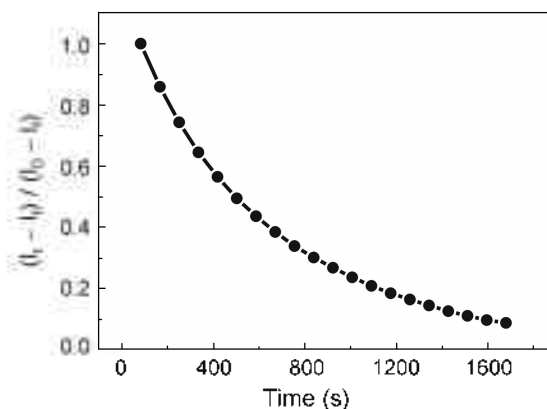


Figure 3. Plot of the reduction peak current vs. time for the data shown in Figure 2(b). I_t is the peak current at time t , I_0 is the initial peak current and I_f is the nonfaradaic residual current. The slope in the plot of $\ln[(I_t - I_f)/(I_0 - I_f)]$ vs. time gave the pseudo-first order rate constant k .

Table 1. Pseudo-first order rate constant k for the interfacial Diels-Alder reaction of CpEF and benzoquinone group at mixed MDH₂Q-SAMs. C_nSH refers to the carbon number of n-alkanethiol used as a diluent thiol in the mixed SAMs

[CpEF]/mM	$k/10^3 \text{ M}^{-1} \text{ s}^{-1}$					
	C ₆ SH	C ₈ SH	C ₁₀ SH	C ₁₂ SH	C ₁₆ SH	C ₁₈ SH
0.5	1.27	1.41	1.09	0.73	0.52	0.40
0.7	1.48	1.70	1.51	0.94	0.74	0.54
1	2.58	2.62	2.31	1.18	0.88	0.73
1.2	3.14	3.28	2.91	2.17	0.90	0.75

Table 2. Second order rate constant k_{DA} for the interfacial Diels-Alder reactions of CpEF and benzoquinone groups at mixed MDH₂Q-SAMs. C_nSH refers to the carbon number of n-alkanethiol used as a diluent thiol in the mixed SAMs

Diluent thiol	$k_{\text{DA}}/10^3 \text{ M}^{-1} \text{ s}^{-1}$
C ₆ SH	2.51
C ₈ SH	2.43
C ₁₀ SH	2.32
C ₁₂ SH	1.71
C ₁₆ SH	0.46
C ₁₈ SH	0.45

obtained in those experiments are presented in Table 1. In all cases, the pseudo-first-order rate constants were linearly related to the concentration of CpEF. Using a relationship that $k' = k_{\text{DA}} [\text{CpEF}]$, k_{DA} was obtained for 6 mixed MDH₂Q-SAMs with different alkyl chain length of simple n-alkanethiol ($n = 6, 8, 10, 12, 16, 18$) and was presented in Table 2. It should be emphasized that a surface coverage of MDH₂Q for 6 mixed SAMs was kept constant to be 20% (± 2) of a full monolayer coverage value to make steric environment around benzoquinone uniform. Figure 4 shows relationship between k_{DA} values for the interfacial D-A reaction and the alkyl chain length of n-alkanethiol. It clearly shows that there are two stages (high and low k_{DA}) located on both sides of $n = 12$, and that k_{DA} value transfers from high to low stage as the length increases. On the high stage (fast D-A reaction), CpEF molecule in solution is freely accessible to the immobilized benzoquinone at the interface because the alkyl chain length of diluent thiol ($n = 6, 8, \text{ and } 10$) is shorter than that ($n = 12$) of MDH₂Q. However, D-A reaction gets slow on the low stage that the length of n-alkanethiol ($n = 16$ and 18) is much longer than that of MDH₂Q. At the low stage, the immobilized benzoquinone is buried within the monolayer surface, resulting in difficulty of accessibility. That is, longer alkyl chain of a diluent surrounding benzoquinone produces steric hindrance to deter the interfacial D-A reaction. Our data shows that the rate constants on the low stage were near $ca. 4.5 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$, which is 5 times lower than those ($ca. 2.5 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$) for mixed SAMs that benzoquinone is in the accessible environment. Though this difference in the second-order rate constants is not so large as expected, the dependence of k_{DA} on the accessibility of benzoquinone demonstrates that a self-assembled monolayer can be used as a model substrate to study kinetics of an interfacial

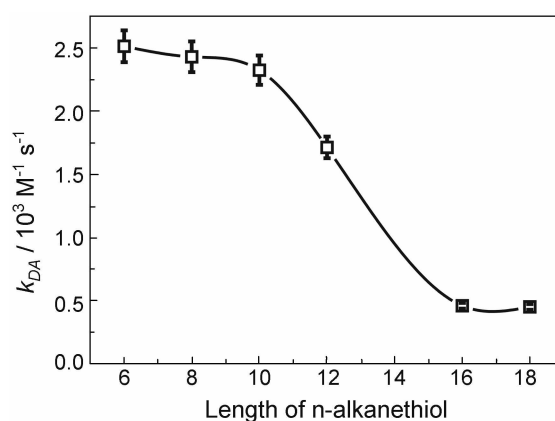


Figure 4. Dependence of second order rate constants presented in Table 2 on the alkyl chain length of a diluent thiol in the mixed MDH₂Q-SAM. At 95% confidence level, the experimental error bars were represented.

reaction. As shown in our work, the modest changes in geometric surface structure can have significant influence on the heterogeneous reaction. Currently, we are studying the effect of temperature on the interfacial D-A reaction rate for those mixed MDH₂Q-SAMs. The temperature study will provide informations on the thermodynamic parameters such as enthalpies and entropies of activation for mechanistic investigation on the modest difference in the second-order rate constant. In conclusion, this work presents that the rate of an interfacial heterogeneous reaction depends on the geometry of a monolayer structure surrounding reactive molecule immobilized on a SAM. In addition, using a well-defined surface monolayer can give us a better understanding of the factors that affect interfacial reactions and in turn provide a mechanistic framework for controlling the reaction of organic molecules at surface. And the combination of self-assembled monolayers and electrochemistry provides a methodology that is well suited for understanding many features characteristics of the interfacial reactions.

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