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### COMMUNICATION

## Pd(0)/Au(1) redox incompatibilities as revealed by Pd-catalyzed homo-coupling of arylgold(1)-complexes<sup>†‡</sup>

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A Pd(II)-catalyzed homo-coupling of Au(I)-aryls is reported. The reaction is driven by a Pd(0)/Au(I) redox reaction that generates a gold mirror and Pd(II), and illustrates one of the challenges for developing dual catalytic Au–Pd systems.

Pd(0)/Pd(II) catalyzed coupling reactions rely on five basic elementary steps: oxidative addition, reductive elimination, migratory insertion,  $\beta$ -elimination, and transmetallation.<sup>1</sup> With the exception of transmetallation, gold complexes rarely facilitate these basic transformations, a partial consequence of their high barriers for Au(I)/Au(0) and Au(III)/Au(1) redox transitions<sup>2</sup> along with their preference for low coordination numbers. Despite these differences Au(1)/Au(III) catalyzed cross-coupling reactions have been reported<sup>3,4</sup> under the action of strong oxidants like selectfluor,<sup>5</sup> PhI(OAc)<sub>2</sub>,<sup>6</sup> or peroxy acids.<sup>7</sup> Mechanistic studies by Toste on systems utilizing selectfluor suggest fascinating bimolecular reductive elimination mechanistic possibilities.<sup>8,9</sup>

Fueled by the seemingly orthogonal reactivity modes of Au and Pd catalysts, are suggestions of tantalizing new crosscoupling schemes that sequence the reactivities of Au and Pd. Reports of at least partial success in interfacing Au- and Pd catalysis in this manner have been published by Blum,10 Hashmi,<sup>11</sup> Sarkar,<sup>12</sup> and Sestelo.<sup>13</sup> In particular, Blum has reported an impressive example of bimetallic catalysis wherein a gold-vinyl intermediate obtained from an allene activation reaction could be intercepted by an in situ formed palladium  $\pi$ -allyl species to perform a vinyl-allyl coupling that was catalytic in *both* gold and palladium.<sup>14</sup> We report herein that undesirable redox reactions between Pd(0) and Au(1) can interfere with the normal operation of several putative catalytic cycles that could couple the reactivity of Au and Pd. These observations may explain the difficulty of developing reactions that are catalytic in both metals.

Motivated by the potential of utilizing aryl and vinyl electrophiles to model the reactivity of  $C(sp^2)$ -Au intermediates in Au(1)-catalysis, we studied the palladium-catalyzed



Fig. 1 Structures of Au-vinyl complexes A and B.

cross-coupling of *isolated* vinyl and arylgold(I)-complexes with aryl-triflates.<sup>15</sup> Unfortunately, attempts to couple complexes  $A^{16}$  and  $B^{17}$  (Fig. 1) and TolOTf with various Pd-catalysts failed.<sup>18</sup> TLC and GC-MS analysis indicated that at best only traces of the desired cross-coupled products were obtained (24 h).

In contrast, the same reaction conditions converted arylgold(1)-complex **1a** into a variety of biaryl products (eqn (1)). The reaction progress was accompanied by the formation of brown particles, which gradually led to a gold mirror on the glass surface. Once TLC indicated complete conversion, GC-MS showed that three biaryl products, **2**, **3**, and **4**, were generated in an 8:85:7 ratio, respectively.<sup>19</sup> The structure of **4** was confirmed by <sup>1</sup>H NMR.



A simple mechanistic scheme for the formation of **2** is shown in cycle **C**, Scheme 1. Whereas cross-coupling to **2** is initiated by oxidative addition of TolOTf, catalytic homo-coupling of **1a** to **3** requires a separate oxidant (cycle **D**, Scheme 1) to



Scheme 1 Mechanistic schemes for cross- and homo-coupling of 1a.

