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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 Caryl−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 Caryl−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 alkenes.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., AuX3 and NaAuX4).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, Zhang7a and our group7b have demonstrated oxidative heteroarylation of alkenes by catalytic Ph3PAuCl and dppm(AuBr)2 (dppm = 1,1-bis(diphenylphosphino)methane), respectively, using Selectfluor as oxidant. Muñiz8 has shown that Ph3PAuOAc catalyzes the oxidative dianimation of alkenes in concert with stoichiometric hypervalent iodine, while Glorius9 has demonstrated that [Ru(bipy)3]3+ (bipy = 2,2’-bipyridine) oxidizes R3PAuCl 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, Cy3PAu(aryl) undergoes photoinitiated oxidative addition with CF3I to access a species that can trifluoromethylate arenes,10 while Nevado11 has exploited Caryl−H activation by Au(III) to oxidatively cross-couple arenes. Additionally, Nocera12 has demonstrated that dppm(AuX3)2 (X = Cl, Br) reductively eliminates X2 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 Caryl−CF310 and cyclobutane15g reductive elimination, are especially small from Ph3PAuCl.

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Figure 1. Examples of observed reductive elimination behavior from phosphine-supported Au(III) complexes.
caticonic 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, our group has reported formation of phosphonium in solution under relatively mild conditions (room temperature) with concomitant catalyst decomposition. Catalyst deactivation via phosphonium reductive elimination has also been observed in Pd-catalyzed Heck reactions. In contrast, Lloyd-Jones has shown that phosphine oxidation in (R3P)AuX3 (in MeOH) activates Au(III) toward oxidative coupling chemistry, a pathway often proposed for activation of Pd(II) salts, as well; 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 (i.e., phosphines, phosphites, and phosphinates). Reductive elimination of phosphonium is far less precedent and is typically observed at group 10 metals. For instance, Yamamoto, Migita, and Chan 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 phosphate-supported organogold(III) complexes.21f

Herein, we present several phosphine-supported Au(III) organometallic complexes that undergo irreversible C−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**

Caryl−P Reductive Elimination of a Monodentate Phosphine. Systems of the type (R3P)Au(aryl)Cl2 are well-suited for study of Caryl−P reductive elimination. The cation [(R3P)Au(aryl)Cl]+ can be discretely prepared by Ag(I)-mediated halide abstraction, and Caryl−P bond formation has to compete with P−Cl and Caryl−Cl reductive elimination, which are likely slow processes.

Oxidation of (R3P)Au(aryl) by PhICl2 is extremely sensitive to phosphine substituents. For instance, triarylphosphines or phosphites are used, 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-(R3P)Au(aryl)Cl undergoes fast Caryl−Caryl reductive elimination (Scheme 1A). Complexes supported by alkyl−diaryl and dialkyl−arylphosphines, such as Bu-JohnPhos, exhibit more complicated behavior resulting from competing Au(I) oxidation and aryl transmetalation. Use of strongly donating, bulky trialkylphosphines, on the other hand, sufficiently slow transmetalation from Au(I) to Au(III), resulting in quantitative oxidation of starting material (Scheme 1B).

cis-(Cy3P)Au(4-F-C6H4)(Cl)2 (1a) was prepared by oxidizing Cy3PAu(4-F-C6H4) with PhICl2 (Scheme 1B). Treatment of 1a with AgSbF6 in CD2Cl2 resulted in the precipitation of Au nanoparticles (implicating a reductive process) and formation of a single product as judged by 31P{1H} and 19FN M NMR (Scheme 2). X-ray analysis of white crystals grown from a reaction solution unambiguously revealed the formation of the phosphonium salt [(4-F-C6H4)PCy3][SbF6] (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 PCy3.

