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Cationic Copper(I) Complexes as Efficient Precatalysts for the Hydrosilylation of Carbonyl Compounds

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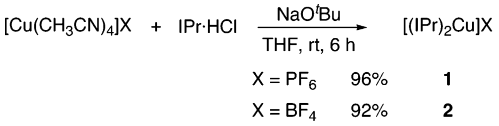
Novel cationic copper complexes bearing two *N*-heterocyclic carbenes (NHCs) have been synthesized and fully characterized. These air- and moisture-stable complexes were found to be highly active toward the hydrosilylation of ketones with varying steric congestion, aldehydes (even enolizable ones), and esters.

"Cu−H" is among the earliest metal hydrides reported in the literature,[1] but for a long time it was considered to have no potential as a reagent in organic chemistry. A stabilized form of copper hydride, the hexameric $[(Ph_3P)CuH]_6$, was first reported by Osborn,[2] but Stryker showed it useful in conjugate reductions of a number of carbonyl derivatives with high regioselectivity.[3] Since then, a number of phosphine-copper hydride systems combined with an external source of hydride have been employed for the catalytic reduction of carbonyl compounds.[4] The use of a hydrosilane as hydride source is especially useful, as it yields the protected alcohols and makes use of simple starting materials.[5]

After the isolation of the first stable free carbene by Arduengo and co-workers,[6] *N*-heterocyclic carbenes (NHCs) have emerged as efficient ligands in metal-mediated reactions.[7] Compared to tertiary phosphines, the NHC ligands have a stronger interaction with the metal center, thereby minimizing ligand dissociation. In addition, their significant steric bulk results in metal−NHC complexes having unique catalytic behavior.[8]

We and others have recently reported the (NHC)CuCl-catalyzed reduction of a wide array of carbonyl compounds.[9−11] Herein, we describe the synthesis, characterization, and catalytic activity of novel (IPr)−Cu cationic complexes (IPr = *N*,*N*′-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene). To our knowledge, only one complex of this kind with two monodentate carbenes on the copper center has been reported. However, its structure was not determined unambiguously by X-ray diffraction.[12]

Scheme 1. Synthesis of $[(IPr)_2Cu]X$ Complexes 1 and 2



In our first attempt, complexes **1** and **2** were prepared from the corresponding tetrakis(acetonitrile)copper complex and free IPr.[13] More interestingly, these complexes can be prepared in good yields from the air-stable and commercially available IPr·HCl salt in the presence of a strong base (Scheme 1).

The structures of these air- and moisture-stable complexes were elucidated by single-crystal diffraction from suitable crystals grown from CH_2Cl_2/MTBE solutions. The resulting thermal ellipsoids for **1** and **2** are shown in Figure 1. The Cu−C(1) bond lengths in **1** and **2** (1.938 and 1.939 Å, respectively) are comparable to reported Cu−C bonds in carbene complexes.[14] On the other hand, the angle of intersection of the planes of the two imidazole rings is 40.71° in **1** and 49.72° in **2**.

We investigated the catalytic activity of **1** and **2** in the hydrosilylation of carbonyl compounds. Using cyclohexanone as substrate under reaction conditions we previously established

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(8) For reviews about NHCs see: (a) Díez-González, S.; Nolan, S. P. *Annu. Rep. Prog. Chem., Sect. B* **2005**, *101*, 171−191. (b) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 2162−2187. (c) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39−91. (d) Arduengo, A. J., III. *Acc. Chem. Res.* **1999**, *32*, 913−921.

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(10) For simple ketones see: Kaur, H.; Zinn, F. K.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2004**, *23*, 1157−1160.

