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Phosphonium Formation by Facile Carbon–Phosphorus Reductive Elimination from Gold(III)

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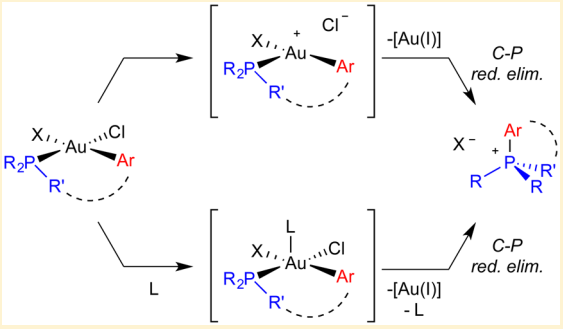
Supporting Information

ABSTRACT: A recent trend in homogeneous gold catalysis has been the development of oxidative transformations relying on Au(I)/Au(III) redox cycling. Typically, phosphine-supported Au(I) precatalysts are used in the presence of strong oxidants to presumably generate phosphine Au(III) intermediates. Herein, we disclose that such Au(III) complexes can undergo facile C_{aryl}–P reductive elimination to afford phosphonium salts, which have been spectroscopically and crystallographically characterized. Mechanistic studies indicate that this process occurs from *cationic* species at temperatures as low as −20 °C but can be accelerated in the presence of nucleophiles, such as acetonitrile and phosphines, via a five-coordinate intermediate. Importantly, this study highlights that irreversible C_{aryl}–P reductive elimination is a feasible decomposition or activation pathway for phosphine-supported Au(III) catalysts and should not be ignored in future reaction development.



INTRODUCTION

Most examples of homogeneous gold(III) catalysis exploit the metal's Lewis acidity to activate heteroatoms or alkynes.[1] As a hard acceptor, Au(III) is often stabilized by hard carbon and nitrogen donors,[2] such as ylides, imines, and pyridines, but many reactions rely on the enhanced Lewis acidity of "ligand-free" Au(III) (i.e., AuX_3 and $NaAuX_4$).[3] Despite their accessibility, broad steric and electronic profiles, and ubiquity in transition metal catalysis,[4] phosphines have largely been avoided as ligands in Au(III) catalysis, due to "mismatch" between the soft donor properties of phosphines and the hard acceptor Au(III).[5] Furthermore, due to the high Au(III)/Au(I) potential (1.401 V),[6] these processes are mostly redox-neutral, and the typically hard donor ligands need only to stabilize the high-valent metal.

The compatibility of unsaturated substrates with certain strong oxidants has fueled recent developments in homogeneous Au(I)/Au(III) redox catalysis. Due to their stability toward air and water, phosphine-supported Au(I) complexes are convenient precatalysts in these processes. For instance, Zhang[7a] and our group[7b] have demonstrated oxidative heteroarylation of alkenes by catalytic Ph_3PAuCl and $dppm(AuBr)_2$ (dppm = 1,1-bis(diphenylphosphino)methane), respectively, using Selectfluor as oxidant. Muñiz[8] has shown that $Ph_3PAuOAc$ catalyzes the oxidative diamination of alkenes in concert with stoichiometric hypervalent iodine, while Glorius[9] has demonstrated that $[Ru(bipy)_3]^{3+}$ (bipy = 2,2′-bipyridine) oxidizes R_3PAuCl in photochemical alkene heteroarylations. Phosphine-stabilized Au(I) and Au(III) complexes have also shown promising stoichiometric redox behavior foundational for catalyst development. For instance, $Cy_3PAu(aryl)$ undergoes photoinitiated oxidative addition with CF_3I to access a species that can trifluoromethylate arenes,[10] while Nevado[11] has exploited C_{aryl}–H activation by Au(III) to oxidatively cross-couple arenes. Additionally, Nocera[12] has demonstrated that $dppm(AuX_3)_2$ (X = Cl, Br) reductively eliminates X_2 upon photoexcitation. Although not observed, reactive phosphine-supported Au(III) intermediates conceivably lie along these catalytic and stoichiometric pathways.[13]

Our group and others' have observed unusually fast reductive eliminations from Au(III) (Figure 1).[10,14,15] The barriers to challenging bond-forming processes, such as C_{aryl}–CF_3[10] and cyclobutane[15g] reductive elimination, are especially small from

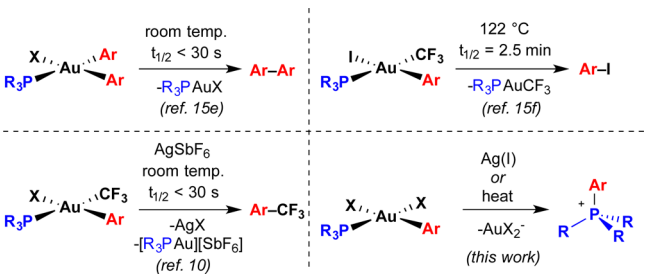


Figure 1. Examples of observed reductive elimination behavior from phosphine-supported Au(III) complexes.