The reaction was monitored by low-temperature NMR. Injection of a AgSbF6 solution to 1a in CD2Cl2 at −78 °C cleanly generated a new species (3a) by 19F and 31P NMR, which reacted at −20 °C to afford 2 (kobs = (7.2 ± 1.5) × 10−4 s−1);
see Supporting Information for more information.) Although Caryl−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 [(Cy3P)Au(4-F-C6H4)(Cl)(pyr)][SbF6] (5) (Scheme 3 and Figure 3). This complex is stable at room temperature but undergoes Caryl−P reductive elimination in the presence of a pyridine-abstracting agent (B(C6F5)3), suggesting that pyridine dissociation from 5 is reversible. The ratio of diffusion coefficients of 3a and 5 (D3a/D5 = 0.467 ± 0.070) obtained by diffusion-ordered spectroscopy (DOSY NMR) supports that 3a is dimeric (see Supporting Information); from the Stokes-Einstein relationship22

\[
\frac{r_3}{r_5} = \frac{D_5}{D_{3a}}
\]

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 (Cy3P)Au(4-CF3-C6H4)(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 dicaticonic N-heterocyclic carbene-stabilized bis(μ-fluoro)-bridged dimer, [(SIPr)Au(CH3)(μ-F)][F2] (SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene).23c

Caryl−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 Caryl−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 PhICl2 (1 equiv) afforded roughly 50% of the phosphonium 7[AuCl4] (Scheme 4 and Figure 2B). Addition of another equivalent of PhICl2 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) Caryl−H activation by Au(III) followed by Caryl−P reductive elimination, (2) P−Cl reductive elimination, and (3) phosphine dissociation from Au(III) and direct oxidation of phosphorus by PhICl2. However, in support of mechanism 3, phosphine
dissociation from Au(III) is facile, and treating the free phosphine 8 with PhICl₂ (1 equiv) results in the fast, quantitative formation of phosphonium [Cl] (eq 1).

We reasoned that exchanging Cl on 6 for a substantially more electron-withdrawing C₆F₅ 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 PhICl₂ 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 Caryl-P reductive elimination to phosphonium salt [AuCl(C₆F₅)] in chlorinated solvents at room temperature. The reaction was monitored by 'H NMR in CDCl₃ and exhibited first-order behavior at 60 °C (Figure 5) (8.3 mM, \( k_{\text{obs}} = (3.4 \pm 0.1) \times 10^{-4} \text{ s}^{-1}, t_{1/2} = 2029 \text{ s} \)), quantitatively generating [AuCl(C₆F₅)]. The first-order behavior in CDCl₃ was conserved between 40 and 70 °C, and kinetic parameters of the rate-determining step \( \Delta H^\ddagger = (21.9 \pm 0.4) \text{ kcal/mol} \) and \( \Delta S^\ddagger = (-9.1 \pm 1.4 \text{ eu}) \) were determined by Eyring analysis (Figure 6 and Figure S6). The rate was not perturbed by the addition of 5 equiv of [Bu₄N][Cl] but nearly doubles (\( k_{\text{obs}} = (7.2 \pm 0.9) \times 10^{-4} \text{ s}^{-1} \)) in CDCl₃ saturated with LiBF₄ (Figure S7), indicative of a kinetic salt effect. Incremental addition of a polar cosolvent, CD₃OD (0–30% v/v in CDCl₃), also results in a rate acceleration (Figure 7 and Figure S8).

These results are consistent with rate-determining chloride dissociation from 10 preceding Caryl-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 S₅Ar at an arene with electron-donating ortho- and para-OMe substituents is unlikely.
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), yet we observe no evidence of the resulting phosphonium. As a unimolecular reaction, formation of [7][AuCl(C6F5)] may be kinetically biased relative to the second-order substitution reaction by exogenous phosphine. However, even in the presence of 10 equiv of PPh3, only [7][Cl] and Ph3PAu(C6F5) were observed (vide infra). This evidence is not definitive but suggestive of an inner-sphere Caryl-P reductive elimination process.

