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Dependence of the Rate of an Interfacial Diels−Alder Reaction on the Steric Environment of the Immobilized Dienophile: An Example of Enthalpy−Entropy Compensation

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Abstract: This paper describes a physical organic study of the relationship between the rate for an interfacial Diels−Alder reaction and the steric environment around the reacting molecules. The study used as a model reaction the cycloaddition of cyclopentadiene with a self-assembled monolayer (SAM) presenting benzoquinone groups surrounded by hydroxyl-terminated alkanethiolates. The accessibility of the quinone was varied by preparing monolayers from hydroquinone-terminated alkanethiols of different lengths [HS-$(CH_2)_n$-HQ, $n = 6-14$] and a hydroxyl-terminated alkanethiol [$HS(CH_2)_{11}$-OH] of constant length. Cyclic voltammetry was used to measure the rate of the reaction by monitoring the decay of the redox-active quinone. The second-order rate constant showed a modest change as the position of quinone was varied relative to the hydroxyl groups of the monolayer. For monolayers wherein the quinone groups were extended from the interface, the rate constants oscillated near 0.20 M^{-1} s^{-1} with an even−odd dependence on the length of the alkanethiol. For monolayers that positioned the quinone groups below the surrounding hydroxyl groups, the rate constants decreased by approximately 8-fold. Examination of the activation parameters revealed that the quinone groups that were positioned below the interface (and in a crowded environment) reacted with an enthalpy of activation that was 4 kcal/mol greater than did the quinones that were accessible at the interface. The reaction of the buried quinone, however, proceeded with an entropy of activation that was more favorable by 13 eu, and therefore with a similar free energy of activation. The combination of SAMs for preparing model interfaces and cyclic voltammetry for measuring rates provides a new opportunity for physical organic studies of interfacial reactions.

Physical organic studies of reactions that occur at the solid−liquid interface have lagged considerably behind studies of reactions in solution.[1−4] The reasons for this difference stem from the added complexity in developing model systems for interfacial reactions, which require substrates that present reactants in defined environments, and from a lack of convenient analytical techniques that have the sensitivity and temporal resolution necessary for measuring the rates of reactions at the interface. The opportunities for mechanistic studies of interfacial reactions have improved with the development of model organic surfaces—and of monolayers of alkanethiolates on gold in particular—which present reactants in well-defined environments and permit wide flexibility in modifying the microenvironment of the immobilized molecules.[5] Early studies have motivated a growing recognition that interfacial reactions can differ in dramatic ways from the corresponding homogeneous phase reactions[6] and that these differences can have substantial practical implications in sensing,[7] catalysis,[8] and combinatorial libraries.[9] In this paper we use as a model reaction the Diels−Alder cycloaddition of cyclopentadiene to benzoquinone immobilized at a monolayer to investigate the dependence of the rate constant on changes in the steric environment of the quinone.

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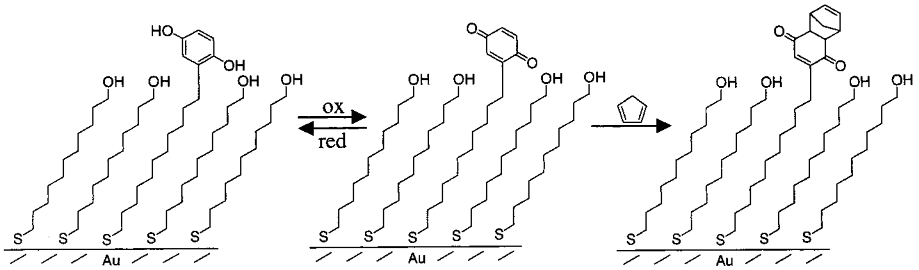

Figure 1. Model substrate for the interfacial Diels–Alder reaction of cyclopentadiene with an immobilized benzoquinone group. The quinone group undergoes a reversible two-electron reduction to give the corresponding hydroquinone and therefore permits the use of cyclic voltammetry to measure the rate of the reaction.

In previous work we described the Diels–Alder reaction of dienes with a self-assembled monolayer (SAM) prepared from an alkanethiol terminated in a benzoquinone group and a second alkanethiol terminated in a hydroxyl group (Figure 1).[10] In this mixed monolayer, the density of the quinone can be controlled (which is important to ensure that the quinones are isolated from one another at the interface) and the choice of the second alkanethiol defines the chemical environment surrounding the quinone.[11] The benzoquinone group was used as the dienophile because it undergoes a reversible two-electron reduction to give the corresponding hydroquinone and therefore permits use of cyclic voltammetry to measure the loss of quinone on the surface.[12] This electrochemical method has the important advantage over many spectroscopic methods in that it measures the rate in situ and does not require the sample to be periodically removed from solution prior to each measurement. For the monolayer shown in Figure 1, we found that the Diels–Alder reaction of immobilized benzoquinone with cyclopentadiene proceeded with a second-order rate constant of $k_{DA} = 0.22\ M^{-1}\ s^{-1}$.

