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# Low-Temperature Carbon−Chlorine Bond Activation by Bimetallic Gold/Palladium Alloy Nanoclusters: An Application to Ullmann Coupling

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*Supporting Information*

**ABSTRACT:** This paper describes the unique catalytic activity of bimetallic Au/Pd alloy nanoclusters (NCs) for Ullmann coupling of chloroarenes in aqueous media at low temperature. The corresponding reaction cannot be achieved by monometallic Au and Pd NCs as well as their physical mixtures. On the basis of quantum chemical calculation, it was found that the crucial step to govern the unusual catalytic activity of Au/Pd is the dissociative chemisorption of ArCl, which is unlikely in the monometallic Au and Pd NCs.

In the past decade, nanoclusters (NCs) of bimetallic alloys have attracted considerable research interest because of their unique catalytic properties, which differ substantially from those of single-phase monometallic counterparts.[1] Among the various bimetallic NCs that have been fabricated to date, gold/palladium alloy NCs are particularly fascinating because of their high catalytic activities.[2]

Because of the relatively high dissociation energy of C−Cl bond in comparison with C−Br or C−I, it is difficult to activate chloroarenes by undergoing oxidative addition on Pd without ligation by nucleophilic ligands.[3] Here, we demonstrate a new method for activation of C−Cl bonds at low temperature as a result of bimetallic Au/Pd synergy and we report the successful examples of the Ullmann coupling of chloroarenes under ambient conditions. Ullmann coupling, which was first reported in 1901,[4] is a conventional method for the synthesis of symmetrical biaryls. Initially, aryl iodides were used in coupling reactions that were promoted by excess amount of copper at high temperatures.[4,5] Recent developments in the Ullmann coupling reaction has permitted the use of aryl bromides or chlorides as reactants in the presence of a coreductant such as Zn powder, formic acid, and dihydrogen under mild conditions. Such reactions can be catalyzed by many types of homogeneous or heterogeneous transition-metal catalysts, such as Ni, Pd, or Au.[6,7] However, to the best of our knowledge, there are no reports of any successful examples of Ullmann coupling reactions of chloroarenes under ambient conditions. It is because of relative difficulty in the activation a C−Cl bond, which needs to occur twice within a single catalytic cycle, and because all C−M intermediates need to resist hydrogenation by external coreductant.[8]

Our investigation started by monitoring the Ullmann coupling of 4-chlorotoluene (**1a**) (0.1 mmol) in *N*,*N*-dimethylformamide (DMF)/ $H_2O$ (1:2 ratio) in the presence of 300 mol % $K_2CO_3$ at 45 °C under argon atmosphere using monometallic Au, Pd or bimetallic Au/Pd-alloy NCs as catalysts. These NCs were stabilized by a hydrophilic polymer, poly(*N*-vinylpyrrolidone) (PVP).[9−11] The results are shown in Table 1 (entries 1−6).

The Ullmann coupling product, 4,4′-dimethylbiphenyl (**2a**), was not obtained when monometallic Au:PVP or Pd:PVP was used as the catalyst (entries 1 and 2). To our delight, however, Au/Pd bimetallic alloy NCs did exhibit Ullmann coupling activities (entries 3−5) with **1a** at 45 °C. When $Au_{0.8}Pd_{0.2}$:PVP (80% of Au and 20% of Pd) was used as a catalyst, the yield of **2a** was only 30% (entry 3). The activity increased markedly for a bimetallic catalyst containing 50% of Pd, giving **2a** in 98% yield with 100% conversion (entry 4). However, an increase in the Pd content to 80% drastically reduced the yield of **2a** to 20% (entry 5). The presence of physical mixtures of 1 atom % Au and 1 atom % Pd did not promote the reaction, indicating that the presence of an alloy structure was essential to the coupling reaction (entry 6). Since no reaction occurred in the absence of a base as shown in entry 7, the effect of the base was screened by quenching the reaction after 3 h. Inorganic bases such as carbonates or hydroxides worked effectively and the reaction rate was in order $Na_2CO_3 < K_2CO_3 < Cs_2CO_3 <$ NaOH < KOH (entries 8−12). The reaction was completed within 1 h in the presence of 300 mol % of KOH. The coupling reaction occurred smoothly even when the reaction temperature was decreased to 35 °C or to 27 °C (room temperature), giving **2a** quantitatively for 6 and 24 h, respectively (entries

