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Homogeneous Catalysis

Mechanistic Surprises in the Gold(I)-Catalyzed Intramolecular Hydroarylation of Allenes**

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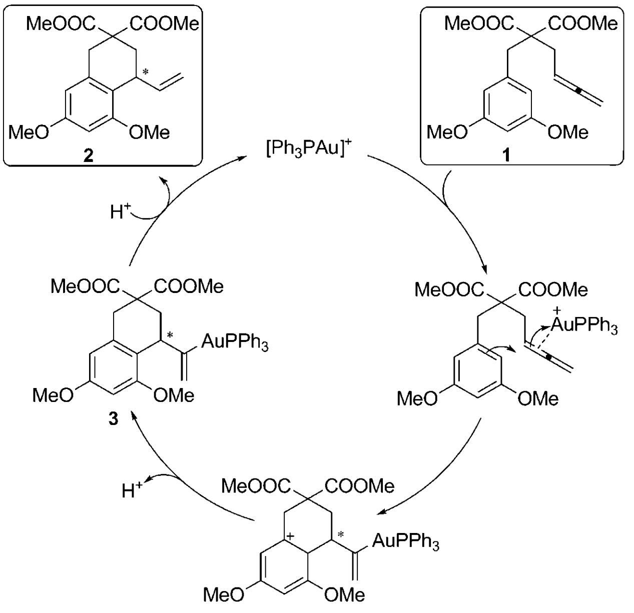
Gold(I)-catalyzed carbon–carbon bond-forming reactions continue to fascinate the synthetic community but are less well investigated than many conventional metal catalysts.[1] In many cases a cationic gold(I) species activates an unsaturated C−C bond and isomerizes or functionalizes it to build molecular complexity via reactive intermediates which include gold–π complexes, gold–vinyl species, and gold–carbene species. Support for these intermediates is mainly based on gold(I) organometallic chemistry, though computational studies and the isolation of proposed catalytic intermediates have been reported.[2–5]

We report mechanistic studies on a seemingly simple gold(I)-catalyzed reaction and demonstrate the importance of dinuclear organometallic intermediates. Whereas similar dinuclear species have been postulated on the basis of density functional theory (DFT) studies,[5b] di-gold intermediates have yet to be detected in situ and their reactivity characterized.

We previously showed that the transformation of **1** into **2** could be catalyzed by $[R_3PAu]^+$.[6] The proposed cycle is shown in Scheme 1, wherein $[R_3PAu]^+$ initiated the process by π coordination to **1**,[7] which activated it for nucleophilic attack by the aromatic ring.[1b] Subsequent rearomatization generated the vinyl–gold(I) complex **3**, which protodeaurated with the generated acid to give **2** and $[R_3PAu]^+$.[8] The seemingly well-behaved nature of this reaction led us to initiate studies to refute or validate this mechanism, and this has led to surprising results concerning the nature of the catalyst resting state.

Preliminary studies identified the Gagosz catalyst $Ph_3PAuNTf_2$ (**4**) as a convenient source of $[Ph_3PAu]^+$, which does not require in situ activation using silver salts.[9] Monitoring, by ^{31}P NMR methods, the reaction of **1** with 10 mol % **4** indicated that the catalyst rests as a single species, **5a**, having two distinct peaks in a 1:1 ratio ($\delta \approx 36$ ppm).[10] Upon completion of the reaction these peaks diminished, and the Gagosz catalyst reappeared with a signal at $\delta = 30$ ppm. The stoichiometric reaction of **1** with **4** in the presence of 2,6-di-*tert*-butylpyridine (to inhibit protodeauration) resulted in the incomplete consumption of **1**, but gave the same peaks at $\delta = 36$ ppm. The addition of a second equivalent of **4** converted all the starting material into **5a**.



Scheme 1. Proposed cycle for the gold(I)-catalyzed hydroarylation of allenes.