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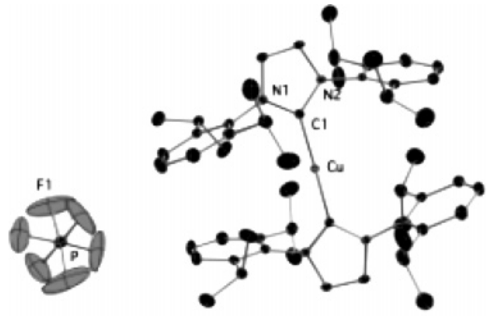
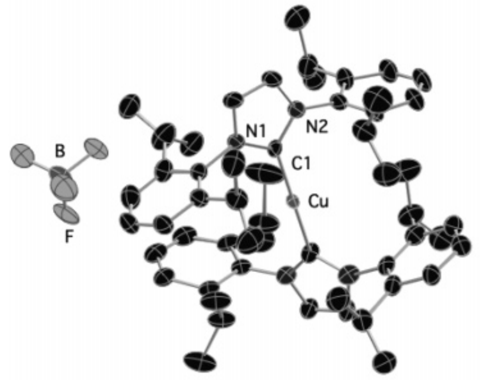
(13) Isolated yields were 93% for **1** and 91% for **2**.

(14) (a) Mankad, N. P.; Gray, T. G.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 1191−1193. (b) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369−3371. (c) Arnold, P. L.; Scarisbrick, A. C.; Blake, A. J.; Wilson, C. *Chem. Commun.* **2001**, 2340−2341. See also refs 10 and 11.

10.1021/om0600487 CCC: $33.50



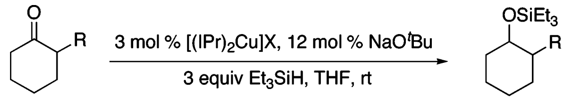
$[(IPr)_2Cu]PF_6$ **1**



$[(IPr)_2Cu]BF_4$ **2**

Figure 1. Thermal ellipsoid plots for **1** and **2** (50% of probability). Selected bond lengths (Å): Cu−C(1) = 1.938(5), Cu···P = 8.789 for **1**, Cu−C(1) = 1.939(18), Cu···B = 8.068 for **2**. Hydrogens have been omitted for clarity.

Scheme 2. Hydrosilylation of Ketones with 1 or 2[a]



		R = H	R = Me
$[(IPr)_2Cu]\ PF_6$	**1**	2 h, 97%	6 h, 92% (*trans:cis* = 90:10)
$[(IPr)_2Cu]\ BF_4$	**2**	0.5 h, 98%	3 h, 90% (*trans:cis* = 85:15)

[a] Isolated yields are average of two runs. Diastereoisomeric ratios were determined by ^{1}H NMR.

for the hydrosilylation of simple ketones with IPrCuCl,[15] no reaction was observed in the presence of **1** or **2** even after long reaction times. Due to the low solubility of our copper salts in toluene, the solvent was replaced by THF. In this case, a homogeneous solution was obtained and the expected silyl ether was formed in good yields and short reaction times (Scheme 2). Surprisingly, an important counterion effect was observed for these complexes and shorter reaction times were observed with the BF_4 complex **2**. This trend was confirmed using 2-methylcyclohexanone as substrate. However, the counterion had no significant influence on the diastereoselectivity of the reaction (Scheme 2). The origin of the different reactivity between **1** and **2** cannot be explained by their structures and is currently being investigated in our laboratories.

Some optimization studies revealed that 12 mol % of NaO^{t}Bu and 2 equiv of Et_3SiH provided the best catalytic system.[16] When lower quantities of these reagents were used, the hydrosilylation of cyclohexanone did not go to completion. No reaction was observed in the absence of base.

Under these optimized conditions, cyclic and acyclic ketones were hydrosilylated in short reaction times and in excellent yields (Table 1). Aromatic ketones required slightly longer reaction times (Table 1, entries 7−9), and the reaction was found compatible with an alkene moiety (Table 1, entry 10). In the case of norcamphor (Table 1, entry 3), the *exo* isomer was observed only in trace amounts (<5%) in the ^{1}H NMR spectrum. In general, this new catalyst system allowed the hydrosilylation of ketones to be performed in shorter or similar reaction times as when (IPr)CuCl is employed with the advantage that only 2 equiv of silane were required.