In subsequent work we investigated the reaction of cyclopentadiene with monolayers that presented quinone groups that were surrounded by methyl-terminated alkanethiolates (in place of the hydroxyl-terminated alkanethiolates).[13] The reaction of cyclopentadiene with the immobilized quinone did not proceed with a second-order rate constant but instead approached a maximum rate with increasing concentrations of diene. A kinetic analysis of this reaction was consistent with a model wherein the diene first adsorbed to the monolayer and then underwent reaction with the immobilized quinone. The analysis provided both an equilibrium association constant for adsorption and a first-order rate constant for the reaction. Further, we found that changes in the solvent composition had an effect on the association constant of diene for the substrate but had no effect on the rate constant for reaction of the adsorbed diene and immobilized quinone.[14] This example illustrates one way in which an interfacial reaction can differ dramatically from the corresponding solution-phase reaction.

This model system is well suited for investigating other aspects of interfacial reactions. In this paper, we investigate the relationship between the second-order rate constant of the reaction and the steric environment around the benzoquinone. Our studies reveal that the rate constant shows a modest decrease as the quinone is positioned below the monolayer interface. A determination of the activation parameters for two limiting cases—where the quinone is either freely accessible at the interface or buried within the monolayer—reveals that the buried quinone reacts with an enthalpy of activation that is 4 kcal/mol larger than that of the accessible quinone but that this difference is nearly compensated by a favorable entropy of activation for the reaction of the buried quinone.

Experimental Design

Our strategy for controlling the steric environment of the benzoquinone group within the monolayer is illustrated in Figure 2. We prepared several mixed monolayers from an alkanethiol terminated in the benzoquinone group and a second alkanethiol terminated in a hydroxyl group. The accessibility of the quinone was systematically altered by adjusting the length of the quinone-terminated alkanethiol, while keeping a constant length of the hydroxyl-terminated alkanethiol. When a linker of seven methylene units is used for the benzoquinone-terminated alkanethiol (C7), for example, the quinone is buried within the monolayer. With a linker of 14 methylene units (C14), the benzoquinone group is freely accessible at the interface. In this work, we used eight analogues of the quinone-terminated alkanethiol, wherein the length of the alkyl groups ranged from seven to 14 methylene units. We report the second-order rate constants for this series of monolayers. We also report activation parameters for the reaction to understand the mechanistic basis for differences in reaction rates that result from the change of steric environment around the benzoquinone. In all cases, the quinone-terminated alkanethiolate was present at a density of 3–5% relative to total alkanethiolate. The low density of benzoquinone isolates the reactant groups at the surface and provides a uniform microenvironment around each group.

Results

Synthesis of Benzoquinone-Terminated Alkanethiol. Each of the benzoquinone-terminated alkanethiols was prepared by a common route (Figure 3). The syntheses started with treatment of the appropriate alkenyl bromides with lithiated 1,4-dimethoxybenzene to give the alkylated hydroquinones (**1a**–**1i**). The terminal olefins were converted to the corresponding

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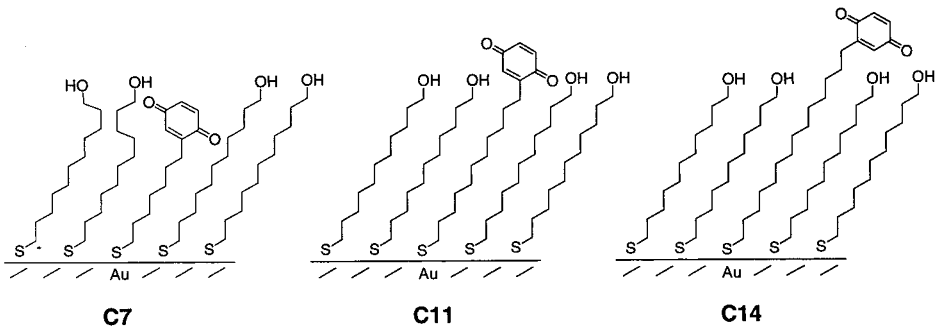

Figure 2. This work investigated the relationship between the rate constant for an interfacial Diels–Alder reaction and the steric environment about the immobilized quinone. A series of mixed SAMs was prepared wherein the quinone group was tethered to an alkanethiolate having from 7 to 14 methylene units and surrounded by a hydroxyl-terminated alkanethiolate of a constant length. The use of a short alkyl group (C7, left) positions the quinone within the monolayer, while an intermediate-sized alkyl group (C11, middle) positions the quinone at the periphery of the monolayer, and a long alkyl group (C14, right) positions the quinone in an accessible environment above the interface.

