ACS Catalysis

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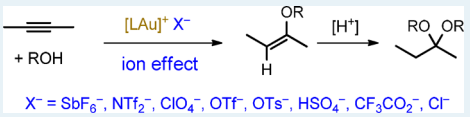
Explanation of Counterion Effects in Gold(I)-Catalyzed Hydroalkoxylation of Alkynes

Alexander Zhdanko* and Martin E. Maier*

Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle 18, 72076 Tübingen, Germany

Supporting Information

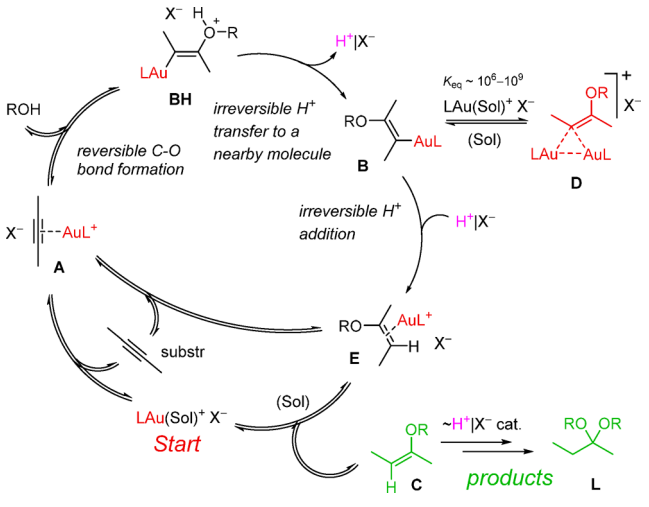
ABSTRACT: Using gold(I)-catalyzed hydroalkoxylation of alkynes as a model reaction with a well-known mechanism, a systematic experimental study was conducted to disclose the influence of the counterion X^- of a gold catalyst $LAuNCMe^+$ X^- on every step of the catalytic cycle. The overall ion effect is determined as a superposition of several effects, operating on different steps of the reaction mechanism. All effects were explained from a position of hydrogen bonding, coordination chemistry at gold, and affinity for a proton.



KEYWORDS: *gold catalysis, hydroalkoxylation, counterion effect, kinetics, reaction mechanism*

Hydroalkoxylation of alkynes catalyzed by cationic gold(I) complexes was first described 15 years ago at the dawn of the era of homogeneous gold catalysis.[1,2] However, only recently has the mechanism of this fundamental reaction been systematically investigated using experimental approaches, yielding a high level of understanding of the process (Scheme 1).[3] Thus, the reaction starts from reversible *anti* addition of an

Scheme 1. Mechanism of Gold-Catalyzed Hydroalkoxylation



alcohol onto alkyne gold π-complex **A** to form a highly unstable adduct **BH** that quickly undergoes proton transfer to give vinyl gold **B**. Subsequently, **B** undergoes protonation by the previously released acid to form enol ether π-complex **E** that participates in global ligand exchange equilibrium, releasing product **C**. Competitively, **B** undergoes reversible addition of a second LAu^+ unit to form diaurated species **D**. Depending on the level of acidity in the system, **C** may stay as the end product or further transform into acetal **L** by means of a classical Brönsted acid catalysis. All cationic species are accompanied by a counterion X^-.

Cationic gold(I) complexes of general composition $[LAu(Sol)]^+$ X^- are the most frequently used type of catalysts for gold-mediated transformations of alkynes. They are typically applied with various anions (most often X^- = SbF_6^-, NTf_2^-, and OTf^-). The dependence of a reaction from the counterion (the counterion effect) is well-documented in many papers on gold catalysis methodology, but the mechanism by which the anion actually influences the process is still largely unknown.[4] An impressive example, highlighting the importance of a counterion, has been reported by Toste and co-workers. They showed that high enantioselectivity in gold-catalyzed reactions can be simply achieved using a catalyst with a chiral counterion.[5] Specific investigations into the counterion effects are scarce and mostly based on theoretical methods.[6] A nuclear magnetic resonance (NMR) investigation revealed that the prevalent position of a counterion within ion pairs is dependent on the ligands at gold.[7,8] This finding suggests that the strength of the ion effect may be dependent on the ligand at gold. In particular, the counterion effect has never been explained properly for hydroalkoxylation.[1b] Herein, using gold(I)-catalyzed hydroalkoxylation of alkynes as a model reaction with a well-established mechanism, we provide a systematic experimental study to disclose the role of counterion X^- on every step of the reaction mechanism.

