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Catalytic Mechanism of Interfacial Water in the Cycloaddition of Quadricyclane and Diethyl Azodicarboxylate

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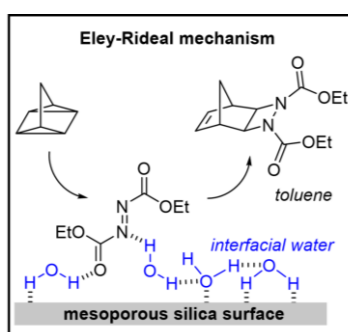
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ABSTRACT: “On-water” catalysis, the unusual activity of water molecules at the organic solvent-water interface, has been demonstrated in many organic reactions. However, the catalytic mechanism has remained unclear, largely due to the irreproducibility of the organic-water interface under the common stirring condition. Here, the interfacial area was controlled by employing adsorbed water on mesoporous silica nanoparticles as the catalyst. Reliable kinetics of the cycloaddition reaction of quadricyclane and diethyl azodicarboxylate (DEAD) at the toluene-water interface within the nanoparticle pores were measured. Data reveal an Eley-Rideal mechanism, wherein DEAD adsorbs at the toluene-water interface via hydrogen bonds formed with interfacial water, which lower the activation energy of the cycloaddition reaction. The mechanistic insights gained and preparation of surface water in silica pores described herein may facilitate the future design of improved “on-water” catalysts.

TOC graphic



Interfacial water plays an essential role in nature, science, and technology. “On-water” catalysis, a term coined for catalysis at the interfaces of organic solvents and water, was discovered by Sharpless and coworkers when they observed a significant increase in product yield after vigorously stirring a heterogeneous mixture of organic reaction solution and water.¹ Since then, “on-water” catalysis has been explored as a venue for inexpensive and environmentally-friendly organic synthesis.²⁻⁵ However, understanding the catalytic mechanism is still challenging,⁶ largely because the stirred mixtures of organic reaction solutions and water create non-uniform water droplets that are difficult to characterize and reproduce. This issue was solved elegantly by using a biphasic fluidic platform in which the water droplets

were created in polytetrafluoroethylene tubes filled with reactants and toluene, and the organic-water interfacial area was determined and correlated with reaction kinetics.⁷ However, mixing within those microchannels is reduced significantly as compared to the common stirring condition in organic synthesis due to the hydrodynamically stable laminar flow.⁸ Consequently, the measured reaction rate may not necessarily reflect the actual kinetics that occur under the well-mixed conditions in common organic synthesis.

In this work, water was confined in mesoporous silica nanoparticles (MP-SNPs) to control the amount of interfacial water, which in turn, facilitated reliable kinetic and spectroscopic studies of the “on-water” catalyzed reaction. The cycloaddition reaction between quadricyclane and diethyl azodicarboxylate (DEAD) at the toluene-water interface serves as a prototypical reaction due to the extensive research on this reaction (Figure 1).^{1, 7, 9-12} The facile tunability of the water-adsorbed MP-SNP catalyst allows for a systematic kinetic study and elucidation of the catalytic mechanism.

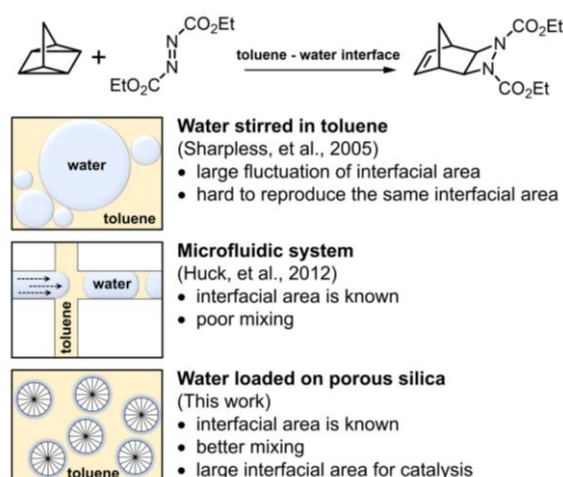


Figure 1. Development of some platforms for studies of “on-water” catalysis.

The MP-SNPs were allowed to adsorb water vapor at room temperature in a home-built humidity-controlled box (Section S1.4). FTIR spectroscopy confirmed water in the pores to be dominantly surface bound due to the characteristic red-shift of the HOH bending vibration as compared to that of bulk water¹³.