The ^{1}H NMR spectra of the isolated **5a** showed a single carbocycle consistent with a vinyl–gold(I) connectivity, as well as other features that were inconsistent with **3**. These included the two peaks at around $\delta = 36$ ppm (^{31}P NMR) rather than the expected singlet at around $\delta = 44$ ppm,[3b–h] and the 2:1 ratio of the PPh_3 to the carbocycle as determined by the resonances in the ^{1}H NMR spectra. A closer examination of the multiplicity of the vinyl peaks in the ^{1}H NMR spectra additionally revealed a heteronuclear coupling between the vinyl proton, which was *anti* to Au, and two phosphorous atoms, rather than the coupling to a single phosphorous atom as expected for a simple vinyl–gold(I) complex such as **3**. These data therefore suggested that the resting state **5a** was a doubly metalated variant of **3**.

Compound **5a** was air stable and amenable to an aqueous workup without protodeauration; however attempts to purify it using Florisil or silica gel chromatography led to immediate decomposition and the elution of **2**. In contrast, neutral alumina cleanly converted **5a** into **3**, whose monometalated nature was confirmed by NMR spectroscopy[11] and X-ray crystallography (Figure 1).[12,13] In contrast to **5a**, the ^{1}H NMR spectra showed large upfield shifts of the *syn* ($\delta =$

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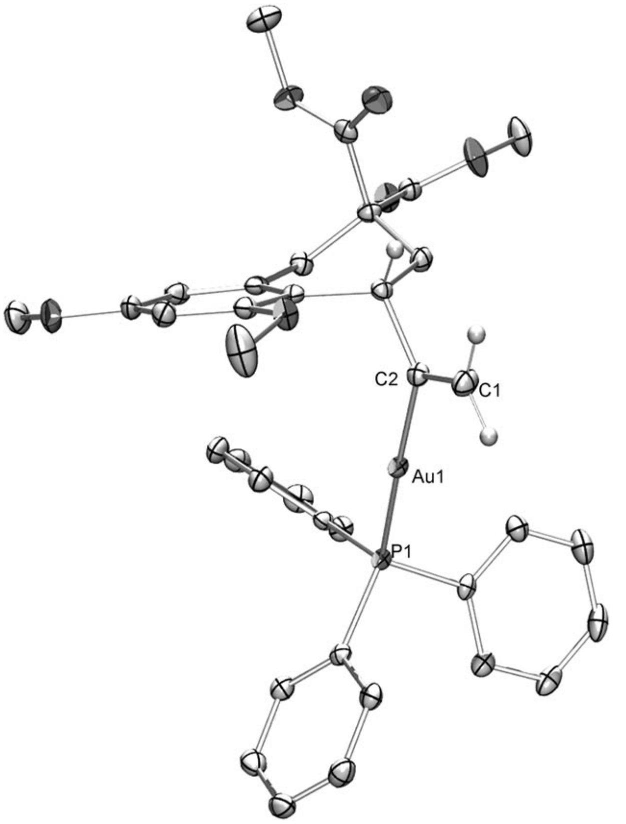


Figure 1. ORTEP diagram of intermediate **3** with 50% probability ellipsoids; most hydrogen atoms omitted for clarity. Key bond lengths [Å] include: Au1–P1 [2.2913(5)], Au1–C2 [2.050(2)], and C1–C2 [1.324(4)].[13]

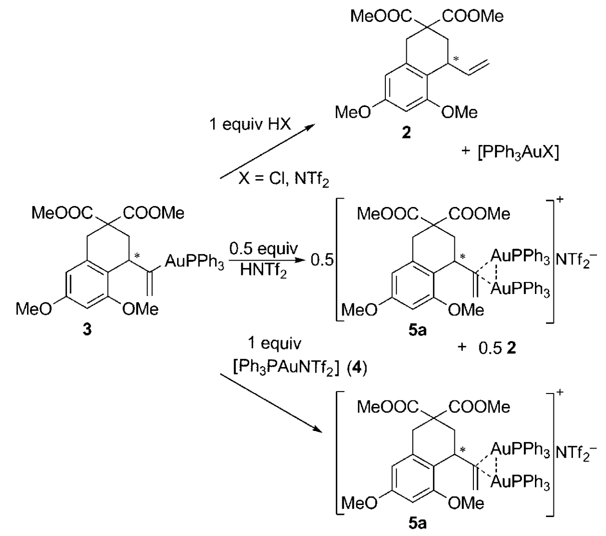
6.43 ppm (**5a**) to $\delta = 4.97$ ppm (**3**)) and *anti* ($\delta = 5.91$ ppm (**5a**) to $\delta = 5.62$ ppm (**3**)) vinyl hydrogen atoms, suggesting significantly different chemical environments in the two compounds.

