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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 XeF₂ to yield *cis*-(NHC)AuMeF₂ 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)AuMeF₂ complex was favored exclusively in solution, and it was found to react with a variety of ArB(OH)₂ reagents to yield Ar-CH₃ 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 towards C-X oxidative addition⁵ 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 XeF₂ in CDCl₃ yielded evidence for Au(III)-F bonds. The ¹H and ¹⁹F NMR spectra of the product mixture indicated the presence of two species assigned as *cis*-(SIPr)AuMeF₂ (**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 ¹⁹F 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

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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>.

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 d⁸-d⁸ interaction,⁸ but also simply could be a result of the small fluoride bridging ligands.⁹ Reversible formation of $\text{Au}_2(\mu\text{-F})_2$ 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}

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)AuMeF₂ (**5**), which exhibits characteristic ¹⁹F NMR features at δ -200 (d, ² $J_{\text{FF}} = 81.3$ Hz) and δ -233 (dq, ² $J_{\text{FF}} = 81.3$ and ³ $J_{\text{HF}} = 8.6$ Hz). Only **5** was observed in typical NMR experiments (Figure 1b); no evidence for dimeric [(IPr)AuMe(μ -F)]₂F₂ (**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 Supporting Information.

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 coworkers have observed closely related complexes (IPr)AuMeX₂ (X = Cl, Br, and I), which at ambient conditions are unstable towards 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 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 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-CH₃ 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 coworkers,^{10a} we generated (IPr)AuMeI₂ 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 appear to be key to unveiling C-C coupling reactivity, both by preventing unproductive C-X elimination and by activating reactivity towards arylboronic acids.

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). In light of this intriguing proposal involving direct attack of the arylboronic acid on the C(sp³) 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.^{1a-b}

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*-RC₆H₄B(OH)₂. Interestingly, there was relatively little electronic bias in the resulting PhCH₃/*p*-RC₆H₄CH₃ ratios (1.0 and 0.72 for R = Br and CO₂Me, 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 d⁰ 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 are rate limiting might be expected to exhibit significant sensitivity to 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(sp³) center. Oxidation of (IPr)Au(*t*-Bu) (**7**) with XeF₂ provided the dimeric complex [(IPr)Au(*t*-Bu)(μ -F)]₂[F]₂ (**9**), with no evidence by NMR spectroscopy for significant population of the monomer (IPr)Au(*t*-Bu)F₂ (**8**) (Figure 1c). Though **9** is much less stable than its less bulky relatives **3** and **6**, it persists for several hours in CDCl₃ 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(sp³) center of an alkylgold(III) fluoride complex is expected to be attenuated at a tertiary C(sp³) 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(μ -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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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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.

Figure 2.

Solid-state structure of dicationic **3** (50% probability ellipsoids). Hydrogen atoms and co-crystallized anions and solvent molecules have been omitted for clarity. Selected bond lengths (Å) and angles (°): 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).

Scheme 1.
Synthesis of alkylgold(III) fluoride complexes

Scheme 2.
Two possible C-C coupling pathways

Table 1

C-C Coupling with Various ArB(OH)₂^a

entry	Ar	yield (%) ^b	entry	Ar	yield (%) ^b
1	C ₆ H ₅	45	5	4-MeO ₂ CC ₆ H ₄	68
2	4-MeOC ₆ H ₄	25	6	4-O ₂ NC ₆ H ₄	51
3	4-MeC ₆ H ₄	28	7	C ₆ F ₅	49
4	4-BrC ₆ H ₄	30	8	C ₆ H 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)AuMeI₂ instead of **5**.