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Entry	Additive	[Pd]	L	Time	<b>2</b> :3:4 <sup>f</sup>
1	TolOTf	Pd(OAc) <sub>2</sub>	L1	<19 h	8:85:7
2	TolOTf	$Pd(OAc)_2$	L3	<19 h	2:84:14
3	TolOTf	$Pd(OAc)_2$	L4	$24 h^d$	1:86:13 <sup>g</sup>
4	TolOTf	dppfPdCl2 <sup>b</sup>	None	<19 h	11:74:15
5	TolOTf	$Pd_2(dba)_3$	L1	19 h <sup>d</sup>	13:73:14 <sup>g</sup>
6	TolOTf	$Pd_2(dba)_3$	L3	$24 h^d$	$5:83:12^{g}$
7	TolOTf	$Pd_2(dba)_3$	L4	$24 h^d$	$7:81:12^{g}$
8	TolOTf	PEPPSI-IPr <sup>c</sup>	None	<29 h	1:88:12
9	TolOTf	None	L1	19 h <sup>e</sup>	
10	TolOTf	None	None	19 h <sup>e</sup>	
11	None	None	None	19 h <sup>e</sup>	_

<sup>*a*</sup> Reaction conditions: 5–10 mol% [Pd]/L; 2.5 equiv. TolOTf; 10 mg (17.7  $\mu$ mol) of **1a**. <sup>*b*</sup> dppf = 1,1'-bis(diphenylphosphino)-ferrocene. <sup>*c*</sup> PEPPSI-IPr = [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride. <sup>*d*</sup> Incomplete conversion to coupled product was indicated by TLC; after the indicated period of time, the reactions was analyzed by GC-MS which thermally converts unreacted **1a** to **3**. <sup>*e*</sup> No conversion indicated by TLC. <sup>*f*</sup> Product ratio determined by GC-MS. <sup>*g*</sup> See ref. 19.

regenerate  $Pd(\pi)$  after reductive elimination of **3**. Since no external oxidant was added (with the exception of TolOTf which would facilitate cross-coupling) further studies were initiated to gain insight.

As shown in Table 1, variation of the Pd catalyst did not significantly increase the amount of 2 (Table 1, entries 1–8), though reaction times did vary from catalyst to catalyst: Pd(II) sources tended to be faster. Control experiments showed that when no Pd catalyst was added, no conversion of 1a to coupled products was observed by TLC (Table 1, entries 9–11). Note: thermolysis of 1a in the GC injector port leads to 3.<sup>19</sup>

The source of 3 and 4 was investigated by examining the role of each reaction component. When TolOTf was omitted, only 3 and 4 were formed (Table 2, entry 1), which clearly showed that TolOTf did not act as the oxidant for the formation of 3. Monitoring the reaction with Pd(OAc)<sub>2</sub> by TLC indicated that 1a was consumed within 5 h (Table 2, entry 2), and that an initial burst<sup>20</sup> of coupled products was followed by a slower but steady reaction. Using Pd<sub>2</sub>(dba)<sub>3</sub> (Table 2, entry 3), the initial burst was not observed and the reaction proceeded slowly. A slightly faster rate could be regained using Pd<sub>2</sub>(dba)<sub>3</sub> in combination with TolOTf, but the reaction time was still not as rapid as when a Pd(II) source was used. These data suggest that it is a Pd(II) species that first engages Au(I) to produce homo-coupled products. Since the aryl groups of PAr<sub>3</sub> ligands are known to transfer in Ni, Pd, and Pt reductive elimination reactions,<sup>21</sup> the possibility that **4** was phosphine derived was tested by utilizing (p-tol)<sub>3</sub>PAuAr (1b) (Table 2, entries 4 and 5). Not surprisingly, a significant amount of 2 was observed. When Ph-Xphos (L1, Fig. 2) was utilized as the

