

Catalysis by Gold(I) and Gold(III): A Parallelism between Homo- and Heterogeneous Catalysts for Copper-Free Sonogashira Cross-Coupling Reactions**

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There is an increasing interest in the chemistry of gold(I) and gold(III) compounds. A major driving force for this interest has been the utility of soluble gold compounds and the observation that gold nanoparticles and supported gold nanoparticles are active, for instance, for CO oxidation,^[1] hydrochlorination of acetylene,^[2] chemoselective reduction of substituted nitroarenes by H₂,^[3] C–C bond formation,^[4] and selective oxidation of alcohols.^[5] Moreover, the use of Au complexes in homogeneous catalysis has undergone a renaissance and spectacular achievements have recently been reported.^[6] Carbon–carbon coupling reactions are ubiquitous in organic synthesis. Heck,^[7] Suzuki,^[8] and Sonogashira couplings,^[9] occupy a special place among those as a result of the mild reaction conditions required. The coupling products are mostly used as intermediates for polymers, natural products, and bioactive compounds. The most commonly used catalytic systems for the Sonogashira reaction include [PdCl₂(PPh₃)₂], PdCl₂/PPh₃, and [Pd(PPh₃)₄] together with CuI as the co-catalyst, and large amounts of amines as the solvents or co-solvents.^[10]

Taking into account that gold has been successful for performing the same role as Pd during carbon–carbon bond formation in the Suzuki–Miyaura condensation,^[11] while Au^I has the same d¹⁰ electronic structure as Cu^I and can easily and properly interact with the acetylenic group,^[12] it appeared to us that gold could catalyze the copper-free Sonogashira cross-coupling reaction. In order to explore this possibility, we chose a solid catalyst formed by gold supported on nanocrystalline CeO₂ (Au/CeO₂). The reason for this choice is that Au^I and Au^{III} species are stabilized on this catalyst,^[13] and X-

ray photoelectron spectroscopy results (see Figure S1 in the Supporting Information) show the presence of Au⁰, Au^I, and Au^{III}. When this solid (5 mol % of gold) was used as a catalyst for the condensation between iodobenzene and phenylacetylene (1:2 molar ratio) in *N,N*-dimethylformamide (DMF) as solvent at 150 °C using sodium carbonate as base (2 equiv), full conversion of iodobenzene was obtained in 24 h. The products observed correspond to 89 % of the cross-coupling product and 11 % of biphenyl (the homocoupling product of iodobenzene). Meanwhile, the phenylacetylene that was present in twofold excess also gives the corresponding homocoupling product, 1,4-diphenylbutadiene, in 30 % yield. We found that when using DMF as solvent, some leaching of gold occurs. Then, the experiment was repeated under the same experimental conditions but using *o*-xylene as solvent. In this case, the conversion was 50 % while the selectivities of the Sonogashira cross-coupling and the homocoupling of iodobenzene and phenylacetylene were nearly the same as before. Au leaching was not observed, and the Au/CeO₂ catalyst could be reused after washing with acetonitrile and maintained its activity and selectivity.

From these results, we can conclude that the Au/CeO₂ catalyst, which contains Au⁰, Au^I, and Au^{III} species, is active for performing the copper-free Sonogashira cross-coupling reaction and also produces, although at a much lower rate, the homocoupling products of iodobenzene and the alkyne. The question now is what species are responsible for which reaction. To answer this question, we used colloidal gold with a gold particle size distribution (mean diameter 5 nm) very similar to that observed for gold nanoparticles supported on nanocrystalline ceria (see the Supporting Information) as catalyst for the Sonogashira reaction. Under the conditions described above and using *o*-xylene as solvent, the conversion attained with colloidal gold was only 6%, with 46 % selectivity for the desired cross-coupling reaction and 54 % selectivity for the homocoupling product of iodobenzene, and less than 1 % yield of the alkyne homocoupling product. From the above results, we conclude that Au⁰ shows much lower activity for these reactions, probably arising from the unsaturated gold atoms presents in the small gold nanoparticles. Thus, we were left with Au^I and Au^{III} as potential active centers for the cross- and homocoupling condensations observed.

