Lawrence Berkeley National Laboratory
Recent Work

Title
Halide-Dependent Mechanisms of Reductive Elimination from Gold(III).

Permalink
https://escholarship.org/uc/item/1849f92n

Journal
Journal of the American Chemical Society, 137(24)

Authors
Winston, Matthew
Wolf, William
TOSTE, F. Dean

Publication Date
2015-06-24

DOI
10.1021/jacs.5b04613

Peer reviewed
Halide-Dependent Mechanisms of Reductive Elimination from Gold(III)

Matthew S. Winston, William J. Wolf, and F. Dean Toste*

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

Supporting Information

ABSTRACT: Two unique organometallic halide series (Ph₃P)Au(4-Me-C₆H₄)(CF₃)(X) and (Cy₃P)Au(4-F-C₆H₄)(CF₃)(X) (X = I, Br, Cl, F) have been synthesized. The PPh₃-supported complexes can undergo both Caryl−X and Caryl−CF₃ reductive elimination. Mechanistic studies of thermolysis at 122 °C reveal a dramatic reactivity and kinetic selectivity dependence on halide ligand. For X = I or F, zero-order kinetic behavior is observed, while for X = Cl or Br, kinetic studies implicate product catalysis. The selectivity for Caryl−CF₃ bond formation increases in the order X = I < Br < Cl < F, with exclusively Caryl−I bond formation when X = I, and exclusively Caryl−CF₃ bond formation when X = F. Thermodynamic measurements show that Au(III)−X bond dissociation energies increase in the order X = I < Br < Cl, and that ground state Au(III)−X bond strength ultimately dictates selectivities for Caryl−X and Caryl−CF₃ reductive elimination.

INTRODUCTION

Transition metal-catalyzed transformations proceed through a series of fundamental steps, i.e., oxidative addition, migratory insertion, and reductive elimination. To minimize deleterious side reactions and maximize overall catalyst efficiency, the metal must undergo the proper series of reactions with excellent selectivity. A fundamental understanding of the factors that affect the selectivity of these elementary steps is critical in designing and improving new metal-catalyzed transformations.

We have recently shown that complexes of the type (Ph₃P)Au(aryl) (aryl = 4-F-C₆H₄, 4-Me-C₆H₄) undergo a photochemical oxidative addition to Ar(I) to give the air- and moisture-stable Au(III) complexes (Ph₃P)Au(CF₃)(aryl)(I). These complexes undergo rapid Caryl−CF₃ reductive elimination when treated with AgSbF₆ (Scheme 1).

Scheme 1. Divergent Reductive Elimination Behavior of Au(III) Complexes

Caryl−X reductive elimination is not necessarily productive, and may be a decomposition pathway for high-valent organometallic species with halide ligands. Importantly, Au(III) catalysts, which are often generated using dihalogen (or formal dihalogen) oxidants and stabilized by halide ligands, could undergo deleterious, irreversible Caryl−X bond formation to deplete active catalyst concentrations. With access to a full family of Au(III) halides, trends in the rates of Caryl−X reductive elimination from Au(III), and C(sp²)−F⁰ and C(sp³)−F³ eliminations from Au(III) have also been demonstrated. Caryl−X reductive elimination is not necessarily productive, and may be a decomposition pathway for high-valent organometallic species with halide ligands. Importantly, Au(III) catalysts, which are often generated using dihalogen (or formal dihalogen) oxidants and stabilized by halide ligands, could undergo deleterious, irreversible Caryl−X bond formation to deplete active catalyst concentrations. With access to a full family of Au(III) halides, trends in the rates of Caryl−X reductive elimination from Au(III) could be established. Perhaps slower Caryl−X bond formation could also be exploited to promote selectivity for otherwise challenging reductive eliminations, such as Caryl−CF₃ bond formation in complexes of the type (R₃P)Au(aryl)(CF₃)(X).

Received: May 3, 2015
Published: June 11, 2015

DOI: 10.1021/jacs.5b04613
J. Am. Chem. Soc. 2015, 137, 7921−7928
reductive eliminations should inform factors dictating selectivity in catalytic cycles.4c,k

Herein, we report the synthesis and characterization of a series of well-defined complexes of the type \((R,P)Au(aryl)-(CF_3)(X)\) (X = I, Br, Cl, F) that undergo both Caryl−X and Caryl−CF_3 reductive elimination with different, halide-dependent kinetic ratios. These ratios vary systematically among the halide series, showing that halide ligands, often considered spectators, can dramatically influence reaction behavior.

