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Strong Electronic and Counterion Effects on Geminal Digold Formation and Reactivity as Revealed by Gold(I)–Aryl Model Complexes**

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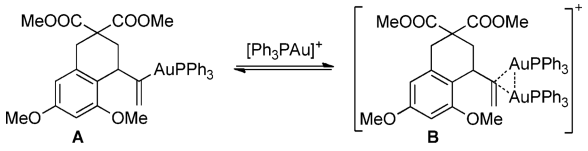
Keywords

aurophilicity; geminal diauration; gold complexes; protodemetalation

Gold(I) cations have emerged as efficient and often times uniquely effective catalysts for the formation of C–X (X=C, O, N) bonds.[1] Its use as a soft **π**-acid for the activation of C–C multiple bonds has led to proposed intermediates that include **π**–gold, Au–vinyl, Au–alkyl, and Au–carbene structures.[2] In many instances a transient Au–C **σ**-bond is converted into a C–E bond through its reaction with an E^+ electrophile.[3] Recently, we provided evidence that the intramolecular hydroarylation of allenes proceeded through two different gold–vinyl intermediates, one mononuclear (**A**), and one dinuclear (**B**), with the latter acting as the catalyst's resting state. The digold structure was proposed to result from the reaction of LAu^+ with monogold–vinyl A [Eq. (1)].[4]



(1)

The proposal that the digold resting state **B** contained a Au_2C three-center-two-electron bond, which was additionally stabilized by an aurophilic closed shell interaction of significant strength (5–10 kcal mol^{-1}),[5] was based on the aromatic digold compounds reported by Schmidbaur, Grandberg, and Nesmeyanov and confirmed by recent digold vinyl complexes from Fürstner et al. (Scheme 1).[6] With the exception of above mentioned studies little is known about digold intermediates in gold catalysis. Grandberg, Nesmeyanov, and Schmidbaur have reported their synthesis and structure, but their properties in catalytic applications has yet to be articulated. Since digold formation consumes an otherwise catalytically active $\{LAu\}^+$ unit and the digold intermediate was shown to be less reactive

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towards H^+, one might reasonably surmise that digold formation is inhibitory to catalysis.[7] These considerations prompted studies to experimentally delineate and quantify those factors influencing digold formation. As Fürstner et al. noted, the availability of stable digold vinyl complexes with a Au_2C three-center-two-electron bond is limited due to their tendency to decompose through a homocoupling pathway.[8] To bypass this situation we instead turned to readily available and easily modifiable aryl complexes as models for catalytically relevant vinyl complexes. This approach has enabled us to determine the affinity of $\{R_3PAu\}^+$ to R_3PAu–aryl compounds and to explore the influence of counterions and Brønsted acids on this equilibrium. These results provide a framework from which to predict and rationalize the equivalent reactivity of gold–vinyl intermediates in catalysis.

Ph_3PAu–aryl complexes (**1**) were synthesized from [Ph_3PAuCl] and the corresponding Grignard reagents, and were found to crystallize either in a monomeric form or with an unsupported Au–Au interaction that pairs the compounds.[9–12] Solutions of these compounds were stable to decomposition in CD_2Cl_2 over a minimum of 12 h.

The digold(I)–aryl complexes were available through a slight variation of the Grandberg–Nesmeyanov synthesis of geminally diaurated ferrocenyl complexes (Scheme 1).[6c,10] Addition of diethyl ether to a 0.8:1 solid mixture of [$Ph_3PAuNTf_2$] (**3a**)[13] and [Ph_3PAuAr] at −78 °C led to precipitation of the desired [$(Ph_3PAu)_2Ar^+$][NTf_2^-] salt [Eq. (2)]. This procedure could be applied to the synthesis of a variety of gold aryl complexes. In two cases single crystals of sufficient quality for X-ray analysis were obtained to confirm atom connectivity, though twinning and disorder did not allow an analysis of metrical parameters.[14] In general, digold compounds were stable in their precipitated state but decomposed slowly in CD_2Cl_2 solution.[6a, 8] Alternatively digold–aryl complexes could also be generated by the addition of **3a** to a solution of monogold **1**.

$$\underset{\mathbf{1}}{[Ph_3PAuAr]} + \underset{\mathbf{3a}}{[Ph_3PAuNTf_2]} \xrightarrow[-78\ ^\circ C]{\text{Addition of } Et_2O} \underset{\mathbf{2}\cdot NTf_2}{[(Ph_3PAu)_2Ar]NTf_2} \qquad (2)$$