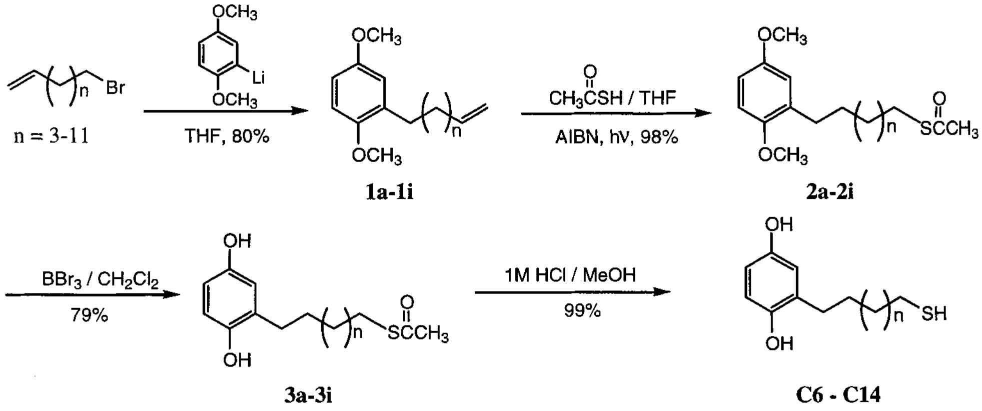

Figure 3. Synthetic route for the preparation of hydroquinone-terminated alkanethiols **C6–C14**. See text for an explanation.

thioacetates by treatment with thiolacetic acid and AIBN under photolytic conditions. Both methyl ethers were efficiently cleaved with boron tribromide to give the unprotected hydroquinones (**3a–3i**). The terminal acetyl groups were removed by refluxing in HCl/MeOH to give the desired alkanethiols (**C6–C14**). Throughout the paper, we refer to the alkanethiols with a nomenclature that indicates the length of the alkyl chain that separates the benzoquinone and thiol groups (C6 through C14).

Preparation of Monolayers. Monolayers were prepared according to standard methods.[15] Gold-coated silicon substrates were immersed in ethanolic solutions of a benzoquinone-terminated alkanethiol and a hydroxyl-terminated alkanethiol (in ratios of 1:12 to 2:3) for 18 h. Because the ratio of alkanethiolates in a mixed SAM is rarely identical to the ratio of alkanethiols in the solution from which the monolayer assembled, we used cyclic voltammetry to independently determine the density of the hydroquinone in the SAM. Integration of the voltammetric wave for reduction of the benzoquinone gave the density of quinone in the monolayer. We found that the longer quinone-terminated alkanethiols were incorporated in the monolayer at higher densities, but we adjusted the solution ratios to ensure that final densities of quinone in all monolayers were between 3% and 5%. For these densities of quinone, all reactions proceeded to completion with a uniform rate, which ensures that the quinone groups are indeed isolated at the interface. When we used monolayers that presented quinone groups at densities of 10–15%, by contrast, the rates showed deviations (usually becoming slower) as the reactions progressed.

Determination of Rate Constant. We used cyclic voltammetry to follow the rate of reaction because the quinone group displays a reversible redox couple and the Diels–Alder adduct is not redox-active over the potential range used here. Hence, the rate of decay of quinone redox waves is proportional to the rate of the Diels–Alder reaction. Cyclic scans were performed between −400 and +600 mV at a scan rate of 25 mV/s in an electrolyte that was equal parts of tetrahydrofuran (THF) and water (154 mM NaCl and 3 mM phosphate, pH 7.7). We used this solvent mixture because a protic solvent is required for the reduction of quinone to the corresponding hydroquinone, while the THF provides solubility for the diene.[10] Equation 1 describes the rate for this second-order reaction (in units of mol·cm^{-2}·s^{-1}), where Γ_Q is the density of quinone groups in the monolayer (in units of mol·cm^{-2}) and k_{DA} is the second-order rate constant (M^{-1} s^{-1}). Under these conditions, the oxidation of hydroquinone was reversible over as many as 100 scans, but when cyclopentadiene was added to the electrolyte the voltammetric waves for both oxidation and reduction decreased over consecutive scans (Figure 4A). Figure 4B shows a representative plot of the peak current, I_t, for the reduction waves as a function of time. Because these experiments were carried out under pseudo-first-order conditions—the amount of diene is in large excess over the immobilized quinone—the apparent rate constant k' is

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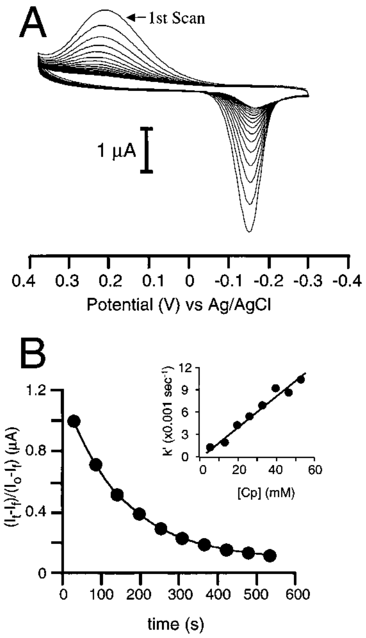

