ORGANOMETALLICS

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pubs.acs.org/Organometallics

Development of N-Heterocyclic Carbene–Copper Complexes for 1,3-Halogen Migration

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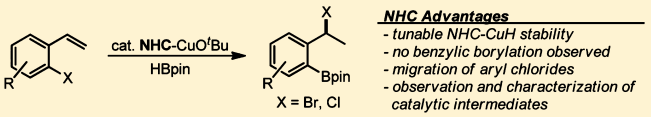
Supporting Information

ABSTRACT: A series of NHC–copper complexes was synthesized and their potential to catalyze 1,3-halogen migration explored. Increasing the steric bulk around the metal drastically improves the lifetime of NHC–CuH species and promotes 1,3-halogen migration of both 2-bromo- and 2-chlorostyrenes through transfer of an aryl halogen to a benzylic carbon with concomitant arene borylation. The NHC-based system displays a broad substrate scope with notable advantages over previously reported phosphine-based catalysts, including complete selectivity for migration versus competing benzylic borylation, increased steric tolerance, efficient aryl chloride migration, and facile formation and characterization of organocopper catalytic intermediates. Experimental evidence and DFT calculations support a mechanism proceeding through dearomatization of a benzyl copper species, followed by a 1,4-halogen shift and borylation of the resulting ArCu(I) intermediate.

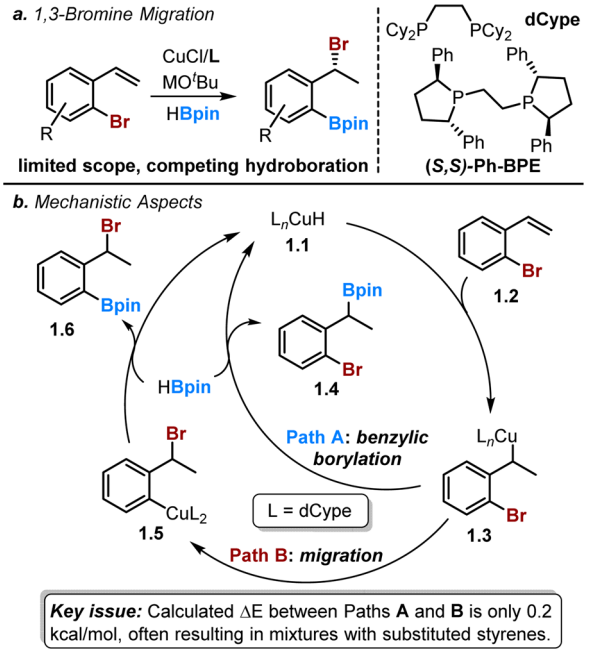


1. INTRODUCTION

Base metal catalysis is a vibrant area of research due to several potential advantages such compounds offer over more widely utilized precious metal catalysts. Earth-abundant metals have a significantly lower cost (Pd: $780/troy oz. vs Cu: $0.20/troy oz.), as well as potential environmental advantages.[1] Perhaps most importantly, first-row transition metals have different electronic structures compared to second- and third-row metals and may exhibit new reactivities that proceed through novel mechanistic pathways.[2] Our group has recently described a new mode of reactivity for Cu(I) involving a migration of a halide from the arene carbon of **1.2** to the benzylic carbon of **1.7** (Scheme 1a).[3] Our initial synthetic studies of copper-catalyzed 1,3-halogen migration/borylation focused on 2-bromostyrenes as substrates and copper catalysts supported by bulky and electron-rich bidentate phosphine ligands, including 1,2-bis(dicyclohexylphosphino)ethane (dCype) and (*S*,*S*)-1,2-bis(2,5-diphenylphospholano)ethane (Ph-BPE).[3,4]

Subsequent mechanistic studies were undertaken to elucidate the reaction pathway (Scheme 1b).[5] Experiment and density functional theory (DFT) calculations established hydrocupration of styrene **1.2** by the dCype–copper hydride to give benzyl copper **1.3** as the initial step. This intermediate could then either undergo σ-bond metathesis with pinacolborane (HBpin) to give the benzylic borylation product **1.4** (path A) or rearrange via dearomatization to form aryl copper **1.5** (path B). Subsequent reaction of **1.5** with HBpin delivers migration product **1.6** and regenerates the active copper hydride. Notably, ligand variations indicated that bulky ligands disfavor the benzylic hydroboration, while electron-rich ligands were necessary to achieve migration. However, our computations predicted that the energy gap between these two paths was very small (0.2 kcal/mol); indeed, minor changes in the nature of the substrate often led to mixtures of products.[5] Thus, it was imperative that we identify ways in which to increase the energy barrier between the undesired hydroboration and the desired migration process.

Scheme 1. Mechanism of 1,3-Halogen Migration Catalyzed by Phosphine-Based Ligands



While the phosphine-based catalyst systems proved successful for a range of substrates, the competing benzylic

Received: July 21, 2015

DOI: 10.1021/acs.organomet.5b00629
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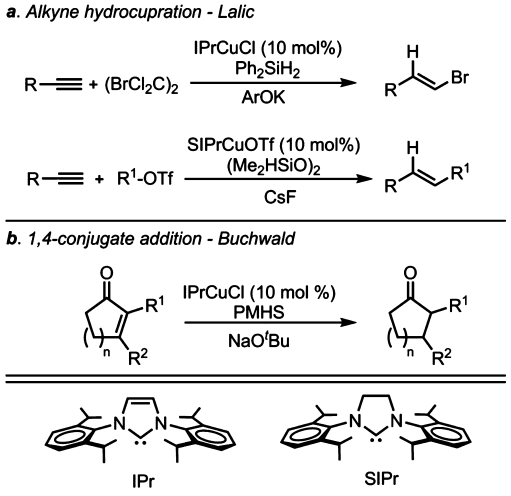
hydroboration pathway impeded successful migration of other functional groups, as well as attempts to selectively functionalize aryl copper **1.5** with different electrophiles. Therefore, we found it necessary to pursue new catalysts with better selectivity for the halogen migration in order to advance our chemistry. Additionally, substantial electron density at the aryl-bromide carbon was necessary for high levels of conversion in the enantioselective chemistry using (*S,S*)-Ph-BPE. Substrates that performed poorly with phosphine-supported Cu catalysts include electron-deficient arenes, those containing substitution *ortho* to either the halogen or the alkene, and 2-chlorostyrenes. Given the success of N-heterocyclic carbene (NHC) ligands as alternatives to electron-rich phosphines, we sought to determine whether this ligand class could successfully promote 1,3-halogen migration with a broader scope than phosphine ligands.[6]

We were encouraged by the prospect of catalyzing 1,3-halogen migration with NHC-supported copper complexes for three main reasons. First, like their phosphine counterparts,[7] NHC−copper hydrides have well-precedented reactivity toward unsaturated functionality, particularly alkynes and α,β-unsaturated carbonyls. For example, Lalic has recently reported alkyne hydrobrominations and hydroalkylations, both catalyzed by the NHC-bound copper hydride (S)IPrCuH generated *in situ* (Scheme 2a).[8] Buchwald has established that IPrCuH promotes 1,4-reduction of α,β-unsaturated carbonyls using stoichiometric polymethylhydrosiloxane (PMHS) as the hydride source (Scheme 2b).[9]

Scheme 2. Selected Functionalizations with NHC−CuH

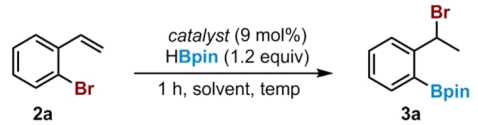


Although catalytic hydrocupration of styrenyl olefins with NHC−copper hydrides had not been investigated prior to our work, NHC−Cu−Bpin complexes were known to successfully add to styrenes in a regioselective manner to place the Cu at the benzylic carbon.[10] Second, a growing body of work has focused on defining the sterics and electronics of NHC ligands through the use of percent buried volume calculations (% V_{Bur})[11] and both Tolman electronic parameters[12] and heteroatom NMR shifts,[13] respectively. These precedents, combined with the synthetic accessibility of a range of NHC ligands, would allow us rational catalyst design that was difficult to achieve using phosphine-based systems. Third, in our efforts to understand the mechanism of 1,3-halogen migration, we found that examining the migration stoichiometrically using catalysts supported by phosphine ligands was challenging. While the aryl copper intermediate could be observed, its instability and inability to form in appreciable quantities precluded a detailed investigation into its chemistry.[5] Thus, we were motivated by the potential for NHC-based catalysts to give well-defined intermediates for further studies.