To study their potential catalytic role, we prepared Au^I and Au^{III} complexes with Schiff base ligands derived from 1,1'-binaphthyl-2,2'-diamine ([Au^I] and [Au^{III}]; Figure 1). The corresponding Pd^{II} complex ([Pd^{II}]) was also prepared for

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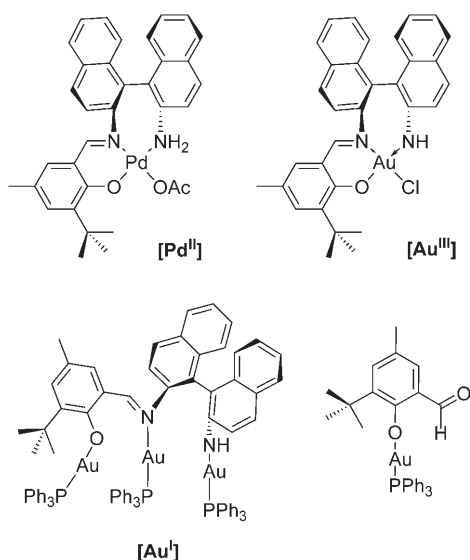
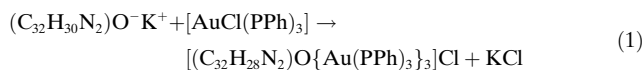


Figure 1. Structures of gold and palladium complexes.

comparison reasons. The soluble ligands and their respective metal complexes were obtained in high yields by using a similar method to that described previously.^[14] In this type of potentially tridentate ligands, there are two types of nitrogen donor ligands and one oxygen phenolate. The nitrogen center on the pyrrolidine ring is expected to act as a hemilabile ligand, while the Schiff base nitrogen and oxygen centers act as the principal donors.

The Au^I complex [**Au^I**] was synthesized according to Equation (1). Thus, [AuCl(PPh₃)₃] (1 mmol) in THF was



added to a solution of the corresponding phenolate ligand (1 mmol) in THF (20 mL) at 40 °C. The resultant mixture was stirred for 2 h, cooled to room temperature, and filtered, and the filtrate was concentrated under vacuum. The residue was extracted with dichloromethane and precipitated with pentane; the precipitate was washed several times, filtered, and dried to afford the yellow-brown, air-stable solid complex in high yield.

The homogeneous complexes were studied with the Sonogashira cross-coupling of R-Ph-I (R = H, COOEt) with a series of alkynes containing electron-donating and electron-withdrawing substituents (R') in the alkyne. The reaction was carried out in a 25-mL vessel at 130 °C during 24 h. In a typical run, a mixture of aryl halide (10 mmol), alkyne (15 mmol), aqueous potassium carbonate or phosphate (20 mmol), and catalyst (0.3 mmol) was stirred in 3 mL of *o*-xylene. The standard reaction conditions were applied to a series of catalysts, including Pd⁰, [Pd(PPh₃)₄], and the Pd^{II}-, Au^{III}-, and Au^I-Schiff base complexes (**[Au^I]**, **[Au^{III}]**, and **[Pd^I]**, respectively). The conversions obtained with those catalysts and the Au^I complex [AuCl(PPh₃)₃] are presented in Table 1. For these reactions, we chose K₃PO₄ as the mild base because longer

Table 1: Palladium- and gold-catalyzed Sonogashira cross-coupling reaction.^[a]

R	R'	Yield [%]			
		Pd ⁰	Pd ^{II}	Au ^I	[AuCl(PPh ₃) ₃]
H	Ph	23	30	54	35
H	<i>n</i> -C ₁₀ H ₁₇	20	25	10 ^[b]	97 ^[b]
				(50) ^[c]	(80) ^[c]
H	CH ₂ CH(CO ₂ Me) ₂	25	15	10	40
COOEt	Ph	25	14	10 ^[b]	95 ^[b]
				(90) ^[c]	(30) ^[c]