Figure 4. (A) Consecutive cyclic voltammetric scans of a monolayer presenting the hydroquinone group (C11) at a density of 4% mixed with hydroxyl-terminated alkanethiolate. The scans were performed in the presence of cyclopentadiene (24 mM) in 1:1 THF/H_2O with phosphate (3 mM) and NaCl (154 mM) at a scan rate of 25 mV/s. (B) Plot of peak current for the reduction wave versus time for the data shown in panel A. I_t is the peak current at time t, I_0 is the peak current for the first scan, and I_f is the residual nonfaradaic current. The pseudo-first-order rate constant k' was obtained from the slope of a plot of ln $[(I_t - I_f)/(I_0 - I_f)]$ versus time. The rate constants k' were determined for several concentrations of diene. These rate constants increased linearly with the concentration of diene (inset) and gave a second-order rate constant, k_{DA}, of 0.22 M^{-1} s^{-1}.

equal to k_{DA}[Cp] (eq 2). The data for decay of quinone were fitted to eq 3 to give the pseudo-first-order rate constant k', where I_t is the peak current at time t, I_0 is the initial peak current, I_f is the residual nonfaradaic current, and t is the reaction time after correction for the fraction of time during which the monolayer presents the nonreactive hydroquinone.

$$v = k_{DA}[\mathrm{Cp}]\Gamma_Q \tag{1}$$

$$v = k'\Gamma_Q \qquad ([\mathrm{Cp}] \gg \Gamma_Q) \tag{2}$$

$$\ln [(I_t - I_f)/(I_0 - I_f)] = -k't \tag{3}$$

We repeated this experiment with concentrations of cyclopentadiene ranging from 3 to 70 mM. A plot of the pseudo-first-order rate constants versus the concentration of cyclopentadiene was linear (Figure 4B, inset). A least-squares fit of these linear data gave the second-order rate constants k_{DA}.

C7−C14 Rate Constants with C11 (-OH) Background. We repeated the analysis described above for each of the eight monolayers prepared from one of the quinone-terminated alkanethiols (C7−C14) and the hydroxyl-terminated alkanethiol. In all cases, the benzoquinone groups displayed a reversible two-electron reduction, though the positions of oxidation and reduction waves showed a slight dependence on the distance of quinone to the gold substrate (~400 mV difference between C7 and C14). For monolayers containing either C11, C12, C13, or C14 quinones, the rate of loss of quinone (due to Diels−Alder reaction) followed an exponential decay to completion of the reaction. For monolayers containing C7, C8, C9, and C10 alkanethiolates (which were shorter than the hydroxyl-terminated alkanethiolate), the disappearance of quinone over the first half of the reaction was described well by a single exponential decay but then deviated from the exponential at longer extents of reaction. Plots of ln $[(I_t - I_f)/(I_0 - I_f)]$ versus time showed an upward deviation (the rate of reaction slowed) as the reaction proceeded, which was likely due to a steric accumulation of the product in the monolayer. For these cases, we fitted data from the start of the reaction to ~60% completion. As described above, for each monolayer (C7−C14), we measured the pseudo-first-order rate constant at concentrations of cyclopentadiene ranging from 3 to 70 mM. In all cases, the first-order rate constants (k') were linearly related to the concentration of diene. The resulting second-order rate constants are listed in Table 1.

Table 1. Second-Order Rate Constants for the Interfacial Diels−Alder Reactions of Cyclopentadiene and Quinone Groups Presented at Self-Assembled Monolayer with Methylene Linkers of Varying Lengths[a]

monolayer	k_{DA} (M^{-1} s^{-1})	error[b]
C7	0.010	0.001
C8	0.027	0.004
C9	0.035	0.004
C10	0.135	0.015
C11	0.219	0.021
C12	0.175	0.016
C13	0.209	0.024
C14	0.188	0.008

[a] The labels for monolayers refer to the number of methylene units in the quinone-terminated alkanethiols. [b] Errors were calculated at the 95% confidence level.

C6 Rate Constant with C6 (-OH) Background. The data presented above show that the rate constant for the Diels−Alder reaction decreases as the quinone is positioned within the monolayer. To verify that the changes in rate were due primarily to changes in the relative positions of quinone and hydroxyl background, we characterized the Diels−Alder reaction for a monolayer prepared from a short hydroquinone-terminated alkanethiol (C6) and mixed with a hydroxyl-terminated alkanethiolate that also had six methylene units. Our hypothesis was that the Diels−Alder reaction with these monolayers should proceed with a rate constant that was similar to that for monolayers having the C11 quinone mixed with 11-hydroxyundecanethiol (as shown in Figure 1). Reactions with this monolayer were kinetically well-behaved and gave first-order rate constants that increased linearly with the concentration of diene (Figure 5, inset). The second-order rate constant k_{DA} of 0.19 M^{-1} s^{-1} was indeed similar to that for monolayer presenting the quinone and hydroxyl groups at longer alkanethiolates.