2. RESULTS AND DISCUSSION

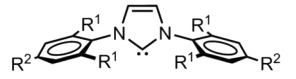
2.1. (NHC)Cu-Catalyzed 1,3-Bromine Migration: Development, Scope, and Comparison to (dCype)CuH System. We began our studies by examining copper complexes of the commercially available NHCs IMes and IPr (Table 1).

Table 1. Initial NHC-Catalyzed 1,3-Br Migration



entry	catalyst	solvent	temp (°C)	conversion	yield **3a**[a]
1	IMesCuCl/KO^{t}Bu	THF	45	73%	0%
2	IPrCuCl/KO^{t}Bu	THF	45	90%	75%
3	IPrCuO^{t}Bu	THF	45	100%	78%
4	SIPrCuO^{t}Bu	THF	45	91%	74%
5	IPrCuO^{t}Bu	THF	rt	56%	30%
6	**IPrCuO^{t}Bu**	**toluene**	**45**	**100%**	**82% (80%)**

[a] ^{1}H NMR yields using 1,1,1,2-tetrachloroethane as standard. Isolated yield in parentheses.



IMes: R^1, R^2 = Me
IPr: R^1 = *i*Pr, R^2 = H
SIPr: saturated imidazole

Subjecting the model styrene **2a** to IMesCuCl/KO^{t}Bu and pinacolborane gave substantial conversion but 0% yield of migration product **3a** (entry 1). We attributed this lack of productive reactivity to the instability of the formed IMesCuH. Upon addition of HBpin to the reaction mixture, a rapid color change from orange to black with substantial precipitation of black solids was observed. In contrast, the bulkier IPrCuCl precatalyst delivered **3a** in 75% yield with nearly complete conversion of styrene **2a**. The IPrCuH formed *in situ* was noticeably more stable, as its orange color persisted in solution and faded to clear over 20 s. The preformed IPrCuO^{t}Bu performed even better as a precatalyst, giving complete conversion of starting material (entry 3). Switching to the saturated analogue SIPr or decreasing the reaction temperature did not improve the yield of **3a** (entries 4 and 5). However, utilizing a less polar solvent, toluene, gave a much cleaner reaction, allowing **3a** to be isolated in 80% yield.

Following the optimization of 1,3-bromine migration, several substituted 2-bromostyrenes were subjected to the reaction conditions, and select examples compared to our initially reported dCype system (Table 2).[3] Like dCype, electron-rich substrates, particularly those with electron-donating groups at the 5-position, gave the best yields (substrates **2b−f**). The efficiency of these substrates with both catalysts possibly hints at mechanistic similarities between the two ligand classes. Unsurprisingly, **2g**, containing an electron-donating group in the 4-position, showed no conversion with IPrCuH; attempts to force conversion at higher temperatures were unsuccessful. It is likely the increased electron density of the olefin substantially disfavors the proposed initial hydrocupration step. As electron-poor, polyhalogenated, and *ortho*-substituted substrates were

DOI: 10.1021/acs.organomet.5b00629
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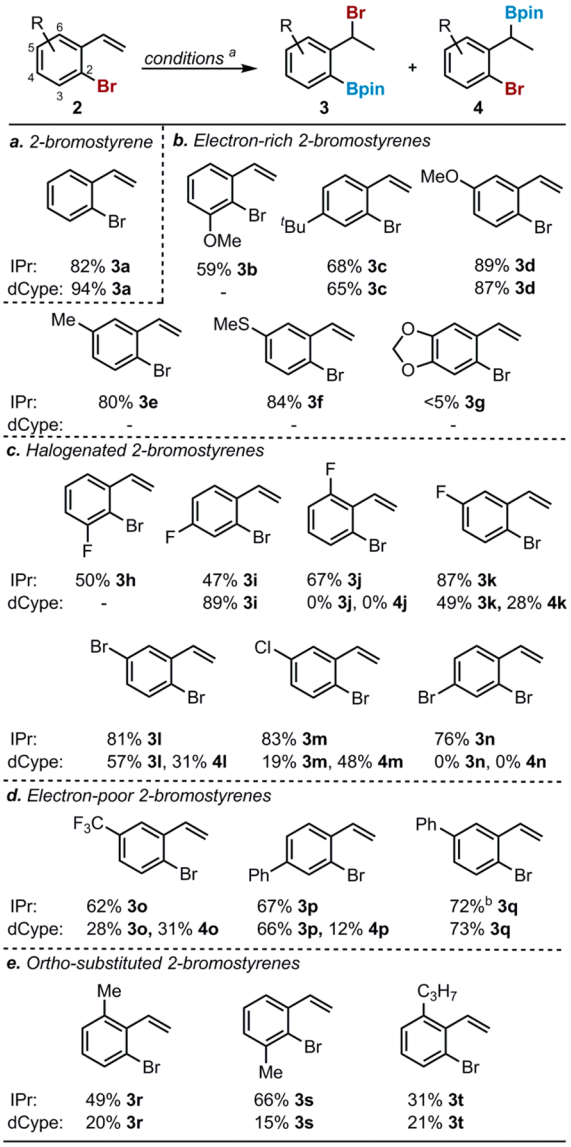
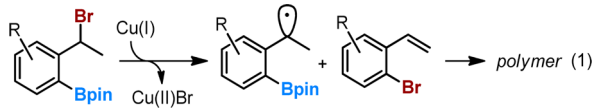
Table 2. Scope of IPrCuH Compared to dCypeCuH



[1]H NMR yields using 1,1,1,2-tetrachloroethane. [a] IPr conditions: IPrCuO^{t}Bu (9 mol%), HBpin (1.2 equiv.), 45°C, tol. dCype conditions: CuCl (9 mol%), dCype (9 mol%), KO^{t}Bu (18 mol%), HBpin (1.2 equiv.), 40°C, thf. [b] SIPrCuO^{t}Bu was used. 50% product with IPrCuO^{t}Bu

particularly problematic in our initial studies using dCype, we were interested in examining them with IPrCuH. While IPrCuH gave moderate to good yields for fluorinated substrates **2h** and **2i**, **2j** underwent migration cleanly to give 67% product, a stark contrast to the lack of reactivity observed with dCypeCuH. Substrates **2k**−**m**, halogenated at the 5-position, gave substantial amounts of hydroboration products **4k**−**m** with the phosphine system, yet showed complete selectivity for 1,3-bromine migration when subjected to the NHC conditions. Styrene **2n** gave a 76% yield of migration product **3n** with IPrCuH, but significant polymerization occurred using dCype. Similarly, other substrates yielding mixtures of migration and hydroboration products with dCype, such as **2o** and **2p**, again resulted in exclusive migration with IPrCuH. *Ortho*-substituted substrates **2r** and **2s** showed poor conversion with the phosphine-based catalyst, which was significantly improved moving to IPrCuH. However, when bulkier substrates, such as **2u**, were subjected to IPrCuH, no significant yield improvement was observed compared to dCypeCuH. This most likely arises from the steric bulk of the NHCs being only marginally further away from the metal center compared to phosphine ligands.[11] *Most significantly, appreciable amounts of benzylic borylation were never observed using the NHC catalyst.*

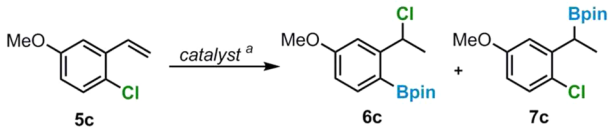
2.2. NHC-Copper-Catalyzed 1,3-Chlorine Migration: Background, Ligand Development, and Scope. *2.2.1. Background.* The complete selectivity of IPrCuH for 1,3-migration, as opposed to benzylic borylation, prompted us to examine the ability of this catalyst to promote 1,3-chloride migration with 2-chlorostyrenes. With phosphine ligands, we recognized that difficulties in both racemic and enantioselective bromine migration stemmed from the lability of the resulting benzyl bromides. We hypothesized the most significant decomposition pathway was due to atom transfer radical polymerization (ATRP).[14] Copper-mediated benzyl bromide fragmentation produces benzylic radicals, which are competent polymerization initiators in the presence of excess styrene (eq 1).