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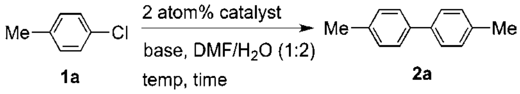
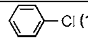
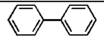
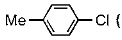
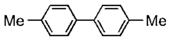
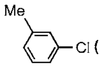
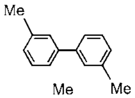
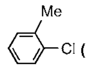
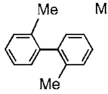
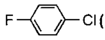
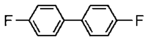
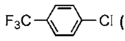
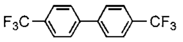
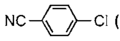
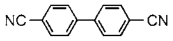
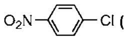
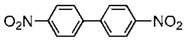
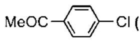
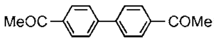
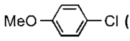
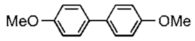
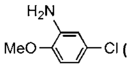
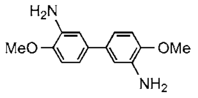
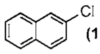
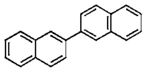
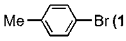
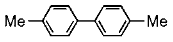
**Table 1. Ullmann Coupling of 4-Chlorotoluene Catalyzed by Monometallic and Bimetallic Catalyst**



| entry | catalyst | base | $T$ (°C) | $t$ (h) | yield[a] (%) |
|---|---|---|---|---|---|
| 1 | Au:PVP | $K_2CO_3$ | 45 | 24 | 0 |
| 2 | Pd:PVP | $K_2CO_3$ | 45 | 24 | 0 |
| 3 | $Au_{0.8}Pd_{0.2}$ | $K_2CO_3$ | 45 | 24 | 30 |
| **4** | **$Au_{0.5}Pd_{0.5}$** | **$K_2CO_3$** | **45** | **24** | **98** |
| 5 | $Au_{0.2}Pd_{0.8}$ | $K_2CO_3$ | 45 | 24 | 20 |
| 6[b] | Au:PVP+Pd:PVP | $K_2CO_3$ | 45 | 24 | 0 |
| 7 | $Au_{0.5}Pd_{0.5}$ | – | 45 | 24 | 0 |
| 8 | $Au_{0.5}Pd_{0.5}$ | $Na_2CO_3$ | 45 | 3 | 66 |
| 9 | $Au_{0.5}Pd_{0.5}$ | $K_2CO_3$ | 45 | 3 | 73 |
| 10 | $Au_{0.5}Pd_{0.5}$ | $Cs_2CO_3$ | 45 | 3 | 85 |
| 11 | $Au_{0.5}Pd_{0.5}$ | NaOH | 45 | 3 | 95 |
| 12 | $Au_{0.5}Pd_{0.5}$ | KOH | 45 | 1 | 98 |
| 13 | $Au_{0.5}Pd_{0.5}$ | KOH | 35 | 6 | 98 |
| **14** | **$Au_{0.5}Pd_{0.5}$** | **KOH** | **27** | **24** | **98** |
| 15[c] | $Au_{0.5}Pd_{0.5}$ | KOH | 35 | 6 | 97 |

[a] Isolated yield. [b] 1 atom % of Au:PVP and 1 atom % of Pd:PVP were used. [c] 150 mol % of KOH was used.

**Table 2. Catalytic Ullmann Coupling of Chloroarenes Using Bimetallic $Au_{0.5}Pd_{0.5}$:PVP Catalyst[a]**

| entry | substrate | product | | t (h) | yield[b] (%) |
|---|---|---|---|---|---|
| 1 |  (1b) |  | (2b) | 12 | 97 |
| 2 |  (1a) |  | (2a) | 6 | 98 |
| 3 |  (1c) |  | (2c) | 16 | 93 |
| 4 |  (1d) |  | (2d) | 24 | 90 |
| 5 |  (1e) |  | (2e) | 12 | 96 |
| 6 |  (1f) |  | (2f) | 12 | 97 |
| 7 |  (1g) |  | (2g) | 12 | 92 (8)[c] |
| 8[d] |  (1h) |  | (2h) | 24 | 88 (6)[c] (5)[e] |
| 9[f] |  (1i) |  | (2i) | 24 | 86 (5)[c] |
| 10 |  (1j) |  | (2j) | 12 | 92 (6)[c] |
| 11 |  (1k) |  | (2k) | 12 | 93 (7)[c] |
| 12[g] |  (1l) |  | (2l) | 24 | 92 (7)[c] |
| 13[g] |  (1m) |  | (2m) | 24 | 48 |