Activation Parameters. To understand the mechanistic basis for the rather modest changes in rate constant observed with the series of monolayers, we measured activation parameters for the Diels−Alder reaction of two monolayers: one in which the benzoquinone was freely accessible (C13) and one in which benzoquinone was partially buried within the monolayer (C9). In both cases, the reaction rates were measured as described above and were repeated at eight different temperatures ranging from 0 to 40 °C. The rate constants are summarized in Table 2. Activation parameters were determined in the normal fashion by a least-squares fit of plots of ln (k_{DA}/T) versus $1/T$ (Figure 6) by use of eq 4, where κ is the transmission coefficient (≈1,

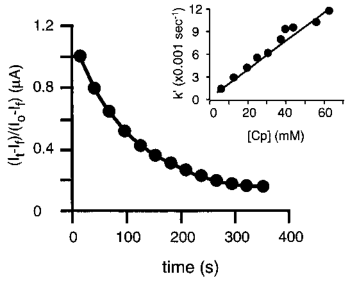

Figure 5. Plot of peak current for the reduction wave versus time for the mixed monolayer of (mercaptohexanyl)hydroquinone (C6) and mercaptohexanol. I_t is the peak current at time t, I_0 is the peak current for the first scan, and I_f is the residual nonfaradaic current. The pseudo-first-order rate constant k' was obtained from the slope of a plot of $\ln((I_t-I_f)/(I_o-I_f))$ versus time. The rate constants k' were determined for several concentrations of diene. These rate constants increased linearly with the concentration of diene (inset) and gave a second-order rate constant, k_{DA}, of 0.19 M^{-1} s^{-1}.

Table 2. Summary of Second-Order Rate Constants for the Diels–Alder Reaction of Cyclopentadiene with Two Monolayers Presenting Quinone Groups (C9 and C13)

C9		C13	
temp (°C)	k (M^{-1} s^{-1})	temp (°C)	k^a (M^{-1} s^{-1})
2	0.009	2	0.065
7	0.020	6.5	0.089
12	0.027^b	10	0.109
17	0.036^b	14	0.102
22	0.042^b	18	0.136
27	0.053^b	21	0.147
32	0.080	25	0.152
37	0.106	33	0.224

[a] Second-order rate constant determined with monolayers presenting quinone groups at 15% density. [b] Average rate constant from two different measurements.

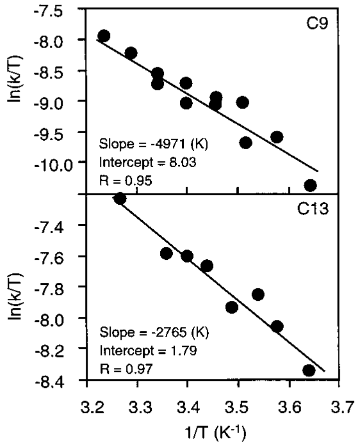

Figure 6. Plot of ln (k/T) versus $1/T$ for the reaction of cyclopentadiene with monolayers presenting quinone groups in either a crowded environment (C9, top) or an accessible environment (C13, bottom). Values for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were calculated from the slope and the intercept of the best-fit lines to these data.

in many cases), k_b is the Boltzmann constant (1.380×10^{-23} J/K), R is the gas constant (1.987 cal/mol•K), and h is Planck's constant (6.626×10^{-34} J•s); the activation parameters are listed in Table 3.

$$\ln (k_{DA}/T) = \ln (\kappa k_b/h) + \Delta S^{\ddagger}/R - \Delta H^{\ddagger}/RT \qquad (4)$$

Discussion

This paper presents a physical organic study of an interfacial Diels–Alder reaction. The use of a self-assembled monolayer as a model substrate was significant for two reasons. First, the well-defined structure of the monolayer gives excellent control over the steric accessibility of the quinone groups and at the same time allows these groups to be diluted in the film so that they are isolated and therefore each reacts with uniform kinetics. The structural order of the monolayers and the synthetic flexibility to adjust the environments of reactive groups is unmatched by other model substrates for studying interfacial reactions. Second, since the benzoquinone group is redox-active, cyclic voltammetry could be used to monitor the rate of the interfacial reaction. This technique has a primary advantage compared to other analytical tools that have been used for interfacial kinetic studies [including X-ray photoelectron spectroscopy, IR, and contact angle measurement] in that it provides kinetic information in real time without causing unwanted damage to the interface. The combination of SAMs and cyclic voltammetry gives an excellent model system for physical organic studies of interfacial reactions.