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cationic Au(III) species. We speculated if reductive elimination of a phosphine and aryl/alkyl ligand on Au(III) to a phosphonium is similarly kinetically feasible. Although O'Hair has provided evidence that this process may occur in the gas phase in a mass spectrometer,[16a] our group has reported formation of phosphonium in solution under relatively mild conditions (room temperature) with concomitant catalyst decomposition.[16b] Catalyst deactivation via phosphonium reductive elimination has also been observed in Pd-catalyzed Heck reactions.[17] In contrast, Lloyd-Jones[18] has shown that phosphine oxidation in $(R_3P)AuX_3$ (in MeOH) activates Au(III) toward oxidative coupling chemistry, a pathway often proposed for activation of Pd(II) salts, as well;[19] likewise, C−P reductive elimination of phosphonium from a phosphine-supported organogold(III) species can result in activation of a Au(I) catalyst.

Most metal-mediated carbon−phosphorus bond-forming reactions generate neutral products[20] (i.e., phosphines, phosphites, and phosphinates). Reductive elimination of phosphonium is far less precedented and is typically observed at group 10 metals.[21] For instance, Yamamoto,[21a] Migita,[21b,c] and Chan[21d,e] have developed Ni- and Pd-catalyzed phosphonium syntheses from phosphines and aryl halides, while phosphonium reductive elimination plays a critical role in aryl−aryl interchange in phosphine-supported organometallic Pd(II) complexes.[21f]

Herein, we present several phosphine-supported Au(III) organometallic complexes that undergo irreversible C_{aryl}−P reductive elimination and our mechanistic studies that identify conditions under which these reductive eliminations are observed. We aim to achieve a thorough understanding of the nonspectator role of phosphines on Au(III) and how they influence the redox behavior of the metal center.

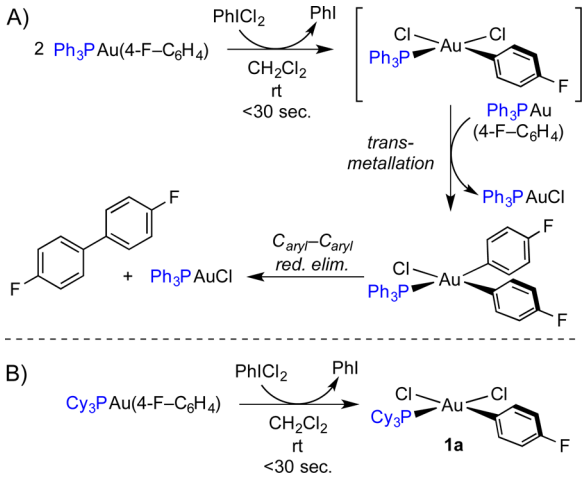
RESULTS AND DISCUSSION

C_{aryl}−P Reductive Elimination of a Monodentate Phosphine. Systems of the type $(R_3P)Au(aryl)Cl_2$ are well-suited for study of C_{aryl}−P reductive elimination. The cation $[(R_3P)Au(aryl)Cl]^+$ can be discretely prepared by Ag(I)-mediated halide abstraction, and C_{aryl}−P bond formation has to compete with P−Cl and C_{aryl}−Cl reductive elimination, which are likely slow processes.[15f]

