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Silica-Supported Cationic Gold(I) Complexes as Heterogeneous Catalysts for Regio- and Enantioselective Lactonization Reactions

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*Supporting Information

ABSTRACT: An efficient method for the synthesis of heterogeneous gold catalysts has been developed. These catalysts were easily assembled from readily available silica materials and gold complexes. The heterogeneous catalysts exhibited superior reactivity in various reactions where protodeauration is the rate-limiting step. Dramatic enhancement in regio- and enantioselectivity was observed when compared to the homogeneous unsupported gold catalyst. The catalysts are easily recovered and recycled up to 11 times without loss of enantioselectivity.

Integration of multiple catalytically relevant functionalities into a single active site is a concept often employed by biological catalysts (Scheme 1a)1 and is an emerging strategy in heterogeneous2 and homogeneous3 catalysis. In an ideal scenario, the functional groups act cooperatively to enhance reactivity and/or selectivity.4,5 The placement of a homogeneous catalyst in proximity to surface active sites of heterogeneous supports offers an opportunity to exploit these cooperative effects while leveraging the benefits of both homogeneous and heterogeneous catalysis.6 However, the use of this strategy to enhance the stability, reactivity, and enantioselectivity of chiral homogeneous catalysts remains illusive.

Homogeneous gold catalysts have proven to be both highly reactive and selective toward a variety of carbon–carbon and carbon–heteroatom bond forming reactions.7 Inspired by recent reports showing that cationic metal complexes can be adsorbed onto mesoporous silica via hydrogen bonding of the counterion,8 we envisioned that chiral cationic gold(I) complexes could be localized near the acidic silica surface to provide a bifunctional gold/Brønsted acid catalyst (Scheme 1b). Moreover, this process allows for a simple one-step synthesis from the homogeneous catalyst and retains the tunable electronic and steric properties of the original molecular catalyst.9 Herein, we report the synthesis of a heterogeneous gold catalyst made by adsorbing molecular gold complexes onto mesoporous silica via such a hydrogen bonding method (Scheme 1b). More importantly, we show that the synergetic effect of the acidic silica surface significantly increases the catalyst’s activity as well as regio- and enantioselectivity for intramolecular additions of allenes and alkynes.

The heterogeneous gold catalyst was prepared by stirring SBA-15 in a CH2Cl2 solution of Ph3PAuBF4 at room temperature for 4 h (Scheme 1c). The catalyst was separated by centrifugation, washed with CH2Cl2, and dried under vacuum to give a white solid, SBA-15@Ph3PAuBF4. The transmission electron microscope (TEM) images of SBA-15@Ph3PAuBF4 show a regular hexagonal array of uniform channels that is characteristic of mesoporous SBA-15 materials (Figure 1a). The catalyst was treated with ascorbic acid to reduce the homogeneous gold complex and enable the direct observation of the gold nanoparticles. Gold nanoparticles formed during the reduction by ascorbic acid are clearly seen inside the mesoporous channels, indicating the successful adsorption of the catalyst onto the pores (Figure 1b). This conclusion was further confirmed through nitrogen sorption experiments. Compared to SBA-15, SBA-15@Ph3PAuBF4 showed less
surface area and smaller pores (Figure 1c), consistent with the presence of molecular catalysts in the mesopores. The type IV isotherm with a H1 hysteresis loop indicates that the heterogeneous catalysts retain the ordered mesoporous channels of SBA-15.

The preservation of the molecular catalyst’s structure in SBA-15@Ph3PAuBF4 was further demonstrated by IR spectroscopy (Figure 2). In addition, a significant red shift of the O−H stretching vibrational band at 3750 cm⁻¹ in SBA-15@Ph3PAuBF4 was observed, consistent with hydrogen bonding of the surface silanol groups in SBA-15 with the molecule catalyst.

The existence of this hydrogen bond was also investigated using ¹⁹F MAS NMR spectroscopy (Figure 3). Three major resonances were detected in SBA-15@Ph3PAuBF4 at −152, −156, and −160 ppm while the homogeneous counterpart only showed a single resonance at −152 ppm in a solution ¹⁹F NMR spectrum. On the basis of previously reported values, the resonances observed in the SBA-15@Ph3PAuBF4 sample were are assigned as follows: −156 ppm (F in BF₄⁻ hydrogen bonded to the surface silanol group), −152 ppm (F in BF₄⁻ not hydrogen bonded), and −162 ("bulk" BF₄⁻ species). The observation of these characteristic peaks further validates the hypothesis that the gold complex was immobilized on the silica surface by hydrogen bonding of the BF₄⁻ anion to surface silanol groups in SBA-15.

Previous studies have revealed that protodeauration of a vinylgold intermediate (3) is the turnover limiting, and often selectivity defining, step in gold-catalyzed addition of oxygen nucleophiles to allenes. On the basis of these reports, we examined their reactivity of the silica-supported gold catalysts in the lactonization reaction of allenoic acid 1a. The heterogeneous gold catalyst SBA-15@Ph3PAuBF4 exhibited superior activity compared to its homogeneous counterpart under the same conditions (eq 1a vs b). Thus, we propose that the enhanced reactivity of SBA-15@Ph3PAuBF4 is likely due to enhancement of protodeauration by the surface acidity of silica (3 to 2a). A series of reactions with the same rate-limiting step was also found to be accelerated by introducing molecular gold catalysts into SBA-15 (eqs 2 and 3).

