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Homogeneous vs Heterogeneous Polymerization Catalysis Revealed by Single-Particle Fluorescence Microscopy

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Supporting Information

ABSTRACT: A high-sensitivity and high-resolution single-particle fluorescence microscopy technique differentiated between homogeneous and heterogeneous metathesis polymerization catalysis by imaging the location of the early stages of polymerization. By imaging single polymers and single crystals of Grubbs II, polymerization catalysis was revealed to be solely homogeneous rather than heterogeneous or both.

One of the most important challenges in transition metal catalysis is determining the true nature of the catalytically active components.[1−5] The resulting fundamental understanding permits the efficient design and improvement of catalysts by obviating a purely empirical development approach. Common questions regard the phase of the active catalyst:[6−8] With a solid precatalyst, does reactivity occur at the interface of the surface and solution (heterogeneous catalysis) or by leached/soluble molecules in solution (homogeneous catalysis) or both?[9] Similarly, with a solution precatalyst, does the activity occur on decomposed heterogeneous particles rather than in solution (e.g., via nanoparticle formation)?[6] The answer to these questions is difficult to discern by existing experimental methods because the simple presence of solid particles or soluble components does not imply catalytic activity. Existing experimental methods therefore are indirect and/or potentially ambiguous,[6] especially when determining if a catalyst is exclusively homogeneous or exclusively heterogeneous in situations when both phases may be active (e.g., the three-phase test[9] and the commonly used mercury drop test[10,11]). For these reasons, there is no single definitive experiment for distinguishing between homogeneous and heterogeneous catalysis.[8] The resulting uncertainty plagues applications as diverse as biomass conversion,[11] industrial-scale pharmaceutical synthesis,[9] and fuel cell optimization.[12] We herein present a single-particle fluorescence imaging[1,13−16] method able to capture the early stages of catalysis and determine if the catalysis is homogeneous or heterogeneous or both based on direct imaging of the *location* of catalysis.

Polymerization of dicyclopentadiene (**1**) by Grubbs catalysts is used in the industrial synthesis of polydicyclopentadiene[17,18] and in self-healing materials.[19] In the case of self-healing materials, the catalytic reaction occurs in the presence of solid particles of metathesis catalyst embedded in wax,[20,21] raising the possibility that the solid catalyst could contribute to the polymerization reactivity. Similarly, in the course of our studies, we noted that Grubbs II catalyst polymerized **1** in proximity to particles of solid Grubbs II, such that polydicyclopentadiene encapsulated the solid (Figure 1a). This macroscale colocalization was consistent with the possibility that the polymerization could be occurring on the solid surface, as has been suggested recently for other

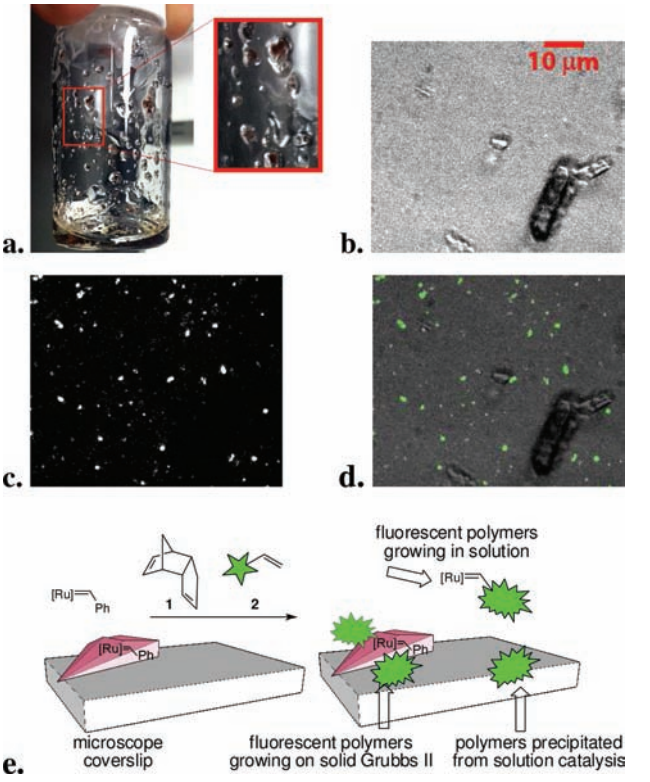

Figure 1. (a) Photograph of bench-scale experiment. Dicyclopentadiene polymerizes around solid particles of Grubbs II, encapsulating the solid maroon-colored precatalyst in clear polydicyclopentadiene. (b) A 53 μm × 63 μm microscope image with ambient light, showing individual crystals of Grubbs II on the surface of a glass microscope slide. (c) Same surface region as in (b) but fluorescence image at t = 170 s; individual polymer particles have precipitated on microscope slide after reaching insolubility in solution. Each white spot is one polymer particle. (d) Overlay of (b) and (c) reveals that polymer growth is not spatially associated with solid particles of Grubbs II precatalyst. Fluorescent polymers are false colored green to facilitate spatial comparison. (e) Experiment schematic. Fluorescent polymers tagged with BODIPY (green star) form upon polymerization of **1**. The location of the polymerization differentiates between homogeneous and heterogeneous catalysis.