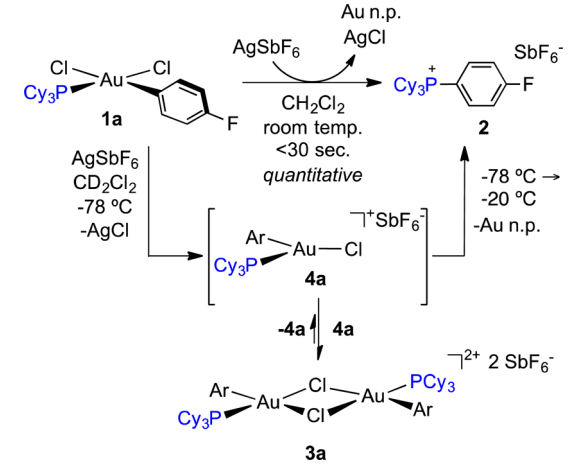
Oxidation of $(R_3P)Au(aryl)$ by $PhICl_2$ is extremely sensitive to phosphine substituents. For instance, when triarylphosphines or phosphites are used,[15e] only half of the starting material is oxidized, and aryl transmetalation from unreacted Au(I) to Au(III) outcompetes oxidation of the remaining half; the resulting *cis*-$(R_3P)Au(aryl)_2Cl$ undergoes fast C_{aryl}−C_{aryl} reductive elimination (Scheme 1A). Complexes supported by alkyl−diaryl and dialkyl−arylphosphines, such as ^{t}Bu-JohnPhos, exhibit more complicated behavior resulting from competing Au(I) oxidation and aryl transmetalation. Use of stongly donating, bulky trialkylphosphines, on the other hand, sufficiently slows aryl transmetalation from Au(I) to Au(III), resulting in quantitative oxidation of starting material (Scheme 1B).

cis-$(Cy_3P)Au(4\text{-}F\text{-}C_6H_4)(Cl)_2$ (**1a**) was prepared by oxidizing $Cy_3PAu(4\text{-}F\text{-}C_6H_4)$ with $PhICl_2$ (Scheme 1B). Treatment of **1a** with $AgSbF_6$ in CD_2Cl_2 resulted in the precipitation of Au nanoparticles (implicating a reductive process) and formation of a single product as judged by $^{31}P\{^1H\}$ and ^{19}F NMR (Scheme 2). X-ray analysis of white crystals grown from a filtered reaction solution unambiguously revealed the formation of the phosphonium salt $[(4\text{-}F\text{-}C_6H_4)PCy_3][SbF_6]$ (**2**), as well (Figure 2A). To our knowledge, this transformation represents the first example of C−P reductive elimination involving a phosphine as bulky as PCy_3

Scheme 1. Solution Behavior of (A) PPh_3-Supported[15e] and (B) PCy_3-Supported Au(I) Aryl Complexes under Oxidizing Conditions



Scheme 2. Proposed Mechanism of Phosphonium Formation from 1a



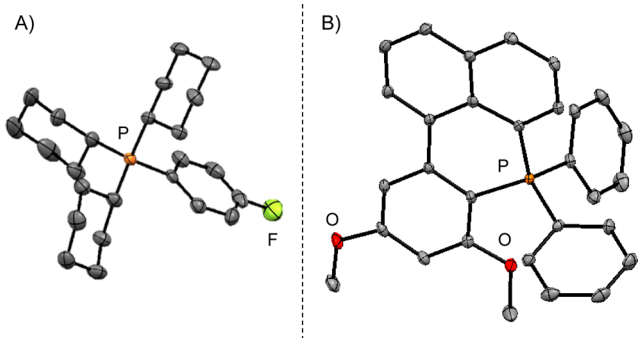


Figure 2. Thermal ellipsoid representations of phosphoniums: (A) **2** at the 50% probability level. Hydrogens and counterion (SbF_6^-) have been omitted for clarity. (B) **7**[**AuCl$_4$**] at the 50% probability level. Hydrogens and counterion have been omitted for clarity.

The reaction was monitored by low-temperature NMR. Injection of a $AgSbF_6$ solution to **1a** in CD_2Cl_2 at −78 °C cleanly generated a new species (**3a**) by ^{19}F and ^{31}P NMR, which reacted at −20 °C to afford **2** (k_{obs} = (7.2 ± 1.5) × 10^{-4} s^{-1};

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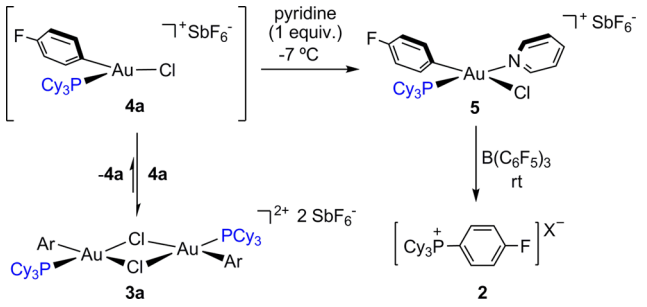
see Supporting Information for more information.) Although C_{aryl}–P reductive elimination likely occurs from **4a**, three-coordinate Au(III) complexes are generally too reactive for observation and isolation;[14,15e–g] thus, we propose that **4a** readily undergoes reversible dimerization to **3a** (Scheme 2).

