# Mechanism of Copper-Catalyzed Hydroalkylation of Alkynes: An Unexpected Role of Dinuclear Copper Complexes

Alison M. Suess,[†] Mycah R. Uehling,[†] Werner Kaminsky, and Gojko Lalic*

Department of Chemistry, University of Washington, Seattle, Washington 98195, United States

Ⓢ *Supporting Information*

ABSTRACT: This article describes a mechanistic study of copper-catalyzed hydroalkylation of terminal alkynes. Relying on the established chemistry of N-heterocyclic carbene copper hydride (NHCCuH) complexes, we previously proposed that the hydroalkylation reaction proceeds by hydrocupration of an alkyne by NHCCuH followed by alkylation of the resulting alkenylcopper intermediate by an alkyl triflate. NHCCuH is regenerated from NHCCuOTf through substitution with CsF

followed by transmetalation with silane. According to this proposal, NHCCuH must react with an alkyne faster than with an alkyl triflate to avoid reduction of the alkyl triflate. However, we have determined that NHCCuH reacts with alkyl triflates significantly faster than with terminal alkynes, strongly suggesting that the previously proposed mechanism is incorrect. Additionally, we have found that NHCCuOTf rapidly traps NHCCuX (X = F, H, alkenyl) complexes to produce $(NHCCu)_2(\mu\text{-}X)(OTf)$ (X = F, H, alkenyl) complexes. In this article, we propose a new mechanism for hydroalkylation of alkynes that features dinuclear $(NHCCu)_2(\mu\text{-}H)(OTf)$ (X = F, H, alkenyl) complexes as key catalytic intermediates. The results of our study establish feasible pathways for the formation of these intermediates, their ability to participate in the elementary steps of the proposed catalytic cycle, and their ability to serve as competent catalysts in the hydroalkylation reaction. We also provide evidence that the unusual reactivity of the dinuclear complexes is responsible for efficient hydroalkylation of alkynes without concomitant side reactions of the highly reactive alkyl triflates.
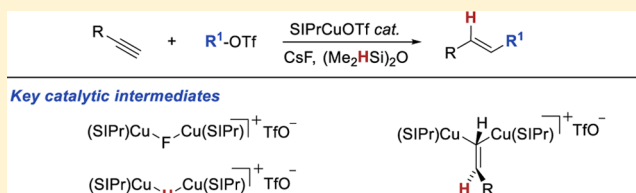
INTRODUCTION

Copper hydride complexes have been known since 1844 when Wurtz described a preparation of copper(I) hydride.[1] However, the modern chemistry of copper hydrides can be traced back to a study of the stability and reactivity of copper hydride complexes, reported by Whitesides in 1969.[2] Soon after, in 1971, the synthesis of the thermally stable and well-characterized $[CuH(PPh_3)]_6$ complex was reported by Osborn and Churchill.[3] The first application of the Osborn complex in organic synthesis followed in 1988, when Stryker published a series of papers describing mild and selective reductions of activated alkenes.[4] The Osborn complex became known in the synthesis community as Stryker's reagent. In 1998, following the initial reports by Brunner,[5] Mori,[6] and Hosomi,[7] Lipshutz introduced the use of silanes as a terminal hydride source in reactions catalyzed by Stryker's reagent.[8] The basic reactivity pattern established by Stryker and Lipshutz led to the development of a wide range of transformations featuring copper hydride complexes as key catalytic intermediates.[9]

Critical for the successful development of copper hydride chemistry was an early realization that properties of the ancillary ligand(s) can have dramatic effects on both the selectivity and reactivity of copper hydride complexes.[10] While excellent results have been obtained using a range of phosphine ligands, the introduction of N-heterocyclic carbene (NHC) ligands has had a particularly significant impact on the chemistry of copper hydride complexes. In 2003, Buchwald

and Sadighi reported the first example of a catalytic reaction in which an NHC copper hydride complex was proposed as a key catalytic intermediate.[11] Since this seminal report, NHC copper hydride complexes have been invoked as intermediates in a wide range of transformations performed in the presence of a silane as a terminal hydride donor. Most common are reduction reactions, such as 1,4-reduction of unsaturated carbonyls,[11] 1,2-reduction of ketones,[12] reduction of carbon dioxide,[13] reduction of propargylic electrophiles to allenes,[14] reduction of alkyl triflates to alkanes,[15] and semireduction of alkynes to alkenes.[16] NHC copper hydride complexes have proven to be particularly important in the development of hydrofunctionalization reactions that are postulated to proceed through the hydrocupration of unsaturated compounds. NHC copper hydride complexes have been invoked as intermediates in hydrocarboxylation,[17] hydroboration,[18] hydrobromination,[19] and hydroalkylation of alkynes.[20]

The first direct evidence for NHC copper(I) hydride complexes invoked as intermediates in these transformations was provided by Sadighi and co-workers in a seminal 2004 paper.[21] They demonstrated the synthesis of the stable and isolable complex IPrCuH (**2**) by transmetalation of the complex IPrCuOt-Bu (**1**) with a silane (Scheme 1, eq 1). They also showed that in the solid state IPrCuH exists as a

