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doi:10.1246/cl.2012.630

Anomalous Efficacy of Bimetallic Au/Pd Nanoclusters in C–Cl Bond Activation and Formal Metathesis-type C–B Bond Activation at Room Temperature

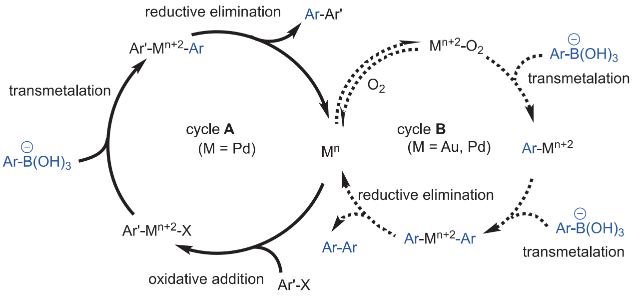
Raghu Nath Dhital[1] and Hidehiro Sakurai*[1,2]
[1]*Department of Functional Molecular Science, School of Physical Sciences,*
Graduate University for Advanced Studies (SOKENDAI), Myodaiji, Okazaki, Aichi 444-8787
[2]*Research Center for Molecular Scale Nanoscience, Institute for Molecular Science,*
Myodaiji, Okazaki, Aichi 444-8787

(Received March 19, 2012; CL-120235; E-mail: hsakurai@ims.ac.jp)

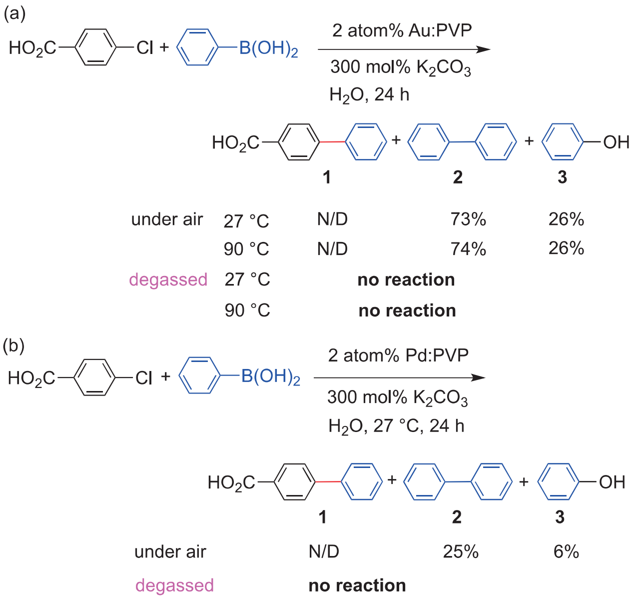
Au/Pd alloy nanoclusters stabilized by poly(*N*-vinylpyrrolidone) catalyze two different reactions of phenylboronic acid with 4-chlorobenzoic acid at room temperature in a single reaction cycle, cross coupling and metathesis-type homocoupling that is normally inaccessible through conventional catalysis.

Bimetallic nanoclusters with an alloy structure have attracted a great deal of interest during the past decade owing to their enhanced catalytic activities, which are superior to those of the corresponding monometallic counterparts.[1,2] Among the various bimetallic nanoclusters fabricated to date, Au/Pd alloy clusters are particularly fascinating because of their excellent catalytic activities for a diversity of chemical transformations.[3] Recent research reports have, however, dealt mainly with the significant extension of catalytic reactivity and selectivity of monometallic nanoclusters.[3,4] Herein, we report the peculiar catalytic activity of bimetallic Au/Pd alloyed nanoclusters in coupling between 4-chlorobenzoic acid (CBA) and phenylboronic acid ($PhB(OH)_2$) under aqueous conditions at room temperature.