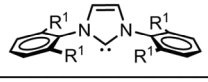
Notably, in addition to consuming both product and starting material, the ATRP pathway also deactivates the catalyst through oxidation to copper(II). We proposed that the stronger benzylic C−Cl bond formed through 1,3-chlorine migration might mitigate this problem. Additionally, aryl chlorides are cheaper and more readily available than the corresponding aryl bromides, an important factor to consider if Cu-catalyzed 1,3-halogen migrations are to be used as tools for rapid synthesis of bioactive scaffolds.[15]

2.2.2. Ligand Effects in 1,3-Chlorine Migration. 1,3-Chlorine migration was initially tested with **5c** as the model substrate (Table 3). Attempted migration of **5c** at elevated

Table 3. Ligand Effects in 1,3-Chlorine Migration



entry	*catalyst*	yield **6c**	yield **7c**
1	dCype/CuCl/KO^{t}Bu	<5%	72%
2	IPrCuO^{t}Bu	44%	trace
3	IPentCuO^{t}Bu	70%	trace
4	IHeptCuOMe	87%	trace



IPr: R^1 = *i*Pr
IPent: R^1 = 3-pentyl
IHept: R^1 = 4-heptyl

[1]H NMR yields using 1,1,1,2-tetrachloroethane as the internal standard. [a] NHC conditions: NHCCuOR (9 mol%), HBpin (1.2 equiv), 70°C, tol. dCype conditions: CuCl, dCype (9 mol%), KO^{t}Bu (18 mol%), HBpin (1.2 equiv), 70°C, THF.

temperatures using dCype gave exclusively the benzyl borylation product **7c** with trace amounts of **6c**. In contrast, utilizing IPrCuO^{t}Bu as the precatalyst completely switches the selectivity from the borylation pathway to the migration pathway, yielding 44% of **6c**. We hypothesized that the decay of the active IPrCuH prevented full conversion in the chlorine

DOI: 10.1021/acs.organomet.5b00629
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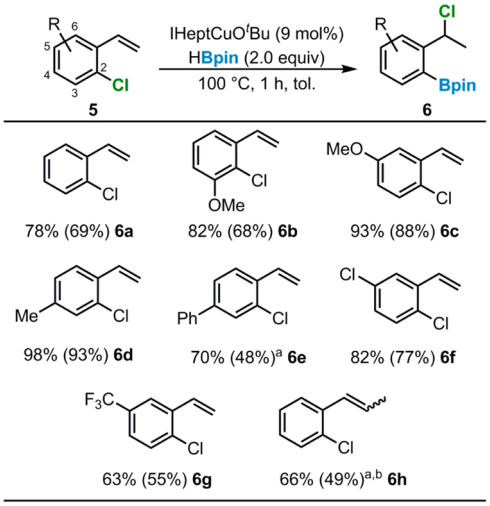
migration; rapid disappearance of the bright yellow color of IPrCuH at elevated temperatures supported this assertion. These results prompted an investigation into more thermally stable NHC−CuH complexes. Preservation of the diaryl-imidazolium motif, while increasing steric bulk around the metal, was accomplished through the synthesis of two copper complexes supported by Organ and Nolan's flexible, bulky NHCs, IPent and IHept (entries 3 and 4).[16] While precatalyst IPentCuO^{t}Bu gave full conversion of **5c** (entry 3), it was found that IHeptCuOMe delivered the best yield of the migration product and was used for further optimization. In addition to ligand design, three other variables were crucial to successful 1,3-chlorine migration: (a) increasing reaction temperature to 100 °C, (b) decreasing the concentration to 0.1 M, and (c) using two equivalents of pinacolborane (see the Supporting Information for optimization studies).

2.2.3. Scope of 1,3-Chlorine Migration. Several substrates were subjected to optimized conditions using IHeptCuOMe in the presence of HBpin (Table 4). Unsubstituted **5a** performed

Table 4. Scope of (NHC)Cu-Catalyzed 1,3-Chlorine Migration



^{1}H NMR yield using 1,1,1,2-tetrachloroethane as an internal standard, isolated yield in parentheses. [a] 15 mol% catalyst was used. [b] *E/Z* ratio: 9:1.

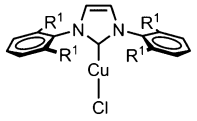
efficient chlorine migration, delivering **6a** in good yields. As observed previously with 1,3-Br migration, electron-donating groups at either the 3- or 5-position gave excellent yields of the migration products (substrates **5b** and **5c**). Both 4-alkyl and aryl substituents were tolerated in the reaction (**5d** and **5e**), although increased catalyst loading was needed for full conversion of **5e**. We suspect the sluggish reactivity is due to steric clashing of the large alkyl arms of the IHeptCu complex with the remote aryl ring, most likely during one or more of the migration steps. Substrates **5f** and **5g**, containing electron-withdrawing groups *para* to the aryl chloride, were expected to be difficult migration substrates due to significantly decreased electron density at the aryl chloride carbon. However, we were pleased to find that the 1,3-chloride migration occurred smoothly in both, yielding **6f** and **6g**. *Trans*-disubstituted styrene **5h** underwent migration, albeit slowly (entry 8). Unfortunately, halogen substitution at either the 3- or 6-position yielded little migration and significant polymerization. Efforts to improve these substrates are under way. Nonetheless, even under forcing conditions, the NHC-based catalyst system showed impressive selectivity for the migration pathway.

2.3. Mechanistic Studies. *2.3.1. Goals.* Following the development and exploration of IPrCuO^{t}Bu and the new complexes IPentCuO^{t}Bu and IHeptCuOMe for 1,3-halogen migration, we initiated a series of mechanistic experiments to accomplish several goals: (a) quantify the increased stability offered by the IPent and IHept ligands, (b) gain insight into why the NHC systems do not perform benzylic borylation relative to the phosphines, (c) observe and characterize potential intermediates in catalysis, and (d) determine if the 1,3-halogen migration by NHC−Cu catalysts proceeds via the dearomatization mechanism proposed for dCypeCuH.

2.3.2. Stability of NHC−CuH Species and Their Solution Behavior. In the initial ligand screen for 1,3-chlorine migration, several qualitative observations prompted examination of the active NHC−CuH catalysts in greater detail. Using the color change (yellow-orange to clear) that occurred upon reaction of **5a** with NHC−CuH as a metric, IPentCuH showed remarkable stability relative to IPrCuH. However, when IHept was employed, faster styrene uptake was seen, indicating a more reactive copper hydride despite the bulkier ligand. This detail contradicted our simple hypothesis that increasing the steric environment of the ligand would increase NHC−CuH stability.

To address this inconsistency, the sterics of IPentCuCl and IHeptCuCl were quantitatively assessed by percent buried volume (%V_{Bur}) calculations on their crystal structures, and the stability of NHC−CuH complexes was assessed by monitoring their decay by NMR (Table 5). Each additional methylene

Table 5. Comparison of NHC−Copper Complexes



NHC	R^1	%V_{Bur}[a]	NHC-Cu-H half-life[b]
IPr	^{i}Pr	47.6%[c]	72 min at 30 °C
IPent	3-pentyl	49.3%[d]	98 min at 58 °C
IHept	4-heptyl	52.8%[e]	80 min at 45 °C

[a] M-NHC length of 2.0 Å, 3.5 Å sphere radius, 0.05 Å mesh step. [b] Measured decay by NMR. [c] From crystal structure in ref. 17. [d] Average of 3 different conformations in the crystal structure. [e] Average of 2 different conformations in the crystal structure.

extension on the alkyl arms on the NHC provides a 2−3% increase in %V_{Bur} values, a smaller increase than that observed in palladium and gold catalysts.[16−18] While the range of stabilities of the NHC−CuH complexes precluded studying their decay at the same temperature, the data in Scheme 4 confirmed our earlier observation that IPentCuH is significantly more stable than both IPrCuH and IHeptCuH; the difference between IPentCuH and IPrCuH is an incredible result given the small increase in %V_{bur}, 1.7%, between the two ligands. The increased stability of IPentCuH versus IHeptCuH inspired us to reevaluate our thoughts on the solution speciation of these complexes, as this detail suggests possible dimer−monomer equilibrium in solution. While Sadighi's isolation and characterization of IPrCuH by X-ray diffraction showed a dimeric structure in the solid state,[19] other studies failed to support the presence of NHC−CuH dimers in solution based on kinetic data.[20] Diffusion NMR experiments (DOSY) were performed on all three NHC−CuH complexes (details in the Supporting Information). Interestingly, IPrCuH, IPentCuH, and IHept-