Scheme 1. IPrCuH: Formation and Reaction with Alkyne

$Ar = 2,6-(i-Pr)_2C_6H_3$
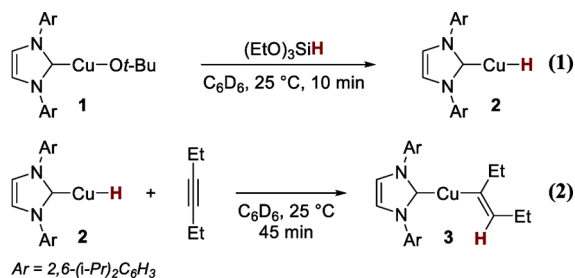
dimer with bridging hydride ligands. However, there are no indications that the dimer is stable in solution, and a recent experimental and theoretical study suggested that the monomeric form is the reactive species in the reduction of ketones.[22] Further stoichiometric studies with IPrCuH provided evidence for the feasibility of key elementary steps of known catalytic reactions. For example, Sadighi demonstrated the ability of IPrCuH to effect facile hydrocupration of alkynes (Scheme 1, eq 2),[21] which has been proposed as the key elementary step in copper-catalyzed hydrofunctionalization reactions. Overall, reactions catalyzed by NHC copper complexes in the presence of a silane have generally been assumed to involve intermediates analogous to the IPrCuH complex originally described by Sadighi.

For the past several years, our group has actively pursued the development of new transformations based on the chemistry of NHC copper hydride complexes.[16b,19,15] As a result of our efforts, we have recently developed the copper-catalyzed hydroalkylation of terminal alkynes.[20] As shown in Scheme 2,

Scheme 2. Copper-Catalyzed Reactions of Alkyl Triflates
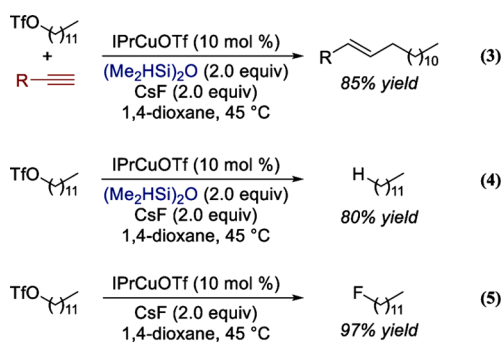
we found that terminal alkynes and alkyl triflates can undergo reductive cross-coupling in the presence of IPrCuOTf as a catalyst, $(Me_2HSi)_2O$ as a hydride donor, and CsF as a turnover reagent (eq 3). Relying on the well-established chemistry of NHCCuH complexes[21] and previous studies of related hydrofunctionalization reactions[16a,b,19] we proposed that the hydroalkylation of terminal alkynes proceeds according to the mechanism shown in Scheme 3. According to this proposal, the hydroalkylation reaction involves (1) the formation of copper hydride complex 2, (2) hydrocupration of the alkyne, and (3) alkylation of an alkenylcopper intermediate (6).

This mechanism raised interesting questions about the selectivity exhibited by IPrCuF and IPrCuH intermediates, considering that the same complexes have also been implicated in two other transformations of alkyl triflates (Scheme 2, eqs 4 and 5).[23,15] Under reaction conditions that are essentially the same as those used in the hydroalkylation reaction, but in the

Scheme 3. Proposed Mechanism of Hydroalkylation
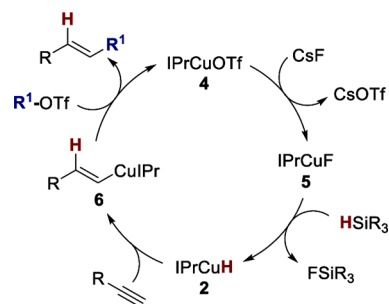
absence of a terminal alkyne, we observe an efficient reduction of the alkyl triflate to an alkane (eq 4).[24] If we omit both the silane and the alkyne from the reaction mixture, we observe facile formation of an alkyl fluoride (eq 5).[25]

Considering the three transformations of alkyl triflates shown in Scheme 2, we were intrigued by the selectivity of the hydroalkylation reaction, as neither the alkane nor the alkyl fluoride are formed in appreciable amount (<5% yield) during the reaction. For the proposed hydroalkylation mechanism to be correct, IPrCuH must selectively react with an alkyne rather than reduce the highly electrophilic alkyl triflate present in the reaction mixture. Similarly, IPrCuF must react with silane to produce IPrCuH rather than fluorinate the alkyl triflate. In this article, we describe our exploration of the mechanism by which hydroalkylation of alkynes is accomplished without concomitant reduction or fluorination of alkyl triflates (eqs 4 and 5). We present the results of our study and propose a new mechanism of the hydroalkylation reaction that explains this remarkable selectivity.