Among the organic halides including triflates, organic chlorides are less reactive due to relatively high C–Cl bond strength and their reluctance to undergo oxidative addition. Recently significant progress has been made toward activation of aryl chlorides by the use of highly electron-donative and bulky ligands.[5] These ligands make the metal more nucleophilic, which facilitates oxidative addition by less active C–Cl bonds, the initial step of cross-coupling reaction. We previously reported that colloidal gold nanoclusters, such as poly(*N*-vinylpyrrolidone)-protected gold (Au:PVP) or chitosan [β-1,4-linked poly(D-glucosamine)]-protected gold (Au:chit), are excellent catalysts for aerobic oxidation including homocoupling reactions of arylboronic acids and their derivatives (cycle B in Scheme 1) in water under ambient conditions.[6,7] One characteristic feature of colloidal nanogold is that a negatively charged surface is generated due to the size effect of the clusters as well as the donation effect from the matrices, realizing the facile adsorption of molecular oxygen on its surface.[8] Such electronically enriched cluster surface would also be expected to accelerate the oxidative addition process in the Suzuki–Miyaura cross coupling (cycle A in Scheme 1). Since Pd always favors the cross coupling against homocoupling as compared with Au, we started to develop PVP-stabilized bimetallic Au/Pd alloy clusters for the activation of C–Cl bond under mild conditions in the Suzuki–Miyaura reaction. The PVP-stabilized Au and Pd monometallic and bimetallic alloy clusters containing 1:1 ratios of two metals ($Au_{0.5}Pd_{0.5}$:PVP) were prepared according to our previous procedure.[9]



Scheme 1. Suzuki–Miyaura cross-coupling reaction (cycle A) and aerobic (oxidative) homocoupling of arylboronic acid (cycle B).



(a)

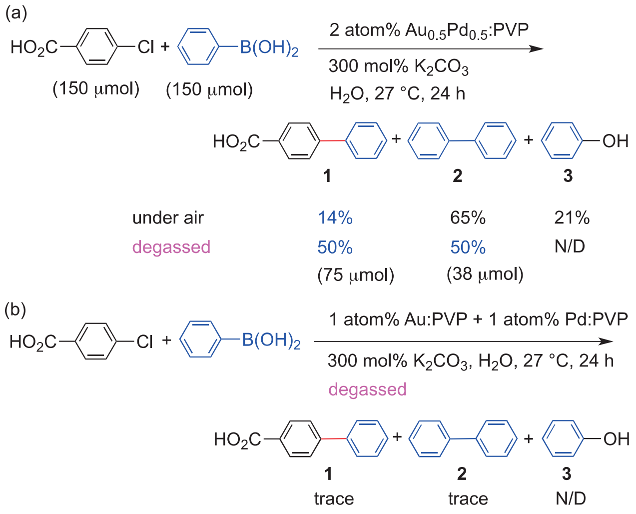
		1	2	3
under air	27 °C	N/D	73%	26%
	90 °C	N/D	74%	26%
degassed	27 °C	no reaction		
	90 °C	no reaction		

(b)

	1	2	3
under air	N/D	25%	6%
degassed	no reaction		

Scheme 2. Coupling reactions between CBA and $PhB(OH)_2$ catalyzed by (a) Au:PVP and (b) Pd:PVP, N/D: not detected.

First, the coupling reactions between CBA and $PhB(OH)_2$ by monometallic clusters were investigated. Equimolar amounts of CBA and $PhB(OH)_2$ were used as reactants. The cross-coupling product, biphenyl-4-carboxylic acid (**1**) was not observed, but biphenyl (**2**) and phenol (**3**) were observed in 73% and 26% yields (Scheme 2a), respectively in water at room temperature, which is in good agreement with our previous



Scheme 3. Coupling reactions between CBA and $PhB(OH)_2$ catalyzed by (a) $Au_{0.5}Pd_{0.5}$:PVP and (b) Au:PVP + Pd:PVP.

report that Au:PVP promotes only homocoupling (and the oxygenation) and no activity towards the cross coupling.[7a] To suppress the oxidative homocoupling and oxygenation, the reaction was performed under carefully degassed conditions, giving no reaction.[7a,10] The results did not change when the reaction was carried out at 90 °C. According to these results, Au:PVP should not be able to catalyze the Suzuki–Miyaura cross-coupling because Au is unable to activate C–Cl bonds.[11] Similar results were observed when Pd:PVP was used as a catalyst although Pd:PVP showed inferior activity as compared to Au:PVP towards the aerobic oxidations for yielding **2** and **3** (Scheme 2b). The lack of cross-coupling activity of Pd:PVP is consistent with previous reports where Pd:PVP-catalyzed coupling of aryl iodides or bromides as coupling partners were described but not aryl chlorides.[12]