DOI: 10.1021/acs.organomet.5b00629
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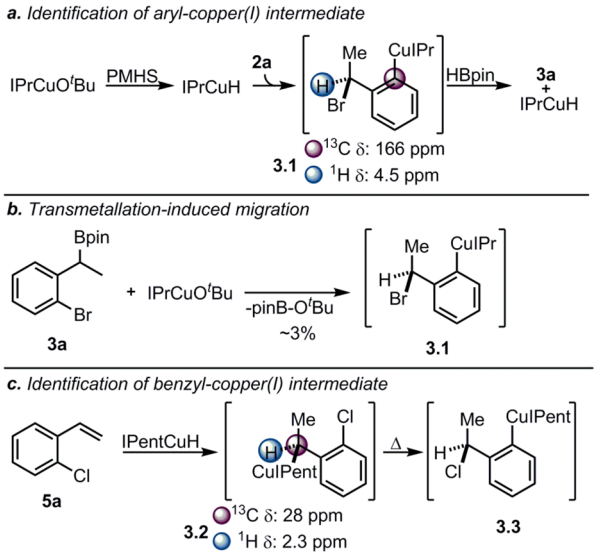
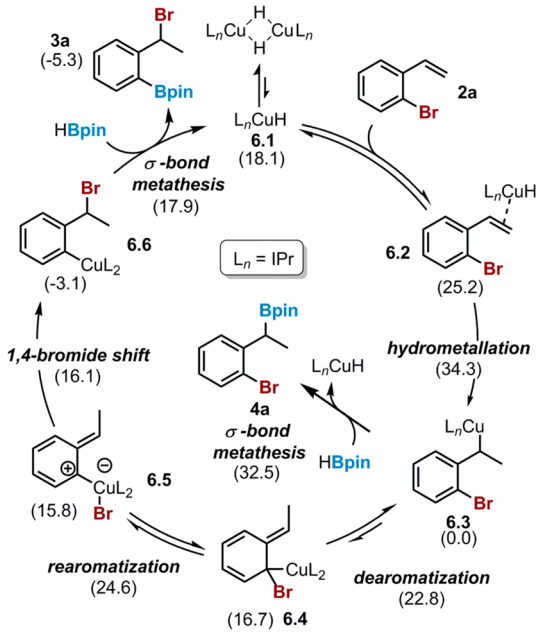
Scheme 3. Stoichiometric Studies of 1,3-Migration

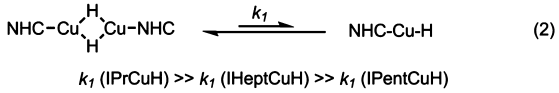


Scheme 4. Proposed Catalytic Cycle



Free energies shown are in kcal mol-1 computed at SMD(THF)-M06/6-311G(d):LANL2TZ+ (Cu).

CuH all appeared to exist as dimers in solution; no evidence was observed for the presence of monomer species for any of the three metal complexes. However, we postulate that the monomer is the active catalyst, regardless of its low concentration relative to the dimer. This suggests three important features of NHC−CuH-catalyzed 1,3-halogen migration: (a) there exists a NHC−CuH dimer−monomer equilibrium in solution (eq 2), heavily favoring the dimer, (b)



k_1 (IPrCuH) >> k_1 (IHeptCuH) >> k_1 (IPentCuH)

the stability of IPentCuH likely originates from its 3-pentyl arms, offering the most steric shielding of the dimer without being too large to disfavor dimer formation, resulting in a very small equilibrium constant k_1, and (c) the increased efficiency of chlorine migration with IHept relative to IPent does not stem from NHC−CuH stability. We posit the larger IHept better stabilizes other intermediates in the catalytic cycle. In a more general context, these studies indicate a tunable spectrum of reactivity versus stability for NHC−CuH complexes, properties difficult to examine with related phosphine-based copper hydrides.

2.3.3. Computations and Rationale on the Difference in the Benzylic Borylation Pathways with Different Ligands. Having rationalized the improvements on catalytic activity afforded by the larger IPent and IHept ligands, efforts were directed toward answering the question of why benzylic borylation, a common side pathway with the dCype catalyst, was never observed with the NHC catalysts in either bromide or chloride migration. In previous mechanistic studies of the dCype catalyst, computations indicated that the difference in energy between the hydroboration pathway versus the migration pathway was small.[5] With evidence that the migration pathways for both catalysts were similar (*vide infra*), two scenarios were possible: either the NHCs were much more efficient at migration or they significantly disfavored the borylation pathway. We performed DFT calculations on the benzylic borylation pathway with both dCype and IPr ligands to examine these possibilities (Figure 1). The borylation has been proposed to proceed through a σ-bond metathesis of benzyl copper **1.4** with HBpin to give benzyl boronic ester **1.9** and regenerate the ligand-supported copper hydride.[5,21] Corroborating our experimental results, the transition state, **1.10-TS1**,

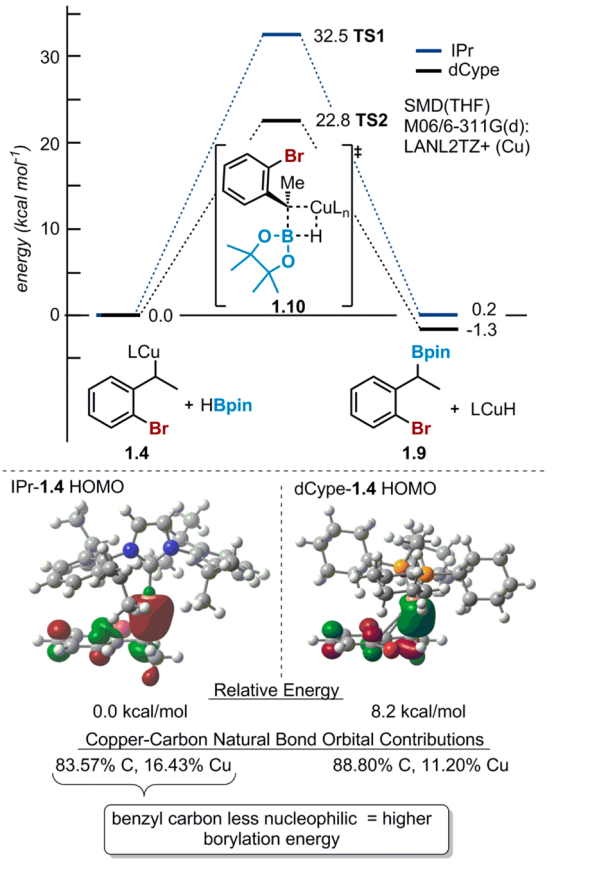


Figure 1. DFT calculations on benzylic borylation.

DOI: 10.1021/acs.organomet.5b00629
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for the IPr ligand lies 9.7 kcal·mol^{-1} uphill relative to the dCype pathway (Figure 1, top). Examination of the HOMOs for both benzyl copper species **1.4** reveals that the IPr HOMO is substantially lower in energy (Figure 1, bottom). In addition, the carbon−copper natural bond orbital in IPr-**1.4** has 83.57% orbital contribution from the benzyl carbon compared to 88.80% of dCype-**1.4**, indicating a less polarized bond and a less nucleophilic carbon in IPr-**1.4**. This attenuated nucleophilicity renders IPr-**1.4** less reactive toward σ-bond metathesis with HBpin. Additionally, it is presumed that increased steric bulk of IPent and IHept further discourages the benzylic borylation pathway, given our previous studies of the impact of steric bulk on the hydroboration pathway.[5] Therefore, despite the higher barrier for chlorine migration, the borylation is equally, if not more, disfavored, resulting in efficient migration.

2.3.4. Stoichiometric Reactions: Identification and Characterization of Relevant Intermediates. Stoichiometric studies of reactions promoted by dCypeCuH were plagued by difficulties in cleanly generating the active catalytic species and observing its reaction with 2-bromostyrene. These issues were due to the insolubility of the phosphine system and the complexity of the NMR spectra. The ability to cleanly generate and react IPrCuH with unsaturated molecules in a stoichiometric fashion[8c,19] was utilized to monitor the addition of 2-bromostyrene (**2a**) to one equivalent of IPrCuH. The reaction was observed by ^{1}H NMR (Scheme 3a) and showed that clean formation of aryl copper **3.1** occurred instantaneously at room temperature. The ^{13}C shift of the aryl carbon bound to copper at 165 ppm closely matches that found by Ball.[22] This species is stable for several hours at room temperature; it cleanly forms migration product **3a** and regenerates IPrCuH upon addition of HBpin.