■ RESULTS

**Reactions of IPrCuH With Alkynes and Alkyl Triflates.** The feasibility of the originally proposed mechanism of hydroalkylation (Scheme 3) hinges on the relative rates of the reactions of IPrCuH with the alkyl triflate and the alkyne. The reaction of the copper hydride complex with the alkyne has to be faster than its reaction with the alkyl triflate. We found that both a terminal alkyne and an alkyl triflate react very quickly in a stoichiometric reaction with IPrCuH (Scheme 4, eqs 6 and 7). In a reaction with a terminal alkyne, a 51% yield of alkenylcopper complex 7 was formed in just 4 s. Complete conversion of the IPrCuH was achieved after less than 5 min,

## Scheme 4. Relative Rates of IPrCuH Reactions
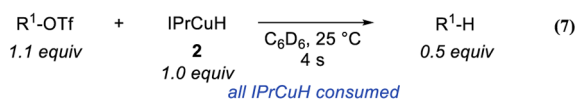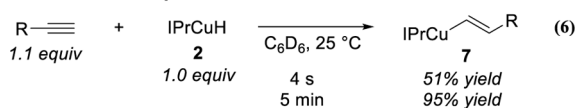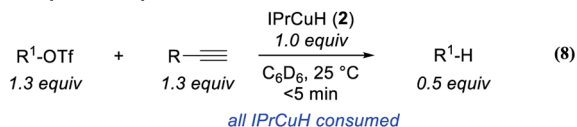
$R = Ph(CH_2)_3, R^1 = CH_3(CH_2)_{11}$

with the concomitant formation of alkenylcopper complex **7** in 95% yield. In a stoichiometric reaction with an alkyl triflate, complete consumption of IPrCuH was achieved in less than 4 s. Surprisingly, only 0.5 equiv of the alkyl triflate was consumed. While the results of these experiments did not allow us to definitively establish the relative rates of the reactions of IPrCuH with a terminal alkyne and an alkyl triflate, they did suggest that the reaction with alkyl triflates may be faster.

To further explore this possibility, we performed a competition experiment in which IPrCuH was exposed to a mixture of an alkyl triflate and an alkyne (Scheme 4, eq 8). The complete consumption of the IPrCuH was accompanied by the consumption of 0.5 equiv of the alkyl triflate and the formation of 0.5 equiv of the alkane. At the same time, >95% of the alkyne was still present in the reaction mixture.[26] The results of this competition experiment allowed us to conclude that the reaction of IPrCuH with an alkyl triflate is significantly faster than the reaction with a terminal alkyne. Importantly, these results allowed us to conclude that the originally proposed mechanism of hydroalkylation is incorrect.

Formation and Reactivity of $(IPrCu)_2(\mu\text{-}H)(OTf)$. The first indication of an alternative mechanism of hydroalkylation emerged when we tried to understand the unusual stoichiometry of the reaction between IPrCuH and alkyl triflate. This reaction results in the consumption of only 0.5 equiv of the alkyl triflate and yet leads to the consumption of a full 1 equiv of IPrCuH (Scheme 4, eq 7). We determined that another major product of the reaction is the complex $(IPrCu)_2(\mu\text{-}H)(OTf)$ **(8)**[27] (Scheme 5, eq 9).[28] One possible explanation for the formation of the hydride-bridged complex **8** is that IPrCuOTf formed in the reduction of the alkyl triflate sequesters IPrCuH before it can be fully consumed by the alkyl triflate. As shown in eq 10 in Scheme 5, we found that the reaction between IPrCuH and IPrCuOTf happens rapidly at room temperature to cleanly produce $(IPrCu)_2(\mu\text{-}H)(OTf)$.
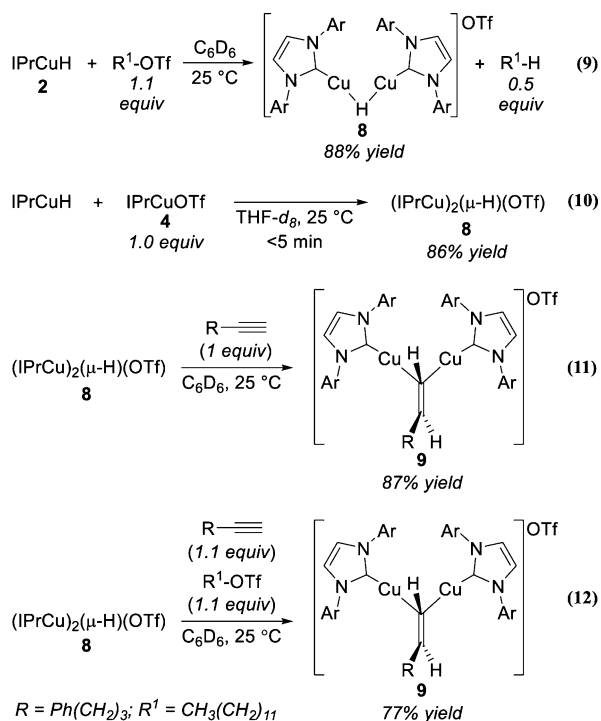
Considering that only 0.5 equiv of the alkyl triflate is consumed (eq 9), we can conclude that the formation of the dinuclear complex is significantly faster than the reaction of IPrCuH with alkyl triflates.