Table 3. Comparison of the Activation Parameters for the Interfacial Diels–Alder Reaction of Cyclopentadiene with Monolayers That Present the Quinone Group in a Buried Environment (C9) and an Accessible Environment (C13)

activation parameter	C9	C13
$\Delta G^{\ddagger}$	19.1 ± 0.4 kcal	18.5 ± 0.4 kcal
$\Delta H^{\ddagger}$	9.8 ± 0.5 kcal	5.5 ± 0.4 kcal
$\Delta S^{\ddagger}$	−31 ± 3 eu	−44 ± 3 eu

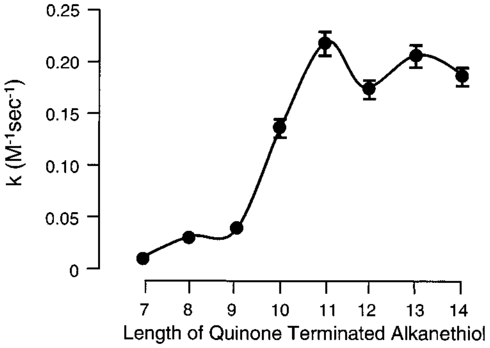

Figure 7. Relationship between the second-order rate constants for interfacial Diels–Alder reactions and the length of the quinone-terminated alkanethiol (the background hydroxyl-terminated alkanethiol has a length of 11 methylene units). The error bars were calculated with 95% confidence level.

We quantitatively measured the dependence of rate constant for the interfacial Diels–Alder reaction on the accessibility of the benzoquinone and found that there is a difference of about 2 kcal/mol between the largest and smallest rate constants (Figure 7). For monolayers presenting quinone groups on alkanethiolates that were as same length as, or longer than the hydroxyl-terminated alkanethiolate (C11–C14), the rate constants were between 0.18 and 0.22 M^{-1} s^{-1} and showed a slight even–odd alternation with the number of methylene units in the alkyl chains. While this finding is consistent with previous studies that have shown a dependence of interfacial properties on an even–odd effect, which derives from the orientation of the terminal group at the interface, the mechanistic significance for the more rapid reaction of vertically oriented quinone groups is unclear.[16] For monolayers presenting quinone groups on alkanethiolates that were shorter than the hydroxyl-terminated alkanethiolates (C7–C9), the rate constants were all near 0.03

M^{-1} s^{-1}, which is approximately 7-fold lower than those for monolayers that present the quinone in an accessible environment.

We had expected to observe a larger difference in rate constants for monolayers that varied the position of the quinone groups relative to the hydroxyl groups. To investigate the mechanistic basis for the modest change in rate constant, we determined the activation parameters for two monolayers: one that presented the quinone above the interface (C13) and one that positioned the quinone below the interface (C9). This experiment showed that the enthalpies and entropies of activation were very different for the two cases and that these differences compensated one another to give similar free energies of activation ($\Delta G^{\ddagger}$). The reaction of cyclopentadiene with the accessible quinone had an enthalpy of activation ($\Delta H^{\ddagger}$) of 5.5 kcal/mol. This value is consistent with (but on the lower end of) values found for analogous Diels−Alder reactions in solution.[17] The interfacial reaction with the buried quinone (C9) had a $\Delta H^{\ddagger}$ of 9.8 kcal/mol, a value that is 4 kcal/mol higher than that for C13. This enthalpic penalty for the buried system is likely due to the following two reasons. First, the steric environment imposed by the dense-packed alkanethiolates likely prevents optimal alignment and orientation of diene with the dienophile, leading to less overlap between the two reacting π-systems in the transition state. Second, the approach of the diene to the quinone group within the monolayer likely requires that the alkanethiolates surrounding the quinones undergo conformational changes to introduce gauche interactions. It is also possible that the activation parameters are influenced by changes in the local dielectric constant (which should be lower for the buried quinone), but we would expect this effect to be minimal because the concerted Diels−Alder reaction proceeds with little charge separation in the transition state. In any case, the ~4 kcal/mol difference in $\Delta H^{\ddagger}$ for the two reactions, in the event that there was no change in $\Delta S^{\ddagger}$, would correspond to a 1000-fold difference in rate constants.