To our delight, bimetallic clusters did exhibit a cross-coupling activity and **1** was obtained in 14% yield, along with 65% of **2** and 21% of **3** in the presence of $Au_{0.5}Pd_{0.5}$:PVP under air (Scheme 3a). Although we knew that Au/Pd bimetallic clusters are potentially active in the cross-coupling reaction, the oxidative homocoupling and oxygenation side reactions could not be suppressed unless the reactions were carried out under anaerobic conditions.[7a,10] We therefore examined the reactions under carefully degassed conditions and as a result 50% of **1** and 50% of **2** (yield based on $PhB(OH)_2$; i.e., 2:1 molar ratios) were obtained with $Au_{0.5}Pd_{0.5}$:PVP as the catalyst. To our surprise, however, biphenyl was still obtained in 50% yield, in the absence of oxidant although none of the oxygenated product **3** was produced. To confirm the significance of the bimetallic cluster structure, the reaction was carried out in the presence of a physical mixture of 1 atom % Au:PVP and 1 atom % Pd:PVP, resulting in the trace amounts of **1** and **2** (Scheme 3b). These results clearly showed that a synergistic effect originating from the presence of an alloyed phase plays a crucial role in the coupling reaction.

The oxidative homocoupling of phenylboronic acid (Scheme 1, cycle B) could only occur in the presence of stoichiometric amount of chemical oxidant or molecular oxygen or air.[7a,10,13] In contrast, we observed the homocoupling of $PhB(OH)_2$ continued to occur in the absence of oxidant in faire competition with cross-coupling product. The constant ratios of **1** and **2** were observed in each time interval suggest that both products are probably formed in a single catalytic cycle (Figure S5, Supporting Information[16]). This result indicates that the observed reaction is unlikely to follow the conventional mechanism (Scheme 1) and is more likely to occur by a new mechanism. To understand the reaction pathway of the homocoupling, the reaction was monitored by ^{11}B NMR spectroscopy to follow the intermediates derived from $PhB(OH)_2$. Pinacol ester of phenylboronic acid (PhBpin) was used as a reactant instead of $PhB(OH)_2$ due to the expectation of these intermediates stabilized by the pinacol ester formation. We confirmed that the same reaction also took place in the case of PhBpin to give cross-coupling product and homocoupling product in 50% and 49% yield, respectively, after prolonged time (27 h). As shown in Figure 1, bis(pinacolato)diborane (pin_2B_2) was detected after 16 h. It can be concluded that a metathesis-type reaction of $PhB(OH)_2$ takes place under anaerobic conditions, giving biphenyl (**2**) and tetrahydroxydiborane $[(HO)_2B–B(OH)_2]$. To the best of our knowledge, this is the first example of the homocoupling reaction of organoboron compounds through the formal metathesis reaction not by oxidative coupling. To summarize, the total reaction occurs between two equivalents of CBA and four equivalents of $PhB(OH)_2$ to give two equivalents of biphenyl-4-carboxylic acid (**1**), one equivalent of biphenyl (**2**), two equivalents of boric acid $[B(OH)_3]$, and one equivalent of tetrahydroxydiborane in the presence of the bimetallic catalyst in H_2O at 27 °C as shown in Scheme 4.

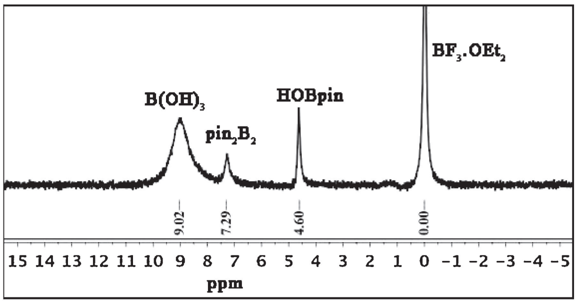
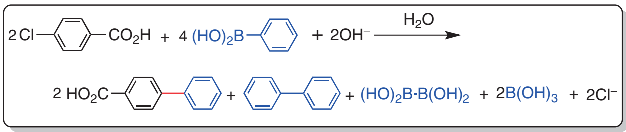
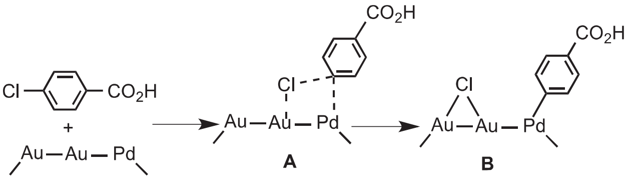


Figure 1. ^{11}B NMR spectra recorded at pH 9.7 in 33% D_2O. Reaction conditions: CBA (0.15 mmol), PhBpin (0.15 mmol), 300 mol % K_2CO_3, 2 atom % $Au_{0.5}Pd_{0.5}$:PVP, 2 mL H_2O, 1 mL D_2O, 27 °C, 24 h degassed.

