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

Neal P. Mankad and F. Dean Toste*

Department of Chemistry, University of California, Berkeley, California 94720

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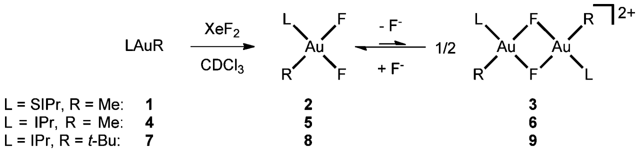
Abstract: Previously, alkylgold(III) fluorides have been proposed as catalytic intermediates that undergo C−C coupling with reagents such as arylboronic acids in Au(I)/Au(III) cross-coupling reactions. Here is reported the first experimental evidence for this elementary mechanistic step. Complexes of the type (NHC)AuMe (NHC = N-heterocyclic carbene) were oxidized with XeF_2 to yield *cis*-(NHC)AuMeF_2 products, which were found to be in equilibrium with their fluoride-dissociated, dimeric [(NHC)AuMe(μ-F)]$_2$[F]$_2$ forms. In one case, a monomeric *cis*-(NHC)AuMeF_2 complex was favored exclusively in solution, and it was found to react with a variety of ArB(OH)$_2$ reagents to yield Ar−CH_3 products.

Recently there has been an emerging literature of catalytic reactions exploiting Au(I)/Au(III) redox cycles to achieve cross-coupling reactivity,[1,2] which complements the more established role of cationic Au(I) and Au(III) catalysts as redox-neutral, carbophilic electrophiles.[3] 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.[4] On the other hand, gold(I) catalysts tend to be unreactive toward C−X oxidative addition[5] and instead require a sacrificial two-electron oxidant to access reactive gold(III) intermediates poised for C−C coupling.[1] Selectfluor, a source of electrophilic fluorine, has met with great success as a common sacrificial oxidant in these Au-catalyzed coupling reactions.[1a−e] Thus, it has been speculated that alkylgold(III) fluoride species are key intermediates despite the paucity of known gold fluoride complexes.[6] Indeed, DFT studies[1a] 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.[1a−c,e] 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)imidazolin-2-ylidene),[6,7] 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_2 in $CDCl_3$ yielded evidence for Au(III)−F bonds. The ^1H and ^{19}F NMR spectra of the product mixture indicated the presence of two species assigned as *cis*-(SIPr)AuMeF_2 (**2**) and [(SIPr)AuMe(μ-F)]$_2$[F]$_2$ (**3**), which presumably are related by reversible fluoride dissociation (Scheme 1). Monomer **2** has characteristic peaks in the ^{19}F NMR spectrum at δ −201 (d, $^2J_{FF} = 84.9$ Hz) and δ −232 (dq, $^2J_{FF} = 85.1$ and $^3J_{HF} = 8.6$ Hz), consistent with a *cis* geometry, while the bridging fluoride ligands in dimer **3** display a singlet resonance at δ −253 (Figure 1a). Diffusion of pentane vapors into a $CDCl_3$ 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)[6] 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^8−d^8 interaction[8] but also simply could be a result of the small fluoride bridging ligands.[9] Reversible formation of $Au_2(\mu\text{-}F)_2$ 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.[1a,b]

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_2 in $CDCl_3$ yielded the spectroscopically pure monomer species *cis*-(IPr)AuMeF_2 (**5**), which

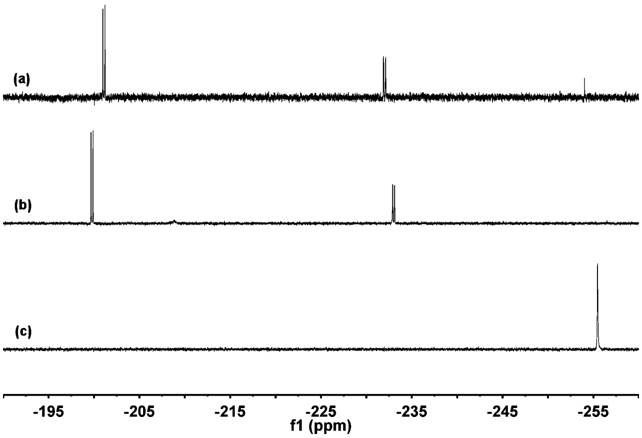


Figure 1. Au−F region of the ^{19}F NMR spectra of (a) a mixture of **2** and **3**, (b) **5**, and (c) **9** in $CDCl_3$ solution at room temperature.