To understand the ion effect, we conducted kinetic studies by NMR. In every such experiment, we monitored the disappearance of the substrate with time, the presence of organic intermediates, and the development of final products. Besides this, particular attention was given to observations of catalytic organogold intermediates (resting states) *in situ* during the whole process. Because of space limitations, complete

Received: April 4, 2014
Revised: July 9, 2014
Published: July 10, 2014

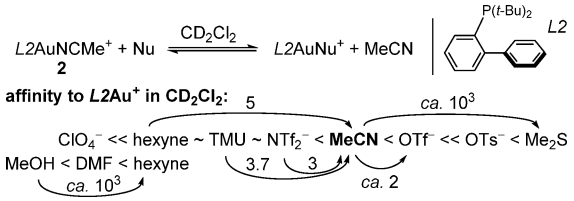
   dx.doi.org/10.1021/cs500446d | ACS Catal. 2014, 4, 2770−2775

tables, diagrams, explanations at a more narrow level, and spectra are given in the Supporting Information.

Gold-catalyzed hydroalkoxylation can be performed in a wide range of solvents: aprotic ones (CH_2Cl_2, toluene, and dioxane) or an alcohol (MeOH). The occurrence and strength of the ion effect will thus depend on the nature of the solvent. We performed the whole study in CD_2Cl_2 because ion pair effects are quite pronounced in this solvent because of its weak solvation ability.[9] At the same time, ionic components are sufficiently soluble in this solvent. Thereafter, we performed a control study in CD_3OD to demonstrate that all ion effects disappear in this highly polar solvent with strong solvation ability. As starting materials for the preparation of catalytic systems, we used $[Ph_3PAuNCMe]^+$ SbF_6^- (catalyst **1**) and $[L2AuNCMe]^+$ SbF_6^- (catalyst **2**) [*L2* = *o*-(di-*tert*-butylphosphino)-biphenyl].

Prior to discussion of the ion effects, we studied simple ligand exchange and proton exchange processes. This was done as in our previous publication on coordination chemistry.[10] Thus, we performed reactions of **2** with various anions as well as some neutral molecules in CD_2Cl_2. Upon direct NMR observation, we have built affinity scales for $L2Au^+$ (Scheme 2).

Scheme 2. Ligand Exchange Equilibria and Affinity Scale in CD_2Cl_2

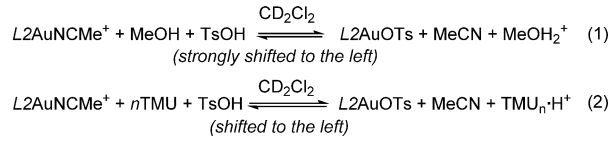


These experiments are described in the Supporting Information. According to this scheme, anions SbF_6^- and ClO_4^- can be regarded as very little-coordinating to LAu^+, NTf_2^- and OTf^- as weakly nucleophilic, and OTs^- as a rather nucleophilic anion. Thus, displacement of OTs^- from LAuOTs by an alkyne substrate is difficult, preventing formation of π-alkyne complex **A**, the necessary intermediate of the catalytic cycle. We can conclude that application of a more nucleophilic anion like carboxylate will further prevent formation of **A** (generally in an aprotic solvent like CD_2Cl_2).

To approximately determine a binding affinity scale to H^+ for our study in CD_2Cl_2, we conducted experiments with TfOH, the strongest acid available to us in a pure state. As described for benzene and $CDCl_3$ in the literature,[11] simple addition of a small amount TfOH (~1 mg) to CD_2Cl_2 upon making an NMR sample caused immediate formation of an emulsion, which is ascribed to protonation of residual water in the solvent. The ^1H and ^{19}F NMR spectra of the emulsion showed several signals. To prepare a clear anhydrous solution of TfOH, a larger amount of the acid (~50 mg) was mixed with CD_2Cl_2 (~0.8 mL) and allowed to settle. The clear CD_2Cl_2 phase was taken for analysis. An NMR spectrum of this solution showed a single ^{19}F resonance at −76.41 ppm and a single ^1H resonance at 9.21 ppm. Addition of a small amount of CF_3CH_2OH allowed us to establish the ratio of H^+ and OTf^- residues through a combination of ^1H and ^{19}F NMR spectra and to confirm the existence of at least 95% pure, water free TfOH in the initial binary TfOH/CD_2Cl_2 solution. Presumably, TfOH exists in such a solution as an undissociated molecule, waiting to protonate anything that would be added. Thus, addition of MeOH to the clear extract immediately gives a heavy emulsion, which is ascribed to the formation of a less soluble $ROH_2^+|OTf^-$ salt, forming the new polar liquid phase.