1 equivalent of **3a** was shown to fully convert [(4-MeO-C_6H_4) $AuPPh_3$] (**1a**) to [(4-MeO-C_6H_4)$(AuPPh_3)_2$]NTf_2 (**2a**·NTf_2). This transformation caused the aromatic and OMe resonances of the 4-anisyl fragment to shift downfield in the ^1H NMR spectrum. Substoichiometric quantities of [Ph_3PAu]NTf_2 (**3a**) provided ^1H NMR spectra where the 4-anisyl fragment was time averaged and located between the signals of pure **1a** and **2a**·NTf_2. Since Grandberg and Nesmeyanov previously observed $\{Ph_3PAu\}^+$ exchange with Au–ferrocenyl complexes (Scheme 1), we surmised a similar exchange was occurring to average gold–aryl, gold–cation, and digold spectra.[15] Evidence for fast exchange was provided by ^1H NMR characterization of solutions obtained from the titration of **3a** into **1a**. Incremental additions caused a steady downfield shifting of the 4-anisyl resonances until one equivalent of **3a** had been added, at which point the chemical shift matched pure **2a**·NTf_2 (Figure 1). More than one equivalent of **3a** had no further effect on the chemical shift, suggesting that the equilibrium in Figure 1 strongly favored digold and that no trigold species were formed.[16]

Averaged signals and a linear dependence of chemical shift on added **3a** were also observed for [$PhAuPPh_3$] (1b) and [(*p*-CF_3-C_6H_4)$AuPPh_3$] (**1c**).[17] Since the averaged signals reflect the weighted average of the mono- and digold aryl chemical shifts, it thus provided the means to determine the equilibrium position as a function of structure and reaction variables. This technique was used to measure how counterions and aryl electronic effects influenced the propensity for digold formation.

When 1 equiv of different [Ph_3PAu]Y complexes were added to a solution of [(4-MeO-C_6H_4)$AuPPh_3$] (**1a**), averaged 4-anisyl signals were observed by ^{1}H NMR spectroscopy. The average percentage of **1a** bound as digold was calculated from the measured chemical shifts of the two inequivalent aromatic hydrogen atoms and the methoxy group, and the correlations in Figure 1 with the explicit assumption that the time averaged 4-anisyl shifts in the digold were not sensitive to Y^-.

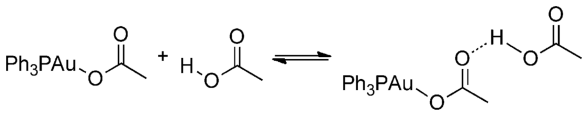
In the case of Y = OAc and OBz, added quantities of [Ph_3PAu]Y to **1a** caused no shifting in the anisyl peaks, suggesting that no digold was formed under these conditions (Table 1). With less binding counterions shifting was observed, allowing equilibrium concentrations of digold to be calculated. In these cases, OONB (ortho-nitrobenzoate) provided 1 ± 1% digold, 12 ± 2% with OPNB (*para*-nitro-benzoate), and 41 ± 1% and 88 ± 1% digold for TFA (trifluoroacetate) and OTs (tosylate), respectively. Complete conversion to the digold form was calculated for the least coordinating NTf_2 (bistriflimide). This trend was reasonably rationalized by the pK_a of the conjugate acids (with the exception of OONB), and suggested that it was strong ion pairing in [Ph_3PAu]Y that inhibited digold formation for the more binding anions. As shown in the final two columns of Table 1, the affinity of [Ph_3PAu]Y to **1b** and **1c** was considerably lower for the less electron-rich aryl ligands, with significant quantities of digold only being observed for the least coordinating anions. This trend supports the notion that the Au_2C three-center-two-electron interaction is electron-deficient, and competes with the counterion.

To determine how the ratio of mono- and digold was affected by concentration, aliquots of CD_2Cl_2 were added to a 1:1 mixture of **1a** and [Ph_3PAu]OTs.[18] As the component concentration was decreased 4.6-fold the percentage of **1a** bound as digold only decreased from 89.2% to 87.5%, which was more muted than expected for a 2:1 stoichiometry, and likely reflects the diminished ion pairing in the more charge-dispersed digold aryl complex compensating for the stoichiometry. In the context of catalysis, this observation suggests that digold formation is not heavily penalized at low catalyst loadings.