The results of the experiment shown in eq 9 clearly demonstrate that the hydride-bridged complex **8** is stable in the presence of an alkyl triflate. This raises the possibility that complex **8** is responsible for the selective hydrocupration of the alkyne in the presence of the alkyl triflate. In agreement with similar observations recently made by Sadighi,[28] we found that the dinuclear hydride reacts with an alkyne to form $(IPrCu)_2(\mu\text{-}$alkenyl$)(OTf)$ complex **9** in good yield (Scheme 5, eq 11). The product precipitates from the reaction mixture to yield colorless crystals suitable for X-ray crystallography, which allowed us to fully characterize this complex.[29] The competition experiment shown in eq 12 in Scheme 5 demonstrates efficient hydrocupration of an alkyne even in the presence of an alkyl triflate. This result suggests that the attenuated reactivity of complex **8** may be responsible for the cross-coupling of alkyl triflates in the hydroalkylation reaction (eq 3) without their concomitant reduction. Furthermore, this result allows us to conclude that hydrocupration of an alkyne by $(IPrCu)_2(\mu\text{-}H)(OTf)$ does not proceed through dissociation and subsequent reaction of IPrCuH with the alkyne. If IPrCuH were involved, we would expect only the reduction of the alkyl triflate according to the results of the experiment shown in eq 8.

With complex **8** as a plausible intermediate responsible for selective hydrocupration of an alkyne in the presence of an alkyl triflate, we explored ways in which this key intermediate could be formed in a catalytic hydroalkylation reaction. As shown in Scheme 5, **8** can be formed in a stoichiometric reduction of alkyl triflate by IPrCuH. However, in the catalytic hydroalkylation reaction, alkane is formed in only trace amounts (<5%), which suggests that the reduction of alkyl triflates is not a relevant method for the formation of the key catalytic intermediate. We also found that IPrCuOTf does not react directly with the silane. Therefore, we decided to explore other ways in which dinuclear hydride **8** can be formed from IPrCuOTf in the presence of a silane and CsF.

We previously demonstrated the formation of NHCCuF from the corresponding triflate complexes in the presence of alkali-metal fluorides in 1,4-dioxane.[23] We have found that like IPrCuH, IPrCuF also readily reacts with IPrCuOTf to form $(IPrCu)_2(\mu\text{-}F)(OTf)$ **(10)** (Scheme 6, eq 13). This suggests that the fluoride-bridged complex is likely present at partial conversions of IPrCuOTf to IPrCuF. We have also found that the fluoride-bridged complex **10** rapidly and quantitatively converts to the hydride-bridged complex **8** after addition of $(Me_2HSiO)_2$ (Scheme 6, eq 14). This reaction sequence provides a plausible pathway for the formation of the key

Scheme 5. Formation and Reactivity of $(IPrCu)_2(\mu\text{-}H)(OTf)$

Scheme 6. Formation and Reactivity of $(IPrCu)_2(\mu\text{-}F)(OTf)$
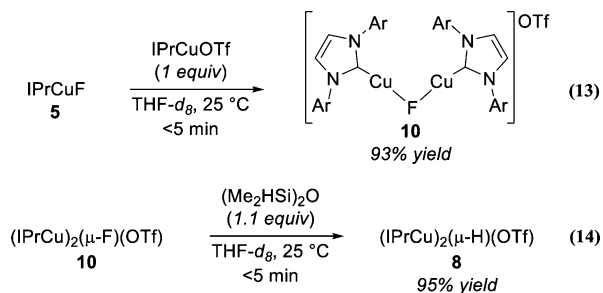
catalytic intermediate **8** under the conditions relevant to the catalytic hydroalkylation reaction (see Scheme 2, eq 3).

Reactivity of IPrCuF and (IPrCu)$_2$(μ-F)(OTf) toward Alkyl Triflates. In light of the reaction shown in eq 5, we found it surprising that fluorination of the alkyl triflate does not occur in the hydroalkylation reaction. We previously showed that the key step in the catalytic fluorination (eq 5) is a fast reaction of IPrCuF with the alkyl triflate.[23] We surmised that in the hydroalkylation reaction the formation of the less reactive (IPrCu)$_2$(μ-F)(OTf) may prevent the fluorination of the alkyl triflate. We have found that (IPrCu)$_2$(μ-F)(OTf) does react with alkyl triflates (Scheme 7, eq 15), albeit at a significantly

Scheme 7. Fluorination of Alkyl Triflates
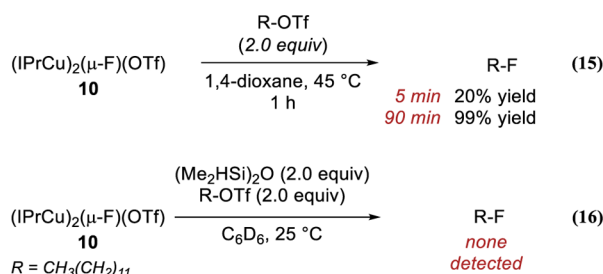
lower rate than IPrCuF.[23] The reaction shown in eq 14 suggests that transmetalation of (IPrCu)$_2$(μ-F)(OTf) with a silane may be faster than its reaction with alkyl triflate. To more firmly establish the relative rates of the two reactions, we performed the competition experiment shown in Scheme 7, eq 16. When (IPrCu)$_2$(μ-F)(OTf) is exposed to a mixture of (Me$_2$HSi)$_2$O and dodecyl triflate, no alkyl fluoride is formed.[30] Instead, (IPrCu)$_2$(μ-H)(OTf) is formed as the major product. This finding confirms that (IPrCu)$_2$(μ-F)(OTf) reacts faster with (Me$_2$HSi)$_2$O than with alkyl triflates[31] and provides a simple explanation for the selective cross-coupling of the alkyl triflates without competing formation of alkyl fluorides.