On the other hand, addition of MeOH (6.5 equiv) to a slight emulsion prepared by addition of TfOH (<1 mg) to an undried CD_2Cl_2 sample (0.5 mL) gives a clear solution. Obviously, the initial polar phase was dissolved with the help of excess MeOH. The ^{19}F resonance in this solution appears at −79.07 ppm, which now corresponds to the OTf^- ion (see the Supporting Information for more details), confirming dissociation of TfOH by MeOH. Because $HSbF_6$, $HNTf_2$, $HClO_4$, and TfOH are all regarded as super acids,[12] they all will protonate an alcohol so the proton will exist in solution as an $ROH_2^+|X^-$ oxonium ion pair. In contrast, TsOH was shown not to dissociate in CD_2Cl_2 even in the presence of MeOH. Interestingly, even $[L2AuNCMe]^+$ does not trigger dissociation of TsOH in the presence of MeOH (neutral [LAuOTs] would be formed), but partial dissociation occurs in the presence of TMU (tetramethylurea) as a weak base (eqs 1 and 2). The last fact points to the higher strength of $TMU{\cdot}H^+$ versus that of TsOH as an acid in CD_2Cl_2. The proton affinity scale was built upon these observations (Scheme 3).

Scheme 3. Proton Exchange Equilibria and Affinity Scale in CD_2Cl_2



The aforementioned basic observations should help us to unambiguously determine the origin of the counterion effect. Because the counterion effect may apply at every step that includes ionic species, the overall effect on the entire reaction may be difficult to understand because of the superposition of the effects. It is therefore important to study the counterion effect under properly selected conditions, excluding the situation with multiple effects. It is convenient first to describe and explain the effects for a reaction in which the transition from **A** to **B** is rate-limiting, because for such a reaction type there is no need to consider diaurated species **D** and protodeauration. A suitable case is the reaction of hexyne **S1** with MeOH catalyzed by **2** ($[L2AuNCMe]^+$ SbF_6^-) in CD_2Cl_2, which was previously shown to fit these requirements.[3b] Now this reaction was conducted in the presence of various salts and neutral additives (Scheme 4). In all runs, except entries 8 and 9 (OTs^-), gold predominantly existed as $[L2Au(\mathbf{S1})]^+$ (**A1**) (^{31}P, δ 65.6 ppm) and the reactions exhibited the apparent "half-order" kinetics in substrate. Obviously, all additives in these cases, being very weak ligands, did not lead to substantial changes in the global equilibrium. This circumstance allows us to assign the observed overall effect to a single effect acting exclusively at the stage of alcohol addition on complex **A1**. However, in the two experiments with OTs^-, gold predominantly existed as [*L2*AuOTs] (^{31}P, δ 56.6 ppm). This is obviously because of the higher binding affinity of OTs^- for gold, which now shifts the global equilibrium entirely to [*L2*AuOTs], establishing an [*L2*AuOTs]/OTs^- auro buffer system. Correspondingly, the kinetics of the reaction entirely

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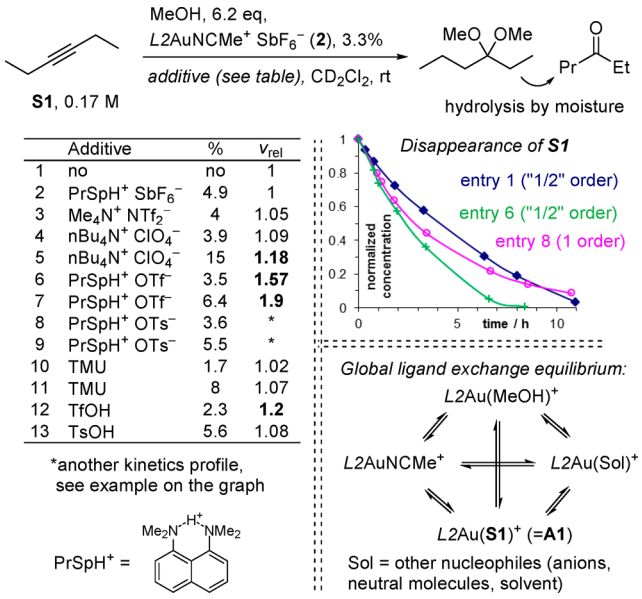
Scheme 4. Ion Effects in CD_2Cl_2