Although the details of the reaction mechanism are still unclear, mechanisms involving a single-metal (Au or Pd) catalytic site can be ruled out for the following reasons. First, it is impossible to express the overall reactions described in Scheme 4 in terms of a single-site catalyst, at least if that single site catalyst behaves in the same manner as in the conventional Suzuki–Miyaura coupling. Next, previous reports[14] have suggested that catalysis in palladium nanocluster-catalyzed cross-coupling reactions might occur in solution involving atomic Pd leached from clusters if oxidative addition occurs on a single palladium atom to afford a Pd^{2+} intermediate. We examined the leaching of Pd and Au by means of inductively coupled plasma atomic-emission spectroscopy (ICP-AES) analysis after completion of the reaction, and the levels of Pd and Au ions were found below the detection limits (<44 ppb of Pd and <50 ppb of



Scheme 4. The overall reaction catalyzed by $Au_{0.5}Pd_{0.5}$:PVP.



Scheme 5. Proposed model for synergistic involvement of atoms of both metals in the oxidative addition processes.

Au). When the reaction was stopped after 8 h in the in situ leaching test and samples of the filtrate were monitored for further reaction, the conversion remained unchanged (Scheme S1, Supporting Information[16]). These experiments strongly support the view that leaching of metal species (Pd or Au) does not form part of the catalytic cycle. In addition, the initial rates of formation of biphenyl-4-carboxylic acid (**1**) and biphenyl (**2**) depend linearly on the concentration of the $Au_{0.5}Pd_{0.5}$:PVP (Figure S7[16]), providing strong evidence that the oxidative addition occurs on the surface of bimetallic Au/Pd:PVP.[12a] Furthermore, the initial rate of formation of **1** and **2** was independent of the concentration of CBA and it showed zero-order kinetics with CBA (Figure S6[16]), which indicated that the oxidative addition of CBA is feasible on a bimetallic surface. Since the presence of a bimetallic structure is essential for the reaction to occur, as judged from the results shown in Scheme 3b, the catalytic cycle of the reaction, particularly the oxidative addition process, must involve multiple metals on the surface of bimetallic clusters.

On the basis of these results, we would like to propose a model, shown in Scheme 5, for the oxidative addition at the gold/palladium surface. In this model, more than two adjacent atoms synergistically assist cleavage of the C–Cl bond (transition state **A**), so that an organic unit becomes attached to one atom (probably Pd) and the chloride ion becomes attached to other atoms, such as those on the Au surface, to form the stable bridged intermediate (**B**). This process might prevent the formation of M^{2+} intermediates through oxidative addition at a single metal site, which would otherwise permit leaching to occur and would also result in the dual-catalyst behavior in the formal cross coupling and metathesis-type homocoupling reactions. On the basis of DFT calculation, Corma and coworkers have also proposed that a similar type of oxidative addition process occurs during the reaction of iodobenzene with Au_{38}.[15]

In summary, we have demonstrated anomalous behavior of bimetallic Au/Pd alloy systems in the coupling reaction of $PhB(OH)_2$ with CBA at room temperature under aqueous conditions. The most important finding is that the reaction mechanism is likely to be completely different from that of the conventional Suzuki–Miyaura coupling, which can be described in terms of the participation of a single metal (Pd). Instead, our reaction involves two processes of cross-coupling and metathesis-type homocoupling in a single reaction cycle where both Au and Pd are synergistically participating. We believe that the modified electronic structure of the catalyst and/or the nature of the active sites, resulting from a synergistic effect by the presence of alloy phases, play a crucial role in generating the unusual catalytic properties and open new possibilities for reactions that are normally inaccessible through conventional catalysis.

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