Reactivity of (IPrCu)$_2$(μ-alkenyl)(OTf). Our next goal was to explore the reactivity of (IPrCu)$_2$(μ-alkenyl)(OTf) (**9**) and its potential role in the C–C bond-forming step of the hydroalkylation reaction. The alkenyl-bridged complex **9** does not react with dodecyl triflate under a variety of conditions (Scheme 8, eq 17), indicating that direct alkylation of **9** is unlikely. However, the reaction of alkenylcopper complex **7** and dodecyl triflate results in complete consumption of **7** and the formation of equal amounts of C–C-coupled product **11** and alkenyl-bridged complex **9** (Scheme 8, eq 18). We propose that IPrCuOTf formed in the coupling reaction sequesters the unreacted IPrCu(alkenyl) before it can react with the remaining alkyl triflate. As shown in Scheme 8, eq 19, this reaction occurs readily at room temperature.

These results suggest that dissociation of alkenyl-bridged complex **9** under the conditions of the catalytic hydroalkylation would be a viable way to accomplish the C–C bond formation. The dissociation of the alkenyl-bridged dinuclear complex may be promoted by the replacement of the triflate ligand with a more electron-donating ligand. The same ligand exchange could alternatively result in the formation of a more reactive alkenyl-bridged dinuclear complex, which would react further with the alkyl triflate.

Unfortunately, our attempts to promote the reaction between the alkenyl-bridged dinuclear complex and the alkyl triflate by addition of individual components of the catalytic

Scheme 8. Reactivity of (IPrCu)$_2$(μ-alkenyl)(OTf)
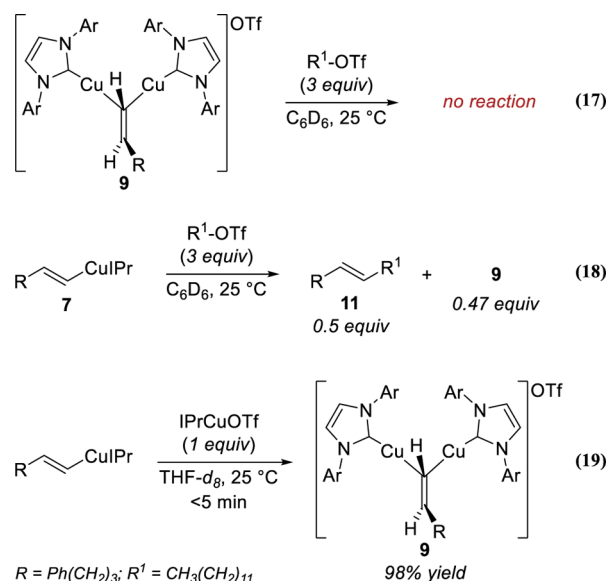
reaction (alkyne, silane, or CsF) were unsuccessful.[29] However, an excellent yield of the cross-coupling product **11** was obtained when 4-methoxyphenylacetylene, CsF, and (Me$_2$HSi)$_2$O were added to the mixture of an alkyl triflate and alkenyl-bridged complex **9**. In this experiment, product **11** was formed exclusively by the cross-coupling of the alkenyl group of complex **9** with the alkyl triflate. We also found that adding alkenyl-bridged complex **9** into an ongoing catalytic reaction between 4-methoxyphenylacetylene and dodecyl triflate results in the formation of cross-coupling product **11** in 71% yield (Scheme 9, eq 20). While these experiments do

Scheme 9. (IPrCu)$_2$(μ-alkenyl)(OTf) in a Catalytic Reaction[a]
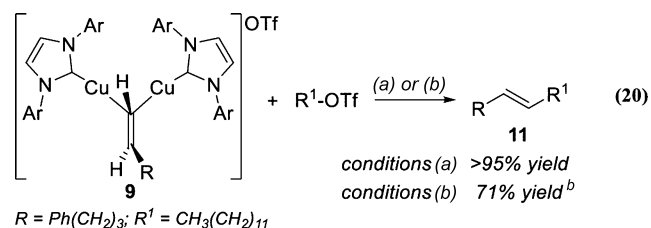
[a]Conditions (a): **9** (0.1 equiv), CH$_3$(CH$_2$)$_{11}$OTf (1.5 equiv), 4-MeOC$_6$H$_4$CCH (1.0 equiv), (Me$_2$HSi)$_2$O (2.0 equiv), CsF (2.0 equiv), 1,4-dioxane, 45 °C. Conditions (b): same as conditions (a) with IPrCuF (10 mol %) added. [b]An 80% yield was obtained when **15** was used instead of **9**.

not unequivocally establish the nature of the species involved in the C–C bond-forming step of the reaction, they establish the feasibility of the cross-coupling of the alkyl triflate and intermediate **9** under the reaction conditions as well as the feasibility of a catalytic cycle featuring **9** as an intermediate.