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exhibits characteristic ^{19}F NMR features at δ −200 (d, $^2J_{FF} = 81.3$ Hz) and δ −233 (dq, $^2J_{FF} = 81.3$ and $^3J_{HF} = 8.6$ Hz). Only **5** was observed in typical NMR experiments (Figure 1b); no evidence for dimeric $[(IPr)AuMe(\mu\text{-}F)]_2[F]_2$ (**6**) was found by NMR spectroscopy except at near-saturation concentrations. Nonetheless, slow diffusion of pentane vapors into $CDCl_3$ 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.

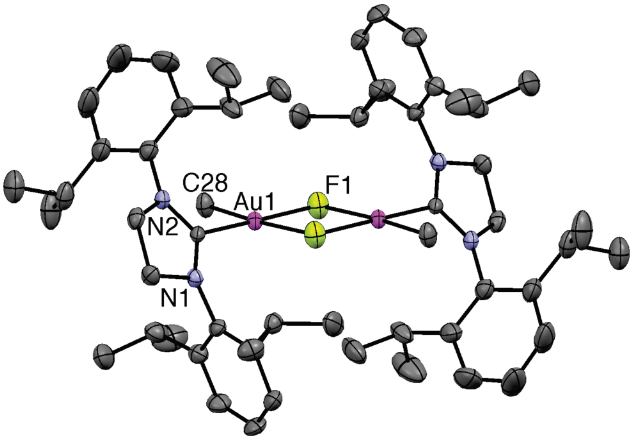


Figure 2. Solid-state structure of dicationic **3** (50% probability ellipsoids). Hydrogen atoms and cocrystallized anions and solvent molecules have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Au(1)−C(1), 1.968(4) Å; Au(1)−C(28), 2.029(4); Au(1)−F(1), 2.034(3); Au(1)−F(1#), 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[7] but also because simple monoalkyl complexes of Au(III) are very rare[10,11] despite the efforts of many researchers to synthesize them.[12] Bercaw and co-workers have observed closely related complexes $(IPr)AuMeX_2$ (X = Cl, Br, and I), which at ambient conditions are unstable toward Me−X elimination.[10a] The higher barrier for C−F elimination relative to other types of 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.[1a−e,13]

Complex **5** is closely related to complexes of the type LAu(R)(F)(X) (X = Cl or Br) that are proposed as the key intermediates that undergo C−C coupling in various Au(I)/Au(III) catalytic cycles.[1a−e] Therefore, it was of fundamental interest to examine the C−C coupling reactivity of **5** with weak nucleophiles such as arylboronic acids that are often used in Au-mediated cross-coupling reactions.[1a−c,e] We were pleased to observe that addition of excess $PhB(OH)_2$ to $CDCl_3$ solutions of **5** at room temperature led to rapid formation of toluene, albeit in modest 45% yield (Table 1, entry 1).[14] The Au-containing product in this reaction was (IPr)AuPh,[15] which presumably formed from reaction between $PhB(OH)_2$ and the initial elimination product (IPr)AuF, which was not observed directly.[16] 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 $Ar-CH_3$ 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,[10a] we generated $(IPr)AuMeI_2$ in the presence of $PhB(OH)_2$ and observed its decay to (IPr)AuI and MeI with no formation of toluene (Table 1, entry 8). Thus, the presence of Au(III)−F bonds appears to be key to unveiling C−C coupling reactivity, both by preventing unproductive C−X elimination and by activating reactivity toward arylboronic acids.