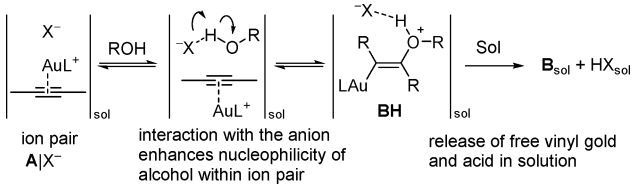
	Additive	%	v_{rel}
1	no	no	1
2	$PrSpH^+ SbF_6^-$	4.9	1
3	$Me_4N^+ NTf_2^-$	4	1.05
4	$nBu_4N^+ ClO_4^-$	3.9	1.09
5	$nBu_4N^+ ClO_4^-$	15	**1.18**
6	$PrSpH^+ OTf^-$	3.5	**1.57**
7	$PrSpH^+ OTf^-$	6.4	**1.9**
8	$PrSpH^+ OTs^-$	3.6	*
9	$PrSpH^+ OTs^-$	5.5	*
10	TMU	1.7	1.02
11	TMU	8	1.07
12	TfOH	2.3	**1.2**
13	TsOH	5.6	1.08

*another kinetics profile, see example on the graph

changed to pure first-order in substrate. In this case, the overall effect of OTs^- is not directly comparable to the effects of the other additives, because it rather consists of two components: the effect on alcohol addition and the effect on binding of gold.

On the basis of the relative reaction rates shown in Scheme 4, we can conclude that the reactivity of the **A**|X^- ion pair toward alcohol addition increases in the following order: SbF_6^- < NTf_2^- < ClO_4^- < OTf^- < OTs^- (following the basicity of anions). This suggests that the origin of this effect is in activation of the incoming MeOH molecule toward addition to **A** within the **A**|X^- ion pair by means of hydrogen bonding (Scheme 5). Observation of positive effects in the presence of

Scheme 5. Explanation of the Counterion Effect for a Reaction with the Rate-Limiting Step Being That from A to B



neutral hydrogen bond acceptors like TMU (entries 10 and 11) and DMF (our previous study)[3b] in this reaction supports this hypothesis. Correspondingly, this effect increases with the ability of the anion to act as a hydrogen bond acceptor. In case of OTs^-, the ion effect should be the strongest, as OTs^- is the most nucleophilic and basic among the other anions tested, but here the strong ion pair effect is mostly overridden by the binding of gold to give the inert neutral species *L*2AuOTs, preventing the formation of **A1** (eq 3). Correspondingly, the rate of reaction in the presence of OTs^- (entry 8) is comparable to the rate of the control reaction (entry 1).

$$\underset{\mathbf{A1}}{[L2\mathrm{Au}(\mathbf{S1})]^+} + \mathrm{OTs}^- \underset{\text{shifted to the right}}{\overset{K_{eq}\sim 10^2-10^3}{\rightleftharpoons}} \mathbf{S1} + [L2\mathrm{AuOTs}] \quad (3)$$

In some cases, a neutral additive may also cause an ion effect if it is, for example, a strong acid. Thus, use of TfOH caused a positive effect (entry 12), which is ascribed to the ion effect of OTf^- arising upon complete dissociation of this acid in the reaction medium (eq 4). Addition of TsOH also caused a

$$\mathrm{TfOH} + \mathrm{MeOH} \longrightarrow \mathrm{MeOH_2}^+ + \mathrm{OTf}^- \quad (4)$$

causes positive ion effect

positive effect (entry 13), but this effect is rather small because the acid stays predominantly undissociated. These two examples demonstrate that care should be taken when considering assignment of an effect. The conclusion is reached upon consideration of several experimental facts (knowledge of the rate-limiting step, resting state of the catalyst, reaction kinetics, and binding affinity of the relevant species for H^+ and LAu^+).

Our reasoning about the origin of the counterion effect was further corroborated in the reaction of pentynol **S2** catalyzed by auro buffer $[L2\mathrm{AuSMe_2}]^+/\mathrm{Me_2S}$ in CD_2Cl_2 in the presence of MeOH. We previously established this reaction to be first-order in substrate, first-order in gold, and minus-first-order in Me_2S.[3b] Under these conditions, the transition from **A** to **B** is rate-limiting and there is no need to consider diaurated species and protonolysis.[3b] Use of the auro buffer system ensures an easy functional dependence of [**A**] from the starting inputs, which is determined from eq 5.

$$\mathbf{S2} + [\mathrm{LAuSMe_2}]^+\mathrm{X}^- \underset{\mathrm{CD_2Cl_2}}{\overset{K_{eq}\sim 10^{-4}}{\rightleftharpoons}} \mathrm{Me_2S} + \underset{\mathbf{A}|\mathrm{X}^-}{[\mathrm{LAu}(\mathbf{S2})]^+\mathrm{X}^-} \quad (5)$$