Reactivity of SIPr Copper Complexes. Previously, we found that IPrCuOTf was the optimal catalyst for both the fluorination[23] and reduction[15] of alkyl triflates. However, the best results in the hydroalkylation reaction were obtained using SIPrCuOTf as a catalyst. The change in the catalyst structure in going from IPrCuOTf to SIPrCuOTf is relatively small, and we found that in the experiments shown in eqs 7–20, SIPr and IPr
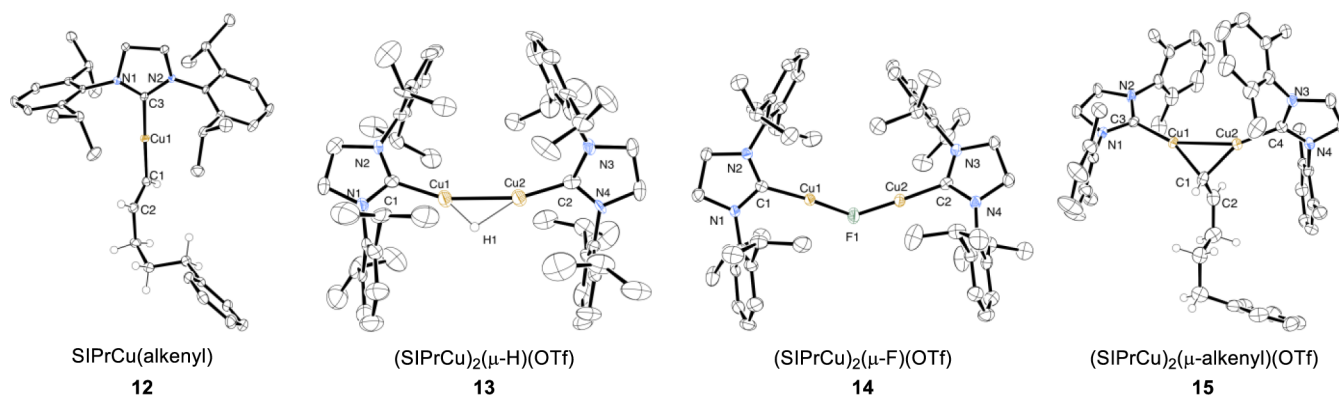
Figure 1. Crystal structure ORTEP images of SIPr copper complexes with ellipsoids at 50% probability. For clarity, triflate counterions and most of the hydrogen atoms have been omitted. For clarity, the methyl substituents of the isopropyl groups in **15** have also been omitted. In **15**, alkenyl = (E)-CH=CH(CH$_2$)$_3$Ph.

complexes performed qualitatively in the same way.[29] We found that in general the SIPr complexes give lower yields in stoichiometric reactions. At the same time, the SIPr copper complexes proved to be easier to crystallize, which allowed us to characterize all of the relevant complexes by X-ray crystallography (see Figure 1).
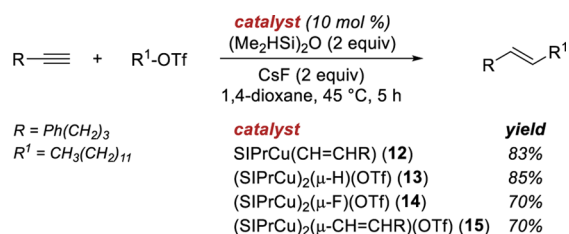
While the reactivities of SIPr and IPr complexes are quite similar in general, we found that (SIPrCu)$_2$(μ-alkenyl)(OTf) (**15**) performed better than the analogous IPr complex **9** in the C−C bond-forming experiment shown in eq 20 (80% vs 71% yield; see Scheme 9). We also found that the hydrocupration of the alkyne is significantly slower with SIPrCuH than with the IPr analogue. The reaction of SIPrCuH with an alkyne took an hour to complete (eq 21), while the same reaction using

$$\text{SIPrCuH} + \text{Ph} \diagdown_3 \xrightarrow[\substack{C_6D_6,\ 25\ °C \\ \textbf{1 h}}]{} \text{Ph} \diagdown_3 \text{CuSIPr} \quad (21)$$
$$\textbf{12}$$
$$\textit{65% yield}$$
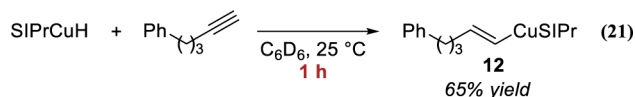
IPrCuH took less than 5 min (eq 6). The reaction of SIPrCuH with alkyl triflate was essentially instantaneous and produced (SIPrCu)$_2$(μ-H)(OTf). These findings further strengthen our conclusion that the originally proposed mechanism for the hydroalkylation reaction is incorrect.[32]

To explore the relevance of the dinuclear SIPr complexes (Figure 1) in the catalytic hydroalkylation performed under the optimal reaction conditions, we tested the ability of these complexes to catalyze the hydroalkylation reaction. We found that all of the complexes were catalytically competent, although the yield of the hydroalkylation was diminished in a few instances (Scheme 10). These results are consistent with the idea that the bridged dinuclear complexes are intermediates in the catalytic hydroalkylation reaction.