[a] Conditions: alkyne (15 mmol), aryl halide (10 mmol), catalyst (20%), and K₃PO₄ (20 mmol) in *o*-xylene at 130 °C. Yields after 24 h are given unless otherwise stated. [b] 48 h. [c] 30% catalyst.

reaction times were necessary with K₂CO₃ to obtain reasonable conversions.

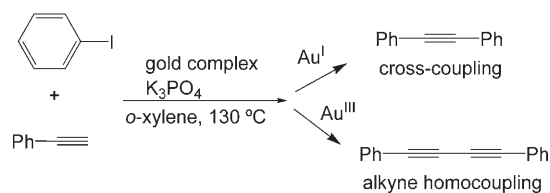
In the case of the Au^I complex [**Au^I**], moderate to excellent yields with very high selectivities (≥ 99%) for the cross-coupling Sonogashira reaction were obtained (Table 1). On the other hand, when the Au^{III} complex was used as the catalyst for several of the reactions, the product observed comprised 10% of alkyne homocoupling product with a very small amount of the iodobenzene homocoupling product. When the reaction was carried out under the same experimental conditions but in the absence of iodobenzene, only the alkyne homocoupling product was detected (8% yield). In contrast, when the reaction was performed in the absence of the Au^{III} complex no reaction occurred which confirms that Au^{III} catalyzes the homocoupling reaction of 1-phenylacetylene.

For comparison purposes, **[Pd^{II}]** and [Pd(PPh₃)₄] complexes were also prepared and tested under the same reaction conditions (Table 1). The results show that the activity of Pd catalysts is similar to that of the gold analogues, with also a very high selectivity for the Sonogashira reaction.

The homogeneous catalytic results presented show that Au^I is able to selectively catalyze the cross-coupling reaction, while Au^{III} complexes do not catalyze the cross-coupling but rather the alkyne homocoupling, although at a much lower reaction rate than Au^I catalyzes the Sonogashira cross-coupling (see Scheme 1).

If we establish a parallelism between the results obtained with Au/CeO₂ and the gold complexes, we conclude the following:

- The homogeneous catalysis studies show us that Au^I, which has the same d¹⁰ electronic configuration as Pd metal and Cu^I, is active and very selective for performing the Sonogashira reaction.



Scheme 1. Product distribution observed in the Sonogashira reaction catalyzed by gold complexes.

- b) Au^{III} does not catalyze the cross-coupling reaction but does catalyze the homocoupling condensation.
 c) Colloidal gold (Au⁰) displays low activity.

Finally, this work shows the interest of gold as a heterogeneous catalyst, in the sense that cationic gold species can be stabilized on the surface and can act as soft Lewis acids.

Experimental Section

Sonogashira reaction: The reaction was carried out in a 25-mL vessel at 130 °C. In a typical run, a mixture of aryl halide (10 mmol), alkyne (15 mmol), aqueous potassium carbonate or phosphate (20 mmol), and catalyst (0.3 mmol) in *o*-xylene (3 mL) was stirred, and the reaction was followed by GC-MS. Gas chromatography analysis were performed in a Hewlett-Packard 5890 II or/and in a Hewlett-Packard G1800 A with a quadrupole mass detector using a cross-linked methylsilicone column. After the desired time, the reaction mixture was allowed to cool, and a 1:1 mixture of ether/water (20 mL) was added. The organic layer was washed and separated, the aqueous layer was further washed with another 10-mL portion of diethyl ether, and the combined organic extracts were dried with anhydrous MgSO₄ and filtered. The solvent and volatiles were completely removed under vacuum to give the crude product, which was subjected to column chromatographic separation to give the pure compounds.

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