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Published in:
CHEMISTRY-A EUROPEAN JOURNAL

DOI:
10.1002/chem.201603162

Link to publication

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A Switchable Gold Catalyst by Encapsulation in a Self-Assembled Cage

Anne C. H. Jans,[a] Adrián Gómez-Suárez,[b] Steven P. Nolan,[c, d] and Joost N. H. Reek*[a]

Abstract: Dinuclear gold complexes have the ability to interact with one or more substrates in a dual-activation mode, leading to different reactivity and selectivity than their mononuclear relatives. In this contribution, this difference was used to control the catalytic properties of a gold-based catalytic system by site-isolation of mononuclear gold complexes by selective encapsulation. The typical dual-activation mode is prohibited by this catalyst encapsulation, leading to typical behavior as a result of mononuclear activation. This strategy can be used as a switch (on/off) for a catalytic reaction and also permits reversible control over the product distribution during the course of a reaction.

There is a growing interest in transition-metal catalysis in confined spaces as the approach provides an additional tool to control selectivity and activity in catalysis.[1] For example, it has been demonstrated that the encapsulation of rhodium complexes in a hemispherical porphyrin assembly results in catalysts with increased activity and unprecedented branched selectivity in the hydroformylation of terminal and internal alkenes.[2] In addition, the encapsulation of transition-metal complexes in preformed cavities through weak interactions can lead to unexpected reactivity: $\text{MA}_{4}^-$ anionic tetrahedral capsules, for instance, can host cationic organometallic catalysts in their hydrophobic cavities.[3] thereby inducing substrate selectivity.[4] Moreover, reaction rates[5] and product distribution[6] can be greatly affected by catalyst encapsulation. Interestingly, many catalytic reactions operate through a dinuclear mechanism[7] or deactivate via a dinuclear pathway[8,9] by encapsulation of a transition metal complex, such decomposition pathways can be suppressed, leading to higher catalytic turnover numbers.[10]

In principle, an encapsulation event could also change the catalytic pathway of a reaction, and as such can be used as a switch for a catalytic transformation. Switchable catalysis is an interesting upcoming field of research as it provides new tools to control the reaction process with external stimuli such as light, pH, or metal coordination, a concept that is important to control reactions in nature.[11] In a recent study, encapsulation of a photoredox catalyst was shown to be a feasible stimulus to steer reactivity.[12] In a previous paper we reported the encapsulation of an N-heterocyclic carbene (NHC) mononuclear gold(I) complex inside a self-assembled hexameric resorcin[4]arene cage $\text{1}_{\text{s}}$ and showed that the encapsulated catalyst gives a different product distribution than the free complex.[13] This supramolecular complex is formed in apolar, water-saturated solvents (Scheme 1].[14,15] In the current contribution, we report how we change the active gold complex from dinuclear to mononuclear by reversible encapsulation and demonstrate that this can be used for both switching on/off a reaction, as well as for controlling its selectivity during the course of a reaction. Changing the reactivity or selectivity of a gold catalyst has been shown before by changing the ligands[16] or Brensted acid/base effects[17] and even by guest binding by a rotaxane,[18] but reversibly changing the active species of a gold-catalyzed reaction as a result of encapsulation has, to the best of our knowledge, not been shown before.

In this study we use a dinuclear hydroxyl-bridged gold complex $\text{[Au(NHC)$_2$(\(\mu\)-OH)]}[X]$ instead of a mononuclear gold complex.[19] This complex reacts through different mechanisms...
than mononuclear gold complexes and is a privileged catalyst for dual activation reactions. It, however, is too large to fit inside the cage  and should be split into mononuclear complexes upon encapsulation. The NHC-Au-X fragment displays the traditional Lewis acidic character of mononuclear cat-ionic gold catalysts, activating unsaturated substrates such as alkynes through π-coordination, making them more electrophilic and susceptible towards nucleophilic attack. Meanwhile, the NHC-Au-OH species behaves as a Brønsted base and is known to σ-activate substrates such as terminal alkynes or phenols. Together the two species, NHC-Au-X and NHC-Au-OH, can dually activate substrates through both π- and σ-activation (Scheme 2). This dual-activation mode was originally proposed by Toste and Houk and is well established and employed nowadays. In addition, this dual activation has elegantly been explored by Hashmi and Zhang for the formation of gold acetylides, which can react as a nucleophile and attack the π-activated bond of the substrate, and as such represents a common strategy in gold-mediated synthesis.

![Scheme 2](image)

**Scheme 2.** Dinuclear complexes [[Au(NHC)],(μ-OH)] can dually activate substrates.

We envisioned that encapsulation of the two fragments of the dinuclear gold catalyst [[Au(NHC)],(μ-OH)] in separate cages would alter its typical reactivity as they undergo transformations in a site isolated fashion. We anticipated that by complex encapsulation we could reversibly switch between the dinuclear and mononuclear catalyst and, therefore, have a tool to shift from dual gold catalysis to a mononuclear reaction mechanism. This forms the basis for an on/off switchable system, but can also alter the product distribution during a gold-catalyzed transformation.

Indeed, when complex [[Au(Pr)],(μ-OH)][BF₄] 2 (Scheme 3) and the capsule were mixed together, encapsulation of a mononuclear gold complex was confirmed by ¹H NMR and ¹H 2D DOSY NMR (see the Supporting Information). To demonstrate the principle of switching catalyst activity by selective encapsulation, the dual gold-catalyzed hydrophenolxylation reaction was studied. This reaction requires σ-activation of a phenol by the NHC-Au-OH moiety and π-activation of an alkylene by the cationic NHC-Au-X fragment (Scheme 4). Indeed, it was observed that the standard reaction between phenol (4) and diphenylacetylene (5) readily takes place when using 2 as catalyst in the absence of the cage (full conversion within 60 min). However, in the presence of the cage, the dinuclear complex 2 is broken and encapsulated as mononuclear spe-
Table 1. Gold catalyzed conversion of 4-phenyl-1-butyne.[a]

<table>
<thead>
<tr>
<th>Entry</th>
<th>t[Au]</th>
<th>Yield 9 (%)</th>
<th>Yield 10 (%)</th>
<th>Yield 11 (%)</th>
<th>Yield 12 (%)</th>
</tr>
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<tbody>
<tr>
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<td>7</td>
<td>0</td>
<td>38</td>
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<tr>
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<td>+</td>
<td>3</td>
<td>16</td>
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</tr>
<tr>
<td>4</td>
<td>–</td>
<td>6</td>
<td>0</td>
<td>47</td>
<td>8</td>
</tr>
</tbody>
</table>


Experimental Section

Hydrophenoxylation experiments: The catalyst 2 (0.025 mol%) was added to a solution of 4 (550 mm) and 5 (500 mm) and in selected experiments cage 1c (50 mm) and/or competing guest 7 (50 mm) in [D6]toluene. The mixture was heated to 80 °C and yields were monitored using GC and 1H NMR of the crude mixture.

Catalytic experiments with substrate 8: The catalyst 2 (2.5 mol%), H2O (44 mm), substrate 8 (66 mm), and, in selected experiments, cage 1c (33 mm) and/or competing guest 7 (33 mm) were mixed in [D6]benzene and heated to 70 °C for 48 h. Yields were monitored using GC and 1H NMR of the crude mixture and were determined as the average of two experiments.

Acknowledgements

Support for this work was generously provided by King Abdullah University of Science and Technology (KAUST) Office of Sponsored Research (OSR) under Award No. OSR-2015-CCF-
Keywords: catalyst encapsulation • catalytic switch • dual catalysis • gold catalysis • supramolecular chemistry