[a] Reaction conditions: 2 atom % $Au_{0.5}Pd_{0.5}$:PVP, chloroarene (0.1 mmol), KOH 150 mol %, DMF/$H_2O$ (1:2, 1 mL DMF, 2 mL $H_2O$), 35 °C, under argon. [b] Yield of isolated product. [c] Yield of hydrodechlorination product. [d] 300 mol % of $Cs_2CO_3$ was used. [e] Yield of 4-$NO_2C_6H_4NMe_2$. [f] 10% of **1i** was recovered. [g] DMF/$H_2O$ 1:1 ratio (1.5 mL DMF and 1.5 mL $H_2O$) was used.

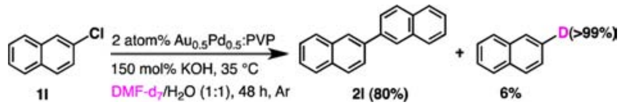
13–14). To the best of our knowledge, this is the first example of Ullmann coupling of chloroarenes under ambient conditions.

Having established the optimal reaction conditions, the protocol was extended to other chloroarenes to verify the scope of the method, and the results are listed in Table 2. The coupling of chlorobenzene (**1b**) proceeded smoothly to yield biphenyl (**2b**) in 97% (entry 1). Sterically less-congested substrates coupled in excellent yields, and in the case of 3-chlorotoluene (**1c**), the reaction was completed in 16 h, whereas sterically hindered 2-chlorotoluene (**1d**) required 24 h for the reaction to reach completion (entry 3–4). Chloroarenes with an electron-withdrawing group in the *para*-position (**1e**–**1i**) also underwent coupling, although byproducts from hydrodechlorination were also obtained in some cases (entries 5–8). For example, the reaction of 4-chlorobenzonitrile (**1g**) gave the corresponding biaryl **2g** in 92% yield together with 8% yield of benzonitrile (entry 7). In the case of 1-chloro-4-nitrobenzene (**1h**), KOH failed to give satisfactory results, but **2h** was obtained in 88% yield after 24 h when 300 mol % of $Cs_2CO_3$ was used (entry 8). Note that two byproducts, nitrobenzene and *N*,*N*-dimethyl-4-nitroaniline, were obtained from this reaction in 6% and 5% yield, respectively. The former is the hydrogenation product and the latter may be formed through amination with dimethylamine generated from DMF (see in the table caption). The reaction of acetyl derivatives (**1i**) was somewhat slower and was incomplete after 24 h, giving **2i** in 86% yield, together with 5% of acetophenone and a 10% recovery of **1i** (entry 9). In addition to chloroarenes containing electron-withdrawing groups, chloroarenes containing electron-donating groups also reacted under the current reaction conditions. 4-Chloroanisole (**1j**) and 5-chloro-2-methoxyaniline (**1k**) were each coupled under mild conditions, to give **2j** and **2k** in 92 and 93% yields, respectively (entry 10–11). 2-Chloronaphthalene (**1l**) also successfully underwent the coupling to afford 2,2′-binaphthyl (**2l**) in 92% yield for 24 h (entry 12).

However, to our surprise, the reaction of bromotoluene (**1m**) was slower than that of **1a**. The reaction was incomplete even after 24 h, giving **2a** in only 65% yield with the recovery of **1m** (entry 13). A comparison of the observed reaction rates[12] for the decay of **1a** ($k_{1a}$) and of **1m** ($k_{1m}$) (see Figures S5 and S6) showed that the value of $k_{1a}$ ($5.6 \times 10^{-2}$ $h^{-1}$) was nearly 3 times that of $k_{1m}$ ($2.0 \times 10^{-2}$ $h^{-1}$). The significant difference in the rates of activation of C–Cl and C–Br showed the opposite trend in the catalytic activity of bimetallic Au/Pd catalyst to that of usual transition-metal catalyst.