This protocol also allowed us to reduce more hindered ketones efficiently by simply increasing the reaction temperature to 55 °C. These results are summarized in Table 2. From 2,6-dimethylcyclohexanone (Table 2, entry 2),[17] the corresponding silyl ether was obtained as a 25:1:74 mixture of *meso trans/trans:cis/trans:meso cis/cis* isomers.[18]

To broaden the scope of this catalytic system, a number of aldehydes were tested. As expected, short reaction times allowed for the hydrosilylation of aromatic aldehydes in excellent yields at room temperature (Table 3). No significant difference of reactivity between aldehydes bearing electron-withdrawing and electron-donating substituents was observed. Remarkably, two enolizable aldehydes could be reduced in good yields (Table 3, entries 8 and 9). In these cases, a larger excess of silane was employed in an attempt to favor the hydrosilylation reaction over the aldol condensation.

To gain insight into the mechanism of this reaction, the hydrosilylation of cyclohexanone in the presence of 3 mol % of $[Cu(CH_3CN)_4]BF_4$ and free IPr under different conditions was studied. First, different loadings of free IPr were tested. Under the optimized conditions, the use of 3 mol % of IPr led to the complete conversion of the ketone after 2 h. Four hours were required to reach the same conversion with 6 mol % of IPr, and only 62% of the silyl ether was formed with 9 mol %.[19] Furthermore, in the absence of base, this reaction led to the isolation of the expected silyl ether in 96% after 2 days in refluxing THF. In the absence of base and after 48 h of reaction in refluxing THF, no conversion was observed using either $[Cu(CH_3CN)_4]BF_4$, IPr, or **2** separately. This suggests that a mono-carbene copper complex may be the active species and that the base most probably plays an activation role in the catalytic cycle.[20]

Finally, the reduction of an ester, a much less reactive carbonyl compound, was also achieved with this catalytic system (Scheme 3). After 6 h at 55 °C the corresponding silyl ether was isolated in 69% yield. Under these conditions, 10% of the starting material and 10% of the *tert*-butyl phenylacetate resulting from a transesterification reaction were also isolated.[21]

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[15] 3 mol % of copper complex, 12 mol % of NaO^{t}Bu, and 3 equiv of Et_3SiH in toluene at room temperature. See ref 10.

[16] Other hydride sources, such as *tert*-butyldimethylsilane or dimethylphenylsilane, led to incomplete conversions even after 20 h. No reaction was observed with NaOMe, NaOAc, NaH, KOH, or Cs_2CO_3 as bases, and no difference of reactivity was observed with NaO^{t}Bu or KO^{t}Bu.

[17] This ketone is sold as an 80:20 mixture of *cis:trans* isomers. The *cis*:*trans* ratio observed for the silyl ether could be explained as a result of the base-catalyzed equilibrium between both isomers of the starting material.

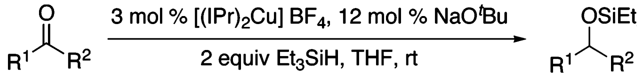
[18] Raban, M.; Lauderback, S. K.; Kost, D. *J. Am. Chem. Soc*. **1975**, *97*, 5178−5183.

[19] 62% after 4 h; no further conversion was observed after longer reaction times. For more details see the Supporting Information.

[20] In a related system, we recently proposed that the base might interact with the hydrosilane to facilitate its σ-bond metathesis with a (NHC)Cu−OR intermediate. See ref 11.

[21] Similar product distribution was observed at room temperature, but 14 h were required to achieve maximal conversion. The use of ethanol as a protic source at 55 °C led only to a lower conversion in silyl ether (39% as determined by ^{1}H NMR).