The entropies of activation ($\Delta S^{\ddagger}$) for the two monolayers, however, differed by a magnitude that negated much of the enthalpic penalty incurred by the buried quinone. For the monolayer that presents the quinone above the interface (C13), the $\Delta S^{\ddagger}$ was −44 eu, a value that is slightly more unfavorable than analogous Diels−Alder reactions in solution.[17] Monolayers having the quinone group in a crowded environment (C9), by contrast, had a $\Delta S^{\ddagger}$ of −31 eu, a value that is less unfavorable than analogous solution-phase reactions. In both cases, the negative values of $\Delta S^{\ddagger}$ reveal that the transition-state complexes are more ordered than the reactants, which is due to a required specific alignment of the π systems in the Diels−Alder reaction. The smaller negative value of $\Delta S^{\ddagger}$ for reaction of the buried quinone shows that two molecules undergo less ordering in the transition state than they do in reaction of the accessible quinone. This smaller absolute value of $\Delta S^{\ddagger}$ for reaction of the buried quinone requires either that the transition-state complex is less ordered or the reactants are more ordered as compared to reaction of the accessible quinone. We favor the explanation that the transition state is less ordered, because it is more consistent with the larger $\Delta H^{\ddagger}$ that accompanies reaction of the buried quinone. As we suggested above, the hydroxyl-terminated alkanethiolates surrounding the buried quinone groups can prevent optimal alignment of the two π systems, thereby relaxing the requirement for strict alignment of the two molecules. We must note that these explanations do not address roles that the solute molecules near the interface can play, which could easily dominate changes in $\Delta S^{\ddagger}$. A sophisticated understanding of interfacial solvation, however, is still lacking due to limited experimental techniques that can assess interfacial properties, and therefore it is not yet possible to fully interpret activation parameters for interfacial reactions.[18]

It is important to recognize that although the monolayer substrates are structurally well-ordered, they do in practice contain defects and display conformational dynamics at the surface, which can lead to structures that deviate from the idealized structures commonly shown in figures. At the same time, they are sufficiently ordered that modest changes in structure, including changing the relative positions of reactive groups and neighboring groups by a single methylene unit, can have a significant influence on the reaction. To gain support that the differences in reactivity observed in this work were due primarily to changes in the relative position of the quinone relative to the interface, we determined the rate constant for reaction with a monolayer presenting quinone groups on a short alkanethiolate (C6) and surrounded by a short hydroxyl-terminated alkanethiolate [$S(CH_2)_6OH$]. Indeed, we found that the rate constant was similar to that for the C11 quinone described above. As we noted above, the reaction of monolayers presenting the quinone group above the interface (C11−C14) proceeded to completion with a uniform rate constant, whereas reaction of monolayers presenting the quinone group below the interface showed deviations in rate as the reaction progressed. This result suggests that, for the latter case, the product exerts a steric influence on unreacted quinone groups.

This paper describes studies of the relationship between the rate constant for an interfacial Diels−Alder reaction and the accessibility of the immobilized dienophile. This work used self-assembled monolayers of alkanethiolates on gold as a model substrate to vary the position of a benzoquinone group within the monolayer and found a modest effect of the environment on the rate constant for reaction. A mechanistic analysis of these rates showed that the enthalpy of activation was strongly dependent on the environment but was largely masked by a compensating entropy of activation. This work is significant because it provides an example that illustrates the importance of steric factors in interfacial reactions. This type of steric effect, which is due to the structure of the interface, does not have an analogue in corresponding solution-phase reactions. The system used in this work has the additional significance that it permits quantitative studies of reaction kinetics at a level that has previously only been possible with reactions that take place in

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a homogeneous phase. We believe that the combination of SAMs and cyclic voltammetry employed here will be valuable in identifying other mechanistic factors that are unique to interfacial reactions.

Experimental Section

Chemicals and solvents were purchased from Aldrich Chemical Co, Pfaltz & Bauer, and Fluka. THF was distilled from sodium benzophenone ketyl, and CH_2Cl_2 was distilled from calcium hydride. Column chromatography was performed with 70−230 mesh silica gel (Fisher Scientific). NMR spectra were acquired on Bruker DRX 400 MHz or DMX 500 MHz spectrometers. For electrochemistry, deionized ultrafiltered water, tetrahydrofuran (optima grade), and absolute ethanol were purchased from Fisher Scientific. Phosphate-buffered saline was purchased from Gibco−BRL. Adsorbates were synthesized or purchased from Aldrich and purified before use. Cyclopentadiene was distilled prior to each experiment in order to remove dimer and was kept at −20 °C as a 10 M solution in THF.

11-(2,5-Dimethoxyphenyl)-1-undecene (1f). To a solution of *n*-butyllithium solution in hexanes (2.5mM, 5.8 mL, 14.5 mmol) was added dry tetramethylethylenediamine (2.19 mL, 14.5 mmol) at room temperature. The reaction mixture was cooled to 0 °C, and a solution of *p*-dimethoxybenzene (2 g, 14.5 mmol) in THF (20 mL) was added over a period of 30 min. The resulting pale yellow solution was stirred for 90 min and a solution of undecenylbromide (1.9 mL, 8.66 mmol) in THF (10 mL) was added. The colorless reaction mixture was warmed to room temperature and stirred for 10 h. The reaction mixture was diluted with ethyl acetate, washed with saturated NH_4Cl solution, water, and brine, and dried over $MgSO_4$. The organic layer was concentrated to a pale yellow oil and purified by column chromatography with 6:1 hexane/methylene chloride to afford 1.97 g (79% yield) of product as colorless oil: ^1H NMR ($CDCl_3$) δ 6.72 (m, 3H, -$C_6H_3(OCH_3)_2$), 5.8 (m, 1H, -C*H*CH_2), 4.95 (dq, *J* = 2.0 and 17.1 Hz, 2H, -CHCH_2), 3.77 (s, 3H, -OCH_3), 3.76 (s, 3H, -OCH_3), 2.57 (t, *J* = 7.6 Hz, 2H, -CH_2-Ar), 2.03 (q, *J* = 6.7 Hz, 2H, -CH_2CHCH_2), 1.58 (br s, 2H, -CH_2CH_2-Ar), 0.96 (br s, 12H, -(CH_2)-).