### RESULTS AND DISCUSSION

Sonicating 1-I or 2-I with excess \(AgX\) (X = Br, Cl, F) afforded metathesis products 1-X and 2-X (X = Br, Cl, F) in high yield (Scheme 2). Interestingly, 1-F represents a rare example of an isolable, terminal organometallic Au(III) fluoride (Figure 1).

All complexes within the 1-X halide series underwent thermolysis to products of Caryl−X and Caryl−CF_3 reductive elimination, and (when X = F) solvent activation. All reactions were followed by \(^{19}F\) NMR at 122 °C in toluene-\(d_8\) \(([1-X]=14.0−16.0 \text{ mM})\). All values were quantified relative to 1-trifluoromethylnaphthalene \((^{19}F \delta: -59 \text{ ppm})\) as an internal standard. Due to irreversible formation of a new Au(III) species upon treatment with \([Bu_4N][X]\) (presumably the aurates \([Bu_4N][Au(aryl)(CF_3)(X)]\) \((^{19}F\) NMR singlet at \(\delta = -21\) to \(-25 \text{ ppm})\), the kinetic order of halide anions could not be determined. Reactions run in the significantly more polar \(PhNO_2\) were only slightly affected (see Supporting Information), providing evidence against an ionic mechanism involving tight or dissociated ion pairs.

#### Thermolysis of Au(III)−Iodide 1-I

As previously reported, complex 1-I underwent thermolysis at 122 °C to exclusively generate \(Ph_3PAuCF_3\) and 4-Me-C_6H_4−I (\(t_{1/2} = 2.5 \text{ min})\). Consumption of 1-I followed unusual zero-order kinetics over a range of concentrations \((k_{obs} = 4.5 \times 10^{-5} \text{ M}^{-1} \text{s}^{-1})\) from 6 to 35 mM [1-I], Figure 2 and Supporting Information Figure S1). When 0.005 equiv PPh_3 (70 \(\mu\)M) was added, the rate slowed substantially \((t_{1/2} = 28 \text{ min})\), and the reaction exhibited first-order behavior in 1-I \((k_{obs} = 4.1 \times 10^{-5} \text{ s}^{-1})\). The observed rate constant \((k_{obs})\) is inverse first-order in PPh_3, implicating PPh_3 predissociation from 1-I and reductive elimination from a short-lived three-coordinate Au(III) complex 3-I under these conditions (Scheme 3). Consistent with this sequence, PCy_3-supported 2-I did not react at 122 °C over 2 days, presumably due to the increased donor strength of the trialkylphosphine.

The zero-order kinetics in the absence of PPh_3 suggest reversible reaction inhibition by starting material. If reductive elimination proceeds through the coordinatively unsaturated 3-I, a reasonable origin of this unusual behavior is trapping by 1-I to \(\mu\)-iodo bimetallic adduct 4-I (Scheme 3). Indeed, \(\mu\)-halide bridges between Au(III) atoms form readily to avoid coordinative unsaturation at the metal; in addition, bimetallic complexes such as \([AuCl_2]\_2, [Me_2AuI]\_2, [(F_3C)AuX]_2\) (X = I, Br), and \(([SIPr)(Me)F]_2\) 2+ (SIPr = 1,3-bis(2′,6′-
Disproportionately, the recombination of PPh3 and

\[ \text{+} \]

added, the rate law simplifies to

\[ k \text{obs} = (0.0013 \, s^{-1}) \left[ \text{Ph}_3\text{PAuCF}_3 \right] + (0.0013 \, M \, s^{-1}) \], \( R^2 = 0.989 \)

Figure 3. (A) Time course for thermolysis of Au(III)–bromide 1-Br in the presence of 9.1–29.9 equiv of Ph3PAuCF3. (B) Direct relationship between \( k_{\text{obs}} \) and \( [\text{Ph}_3\text{PAuCF}_3] \) indicating first-order behavior of Ph3PAuCF3 in the thermolysis of 1-Br.

