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Catalyst Decomposition during Olefin Metathesis Yields Isomerization-Active Ruthenium Nanoparticles

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The second-generation Grubbs catalyst, $RuCl_2(H_2IMes)(PCy_3)(=CHPh)$ [**GII**; H_2IMes = 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene, Cy = cyclohexyl], is shown to decompose during olefin metathesis to generate Ru nanoparticles (RuNPs). These RuNPs appear to contribute significantly to competing isomerization during metathesis. Larger, partially oxidized RuNPs are also observed in commercial **GII**, but these exhibit modest isomerization activity. Removal of RuNPs from the precatalyst does not prevent isomerization, because new, more reactive NPs are generated by catalyst decomposition during metathesis.

Ruthenium-catalyzed olefin metathesis is a core tool in organic synthesis[1] and an emerging protagonist in the pharmaceutical industry.[2] Notwithstanding the importance of these advances, a number of reports cite challenges arising from competing olefin isomerization,[3] the dominant non-metathetical side reaction.[4] Isomerization is particularly pronounced for the second-generation Grubbs catalyst (**GII**), relative to its predecessor **GI** (Figure 1).[3]

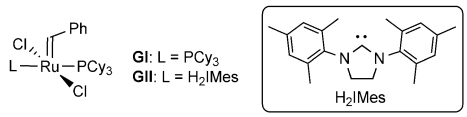

Figure 1. Grubbs catalysts **GI** and **GII**. Cy = cyclohexyl, H_2IMes = 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene.

Tandem metathesis–isomerization or isomerization–metathesis protocols, employed as a deliberate synthetic strategy, can enable access to targets that are otherwise challenging or inaccessible.[5–7] More commonly, however, isomerization is an unintended, often capricious side reaction that results in variable control over product selectivity and yields, in processes ranging from ring-closing metathesis (RCM) to cross-metathesis (CM) and metathesis polymerization.[2,3,8,9] Ruthenium hydride complexes generated by catalyst decomposition are widely viewed as responsible. Until now, only molecular complexes have been considered as potential culprits, despite the low isomerization activity documented for leading candidates.[10] Herein, we show that ruthenium nanoparticles (RuNPs) are formed by decomposition of **GII** during metathesis, and that these are important, hitherto unrecognized contributors to competing olefin isomerization. Notably, whereas NP formation is common for low-coordinate Pd catalysts that cycle between Pd^{II} and Pd^0,[11] reports of such behavior for well-defined monoruthenium complexes operating in organic media are rare, outside hydrogenation reactions mediated by η^6-arene complexes of ruthenium.[12] This is the first report of metal NP formation by decomposition of a molecular metathesis catalyst.

Olefin isomerization by RuNPs has not, to our knowledge, previously been reported. Given the activity of such entities in other catalytic contexts, however,[13] we speculated that they might function as viable isomerization catalysts. This proved to be the case. RuNPs were prepared by a range of methods (see the Supporting Information)[14–16] and were tested for their activity toward isomerization of estragole (**1**). Estragole is an important renewable allylbenzene used in metathesis reactions,[17] which, as with its congeners,[9,18] is readily isomerized. Figure 2 shows the isomerization activity recorded for four different Ru-containing nanostructures. All are clearly capable of inducing **1**→**2** isomerization. By far most active, however, were the Chaudret–Philippot NPs (type **D**), prepared under rigorously anaerobic conditions, and stabilized by N-heterocyclic carbene (NHC) ligands.[14,19] The dramatically higher isomerization activity of these NHC-stabilized NPs is consistent with the absence of oxidized surface species.

Given this evidence that RuNPs promote olefin isomerization, and prior reports that such side reactions declined if com-

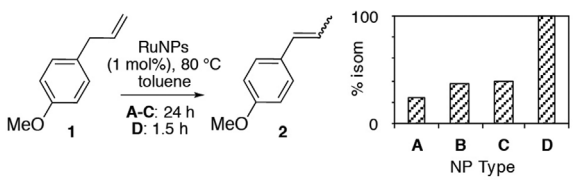

Figure 2. Isomerization promoted by RuNPs prepared by methods shown in the Supporting Information. Type **A**) RuNPs on mesoporous silica MCM-41 (Ru@MCM), **B**) RuNPs on crystal nanodiamonds (Ru@CND), **C**) RuNPs stabilized with ethylene glycol, and **D**) RuNPs stabilized with the NHC 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene (IPr).

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mercial **GII** was chromatographed prior to use,[20,21] we questioned whether RuNP contaminants might be present in **GII**,[22] which trigger competing isomerization during metathesis. We found that commercial **GII** catalysts do indeed contain RuNPs, present as aggregates that agglomerate on isolation to an average size of >500 nm (see the Supporting Information). However, the isolated particles induced olefin isomerization with low efficiency. They required 24 h to reach 45% yield of **2** under the conditions of Figure 2. This is unsurprising given their large size and partial oxidation, both of which limit the number of active surface sites.

