Organic LETTERS

Letter

pubs.acs.org/OrgLett

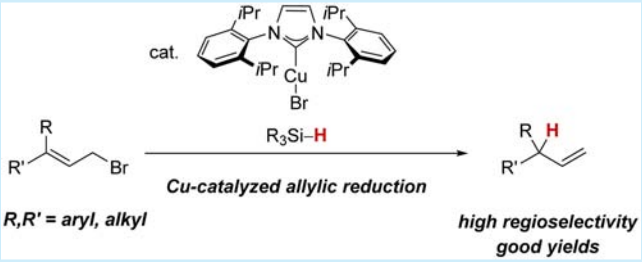
Copper(I)-Catalyzed Allylic Substitutions with a Hydride Nucleophile

T. N. Thanh Nguyen, Niklas O. Thiel,[†] Felix Pape,[†] and Johannes F. Teichert*

Institut für Chemie, Technische Universität Berlin, Straße des 17. Juni 115, 10623 Berlin, Germany

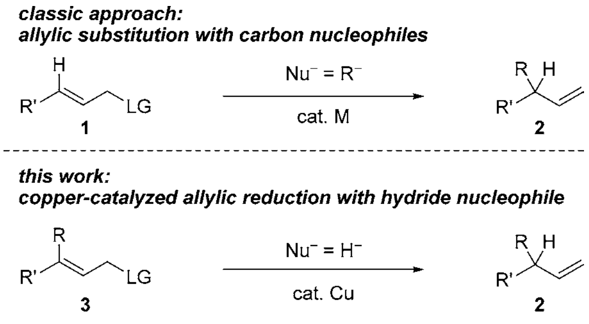
Supporting Information

ABSTRACT: An easily accessible copper(I)/N-heterocyclic carbene (NHC) complex enables a regioselective hydride transfer to allylic bromides, an allylic reduction. The resulting aryl- and alkyl-substituted branched α-olefins, which are valuable building blocks for synthesis, are obtained in good yields and regioselectivity. A commercially available silane, (TMSO)$_2$Si(Me)H, is employed as hydride source. This protocol offers a unified alternative to the established metal-catalyzed allylic substitutions with carbon nucleophiles, as no adaption of the catalyst to the nature of the nucleophile is required.



The transition-metal-catalyzed allylic substitution is a widely applicable method to generate terminal alkenes bearing α-substitutions. Branched α-olefins **2** bearing alkyl and/or aryl substituents can be accessed by appropriate catalytic systems from **1** and a nonstabilized carbon nucleophile (Scheme 1, top). While for these transformations copper catalysts have been most thoroughly studied,[1−7] a variety of other metal catalysts have also been disclosed.[8−13]

Scheme 1. Allylic Substitution vs Allylic Reduction[a]



[a] Nu^- = nucleophile, LG = leaving group.

In contrast, the alternative pathway employing a hydride nucleophile with the corresponding higher substituted allylic substrates **3** has been less investigated (Scheme 1, bottom).[14−21] This approach—the allylic reduction—bears the advantage that a single catalyst could give rise to a wide variety of alkene products **2** if the catalytic process equally tolerates aryl and alkyl substituents. The required allylic acceptors **3** could be accessed employing similar routes as for **1**, e.g., by formation of the alkene by Horner–Wadsworth–Emmons reaction followed by reduction and generation of the appropriate leaving group.

Pd-catalyzed allylic substitutions with hydride nucleophiles have been reported.[14−20,22] These transformations have mainly been applied in protecting group manipulations.[23] It should be noted that recently an alternative organocatalytic approach to allylic reduction employing phosphetanes and an aluminum hydride has been reported.[24]

We reasoned that a protocol relying on cheap and readily available copper catalysts employing silanes as hydride source would be a useful approach to catalytic allylic reductions, given the success of copper-catalyzed allylic alkylations.[1] An allylic reduction based upon Cu–H complexes would be synthetically attractive, since these compounds generally display high functional group tolerance.[25] We herein report an unprecedented[26,27] copper(I)-catalyzed allylic reduction protocol with silanes.