Figure 4. (A) Time course for thermolysis of Au(III)–chloride 1-Cl in the presence of 8.9–28.4 equiv of Ph3PAuCF3. (B) Direct relationship between \( k_{\text{obs}} \) and \( [\text{Ph}_3\text{PAuCF}_3] \) indicating first-order behavior of Ph3PAuCF3 in the thermolysis of 1-Cl.

disproportionately, the recombination of PPh3 and electronic diversity that can complement \( \mu \)-halide interactions.\(^{10}\)

Treating 3-I as a steady-state intermediate, a complex rate law consistent with experimental observations can be derived (eq 1, see Supporting Information for derivation).

\[
\frac{d[1-1]}{dt} = \frac{k_{C_{-1}} (k_1[1-1] + k_{-1}[4-1])}{k_{-1}[\text{PPh}_3] + k_{1}[1-1] + k_{C_{-1}}}
\] (1)

Since \([4-1] \approx 0\) is valid. If the formation of \([4-1]\) is significantly faster than the recombination of PPh3 and 3-I, then \(k_{C_{-1}} \gg k_{-1}[\text{PPh}_3] + k_{1}[1-1]\) and eq 1 simplifies to the zero-order rate law 

\[
\frac{d[1-1]}{dt} = k_{C_{-1}} k_1 \left(1 \text{[1-1]} - [1-1] \right)
\] (2)

where \(k_{C_{-1}} k_1 / k_{-1} = 2.9 \times 10^{-8} \, M \, s^{-1}\). Thus, \(k_{-1} = (1600) k_1\) in accordance with our previous conclusion that \(k_{C_{-1}} \gg k_2\).

**Thermolyses of Au(III)–Bromide 1-Br and Au(III)–Chloride 1-Cl.** Qualitatively, the thermolyses of 1-Br and 1-Cl were notably slower (1/2d ~ 75 and 400 min, respectively) than 1-I, and products of both \( C_{\text{aryl}} \text{X} \) and \( C_{\text{aryl}} \text{CF}_3 \) reductive elimination were detected after full conversion ([4-Me-C\(_6\)H\(_4\)-Br]/[4-Me-C\(_6\)H\(_4\)-CF\(_3\)] = 1.3:1) for 1-Br, and [4-Me-C\(_6\)H\(_4\)-Cl]/[4-Me-C\(_6\)H\(_4\)-CF\(_3\)] = 1:4.5 for 1-Cl). To our surprise, reaction rates increased with time for both thermolyses (Figures 3A and 4A), suggestive of catalysis by products or nanoparticles.\(^{11}\) Indeed, in the presence of excess Ph3PAuCF3, the rates of these thermolyses dramatically accelerated, behaving first-order in 1-Br or 1-Cl and Ph3PAuCF3 (Figures 3B and 4B, and see Supporting Information). The addition of 0.01 equiv (0.014 mM) PPh3 dramatically slowed thermolysis of 1-Br and 1-Cl with and without excess Ph3PAuCF3, consistent with phosphine dissociation preceding reductive elimination in both the nonaccelerated and product-accelerated pathways.

Consistent with at least two processes with different product-determining steps, the ratios [4-Me-C\(_6\)H\(_4\)-X]/[4-Me-C\(_6\)H\(_4\)-CF\(_3\)] vary over time during the thermolyses of 1-Br and 1-Cl. For instance, when \( t < 20 \, \text{min} \), the accelerated pathway had not significantly contributed to consumption of 1-Br, and there was almost no kinetic preference for \( C_{\text{aryl}} \text{Br} \) or \( C_{\text{aryl}} \text{CF}_3 \) bond formation ([4-Me-C\(_6\)H\(_4\)-Br]/[4-Me-C\(_6\)H\(_4\)-CF\(_3\)] is roughly 2:1:1). However, in the presence of a large excess of Ph3PAuCF3 (140 mM), the accelerated pathway dominated even at early reaction times, and \( C_{\text{aryl}} \text{Br} \) reductive elimination was slightly favored (2.3:1, presumably the intrinsic kinetic product distribution of the accelerated pathway.) For 1-Cl, the product ratio [4-Me-C\(_6\)H\(_4\)-Cl]/[4-Me-C\(_6\)H\(_4\)-CF\(_3\)] for the nonaccelerated pathway was roughly 1:2.8, while the accelerated...
pathway heavily favored Caryl\textsubscript{aryl}−CF\textsubscript{3} reductive elimination (1:7.6).

We propose that the electron-withdrawing effect\textsuperscript{12} of the CF\textsubscript{3} ligand renders Ph\textsubscript{3}PAuCF\textsubscript{3} sufficiently Lewis acidic to coordinate the halide of 1-Br or 1-Cl in a μ-bridging fashion,\textsuperscript{13} effectively withdrawing electron density from the Au(III) center and perturbing the relative kinetic preferences for Caryl\textsubscript{aryl}−X and Caryl\textsubscript{aryl}−CF\textsubscript{3} reductive elimination from 6-X. Inhibition by PPh\textsubscript{3}, the absence of saturation behavior at high [Ph\textsubscript{3}PAuCF\textsubscript{3}], and unobserved intermediates suggest a process involving fast, reversible coordination of Ph\textsubscript{3}PAuCF\textsubscript{3} to 1-Br or 1-Cl, followed by PPh\textsubscript{3} dissociation and slow Caryl\textsubscript{aryl}−X and Caryl\textsubscript{aryl}−CF\textsubscript{3} reductive elimination (Scheme 4).

