Supported Catalysts

Supported Gold Catalyzes the Homocoupling of Phenylboronic Acid with High Conversion and Selectivity**

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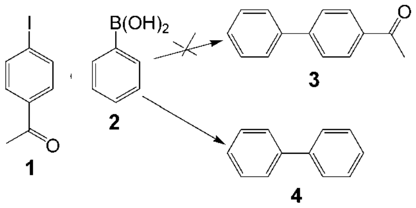
Coupling reactions are largely dominated by the use of palladium catalysts and are a powerful and versatile tool in synthetic organic chemistry for the formation of carbon–carbon bonds.[1,2] Among the different coupling reactions, the Suzuki reaction plays an important role and it is already used in some industrial processes.[3] The possible products include biaryls which are interesting because of their presence in many natural products and biologically active compounds.[4] This class of compounds can be prepared by two different types of reactions: homocoupling or cross-coupling.

The general mechanism for the Suzuki cross-coupling reaction involves the transmetalation of a boronic acid by Pd^{2+} ions. Various examples have recently been reported for the homocoupling of boronic acids by different metals.[5] One of these[5a] shows that homocoupling of boronic acids occurs by a double transmetalation at Pd^{2+} centers formed by oxidative addition of an α-halocarbonyl compound to an initial Pd^0 complex. The authors found that there was no reaction in the absence of the α-halocarbonyl compound, thus confirming that the transmetalation of the boronic acid occurs at Pd^{2+} species. Taking this into account, we thought that as Au^{3+} is isoelectronic with Pd^{2+} and able to undergo the redox cycle $Au^{3+} \rightleftarrows Au^+$, it may be possible for a solid catalyst containing Au^{3+} species to be active in the cross-coupling as well as the homocoupling reaction (Scheme 1). To the best of our knowledge the only examples of C–C bond formation catalyzed by gold have been performed using homogeneous catalytic systems.[6,7]



Scheme 1. Possible Suzuki and homocoupling reactions catalyzed by gold; reaction conditions: 2.25 wt% Au/CeO_2, toluene, K_2CO_3, $T = 333$ K.

To investigate our hypothesis, we prepared a supported gold catalyst containing cationic gold species. The support consists of nanocrystalline ceria particles, which are able to stabilize ionic states of gold because of their electron-withdrawing properties.[8] Indeed, the IR spectrum of CO adsorbed on an Au/CeO_2 catalyst[9] shows a band at 2148 cm^{-1} that confirms the presence of Au^{3+} ions. This result was supported by XPS data, which display a peak at 86.2 eV corresponding to the binding energy ($4f_{7/2}$) of Au^{3+} (Supporting Information).

To test the reactivity of gold supported on nanocrystalline CeO_2 for Suzuki cross-coupling, reactions were carried out between *p*-iodobenzophenone and phenylboronic acid (Experimental Section, Reaction a). We observed that all the boronic acid was transformed into biphenyl, thus indicating that the homocoupling reaction occurs with practically 100% conversion and selectivity (Supporting Information). The product of Suzuki cross-coupling condensation was detected in very small amounts (< 0.5%).

Interestingly, the reaction also proceeds with the same conversion and selectivity in the absence of the α-halocarbonyl compound and K_2CO_3. When the reaction is carried out without K_2CO_3, the only difference observed is the degradation of the catalyst. The base is known to activate phenylboronic acid;[1] however, our results indicate that with our catalytic system base is not needed for the activation of phenylboronic acid, and its only role is to neutralize the boric acid. Furthermore, the turnover number (TON) of 20 (calculated as the moles of boronic acid converted divided by two and by the moles of gold in the catalyst per hour) indicates that the process is catalytic. It should be noted that because not all the gold atoms are available for the reaction, the real TON is likely to be much higher than 20.

Blank experiments without catalyst or using gold-free nanocrystalline ceria gave no conversion, thus showing that the catalytically active sites are associated with gold. Possible Au leaching during the reaction was checked by analyzing gold in the supernatant liquid by AAS; 0.3 ± 0.1 ppm of gold was detected (Supporting Information). The activity of the leached gold was found to be negligible by carrying out an experiment in which 3 ppm of gold (ten times the amount of leached gold) in the form of $HAuCl_4$ was introduced as catalyst. After 6 h at 333 K the conversion was 1.1%. Under the same conditions using our gold catalyst the conversion was 100%.