A monomeric, cationic Au(III) complex can be trapped by addition of pyridine to a solution of **3a** at −7 °C to generate [(Cy_3P)Au(4-F-C_6H_4) (Cl) (pyr)][SbF_6] (**5**) (Scheme 3 and Figure 3). This complex is stable at room temperature but

Scheme 3. Trapping of Mononuclear Cation 4a with Pyridine



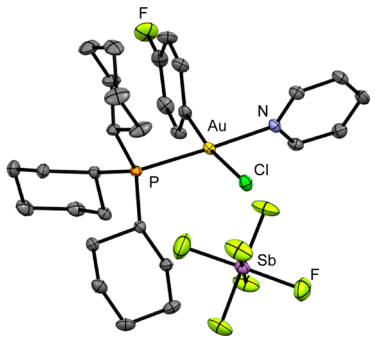


Figure 3. Thermal ellipsoid representations of **5** at the 50% probability level. Hydrogens have been omitted for clarity.

undergoes C_{aryl}–P reductive elimination in the presence of a pyridine-abstracting agent ($B(C_6F_5)_3$), suggesting that pyridine dissociation from **5** is reversible. The ratio of diffusion coefficients of **3a** and **5** (D_{3a}/D_5 = 0.467 ± 0.070) obtained by diffusion-ordered spectroscopy (DOSY NMR) supports that **3a** is dimeric (see Supporting Information); from the Stokes–Einstein relationship[22]

$$\frac{r_{3a}}{r_5} = \frac{D_5}{D_{3a}}$$

where r is the van der Waals radius of a molecule and the ratio of radii of dimer **3a** to **5** is 2.13 ± 0.31. Furthermore, halide abstraction from **1a** and (Cy_3P)Au(4-CF_3-C_6H_4) ($Cl)_2$ (**1b**) results in a statistical mixture of *three* intermediates observable at low-temperature—homodimers **3a** and **3b** and heterodimer **3c**. If, instead, we observed a monomeric species by NMR (either **4** or a solvento adduct, for instance), this crossover experiment would have resulted in just *two* observable intermediates (Figure 4). Indeed, bis(μ-halo)-bridged Au(III) dimers are well-precedented,[23] and our group has recently reported solution-state and crystallographic evidence of a *dicationic* N-heterocyclic carbene-stabilized bis(μ-fluoro)-bridged dimer, $[(SIPr)Au(CH_3)(\mu\text{-}F)]_2[F]_2$ (SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene).[23c]

C_{aryl}–P Reductive Elimination of a Bidentate Phosphine. Given the preference for linear geometries of Au(I) enforced by relativistic mixing of 5d, 6s, and 6p orbitals,[6b] new modes of catalysis rely on the development of novel, often complex, phosphines. Furthermore, the Lewis acidity of Au(III) has long been recognized to effect arene C–H activation by electrophilic aromatic substitution;[24] while this reactivity has been exploited in catalysis, it has also led to ligand activation. To assess whether irreversible C_{aryl}–P reductive elimination also occurs from auracycles, we developed a naphthalene-based phosphine that would place an electron-rich arene in the proper orientation for activation by a Au(III) center.

Treatment of **6** with $PhICl_2$ (1 equiv) afforded roughly 50% of the phosphonium 7[**$AuCl_4$**] (Scheme 4 amd Figure 2B). Addition of another equivalent of $PhICl_2$ brings the reaction to full conversion, implicating a mechanism involving *two* oxidations: P(III) → P(V) and Au(I) → Au(III). Since the first step is rate-determining oxidation of Au(I), we cannot distinguish between pathways of phosphorus oxidation, including (1) C_{aryl}–H activation by Au(III) followed by C_{aryl}–P reductive elimination, (2) P–Cl reductive elimination, and (3) phosphine dissociation from Au(III) and direct oxidation of phosphorus by $PhICl_2$. However, in support of mechanism 3, phosphine