¹⁴ (Figure S1). This adsorption fashion is consistent with a previous study on mesoporous silica MCM-41 with pore sizes of 2-6 nm in which the adsorbed water spreads evenly on the surface within the pores for low amounts of adsorbed water.¹⁵ The amount of surface water was determined by the peak area of the HOH bending mode and tuned by adjusting the adsorption time within the humidity-controlled box (Figure 2b, Section S1.5). Under typical conditions for preparing the catalyst in our kinetic studies, the adsorbed water can reach up to an average of four molecules per nm² of porous silica surface, which is comparable to the number of silanol groups on the same surface.¹⁶

To confirm that the majority of catalytic sites comprise surface-adsorbed water within the pores of MP-SNPs, the reaction conversion was monitored for three control samples in which the mass of MP-SNPs and amount of adsorbed water were kept constant, but the external surface area varied by changing the particle diameter (Figure 2c and 2d). If the reaction were to happen only on the external surface of the particles (*i.e.*, the outermost part), the conversion would be reduced significantly for larger particles due to the reduction of external particle surface area. In fact, the observed conversions after background correction (*vide infra*, 27%) are strongly correlated to the internal surface areas, but not to the external surface areas (Figure 2d). This result suggests that most of the catalyst sites are within the pores. Considering the relatively small pore diameter (ca. 2.1 nm)¹⁷, the reactants, products, and toluene solvent can still efficiently diffuse in and out of the pores for the reaction to happen. At high water loading conditions, the conversion reaches an upper limit (Figure 2b). This suggests that water may begin to adsorb in a multi-layer fashion and the percentage of active sites relative to the total amount of loaded water is reduced. Note that the reaction conversion was kept well below 100% for reliable kinetic comparisons in this study; however, a higher conversion can be achieved with longer reaction times.

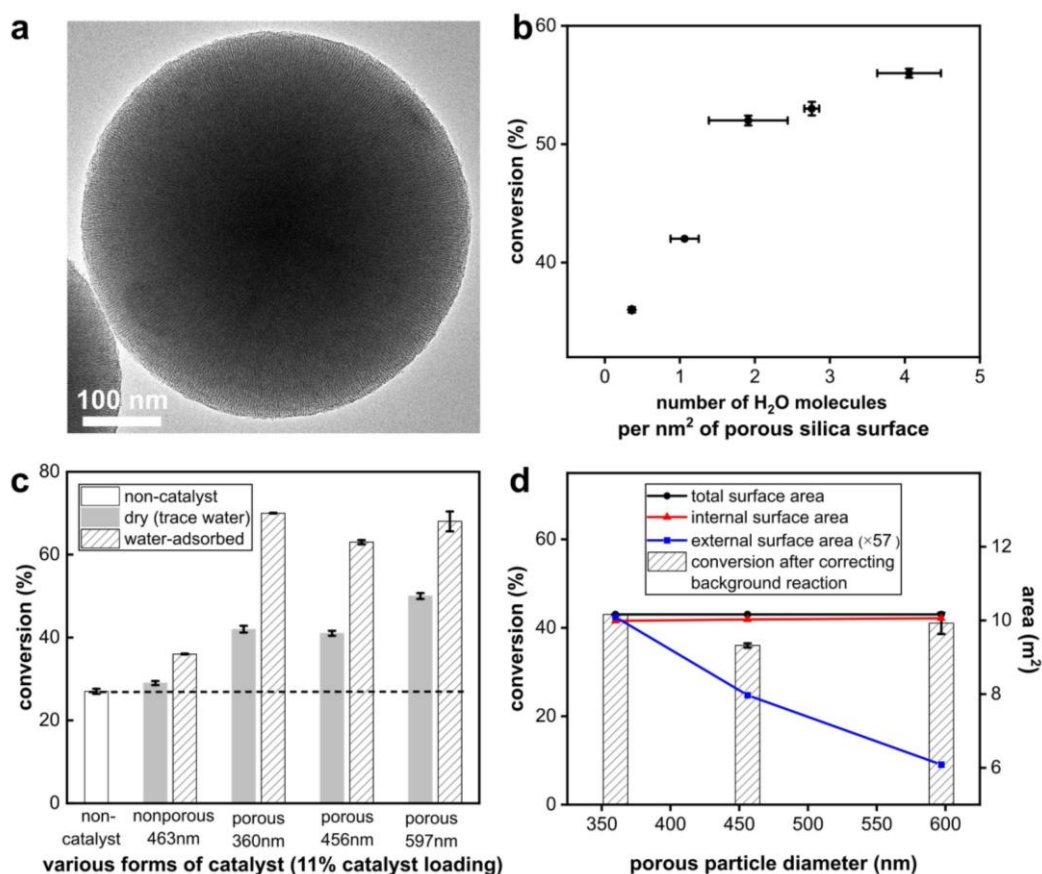


Figure 2. Water-adsorbed mesoporous silica nanoparticle catalyst for the cycloaddition of quadricyclane and DEAD. a) A representative TEM image of 597 ± 22 nm mesoporous silica nanoparticles. b) Reaction conversion vs. amount of surface water adsorbed on the silica surface under the same catalyst loading condition (11% in w/w, particle size of 425 ± 23 nm, 24h reaction). c) Reaction conversion when using different forms of catalysts after 24h reaction. d) Correlation between conversion in (c) (after subtracting conversion of the background reaction) and surface areas of the catalysts. Error bars represent one standard deviation of the means.