For both 1-Br and 1-Cl, kinetic details of the nonaccelerated pathway were masked by the accelerated reaction. However, the slower pathway is likely analogous to 1-I thermolysis (Scheme 3), given the reaction’s sensitivity to excess phosphine and the diversity of Au(III)-supported μ-halide bridges.\textsuperscript{11} The unambiguous first-order behavior in the presence of excess Ph\textsubscript{3}PAuCF\textsubscript{3} clearly indicates that the accelerated reaction is substantially faster than the nonaccelerated process (see Supporting Information for rate laws).

**Thermolysis of Au(III)−Fluoride 1-F.** The thermolysis of 1-F was slower (t\textsubscript{1/2} = 33 min) than that of 1-I, but significantly faster than that of 1-Br and 1-Cl. Consistent with the apparent trend of decreasing selectivity of Caryl\textsubscript{aryl}−X reductive elimination in the order X = I > Br > Cl, we observed no 4-Me-C\textsubscript{6}H\textsubscript{4}−1-F, the kinetic behavior for both thermolyses is essentially constant (~8.3 M at 122 °C in a sealed tube),\textsuperscript{16} and the ratio of products expressed as rate terms k\textsubscript{C−CF\textsubscript{3}}/(k\textsubscript{Ar}(toluene-d\textsubscript{8})) is also constant (3.6) (Scheme 5). That 3-F can activate solvent implicates an ionic Au(III)−F bond that imparts sufficient Lewis acidity for formal C−H activation by electrophilic aromatic substitution, fluoride-assisted deprotonation, or σ-bond metathesis.\textsuperscript{17}

Like 1-I, addition of 0.1 equiv PPh\textsubscript{3} (1.4 mM) slowed the reaction (t\textsubscript{1/2} = 300 min) and altered the order in 1-F from zero to first (see Supporting Information ). However, only biaryl-d\textsuperscript{7} was formed under these conditions, suggesting an alternative, slower solvent activation pathway that does not involve 3-F. Although the Au(III) center in 1-F is less electron-deficient and more sterically shielded than in 3-F due to coordinative saturation, it may still be sufficiently Lewis acidic to activate solvent (Scheme 6). Consistent with this proposal, the reaction rate was independent of [PPh\textsubscript{3}] (from 1.4 to 14 mM), and the more electron-rich, sterically encumbered 2-F did not react with toluene-d\textsubscript{8}.

A rate law consistent with the mechanism of 1-F thermolysis is shown in eq 3 where the zero-order term is significantly larger than the pseudo-first-order term in the absence of PPh\textsubscript{3}, and k\textsubscript{2}(k\textsubscript{C−CF\textsubscript{3}} + k\textsubscript{Ar}(toluene-d\textsubscript{8}))/k\textsubscript{2} = 3.9 × 10\textsuperscript{−6} M\textsuperscript{−1}s\textsuperscript{−1} (see Supporting Information for derivation).

\[
\frac{d[1-F]}{dt} = \frac{k_2}{k_2}(k_{C−CF_3} + k_{Ar}(toluene-d^8)) + k'_{Ar}(toluene-d^8)[1-F] \\
(3)
\]

These kinetic investigations reveal that selectivity for Caryl\textsubscript{aryl}−X versus Caryl\textsubscript{aryl}−CF\textsubscript{3} reductive elimination from Au(III) decreases in the order X = I > Br > Cl > F (Figure 6). While rate of Caryl−
X bond formation corresponds to halide polarizability, thermodynamic studies were necessary to determine the role of ground state effects in the reaction selectivities.

Relative Au(III)–X Bond Dissociation Enthalpies (X = I, Br, Cl). To gain insight into what extent thermodynamics govern reductive elimination selectivity, van’t Hoff analyses between 2-X and trityl halides were carried out. The halide metathesis equilibria were monitored in toluene-d8 by 19F NMR at temperatures between 25 and 78 °C. Complexes 2-I and 2-Br were treated with an excess of Ph3C–Cl (30 equiv) to ensure fast approach to equilibrium, and to hold [Ph3C–Cl] constant for determination of the equilibrium constant. The equilibrium between 2-Cl (+ Ph3C–I) and 2-I (+ Ph3C–Cl) was moderately exothermic ($\Delta H^o = -4.8$ kcal/mol) with a negligible loss of entropy ($\Delta S^o = -2.1$ e.u.) (Figure 7).