From a stoichiometric point of view, the formation of boric acid from boronic acid requires the participation of either a surface hydroxy group (associated to gold[10] and/or to the cerium oxide[11]) or molecular water that will dissociate and subsequently hydrolyze the boronic acid to boric acid. For either case, it is clear that hydroxy groups participate in the catalytic reaction, and regeneration of such species requires dissociation of molecular water on the surface of the support to restore the surface hydroxy groups and generate molecular hydrogen.[11] The overall homocoupling reaction is therefore as described in [Eq. (1)].

$$2\,(HO)_2BPh + 2\,H_2O + Au^{3+} \rightarrow 2\,B(OH)_3 + PhPh + Au^+ + H_2 \quad (1)$$

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To prove experimentally that this reaction is taking place we monitored the homocoupling reaction by Raman spectroscopy to detect H_2 formation. The results presented in Figure 1 clearly show the presence of molecular hydrogen, as indicated by the band at 4104 cm^{-1}.[12]

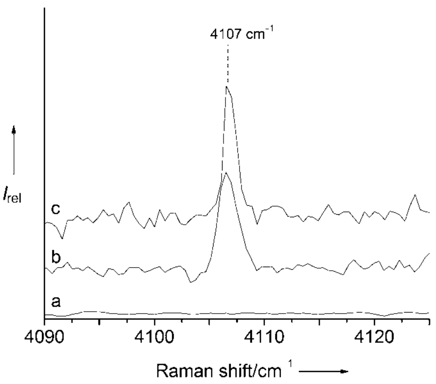


Figure 1. Raman spectra of a) toluene; b) H_2 in toluene; and c) homocoupling reaction in toluene.

The presence of H_2O is required for this reaction. To confirm this we performed a set of experiments using anhydrous materials (Experimental Section, Reaction b) which lead to only 17 % conversion after 7 h. At this point 30 μL of H_2O was added, and the conversion increased to 47.5 % after another 7 h. Furthermore, when 50 μL of H_2O was added to the dried catalyst and reactants the conversion increased to 61 %. These results clearly support the importance of H_2O in the catalytic reaction, and suggest the participation of hydroxy groups in hydrolyzing the boronic acid.

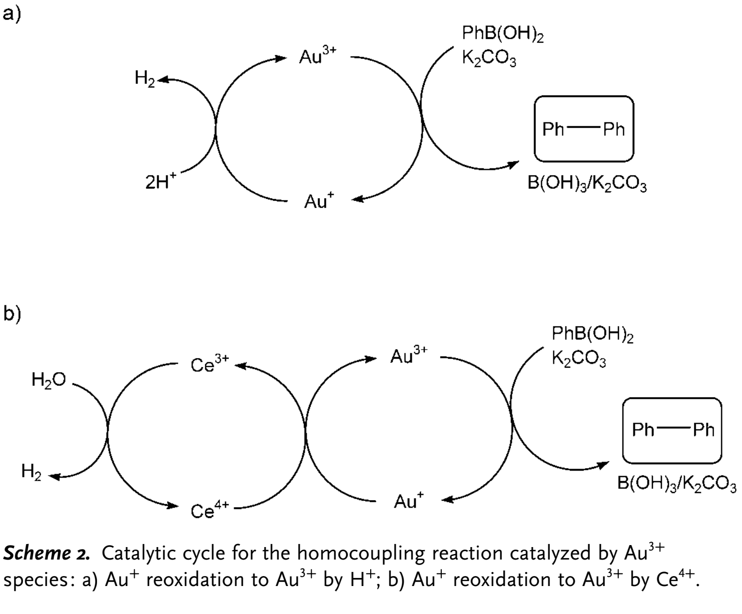
Raman spectroscopy was used to characterize the addition of water to the gold catalyst and the support alone. The spectrum of the Au/CeO_2 catalyst treated with water shows the formation of hydroxy groups on the support, as evidenced by new bands at 3427 and 3594 cm^{-1} (Supporting Information). These hydroxy groups disappeared after addition of phenylboronic acid, thereby indicating the participation of OH species in the activation of the phenylboronic acid. In contrast, when the same experiment was carried out with the CeO_2 support, the Raman bands representing the hydroxy groups showed no variation after addition of boronic acid. These results indicate that gold is required to enhance the interaction between OH species and the boronic acid. It has been shown previously that the presence of gold weakens the surface oxygen species of ceria.[13]

When boronic acid was mixed with water or with water and cerium oxide at the reaction temperature in the absence of gold, neither product formation nor substrate decomposition were observed. We can therefore conclude that the OH groups on the surface of the CeO_2 support interact with the boronic acid to form boric acid, while two phenyl species interact with Au^{3+} to form a carbon–metal bond. Thus, homocoupling occurs and Au^{3+} is reduced to Au^{+}.