Because $[\mathrm{LAuSMe_2}^+] = c_0(\mathrm{LAuSMe_2}^+)$ and $[\mathrm{Me_2S}] = c_0(\mathrm{Me_2S})$ during the entire reaction course, the following expression for [**A**] is obtained (eq 6).

$$[\mathbf{A}|\mathrm{X}^-] = \frac{Kc_0(\mathrm{LAuSMe_2}^+)[\mathbf{S2}]}{c_0(\mathrm{Me_2S})} \quad (6)$$

Taking this expression into the rate law defined by eq 7 gives a simple overall reaction rate expression (eq 8).

$$\mathbf{A}|\mathrm{X}^- \underset{\text{rate-limiting}}{\overset{k}{\longrightarrow}} \mathbf{B} \rightarrow \text{products} \quad (7)$$

$$\frac{\mathrm{d}[\mathbf{S2}]}{\mathrm{d}t} = -k[\mathbf{A}|\mathrm{X}^-] = -k\frac{Kc_0(\mathrm{LAuSMe_2}^+)[\mathbf{S2}]}{c_0(\mathrm{Me_2S})} = -k_{\mathrm{eff}}[\mathbf{S2}] \quad (8)$$

To study the ion effect, this reaction was conducted in the presence of various salts but at constant starting concentrations of all other inputs (Scheme 6). Here again, all the reactions were pure first-order in substrate; the resting state was solely $[L2\mathrm{AuSMe_2}]^+$, and the positive ion effect increased in the same order: SbF_6^- < NTf_2^- < ClO_4^- < OTf^- < OTs^-. Notably, the ion effect in this reaction was much more pronounced than the effect in the reaction of **S1** described above. Thus, addition of 2.9% OTs^- led to a 33-fold increase in the reaction rate! Because this reaction occurs through a ligand exchange equilibrium (eq 5), we hypothesized that an additional positive effect was provided by shifting this equilibrium toward **A** because of the presence of the OH group already in the

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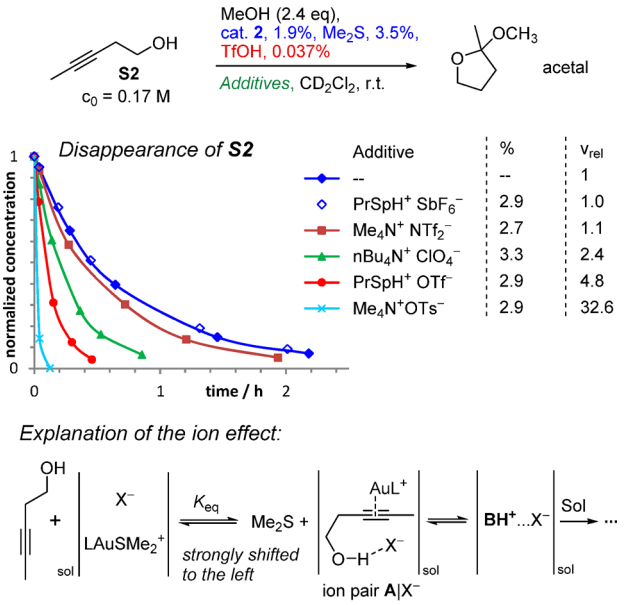
Scheme 6. Ion Effects in CD_2Cl_2

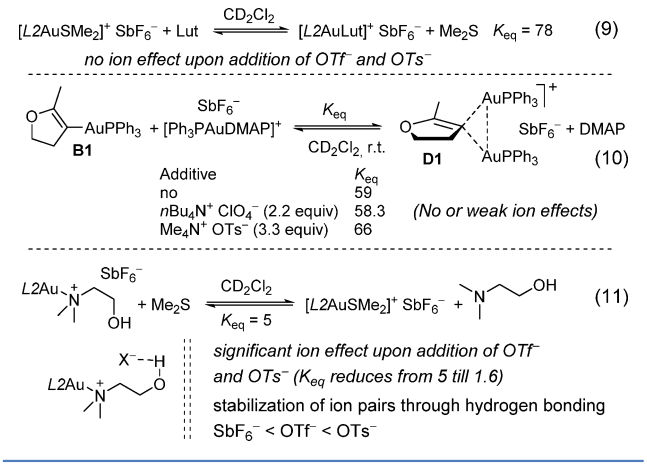


interaction with X^- enhances *both* K_{eq} and nucleophilicity of the alcohol in the ion pair **A**|X^-.

molecule available for hydrogen bonding within the internal ion pair.