Following characterization of **3.1**, we focused on obtaining evidence for IPr-**1.4**, as it would support our hypothesis that both IPrCuH- and dCypeCuH-catalyzed halogen migration proceed via the same dearomatization mechanism (Scheme 1, bottom). Additionally, the benzyl-copper(I) species represents an important intermediate of the catalytic cycle that could not be observed in our phosphine studies.[5] Toward this goal, we wondered if we could successfully achieve migration if we formed benzyl copper IPr-**1.4** by transmetalation instead of hydrocupration. While transmetalation of sp^3 centers is notoriously difficult, Ball's report detailing transmetalation from a benzyl silane using SICyCuF[23] inspired us to attempt such a strategy. Thus, we subjected benzyl boronic ester **3a** to an equivalent of IPrCuO^{t}Bu at room temperature (Scheme 3b). While conversion was poor and could not be improved upon increased heating, the aryl copper **3.2** was observed spectroscopically, supporting the formation of IPr-**1.4** as a competent migration intermediate.

Based on the hypothesis that one of the shifts during migration is the rate-limiting step of the chlorine migration, and the hope that the benzyl copper species IPr-**1.4** could be observed spectroscopically, 2-chlorostyrene (**5a**) was introduced to a solution of IPentCuH at 40 °C (Scheme 3c). As hypothesized, this reaction delivered benzyl copper **3.2**. It is noteworthy that **3.2** is a 14-electron η^1-complex and that the η^3-benzyl complex was not observed.[24] Its competency for migration was assessed by heating **3.2** in the NMR tube to 90 °C, which induced migration, resulting in aryl copper complex **3.3**. Not only does characterization of these intermediates lend robust evidence toward the dearomatization mechanism, but the ease and efficiency of these stoichiometric experiments highlight a substantial advantage offered by the NHC system.

2.3.5. DFT-Supported Mechanism. To support our stoichiometric studies, DFT calculations (SMD(THF)-M06/6-311G(d):LANL2TZ+ (Cu)) were then performed on the dearomatization pathway using IPr as the supporting ligand (see the Supporting Information for full details). The full proposed mechanism is shown in Scheme 4.

Following dissociation from the dimer, the active monomer, IPrCuH or **4.1**, initially forms a π-acid complex **4.2** with the substituted styrene. This species undergoes olefin insertion to yield the benzyl copper **4.3**. Subsequent dearomatization, rearomatization, and 1,4-bromide shift occur on a relatively flat energy surface, completing the migration process to the aryl copper **4.6**. Finally, σ-bond metathesis of **4.6** with HBpin yields the migration product **4.7** and regenerates the active IPrCuH. The crucial point of Scheme 4 is that the NHC ligand greatly increases the energy difference between the undesired hydroboration and the desired migration, key achievements for extending Cu-catalyzed 1,3-migration processes to nonhalogenated activating groups, particularly those based on readily available phenols and anilines.

3. CONCLUDING REMARKS

The utility of more stable NHC−CuH species based on the flexible and bulky IPent and IHept ligands has enabled substantial improvements in 1,3-halogen migration methodology and increased our understanding of the reaction mechanism. Notable advancements include increased scope of migration for difficult substrates, specifically sterically encumbered 2-bromostyrenes and 2-chlorostyrenes, suppression of the competing benzylic borylation pathway, insight into the nature of NHC−CuH species, and compelling evidence for the proposed catalytic cycle. These studies will provide a strong foundation for the future development of NHC−Cu-catalyzed 1,3-halogen migration. We anticipate our insight into the reactivity of NHC−Cu-hydrides for 1,3-migration will prove useful in the broader context of developing an array of Cu-catalyzed arene functionalizations that result in the formation of new C−C and C−heteroatom bonds.

4. EXPERIMENTAL SECTION

All glassware was either oven-dried overnight at 130 °C or flame-dried under a stream of dry nitrogen prior to use. Unless otherwise specified, reagents were used as obtained from the vendor without further purification. Tetrahydrofuran, deuterated tetrahydrofuran, and toluene were vacuum transferred from purple Na/benzophenone ketyl. Dichloromethane and acetonitrile were dried over CaH_2 and freshly distilled prior to use. IPrCuO^{t}Bu was synthesized according to the literature procedure.[25] All other solvents were purified in accordance with *Purification of Laboratory Chemicals*.[26] Air- and moisture-sensitive reactions were performed either in an MBraun LabStar glovebox under an atmosphere of nitrogen or using standard Schlenk techniques under an atmosphere of nitrogen. Analytical thin layer chromatography (TLC) was performed utilizing precoated silica gel 60 F_{254} plates containing a fluorescent indicator, while preparative chromatography was performed using SilicaFlash P60 silica gel (230−400 mesh). Unless otherwise stated, the mobile phases for column chromatography were mixtures of hexanes/ethyl acetate. Columns were typically run using a gradient method, beginning with 100% hexanes and gradually increasing the polarity using ethyl acetate. A UV lamp was used to visualize reaction products. ^{1}H NMR and ^{13}C NMR spectra were obtained using Bruker-300, Varian Inova-500, Varian Unity-500, or Varian Inova-600 NMR spectrometers. For ^{1}H NMR, chemical shifts are reported relative to residual protiated solvent peaks (δ 7.26,

DOI: 10.1021/acs.organomet.5b00629
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2.49, 7.15, and 4.80 ppm for $CDCl_3$, $(CD_3)_2SO$, C_6D_6, and CD_3OD, respectively). ^{13}C NMR spectra were measured at either 125 or 150 MHz on the same instruments noted above for recording ^1H NMR spectra. Chemical shifts were again reported in accordance with residual protiated solvent peaks (δ 77.0, 39.5, 128.0, and 49.0 ppm for $CDCl_3$, $(CD_3)_2SO$, C_6D_6, and CD_3OD, respectively). Accurate mass measurements were acquired at the University of Wisconsin−Madison using a Micromass LCT (electrospray ionization, time-of-flight analyzer, or electron impact methods).

IPentCuCl.[27] CuCl (1.0 equiv), NaO^{t}Bu (1.0 equiv), IPentHCl (1.0 equiv),[28] and THF (0.2 M) were added to a dry Schlenk flask and stirred at rt. The progress of the reaction was checked via ^1H NMR after 30 min. Additional equivalents of CuCl and NaO^{t}Bu were added as needed to reach full conversion to IPentHCl and IHeptHCl. The reaction mixture was stirred with Celite for 15 min and then filtered over additional Celite. The filtrate was concentrated to yield an off-white solid, which was purified by either column chromatography (small scale, 20% EtOAc/hexanes) or recrystallization (large scale, hot toluene) to give a white solid (yields typically 60−75%). Although the complex was air stable, it was brought into the glovebox immediately for the next step. ^1H NMR (500 MHz, $CDCl_3$): δ 7.48 (t, J = 7.8 Hz, 2H), 7.21 (d, J = 7.8 Hz, 4H), 7.01 (s, 2H), 2.15 (p, J = 7.3 Hz, 4H), 1.73 (m, 8H), 1.65 (m, 4H), 1.50 (m, 4H), 0.92 (t, J = 7.4 Hz, 12H), 0.78 (t, J = 7.4 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 180.3, 143.2, 137.2, 130.1, 124.6, 123.7, 42.8, 29.3, 28.6, 13.0, 12.6. HRMS (ESI): m/z calculated for $[C_{35}H_{51}N_2CuCH_3CN + H]^+$ 604.3687, found 604.3693. For further crystallographic information, see the Supporting Information, Table S8 and Figure S4.

IPentCuO^{t}Bu. The procedure was adapted from the literature.[25] IPentCuCl (1.0 equiv) and NaO^{t}Bu (1.0 equiv) were stirred in THF under an inert atmosphere at rt. After 2 h, the reaction was filtered under N_2 and concentrated *in vacuo* overnight to yield an air-sensitive white solid (yields typically 60−85%). ^1H NMR (500 MHz, d_8-THF): δ 7.50 (t, J = 7.8 Hz, 2H), 7.29 (d, J = 7.9 Hz, 4H), 7.28 (s, 2H), 2.33 (p, J = 7.2 Hz, 4H), 1.90 (m, 4H), 1.79 (m, 4H), 1.68 (m, 4H), 1.60 (m, 4H), 0.98 (t, J = 7.4 Hz, 12H), 0.84 (t, J = 7.4 Hz, 12H), 0.73 (s, 9H). ^{13}C NMR (126 MHz, d_8-THF): δ 182.8, 143.3, 138.0, 129.2, 124.3, 123.6, 67.7, 42.5, 36.0, 28.7, 27.9, 12.4, 11.8.