Non-porous SNPs prepared with adsorbed water showed lower catalytic activities due to the decreased surface area and interfacial water (Figure 2c). Dry MP-SNPs which still have trace amounts of adsorbed water also gave lower conversions. Due to the unavoidable trace of adsorbed water when handling the dry MP-SNPs, this trace of water, confirmed by FTIR spectroscopy (see one example in Figure S1), may partially contribute to the observed conversion. Nevertheless, the lower conversion obtained from these

dry MP-SNPs indicates that the interfacial water generates greater catalytic activity than the bare silica surface. When pure water was used as the catalyst at the same loading in the reaction mixture as the water-loaded MP-SNPs (Figure S2), the conversion dropped significantly, indicating lower surface areas for water droplets. Note that the non-catalyzed reaction occurs in the bulk of toluene solvent (background reaction) in parallel with the water-catalyzed reaction occurring at the toluene-water interface. When necessary, the conversion due to non-catalyzed reaction in the bulk are subtracted from those of the catalyzed reaction. The effect of the background reaction was estimated from the non-catalyzed reaction under similar experimental conditions; this approximation is reasonable since the majority of reactant molecules exist in the bulk, as confirmed by UV-Vis spectroscopy measurements on the reaction solution before and after centrifuging MP-SNPs. Given these results, MP-SNPs with an average of four water molecules per nm^2 of silica surface were selected for further kinetic study (Table S1).

Second harmonic scattering (SHS) spectroscopy was used to investigate the molecular interaction between DEAD and interfacial water adsorbed within the pores. In this surface-specific technique, the 400 nm SHS signal generated from the 800 nm laser beam is resonantly enhanced by the strong optical absorbance of DEAD molecules ($\lambda_{\text{max}} = 405 \text{ nm}$) that adsorb at the toluene-water interface within the pores. Although coherent second harmonic generation is not allowed in bulk centrosymmetric media under the electric dipole approximation, SHS signal is still detected from our sample. The micron or sub-micron size centrosymmetric particles like the MP-SNPs used in this study have non-centrosymmetric local surface because the size of the particles is much larger than the coherence length of the second harmonic generation process.^{18, 19} Based on the SHS intensity, the surface coverage of DEAD was extracted and the adsorption isotherm was shown to follow a Langmuir model (Section S1.8 and Figure S3). This result suggests that DEAD adsorbs at the toluene-water interface, most likely via hydrogen bonding. A control measurement on the dry porous version showed no dependence of SHS intensity on the bulk concentration of DEAD; therefore, the surface water plays a critical role in adsorption. Quadricyclane is expected not to adsorb strongly at the toluene-water interface due to its nonpolar nature.

