(NHC)Cu^{I} (NHC = N-Heterocyclic Carbene) Complexes as Efficient Catalysts for the Reduction of Carbonyl Compounds

Harneet Kaur, Fabiano Kauer Zinn, Edwin D. Stevens, and Steven P. Nolan*

Department of Chemistry, University of New Orleans, New Orleans, Louisiana 70148

Received November 7, 2003

Summary: The hydrosilylation of various ketones is mediated by an imidazolium salt/Cu(I) salt system or by a well-defined (NHC)CuCl (NHC = N-heterocyclic carbene) catalyst precursor system. Reactions are conducted at room temperature. The synthesis and characterization of well-defined (NHC)CuCl complexes are described.

Introduction

Organic transformations mediated by organocuprates represent a well-developed area of research.[1] Copper complexes have been used in numerous reaction types, including nucleophilic substitutions with alkyl halides, epoxide ring opening, and Michael additions to α,β-unsaturated compounds.[2] However, in these classical reactions, the copper reagent is used in stoichiometric amounts, making the chemistry less economically and environmentally attractive and rendering product isolation and workups more tedious. The use of catalytic amounts of copper has been demonstrated, but such applications have been restricted to date to couplings of aryl halides[3] and reductions of various substrate types.[4,5] The use of the thermally stable organocopper(I) hydride cluster $[(Ph_3P)CuH]_6$ [6] in the selective reduction of enones was introduced by Stryker as an effective metal-mediated reaction.[7] Initially, the copper complex was used in stoichiometric amounts in this transformation, but the use of hydrogen sources such as hydrogen gas[8] and silanes[9] enabled the generation of a Cu−H complex in a catalytic fashion.

During the last 10 years, *N*-heterocyclic carbenes (NHC) have emerged as efficient ligands in metal-mediated reactions.[10] As strong σ-donors, the NHC ligands have a stronger interaction with the metal center compared to tertiary phosphines, thereby minimizing ligand dissociation. This characteristic ligand property, in addition to the significant steric bulk associated with the NHC ligand family, results in metal−NHC complexes having unique and distinct catalytic behavior compared to their phosphine-based analogues.[11]

The catalytic hydrosilylation of carbonyl compounds, which leads directly to protected alcohols, is a useful synthetic alternative to the reduction of carbonyl groups by main-group hydrides or catalytic hydrogenation methods.[12] A number of transition-metal-centered catalytic methods have been employed to mediate this transformation.[13]

---

* To whom correspondence should be addressed. E-mail: snolan@uno.edu.

(1) For leading references, see: (a) Taylor, R. J. K. *Organocopper Reagents, a Practical Approach*; Oxford University Press: New York, 1994. (b) Lipshutz, B. H. In *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1991; Vol. 1, Chapter 14. (c) Krause, N. *Modern Organocopper Chemistry*, 1st ed.; Wiley-VCH: Weinheim, Germany, 2002.

(2) For reviews, see: (a) Krause, N. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 186−204. (b) Woodward, S. *Chem. Soc. Rev.* **2000**, 393−401. (c) Nakamura, E.; Mori, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 3751−3771.

(3) (a) Antilla, J. C.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 11684−11688. (b) Job, G. E.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3703−3706. (c) Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844−14845. (d) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517−3520. (e) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 793−796. (f) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803−2806.

(4) (a) Lipshutz, B. H.; Noson, K.; Chrisman, W.; Lower, A. *J. Am. Chem. Soc.* **2003**, *125*, 8779−8789. (b) Appella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9473−9474. (c) Moritani, Y.; Appella, D. H.; Jurkauskas, V.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 6797−6798. (d) Sirol, S.; Courmarcel, J.; Mostefai, N.; Riant, O. *Org. Lett.* **2001**, *3*, 4111−4113. (e) Lipshutz, B. H.; Caires, C. C.; Kuipers, P.; Chrisman, W. *Org. Lett.* **2003**, *5*, 3085−3088.