To confirm this hypothesis, we conducted a model study to determine if counterions may influence simple ligand exchange equilibria between various $[LAuNu]^+$ cationic species. Thus, model equilibria (eqs 9 and 10, in which Lut = 2,6-lutidine) were found to be rather independent, but the equilibrium with dimethylaminoethanol (eq 11) appeared to be obviously dependent on the counterion (Scheme 7). This result nicely

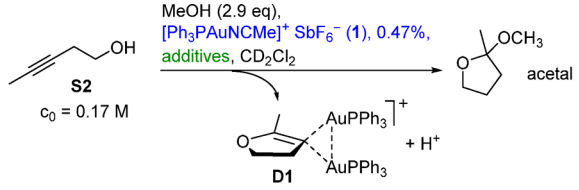
Scheme 7. Ion Effects on Ligand Exchange Equilibria in CD_2Cl_2

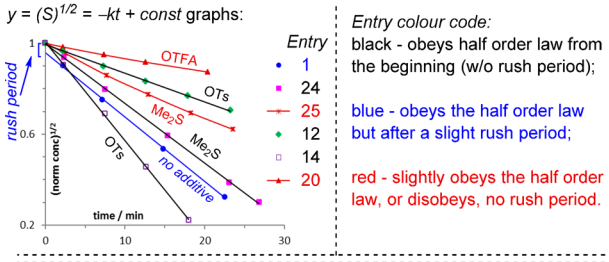


demonstrates that simple equilibria should be generally unaffected by the counterion unless some specific interaction becomes possible within the ion pairs. Presumably, the presence of a hydrogen bond donor (OH group) in dimethylaminoethanol does indeed provide substantial stabilization of ion pairs increasingly as the basicity of the counterion increases (eq 11). We can conclude that the equilibrium (eq 5) must also depend on the counterion (although it is always shifted to the left). It becomes clear that the strong counterion effect in the reaction of Scheme 6 consists of two cumulative effects: enhanced formation of **A** by stabilization of the **A**|X^- ion pair through hydrogen bonding and, at the same time, enhanced reactivity of the alcohol toward the intramolecular attack (Scheme 6, bottom).

With these explanations in hand, we are ready to explain the ion effects for a more complicated system, a reaction accompanied by the complete formation of diaurated species. A suitable reaction is the cyclization of pentynol **S2** catalyzed by **1** ($[Ph_3PAuNCMe]^+$ SbF_6^-) in CD_2Cl_2 in the presence of MeOH. As shown in our previous work, this reaction is characterized by immediate and complete formation of the off-cycle diaurated species **D1**, correspondingly releasing an equal amount of H^+.[3b] The overall reaction is half-order in substrate, half-order in **D1**, and half-order in H^+ (being always dependent on acidity regardless of whether protodeauration is the rate-limiting step of the catalytic cycle).[3b] Therefore, not only the aforementioned ion effects but also the effects associated with the reactivity of H^+ are expected here. In the work presented here, this reaction was repeated in the presence of various salts and neutral additives (Scheme 8). Rather in contrast with the

Scheme 8. Ion Effects in CD_2Cl_2





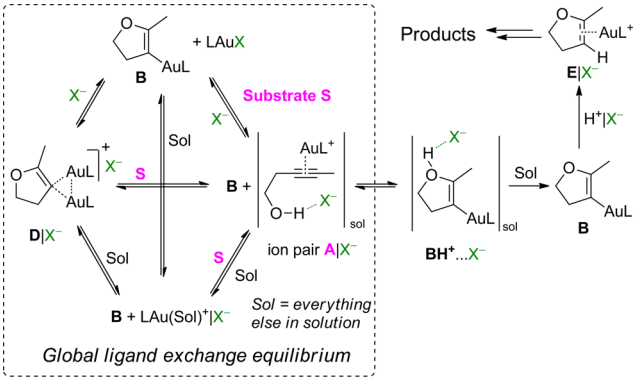
	Additive	%	v_{rel}
1	no	no	1
2	$PrSpH^+$ SbF_6^-	0.53	0.95
3	Me_4N^+ NTf_2^-	0.55	0.9
4	nBu_4N^+ ClO_4^-	0.90	0.78
5	"	1.16	0.84
6	"	2	0.98
7	"	2.17	0.86
8	$PrSpH^+$ OTf^-	0.35	0.67
9	"	0.4	0.81
10	"	0.42	0.77
11	"	2.42	0.87
12	$PrSpH^+$ OTs^-	0.24	0.43
13	"	0.54	0.99
14	"	1.1	1.48
15	"	2.07	1.58
16	$PrSpH^+$ OMs^-	0.2	0.37
17	"	0.8	1.00
18	"	1.6	1.21
19	nBu_4N^+ HSO_4^-	0.9	0.97
20	$PrSpH^+$ $OTFA^-$	0.33	0.20
21	"	0.67	0.24