To regenerate the active species and to close the catalytic cycle, Au^{+} has to be reoxidized to Au^{3+}. This oxidation can occur by three different routes: by air, by H^{+} generated in the media, or by Ce^{4+} present in the support. We have seen that the reaction proceeds in the absence of oxygen with the same activity, therefore the first possibility can be rejected. To investigate the second option—oxidation of Au^{+} by H^{+} to give Au^{3+} and H_2—we monitored the homocoupling reaction by Raman spectroscopy; formation of H_2 was observed.[12] However, it would appear that the redox potential for the whole reaction ($2H^{+}$ to H_2 and Au^{+} to Au^{3+}) is not high enough to cause a spontaneous electron transfer. Nevertheless, it should be taken into account that in the case of nanoparticles, as the number of atoms n per particle decreases, a nonlinear relationship exists between n, the redox potential (E_0), and the lattice stabilization energy of the atoms involved. As a consequence, E_0 decreases drastically with decreasing n.[14] Therefore, considering the formation of H_2 and the effect of small particle sizes on the oxidation potential of gold, it is possible that Au^{+} present as a gold nanoparticle could be reoxidized to Au^{3+} by H^{+}.

Looking into the third possibility—Ce^{4+} acting as an oxidant for Au^{+}—it has been reported[11] that water dissociates on the surface of cerium oxide to form OH groups and oxidize Ce^{3+} to Ce^{4+}. This reaction produces the H_2 that was detected by Raman spectroscopy.[12] In this case the redox potential for the reduction of Ce^{4+} to Ce^{3+} is high enough to oxidize Au^{+} to Au^{3+}, therefore this is also a promising candidate for the process that closes the catalytic cycle. Consistent with this hypothesis, XPS data characterizing the gold catalyst support the presence of Ce^{4+} and Ce^{3+} species (Supporting information).

We can therefore postulate two possible mechanisms for the homocoupling of phenylboronic acid on Au/CeO_2 catalysts (Scheme 2). For both catalytic mechanisms we infer that Au^{3+} is present at the active sites. To confirm this we investigated a series of Au/CeO_2 catalysts with different Au^{3+}/Au^{0} and Au^{+}/Au^{0} ratios, as determined by IR spectroscopy using CO as a probe molecule. The results presented in Figure 2 clearly show a direct correlation between the



Scheme 2. Catalytic cycle for the homocoupling reaction catalyzed by Au^{3+} species: a) Au^{+} reoxidation to Au^{3+} by H^{+}; b) Au^{+} reoxidation to Au^{3+} by Ce^{4+}.