The reactivity of **3** and **5a** also differed greatly.[3b–d,4] Treatment with excess acetic acid ($\mathrm{p}K_a = 4.76$) immediately protodeaurated **3** (to give **2**),[14] whereas **5a** was untouched and unreactive with even α-bromoacetic acid ($\mathrm{p}K_a = 2.86$; 12 h). Excess TFA ($\mathrm{p}K_a = -0.25$), however, resulted in the rapid decomposition to give only traces of **2**. The second equivalent of $[Ph_3PAu]^+$ in **5a** therefore hinders protodeauration.

These spectroscopic data and reactivity observations coupled with the work of Grandberg and Dyadchenko,[4] Nesmeyanov et al.,[15b,c] and Schmidbaur and co-workers[3g] on aryl–gold(I) organometallic complexes suggested that **5a** was a diaurated structure which engaged the vinyl anion in a bridging three-center two-electron mode, and was stabilized by a Au–Au interaction. X-ray crystal structures of numerous bridging aryl compounds are known,[15] and a recent computational study implicated the intermediacy of a bridging vinyl group in the cycloisomerization of ene-ynes.[5b] The phosphorous center in such a chiral structure would be diastereotopic and account for the inequivalent resonances in the ^{31}P NMR spectra.

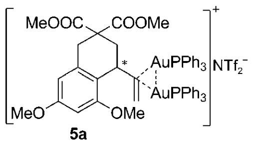
Grandberg et al. have reported the geminally diaurated parent species $[(Ph_3PAu)_2CH{=}CH_2]^+[BF_4]^-$ to be unstable and characterizable only by its IR spectra and its reactivity;[16] the more crowded nature of **5a** presumably contributes to its thermal stability. The enhanced acid stability of a bridging vinyl group can be rationalized by noting that the three-center two-electron bond should be more electron deficient and crowded than the traditional vinyl–gold(I) complex **3**. The stabilizing Au–Au bond interactions are well established and worth 5–10 kcal mol^{-1}.[17]

The isolation of **3** and **5a** provided a rare opportunity to study the comparative reactivity of genuine reaction intermediates. Compound **3** was found to readily react with stoichiometric quantities of HX (X = Cl, NTf_2) to yield **2** and the expected gold(I) species (Scheme 2).[18] When only 0.5 equivalent of $HNTf_2$ was added, clean conversion into **5a** and **2** occurred. Similarly, clean and rapid was the conversion of **3** and **4** into **5a**, a process that presumably competes favorably with protodeauration under catalysis conditions.

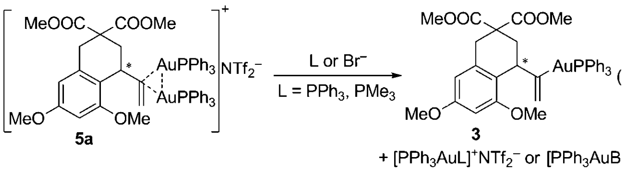


Scheme 2. Reactivity of intermediate **3**.

In reactivity paralleling that for diaurated aryl compounds reported by Nesmeyanov and Grandberg, **5a** extrudes $[Ph_3PAuL]$ and **3** upon reaction with a suitable ligand [Eq. (1)]. Although **5a** and **3** were expectedly unreactive

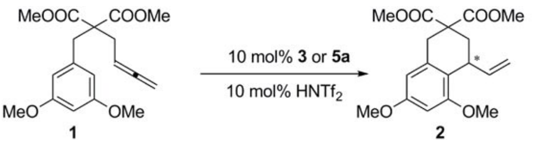


5a



(1)

with **1**, they could each be activated with $HNTf_2$ to reveal **4**. The subsequent conversion of **1** into **2** showed the viability of both **3** and **5a** as catalytic intermediates [Eq. (2)].