Similarly, the equilibrium between 2-Cl (+ Ph3C–Br) and 2-Br (+ Ph3C–Cl) also lies to the right ($\Delta H^o = -3.1$ kcal/mol) with a negligible entropy loss ($\Delta S^o = -1.8$ e.u.) (Figure 8).

Using the thermodynamic parameters above, and differences in Benson group increments for tertiary alkyl halide groups (see Supporting Information for derivation), we obtain the differences in heats of formation ($\Delta\Delta H^o$) of 2-Cl, 2-Br, and 2-I: $\Delta H^o(2-I) = 13$ kcal/mol greater than $\Delta H^o(2-Br)$, and $21$ kcal/mol greater than $\Delta H^o(2-Cl)$.

The differences in bond dissociation energies ($\Delta$BDE) of each Au(III)–X bond are functions of $\Delta\Delta H^o$ (2-X) and BDEs of the diatomic halogens (see Supporting Information for derivation). Although rough approximations, these values suggest that the Au(III)–I bond in 2-I is 18 kcal/mol weaker than the Au(III)–Br bond in 2-Br, and 33 kcal/mol weaker than the Au(III)–Cl bond in 2-Cl. The trend in Au(III)–X bond strengths follows Caryl-X bond strengths, with the variation in Au(III)–X BDEs only slightly greater. That the bond dissociation energies decrease in the order Au(III)–Cl > Au(III)–Br > Au(III)–I suggests that selectivities for Caryl–CF3 reductive elimination are strongly influenced by the strength of the Au(III)–X bond in the starting material (Figure 8), and that Au–X bonding must be substantially diminished in the transition state to Caryl–X reductive elimination. Halide polarizability, or softness, is correlated with nucleophilicity, and may also play a role in dictating relative rates of Caryl–X bond formation, as noted by Hartwig for Pd(II) systems.

CONCLUSIONS

We have accessed full Au(III) halide families through formal oxidative addition of CF3I to Au(I) followed by halide metathesis, and have systematically studied the thermolysis of 1-X (X = F, Cl, Br, I) and the competitive Caryl–X and Caryl–CF3 reductive eliminations from Au(III). The mechanisms and kinetic selectivities for these steps are highly dependent on the identity of the halide ligand. When X = I, thermolysis exclusively generates the products of Caryl–I bond formation. The selectivity for Caryl–CF3 reductive elimination increases in the order X = I < Br < Cl < F, and is completely selective for Caryl–CF3 bond formation when X = F (Figure 6). Thermodynamic studies reveal that the Au(III)–X bond strength increases in the order X = I < Br < Cl, a trend that mirrors selectivity for Caryl–CF3 reductive elimination. These
Halide Metathesis between 1-I or 2-I with AgX. 1-I (75 mg, 0.10 mmol) or 2-I (77 mg, 0.10 mmol) was dissolved in CHCl₃ (5 mL) in a vial. AgX (X = Br, Cl, F) (1.0 mmol) was added at once, and the reaction was capped and sonicated for 5 min in the dark, followed by a second addition of AgX (1.0 mmol) and further sonication for 5 min. When X = Br or Cl, the solid turned increasingly yellow with the formation of AgI. The suspension was filtered through a bed of Celite and concentrated in vacuo to a white powder that was recrystallized twice in 1:3 CH₂Cl₂/pentane to afford 1-Br (52 mg, 0.074 mmol), 2-Br (61 mg, 0.081 mmol), 1-Cl (51 mg, 0.078 mmol), 2-Cl (60 mg, 0.089 mmol), 1-F (45 mg, 0.071 mmol) or 2-F (55 mg, 0.083 mmol) in analytical purity as white solids.