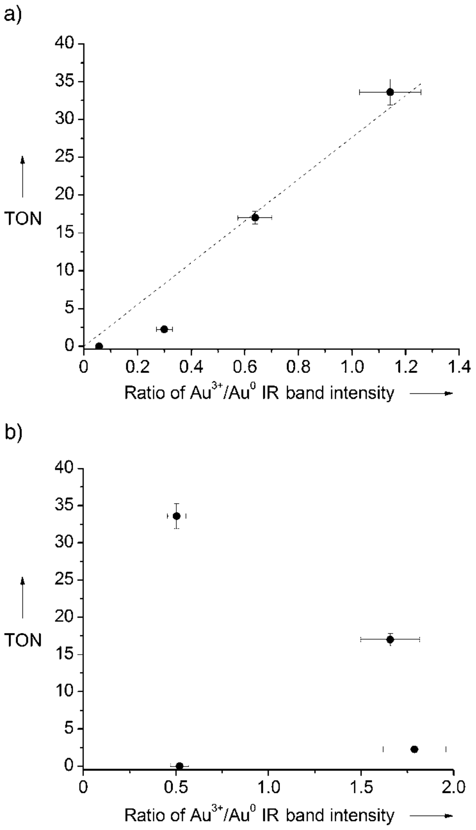


Figure 2. a) Correlation between Au^{3+} and Au^0 species and TON for the homocoupling reaction catalyzed by gold; b) correlation between Au$^+$ and Au^0 species and TON for the homocoupling reaction catalyzed by gold. The frequency and intensity of the IR band of CO adsorbed on gold catalysts were used to identify Au^{3+} (band at 2148 cm^{-1} representing Au^{3+}-bound CO), Au$^+$ (2130 cm^{-1}, Au$^+$-bound CO) and Au^0 (2104 cm^{-1}, Au^0-bound CO).

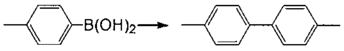
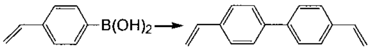
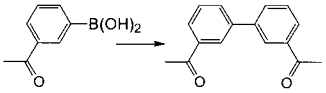
concentration of Au^{3+} species and catalytic activity; no correlation was found between catalytic activity and the concentration of Au$^+$ or Au^0.

Gold on nanocrystalline CeO$_2$ is a much more active catalyst than gold on precipitated CeO$_2$ for the homocoupling reaction. Consistent with these results, our group has recently demonstrated that the characteristics of the cerium oxide surface are extremely important for CO oxidation on an Au/CeO$_2$ catalyst.[9] We found that nanocrystalline CeO$_2$ (nanoparticles of about 4 nm in size with fluorite structure) increases the activity of gold for CO oxidation by two orders of magnitude with respect to a precipitated CeO$_2$ support. The results obtained for gold on different metal-oxide catalysts tested for CO oxidation and for homocoupling show a direct correlation between the activities (Supporting Information).

We also studied the homocoupling of other aryl boronic acids to determine the possible influence of substituents on the aromatic ring. The Au/CeO$_2$ catalyst gave practically 100 % conversion and selectivity in all cases (Table 1).

In conclusion, we have found that gold supported on nanocrystalline cerium oxide catalyzes the homocoupling reaction of phenylboronic acid with very high activity and selectivity in the absence of an α-halocarbonyl compound and presence of a base. Au^{3+} species are the active sites for the reaction and water is required to hydrolize the boronic acid through surface hydroxy groups.

Table 1: Homocoupling of phenylboronic acids.[a]

Reaction	Yield [%]
	100
	100
	97[b]

[a] Reaction conditions: 5 mL toluene, 0.3 mmol of phenylboronic acid, 5 mol % of Au, T = 333 K, 15 h; yield determined by GC-MS with *n*-decane as internal standard. [b] 3 % Acetophenone was formed as byproduct.

Experimental Section

Au/CeO$_2$ catalysts were prepared by precipitation of HAuCl$_4$ with NaOH following a procedure described elsewhere.[9] The total Au content of the final catalyst was determined by chemical analysis to be 2.25 wt %.

The solvent (5 mL) and the catalyst (the amount depends on the mol percent of gold required) were added to a 10-mL round-bottomed flask containing phenylboronic acid (0.3 mmol) and K$_2$CO$_3$ (0.4 mmol). The reactions were carried out at 333 K (unless otherwise specified) for 15 h with vigorous stirring. The yields and conversions were determined by GC-MS analysis using decane as internal standard.

Reaction a (Suzuki cross-coupling): The catalyst (100 mg; 5 mol % of Au per mol of PhB(OH)$_2$) was added to a round-bottomed flask together with DMF (5 mL), *p*-iodobenzophenone (0.2 mmol), and phenylboronic acid (0.3 mmol). The reaction was carried out at 433 K.

Reaction b: The catalyst and reactants were dried at 333 K and 10^{-3} Torr and anhydrous solvent was used; the reaction was carried out at 333 K under nitrgoen.