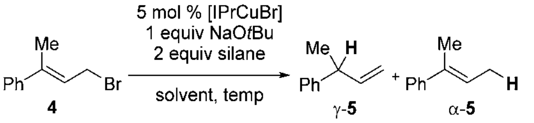
The reaction of β-methyl cinnammic acid derived bromide **4** to the corresponding terminal and internal alkenes **5** served as test reaction for optimization studies (Table 1). We opted for readily available and well-defined[28] copper(I)/NHC complexes as a starting point of our investigation, as these compounds had been described as effective catalysts for related hydrosilylation reactions[25] and S_N2'-type hydride transfer to propargylic acceptors.[27a,b] Initial optimization studies revealed two general trends:[29] (i) Halogen leaving groups (Cl and Br) showed conversion in the allylic reduction, whereas oxygen-based leaving groups are not reactive. The reaction with allylic chlorides proceeded with significantly lower conversion and regioselectivity than with allylic bromides. (ii) With catalytic amounts of NaO*t*Bu (10 mol %), the reaction proceeds as well, but extended reaction times (>72 h) are required to reach full conversion.

Employing polymethylhydrosiloxane (PMHS), a commonly used silane in Cu–H catalysis,[25] and [IPrCuBr][28d,e,31] as

Received: April 8, 2016
Published: May 6, 2016

DOI: 10.1021/acs.orglett.6b00941
Org. Lett. 2016, 18, 2455−2458

Table 1. Optimization of the Copper(I)-Catalyzed Allylic Reduction



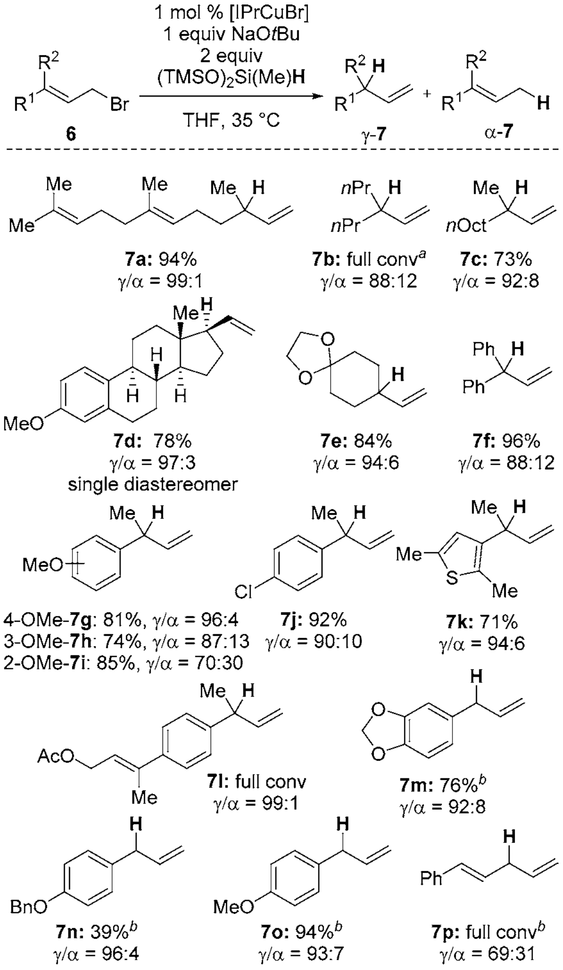
entry	solvent	temp (°C)	silane	conv[a]	γ/α ratio[a]
1	THF	35	PMHS[b]	95%	61:39
2	THF	35	monomer[c]	full	>95:5
3	THF	0	monomer[c]	full	>95:5
4	THF	−78	monomer[c]	50%	>95:5
5	PhMe	35	monomer[c]	full	66:34
6	1,4-dioxane	35	monomer[c]	full	83:17
7	CyH	35	monomer[c]	full[d]	22:78
8	*o*-$C_6H_4Cl_2$	35	monomer[c]	full	93:7
9	PhCl	35	monomer[c]	full	>95:5
10[e]	PhCl	35	monomer[c]	full	95:5
11[e]	**THF**	**35**	monomer[c]	**full**[f]	**>95:5**

