

## C–C Coupling Reactivity of an Alkylgold(III) Fluoride Complex with Arylboronic Acids

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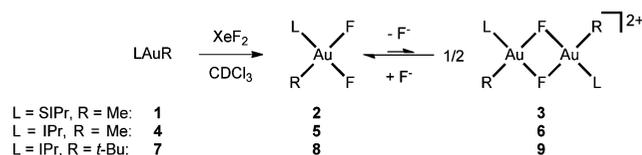
**Abstract:** Previously, alkylgold(III) fluorides have been proposed as catalytic intermediates that undergo C–C coupling with reagents such as arylboronic acids in Au(I)/Au(III) cross-coupling reactions. Here is reported the first experimental evidence for this elementary mechanistic step. Complexes of the type (NHC)AuMe (NHC = N-heterocyclic carbene) were oxidized with XeF<sub>2</sub> to yield *cis*-(NHC)AuMeF<sub>2</sub> products, which were found to be in equilibrium with their fluoride-dissociated, dimeric [(NHC)AuMe( $\mu$ -F)]<sub>2</sub>[F]<sub>2</sub> forms. In one case, a monomeric *cis*-(NHC)AuMeF<sub>2</sub> complex was favored exclusively in solution, and it was found to react with a variety of ArB(OH)<sub>2</sub> reagents to yield Ar–CH<sub>3</sub> products.

Recently there has been an emerging literature of catalytic reactions exploiting Au(I)/Au(III) redox cycles to achieve cross-coupling reactivity,<sup>1,2</sup> which complements the more established role of cationic Au(I) and Au(III) catalysts as redox-neutral, carbophilic electrophiles.<sup>3</sup> Traditional cross-coupling methodologies, for example with Pd(0)/Pd(II) cycles, involve the well-established mechanistic series of C–X oxidative addition, transmetalation, and C–C reductive elimination.<sup>4</sup> On the other hand, gold(I) catalysts tend to be unreactive toward C–X oxidative addition<sup>5</sup> and instead require a sacrificial two-electron oxidant to access reactive gold(III) intermediates poised for C–C coupling.<sup>1</sup> Selectfluor, a source of electrophilic fluorine, has met with great success as a common sacrificial oxidant in these Au-catalyzed coupling reactions.<sup>1a–c</sup> Thus, it has been speculated that alkylgold(III) fluoride species are key intermediates despite the paucity of known gold fluoride complexes.<sup>6</sup> Indeed, DFT studies<sup>1a</sup> have supported this mechanistic proposal and indicated that alkylgold(III) fluoride intermediates would be competent to undergo C–C coupling with arylboronic acid reagents often employed as coupling partners.<sup>1a–c,e</sup> Here we present the first experimental corroboration for this hypothesis by reporting the synthesis of a methylgold(III) fluoride complex and its reactivity with arylboronic acids to generate C–C coupled, Ar–Me products.

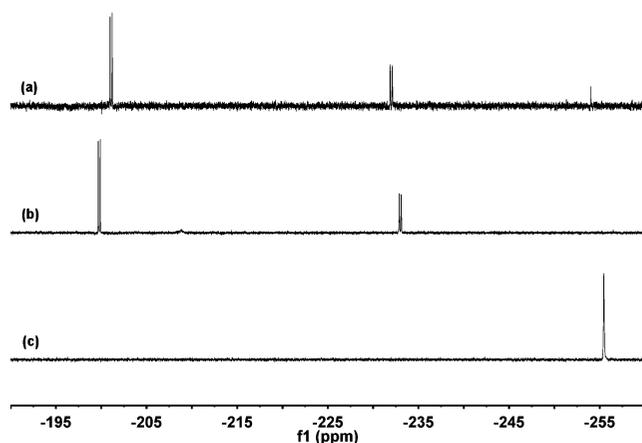
Because the only known molecular gold–fluoride complex is Sadighi's (SIPr)AuF (SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene),<sup>6,7</sup> as a starting point we sought to use SIPr as an ancillary ligand to stabilize a potential alkylgold(III) fluoride target molecule. Indeed, oxidation of (SIPr)AuMe (**1**) with XeF<sub>2</sub> in CDCl<sub>3</sub> yielded evidence for Au(III)–F bonds. The <sup>1</sup>H and <sup>19</sup>F NMR spectra of the product mixture indicated the presence of two species assigned as *cis*-(SIPr)AuMeF<sub>2</sub> (**2**) and [(SIPr)AuMe( $\mu$ -F)]<sub>2</sub>[F]<sub>2</sub> (**3**), which presumably are related by reversible fluoride dissociation (Scheme 1). Monomer **2** has characteristic peaks in the <sup>19</sup>F NMR spectrum at  $\delta$  –201 (d, <sup>2</sup>J<sub>FF</sub> = 84.9 Hz) and  $\delta$  –232 (dq, <sup>2</sup>J<sub>FF</sub> = 85.1 and <sup>3</sup>J<sub>HF</sub> = 8.6 Hz), consistent with a *cis* geometry, while the bridging fluoride ligands in dimer **3** display a singlet resonance at  $\delta$  –253 (Figure 1a). Diffusion of pentane vapors into a CDCl<sub>3</sub>