(5) For asymmetric hydrosilylation, see: (a) Lipshutz, B. H.; Noson, K.; Chrisman, W. *J. Am. Chem. Soc.* **2001**, *123*, 12917−12918. (b) Lipshutz, B. H.; Lower, A.; Noson, K. *Org. Lett.* **2002**, *4*, 4045−4048.

(6) (a) Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, J. *J. Am. Chem. Soc.* **1971**, *93*, 2063−4113. (b) Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, J. *Inorg. Chem.* **1972**, *11*, 1818−1825.

(7) (a) John, F.; McGettigan, C.; Stryker, J. M. *Tetrahedron Lett.* **1990**, *31*, 2397−2400. (b) Brestensky, D. M.; Stryker, J. M. *Tetrahedron Lett.* **1989**, *30*, 5677−5680. (c) Mahoney, W. S.; Brestensky, D. M.; Stryker, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 291−293. (d) Brestensky, D. M.; Huseland, D. E.; McGettigan, C.; Stryker, J. M. *Tetrahedron Lett.* **1988**, *29*, 3749−3752. (e) Chiu, P.; Li, Z.; Fung, K. C. M. *Tetrahedron Lett.* **2003**, *44*, 455−457.

(8) Mahoney, W. S.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 8818−8823. (b) Chen, J.-X.; Daeuble, J. F.; Stryker, J. M. *Tetrahedron* **2000**, *56*, 2789−2798.

(9) (a) Lipshutz, B. H.; Keith, J.; Papa, P.; Vivian, R. *Tetrahedron Lett.* **1998**, *39*, 4627−4630. (b) Lipshutz, B. H.; Chrisman, W.; Noson, K.; Papa, P.; Sclafani, J. A.; Vivian, R. W.; Keith, J. M. *Tetrahedron* **2000**, *56*, 2779−2788.

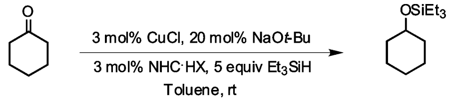
(10) For selected examples see: (a) Huang, J.; Schanz, H.-J.; Stevens, E. D.; Nolan, S. P. *Organometallics* **1999**, *18*, 2370−2375. (b) Frenzel, U.; Weskamp, T.; Kohl, F. J.; Schattenman, W. C.; Nuyken, O.; Herrmann, W. A. *J. Organomet. Chem.* **1999**, *586*, 263−265. (c) Louie, J.; Bielawski, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 11312−11313. (d) Herrmann, W. A.; Bohm, V. P. W.; Gstottmayr, C. W. K.; Grosche, M.; Reisinger, C. P.; Weskamp, T. *J. Organomet. Chem.* **2001**, *617*, 616−628. (e) Lee, C. W.; Choi, T.-L.; Grubbs, R. H.; *J. Am. Chem. Soc.* **2002**, *124*, 3224−3225.

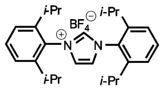
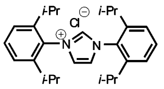
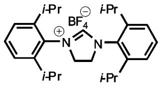
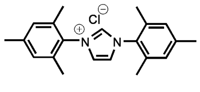
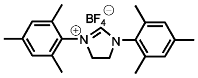
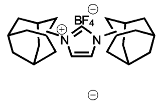
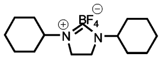
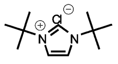
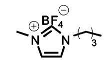
(11) For reviews discussing NHC see: (a) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39−91. (b) Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2162−2187. (c) Arduengo, A. J., III. *Acc. Chem. Res.* **1999**, *32*, 913−921. (d) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 2162−2187.

(12) (a) Ojima, I. In *The Hydrosilylation Reaction: The Chemistry of Organosilicon Compounds*; Patai, S., Rappaport, Z., Eds.; Wiley: New York, 1989; p 1479. (b) Ojima, I.; Li, Z.; Zhu, J. In *Recent Advances in the Hydrosilylation Reaction: Chemistry of Organic Silicon Compounds*; Rappaport, Z., Apeloig, Y., Eds.; Wiley: New York, 1998; Vol. 2, p 1687.