[a] Determined by ^{1}H NMR and GC analysis. [b] PMHS = polymethylhydrosiloxane. [c] Monomer = 1,1,1,3,5,5,5-heptamethyltrisiloxane. [d] 10% of an uncharacterized olefinic compound detected. [e] With 1 mol % of [IPrCuBr]. [f] 69% isolated yield.

catalyst, 95% conversion of **4** was detected with a slight preference for the terminal alkene γ-**5** (γ/α = 61:39, Table 1, entry 1). With structurally related "monomeric PMHS", 1,1,1,3,5,5,5-heptamethyltrisiloxane, full conversion and high regioselectivity toward γ-**5** was obtained at 35 °C (Table 1, entry 2). Similar results in terms of regioselectivity were also found at 0 °C and −78 °C, albeit with reduced conversion of 50% at −78 °C (Table 1, entries 3 and 4). During investigation of the substrate scope, it was found that allylic bromides bearing electron-withdrawing groups would reach full conversion only at 35 °C; therefore, all of the ensuing reactions were carried out at this temperature. The influence of the solvent on the regioselectivity is profound: While the γ/α ratio was lower in toluene and 1,4-dioxane (Table 1, entries 5 and 6), the regioselectivity was reversed in cyclohexane, favoring internal alkene α-**5** (Table 1, entry 7). High regioselectivities were also found in chlorinated aromatic solvents, such as *o*-dichlorobenzene and PhCl (Table 1, entries 8 and 9). In the latter and in THF, lowering the catalyst loading to 1 mol % of [IPrCuBr] was possible without jeopardizing regioselectivity or conversion (Table 1, entries 10 and 11, 69% yield of γ-**5** in THF). With foresight to a practical overall process, the scope of this copper(I)-catalyzed allylic reduction was investigated employing THF as solvent.

With regard to substrate scope, generally, *E*-isomers of the allylic bromides **6** were employed, however, with **6g** (*E*/*Z* 74:26) and **6k** (*E*/*Z* 56:44) mixtures of isomers were used.[29] A preference in reactivity of the catalyst for either alkene stereoisomer or an influence on regioselectivity could not be detected. We found that allylic bromides **6** bearing both aryl and alkyl substituents were amenable to the optimized reaction conditions (Scheme 2): Farnesyl bromide (**6a**) could be converted to the corresponding terminal alkene **7a** with excellent yield and regioselectivity. Other dialkyl-substituted alkenes such as **7b** and **7c** were produced with similar γ/α ratios. Methyl-substituted estrone derivative **7d** was isolated with excellent diastereo- and regioselectivity (78%, as a single diastereomer, γ/α = 97:3). Acetal **6e** undergoes the allylic reduction without removal of the protecting group (**7e**, 84%).

Scheme 2. Substrate Scope of the Copper(I)-Catalyzed Allylic Reduction



[a] Product is volatile. [b] Reactions were carried out at 0 °C.

Regarding the chemoselectivity of the present protocol, it was shown by competition experiments that the other common reaction of Cu−H complexes, such as the 1,2- and 1,4-reduction,[25] can occur, but generally, the allylic reduction proceeds faster.[29] Of particular note is the fact that diphenyl-substituted allylic bromide **6f** can be transformed to alkene **7f** in excellent yield and good regioselectivity (96%, γ/α = 88:12). This successful result marks a rare case of γ,γ-diaryl-substituted substrates for metal-catalyzed allylic substitutions.[13b,24,30] Aryl,alkyl-substituted allylic bromides are viable substrates for the allylic reduction: Both electron-rich (OMe-substituted **6g**−**i**) and electron-poor allylic bromides (chloro-substituted **6j**) undergo the allylic reduction.