Scheme 10. Proposed Intermediates as Catalysts in the Hydroalkylation Reaction

$$R\!\!\equiv\!\! + R^1\text{-OTf} \xrightarrow[\substack{(Me_2HSi)_2O\ (2\ equiv) \\ CsF\ (2\ equiv) \\ 1,4\text{-dioxane},\ 45\ °C,\ 5\ h}]{\textit{catalyst}\ (10\ mol\ \%)} R\diagup\!\!\diagdown R^1$$

R = Ph(CH$_2$)$_3$
R^1 = CH$_3$(CH$_2$)$_{11}$

| catalyst	yield
SIPrCu(CH=CHR) (**12**)	83%
(SIPrCu)$_2$(μ-H)(OTf) (**13**)	85%
(SIPrCu)$_2$(μ-F)(OTf) (**14**)	70%
(SIPrCu)$_2$(μ-CH=CHR)(OTf) (**15**)	70%

■ DISCUSSION

One of the major questions about the mechanism of the catalytic hydroalkylation reaction shown in eq 3 is the question of selectivity: why do alkyl triflates selectively couple with alkynes rather than undergo reduction or fluorination during the course of the hydroalkylation reaction? Our attempts to understand this aspect of the hydroalkylation reaction led us to conclude that the initially proposed mechanism of hydroalkylation (Scheme 3) is incorrect. We found that the postulated IPrCuH intermediate reacts with alkyl triflates significantly faster than it does with terminal alkynes. Further studies of the reaction between alkyl triflates and IPrCuH led us to identify the complexes (IPrCu)$_2$(μ-X)(OTf) (X = H, F, alkenyl) as possible intermediates in the catalytic hydroalkylation reaction. These dinuclear copper complexes are not unprecedented. Although in a different context, the closely related complexes (IPrCu)$_2$(μ-X)(BF$_4$) (X = H, F, alkenyl) have recently been prepared and characterized by Sadighi and co-workers.[28,33] The same authors have also demonstrated a stoichiometric hydrocupration of phenylacetylene using (IPrCu)$_2$(μ-H)(BF$_4$).[28] However, complexes of this type have rarely been proposed as intermediates in catalytic reactions.[34]

The results of our study led us to postulate a new mechanism for the hydroalkylation reaction with (SIPrCu)$_2$(μ-X)(OTf) complexes (X = H, F, alkenyl) as key catalytic intermediates. According to the mechanism shown in Scheme 11, we propose that SIPrCuOTf reacts with CsF to form SIPrCuF, which is immediately trapped by remaining SIPrCuOTf to form (SIPrCu)$_2$(μ-F)(OTf) (**14**). The fluoride-bridged complex **14** reacts with silane to quickly form the hydride-bridged complex (SIPrCu)$_2$(μ-H)(OTf) (**13**). Complex **13** does not react with alkyl triflates and allows selective hydrocupration of terminal alkynes in the presence of these strong electrophiles. The reaction of alkenyl-bridged complex **16** with an alkyl triflate leads to the formation of the cross-coupling product. At the same time, either fluoride- or hydride-bridged dinuclear complex would be regenerated. The detailed mechanism of the cross-coupling step and the catalyst turnover remains to be elucidated. However, the results of the experiments shown in Scheme 9 provide strong evidence for the feasibility of the cross-coupling of the alkenyl group of intermediate **9** and an alkyl triflate under the reaction conditions. At the same time, the results of the experiment shown in eq 18 suggest a mononuclear NHC copper alkenyl complex as the active intermediate involved in the formation of the C−C bond.

Scheme 11. Proposed Mechanism of the Hydroalkylation
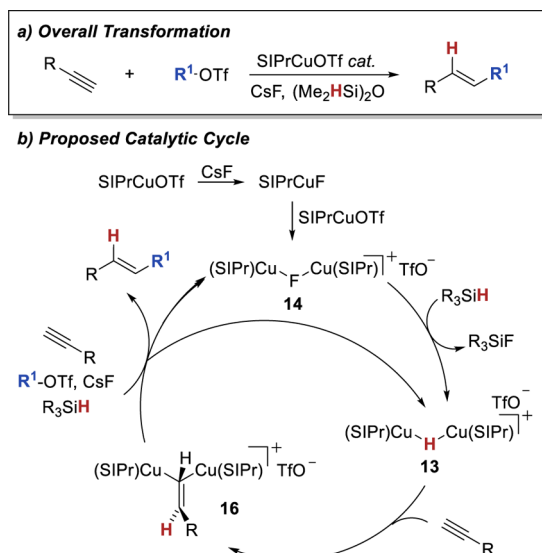
The key aspect of the mechanism shown in Scheme 11 is the intermediacy of $(NHCCu)_2(\mu\text{-}X)(OTf)$ complexes (X = H, F, alkenyl). In this new proposal, the intermediates of the initially proposed catalytic cycle are all replaced by the related dinuclear complexes. In light of the results presented in the previous section, this is not surprising. We showed that the complexes $(NHCCu)_2(\mu\text{-}X)(OTf)$ (X = H, F, alkenyl) are all readily formed in reactions of the corresponding NHCCuX with NHCCuOTf. Therefore, if there is a sufficient amount of NHCCuOTf relative to other intermediates in the reaction mixture, the dinuclear complexes will dominate. Our kinetics data suggest phase transfer of fluoride from solid CsF as the turnover-limiting step,[20] which would ensure that a sufficient amount of NHCuOTf is available under the reaction conditions.[35] Furthermore, the feasibility of the proposed elementary steps involving $(NHCCu)_2(\mu\text{-}F)(OTf)$ and $(NHCCu)_2(\mu\text{-}H)(OTf)$ as intermediates has been demonstrated through stoichiometric reactions. It is important to point out that the exact mechanism of the transformation of $(NHCCu)_2(\mu\text{-alkenyl})(OTf)$ into the final product remains unclear.