With this increased understanding of digold formation, we attempted to study its competing, but essential product yielding step, protodemetalation. To understand this process independent of digold formation the reaction of **1a** with 4 equiv of AcOH was monitored by ^{1}H NMR spectroscopy. Based on data in Table 1 we expected that these conditions would avoid the presence of digold, which should inhibit protodemetalation. Acetic acid was chosen because it enabled pseudo-first order reaction conditions to be established.[19] As expected, a smooth conversion of **1a** to **4a** and [Ph_3PAu]OAc was observed. Unexpected, however, was a steady downfield movement of the 4-anisyl resonances of **1a** as the protodemetallation progressed (Figure 2, ♦).[20] An even larger shift to digold was detected in the reaction of **1a** and 10 equiv of AcOH.[21] Although this observation suggested that digold was being formed during the protodemetalation with AcOH, no digold was detected on mixing **1a** and [Ph_3PAu]OAc in the absence of AcOH (entry 1, Table 1). To probe whether the Dd was due to a build-up of [Ph_3PAu]OAc, the reaction was repeated in the presence of 1 equiv of [Ph_3PAu]OAc. As shown in Figure 2 (●), a near doubling in equilibrium digold was observed.

This behavior suggested that under these reaction conditions, acetate anion was effectively less coordinating. The data suggests that an acid/base interaction between AcOH and [R_3PAu]OAc [Eq. (3)] creates a homoconjugate acid/base pair which causes the acetate to become less coordinating.[22] Since the amount of digold was highly sensitive to the donor properties of the counterion (Table 1), such an interaction could reduce the degree of contact ion pairing.[23] Titration of AcOH into [Ph_3PAu]OAc, however, lead to only a tiny shift in the phosphine resonance in the ^{31}P NMR spectrum, suggesting that the thermodynamic

effect was small, though the kinetic effect could be larger. Similar experiments with alternative counterions confirmed the generality of the observation as all cases (Y = OBz, OPNB, OONB, TFA, and OTs) led to significant downfield shifts consistent with an increase in digold formation.[24]



(3)

When the kinetics of protodemetalation for these latter experiments was determined, it became clear that the gold salts also affected the rate of this key catalytic step. As shown in Table 2, the effect of added [Ph_3PAu]Y on the kinetics for protodemetalation of **1a** by AcOH depended non-linearly with the coordinating character of the anion. At the extreme of non-coordination, Y = NTf_2, a very low rate was expected, as the digold does not react with AcOH.[4] The increase in rate at intermediate donating ability, however, was unexpected and will require further study.

Our studies have thus established, by using [Ph_3PAuAr] complexes as models for catalytic gold vinyl intermediates, a number of important reactivity principles of relevance to catalytic activity and speciation. 1) electron-rich aryl (and thus vinyl) ligands have a heightened propensity to form less reactive digold structures, 2) digold formation is more favorable for the less coordinating counterions (which is also influenced by Brønsted acids), and 3) exogenous gold salts can affect the rate of fundamental processes like protodemetalation even though they do not appear in the balanced equation. Each of these scenarios are commonly encountered in gold(I) catalysis. For example, point (1) explains why the isolable electron-deficient Hammond vinyl rests (and is isolated) in a monomeric form,[25] while the gold vinyl generated by the hydroarylation of allenes rests (and is isolated) in the digold form. These results additionally illuminate on the challenges of developing highly efficient multi-step catalysts. To maximize substrate activation, one typically aims for the least coordinating anions, and while this almost certainly maximizes the initiation step of a catalytic cycle, point (2) demonstrates that these more activated $[LAu]^+$ ions are also more apt to intercept gold vinyl intermediates and generate more stable, less reactive, digold intermediates (e.g. for protodemetalation). The results reported herein help provide a rationale for the inevitable search for catalysts that balance the competing demands of efficiently circumnavigating a catalytic cycle.