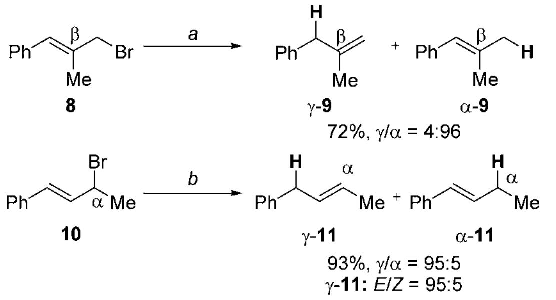
Shifting the methoxy substituent of substrates **6g**−**i** from the *para*- to *meta*- to *ortho*-position, the regioselectivity of the allylic reduction decreased (γ/α = 96:4 for **7g**, 87:13 for **7h**, 70:30 for **7i**). The relatively low regioselectivity for **7i** could be explained by steric hindrance or coordination to the copper catalyst. Thiophene-substituted **7k** (71%, 94:6) could successfully be synthesized via the allylic reduction protocol. Terminal alkene **7l** was obtained (γ/α > 99:1) without jeopardizing the allylic acetate, showcasing the high chemoselectivity of the catalyst for allylic bromides.

The copper(I)-catalyzed allylic reduction could be extended to disubstituted allylic bromides; for best results in terms of γ/

α-selectivity, the reactions were carried out at 0 °C: Safrol (**7m**) was obtained with good yields and selectivities (76%, 92:8). Protected phenol derivatives **7n** and **7o** showed similar regioselectivities. Finally, the allylic reduction method can be used to produce skipped dienes: Cinnamylideneacetic acid-derived bromide **6p** could be converted to terminal alkene **7p**, albeit with a somewhat lower regioselectivity (69:31).

Next, the influence of substitutions at different positions of the allylic bromide on the regioselectivity of the catalytic hydride transfer was investigated. Employing β-methyl-substituted allylic bromide **8** resulted in reversed selectivity favoring the internal alkene α-**9** (Scheme 3, top). In contrast, α-methyl-substituted allylic bromide **10** gave the usual regioselectivity in favor of the unconjugated alkene γ-**11** (Scheme 3, bottom).

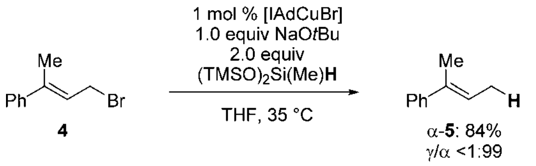
Scheme 3. Copper(I)-Catalyzed Allylic Reduction: Influence of Substitution on Regioselectivity



[a] 1 mol % of [IPrCuBr], 1 equiv of NaO*t*Bu, 2 equiv of $(TMSO)_2Si(Me)H$, THF, 35 °C. [b] As in *a*, but at 0 °C.

Through optimization studies,[29] it was found that by strategic choice of copper(I)/NHC complexes the regioselectivity of the allylic reduction could be reversed toward the α-substitution product. Adamantyl-substituted copper(I) complex [IAd-CuBr][31] gives rise to internal alkene α-**5** as only detectable regioisomer under otherwise identical reaction conditions (84% yield, Scheme 4). This switch in regioselectivity could be controlled by the stronger electron-donating ability of the NHC ligand in [IAdCuBr], favoring σ → π isomerization of the allylcopper intermediates,[32] leading to α-**5**.

Scheme 4. Allylic Reduction: Reversal of Regioselectivity



In summary, we have developed an allylic reduction protocol with readily available copper(I)/NHC catalysts and a silane as hydride source. The corresponding substituted branched α-olefins are obtained with good yields and high regioselectivity. Aryl and alkyl substituents on the allylic bromides are tolerated. Therefore, this approach offers a practical and unified alternative to other catalytic allylic substitutions, which generally are highly optimized for one particular class of nucleophiles. Studies toward the development of an asymmetric variant are currently underway.

■ ASSOCIATED CONTENT

Supporting Information

Detailed starting material synthesis, general procedures, characterization data, and NMR spectra for all compounds. The Supporting Information is available free of charge on the ACS Publications Web site. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00941.

Detailed starting material synthesis, general procedures, characterization data, and spectra for catalysis products (PDF)

Spectra for synthetic intermediates (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: johannes.teichert@chem.tu-berlin.de.