solution of a **2/3** mixture resulted in crystals of **3** as judged by X-ray diffraction (Figure 2). Attempts to isolate **2** by fractional crystallization led only to **3**; apparently **3** crystallizes preferentially due to its lower solubility and crystallographically imposed inversion symmetry. The Au–F bond distance *trans* to the SIPr ligand in **3** (2.034(3) Å) is slightly longer than that in (SIPr)AuF (2.021(17) Å)<sup>6</sup> and significantly shorter than the Au–F bond distance *trans* to the methyl ligand in **3** (2.124(3) Å). The Au⋯Au distance in **3** of 3.1789(6) Å is relatively short and could be indicative of significant d<sup>8</sup>–d<sup>8</sup> interaction<sup>8</sup> but also simply could be a result of the small fluoride bridging ligands.<sup>9</sup> Reversible formation of Au<sub>2</sub>( $\mu$ -F)<sub>2</sub> cores such as that in **3** could contribute to catalyst stability and therefore might account for the superior performance of dinuclear Au compounds in cross-coupling catalysis.<sup>1a,b</sup>

### Scheme 1. Synthesis of Alkylgold(III) Fluoride Complexes

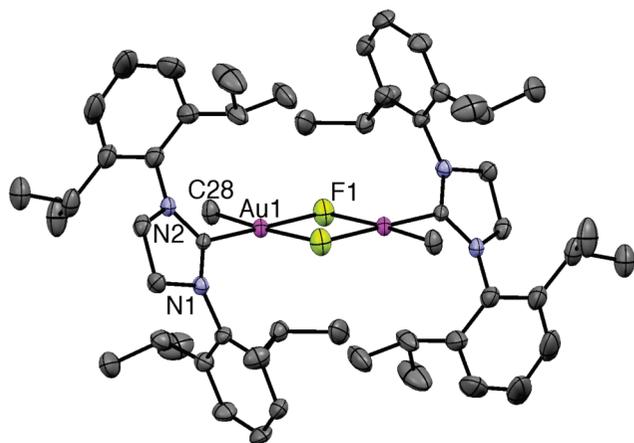


Measurement of  $K_{eq}$  for the **2/3** equilibrium over the temperature range 295–320 K allowed for approximation of the thermodynamic parameters  $\Delta H = -13$  kJ/mol and  $\Delta S = -56$  J/mol·K for the dimerization process. We thus determined that a relatively minor perturbation to this near-thermoneutral equilibrium could allow a monomeric Au(III) difluoride species to be favored exclusively by slight modification of the ancillary ligand. Accordingly, we found that oxidation of (IPr)AuMe (**4**, IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) with XeF<sub>2</sub> in CDCl<sub>3</sub> yielded the spectroscopically pure monomer species *cis*-(IPr)AuMeF<sub>2</sub> (**5**), which



**Figure 1.** Au–F region of the <sup>19</sup>F NMR spectra of (a) a mixture of **2** and **3**, (b) **5**, and (c) **9** in CDCl<sub>3</sub> solution at room temperature.

exhibits characteristic  $^{19}\text{F}$  NMR features at  $\delta -200$  (d,  $^2J_{\text{FF}} = 81.3$  Hz) and  $\delta -233$  (dq,  $^2J_{\text{FF}} = 81.3$  and  $^3J_{\text{HF}} = 8.6$  Hz). Only **5** was observed in typical NMR experiments (Figure 1b); no evidence for dimeric  $[(\text{IPr})\text{AuMe}(\mu\text{-F})_2][\text{F}]_2$  (**6**) was found by NMR spectroscopy except at near-saturation concentrations. Nonetheless, slow diffusion of pentane vapors into  $\text{CDCl}_3$  solutions of **5** yielded only X-ray quality crystals of **6**. The solid-state structure of **6**, which also possesses crystallographically imposed inversion symmetry, is very similar to that of **3** and has been placed in the Supporting Information.