Table 1. Hydrosilylation of Simple Ketones[a]



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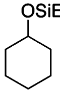
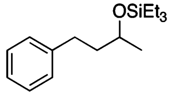
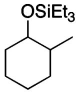
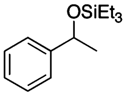
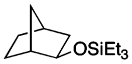
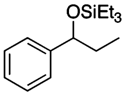
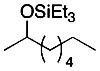
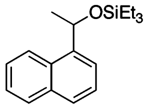
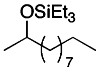
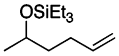
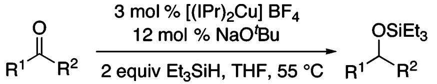
1		0.5	98	6		1	95
2		3	90[b]	7		4	98
3		1	96	8		4	93
4		0.66	92	9		4	94
5		0.33	99	10		0.33	98

[a] Isolated yields are average of two runs. Product isolated as a 85:15 mixture of *trans*:*cis* isomers.

Table 2. Hydrosilylation of Hindered Ketones[a]



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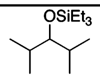
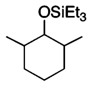
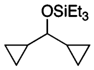
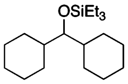
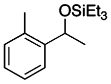
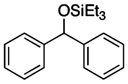
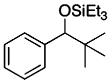
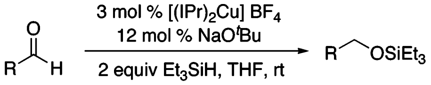
1		0.3	94
2		6	93[b]
3		0.15	94
4		3	98[c]
5		0.15	96
6		5	93
7		7	99

[a] Isolated yields are average of two runs. [b] 20 mol % NaO^{t}Bu. [c] 3 equiv of Et$_3$SiH.

Table 3. Hydrosilylation of Aldehydes[a]



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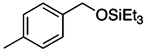
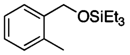
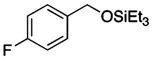
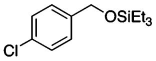
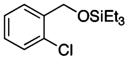
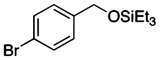
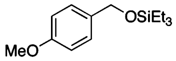
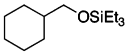
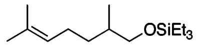
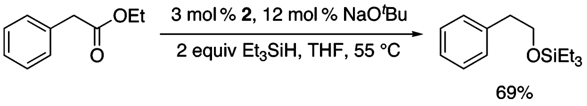
1		20	92
2		25	94
3		10	96
4		15	91
5		30	93
6		20	93
7		15	89
8		40	70[b]
9		45	71[b]

[a] Isolated yields are average of two runs. [b] 5 equiv of Et$_3$SiH.

In summary, the cationic bis-carbenic copper complexes **1** and **2** can be prepared from readily available materials and are extremely air- and moisture-stable. An interesting counterion effect was observed. Most notably, **2** displays remarkable activity in the hydrosilylation of ketones, aldehydes, and an ester. When compared with (IPr)CuCl, this precatalyst allows the hydrosilylation reaction to proceed under smoother reaction conditions and using a lower hydrosilane loading. Applications to other carbonyl-containing substrates and further studies on the mechanism of this reaction are currently ongoing in our laboratories.

Scheme 3. Hydrosilylation of an Ester



Experimental Section

General Considerations. All ketones were used as received. All solid reagents were stored under argon in a glovebox containing less than 1 ppm O_2. Tetrakis(acetonitrile)copper(I) hexafluorophosphate and tetrafluoroborate,[22] IPr•HCl, and free IPr[23] were synthesized according to literature procedures. Solvents were distilled from appropriate drying agents. ^{1}H NMR and ^{13}C NMR were recorded on a 400 MHz spectrometer at room temperature. Chemical shifts (δ) are reported with respect to tetramethylsilane as internal standard in ppm. All reported yields are isolated yields and are averages of at least two runs.