10.1021/om034285a CCC: $27.50
Publication on Web 02/04/2004

Table 1. Catalytic Reduction of Cyclohexanone Using in Situ Generated Catalysts



entry	NHC·HX	time(h)	conversion(%)[a]
1	 IPr·HBF$_4$	2	99
2	 IPr·HCl	2	80
3	 SIPr·HBF$_4$	2	88
4	 IMes·HCl	8	92
5	 SIMes·HBF$_4$	8	35
6	 IAd·HBF$_4$	2	99
7	 ICy·HBF$_4$	8	71
8	 I^{t}Bu·HCl	8	38
9	 BMIM·HBF$_4$	24	3
10	no ligand	24	0

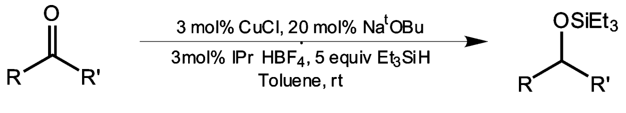
[a] Average of two runs.

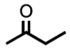
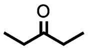
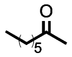
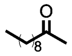
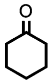
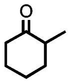
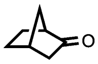
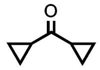
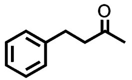
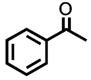
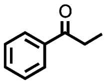
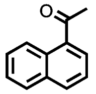
Results and Discussion

Expanding on our work on the use of NHCs as ligands in metal mediated reactions,[14] we now wish to report on the reactivity of these ligands in the hydrosilylation reaction of ketones catalyzed by (NHC)Cu^I complexes.[15] We initially examined the influence of various imidazolium salts as ligand precursors in the copper-catalyzed hydrosilylation using cyclohexanone as a model substrate. Results of this initial screening are shown in Table 1.

Control reactions were examined, where no ligand and/or copper was used. These control reactions do not lead to product formation even after 24 h. The best conversion and shortest reaction times were obtained using 1,3-bis(2,6-diisopropylphenyl)imidazolium tetrafluoroborate, IPr·HBF$_4$, as an NHC precursor (Table 1, entry 1). Interestingly, a counterion effect was observed (entries 1 and 2, Table 1). The reasons behind this trend are presently being examined, but we suspect at this stage a simple solubility difference between the two salts in toluene. IPr·HBF$_4$ was selected as the optimum ligand precursor and used in further testing. Reaction parameters, such as metal loading and amount of base, solvent, and silane, were optimized. As illustrated in Table 2, the hydrosilylation reaction can be performed with alkyl, aryl, and even cyclic ketones, with excellent yields at room temperature.

Table 2. Catalytic Reductive Silylation of Ketones



entry	ketone	time(h)	yield(%)[a]
1		4	96 (80)
2		2	99 (91)
3		3	98 (82)
4		5	99 (86)
5		2	99 (93)
6		2	98 (91)
7		4	97 (88)
8		8	90 (87)
9		5	96 (85)
10		3	99 (94)
11		3	98 (96)
12		3	99 (93)

[a] GC yields (isolated yields) are the averages of two runs.

The synthesis of well-defined (NHC)CuCl complexes was achieved by the reaction of an imidazolium salt, copper(I) chloride, and sodium *tert*-butoxide (Scheme 1).[16] This appears to be a general scheme applicable to numerous imidazolium salts. Suitable crystals of one of these complexes, (IPr)CuCl, were grown from CH_2Cl_2/hexane solutions and subjected to single-crystal

---

(13) For recent examples see: (a) Reyes, C.; Prock, A.; Giering, W. P. *Organometallics* **2002**, *21*, 546–554. (b) Niyomura, O.; Tokunaga, M.; Obora, Y.; Iwasawa, T.; Tsuji, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 1287–1289.

(14) For selected examples see: (a) Huang, J.; Grasa, G.; Nolan, S. P. *Org. Lett.* **1999**, *1*, 1307–1309. (b) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674–2678. (c) Viciu, M. S.; Grasa, G. A.; Nolan, S. P. *Organometallics* **2001**, *20*, 3607–3612. (d) Viciu, M. S.; Germaneau, R. F.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 4053–4056.