**Figure 2.** Solid-state structure of dicationic **3** (50% probability ellipsoids). Hydrogen atoms and cocrystallized anions and solvent molecules have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Au(I)–C(1), 1.968(4) Å; Au(1)–C(28), 2.029(4); Au(1)–F(1), 2.034(3); Au(1)–F(1#), 2.124(3); Au(1)–Au(1#), 3.1789(6); Au(1)–F(1)–Au(1#), 99.69(12).

The ability to observe pure solutions of **5** is significant not only because the complexes reported here are the first examples of Au(III) fluorides<sup>7</sup> but also because simple monoalkyl complexes of Au(III) are very rare<sup>10,11</sup> despite the efforts of many researchers to synthesize them.<sup>12</sup> Bercaw and co-workers have observed closely related complexes  $(\text{IPr})\text{AuMeX}_2$  ( $X = \text{Cl}, \text{Br}, \text{and I}$ ), which at ambient conditions are unstable toward  $\text{Me-X}$  elimination.<sup>10a</sup> The higher barrier for  $\text{C-F}$  elimination relative to other types of  $\text{C-X}$  elimination is therefore critical to the stability of **5** and might contribute to why fluorine-containing oxidants have proven to be so successful in Au(I)/Au(III) catalysis.<sup>1a–e,13</sup>

Complex **5** is closely related to complexes of the type  $\text{LAu}(\text{R})(\text{F})(\text{X})$  ( $X = \text{Cl}$  or  $\text{Br}$ ) that are proposed as the key intermediates that undergo  $\text{C-C}$  coupling in various Au(I)/Au(III) catalytic cycles.<sup>1a–e</sup> Therefore, it was of fundamental interest to examine the  $\text{C-C}$  coupling reactivity of **5** with weak nucleophiles such as arylboronic acids that are often used in Au-mediated cross-coupling reactions.<sup>1a–c,e</sup> We were pleased to observe that addition of excess  $\text{PhB}(\text{OH})_2$  to  $\text{CDCl}_3$  solutions of **5** at room temperature led to rapid formation of toluene, albeit in modest 45% yield (Table 1, entry 1).<sup>14</sup> The Au-containing product in this reaction was  $(\text{IPr})\text{AuPh}$ ,<sup>15</sup> which presumably formed from reaction between  $\text{PhB}(\text{OH})_2$  and the initial elimination product  $(\text{IPr})\text{AuF}$ , which was not observed directly.<sup>16</sup> The remainder of the mass balance was comprised of trace amounts of biphenyl, benzene, and a significant amount of insoluble material that was not characterized. It is possible that these side reactions stem from arylboronic acid oxidation: accordingly, yields of  $\text{Ar-CH}_3$  were lower for more electron-rich boronic acids (Table 1, entries 2–3) and slightly higher for electron-deficient boronic acids (Table 1, entries 5–7). Following the procedure of Bercaw and co-workers,<sup>10a</sup> we generated  $(\text{IPr})\text{AuMeI}_2$  in the presence of  $\text{PhB}(\text{OH})_2$  and observed its decay to  $(\text{IPr})\text{AuI}$  and  $\text{MeI}$

with no formation of toluene (Table 1, entry 8). Thus, the presence of Au(III)–F bonds appears to be key to unveiling  $\text{C-C}$  coupling reactivity, both by preventing unproductive  $\text{C-X}$  elimination and by activating reactivity toward arylboronic acids.

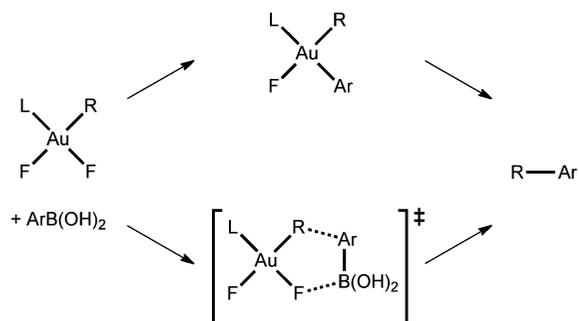
**Table 1.**  $\text{C-C}$  Coupling with Various  $\text{ArB}(\text{OH})_2$ <sup>a</sup>

		$\xrightarrow[\text{CDCl}_3]{\text{ArB}(\text{OH})_2}$			
<b>5</b>		$\text{ArCH}_3 + (\text{IPr})\text{AuAr}$			
entry	Ar	yield (%) <sup>b</sup>	entry	Ar	yield (%) <sup>b</sup>
1	$\text{C}_6\text{H}_5$	45	5	$4\text{-MeO}_2\text{CC}_6\text{H}_4$	68
2	$4\text{-MeOC}_6\text{H}_4$	25	6	$4\text{-O}_2\text{NC}_6\text{H}_4$	51
3	$4\text{-MeC}_6\text{H}_4$	28	7	$\text{C}_6\text{F}_5$	49
4	$4\text{-BrC}_6\text{H}_4$	30	8	$\text{C}_6\text{H}_5$	0 <sup>c</sup>

<sup>a</sup> 18 mM **5**, 46 mM  $\text{ArB}(\text{OH})_2$ , room temp. <sup>b</sup> Based on *in situ*  $^1\text{H}$  NMR integration against an internal standard (1,3-dinitrobenzene). <sup>c</sup> Used  $(\text{IPr})\text{AuMeI}_2$  instead of **5**.