To determine whether isomerization could be inhibited by removing the RuNPs present in the precatalyst, we generated NP-free **GII** by ultracentrifugation under an atmosphere of N_2. As illustrated in Figure 3, the purified **GII** effected both metathesis and isomerization of estragole (**1**). Thus, yields of metathesis product **3** increased over the first hour of the reaction but then declined as **3** underwent isomerization (Figure 3a). Strikingly, the extent of isomerization was only 15% less than that effected by non-purified **GII** (Figure 3b). Freshly decomposed Ru products thus appear to be important contributors to isomerization, with a level of activity much higher than that of the RuNP impurities present in the precatalyst.

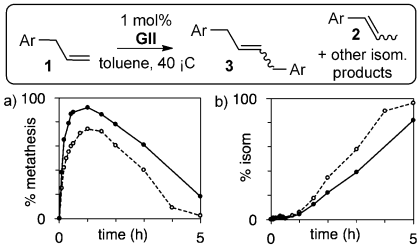
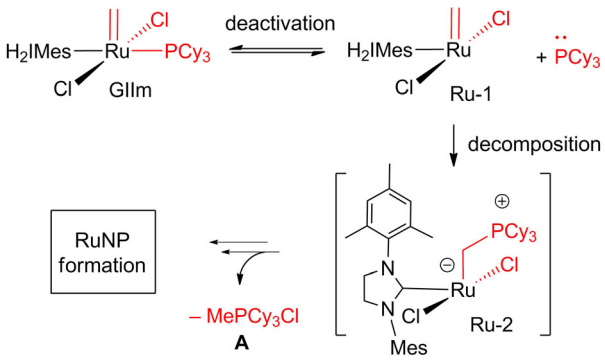


Figure 3. Performance of NP-depleted (——) versus NP-rich **GII** (-----) in metathesis of estragole (**1**). a) Formation and consumption of the self-metathesis product **3**. b) Net isomerization (sum of reagent and product isomerization). See Section S5.2 in the Supporting Information.

Also notable in Figure 3b is the approximately 30 min induction period that precedes the onset of isomerization. Formation of NPs over this timescale was confirmed by in situ nephelometry experiments, in which the intensity of scattered light was detected by synchronous wavelength scanning. As with conventional dynamic light scattering, increases in scattering intensity indicate NP formation. Intensity changes were monitored in the $\lambda = 600$–700 nm region to eliminate perturbation arising from absorption by the sample. The intensity of scattering increased over the first 30 min (see the Supporting Information), a change that maps onto the induction period in isomerization. In the absence of substrate, scattering was significantly reduced.

This evidence implies that RuNPs are formed by decomposition of ruthenium species generated *during* metathesis. We attribute the formation of nanoparticles, as opposed to molecular Ru products, to the loss of multiple ligands in the process of catalyst decomposition. Relevant in this context is the established pathway by which free PCy_3, liberated from the resting-state complex **GIIm** (Scheme 1), attacks the methylidene ligand of active species **Ru-1**.[23,24] Elimination of the σ-alkyl ligand thus formed occurs by abstraction of a proton (most plausibly from the H_2IMes ligand) and bound chloride. This process culminates in the extrusion of [$MePCy_3$]Cl (**A**), a net loss of three ligands per Ru center. Whereas isolation of the putative σ-alkyl intermediate **Ru-2** is precluded by its short lifetime, we recently succeeded in trapping out such a complex in the first-generation Grubbs system.[25] The details of NP formation are now being probed by in situ X-ray absorption studies, but the low-coordinate Ru species resulting from such "ligand stripping" represents a plausible starting point.



Scheme 1. Ejection of [$MePCy_3$]Cl (**A**) from the metathesis-active species **Ru-1**.

Further experimental evidence for RuNP formation during metathesis comes from electron microscopy. In these experiments, styrene **4** was chosen as the substrate, because the low solubility of its self-metathesis product **5** facilitates removal of organic species that otherwise occlude the micrographs. Scanning electron microscopy (SEM, Figure 4a) revealed NP-free solutions. Likewise, transmission electron microscopy (TEM) showed no NPs in analysis of multiple samples, down to the 0.2 nm detection level of the instrument. In contrast, abundant RuNP formation was evident following metathesis of **4**, as shown in Figure 4b.