IHeptCuCl. The same procedure employed for the synthesis of IPentCuCl was used. The crude product was purified by column chromatography (0−20% EtOAc/hexanes gradient), as the nonpolar ligand arms made recrystallization difficult. IHeptCuCl was isolated as a white solid (yields typically 60−75%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.45 (t, J = 7.8 Hz, 2H), 7.21 (d, J = 7.8 Hz, 4H), 6.96 (s, 2H), 2.29 (p, J = 7.2 Hz, 4H), 1.61 (m, 12H), 1.42 (m, 8H), 1.22 (m, 8H), 1.08 (m, 4H), 0.85 (t, J = 6.5 Hz, 12H), 0.82 (t, J = 7.3 Hz, 12H). ^{13}C NMR (500 MHz, $CDCl_3$): δ 180.3, 143.8, 136.7, 130.0, 124.6, 123.7, 39.9, 39.6, 38.8, 22.1, 21.2, 14.5, 14.3. HRMS(ESI): m/z calculated for $[C_{43}H_{68}N_2CuCH_3CN]^+$ 716.4939, found 716.4950. For further crystallographic information, see the Supporting Information, Table S9 and Figures S5−8.

IHeptOMe. The same procedure employed for the synthesis of IPentCuO^{t}Bu was used, except NaOMe was used as the base as attempts to prepare IHeptCuO^{t}Bu produced significant impurities. IHeptCuOMe was isolated as an off-white solid in yields typically around 70%. ^1H NMR (500 MHz, d_8-THF): δ 7.35 (t, J = 7.8 Hz, 2H), 7.16 (d, J = 7.8 Hz, 4H), 7.08 (s, 2H), 3.36 (s, 3H), 2.30 (p, J = 7.2 Hz, 4H), 1.48 (m, 20H), 1.09 (m, 12H), 0.74 (m, 24H). ^{13}C NMR (126 MHz, d_8-THF): δ 182.2, 143.8, 137.5, 129.4, 124.3, 123.8, 56.1, 39.7, 39.4, 38.5, 21.5, 21.1, 14.3, 13.8.

The substrates **2a**, **2c**, **2d**, **2i**, **2k**, **2l**, **2n**, **2p**, **2q**,[3] **2b**, **2e**, **2f**, **2h**,[4] **2j**,[29] **2g**,[30] **2o**,[5] **5a**,[31] **5b**,[32] **5c**,[33] **5f**,[34] **5g**,[32] and **5h**[35] were prepared according to literature procedures. Substrates **2m**, **2r**, **2s**, **2t**, **5d**, and **5e** were prepared as described in the Supporting Information.

General Procedure for NHC−Cu-Catalyzed 1,3-Bromine Migration and Trapping with 2-Naphthalenethiol. In a glovebox, a round-bottom flask was charged with IPrCuO^{t}Bu (11.8 mg, 0.0225 mmol, 0.09 equiv) and toluene (0.5 mL). The flask was brought out of the glovebox, placed in a preset oil bath at 45 °C, and stirred for 10 min. The substrate (0.25 mmol, 1.0 equiv) was added via syringe, followed immediately by addition of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (HBpin) (43.5 μL, 0.3 mmol, 1.2 equiv). After 1 h, the reaction mixture was filtered through Celite with diethyl ether and concentrated. Stable benzyl bromides were purified by column chromatography. Unstable benzyl bromides were trapped with 2-naphthalenethiol. Potassium carbonate (2.0 equiv), 2-napthalenethiol (1.5 equiv), and DMF (0.25−0.5 M in benzyl bromide) were added to the concentrated product mixture. The reaction was stirred for 1 h at rt and diluted with EtOAc, and the aqueous phase was extracted three times. The combined organic phase was washed five times with water, followed by brine (avoiding vigorous shaking, which can lead to emulsions). The organic layer was dried with Na_2SO_4, decanted, and concentrated *in vacuo*. The crude mixture was purified by column chromatography. NMR spectra have been included in the Supporting Information as a measure of purity.

Compound 3a. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **3a** as a clear oil in 81% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[27]

Compound 3b. Following the general procedure, column chromatography (50% CH_2Cl_2/hexanes) yielded **3b** as a clear oil in 81% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[28]

Compound 3c. Following the general procedure and trapping, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3c** as a clear oil in 55% yield over two steps. ^1H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 2.3 Hz, 1H), 7.76 (m, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.43 (m, 5H), 5.56 (q, J = 7,0 Hz, 1H), 1.63 (d, J = 6.9 Hz, 3H), 1.32 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.7, 146.1, 134.0, 133.7, 132.5, 131.9, 129.0, 128.9, 128.3, 127.8, 127.6, 127.2, 126.2, 125.9, 125.5, 83.6, 44.1, 34.4, 31.3, 24.9, 24.9, 22.4. HRMS (ESI): m/z calculated for $C_{28}H_{39}NBO_2S$ $[M + NH_4]^+$ 464.2794, found 464.2801.

Compound 3d. Following the general procedure, column chromatography (50% CH_2Cl_2/hexanes) yielded **3d** as a clear oil in 75% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[27]

Compound 3e. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **3e** as a clear oil in 49% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[28]

Compound 3f. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **3f** as a clear oil in 76% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[28]

Compound 3h. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **3h** as a clear oil in 30% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[28]

Compound 3i. Following the general procedure and trapping, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3i** as a clear oil in 29% yield over two steps. ^1H NMR (500 MHz, $CDCl_3$): δ 7.68 (m, 2H), 7.60 (m, 2H), 7.45 (dd, J = 8.7, 5.2 Hz, 1H), 7.34 (m, 4H), 6.98 (td, J = 8.5, 3.0 Hz, 1H), 5.44 (q, J = 6.9 Hz, 1H), 1.54 (d, J = 6.9 Hz, 3H), 1.25 (s, 6H), 1.24 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1 (d, J = 246.3 Hz), 144.1 (d, J = 3.1 Hz), 132.6, 132.2, 131.0, 128.7, 128.1, 127.2 (d, J = 7.3 Hz), 126.9, 126.6, 126.2, 125.2, 124.7, 120.9 (d, J = 19.6 Hz), 116.9 (d, J = 116.93 Hz), 83.0, 42.8, 23.8, 23.8, 21.5. HRMS (ESI): m/z calculated for $C_{24}H_{27}BFO_2S$ $[M + H]^+$ 408.1840, found 408.1849.

Compound 3j. Following the general procedure, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3j** as a clear oil in 55% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.47 (dd, J = 7.5, 1.4 Hz, 1H), 7.19 (m, 1H), 7.06 (ddd, J = 12.0, 8.2, 1.4 Hz, 1H), 6.12 (qd, J = 7.1, 1.9 Hz, 1H), 2.03 (dd, J = 7.0, 1.8 Hz, 3H), 1.30 (s, 6H), 1.29 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0 (d, J = 252.3 Hz), 134.5 (d, J = 9.3 Hz), 130.5 (d, J = 3.5 Hz), 128.2 (d, J = 8.6 Hz), 118.4 (d, J = 22.5 Hz), 83.2, 43.0, 24.3 (d, J = 6.1 Hz), 23.9, 23.7. HRMS (ASAP): m/z calculated for $C_{14}H_{19}BBrFO_2$ $[M + NH_4]^+$ 345.1021, found 345.1015.

DOI: 10.1021/acs.organomet.5b00629
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Compound 3k. Following the general procedure, column chromatography (50% CH_2Cl_2/hexanes) yielded **3k** as a clear oil in 86% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[28]

Compound 3l. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **3l** as a clear oil in 75% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[27]

Compound 3m. Following the general procedure, column chromatography (37.5% CH_2Cl_2/hexanes) yielded **3m** as a white solid in 75% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 2.2 Hz, 1H), 7.23 (dd, J = 8.0, 2.2 Hz, 1H), 6.18 (q, J = 6.9 Hz, 1H), 1.99 (d, J = 6.9 Hz, 3H), 1.36 (s, 6H), 1.35 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5, 137.7, 137.4, 127.5, 126.9, 84.1, 47.1, 26.9, 25.0, 24.7. HRMS (ESI): m/z calculated for $C_{14}H_{19}BBrClO_2$ $[M + H]^+$ 344.0460, found 344.0468.

Compound 3n. Following the general procedure and trapping, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3n** as a clear oil in 58% yield over two steps. ^1H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, J = 2.3 Hz, 1H), 7.67 (m, 2H), 7.59 (m, 2H), 7.41 (dd, J = 8.4, 2.3 Hz, 1H), 7.33 (m, 4H), 5.41 (q, J = 6.9 Hz, 1H), 1.52 (d, J = 6.9 Hz, 3H), 1.24 (s, 6H), 1.23 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 147.5, 137.3, 133.0, 132.5, 132.0, 131.0, 128.7, 128.0, 127.2, 126.9, 126.6, 126.2, 125.3, 124.8, 119.5, 83.1, 42.9, 23.8, 23.8, 21.3. HRMS (ESI): m/z calculated for $C_{24}H_30NBrO_2S$ $[M + NH_4]^+$ 488.1254, found 488.1253.