Author Contributions

†N.O.T. and F.P. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

T.N.T.N. and J.F.T. acknowledge support by the Fonds der Chemischen Industrie through a Liebig-Stipendium. F.P. is supported by a predoctoral fellowship from the Berlin International Graduate School of Natural Sciences and Engineering (BIG-NSE). We thank Kirandeep Kaur (TU Berlin) for initial experiments. Dr. Sebastian Kemper (TU Berlin) is acknowledged for assistance with NMR experiments. Prof. Dr. Martin Oestreich (TU Berlin) is kindly thanked for generous support.

■ REFERENCES

(1) Reviews Cu-catalyzed allylic substitution: (a) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796−2823. (b) Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824−2852. (c) Langlois, J.-B.; Alexakis, A. In *Transition Metal Catalyzed Allylic Substitution in Organic Synthesis*; Kazmaier, U.; Ed.; Springer: Heidelberg, 2012; Topics in Organometallic Chemistry, Vol. 38, pp 235−268.

(2) Zn-based nucleophiles, selected examples: (a) Dübner, F.; Knochel, P. *Tetrahedron Lett.* **2000**, *41*, 9233−9237. (b) Börner, C.; Goldsmith, P. J.; Woodward, S.; Gimeno, J.; Gladiali, S.; Ramazzotti, D. *Chem. Commun.* **2000**, 2433−2434. (c) Murphy, K. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4690−4691. (d) Malda, H.; van Zijl, A. W.; Arnold, L. A.; Feringa, B. L. *Org. Lett.* **2001**, *3*, 1169−1171. (e) Larsen, A. O.; Leu, W.; Oberhuber, C. N.; Campbell, J. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 11130−11131. (f) Goldsmith, P. J.; Teat, S. J.; Woodward, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 2235−2237.

(3) Mg-based nucleophiles, selected examples: (a) van Klaveren, M.; Persson, E. S.; del Villar, A.; Grove, D. M.; Bäckvall, J.-E.; van Koten, G. *Tetrahedron Lett.* **1995**, *36*, 3059−3062. (b) Tissot-Croset, K.; Polet, D.; Alexakis, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 2426−2428. (c) Tominaga, S.; Oi, Y.; Kato, T.; An, D. K.; Okamoto, S. *Tetrahedron Lett.* **2004**, *45*, 5585−5588. (d) López, F.; van Zijl, A. W.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2006**, 409−411. (e) Selim, K. B.; Matsumoto, Y.; Yamada, K.-i.; Tomioka, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 8733−8735.

(4) Al-based nucleophiles, selected examples: (a) Lee, Y.; Akiyama, K.; Gillingham, D. G.; Brown, M. K.; Hoveyda, A. H. *J. Am. Chem. Soc.*

2008, *130*, 446−447. (b) Dabrowski, J. A.; Gao, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 4778−4781.

(5) B-based nucleophiles, review: (a) Shintani, R. *Synthesis* **2016**, *48*, 1087−1100. Selected examples: (b) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 2895−2897. (c) Ohmiya, H.; Yokokawa, N.; Sawamura, M. *Org. Lett.* **2010**, *12*, 2438−2440. (d) Whittaker, A. M.; Rucker, R. P.; Lalic, G. *Org. Lett.* **2010**, *12*, 3216−3218. (e) Shintani, R.; Takatsu, K.; Takeda, M.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 8656−8659. (f) Shido, Y.; Yoshida, M.; Tanabe, M.; Ohmiya, H.; Sawamura, M. *J. Am. Chem. Soc.* **2012**, *134*, 18573−18576. (g) Hojoh, K.; Shido, Y.; Ohmiya, H.; Sawamura, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 4954−4958.

(6) Li-based nucleophiles, selected examples: (a) Pérez, M.; Fañanás-Mastral, M.; Bos, P. H.; Rudolph, A.; Harutyunyan, S. R.; Feringa, B. L. *Nat. Chem.* **2011**, *3*, 377−381. (b) Fañanás-Mastral, M.; Pérez, M.; Bos, P. H.; Rudolph, A.; Harutyunyan, S. R.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 1922−1925. (c) Guduguntla, S.; Hornillos, V.; Tessier, R.; Fañanás-Mastral, M.; Feringa, B. L. *Org. Lett.* **2016**, *18*, 252−255.