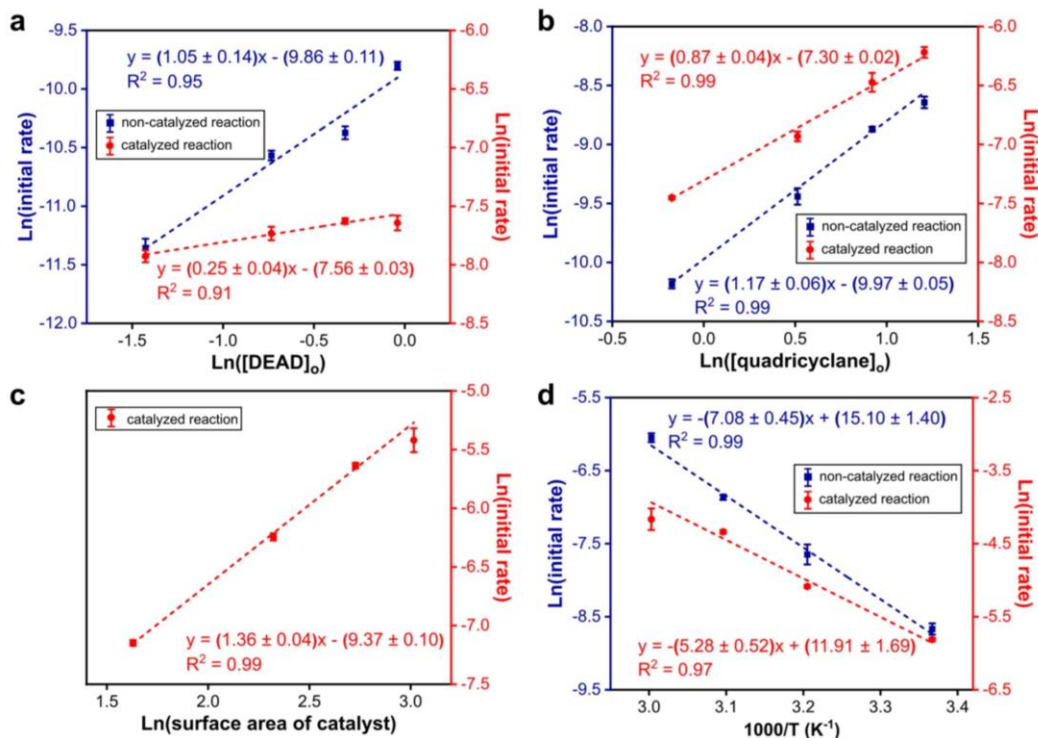


Figure 3. Kinetics of quadricyclane and DEAD reaction without catalyst (left axis) and with catalyst (right axis). a, b, and c) Initial reaction rates with various initial concentrations of DEAD, quadricyclane and catalyst surface area. d) Arrhenius plots show the activation energies of non-catalyzed and catalyzed reactions to be 14.1 ± 0.9 and 10.5 ± 0.9 kcal/mol, respectively. Error bars represent one standard deviation of the means.

To determine the reaction order, initial reaction rates were measured with different initial reactant concentrations. When a reaction proceeded, a small volume of the reaction solution was extracted, diluted in cold toluene (10°C) to quench the reaction, centrifuged to remove MP-SNPs, and the absorbance peak of DEAD at 405 nm was measured to obtain the initial reaction rate (Table S3, Section S1.7). Without any catalyst, both quadricyclane and DEAD followed first-order kinetics, as expected for a homogeneous bimolecular reaction.⁹ When using the catalyst, the initial rates of the catalyzed reactions were corrected by subtracting the initial rates of the corresponding

background reactions. The kinetic plot in Figure 3a shows the reaction order of DEAD as pseudo-zeroth order, implying that DEAD adsorbs readily at the catalyst surface. This observation is well-aligned with the SHS results that show saturated coverage at relatively low bulk DEAD concentration. The oxygen and nitrogen atoms in DEAD are expected to form hydrogen bonds with interfacial water, and the amount of pre-adsorbed DEAD on the catalyst surface is constantly high enough to make DEAD follow pseudo-zeroth order kinetics. Quadricyclane, however, follows closely to first-order kinetics due to its non-adsorption at the toluene-water interface. The observed dependence of reaction rate on the catalyst surface area (*i.e.*, proportional to the amount of surface water) also resembles first-order kinetics for the catalytic sites.

The apparent activation energy (E_a) of the catalyzed reaction is 10.5 ± 0.9 kcal/mol (Figure 3d), which is comparable to an estimated E_a of 12 kcal/mol for the reaction of dimethyl azodicarboxylate (DMAD) with quadricyclane in the stirring mixture of toluene and water.^{1, 9} However, the E_a of the same reaction between DEAD and quadricyclane was measured as 3.9 ± 0.4 kcal/mol from the toluene-water fluidic platform⁷, likely due to the aforementioned difference between the two experimental conditions. The lowering of the activation energy ($\Delta E_a = E_{a/\text{without catalyst}} - E_{a/\text{with catalyst}}$) with our water-loaded MP-SNPs is $\Delta E_a = 3.6$ kcal/mol, comparable to 5.4 kcal/mol determined by the toluene-water fluidic platform⁷. A previous molecular simulation reported an estimated ΔE_a of 7.5 kcal/mol for the reaction between DMAD and quadricyclane when moving the reaction from the neat solution to the aqueous interface, where the main contribution to ΔE_a is the hydrogen-bonding between the surface water molecules and the transition state.⁹ Considering these data, we expect that the hydrogen bonding of interfacial water contributes significantly to the observed ΔE_a .