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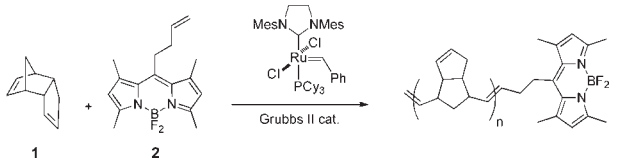

Figure 2. Ring-opening metathesis polymerization of **1** tagged with fluorescent BODIPY **2** catalyzed by Grubbs II.

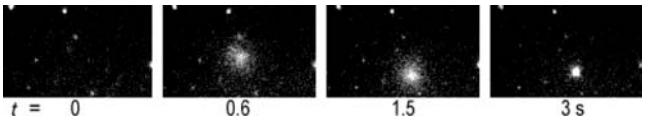

Figure 3. A single polymer particle of diameter ~3 μm that formed in solution by homogeneous catalysis, precipitating from solution over 3 s as observed by epifluorescence. A 31 μm × 18 μm region is shown.

polymerization catalysts.[22] We then asked the fundamental question: Does this reaction occur by heterogeneous catalysis, homogeneous catalysis, or both? Due to the known solution-phase reactivity of Grubbs II, it was anticipated that, at a minimum, some polymerization would occur in solution from leaching of the solid even though Grubbs II was only sparingly soluble in the reaction mixture. The presence of a homogeneous catalyst, however, does not rule out simultaneous heterogeneous catalysis.[6,10] We developed and applied an analytical technique capable of directly imaging the location of polymer growth to differentiate between homogeneous and heterogeneous catalysis. Our data revealed that polymer growth of **1** occurred exclusively in solution by soluble homogeneous Grubbs II catalysts. The solid precatalyst was unreactive toward polymerization and even single metathesis reactions. This method therefore provided an understanding of the nature of the active catalyst at a level of detail that would not be available from prior methods.

A schematic of the in situ imaging of polymerization is shown in Figure 1e. A sample of solid crystalline Grubbs II was placed on a microscope slide containing a reaction well. Individual crystals of Grubbs II were identified by ambient light imaging (Figure 1b). Polymerization was initiated upon injection of a heptane solution containing both fluorescent BODIPY-tagged olefin **2**[13,23] (BODIPY = boron dipyrromethene) and monomer **1** into the reaction well. The imaging mode then was switched to total internal reflection fluorescence (TIRF) mode.[24] In TIRF, only fluorophores near the surface are excited and therefore detected. Polymers freely diffusing in solution are not detected because they are diffusing rapidly or not present in the illumination area. Ambient light images of the Grubbs II crystals were periodically obtained during the experiment for comparison with the fluorescence images of the same surface.

Polymers of **1** were anticipated to be tagged with **2** through chain termination (Figure 2) or backbone elaboration steps[25] (not shown), causing the polymers to be fluorescent. Because Grubbs II was not readily soluble in this solution, individual crystals could be followed for the duration of the imaging experiment and longer (>30 min). If the solid Grubbs II was catalytically active, then fluorescent polymers would grow from the crystal surface (i.e., heterogeneous catalysis). If solid Grubbs II was catalytically inactive, then polymers would grow only in solution (i.e., homogeneous catalysis). If both the solid and solution catalysts were active, then the polymer would form both on the surface of the catalyst and in solution (i.e., both heterogeneous and homogeneous catalysis).

The ability to resolve and localize single polymer particles and single crystals of Grubbs II on the submicrometer scale was critical to this experiment. After about 10 s, polymers of fluorophore-tagged polydicyclopentadiene began to precipitate onto the surface of the microscope slide when they reached the size for insolubility in solution. After 170 s, many polymers had precipitated from solution, and the location of each polymer could be determined (Figure 1c). In Figure 1c, each white spot is one polymer particle with diameter ~2−5 μm.[26] These polydicyclopentadiene particles exhibited no spatial association with the solid Grubbs II precatalyst (Figure 1d). This lack of colocalization strongly suggested that the surface of Grubbs II was not contributing to polymer chain growth.[27,28] Notably, the lack of colocalization on the single-particle level contrasted with the rough colocalization visualized on the ensemble level, which clearly had not provided the high resolution needed to determine where polymer growth was occurring (Figure 1a).