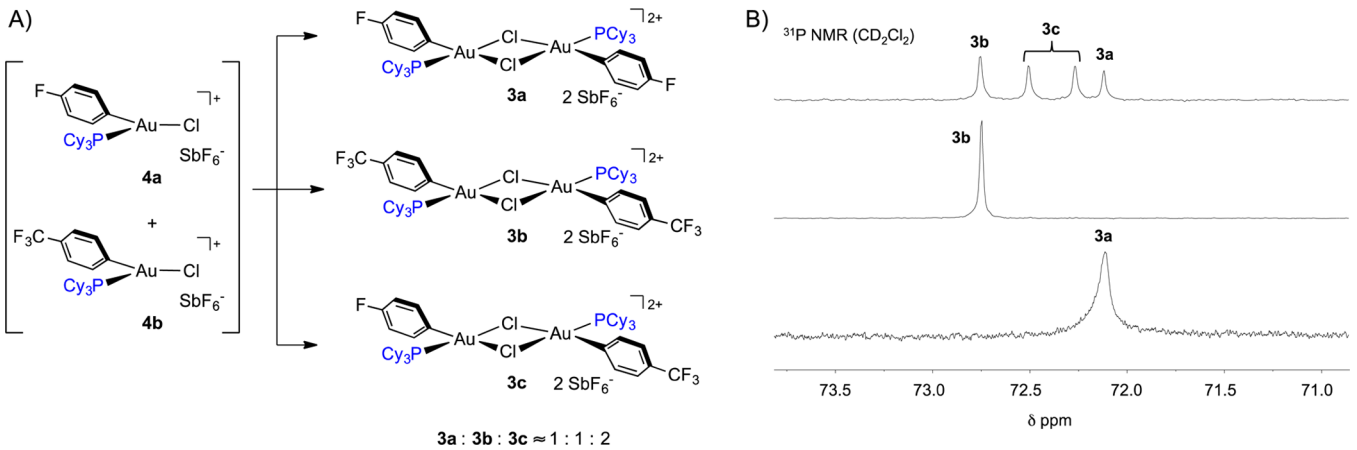


Figure 4. (A) Crossover experiment with **4a** and **4b** generated simultaneously should produce a statistical mixture of **3a**, **3b**, and **3c**. (B) ^{31}P NMR spectra of **3a** (bottom), **3b** (middle), and crossover experiment (top) in CD_2Cl_2 at −60 °C. ^{31}P NMR spectra referenced to H_3PO_4.

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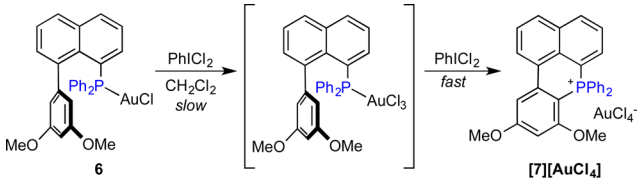
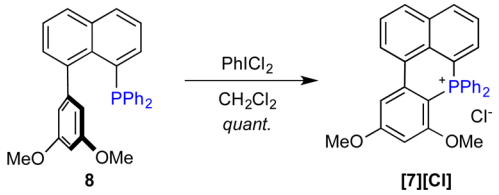
Scheme 4. Synthesis of [7][AuCl$_4$]



dissociation from Au(III) is facile,[14] and treating the free phosphine **8** with $PhICl_2$ (1 equiv) results in the fast, quantitative formation of phosphonium 7[**Cl**] (eq 1).



(1)

We reasoned that exchanging Cl on **6** for a substantially more electron-withdrawing C_6F_5 ligand (**9**) might discourage oxidation of the Au(I) product *and* slow phosphine dissociation relative to oxidation of starting material. Gratifyingly, treating **9** with stoichiometric $PhICl_2$ resulted in quantitative metal oxidation and ligand activation to form cyclometalated **10** (Scheme 5). Unfortunately, crystals of **10** suffered extensive disorder but established the relative geometry around the metal center, with the two aryl ligands in a *cis* relationship, in agreement with their relatively large *trans* influence (Figure S16).

Complex **10** was reasonably stable in the solid state, although it underwent very slow C_{aryl}–P reductive elimination to phosphonium salt [7][**AuCl**($\mathbf{C_6F_5}$)] in chlorinated solvents at room temperature. The reaction was monitored by ^{1}H NMR in $CDCl_3$ and exhibited first-order behavior at 60 °C (Figure 5) (8.3 mM, k_{obs} = (3.4 ± 0.1) × 10^{-4} s^{-1}, $t_{1/2}$ = 2029 s), quantitatively generating [7][**AuCl**($\mathbf{C_6F_5}$)]. The first-order behavior in $CDCl_3$ was conserved between 40 and 70 °C, and kinetic parameters of the rate-determining step $\Delta H^{‡}$ (21.9 ± 0.4 kcal/mol) and $\Delta S^{‡}$ (−9.1 ± 1.4 eu) were determined by Eyring analysis (Figure 6 and Figure S6). The rate was not perturbed by the addition of 5 equiv of [Bu_4N][Cl] but nearly doubles (k_{obs} = (7.2 ± 0.9) × 10^{-4} s^{-1}) in $CDCl_3$ saturated with $LiBF_4$ (Figure S7), indicative of a kinetic salt effect. Incremental addition of a polar cosolvent, CD_3OD (0–30% v/v in $CDCl_3$), also results in a rate acceleration (Figure 7 and Figure S8).