Experimental Section

Reaction conditions were chosen to mimic concentrations and temperatures commonly used in gold(I) catalysis. See the Supporting Information for details.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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18. Concentration of both reagents was 0004 M; see the Supporting Information for details.
19. Protodemetalation of **1c** could not be performed due to overlapping aryl and PPh_3 signals in the ^1H NMR spectrum.
20. A slight downfield shift indicating digold formation was also observed during the protodemetalation of **1b**, but was less pronounced than with **1a**.
21. See the Supporting Information for reaction conditions and tables.
22. An activation of a Brønsted acid by a gold Lewis acid was recently reported: Kanno O, Kuriyama W, Wang ZJ, Toste FD. Angew. Chem. 2011; 123:10093–10096. Angew. Chem. Int. Ed. 2011; 50:9919–9922.
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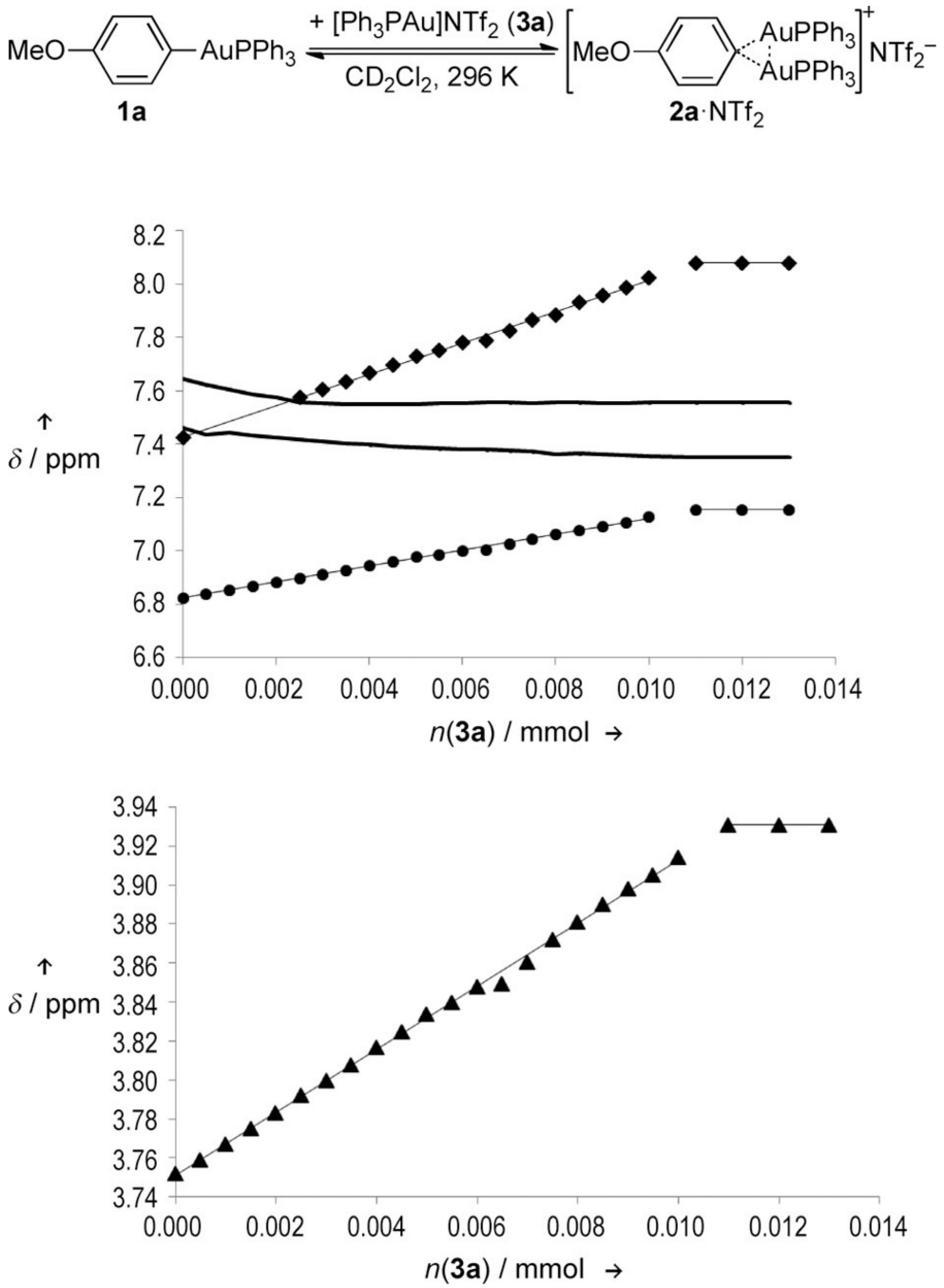
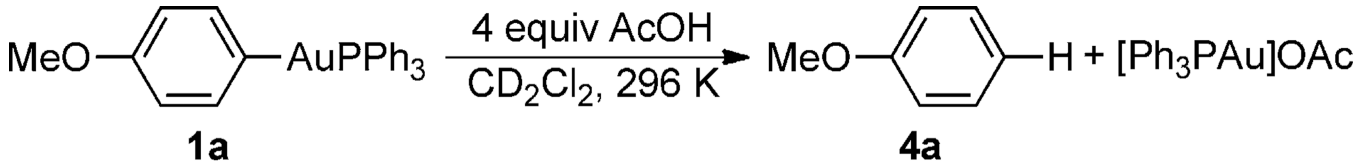


Figure 1.