Table 1. C−C Coupling with Various $ArB(OH)_2$[a]

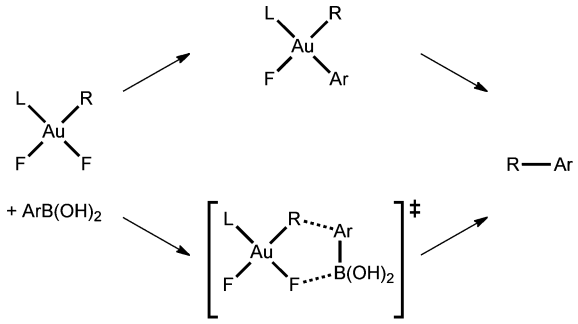
$$\mathbf{5} \xrightarrow[CDCl_3]{ArB(OH)_2} ArCH_3 + (IPr)AuAr$$

entry	Ar	yield (%)[b]	entry	Ar	yield (%)[b]
1	C_6H_5	45	5	$4\text{-}MeO_2CC_6H_4$	68
2	$4\text{-}MeOC_6H_4$	25	6	$4\text{-}O_2NC_6H_4$	51
3	$4\text{-}MeC_6H_4$	28	7	C_6F_5	49
4	$4\text{-}BrC_6H_4$	30	8	C_6H_5	0[c]

[a] 18 mM **5**, 46 mM $ArB(OH)_2$, room temp. [b] Based on *in situ* ^1H NMR integration against an internal standard (1,3-dinitrobenzene). [c] Used $(IPr)AuMeI_2$ instead of **5**.

Recently, it has been proposed that 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 C−C and B−F bonds form simultaneously (Scheme 2).[1a,b] In light of this intriguing proposal involving direct attack of the arylboronic acid on the C(sp^3) center rather than on the Au center in alkylgold(III) fluorides, we have begun to examine the mechanism of C−C coupling with the isolable alkylgold(III) fluoride compounds reported here.

Scheme 2. Two Possible C−C Coupling Pathways



First, we sought to examine the effect of electronics on the C−C coupling reaction by conducting competition experiments in which complex **5** was allowed to react with 1:1 mixtures of $PhB(OH)_2$ and $p\text{-}RC_6H_4B(OH)_2$. Interestingly, there was relatively little electronic bias in the resulting $PhCH_3/p\text{-}RC_6H_4CH_3$ ratios (1.0 and 0.72 for R = Br and CO_2Me, respectively). This observation is possibly consistent with the proposed concerted bimolecular elimination mechanism. Such a pathway is conceptually related to concerted σ-bond metathesis reactions of d^0 metal−alkyl complexes with arenes, whose rates also are relatively insensitive to the electronics of the arene substrates.[17] 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.[18]

Second, we sought to examine the effect of sterics on the C−C coupling reaction by examining a tertiary rather than primary C(sp^3) center. Oxidation of (IPr)Au(*t*-Bu) (**7**) with XeF_2 provided the dimeric complex $[(IPr)Au(t\text{-}Bu)(\mu\text{-}F)]_2[F]_2$ (**9**), with no evidence by NMR spectroscopy for significant population of the monomer $(IPr)Au(t\text{-}Bu)F_2$ (**8**) (Figure 1c). Though **9** is much less stable than its less bulky relatives **3** and **6**, it persists for several hours in $CDCl_3$ solution. When **9** was thus generated *in situ* and then added to

$PhB(OH)_2$, no evidence for *tert*-butylbenzene formation was apparent prior to the thermal decomposition of **9**. Direct attack of an arylboronic acid on the $C(sp^3)$ center of an alkylgold(III) fluoride complex is expected to be attenuated at a tertiary $C(sp^3)$ 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., $L(R)(Ar)Au^{III}X$) resulting from transmetalation might be expected to undergo reductive elimination more rapidly with a bulkier R group.[18,19]

In conclusion, we have reported the first isolable gold(III) fluoride complexes and noted the stabilizing influence of $Au^{III}_2(\mu\text{-}F)_2$ 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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