Analysis of the reaction mixture by gel permeation chromatography (GPC) confirmed the presence of polymers (M_n = 9.8 × 10^4 g/mol, M_w = 1.3 × 10^5 g/mol, PDI = 1.4). The average molecular weight corresponded to 750-mer strands. Comparison of the fluorescence microscopy and GPC data established that the observed polymer particles were larger than 750-mers. Thus, either a subset of the largest strands or aggregates of strands precipitated and were observed as individual particles by fluorescence microscopy.

Verification that these polymers formed in solution by homogeneous catalysis prior to migrating to the microscope slide was obtained by comparing the previous images obtained in TIRF with additional images obtained in epifluorescence mode.[24] Epifluorescence mode permitted the excitation and imaging of fluorophores above the surface of the microscope slide. No colocalization of polydicyclopentadiene and the solid particles of Grubbs II was observed in epifluorescence mode, similar to the lack of colocalization noted in TIRF. Single particles of polydicyclopentadiene were observed precipitating out of solution in real time, sampling the glass coverslip surface before becoming fixed in position. The precipitation of an individual polymer particle was observable as a particle above the focal plane, slightly out of focus, that diffused across the surface for up to several seconds before becoming sharply in focus at a fixed position on the microscope coverslip at the end of the precipitation process (Figure 3; movie available in the Supporting Information).

Finally, it was examined if Grubbs II was present in solution at a sufficient concentration and with sufficient activity to serve as a catalyst under these conditions. To probe this question, solid Grubbs II was added to heptane in the same quantities as used previously. After 30 s, however, the solid was filtered from solution through a 0.2 μm filter. The resulting solution was transferred to the microscope slide. To this solution were added monomer **1** and fluorescent olefin **2**, and then imaging was initiated. Fluorescent polymers again formed. This result established that, although sparingly soluble, Grubbs II was sufficiently soluble to result in homogeneous polymerization activity. The activity of a soluble catalyst, however, does not imply that catalysis is exclusively homogeneous.[6,10] By combining this solution-phase information with the colocalization experiments of each individual nascent polymer described in Figure 1, it was concluded that polymerization catalysis by Grubbs II was solely homogeneous rather than heterogeneous or both. The resolution

of single particles excluded a contributing heterogeneous pathway.

We considered the alternative possibility that polymer growth occurred on the surface of solid Grubbs II but that the growing polymer dissolved prior to becoming tagged with fluorophore, which could result in catalytic reactivity of the surface that was not visible under the previously described conditions. In order to assess this possibility, we leveraged the single-molecule sensitivity[13] of our instrument to directly probe the reactivity of solid Grubbs II toward individual metathesis reactions with fluorescent olefin **2**. Olefin **2** was added to Grubbs II in the absence of **1**. If the surface of Grubbs II was reactive, then **2** would undergo metathesis reactions that would chemically incorporate fluorescent molecules onto the surface. No incorporation of **2**, however, was observed. This lack of surface metathesis reactivity supported the prior observations that the surface was not a viable heterogeneous catalyst under the examined conditions.

In conclusion, imaging of single crystals of Grubbs II and of the location of individual nascent polymer particles revealed that the active catalyst was exclusively homogeneous without simultaneous heterogeneous catalysis, information that would not be readily available through prior analytical techniques. Under conditions with both solid- and solution-phase ruthenium metathesis catalysts, such as in self-healing materials,[19,20] these data suggest that the reactivity is solely from soluble molecular catalysts.

This is the first report of imaging transition-metal-catalyzed polymerization using single-particle/molecule fluorescence microscopy.[29,30] An advantage of this method is in situ imaging. A disadvantage of this method is that a fluorophore probe molecule is required. Due to the sensitivity of this fluorescence method, however, the probe molecule can be present at very low concentrations (in this case 10^{-12} M). Under these conditions, the presence of the probe is unlikely to affect the homo-/heterogeneity of the majority of catalytic reactions. This technique provided a straightforward method for the identification of and differentiation between homogeneous and heterogeneous catalysis, a widespread challenge with profound academic and industrial implications. The imaging method works by determining the location—and thus the nature—of active catalysts. This approach should have especially broad applicability.

■ ASSOCIATED CONTENT

Supporting Information. Synthetic methods and experimental protocols, and movies of polymerization catalysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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