	Additive	%	v_{rel}
22	$ArCO_2H$[a]	1	0.93
23	Me_2S	0.08	1.02
24	"	0.11	0.90
25	"	0.34	0.82
26	"	0.57	0.58
27	"	0.8	0.55
28	MeOH	(3)[b]	1
29	"	(3.1)[b]	1
30	"	(4.1)[b]	1.03
31	"	(7.1)[b]	0.93
32	"	(8.6)[b]	0.9
33	"	(12)[b]	0.9
34	TMU	2	0.43
35	"	7.9	0.32
36	DMF	2.8	0.77
37	"	4.1	0.68
38	PhOH	(7.4)[c]	0.63

[a] 4-nitrobenzoic acid,
[b] total amount of MeOH, equiv
[c] amount of PhOH, equiv

dx.doi.org/10.1021/cs500446d | ACS Catal. 2014, 4, 2770−2775

previous reactions, weak negative effects were noted here, increasing in the following order: SbF_6^- < NTf_2^- < ClO_4^- < OTf^- (Scheme 8, entries 1−11). This indicates that the positive ion effect operating at the alcohol addition stage was overridden by some negative effect. The origin of the negative part is definitely not associated with a change in the equilibrium toward **A** [see the global ligand exchange equilibrium in Figure 1 (because, as we know from the previous paragraph, this effect



General ion effects:

1) hydrogen bonding of ROH to X^- will enhance every equilibrium with alkynol **S** to the side of **A**. Besides that, there is no ion effect on any simple ligand exchange equilibriums (not to confuse with binding of LAu^+ by X^- to form LAuX);

2) nucleophilicity of X^- enhances formation of LAuX (which should be avoided)

3) hydrogen bonding of ROH to X^- will enhance reactivity of **A** towards alcohol addition (valid for intra- and intermolecular alcohol addition);

4) solvation of H^+ with X^- will decrease reactivity of acid for protodeauration of **B**. Also any other parallel Brönsted acid catalyzed processes will be affected.

Figure 1. General ion effects.

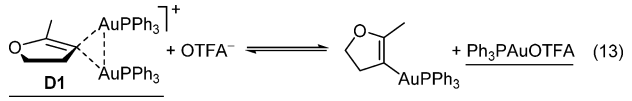
should also be positive)]. Because the overall process was demonstrated to be always dependent on acidity (the aforementioned half-order in H^+), it is now the only possibility to associate the negative effect with the reduced reactivity of the acid. The predominant acid under these conditions will be an $ROH_2^+|X^-$ oxonium ion pair (for X^- = SbF_6^-, NTf_2^-, ClO_4^-, or OTf^-), or neutral acid in the case of TsOH. In the case of the oxonium ion pair, we suggest that the reactivity of this ion pair should decrease as the affinity of the anion for a proton increases (to form a hydrogen bond). In other words, H^+ is better solvated and less reactive in the presence of a more basic anion. This provides a logical explanation for why the more nucleophilic anions led to retardation of the reaction.

The behavior of OTs^- deserves special consideration (entries 12−15). Thus, if OTs^- is present in a small amount [~0.5 equiv to gold (entry 12)], it causes a negative effect. This is associated with quantitative quenching of $MeOH_2^+|X^-$ pairs to form a neutral molecule of TsOH, which is a weak acid in comparison to $MeOH_2^+|X^-$ ion pairs (eq 12).

$$MeOH_2^+ + OTs^- \rightarrow TsOH + MeOH \quad (12)$$

Therefore, as all $MeOH_2^+$ is titrated, there is no more OTs^- left in solution, and the catalytic system is equivalent to **D1**|SbF_6^- + TsOH in a 1:1 ratio. Next, if more OTs^- is added, the overall effect becomes positive (entries 13−15). Now an excess of OTs^- is present in solution (together with neutral TsOH). As we already know, OTs^- possesses a huge positive effect, which now overrides the negative effect of the reduced acidity. The same explanations apply for OMs^- and HSO_4^- (entries 16−18 and 19, respectively).