(Ph₃P)Au(4-Me-C₆H₄)(CF₃)(Cl) (1-Br).¹¹ H NMR (CDCl₃, 500 MHz, δ): 7.54—7.49 (m, 3H), 7.46—7.35 (m, 12H), 6.77 (d, J = 8.4 Hz, 2H), 6.64 (d, J = 8.4 Hz, 2H), 2.15 (s, 3H). ¹³C H NMR (CDCl₃, 125 MHz, δ): 135.9, 134.9 (d, J = 10 Hz), 133.2 (d, J = 3 Hz), 130.7 (d, J = 3 Hz), 130.6, 129.1 (d, J = 11 Hz), 126.2, 125.7, 20.6. ipsi-¹³C signals not observed due to heteroatom coupling.¹¹F NMR (CDCl₃, 172 MHz, δ): −27.6 (d, J = 6 Hz). Anal. Calcld for C₂₅H₃₇AuClF₄P: C, 44.66; H, 3.17. Found: C, 44.94; H, 3.33.

(Ph₃P)Au(4-Me-C₆H₄)(CF₃)(Br) (2-Br).¹¹ H NMR (CDCl₃, 500 MHz, δ): 7.31—7.26 (m, 2H), 7.01—6.96 (m, 2H), 2.38—2.26 (m, 3H), 1.91—1.76 (m, 12H), 1.73—1.55 (m, 9H), 1.32—1.20 (m, 3H), 1.14—1.00 (m, 6H). ¹³C H NMR (CDCl₃, 125 MHz, δ): 161.7 (d, J = 246 Hz), 139.3—139.1 (m), 133.0 (d, J = 20 Hz), 132.2 (d, J = 25 Hz), 129.8 (d, J = 3 Hz), 27.6 (d, J = 11 Hz), 26.3 (d, J = 1 Hz), ipsi-¹³C signals not observed due to heteroatom coupling.¹¹F NMR (CDCl₃, 172 MHz, δ): 28.0 (q, J = 7 Hz, J = 6 Hz). Anal. Calcld for C₂₅H₃₇AuBrF₄P: C, 41.62; H, S.17. Found: C, 41.47; H, 5.33.

(Cy₃P)Au(4-F-C₆H₄)(CF₃)(Br) (2-Br).¹¹ H NMR (CDCl₃, 500 MHz, δ): 7.31—7.26 (m, 2H), 7.01—6.96 (m, 2H), 2.38—2.26 (m, 3H), 1.91—1.76 (m, 12H), 1.73—1.55 (m, 9H), 1.32—1.20 (m, 3H), 1.14—1.00 (m, 6H). ¹³C H NMR (CDCl₃, 125 MHz, δ): 140.0, 134.8 (d, J = 11 Hz), 132.2 (d, J = 25 Hz), 129.8 (d, J = 3 Hz), 27.6 (d, J = 11 Hz), 26.3 (d, J = 1 Hz), ipsi-¹³C signals not observed due to heteroatom coupling.¹¹F NMR (CDCl₃, 172 MHz, δ): 28.0 (q, J = 7 Hz, J = 6 Hz). Anal. Calcld for C₂₅H₃₇AuBrF₄P: C, 41.62; H, S.17. Found: C, 41.47; H, 5.33.
Kinetic Experiments. A 14–16 mM solution of I-X in toluene was prepared in an inert atmosphere glovebox. Standard (1-trihalomethyl-1-naphthalene) was added by microsyringe, and 500 μL aliquots of the solution were transferred to oven-dried NMR tubes. The tubes were capped with greased rubber septa and sealed with Tetlon tape. When appropriate, PPh₃ or Ph₃PAuF₅ were added directly to the NMR tube as a solid prior to injection of the toluene solution of I-X and standard.

The thermolyses of I-I and I-F were carried out in a Bruker DRX-500 NMR probe that was temperature calibrated using ethylene glycol and preheated to 122 °C for 30 min. The spectrometer was shimmed and tuned with a solution of standard, then the NMR tube containing the solution of interest was lowered into the probe. All other reactions were carried out at 122 °C in an oil bath shielded from light and the samples were periodically removed from the bath, cooled to room temperature, and monitored by ¹⁷F NMR.

Thermodynamic Experiments. A 14–16 mM solution of 2-X in toluene was prepared in an inert atmosphere glovebox. Standard (3,5-ditrifluoromethyl-1-bromobenzene) was added by microsyringe, and 500 μL aliquots of the solution were transferred to oven-dried NMR tubes charged with Ph₃C–Cl (63 mg, 0.23 mmol). The tubes were capped with Ph₃C–Cl (63 mg, 0.23 mmol). The tubes were capped with greased rubber septa and sealed with Tetlon tape. All experiments were heated in an NMR probe that was calibrated as described above. The equilibria were first monitored at 25 °C after 10 min at room temperature. After each increase in temperature, the probe was recalibrated, and the solution of interest was heated in the probe for 10 min. After equilibrium at maximum temperature (78 °C) was reached, the reaction was cooled to 25 °C and the equilibrium was measured.