These results are consistent with rate-determining chloride dissociation from **10** preceding C_{aryl}–P reductive elimination (Scheme 6), and the negative entropy of activation likely arises from solvent reorganization to stabilize the forming ion pair. Alternate mechanisms can be discounted based on simple electronic arguments. For instance, phosphine dissociation from **10** followed by slow nucleophilic aromatic substitution at the *ipso* position of the aryl ligand would certainly generate a charged Meisenheimer intermediate, but S_NAr at an arene with electron-donating *ortho*- and *para*-OMe substituents is unlikely;

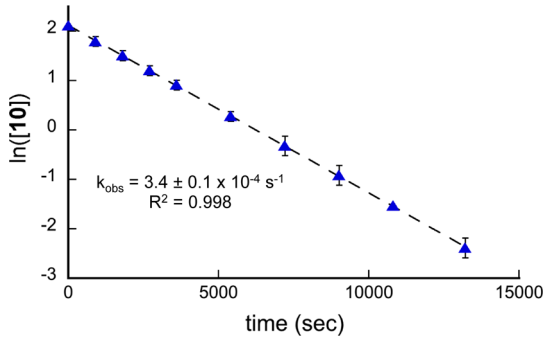


Figure 5. Log plot for thermolysis of **10** in $CDCl_3$ at 60 °C.

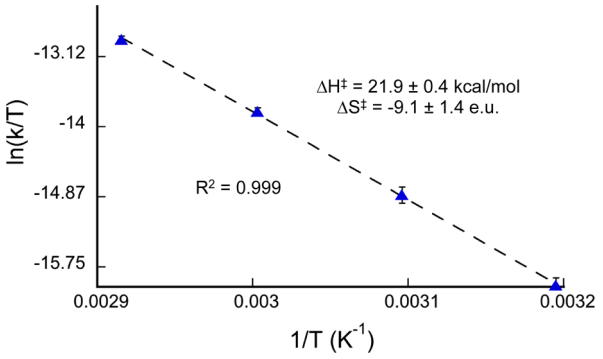


Figure 6. Eyring plot of the thermolysis of **10** in $CDCl_3$ between 40 and 70 °C.

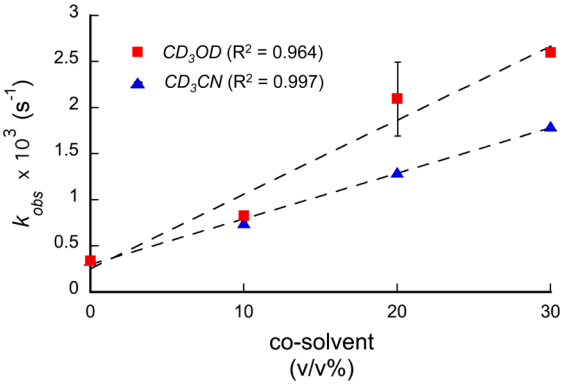
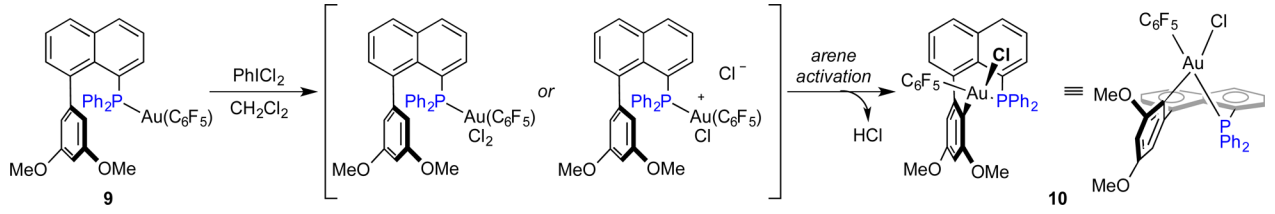


Figure 7. Effect of cosolvents CD_3OD or CD_3CN on rates of thermolysis of **10** in $CDCl_3$ at 60 °C. Although [CD_3CN] exhibits a stronger linear correlation with k_{obs}, linear regressions for both cosolvents are shown.