Combining the above kinetic data, the rate law for the catalyzed reaction closely follows the relationship of $(\# \text{ of catalyst sites})^1 \cdot [\text{quadricyclane}]^1 \cdot [\text{DEAD}]^0$. The proposed mechanism here is that the catalyzed reaction starts with the adsorption of DEAD from bulk toluene onto the interfacial water adsorbed on the silica surface, then the quadricyclane diffuses to the toluene-water interface and reacts with DEAD. The reaction occurs at the interface and hydrogen bonding discussed above lowers the activation barrier. The entire mechanism follows the Eley-Rideal process as illustrated in Figure 4. Since FTIR spectroscopy did not detect any signal from the free silanol groups in our catalyst, apparently silica only serves as a substrate for water adsorption and has no significant contribution to the catalytic mechanism.

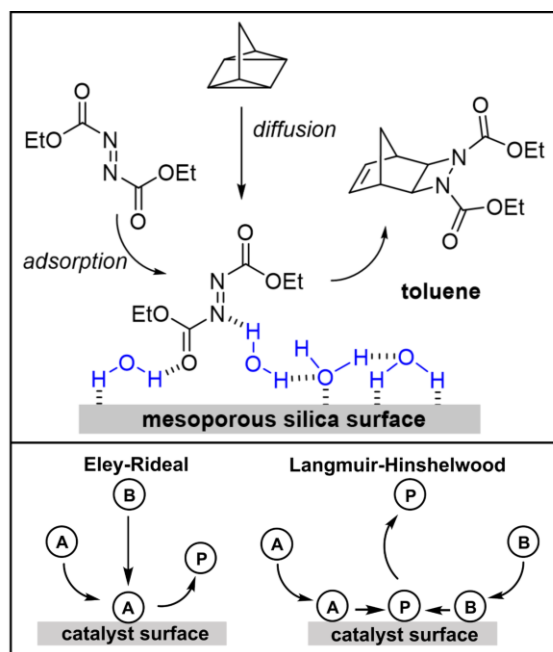


Figure 4. Proposed Eley-Rideal mechanism for the “on-water” reaction of quadricyclane and DEAD at the toluene-water interface on the surface of mesoporous silica.

To elucidate the catalytic mechanism, possible kinetic isotope effects (KIE) were explored by comparing the conversion when the catalyst was loaded with the same amount of water and heavy

water (85% D₂O, 15% H₂O) (Section S1.4). After 24 hours of reaction, the conversions were 75% and 72% for the pure H₂O and 85% D₂O/15% H₂O loaded catalysts, respectively. Assuming the catalytic contribution of D₂O and H₂O to the total conversion is independent, the actual conversion of the presumably 100% D₂O loaded catalyst is estimated to be 71%. This small KIE of 1.1 suggests that breaking of OH bonds does not occur in the rate-determining step; this agrees with the proposed mechanism in a previous simulation that the interfacial water-DEAD hydrogen bonds lower the transition state but does not break the OH bond at the transition state⁹. This result is also consistent with an observation of $k_H/k_D = 1.1$ from toluene-water fluidic platform.⁷ We note the original experiments by Sharpless and coworkers for the reaction between DMAD and quadricyclane showed a significant kinetic isotope effect ($k_H/k_D \sim 4.5$)¹. However, this result could arise from the uncertain surface areas of the organic solvent-water droplets. As Marcus and Jung have pointed out, many physical factors, other than the KIE, must be considered to explain this surprisingly high k_H/k_D .⁹ The Diels-Alder reaction between cyclopentadiene and dimethylfumarate has shown a KIE of 1.4, suggesting that protons transfer from water to the organic phase to catalyze the reaction.¹⁰ However, this mechanism is not supported by our experimental data for the reaction studied here. In previous studies, there is an assumption that the very low solubility of the organic reactants in the water phase of the organic solvent-water heterogeneous mixture may contribute to the “in-water” catalytic mechanism.^{4, 20} This possibility is eliminated from our study due to the molecularly thin layer of adsorbed water on the silica surface. Finally, we would like to point out that the structure of interfacial water adsorbed in the silica pores during the course of catalysis in our experiment is currently unknown and may be somewhat different from the structure of interfacial water at the organic solvent-water interface. We hope our result will facilitate some future simulation studies to gain a clearer physical picture of this complex aqueous interface.

To conclude, the highly controllable adsorption of surface water on MP-SNPs enables reliable kinetic studies of “on-water“ catalysis, and the catalytic mechanism is elucidated. While the mechanism of the studied reaction may depend significantly on the properties of the reactants, the method of preparing interfacial water demonstrated in this study can be applied to many other interesting reactions at organic solvent-water interfaces.

ASSOCIATED CONTENT

Supporting information

Experimental details: preparation of silica nanoparticles and water-adsorbed silica nanoparticles, second harmonic scattering and FTIR spectroscopic data, SEM and TEM images of silica nanoparticles.

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Notes

The authors declare no competing financial interest.

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