■ ASSOCIATED CONTENT

Supporting Information
Detailed experimental characterization data, and crystallographic information ( cif). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b04613.

■ AUTHOR INFORMATION

Corresponding Author
*fdtoste@berkeley.edu

Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge Professor Robert G. Bergman, Andrew Samant, and David Kaphan for helpful discussions. This work was generously funded by the NIHGMs (RO1 GM073932), a NIH fellowship to M.S.W. (F32 GM103238-02) and an NSF fellowship to W.J.W. (DGE 1106400). X-ray crystallography was performed using the UC Berkeley College of Chemistry CheXray facility supported by the NIH Shared Instrumentation Grant S10-RR027172; we thank Guoqing Geng and the Chemistry 208 class at UC Berkeley for assistance with the X-ray structure of 1-Cl.

■ REFERENCES

(1) Winston, M. S.; Wolf, W. J.; Toste, F. D. J. Am. Chem. Soc. 2014, 136, 7777.
(2) Roy, A. H.; Hartwig, J. F. J. Am. Chem. Soc. 2003, 125, 13944.
(3) (a) Klapars, A.; Buchwald, S. L. J. Am. Chem. Soc. 2002, 124, 14844. (b) Zanon, J.; Klapars, A.; Buchwald, S. L. J. Am. Chem. Soc. 2003, 125, 2890. (c) Casitas, A.; Poater, A.; Solá, M.; Stahl, S. S.; Costas, M.; Ribas, X. Dalton Trans. 2010, 39, 10458. (d) Lin, B.-L.; Kang, P.; Stack, T. D. P. Organometallics 2010, 29, 3683. (e) For a review see: Sheppard, T. D. Org. Biomol. Chem. 2009, 7, 1043.
(4) (a) Dekleva, T. W.; Forster, D. Adv. Catal. 1986, 34, 81. (b) Goldberg, K. I.; Yan, J.; Winter, E. L. J. Am. Chem. Soc. 1994, 116, 1573. (c) Goldberg, K. I.; Yan, J.; Brittung, E. M. J. Am. Chem. Soc. 1995, 117, 6889. (d) Mattilis, P. M.; Haynes, A.; Sunley, G. J.; Howard, M. J. J. Chem. Soc., Dalton Trans. 1996, 2187. (f) Frech, C. M.; Millet, D. J. Am. Chem. Soc. 2006, 128, 12434. (f) Whitfield, S. R.; Sanford, M. S. J. Am. Chem. Soc. 2007, 129, 15142. (g) Furuya, T.; Ritter, T. J. Am. Chem. Soc. 2008, 130, 10060. (h) Racowski, J. M.; Gao, B. G.; Sanford, M. S. Angew. Chem., Int. Ed. 2012, 51, 3414.
(i) O’Reilly, M. E.; Pahls, D. R.; Cundari, T. R.; Gunnoe, T. B. Organometallics 2014, 33, 6504. (j) Rivada-Wheelaghan, O.; Roselló-Merino, M.; Diez, J.; Maya, C.; López-Serrano, J.; Conejero, S. Organometallics 2014, 33, 5944. (k) Pérez-Temprano, M. H.; Racowski, J. M.; Rampa, J. W.; Sanford, M. S. J. Am. Chem. Soc. 2014, 136, 4097. (l) Canassos, N. M.; Sanford, M. S. Science 2015, 347, 1218.
(5) For examples, see: (a) Qiu, D.; Mo, F.; Zheng, Z.; Zhang, Y.; Wang, J. J. Org. Lett. 2010, 12, 5475. (b) Nguyen, K. H.; Tomasi, S.; Le Roch, M.; Toupet, L.; Renaud, J.; Uricar, P.; Gouault, N. J. Org. Chem. 2013, 78, 7809.
(6) Mankad, N. P.; Toste, F. D. Chem. Sci. 2012, 3, 72.
(7) Scott, V. J.; Labinger, J. A.; Bercaw, J. E. Organometallics 2010, 29, 4090.
(8) See references contained in: Toste, F. D.; Mierecze, V., Eds. Gold Catalysis: An Homogeneous Approach; Imperial College Press: London, U.K., 2014.
(9) Relative solvatochromic values (Ee) are 0.099 (toluene) and 0.324 (nitrobenzene). For a review, see: Reichardt, C. Chem. Rev. 1994, 94, 2319.
(10) For examples, see: (a) Margrave, J. L.; Whitmire, K. H.; Hauge, R. H.; Noren, N. T. Inorg. Chem. 1990, 29, 3252. (b) Zharkova, G. I.; Baldina, I. A.; Igumenov, I. K. J. Struct. Chem. 2007, 48, 108.
(11) (a) Mankad, N. P.; Toste, F. D. J. Am. Chem. Soc. 2010, 132, 12859.
(11) To discount heterogeneous effects, nanoparticles isolated by heating 1-Br, 1-Cl or Ph₃PAuCF₃ at 122 °C over 3 days did not accelerate the reaction, nor did any solids (unobservable to the naked eye) centrifuged from a reaction halfway to completion. Filtration of reaction mixtures (0.2 μm PTFE filter) at 50% conversion also did not affect the reaction rates when thermolyses were resumed.
(12) The anodic peak potential of (SIPr)CuCF₃ is 0.59 V greater than the potential of (SIPr)CuCl. Likewise, the anodic peak potential of (dtbpe)Ni(CF₃)₂ is 1.17 V greater than the potential of (dtbpe)Ni(CHR)₂. See: Kielsch, I.; Dubinina, G. G.; Hamacher, C.; Kaiser, A.; Torres-Nieto, J.; Hutchison, J. M.; Klein, A.; Budnikova, Y.; Vicic, D. A. Organometallics 2010, 29, 1451.
(13) Three-coordinate AuI complexes are well-known, and may be coordinatively fluxional in solution. See: Concepción Gimeno, M.; Laguna, A. Chem. Rev. 1997, 97, 511.
(14) (a) Vicente, J.; Bermudez, M. D.; Escobedo, J.; Carrillo, M. P.; Jones, P. G. J. Chem. Soc., Dalton Trans. 1990, 3083. (b) Vicente, J.; Bermudez, M. D.; Escobedo, J. Organometallics 1991, 10, 3380.
(15) Ph,PAuF and deuterio-fluoric (DF) acid are products of C₉F₆–CF₃, reductive elimination and tol–d₇ activation, respectively. We observe several silylfluoride species by ¹³C NMR resulting from facile Ph,PAuF ionization and quenching of fluoride and DF with the borosilicate NMR tube.
(16) McMclen, M. O.; Splett, J. P. J. Res. Natl. Inst. Stand. Technol. 2008, 113, 29.
(17) The mechanism of C₉F₆–H activation is unclear. Mechanisms involving electrophilic aromatic substitution have been observed with Au(III), see: (a) Kar, A.; Mangu, N.; Kaiser, H. M.; Tse, M. K. J. Organomet. Chem. 2009, 694, 524. (b) Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. J. Am. Chem. Soc. 2014, 136, 254. However, although