Recently, it has been proposed that  $\text{C-C}$  coupling between alkylgold(III) fluoride complexes and arylboronic acids proceeds not by a traditional transmetalation/reductive elimination sequence, but rather by a concerted process wherein  $\text{C-C}$  and  $\text{B-F}$  bonds form simultaneously (Scheme 2).<sup>1a,b</sup> In light of this intriguing proposal involving direct attack of the arylboronic acid on the  $\text{C}(\text{sp}^3)$  center rather than on the Au center in alkylgold(III) fluorides, we have begun to examine the mechanism of  $\text{C-C}$  coupling with the isolable alkylgold(III) fluoride compounds reported here.

**Scheme 2.** Two Possible  $\text{C-C}$  Coupling Pathways



First, we sought to examine the effect of electronics on the  $\text{C-C}$  coupling reaction by conducting competition experiments in which complex **5** was allowed to react with 1:1 mixtures of  $\text{PhB}(\text{OH})_2$  and  $p\text{-RC}_6\text{H}_4\text{B}(\text{OH})_2$ . Interestingly, there was relatively little electronic bias in the resulting  $\text{PhCH}_3/p\text{-RC}_6\text{H}_4\text{CH}_3$  ratios (1.0 and 0.72 for  $\text{R} = \text{Br}$  and  $\text{CO}_2\text{Me}$ , respectively). This observation is possibly consistent with the proposed concerted bimolecular elimination mechanism. Such a pathway is conceptually related to concerted  $\sigma$ -bond metathesis reactions of  $d^0$  metal–alkyl complexes with arenes, whose rates also are relatively insensitive to the electronics of the arene substrates.<sup>17</sup> By contrast, mechanisms in which either transmetalation or reductive elimination is rate limiting might be expected to exhibit significant sensitivity to the electronics of the transferring aryl group.<sup>18</sup>

Second, we sought to examine the effect of sterics on the  $\text{C-C}$  coupling reaction by examining a tertiary rather than primary  $\text{C}(\text{sp}^3)$  center. Oxidation of  $(\text{IPr})\text{Au}(t\text{-Bu})$  (**7**) with  $\text{XeF}_2$  provided the dimeric complex  $[(\text{IPr})\text{Au}(t\text{-Bu})(\mu\text{-F})_2][\text{F}]_2$  (**9**), with no evidence by NMR spectroscopy for significant population of the monomer  $(\text{IPr})\text{Au}(t\text{-Bu})\text{F}_2$  (**8**) (Figure 1c). Though **9** is much less stable than its less bulky relatives **3** and **6**, it persists for several hours in  $\text{CDCl}_3$  solution. When **9** was thus generated *in situ* and then added to

PhB(OH)<sub>2</sub>, no evidence for *tert*-butylbenzene formation was apparent prior to the thermal decomposition of **9**. Direct attack of an arylboronic acid on the C(sp<sup>3</sup>) center of an alkylgold(III) fluoride complex is expected to be attenuated at a tertiary C(sp<sup>3</sup>) center, and thus the observed lack of *t*-Bu-Ar coupling is consistent with the proposed concerted bimolecular elimination pathway. On the other hand, an alkylgold(III) aryl intermediate (i.e., L(R)(Ar)Au<sup>III</sup>X) resulting from transmetalation might be expected to undergo reductive elimination more rapidly with a bulkier R group.<sup>18,19</sup>

In conclusion, we have reported the first isolable gold(III) fluoride complexes and noted the stabilizing influence of Au<sup>III</sup><sub>2</sub>(μ-F)<sub>2</sub> moieties. The alkylgold(III) difluoride complexes reported here are closely related to speculative catalytic intermediates in Au(I)/Au(III) cross-coupling reactions, and we have shown that they are indeed competent at performing C–C coupling with arylboronic acids, reactivity that appears to be unique to gold(III) fluorides among the halide series. Further experiments aimed at elucidating the intimate mechanism of C–C coupling are currently underway in our laboratory.

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**Supporting Information Available:** Synthetic and crystallographic details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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