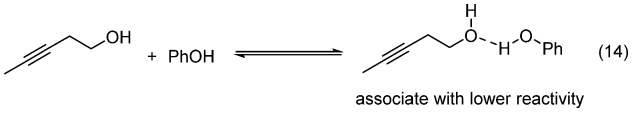
Application of a more basic $OTFA^-$ anion causes a substantial negative effect (entries 20 and 21), which is associated with its higher affinity for both gold and a proton. It binds a proton to form a weak acid TFA, and its high binding affinity for gold inhibits the reaction so that even **D1** is not completely formed, leaving the rest of gold to stay as $Ph_3PAuOTFA$ (eq 13). A similar equilibrium accounts for the



(13)

decrease in rate upon addition of neutral nucleophile Me_2S [to increasingly form $[Ph_3PAuSMe_2]^+$ as the amount of Me_2S increases (entries 23−27)]. We can conclude that highly nucleophilic anions are not beneficial for gold catalysis even though they would exhibit a high level of activation of the alcohol toward addition into the **A**|X^- ion pair simply because the ligand exchange equilibrium for forming this pair is too small.

Like anions, neutral weak bases TMU and DMF also exhibited a substantial negative effect (entries 34−37). Because they are known to exhibit a positive effect on the alcohol addition step,[3b] the negative effect associated with their basicity obviously overrides the positive effect. MeOH exhibited no notable effect, which suggests that positive and negative effects were equal (entries 28−33). Addition of a hydrogen bond donor PhOH (entry 38) caused a negative effect, which is associated with alcohol deactivation (eq 14), as demonstrated in our previous study.[3b]



(14)

In summary, the overall effect of an inert additive (be it an ionic salt or a neutral compound) is determined as a superposition of effects, which are different on different steps of the reaction mechanism (Figure 1).

To demonstrate that the aforementioned effects indeed are present within contact ion pairs, we conducted a small study in methanol. In this highly polar solvent, the salts would exist as freely solvated separate ions; therefore, most of the effects must disappear. Indeed, we found that catalytic hydroalkoxylation of **S2** in CD_3OD in the presence of catalyst **1** is not influenced by the presence of any weakly coordinating anions [SbF_6^-, NTf_2^-, ClO_4^-, OTf^-, or OTs^- (Supporting Information)]. However, strong inhibition is observed if the anion possesses a higher affinity for LAu^+ (Cl^-) or H^+ ($CF_3CO_2^-$). In the case of Cl^-, the catalyst is stoichiometrically transformed into LAuCl and the catalytic reaction becomes strongly inhibited. In the case of $CF_3CO_2^-$, the catalyst is not inhibited, the diaurated species is still formed, but the whole reaction is inhibited because the active H^+ is bound to form weak acid CF_3CO_2H. This result can be easily generalized: weakly coordinating anions of strong acids (at least TsOH and stronger) will have no influence on gold catalysis in methanol, regardless of whether diaurated species are formed. These anions are weakly aurophilic, and

dx.doi.org/10.1021/cs500446d | ACS Catal. 2014, 4, 2770−2775

their conjugated acids are equally strong in methanol because of complete dissociation, providing equally efficient protodeauration.

In summary, various counterion effects were established in gold(I)-catalyzed hydroalkoxylation of alkynes. By hydrogen bonding with ROH, the counterion X^- facilitates the transition from **A** to **B** within **A**|X^- ion pairs in the following order: SbF_6^- < NTf_2^- < ClO_4^- < OTf^- < OTs^-. However, the use of anions with a higher affinity for gold should be avoided because they disfavor formation of **A**|X^- simply by binding gold into LAuX (provided there are no stronger nucleophiles in the system and no diaurated species formed). We suggest OTf^- to be a good compromise for the majority of cases. Counterions X^- reduce the reactivity of H^+ in the following order: SbF_6^- < NTf_2^- < ClO_4^- < OTf^- < OTs^- (reducing the rate of protodeauration). Counterions X^- negligibly influence (if at all) simple ligand exchange equilibria at cationic gold species, unless there is specific interaction arising within the ion pairs or unless the counterion itself binds the metal to form neutral LAuX species. In summary, the overall ion effect is generally determined as a superposition of (at least) the aforementioned elementary effects.

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental procedures and detailed NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: vinceeero@gmail.com.

*E-mail: martin.e.maier@uni-tuebingen.de.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support by the state of Baden-Württemberg is gratefully acknowledged. We thank Dr. K. Eichele and the Institut für Anorganische Chemie for allowing us to use the NMR spectrometer.

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