(15) For a well-defined copper NHC complex, see: (a) Arduengo, A. J., III; Dias, H. V. R.; Calabrese, J. C.; Davidson, F. *Organometallics* **1993**, *12*, 3405–3409. (b) Hu, X.; Castro-Rodriguez, I.; Meyer, K. *J. Am. Chem. Soc.* **2003**, *125*, 12237–12245.

(16) Concomitant with our work, Buchwald and Sadighi recently reported the isolation of such a complex: Jurkauskas, V.; Sadighi, J. P.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2417–2420.

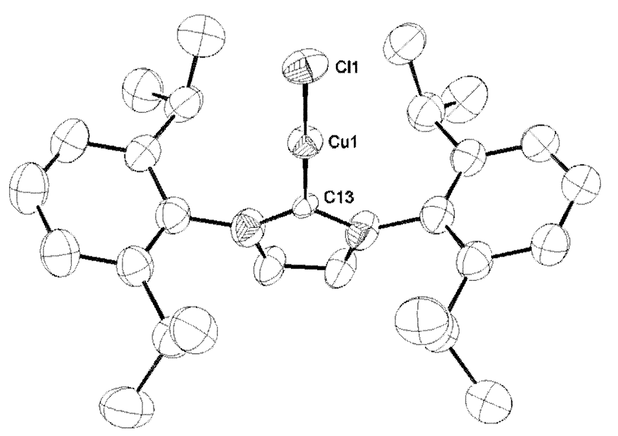
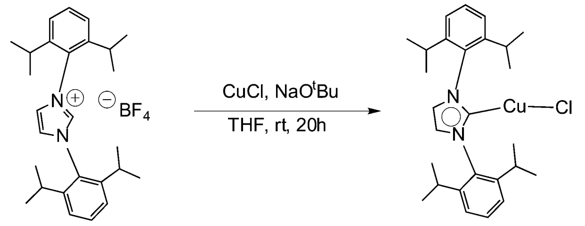


Figure 1. Molecular structure of IPrCuCl with thermal ellipsoids drawn at the 40% level (hydrogens are omitted for clarity). Selected bond lengths (Å): C13−Cu1 = 1.953, Cu1−Cl1 = 2.089. Selected bond angles (deg): C13−Cu1−Cl1 = 180.00.

Scheme 1. Synthetic Route to Well-Defined (NHC)CuCl Complexes



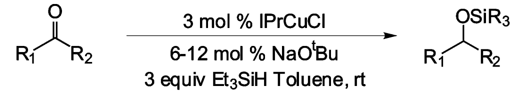
diffraction study. The resulting ORTEP for (IPr)CuCl is shown in Figure 1.

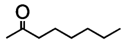
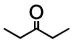
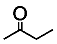
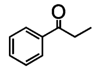
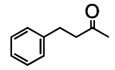
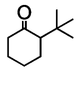
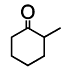
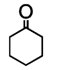
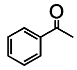
With a well-defined catalyst in hand, the hydrosilylation of ketones was examined and compared to the in situ generated catalytic system.

The well-defined system performs generally better than the in situ generated catalytic system, achieving similar conversions in shorter reaction times (Table 3). As expected, sterically hindered ketones required longer reaction times to reach completion, compared to unhindered ones (entry 6, Table 3). This is in line with the proposed mechanism (discussed below). Efforts aimed at reducing the amount of base were unsuccessful, leading not only to increased reaction times but also to lower conversions. The exact role of the base is presently being investigated. The use of a smaller amount of silane was also tested, and after examination of different sources and concentrations, in some instances, we were able to perform reactions with as little as 3 equiv of triethylsilane.

To test the compatibility of the copper systems examined with reducible functional groups, reaction with an unsaturated ketone was examined (Scheme 2). The chemoselective reduction of the carbonyl moiety in 5-hexen-2-one was achieved without reduction of the alkene fragment. Further studies aimed at examining the scope of this selectivity are in progress.