7927
DOI: 10.1021/jacs.5b04613
J. Am. Chem. Soc. 2015, 137, 7921–7928
PhNO₂ is substantially less active toward electrophilic aromatic substitution, selectivity for arene activation in PhNO₂ increases by a factor of 18 (see Supporting Information). Given the greater acidity of aromatic protons of PhNO₂ relative to the deuterons of toluene-d₈, we favor a mechanism involving fluoride-assisted deprotonation. We observe no benzylic activation of toluene-d₈, suggesting that activation at the arene is kinetically preferred. Such selectivity has been observed in σ-bond metatheses at late metals, see: (c) Butschke, B.; Schwarz, H. Organometallics 2011, 30, 1588.

(18) Since [Ph₃C⁻X] = [2-Cl], the equilibrium constant expression simplifies to $K_{eq} = [2-X][Ph₃C-Cl]/[2-Cl]^2$, and can be solved from the relative intensities of ¹⁹F NMR signals for 2-Cl and 2-Br or 2-I.

(19) Domalski, E. S.; Hearing, E. D. J. Phys. Chem. Ref. Data 1993, 22, 805.

(20) CRC Handbook of Chemistry and Physics, 95th ed.; Haynes, W. M., Ed.; CRC Press: Boca Raton, FL, 2015; Section 9, pp 65–68.

(21) The qualitative trend of decreasing Au(III)–X BDEs with higher halides is in marked contrast with gas-phase diatomic Au(I)–X BDEs, which are lowest for Au(I)–Br and highest for Au(I)–Cl and Au(I)–I, see: Reuben Brown, J.; Schwerdtfeger, P.; Schröder, D.; Schwarz, H. J. Am. Soc. Mass Spectrom. 2002, 13, 485.

(22) Oishi, M.; Yamamoto, H. Bull. Chem. Soc. Jpn. 2001, 74, 1445.