The role of DMF might be critical. We have previously reported that DMF behaves as an excellent reductant in Au:PVP-catalyzed intramolecular hydroalkoxylation of alkenes through donation of hydrogen from its formyl group.[13] Indeed, it was confirmed that DMF can play the role of a reductant in Ullmann coupling. The greater kinetic isotope effect on the pseudo-first-order kinetics of decay of **1a** in the reaction of **1a** to form **2a** ($k_H/k_D$ = 7.0) between DMF and DMF-$d_7$ (see Figure S7) showed that DMF participates in the rate-limiting step, which is probably a hydrogen-transfer process. The reaction of **1l** in DMF-$d_7$/$H_2O$ proceeded significantly slower than that in DMF/$H_2O$, and after 48 h, it gave **2l** in only 80% yield together with 6% of deuterated **3l** (Scheme 1). The results confirmed that the source of hydrogen for the hydrodechlorination side reaction was DMF. As a result, no external

**Scheme 1. Ullmann Coupling of 1l Catalysed by Bimetallic $Au_{0.5}Pd_{0.5}$:PVP in the Presence of DMF-$d_7$/$H_2O$ (1:1 Ratio)**



reductant such as Zn or formic acid was necessary under the reaction conditions.

An essential step, which determines the characteristics difference in the catalytic activities of Au, Au/Pd, and Pd NCs, is the oxidative addition of chloroarene followed by the spill over of Cl,[11a] and we therefore intensively studied only this step at present. Our previous report demonstrated that $Au_{20}^-$, a negatively charged homogeneous Au NCs, is a suitable model for simulating reaction on the surface of Au:PVP.[14] We therefore examined the model systems $Au_{20}^-$, $Au_{16}Pd_4^-$, $Au_{10}Pd_{10}^-$, and $Pd_{20}$ to compare the reaction pathway for oxidative additions on Au, Pd, and Au/Pd alloy clusters. Fundamental consideration of these models and the computational details are given in Supporting Information. The calculations were performed by the Gaussian09 suite of programs.[15] The energy diagram of the oxidative addition of chlorobenzene (**1b**) on $Au_{20}^-$ and $Au_{10}Pd_{10}^-$ is shown in Figure 1 where the energies are shown by taking those of adsorption complexes being the same for these clusters.

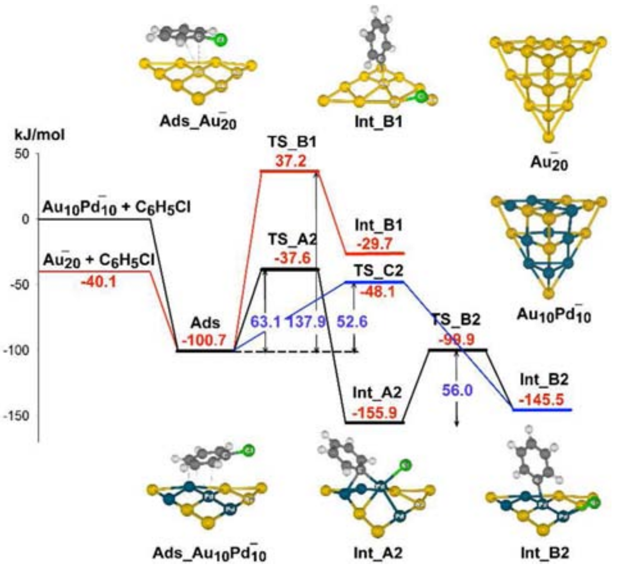


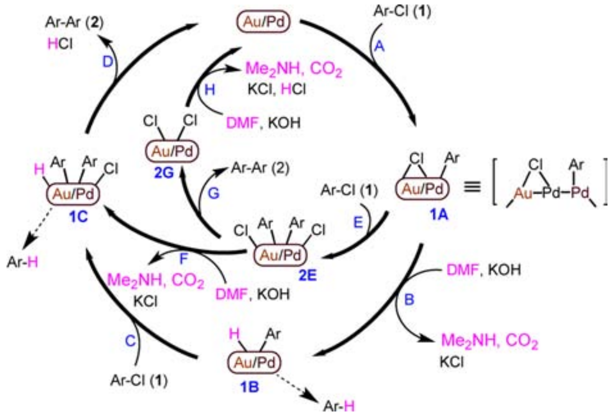
**Figure 1.** Energy profile diagram of oxidative addition of chlorobenzene on $Au_{20}^-$ and $Au_{10}Pd_{10}^-$ NCs.