11-(2,5-Dimethoxyphenyl)-1-(thioacetyl)undecane (2f). To a solution of **1f** (800 mg, 2.7 mmol) in THF (30 mL) was added thiolacetic acid (0.49 mL, 6.95 mmol) and azobis(isobutylnitrile) (46 mg, 0.28 mmol). The reaction mixture was irradiated in a photochemical reactor (Rayonet reactor lamp, Southern New England Ultraviolet Co., model RPR-100) for 5 h under a nitrogen atmosphere. The reaction mixture was concentrated and purified by column chromatography with 1:20 ethyl acetate/hexane to give 970 mg (98%) of product as a yellowish oil: ^1H NMR ($CDCl_3$) δ 6.71 (m, 3H, -$C_6H_3(OCH_3)_2$), 3.75 (s, 3H, -OCH_3), 3.74 (s, 3H, -OCH_3), 2.84 (t, *J* = 7.4 Hz, 2H, -CH_2SCOCH_3), 2.54 (t, *J* = 7.7 Hz, 2H, -CH_2Ar), 2.3 (s, 3H, -SCOCH_3), 1.54 (br s, 4H, -CH_2CH_2SCOCH_3, -CH_2CH_2Ar), 1.28 (br s, 14H, -$(CH_2)_7$-).

11-(2,5-Dihydroxyl)-1-(thioacetyl)undecane (3f). A solution of **2f** (3.14 g, 7.68 mmol) in methylene chloride (50 mL) was cooled to −78 °C and a solution of boron tribromide (7.26 mL, 76.8 mmol) was added. The mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was then cooled to −78 °C and quenched by addition of diethyl ether and water. The reaction mixture was washed with water and brine and dried over $MgSO_4$. The organic layer was concentrated and purified by column chromatography with 1:6 ethyl acetate/hexane to give 2.71 g (93%) of product as a white powder: ^1H NMR ($CDCl_3$) δ 6.6 (m, 3H, -$C_6H_3(OH)_2$), 2.83 (t, *J* = 7.3 Hz, 2H, -CH_2SCOCH_3), 2.54 (t, *J* = 7.7 Hz, 2H, -CH_2Ar), 2.3 (s, 3H, -SCOCH_3), 1.56 (br s, 4H, -CH_2CH_2SCOCH_3, -CH_2CH_2Ar), 1.27 (br s, 14H, -$(CH_2)_7$-).

11-(2,5-Dihydroxyl)-1-mercaptoundecane (4f). To a solution of **3f** (2.30 g, 6 mmol) in methyl alcohol (50 mL) was added concentrated HCl (5 mL, 60 mmol), and the mixture was then heated to reflux for 10 h. The reaction mixture was washed with water and dried over $MgSO_4$. The organic layer was concentrated to give a white powder, which was purified by column chromatography with 1:3 ethyl acetate/hexane to give 1.76 g (99%) of product as a white powder: ^1H NMR ($CDCl_3$) δ 6.6 (m, 3H, -$C_6H_3(OH)_2$), 2.9 (m, 4H, -CH_2SCOCH_3, -CH_2-Ar), 1.58 (br s, 4H, -CH_2CH_2SCOCH_3, -CH_2CH_2Ar), 1.34 (br s, 14H, -$(CH_2)_7$-).

Preparation of Monolayer Substrates. Substrates were prepared by vacuum deposition titanium (100 Å) and then gold (1000 Å) onto the silicon wafers (111, Silicon Sense) by use of a Thermionics e-GUN evaporator. Mixed monolayers were formed by immersing the gold-coated substrates into ethanolic solutions of hydroxyl-terminated alkanethiol (0.6−0.92 mM) and hydroxyquinone-terminated alkanethiol (0.4−0.08 mM, respectively) for 12−24 h. The substrates were removed from the solution, washed with deionized water and absolute ethanol, and dried with a stream of nitrogen gas.

Electrochemical Measurement. Cyclic voltammetry was performed with a Bioanalytical Systems CV-50W potentiostat in an electrolyte comprising equal parts of THF and phosphate-buffered saline solution. The apparent pH of the electrolyte was adjusted to 7.7 with 0.1 N HCl solution and 1 N NaOH solution. All experiments used the monolayer as a working electrode, with a platinum wire counterelectrode and Ag/AgCl reference electrode. Cyclic scans were performed within −400 mV ∼ +600 mV at a scan rate of 25 mV/s.

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