Compound 3o. Following the general procedure, column chromatography (37.5% CH_2Cl_2/hexanes) yielded **3o** as a clear oil in 56% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[28]

Compound 3p. Following the general procedure and trapping, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3p** as a white solid in 51% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, J = 2.2 Hz, 1H), 7.80 (s, 1H), 7.75 (d, J = 7.5, 1H), 7.64 (m, 6H), 7.42 (m, 5H), 7.32 (tt, J = 7.3, 1.3 Hz, 1H), 5.62 (q, J = 6.9 Hz, 1H), 1.68 (d, J = 6.9 Hz, 3H), 1.33 (s, 6H), 1.33 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.4, 140.8, 139.0, 134.7, 133.6, 133.6, 132.0, 129.8, 129.3, 129.0, 128.6, 127.9, 127.6, 127.2, 127.1, 127.1, 126.8, 126.2, 125.6, 83.8, 44.2, 24.9, 24.8, 22.4. HRMS (ESI): m/z calculated for $C_{30}H_{31}BO_2S$ $[M + NH_4]^+$ 484.2481, found 484.2477.

Compound 3q. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **3q** as a clear oil in 53% yield. ^1H NMR and ^{13}C NMR were consistent with the literature.[27]

Compound 3r. Following the general procedure, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3r** as a clear oil in 31% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, J = 7.3 Hz, 1H), 7.21 (d, J = 7.5 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 6.24 (q, J = 7.4 Hz, 1H), 2.56 (s, 3H), 2.08 (d, J = 7.2 Hz, 3H), 1.37 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.5, 136.8, 134.6, 133.4, 127.3, 84.0, 49.0, 25.4, 24.9, 24.8, 21.0. HRMS (ASAP): m/z calculated for $C_{15}H_{22}BBrO_2$ $[M + NH_4]^+$ 341.1271, found 341.1260. For **3r** and **3t**, HMBCs are included in the Supporting Information, as several aryl carbons were difficult to assign based on ^{13}C data alone.

Compound 3s. Following the general procedure, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3s** as a white solid in 60% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, J = 7.9 Hz, 1H), 7.27 (t, J = 7.9 Hz, 1H), 7.05 (d, J = 7.9 Hz, 1H), 5.65 (q, J = 6.9 Hz, 1H), 2.42 (s, 3H), 2.04 (d, J = 6.9 Hz, 1H), 1.43 (s, 6H), 1.41 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3, 142.1, 129.8, 129.2, 123.1, 84.1, 49.3, 25.9, 25.1, 25.0, 22.3. HRMS (EI): m/z calculated for $C_{15}H_{22}BBrO_2$ $[M + NH_4]^+$ 342.1248, found 342.1252.

Compound 3t. Following the general procedure, column chromatography (0 to 37.5% CH_2Cl_2/hexanes) yielded **3t** as a clear oil in 20% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.51 (d, J = 7.2 Hz, 1H), 7.20 (m, 2H), 6.07 (m, 1H), 2.81, (m, 2H), 2.10 (d, J = 7.1 Hz, 3H), 1.66 (sextet, J = 6.7, 2H), 1.39 (s, 6H), 1.37 (s, 6H), 1.02 (t, J = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 140.8, 133.3, 132.9, 127.2, 84.0, 48.4, 35.5, 35.49, 26.7, 24.9, 24.9, 24.8, 14.3. HRMS (ASAP): m/z calculated for $C_{17}H_{26}BBrO_2$ $[M + NH_4]^+$ 369.1584, found 369.1584.

General Procedure for 1,3-Chlorine Migration. In a glovebox, a round-bottom flask was charged with IHeptCuOMe (16.0 mg, 0.0225 mmol, 0.09 equiv) and toluene (2.5 mL). The flask was brought out of the glovebox, placed in a preset oil bath at 45 °C, and stirred for 5 min. The substrate (0.25 mmol, 1.0 equiv) was added via syringe, followed immediately by addition of HBpin (72 μL, 0.5 mmol, 2.0 equiv). The reaction mixture was then put in an oil bath preset at 100 °C. After 1 h, the reaction mixture was concentrated. Stable benzyl chlorides were purified by column chromatography.

Compound 6a. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **6a** as a clear oil in 69% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.27 (t, J = 7.9 Hz, 1H), 6.07 (q, J = 6.7 Hz, 1H), 1.81 (d, J = 6.7 Hz, 3H), 1.36 (s, 6H), 1.35 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 149.2, 135.8, 131.5, 127.1, 125.9, 83.8, 57.3, 27.3, 24.9, 24.8. HRMS (EI): m/z calculated for $C_{14}H_{20}BClO_2$ $[M + NH_4]^+$ 283.1620, found 283.1621.

Compound 6b. Following the general procedure, column chromatography (50% CH_2Cl_2/hexanes) yielded **6b** as a yellow oil in 68% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.32 (t, J = 8.0 Hz, 1H), 7.15 (d, J = 7.8 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 5.21 (q, J = 6.8 Hz, 1H), 3.78 (s, 3H), 1.83 (d, J = 6.8 Hz, 3H), 1.40 (s, 6H), 1.39 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 162.6, 147.8, 131.0, 118.1, 109.5, 84.1, 58.2, 55.7, 26.8, 24.8, 24.8. HRMS (ESI): m/z calculated for $C_{15}H_{22}BClO_3$ $[M + NH_4]^+$ 313.1726, found 313.1718.

Compound 6c. Following the general procedure, column chromatography (50% CH_2Cl_2/hexanes) yielded **6c** as a clear oil in 88% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J = 8.3 Hz, 1H), 7.23 (d, J = 2.5 Hz, 1H), 6.80 (dd, J = 8.4, 2.5 Hz, 1H), 6.08 (q, J = 6.7, 1H), 3.84 (s, 3H), 1.78 (d, J = 6.7 Hz, 3H), 1.34 (s, 6H), 1.32 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 162.3, 151.7, 137.9, 112.6, 111.9, 57.2, 55.2, 27.5, 24.9, 24.8. HRMS (EI): m/z calculated for $C_{15}H_{22}BClO_3$ $[M + NH_4]^+$ 313.1726, found 313.1724.

Compound 6d. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **6d** as a clear oil in 93% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.6 (s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 7.8 Hz, 1H), 6.02 (q, J = 6.8 Hz, 1H), 2.33 (s, 3H), 1.80 (d, J = 6.7 Hz, 3H), 1.36 (s, 6H), 1.34 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.4, 136.7, 136.2, 132.2, 125.9, 83.8, 57.2, 27.2, 24.9, 24.8, 20.93. HRMS (EI): m/z calculated for $C_{15}H_{22}BClO_2$ $[M + NH_4]^+$ 297.1776, found 297.1768.

Compound 6e. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **6e** as a white solid in 48% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 8.0 (s, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.69 (dd, J = 8.2, 2.0 Hz, 1H), 7.61 (d, J = 7.61 Hz, 2H), 7.43 (t, J = 7.48 Hz, 2H), 7.34 (t, J = 7.20 Hz, 1H), 6.74 (q, J = 6.7 Hz, 1H), 1.85 (d, J = 6.7 Hz, 3H), 1.37 (s, 6H), 1.36 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.3, 140.7, 139.9, 134.6, 130.2, 128.7, 127.3, 127.2, 126.5, 84.0, 57.1, 27.2, 24.9, 24.8. HRMS (EI): m/z calculated for $C_{20}H_{24}BClO_2$ $[M + NH_4]^+$ 359.1933, found 359.1931.

Compound 6f. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **6f** as a white solid in 77% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.18 (d, J = 8.0 Hz, 1H), 5.94 (q, J = 6.8 Hz, 1H), 1.70 (d, J = 6.8 Hz, 3H), 1.28 (s, 6H), 1.27 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.3, 136.8, 136.3, 126.3, 125.4, 83.0, 55.3, 26.2, 23.8, 23.75. HRMS (ASAP): m/z calculated for $C_{14}H_{19}BCl_2O_2$ $[M + NH_4]^+$ 317.1230, found 317.1236.