Scheme 5. Proposed Mechanism for Oxidation of 9 by $PhICl_2$ and Ligand Activation



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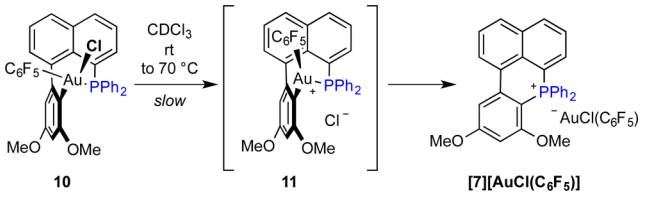
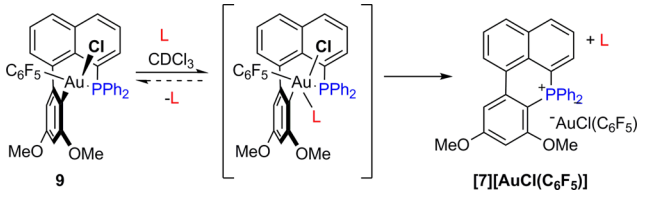
Scheme 6. Proposed Mechanism for the Thermolysis of 10



in other words, the arene must be *both* electrophilic and nucleophilic toward aromatic substitution, even upon coordination to a Lewis acidic Au(III) center. In fact, the phosphine might be expected to react preferentially at the *ipso* position of the electron-deficient perfluorophenyl ligand (ring strain notwithstanding),[11] yet we observe no evidence of the resulting phosphonium. As a unimolecular reaction, formation of [7][**AuCl**(C_6F_5)] may be kinetically biased relative to the second-order substitution reaction by exogenous phosphine. However, even in the presence of 10 equiv of PPh_3, *only* [7][**Cl**] and $Ph_3PAu(C_6F_5)$ were observed (vide infra). This evidence is not definitive but suggestive of an inner-sphere C_{aryl}–P reductive elimination process.

Incremental addition of CD_3CN (0–30% v/v in $CDCl_3$) also accelerated the reaction, although unexpectedly, we observed a linear correlation between k_{obs} and [CD_3CN] (Figure 7, with k_{obs} in $CDCl_3$ as the nonzero *y*-intercept, and Figure S9). This clean, first-order behavior cannot be attributed simply to changes in polarity of the medium[25] but more likely to a second, competitive reductive elimination mechanism involving intimate participation of CD_3CN. In this process, we propose that the nucleophilic cosolvent coordinates to **10** and induces C_{aryl}–P reductive elimination from a five-coordinate solvento complex (Scheme 7). We cannot discount that the sterics and

Scheme 7. Proposed Mechanism for Phosphine-Accelerated C_{aryl}–P Reductive Elimination



nucleophilicity of CD_3OD absolutely preclude this solvent-assisted reductive elimination pathway in CD_3OD, but a weaker correlation between k_{obs} and [CD_3OD] suggests that stabilization of the ionic transition state in the dissociative pathway dominates. This conclusion is reasonable considering that the alcoholic cosolvent can hydrogen bond to the chloride.

To further interrogate this hypothesis and to avoid potentially complicating solvent effects at higher cosolvent ratios, we speculated if larger yet substantially more nucleophilic PPh_3 can accelerate C_{aryl}–P reductive elimination from **10**. Indeed, the reaction was significantly accelerated in the presence of PPh_3, although the formation of $Ph_3PAuC_6F_5$ upon reductive elimination complicated the kinetics.[26,27] With ≥10 equiv excess PPh_3, the reaction maintained well-behaved pseudo-first-order behavior and was first-order in PPh_3 (Figure 8 and Figure S10). Because consumption of **10** was so fast at elevated temperatures under these conditions, the reactions were monitored at 20 °C with 10–15 equiv of PPh_3. With 10 equiv of PPh_3, the reaction was complete within 20 min (k_{obs} = (1.2 ± 0.0) × 10^{-3} s^{-1},

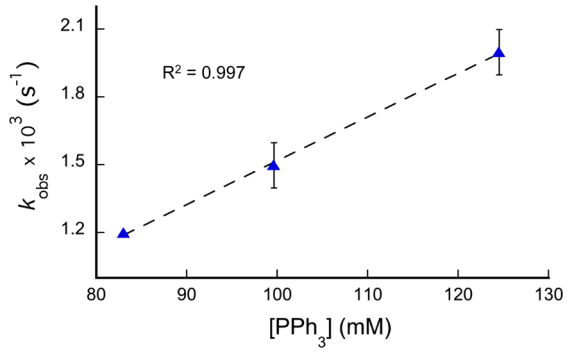


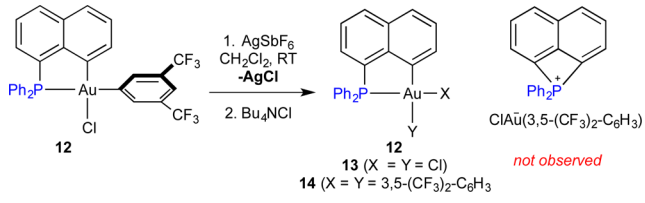
Figure 8. First-order relationship between pseudo-first-order rate constant k_{obs} and [PPh_3] at 20 °C.