Synthesis of [(IPr)$_2$Cu] X Complexes (X = PF$_6$ or BF$_4$). In an oven-dried vial fitted with a septum screw cap, tetrakis(acetonitrile)copper(I) hexafluoroborate (0.186 g, 0.5 mmol) or tetrafluoroborate (0.157 g, 0.5 mmol), IPr•HCl (0.424 g, 1 mmol), and sodium *tert*-butoxide (96 mg, 1 mmol) were loaded inside a glovebox and stirred in dry THF (10 mL) outside the glovebox for 6 h. After filtering the reaction mixture through a plug of Celite (THF), the filtrate was mixed with hexane to form a precipitate. A second filtration led to the isolation of the expected complexes.

Bis[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]copper Hexafluorophosphate (1). A 0.474 g sample of the title compound was isolated as a pure white solid (96%). ^{1}H NMR (400 MHz, acetone-d_6): δ 7.54 (t containing a singlet at 7.55, J = 7.8 Hz, 8H, *p*-CH + NC*H*), 7.25 (d, J = 7.8 Hz, 8H, *m*-CH), 2.42 (septet, J = 6.8 Hz, 8H, $(CH_3)_2CH$), 1.04 (d, J = 6.8 Hz, 18H, CH_3), 0.94 (d, J = 6.8 Hz, 18H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.4 (N−C−N), 145.0 (CH aromatic), 134.6 (C aromatic), 130.6 (C aromatic), 125.2 (=CH−N), 124.5 (CH aromatic), 28.6 ($CH(CH_3)_2$), 24.25 (CH_3), 24.12 (CH_3). Anal. Calcd for $C_{54}H_{72}CuF_6N_4P$ (985.69): C, 65.80; H, 7.36; N, 5.68. Found: C, 65.49; H, 7.42; N, 5.99.

Bis[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]copper Tetrafluoroborate (2). A 0.452 g sample of the title compound was isolated as a pure white solid (92%). ^{1}H NMR (400 MHz, acetone-d_6): δ 7.54 (t containing a singlet at 7.55, J = 7.5 Hz, 8H, *p*-CH + NCH), 7.25 (d, J = 7.5 Hz, 8H, *m*-CH), 2.40 (septet, J = 6.8 Hz, 8H, $CH(CH_3)_2$), 1.04 (d, J = 6.8 Hz, 24H, CH_3), 0.94 (d, J = 6.8 Hz, 24H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4 (N−C−N), 145.0 (CH aromatic), 134.7 (C aromatic), 130.6 (C aromatic), 125.3 (=CH−N), 124.5 (CH aromatic), 28.6 ($CH(CH_3)_2$), 24.3 (CH_3), 24.2 (CH_3). Anal. Calcd for $C_{54}H_{72}BCuF_4N_4$ (927.53): C, 69.93; H, 7.82; N, 6.04. Found: C, 69.57; H, 7.60; N, 5.87.

General Procedure for the Hydrosilylation of Carbonyl Compounds. In an oven-dried vial fitted with a septum screw cap, **2** (27 mg, 0.03 mmol, 3 mol %) and sodium *tert*-butoxide (12 mg, 12 mol %) were charged inside a glovebox and stirred in dry THF (2 mL) at room temperature or at 55 °C outside of the glovebox for 10 min before adding triethylsilane (0.33 mL, 2 mmol, 2 equiv) through the septum using a syringe. After 10 more minutes of stirring, the carbonyl compound (1 mmol) was added. When the starting material was a solid, it was added as a solution in THF. The reaction was monitored by GC, after consumption of the starting material or no further conversion, the reaction mixture was opened to air and filtered through a plug of active charcoal and Celite using ethyl acetate as solvent. The organic phase was concentrated in vacuo and the purity of the residue checked on GC and ^{1}H NMR. Flash chromatography was then performed unless crude product was estimated to be greater than 95% pure.

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Supporting Information Available: Experimental procedures, product characterizarion, and cif files. This material is available free of charge via the Internet at http://pubs.acs.org.

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