(7) Zr-based nucleophiles, selected examples: (a) You, H.; Rideau, E.; Sidera, M.; Fletcher, S. P. *Nature* **2015**, *517*, 351−355. (b) Sidera, M.; Fletcher, S. P. *Chem. Commun.* **2015**, *51*, 5044−5047.

(8) For a general review, see: Begouin, J.-M.; Klein, J. E. M. N.; Weickmann, D.; Plietker, B. In *Transition Metal Catalyzed Allylic Substitution in Organic Synthesis*; Kazmaier, U., Ed.; Springer: Heidelberg, 2012; Topics in Organometallic Chemistry, Vol. *38*, pp 269−320.

(9) For a review of Pd-catalyzed allylic substitution with non-stabilized nucleophiles, see: Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395−422.

(10) Review of Fe catalysis: Plietker, B.; Dieskau, A. *Eur. J. Org. Chem.* **2009**, *2009*, 775−787.

(11) Review of Co catalysis: Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1435−1462.

(12) Reviews of Ni catalysis: (a) Kobayashi, Y. In *Modern Organonickel Chemistry*; Tamaru, T., Ed.; Wiley−VCH: Weinheim, 2015; pp 56−101. (b) Shintani, R.; Hayashi, T. In *Modern Organonickel Chemistry*; Tamaru, T., Ed.; Wiley−VCH, Weinheim, 2015; pp 240−272.

(13) For related transition-metal-free variants, see, for example: (a) Jackowski, O.; Alexakis, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 3346−3350. (b) Grassi, D.; Alexakis, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 13642−13646. (c) Grassi, D.; Alexakis, A. *Chem. Sci.* **2014**, *5*, 3803−3807.

(14) For a review, see: (a) Tsuji, J.; Mandai, T. *Synthesis* **1996**, *1996*, 1−24. For selected early examples, see: (b) Tsuji, J.; Yamakawa, T. *Tetrahedron Lett.* **1979**, *20*, 613−616. (c) Tsuji, J.; Shimizu, I.; Minami, I. *Chem. Lett.* **1984**, *13*, 1017−1020. (d) Tsuji, J.; Minami, I.; Shimizu, I. *Synthesis* **1986**, *1986*, 623−627.

(15) For examples of regio- and diastereoselective reactions, see: (a) Hughes, G.; Lautens, M.; Wen, C. *Org. Lett.* **2000**, *2*, 107−110. (b) Lautens, M.; Paquin, J.-F. *Org. Lett.* **2003**, *5*, 3391−3394. (c) Chau, A.; Paquin, J.-F.; Lautens, M. *J. Org. Chem.* **2006**, *71*, 1924−1933. (d) Cheng, H.-Y.; Sun, C.-S.; Hou, D.-R. *J. Org. Chem.* **2007**, *72*, 2674−2677.

(16) For asymmetric variants, see: (a) Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y.; Miki, M.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 775−776. (b) Hayashi, T.; Kawatsura, M.; Iwamura, H.; Yamaura, Y.; Uozumi, Y. *Chem. Commun.* **1996**, 1767−1768. (c) Fuji, K.; Sakurai, M.; Kinoshita, T.; Kawabata, T. *Tetrahedron Lett.* **1998**, *39*, 6323−6326. (d) Kawatsura, M.; Uozumi, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron* **2000**, *56*, 2247−2257.

(17) For an example employing SmI_2 as reducing agent, see: Yoshida, A.; Hanamoto, T.; Inanaga, J.; Mikami, K. *Tetrahedron Lett.* **1998**, *39*, 1777−1780.

(18) For an example using Pd/C and H_2 as reductant, see: Caspi, D. D.; Garg, N. K.; Stoltz, B. M. *Org. Lett.* **2005**, *7*, 2513−2516.

(19) For an example with Au nanoparticles and H_2 as reductant, see: Noujima, A.; Mitsudome, T.; Mizugaki, T.; Jitsukawa, K.; Kaneda, K. *Chem. Commun.* **2012**, *48*, 6723−6725.