Addition of aliquots of **3a** to a solution of **1a** caused a linear downfield shifting of the time-averaged ^{1}H signals of **1a** and **2a**·NTf_2. Upper diagram: ♦ *ortho*-H ($y = 58.686\ x + 7.428$, $R^2 = 0.998$), ● *meta*-H ($y = 29.727\ x + 6.824$, $R^2 = 0.998$), —— PPh_3; lower diagram: ▲ *para*-OMe ($y = 16.156\ x + 3.751$, R^2=0.999).



1a **4a**

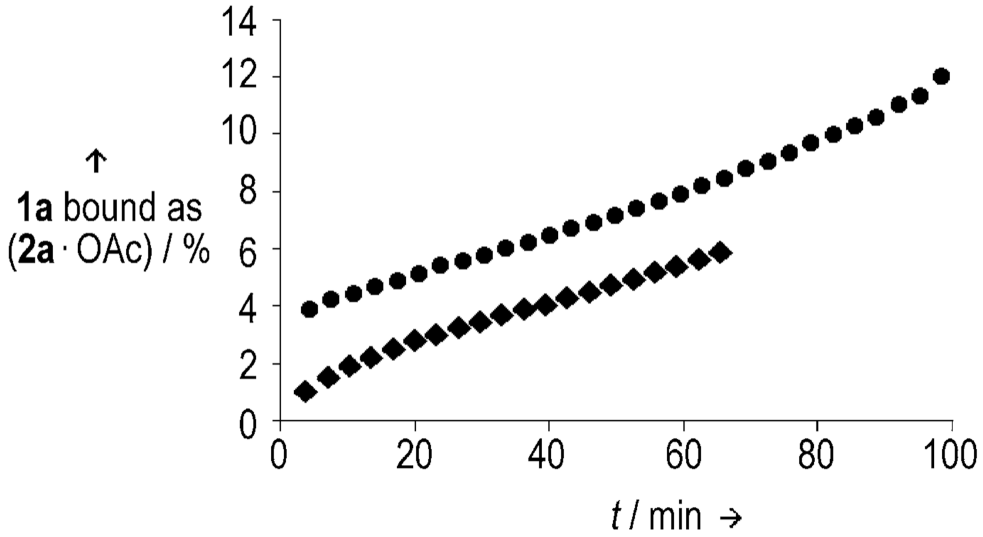
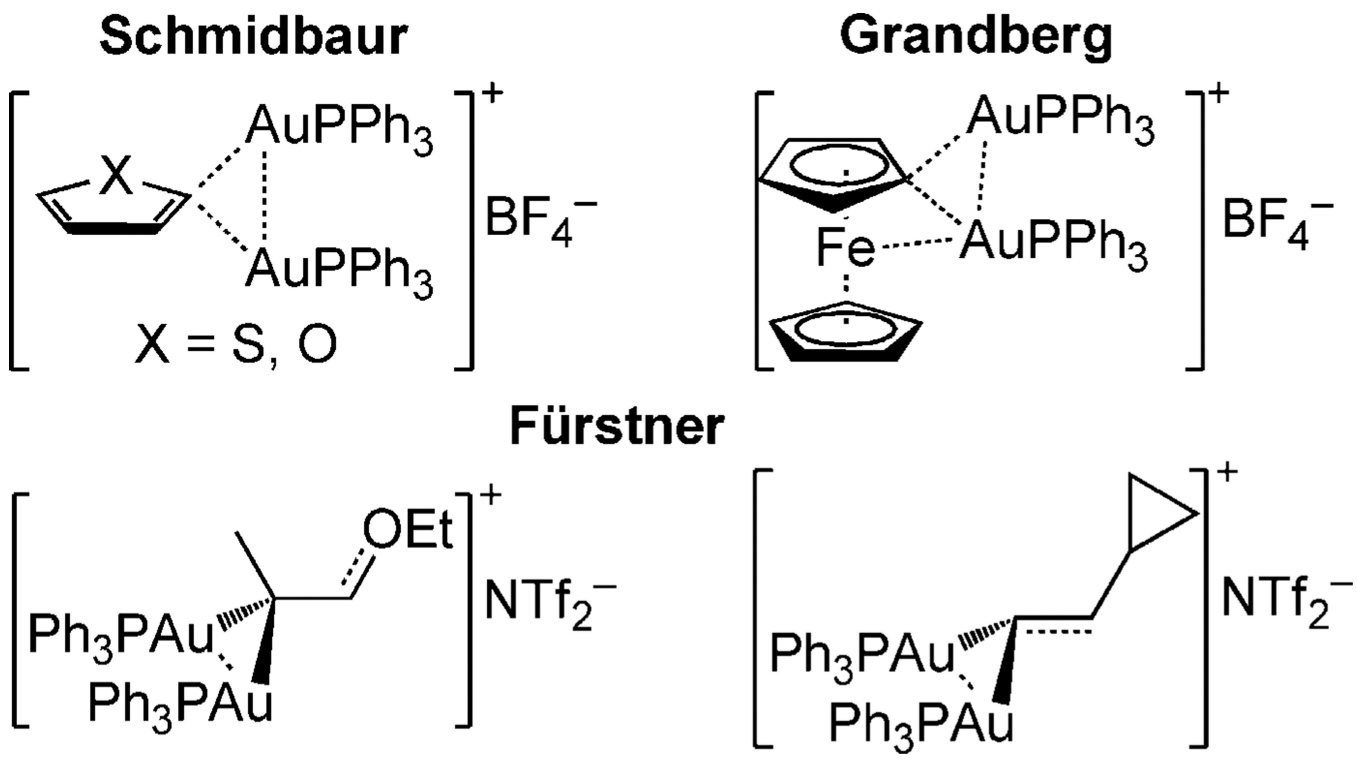