Reactions in the silica mesopores gave a different selectivity than those occurring in solution. The cyclization of alkylic acid was then studied, and the regioselectivity obtained from SBA-15@Ph3PAuBF4 is 3 times greater than that of the homogeneous counterpart (Scheme 2 a−c). By introducing substituents at the α-carbon of the acid, the 5-exo cyclization products were obtained, with 100% purity using a heterogeneous gold catalyst (Scheme 2d−e).

We next examined the application of the supported catalysts to the transition-metal-catalyzed enantioselective nucleophilic addition reactions of allenes. Although intramolecular hydroamination and -alkoxylation of allenes have been well established, the lactonization reactions remain challenging. The unique feature of our method is that chiral heterogeneous gold catalysts are easily assembled from readily available molecular catalysts, thereby allowing for rapid catalysts assessment. Thus, a series of heterogeneous gold catalysts with enhanced reactivity of SBA-15@Ph3PAuBF4 is likely due to enhancement of protodeauration by the surface acidity of silica (3 to 2a). A series of reactions with the same rate-limiting step was also found to be accelerated by introducing molecular gold catalysts into SBA-15 (eqs 2 and 3).

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different chiral phosphine ligands were prepared and explored as catalysts for the enantioselective hydrocarboxylation of allenoic acid 1a (Table 1). Although no enantioselectivity was obtained using molecular gold complexes as a homogeneous catalyst, gold complexes adsorbed on SBA-15 all exhibit considerable enantioselectivity. Among them, the BIPHEP ligand stood out as most effective (entries 2−4). While a less electron-rich ligand did not enhance the selectivity (entry 5), a decrease in the ligand size significantly improved the enantioselectivity and gave (S)-2a in 84% ee (entry 6). However, a further decrease in steric of the ligand gave an inferior result (entries 7).

The versatility of heterogeneous catalyst SBA-15@L5-(AuBF₄)₂ toward cyclization of various allenoic acids was further studied (Table 2). When a dimethyl group was introduced at the α-position of the acid, the enantioselectivity was increased (2b and 2c). A 93% ee was observed for the synthesis of six-membered lactone 2d. Both linear and cyclic substituents in the allenoic were tolerated (2e and 2f).

Table 2. Enantioselective Lactonization of Allenoic Acid Catalyzed by Heterogeneous Gold Catalyst

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L1(AuBF₄)₂</td>
<td>91</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>SBA-15@L1(AuBF₄)₂</td>
<td>93</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>SBA-15@L2(AuBF₄)₂</td>
<td>95</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>SBA-15@L3(AuBF₄)₂</td>
<td>92</td>
<td>75</td>
</tr>
<tr>
<td>5</td>
<td>SBA-15@L4(AuBF₄)₂</td>
<td>92</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>SBA-15@L5(AuBF₄)₂</td>
<td>93 (87)</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>SBA-15@L6(AuBF₄)₂</td>
<td>94</td>
<td>47</td>
</tr>
<tr>
<td>8</td>
<td>MCM-41@L5(AuBF₄)₂</td>
<td>95</td>
<td>81</td>
</tr>
<tr>
<td>9</td>
<td>micelle[L5(AuBF₄)₂]</td>
<td>93</td>
<td>81</td>
</tr>
<tr>
<td>10</td>
<td>L5(AuBF₄)₂ + nonmesoporous silica</td>
<td>90</td>
<td>50</td>
</tr>
</tbody>
</table>

Substituents at the α-carbon of allenoic acid could be alkyl, aryl, and unsaturated rings (2g−2j). Low enantioselectivities were obtained in the presence of a homogeneous catalyst in all cases.

Silica materials with varying pore size and particle morphology demonstrated analogous behaviors to those observed of SBA-15. For example, similar enantioselectivity was achieved in the lactonization of 1a catalyzed by MCM-41@L5(AuBF₄)₂ and micelle@L5(AuBF₄)₂ (Table 1, entries 8 and 9). On the other hand, the combination of the chiral gold catalyst and silica in which the pores are occupied by cetyltrimethylammonium bromide (CTAB) produced lactone 2a with lower enantioselectivity. While confinement of the catalyst in the mesopore may enhance selectivity, the observation that the structure of the support has little impact on enantioselectivity suggests that the cooperative effect of surface silanols is primarily responsible for the observed enhancements in selectivity.

In conclusion, we have developed an efficient method for the synthesis of heterogeneous gold catalysts. The tunable catalysts can be easily assembled from readily available silica supports and cationic gold(I) complexes. Compared with homogeneous catalysts, the heterogeneous gold catalysts exhibited superior catalytic activity toward various reactions with protodeauration as the rate-limiting step, and showed significant enhancement...
in regio- and enantioselectivity. More importantly, the present work highlights the potential of ionic interactions with charged catalysts as a strategy for rapid assembly and assessment of cooperative effects between supports and chiral homogeneous catalysts for the develop of heterogeneous asymmetric catalysts.

**ASSOCIATED CONTENT**

**Supporting Information**
Details of experimental procedures, NMR spectra, and spectroscopic data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b04294.

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**Notes**
The authors declare no competing financial interest.

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**REFERENCES**