While the mechanism of the hydroalkylation reaction shown in Scheme 11 is closely related to the originally proposed mechanism (Scheme 3), the two mechanisms feature catalytic intermediates that have profoundly different reactivities. The finely tuned reactivities of hydride-bridged dicopper complex **13** and fluoride-bridged dicopper complex **14** are essential for the selective transformation of alkyl triflates in the hydroalkylation reaction. The $(SIPrCu)_2(\mu\text{-}H)(OTf)$ complex is perfectly suited for its role in the hydroalkylation reaction. It reacts with alkynes to give the hydrocupration product **16**, but unlike SIPrCuH, it does not react with alkyl triflates. Similarly, $(SIPrCu)_2(\mu\text{-}F)(OTf)$ reacts with silanes much faster than it reacts with alkyl triflates. Overall, the reactivities of these two complexes explain why reduction or fluorination of alkyl triflates does not occur during the course of the hydroalkylation reaction.

Another key feature of the catalytic cycle worth mentioning is that the low solubility of the fluoride source is essential for the success of the hydroalkylation reaction. The low solubility and reactivity of CsF prevents the direct fluorination of alkyl triflates and ensures that the only way fluoride can participate in the reaction is through the formation of copper fluoride complexes. The fact that phase transfer of fluoride is turnover-limiting in catalytic hydroalkylation is essential for maintaining a sufficiently high concentration of NHCCuOTf complex necessary to sequester NHCCuH and prevent unwanted reduction of the alkyl triflate. As a result, in a catalytic hydroalkylation reaction performed with a more soluble and reactive source of fluoride we would expect to see competing fluorination and reduction of alkyl triflates. Indeed, we found that catalytic hydroalkylation reactions performed with either tetrabutylammonium difluorotriphenylsilicate (TBAT) or tetramethylammonium fluoride (TMAF) instead of CsF result in the formation of alkyl fluorides as well as in the reduction of the alkyl triflate.[29]

In conclusion, we believe that the new mechanism of the hydroalkylation reaction provides opportunities for better understanding of other transformations as well as for the development of new ones. For example, our study suggests that the $(IPrCu)_2(\mu\text{-}H)(OTf)$ complex is also a likely intermediate in the catalytic reduction of alkyl triflates (eq 4). Additionally, the unique reactivity of $(NHCCu)_2(\mu\text{-}H)(OTf)$ opens the possibility for the development of hydrofunctionalization reactions of alkynes using other strong electrophiles that are not compatible with the IPrCuH intermediate.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and characterization of new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b03086.

■ AUTHOR INFORMATION

Corresponding Author

*lalic@chem.washington.edu

Author Contributions

[†]A.M.S. and M.R.U. contributed equally.

Notes

The authors declare no competing financial interest.

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(24) The reaction conditions shown in eq 4 are different from the optimal conditions for the reduction of alkyl triflates. See ref 15 for details.

(25) The reaction conditions shown in eq 5 are different from the optimal conditions for the fluorination of alkyl triflates. See ref 23 for details.

(26) After a longer period of time, the reaction proceeds according to the reactions described in eqs 9 and 11 in Scheme 5.

(27) A closely related hydride-bridged dicopper complex has recently been described by Sadighi. See ref 28.

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(29) See the Supporting Information.

(30) Control experiments excluded the possibility that the initially formed alkyl fluoride gets reduced under the reaction conditions.

(31) The analogous competition experiment with IPrCuF suggested that transmetalation with $(Me_2HSi)_2O$ is again faster than the reaction with an alkyl triflate.

(32) It is interesting to point out that the different reactivities of IPrCuH and SIPrCuH may explain performance of different catalysts in other hydrofunctionalization reactions. We have previously shown that semireduction of alkynes and hydrobromination of alkynes involve hydrocupration of alkynes by IPrCuH. In both reactions, the IPr copper catalyst performed significantly better than the closely related SIPr copper catalyst.

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(35) Our attempts to determine the resting state of the catalyst using NMR spectroscopy were hampered by the heterogeneous nature of the reaction mixture.