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[1] a) A. de Meijere, F. Diederich, *Metal-Catalyzed Cross-Coupling Reactions, Vol. 1–2*, Wiley-VCH, Weinheim, **2004**; b) G. C. Fu, A. F. Littke, *Angew. Chem.* **2002**, *114*, 4350–4386; *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211.
[2] K. C. Nicolaou, E. I. Sorensen, *Classics in Total Synthesis*, VCH, New York, **1996**.
[3] G. B. Smith, G. C. Dezeny, D. L. Hughes, A. O. King, T. R. Verhoeven, *J. Org. Chem.* **1994**, *59*, 8151–8156.
[4] J. Hassan, V. Penalva, L. Lavenot, C. Gozzi, M. Lamaire, *Tetrahedron* **1998**, *54*, 13793–13804.

[5] a) A. Lei, X. Zhang, *Tetrahedron Lett.* **2002**, *43*, 2525 – 2528, and references cited therein; b) J. R. Falck, S. Mohapatra, M. Bondlela, S. K. Venkataraman, *Tetrahedron Lett.* **2002**, *43*, 8149 – 8151; c) A. S. Demir, Ö. Reis, M. Emrullahoglu, *J. Org. Chem.* **2003**, *68*, 578 – 580; d) J. P. Parrish, Y. C. Jung, R. J. Floyd, K. W. Jung, *Tetrahedron Lett.* **2002**, *43*, 7899 – 7902; e) A. Demir, Ö. Reis, M. Emrullahoglu, *J. Org. Chem.* **2003**, *68*, 10130 – 10134; f) C. J. Li, *Angew. Chem.* **2003**, *115*, 5004 – 5006; *Angew. Chem. Int. Ed.* **2003**, *42*, 4856 – 4858.

[6] a) G. Dyker, *Angew. Chem.* **2000**, *112*, 4407 – 4409; *Angew. Chem. Int. Ed.* **2000**, *39*, 4237 – 4239, and references cited therein; b) A. S. K. Hashmi, L. Ding, J. W. Bats, P. Fisher, W. Frey, *Chem. Eur. J.* **2003**, *9*, 4339 – 4345.

[7] One of the referees pointed out an ASAP publication where colloidal gold is used as a catalyst for the homocoupling of phenylboronic acids. However, the activity is low and, more importantly, the selectivity is always below 80 %: H. Tsunoyama, H. Sakurai, N. Ichikuni, Y. Negishi, T. Tsukuda, *Langmuir* **2004**, *20*, 11293 – 11296.

[8] a) Q. Fu, H. Saltsburg, M. Flytzani-Stephanopoulos, *Science* **2003**, *301*, 935 – 938; b) F. Zhang, S. W. Chan, J. E. Spanier, E. Apak, Q. Jin, R. D. Robinson, I. P. Herman, *Appl. Phys. Lett.* **2002**, *80*, 127 – 129; c) A. N. Pestryakov, V. V. Lunin, A. N. Kharlanov, N. E. Bogdanchikova, I. V. Tuzovskaya, *Eur. Phys. J. D* **2003**, *24*, 307 – 309; d) A. N. Pestryakov, V. V. Lunin, *J. Mol. Catal. A* **2000**, *158*, 325 – 329.

[9] S. Carrettin, P. Concepción, A. Corma, J. M. López-Nieto, V. F. Puntes, *Angew. Chem.* **2004**, *116*, 2592 – 2594; *Angew. Chem. Int. Ed.* **2004**, *43*, 2538 – 2540.

[10] E. D. Park, J. S. Lee, *J. Catal.* **1999**, *186*, 1 – 11.

[11] a) T. Tabakova, F. Boccuzzi, M. Manzoli, D. Andreeva, *Appl. Catal. A* **2003**, *252*, 385 – 397; b) Lj. Kundakovic, D. R. Mullins, S. H. Overbury, *Surf. Sci.* **2000**, *457*, 51 – 62.

[12] a) D. Gracin, I. Bogdanovic, V. Bojanovic, M. Jaksic, Z. Pastuovic, J. M. Dutta, V. Vlahovic, R. J. Nemanich, *Vacuum* **2001**, *61*, 303 – 308; b) A. W. R. Leitch, J. Weber, V. Alex, *Mater. Sci. Eng. B* **1999**, *58*, 6 – 12.

[13] D. Andreeva, V. Idakiev, T. Tabakova, L. Ilieva, P. Falaras, A. Bourlinos, A. Travlos, *Catal. Today* **2002**, *72*, 51.

[14] L. D. Burke, A. J. Ahern, A. P. O'Mullane, *Gold Bull.* **2002**, *35*, 3 – 10.