Figure 2.

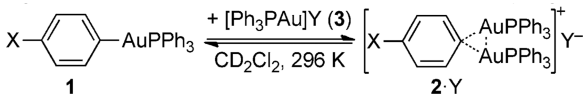
Growth in calculated percentage of **1a** bound as digold **2a**·OAc over the course of the protodemetalation of **1a** with 4 equiv of AcOH (♦). The round data points (●) correspond to the experiment with an additional equivalent of $[Ph_3PAu]OAc$.



Scheme 1.
Selected examples of digold–aryl and digold–vinyl complexes.

Table 1

Digold equilibrium percentages determined by the averaged proton signal method as a function of counterion and aryl ligand.

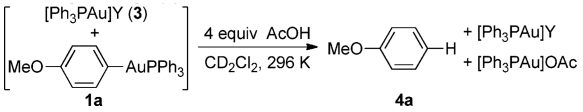


Entry	Y	(2·Y) [%][a] X=OCH3 (1a)	X=H (1b)	X=CF3 (1c)
1	OAc	0 ± 1	0 ± 1	0 ± 1
2	OBz	0 ± 1	0 ± 1	0 ± 1
3	OPNB	12 ± 2	6 ± 1	0 ± 1
4	OONB	1 ± 1	0 ± 1	0 ± 1
5	TFA	41 ± 1	8 ± 2	0 ± 1
6	OTs	88 ± 1	73 ± 1	6 ± 1
7	NTf_2	100 ± 1	100 ± 1	93 ± 3

[a]Determined by averaged ^{1}H NMR signals of 0.1 mL of **1** (0.01 M), 0.1 mL of 3 (0.01 M), 0.3 mL of CD_2Cl_2.

Table 2

Rate of protodemetalation of **1a** with AcOH in the presence of different [Ph_3PAu]Y (**3**) complexes.



Entry	Y	k_{rel}[c]
1	none[a]	1.0
2	OAc[b]	0.9
3	OBz[b]	1.6
4	OPNB[b]	≥2.5
5	OONB[b]	≥3.4
6	TFA[b]	≥3.0
7	OTs[b]	0.4
8	NTf_2[b]	0.0[d]

[a] 0.1 mL of **1a** (0.01 M), 0.1 mL of CD_2Cl_2, 0.1 mL of internal standard mesitylene (0.025 M), 0.2 mL of AcOH (0.02 M).

[b] 0.1 mL of **1a** (0.01 M), 0.1 mL of 3 (0.01 M), 0.1 mL of internal standard mesitylene (0.025 M), 0.2 mL of AcOH (0.02 M).

[c] For determination of k_{rel} see the Supporting Information.

[d] In this reaction, all of **1a** was bound as digold and no conversion to **4a** was observed for 1 h.