 Table 2
 No addition of TolOTf and variation of substrate<sup>a</sup>



Entry	Substrate	[Pd]	$\mathbf{L}'$	Time	2:3:4 <sup>f</sup>
1	1a	Pd(OAc) <sub>2</sub>	L1	<19 h	0:76:24
2	1a	$Pd(OAc)_2$	L1	<5 h	0:75:25
3	1a	$Pd_2(dba)_3$	L1	19 h <sup>c</sup>	$0:98:2^{g}$
4	1b	$Pd(OAc)_2$	L1	5 h <sup>c</sup>	19:80:1 <sup>g</sup>
5	1b	$Pd(OAc)_2$	L2	5 h <sup>c</sup>	18:82:0 <sup>g</sup>
6	1c	$Pd(OAc)_2$	L1	$5 h^d$	_
7	1d	$Pd(OAc)_2$	L1	$12 h^d$	_
8	1a	$Pd(OAc)_2$	None	<2 h	0:83:17 <sup>h</sup>
9	1a	$Pd(OAc)_2$	$PPh_3^b$	12 h <sup>e</sup>	—

<sup>*a*</sup> Reaction conditions: 5–10 mol% [Pd]/L; 10 mg (17.7 μmol) of **1a**. <sup>*b*</sup> 3.1 equivalents of PPh<sub>3</sub> *vs*. **1a** were added. <sup>*c*</sup> Incomplete conversion to coupled product was indicated by TLC; after the indicated period of time, the reactions was analyzed by GC-MS which thermally converts **1** to **3**. <sup>*d*</sup> Only an initial burst to coupled product was observed. <sup>*e*</sup> No conversion indicated by TLC. <sup>*f*</sup> Product ratio determined by GC-MS. <sup>*g*</sup> See ref. 19. <sup>*h*</sup> An 0:84:16 mixture (NMR ratio) of products was isolated by flash column chromatography on silica (45% yield of **3**, and a 5% yield of **4**).

phosphine ligand for Pd a small amount of **4** was also observed, pointing to two ligand sources for the aryl group.

In the case of the non-phosphine NHC complexes (IPr-NHC)AuAr (1c) and (IMes-NHC)AuAr (1d) (Ar = 3,5-Xyl) only an initial burst of homo-coupling was observed, with neither reaction progressing beyond this point (Table 2, entries 6 and 7). This experiment suggests that either the PAr<sub>3</sub> ligand is necessary to facilitate the reaction or that NHC ligands sufficiently stabilize the Au(1) state to inhibit the redox process. In the absence of added phosphine ligand Pd(OAc)<sub>2</sub> fully converted 1a within 2 h at 58 °C (Table 2, entry 8). Conversely, 3.1 equivalents of PPh<sub>3</sub> completely inhibit the conversion to 3 (Table 2, entry 9), supporting the notion that stabilizing Au(1) either through NHC's or excess phosphine can inhibit the redox reaction.<sup>22</sup>

We also attempted to elucidate whether the reaction was homogenous or heterogeneous with a Hg drop test.<sup>23</sup> Unfortunately, this led to an instant decomposition of **1a** as previously observed by Grandberg while studying the redox potential of gold complexes on Hg electrodes (eqn (2)).<sup>24</sup>

$$2RAuPPh_3 + Hg(0) \rightarrow R_2Hg + 2Au(0) + 2PPh_3 \quad (2)$$



Fig. 2 Various ligands utilized in attempted cross-coupling.

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The catalytic coupling of two nucleophiles requires an oxidant. Based on the Grandberg redox precedent, the observed gold mirror, and the experimental results we propose that reduction of Au(1) to Au(0) accounts for the necessary redox equivalents. As outlined in step *a* of Scheme 2, two equivalents of Au(1) are consumed to regenerate Pd(1) with the Au(0) eventually forming the gold mirror.<sup>25</sup> Since the Hg drop experiment failed, the role of Pd and/or Au nanoparticles cannot be eliminated from consideration.



Scheme 2 Proposed mechanism for the homo-coupling of 1a.

In conclusion, a Pd-catalyzed homo-coupling of arylgold(I)complexes has been observed. While of limited applicability in synthesis, these results have illuminated a point of incompatibility between these two metals and suggested strategies for overcoming these shortcomings. Since Au-mirrors are relatively common occurrences in gold-catalyzed reactions, these results demonstrate how two elements with orthogonal reactivity profiles can be redox incompatible and thus impede the development of dual Au(I)/Pd(0) catalysts.

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