(20) For an example using Zn as reducing agent, see: Li, L.-P.; Rayabarapu, D. K.; Nandi, M.; Cheng, C.-H. *Org. Lett.* **2003**, *5*, 1621−1624.

(21) For the related Ni-catalyzed ring opening with hydrides, see: (a) ref 12b. For selected examples, see: (b) Lautens, M.; Chiu, P.; Ma, S.; Rovis, T. *J. Am. Chem. Soc.* **1995**, *117*, 532−533. (c) Lautens, M.; Rovis, T. *J. Am. Chem. Soc.* **1997**, *119*, 11090−11091.

(22) For a review employing silanes, see: (a) Keinan, E.; Greenspoon, N. *Isr. J. Chem.* **1984**, *24*, 82−87. Selected examples: (b) Keinan, E.; Greenspoon, N. *J. Org. Chem.* **1983**, *48*, 3545−3548. (c) Greenspoon, N.; Keinan, E. *J. Org. Chem.* **1988**, *53*, 3723−3731.

(23) (a) Hey, H.; Arpe, H.-J. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 928−929. (b) Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, 2004.

(24) Reichl, K. D.; Dunn, N. L.; Fastuca, N. J.; Radosevich, A. T. *J. Am. Chem. Soc.* **2015**, *137*, 5292−5295.

(25) Reviews of Cu−H catalysis: (a) Rendler, S.; Oestreich, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 498−504. (b) Deutsch, C.; Krause, N.; Lipshutz, B. H. *Chem. Rev.* **2008**, *108*, 2916−2927. (c) Lipshutz, B. H. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley−VCH: Weinheim, 2002; pp 167−187.

(26) The absence of a Cu-catalyzed hydride transfer to allylic systems has recently been highlighted: Zhu, S.; Niljianskul, N.; Buchwald, S. L. *Nat. Chem.* **2016**, *8*, 144−150.

(27) For the related S_N2'-substitution of propargylic compounds catalyzed by Cu−H compounds, see, for example: (a) Deutsch, C.; Lipshutz, B. H.; Krause, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 1650−1653. (b) Deutsch, C.; Lipshutz, B. H.; Krause, N. *Org. Lett.* **2009**, *11*, 5010−5012. (c) Zhong, C.; Sasaki, Y.; Ito, H.; Sawamura, M. *Chem. Commun.* **2009**, 5850−5852.

(28) For reviews, see: (a) Lazreg, F.; Nahra, F.; Cazin, C. S. J. *Coord. Chem. Rev.* **2015**, *293−294*, 48−79. (b) Díez-González, S.; Nolan, S. P. *Synlett* **2007**, *2007*, 2158−2167. (c) Lin, J. C. Y.; Huang, R. T. W.; Lee, C. S.; Bhattacharyya, A.; Hwang, W. S.; Lin, I. J. B. *Chem. Rev.* **2009**, *109*, 3561−3598. For the synthesis of ligands and complexes, see: (d) Hintermann, L. *Beilstein J. Org. Chem.* **2007**, *3*, 22. (e) Santoro, O.; Collado, A.; Slawin, A. M. Z.; Nolan, S. P.; Cazin, C. S. J. *Chem. Commun.* **2013**, *49*, 10483−10485.

(29) See the Supporting Information for details.

(30) (a) van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877−6882. (b) For a related Pd-catalyzed internal cross-coupling, see: Le, H.; Batten, A.; Morken, J. P. *Org. Lett.* **2014**, *16*, 2096−2099.

(31) Díez-González, S.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Stevens, E. D.; Slawin, A. M. Z.; Nolan, S. P. *Dalton Trans.* **2010**, *39*, 7595−7606.

(32) (a) Bäckvall, J.-E.; Sellén, M.; Grant, B. *J. Am. Chem. Soc.* **1990**, *112*, 6615−6621. (b) Thalén, L. K.; Sumic, A.; Bogár, K.; Norinder, J.; Persson, A. K. A.; Bäckvall, J.-E. *J. Org. Chem.* **2010**, *75*, 6842−6847. (c) Warner, M. C.; Nagendiran, A.; Bogár, K.; Bäckvall, J.-E. *Org. Lett.* **2012**, *14*, 5094−5097.