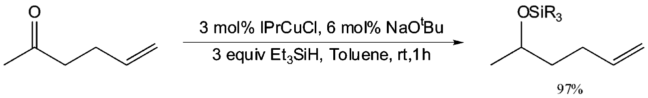
Table 3. Catalytic Reduction of Ketones Using a Well-Defined System



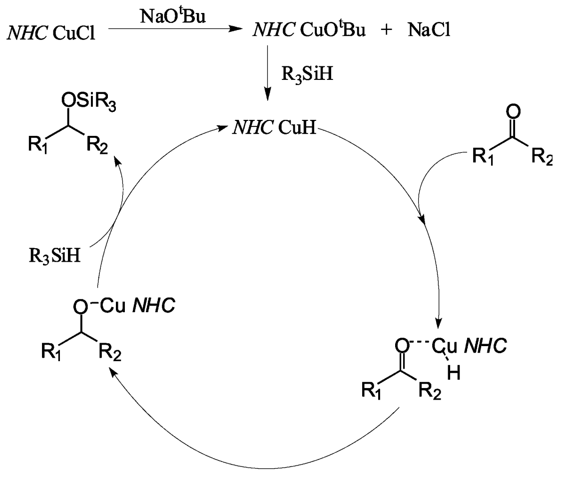
entry	substrate	time (h)	yields (%)[a]
1		0.75	100 (96)
2		1	90 (82)
3		1	100 (93)
4		1 3	40 100 (95)
5		1 2	73 100
6		1 20	9[b] 35
7		1	95
8		1 3	73[b] 86 (83)
9		1 3	48[b] 98 (94)

[a] GC yields (isolated yields). [b] NaOtBu 12 mol %.

Scheme 2



Scheme 3



A proposed mechanism for the copper-catalyzed hydrosilylation of ketones is illustrated in Scheme 3. The initial formation of a (NHC)Cu−alkoxide species is proposed, followed by reaction with Et_3SiH, which generates the active copper hydride species. This Cu−H complex can then react with the carbonyl function, forming a new Cu−OR complex. In the last step, the Cu−H species is regenerated by action of the silane liberating the silyl ether.

Conclusion

In conclusion, the use of $(NHC)Cu^I$ complexes that mediate the efficient hydrosilylation of ketones has been achieved, with excellent yields. Studies aimed at expanding the scope of this method to different substrates as well as examining mechanistic details involving the use of copper hydride NHC complexes are currently ongoing in our laboratories.

Experimental Section

Typical Procedure for Catalysis Using an in Situ Catalyst System. In a scintillation vial fitted with a septum cap containing a magnetic stirring bar were added copper(I) chloride (6 mg, 0.06 mmol) and sodium *tert*-butoxide (38 mg, 0.4 mmol). Under an inert atmosphere, dry toluene (4 mL) was added, and the mixture was magnetically stirred. To this solution was added triethylsilane (1.6 mL, 10 mmol). After 20 min of stirring, cyclohexanone (0.207 mL, 2 mmol) was added. The reaction was allowed to proceed at room temperature for 1 h. The mixture was filtered using a plug of active charcoal and Celite. The organic phase was evaporated using a rotary evaporator, yielding a colorless oil as the pure product (398 mg, 1.85 mmol, 93%).

Typical Procedure for the Synthesis of Copper Catalysts. In a 250 mL Schlenk flask were added copper(I) chloride (1.0 g, 10.10 mmol), 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (4.29 g, 10.10 mmol), and sodium *tert*-butoxide (0.97 g, 10.10 mmol). To this flask was added dry tetrahydrofuran (THF; 100 mL) under an inert atmosphere of argon, and the mixture was magnetically stirred for 20 h at room temperature. After the mixture was filtered through a plug of Celite and the solvent was evaporated under vacuum, a white solid was obtained (4.59 g, 9.40 mmol, 94%).[16]

Acknowledgment. The National Science Foundation and Board of Regents of the State of Louisiana are gratefully acknowledged for support of this research.

Supporting Information Available: Text giving details of the synthesis and characterization data for all compounds synthesized and crystallographic data for IPrCuCl as a CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

OM034285A