Compound 6g. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **6g** as a clear oil in 55% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.90 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 7.9 Hz, 1H), 6.06 (q, J = 6.7 Hz, 1H), 1.82 (d, J = 6.7 Hz, 3H), 1.37 (s, 6H), 1.36 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.1, 136.3, 133.2 (q, J = 32.3 Hz), 124.9 (q, J = 272.8 Hz), 123.6 (q, J = 3.82 Hz), 122.7 (q, J = 3.85 Hz), 84.4, 56.3, 27.2, 24.9, 24.8. HRMS (EI): m/z calculated for $C_{15}H_{19}BF_3O_2$ $[M + H]^+$ 334.1228, found 334.1222.

DOI: 10.1021/acs.organomet.5b00629
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Compound 6h. Following the general procedure, column chromatography (25% CH_2Cl_2/hexanes) yielded **6h** as a clear oil in 49% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 7.7 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.26 (t, J = 7.1 Hz, 1H), 5.83 (t, J = 6.9 Hz, 1H), 2.03 (m, 2H), 1.35 (s, 6H), 1.34 (s, 6H), 1.00 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 148.4, 135.7, 131.4, 126.9, 126.6, 83.8, 63.8, 34.4, 24.9, 24.8, 11.7. HRMS (EI): m/z calculated for $C_{15}H_{22}BClO_2$ $[M + NH_4]^+$ 297.1776, found 297.1781.

General Procedure for 1,3-Halogen Migration and Hydroboration Catalyzed by dCype.[3] In a glovebox, CuCl (4.5 mg, 0.045 mmol, 0.09 equiv), 1,2-bis(dicyclohexanephosphino)ethane (19 mg, 0.045 mmol, 0.09 equiv), and potassium *tert*-butoxide (10 mg, 0.090 mmol, 0.18 equiv) were added to a 5 mL round-bottom flask. The flask was charged with 1 mL of dry, degassed THF, fitted with a septum, and removed from the glovebox. The mixture was allowed to stir at ambient temperature for approximately 10 min. A portion of HBpin (0.087 mL, 0.6 mmol, 1.2 equiv) was added, and the reaction was allowed to stir for an additional 10 min. An aliquot of 2-bromostyrene (0.063 mL, 0.05 mmol) was added to the reaction, and the flask moved to an oil bath preset to 40 °C. The mixture was stirred for 2 h, cooled, filtered through a pad of Celite, and washed with 10 mL of diethyl ether.

Compound 4m. An integrated ^{1}H NMR yield of 48% was obtained using 1,1,1,2-tetrachloroethane as an internal standard. The crude material was purified by column chromatography (20% CH_2Cl_2/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, J = 8.5 Hz, 1H), 7.23 (d, J = 2.5 Hz, 1H), 6.99 (dd, J = 8.5, 2.6 Hz, 1H), 2.74 (q, J = 7.5 Hz, 1H), 1.34 (d, J = 7.5 Hz, 3H), 1.24 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.4, 144.0, 133.4, 128.7, 126.7, 122.7, 83.7, 24.7, 24.6, 15.4. HRMS (ASAP): m/z calculated for $C_{14}H_{19}BBrClO_2$ $[M + H]^+$ 344.0460, found 344.0461.

Copper Hydride Stability Measurements. In the glovebox, the precatalyst NHC−Cu-OR (0.025 mmol) and d_8-THF (0.5 mL) were added to a dry NMR tube. The tube was capped with a septum and brought out of the glovebox. Mesitylene (2 μL, 0.014 mmol) was added, and the sample inserted into the spectrometer. After reaching the desired temperature, the sample was ejected, PMHS (1.8 μL, 0.03 mmol) was added, and the sample was reinserted into the spectrometer. ^{1}H NMR spectra (1 scan) were taken every 1−2 min over several hours. The hydride peaks were used for integration (Supporting Information, Tables S2−S4).

Copper Hydride Diffusion Constants. Insight into the nature of the NHC−CuH species in solution was obtained using pulse gradient spin echo (PGSE) NMR. The PGSE experiment measures the translational motion of molecules and weakly associated complexes through a solution, permitting the extraction of diffusion coefficients for individual compounds.[36] As these coefficients are inversely related to the hydrodynamic volume of the complexes, they can be used to probe monomer−dimer equilibria in solution and yield information about the relative molecular weights of species that cannot be isolated in the solid state.[36,37a,b] In our studies, $Rh_2(TPA)_4$ (TPA = triphenylacetate), IPrCuO^{t}Bu, (dCype)$NiCl_2$, and $PdCl_2(PPh_3)_2$ were used as reference compounds to obtain diffusion coefficients for the Cu complexes (Supporting Information, Tables S5−S7).

Stoichiometric Reactions. The aryl Cu(I) intermediate was identified and characterized in the following manner. In the glovebox, IPrCuO^{t}Bu (13.1 mg, 0.025 mmol) was weighed into an NMR tube and suspended in d_8-toluene (0.5 mL). The tube was capped with a septum and removed from the glovebox. PMHS (1.8 μL, 0.03 mmol) was added via syringe, giving a bright yellow solution that became homogeneous after several rounds of inverting the NMR tube. A ^{1}H NMR spectrum was acquired on IPrCuH[25] to ensure its complete formation. After acquisition, **2a** (3.2 μL, 0.025 mmol) was added. After several seconds, a color change from bright yellow to clear was observed and the sample reinserted into the spectrometer. Complete conversion of IPrCuH to aryl-copper(I) **3.1** was observed, and the complex was characterized by ^{1}H NMR and HMBC. It should be noted the ^{13}C shift of the *ipso*-copper aryl carbon, 164.6 ppm, closely matched that seen by Herron (166.1 ppm).[38] Following characterization of **3.1**, HBpin (7.3 μL, 0.05 mmol) was added, product **3a** was formed, and the colored IPrCuH was regenerated (Figure S1, Supporting Information).

Transmetalation-Induced 1,3-Migration. In the glovebox, IPrCuO^{t}Bu (13.1 mg, 0.025 mmol) was weighed into an NMR tube and suspended in d_8-toluene (0.5 mL). The tube was capped with a septum and removed from the glovebox. Benzyl boronic ester **3a** (5.6 μL, 0.025 mmol) was added via syringe, and the sample inserted into the spectrometer at rt. Approximately 3% (relative to **3a**) of aryl copper **3.1** was observed. Both the chemical shifts and the decomposition to styrene at higher temperature, a pathway previously observed, confirmed this assignment (Figure S2, Supporting Information).

Identification of the Benzyl Cu(I) Species. In the glovebox, IPentCuO^{t}Bu (15.9 mg, 0.025 mmol) was weighed into an NMR tube and dissolved in d_8-toluene (0.5 mL). The tube was capped with a septum and removed from the glovebox. PMHS (1.8 μL, 0.03 mmol) was added via syringe, giving a bright yellow solution. A ^{1}H NMR spectrum was acquired on IPentCuH to ensure its complete formation. After acquisition, **5a** (3.2 μL, 0.025 mmol) was added, the sample was reinserted into the spectrometer, and the probe was warmed to 40 °C to facilitate hydrocupration. Complete conversion of IPentCuH to benzyl-copper(I) **3.2** was observed, and the complex was characterized by ^{1}H, HSQC, and HMBC. Following characterization of **3.2**, the sample was heated to 90 °C and migration to aryl-copper(I) **3.3** observed (**3.3** assigned based on **3.1**). HBpin (7.3 μL, 0.05 mmol) was added to this solution, product **6a** was formed, and the colored IPentCuH was regenerated (Figure S3, Supporting Information).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00629.

Experimental procedures, computational details, and characterization data for all new compounds (PDF)

om5b00629_si_002.xyz - IPentCuCl crystal structure (XYZ)

om5b00629_si_003.xyz - IHeptCuCl crystal structure (XYZ)

om5b00629_si_004.cif - IPentCuCl crystal data (CIF)

om5b00629_si_005.cif - IHeptCuCl crystal data (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by startup funds provided by the University of Wisconsin−Madison and the ACS-PRF No. 53146-ND1. J.M.S. is an Alfred P. Sloan Fellow. The NMR facilities at UW−Madison are funded by the National Science Foundation (NSF; CHE-9208463, CHE-9629688) and National Institutes of Health (NIH; RR08389-01). The computational cluster at UW−Madison is funded by NSF Grant CHE-0840494. Dr. Charlie Fry, Dr. Heike Hofstetter, and Dr. Monika Ivancic of the University of Wisconsin are thanked for their assistance with NMR spectroscopy, Dr. Martha Vestling is acknowledged for her assistance with MS data, and Dr. Maik Tretbar, Dr. Ilia Guzei, and Brian Dolinar are thanked for their assistance with XRD data collection and processing.

DOI: 10.1021/acs.organomet.5b00629
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DOI: 10.1021/acs.organomet.5b00629
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