In the case of the $Au_{20}^-$ system, **1b** is adsorbed on the facet site and a local minimum is obtained for the dissociative chemisorption (Int_B1). However, the calculated activation energy barrier for this (C−Cl) dissociative chemisorption is very high at 137.9 kJ/mol. In $Au_{10}Pd_{10}^-$ bimetallic cluster which simulates $Au_{0.5}Pd_{0.5}$ alloy, we found two types of intermediates for chemisorption. The adsorption was calculated to proceed with low activation energy barrier of 63.1 kJ/mol to give adsorption intermediate (Int_A2) in which both the phenyl group and the Cl atom are attached to the same Pd site. The other intermediate for dissociative chemisorption (Int_B2) is also stable as the adsorbed complex (Ads) or Int_A2. The calculated activation energy barrier from Int_A2 is 56.0 kJ/mol. The reaction pathway, which directly provides Int_B2 from the adsorption complex, is also possible and has a moderate energy barrier of 52.6 kJ/mol. Note that an intermediate corresponding to Int_A2 was not obtained in the case of $Au_{20}^-$ system. These results clearly show that the inclusion of Pd has an effect of stabilizing the dissociative adsorption and reducing activation energy, which is not possible in pure Au cluster.

The model cluster $Au_{16}Pd_4^-$ that simulates $Au_{0.8}Pd_{0.2}$ alloy also shows catalytic activity. The structure relaxation of $Pd_{20}$ cluster, on the other hand, is very large in adsorption intermediate (Int_A3) and this intermediate is very stable, which prevents the further reaction. These results show that the catalytic activity is high in the Au/Pd alloy NCs while the activity is lost in the case of pure Pd NCs. Details of these results are described in Supporting Information. Our results indicated that involvement of Au as a nearest heteroatom is crucial to initiate the reaction on the one hand and its composition up to 50% in bimetallic catalyst enhances the catalytic activities on the other hand. Therefore, in the current Au/Pd bimetallic system, both alloy effects[2d] such as "ligand effect" and "ensemble effect" are significant that enhances catalytic performance.

Possible catalytic pathways are depicted in Scheme 2. The inclusion of Au as a nearest heteroatom might promote the spill over of Cl during the oxidative addition, forming an intermediate **1A** (process A).[16] Possible routes for the involvement of DMF to complete the redox cycle are displayed in the mechanism. In the process B, DMF donates the hydrogen to form Cl free intermediate **1B**, followed by the oxidative addition of ArCl to form intermediate **1C**. Subsequent reductive elimination of Ar−Ar and HCl would lead to regenerate the catalyst. The oxidative addition of second molecule of ArCl before the participation of DMF may also be possible, leading to the intermediate **2E** (process E). Reductive elimination of Ar−Ar from **2E** would afford the intermediate **2G**, followed by the reduction by DMF to complete the redox cycle. The preliminary theoretical calculations for these other steps indicate that the present reaction proceeds smoothly with low energy barriers after the dissociative chemisorption of ArCl (Int_B).

**Scheme 2. Possible Pathways for Ullmann Coupling of Chloroarenes Catalyzed by Bimetallic $Au_{0.5}Pd_{0.5}$:PVP**



In summary, Ullmann coupling of chloroarene under ambient conditions was achieved by using bimetallic Au/Pd alloy NCs as a catalyst and DMF as both a co-solvent and reducing agent. We successfully demonstrated the unique example of bimetallic effect where each monometallic NC and their physical mixture did not catalyze the reaction. The observed synergistic effect of Au/Pd alloy is different from the reported bimetallic effect where at least one metal is mainly in charge of catalytic activity. In addition, the unusual character of bimetallic Au/Pd alloy NCs, which display a higher catalytic activity toward chloroarenes than for bromoarenes, is interesting. We hope our simplified approach for activation of strong C−Cl bonds might create new opportunities for the development of designer multimetallic catalyst for C−C coupling reactions.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Experimental details, characterization, kinetics data and other theoretical results. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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