(2)

To elucidate whether the resting state of the catalyst at **5a** was dependent on NTf_2^-, different silver salts were investigated in an in situ activation protocol (Table 1). In each case, **5a–e** was observed by ^{31}P NMR spectroscopy suggesting a purely outer-sphere role for the anions with the possible exception of OTf^-, which generated a broadened singlet at $\delta = 36$ ppm.

Table 1: Activation protocol using different silver salts.

Entry	Catalyst/Activator	Resting state[a]
1	$[Ph_3PAuNTf_2]$	**5**
2	$[Ph_3PAuCl]/AgNTf_2$	**5a**
3	$[Ph_3PAuCl]/AgPF_6$	**5b**[b]
4	$[Ph_3PAuCl]/AgSbF_6$	**5c**[c]
5	$[Ph_3PAuCl]/AgOTf$	**5d**[d]
6	$[Ph_3PAuCl]/AgBF_4$	**5e**[e]

[a] Monitored by ^{31}P NMR methods. [b] Counter ion to the gold complex is PF_6^-. Signals at $\delta = 35.4$ and 35.1 ppm were observed. [c] Counter ion to the gold complex is SbF_6^-. Signals at $\delta = 35.7$ and 35.4 ppm were observed. [d] Counter ion to the gold complex is OTf^-. A broad peak 35.8 ppm was observed instead of two sharp singlets. [e] Counter ion to the gold complex is BF_4^-. Signals at $\delta = 35.9$ and 35.6 ppm were observed.

The above results indicate that **3** and **5a** are each viable intermediates in the intramolecular hydroarylation of allenes, and that an additional structure needs to be added to the mechanism in Scheme 1. The bridging structure in **5a** was found to be considerably more stable than **3**, and served to sequester the key Lewis acidic species $[Ph_3PAu]^+$ more quickly than the latter promoted allene activation. Although **5a** was less reactive to Brønsted acids than **3**, both could be activated by $HNTf_2$ to generate catalytically active **4**. It is not yet clear whether **5a** operates "on" or "off" the cycle under true catalytic conditions (is **5a** directly protodeaurated?), but it is clear that the mechanism is more complex than previously envisioned.

In conclusion, this report describes the synthesis, characterization, and reactivity of two intermediates in the $[Ph_3PAu]^+$-catalyzed cycloisomerization of allenic arenes. It reports, for the first time, the experimental viability of computationally predicted diaurated reaction intermediates, and therefore provides important insights into the burgeoning field of gold catalysis.

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Keywords: allenes · gold · homogeneous catalysis · hydroarylation · reaction mechanisms

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[11] The ^{31}P NMR spectra showed the expected singlet at $\delta =$ 43.0 ppm for a classical [Ph$_3$PAu]–vinyl complex; see reference [3d].

[12] Compound **3** is one of only a few vinyl–gold(I) species not stabilized by an electron-withdrawing group; see reference [3d].

[13] The observed distances are similar to those published by Laguna; see reference [3d]. X-ray crystal structure data for **3** at 100 K: $C_{36}H_{36}AuO_6P$, $M_r = 792.61\ \mathrm{g\,mol^{-1}}$, triclinic, space group $P\bar{1}$, $a = 8.7814(5)$, $b = 13.7359(7)$, $c = 14.3110(7)$ Å, $\alpha = 105.099(2)$, $\beta = 96.500(2)$, $\gamma = 97.267(2)°$, $V = 1633.85(15)$ Å^3, $Z = 2$, $\rho_{\mathrm{calcd}} = 1.611\ \mathrm{g\,cm^{-3}}$, $R_1 = 0.0186$ (0.0188), $wR_2 = 0.0448$-(0.0449), for 5692 reflections with $I > 2\sigma(I)$ (for 5759 reflections ($R_{\mathrm{int}} = 0.0294$) with a total of 27480 measured reflections), goodness of fit on $F^2 = 1.121$, largest diff. peak (hole) = 0.0930 (-0.725 e Å^{-3}); see the Supporting Information. CCDC 736429 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[18] Products were not isolated but characterized by ^{1}H and ^{31}P NMR methods, and compared to literature values (see the Supporting Information).