To examine whether isomerization is promoted by RuNPs generated by catalyst decomposition during metathesis, or by molecular species formed at an earlier stage, we performed

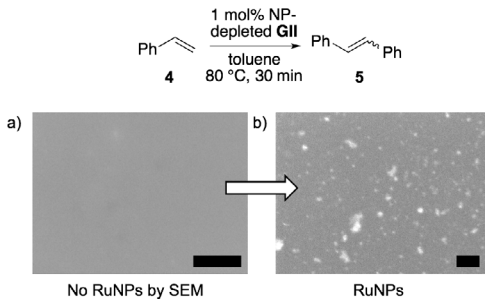


Figure 4. Decomposition of NP-depleted **GII** into RuNPs during styrene metathesis. a) SEM image of GII solution prior to metathesis and b) SEM image after metathesis (COMPO mode). Scale bar: 1 μm. Average particle size: (100±25) nm.

mercury-poisoning experiments. Poisoning by elemental mercury is a common test for the involvement of surface-active metal(0) sites in catalysis.[26–28] As shown in Figure 5, isomerization of **1** dropped by approximately 50% in the presence of Hg. Control experiments indicated that Hg had a negligible impact on the isomerization activity of common Ru hydride complexes (see the Supporting Information), or on the formation of **A**. Indeed, the Hg test may under-report the contribution of RuNPs in Figure 5, given the reported instability of the Ru–Hg amalgam[29] or adsorbate.[26]

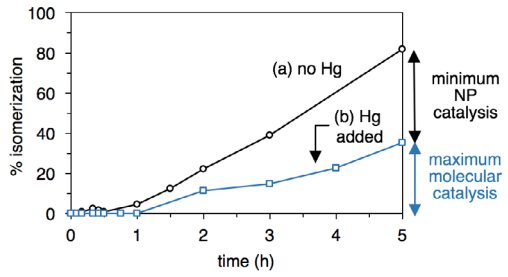


Figure 5. Impact of added Hg on the isomerization of **1** by initially NP-depleted **GII**. Conditions as in Figure 3.

Substoichiometric poisoning experiments (Figure 6) were performed to further probe the involvement of RuNPs in isomerization. Such experiments are predicated on the requirement for $\geq$1 equivalent of a poisoning ligand to inhibit catalysis by molecular Ru species, in contrast with the smaller number of ligands required to inhibit NP catalysis (in which much of the initial metal charge is inaccessible in the NP core). Accordingly, we assessed the impact of PMe_3, $P(OMe)_3$, and PPh_2Me (0.1 equiv. vs. **GII**) on the rate of isomerization during self-metathesis of estragole (**1**). These experiments were performed at 24 °C to maximize the poisoning effect.[30] To compensate for the negative impact of the lower temperature on catalysis, we used a batch of estragole that showed much higher rates of isomerization.[31] Isomerization ceased immediately on adding the phosphine/phosphite poison (Figure 6).

The foregoing demonstrates that RuNPs can show high activity for olefin isomerization, that RuNPs are formed by catalyst decomposition during **GII**-catalyzed metathesis, that Hg poisoning reduces isomerization, and that the addition of a small proportion of a phosphine or phosphite poison, relative to the total Ru loading, is sufficient to completely shut down isomerization. On the basis of this cumulative picture, we propose that RuNPs formed by catalyst decomposition are important contributors to unwanted isomerization during olefin metathesis.

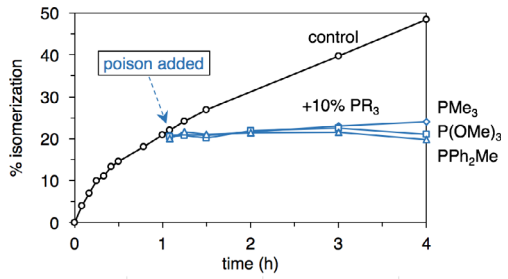


Figure 6. Substoichiometric poisoning experiments: impact of adding 10 mol% PR_3 on the rate of isomerization during metathesis of **1**. Conditions as in Figure 3 with the use of NP-depleted **GII** at 24 °C; poisons added at 1 h.

The context above focuses on unintended isomerization as a problem encountered during olefin metathesis. Insight into its origin, however, points toward new opportunities. The reaction conditions explored above were designed for metathesis, rather than nanoparticle formation or isomerization. Optimizing the synthesis of ruthenium nanoparticles, as well as the isomerization conditions, is expected to open new doors for the design of novel isomerization catalysts.

Acknowledgements

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Keywords: catalyst decomposition · isomerization · metathesis · nanoparticles · side reactions

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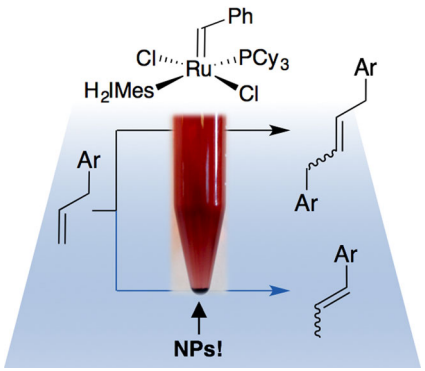
Nanoparticles in metathesis: A previously unrecognized decomposition pathway is reported for the Grubbs catalyst, which results in the formation of isomerization-active nanoparticles (NPs). Cy = cyclohexyl, H_2IMes = 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene.



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