$t_{1/2}$ = 575 s), while in the absence of phosphine, we observed less than 50% consumption of **10** in 2 days (k_{obs} = 3.1 × 10^{-6} s^{-1}, extrapolated from Eyring data). We have previously observed a similar associative process in the C_{aryl}–C_{aryl} reductive elimination from Au(III),[15e] and others have shown coordination-induced reductive bond-forming process from five-coordinate Ni(II) and Pd(II) complexes.[28]

Comparison of the thermolysis of **10** and silver-mediated chloride abstraction from **1a** provided valuable insight into the general C_{aryl}–P reductive elimination reaction. Both processes involve the intermediacy of mononuclear Au(III) cations, which have been recently shown to undergo low-barrier reductive transformations that are often challenging at other metals. However, an even lower barrier dimerization process dominated when **4a** was generated from **1a**, allowing trapping of the reactive cation and spectroscopic observation of dication **3a** at low temperature. Due to the poor bridging ability of perfluorophenyl ligands, cation **11** likely cannot dimerize, and any step following *formation* of this cation is fast. Alternative reductive eliminations from the Au(III) intermediates are also clearly slower than C_{aryl}–P bond formation. For instance, C_{aryl}–C_6F_5 or P–C_6F_5 reductive elimination in **11** is undoubtedly discouraged by the strong Au–C_6F_5 bond.[29] Thus, deleterious C_{aryl}–P reductive elimination may become non-negligible in catalytic cycles, particularly when Au(III) is stabilized by halides that may dissociate. Since initial chloride dissociation is slow, polar solvents will also accelerate phosphonium formation.

Nevertheless, the use of rigid bidentate phosphines can preclude C_{aryl}–P reductive elimination. For instance, in the presence of $AgSbF_6$, **10** undergoes instantaneous C_{aryl}–P reductive elimination, while **12**,[30] which would reductively eliminate to a strained phosphonium, converts to several cationic species persistent at room temperature. The oxidation state of the metal in these complexes is undoubtedly +3 since addition of [Bu_4N]Cl regenerates **12** and disproportionation products (P–C)$AuCl_2$ (**13**) and (P–C)Au(3,5-$(CF_3)_2$-C_6H_3)$_2$ (**14**) (Scheme 8). Reductive elimination to generate the highly strained, phosphacyclobutane did not occur.

Scheme 8. Behavior of a Sterically-Constrained Auracycle



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CONCLUSION

These studies suggest that deleterious C_{aryl}–P reductive elimination is not only facile from Au(III) cations, but that this process is kinetically accessible from *neutral* Au(III) species via the cation under certain conditions (i.e., the Au(III)–Cl bond is weakened by strongly donating *trans* ligands, and C–Cl reductive elimination is discouraged due to a strong Au(III)–C bond). In fact, because Au(III)–X bonds weaken in the order Cl > Br > I,[15f] application of the Bell-Evans-Polanyi principle to the initial Au(III)–Cl heterolysis from **10** suggests that this rate-determining step should be faster with heavier halides. We are currently investigating this hypothesis, as well as the influence of pseudohalides on this process.

Au(III) is often stabilized by hard, neutral donors, such as nitrogen (i.e., pyridines, bipyridines, imines) and N-heterocyclic carbenes. In a catalytic cycle proceeding through multiple intermediates of varying ionicity and coordination environment around the reactive Au(III) center, a polarizable phosphine ligand can engage in redox transformations that deplete active species. The high reduction potential of Au(III) complicates reports of Lewis acidic Au(III) catalysis, for instance, in which it is often ambiguous whether Au(I) or Au(III) is the active catalyst; in these cases, phosphonium reductive elimination from a precatalyst can lead to an active Au(I) species.[18b,31] Phosphines are far too broad and accessible a ligand class to avoid completely, however, and these studies shed light on several pathways that can irreversibly alter a phosphine-supported Au(III) catalyst or Au(I) catalyst under oxidizing conditions. We have also shown that this deleterious process can be avoided (or at least slowed) by rational ligand design.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b10720.

X-ray data (**5**) (CIF)
X-ray data (**2**) (CIF)
X-ray data (**12**) (CIF)
X-ray data ([7][$AuCl_4$]) (CIF)
X-ray data ([7][AuCl-C_6F_5]) (CIF)
X-ray data ([7][Cl]) (CIF)
X-ray data (**10**) (CIF)
Experimental details and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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