Incremental addition of CD3CN (0–30% v/v in CDCl3) also accelerated the reaction, although unexpectedly, we observed a linear correlation between \( k_{obs} \) and [CD3CN] (Figure 7, with \( k_{obs} \) in CDCl3 as the nonzero y-intercept, and Figure S9). This clean, first-order behavior cannot be attributed simply to changes in polarity of the medium but more likely to a second, competitive reductive elimination mechanism involving intimate participation of CD3CN. In this process, we propose that the nucleophilic cosolvent coordinates to 10 and induces Caryl-P reductive elimination from a five-coordinate solvento complex (Scheme 7). We cannot discount that the steric and nucleophilicity of CD3OD absolutely preclude this solvent-assisted reductive elimination pathway in CD3OD, but a weaker correlation between \( k_{obs} \) and [CD3OD] 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 PPh3 can accelerate Caryl-P reductive elimination from 10. Indeed, the reaction was significantly accelerated in the presence of PPh3 although the formation of Ph3PAuC6F5 upon reductive elimination complicated the kinetics. With \( \geq 10 \) equiv excess PPh3, the reaction maintained well-behaved pseudo-first-order behavior and was first-order in PPh3 (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 PPh3. With 10 equiv of PPh3, the reaction was complete within 20 min (\( k_{obs} = (1.2 \pm 0.0) \times 10^{-3} \) s\(^{-1}\), \( t_{1/2} = 575 \) s), while in the absence of phosphine, we observed less than 50% consumption of 10 in 2 days (\( k_{obs} = 3.1 \times 10^{-6} \) s\(^{-1}\), extrapolated from Eyring data). We have previously observed a similar associative process in the Caryl-Caryl reductive elimination from Au(III),\(^{13e} \) 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 Caryl-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 Caryl-P bond formation. For instance, Caryl-C6F5 or P-C6F5 reductive elimination in 11 is undoubtedly discouraged by the strong Au-C6F5 bond.\(^{29} \) Thus, deleterious Caryl-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 Caryl-P reductive elimination. For instance, in the presence of AgSbF6, 10 undergoes instantaneous Caryl-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 [Bu4N]Cl regenerates 12 and disproportionation products (P=C)AuCl2 (13) and (P=C)Au(3,5-(CF3)2-C6H4)2 (14) (Scheme 8). Reductive elimination to generate the highly strained, phosphacyclobutane did not occur.

**Scheme 7. Proposed Mechanism for Phosphine-Accelerated Caryl-P Reductive Elimination**

![Scheme 7. Proposed Mechanism for Phosphine-Accelerated Caryl-P Reductive Elimination](image)

**Scheme 8. Behavior of a Sterically-Constrained Auracycle**

![Scheme 8. Behavior of a Sterically-Constrained Auracycle](image)
CONCLUSION

These studies suggest that deleterious Cα−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)−Cl bond). In fact, because Au(III)−X bonds weaken in the order Cl > Br > I, 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 it is often ambiguous whether Au(I) or Au(III) is the active species. The authors gratefully acknowledge Andrew Samant for helpful discussions.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.B10720.

X-ray data (5) (CIF)

Experimental details and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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(22) The Stokes–Einstein equation is \( r = kT/6\eta D \), where \( r \) is van der Waals radius of a molecule, \( D \) is the diffusion coefficient, \( k \) is Boltzmann’s constant, \( T \) is temperature, and \( \eta \) is solution viscosity. The ratio of two van der Waals radii obtained under the same experimental conditions ensures that \( k \), \( T \), and \( 6\eta \) cancel.


(27) Ph2PMe3,C6F5Fe, can be independently synthesized by treating a CDCl3 solution of [AuCl(C6F5)] with PPh3 at room temperature. The reaction is quantitative after 1 min.


(30) Amgoun and Bourissou have generated structurally similar reactive Au(III) cations by –CH, abstraction with B(C6F5)3. See: Rekhroukh, F.; Brousse, R.; Amgoun, A.; Bourissou, D. Angew. Chem., Int. Ed. 2015, 54, 1266.