A new alternative to Stryker's reagent in hydrosilylation: synthesis, structure, and reactivity of a well-defined carbene–copper(II) acetate complex†

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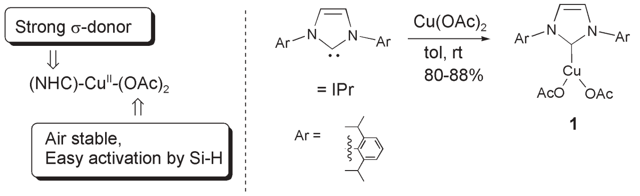
A new, air stable and well-defined carbene–copper(II) complex has been prepared, which is an efficient precatalyst for the 1,2- and 1,4-reduction of carbonyl compounds under hydrosilylation conditions.

Copper hydride mediated chemoselective conjugate reduction of α,β-unsaturated carbonyl compounds is an important transformation for organic synthesis.[1] Since the first report on the use of the organocopper hydride, $[(PPh_3)CuH]_6$, in the conjugate reduction of enones by Stryker and coworkers,[2] the copper complex, known as Stryker's reagent, has been widely employed in organic reductions. A major disadvantage of this reagent is its sensitivity to air;[2] the quality of the commercially available Stryker's reagent is quite variable[3] and special precautions are needed for its storage.

We have recently described a new copper(II) system employing $Cu(OAc)_2$ as a precatalyst that can be easily activated *in situ* by hydrosilanes without using strong bases[4] and that efficiently reduces aromatic ketones[4] and α,β-unsaturated nitriles[5] in combination with a chelating phosphine. Based on our previous studies, we envisioned that a well-defined copper(II) complex incorporating the acetate moieties and a strong σ-donor N-heterocyclic carbene (NHC) ligand would work as an efficient and convenient precatalyst for hydrosilylation and might be a good alternative to Stryker's reagent. N-heterocyclic carbenes have emerged as a new family of ligands for homogeneous catalysis during the past decade.[6] However, their use as ligands for copper complexes remains relatively rare.[7] The first NHC–Cu(I) complex was reported by Arduengo *et al.* in 1993[8] and such copper complexes were shown to catalyze conjugate additions of diethyl zinc to enones by other groups.[9] Recently, Buchwald *et al.*[10] and Nolan *et al.*[11] independently reported the synthesis of a carbene–copper(I) complex, $(IPr)Cu^{I}Cl$ (IPr = 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene). The latter complex efficiently catalyzes the conjugate reduction of enones and esters[10] and hydrosilylation of ketones[11] when activated, however, the use of excess base is required for catalyst activation.

Herein, we wish to report the successful synthesis of the new copper(II) complex **1**, its X-ray structure, and a direct comparison of its activity to Stryker's reagent.

The synthesis of **1** was achieved by the reaction of a free carbene, IPr[12] and copper(II) acetate in toluene at room temperature (Scheme 1).‡ Single crystals for X-ray diffraction were obtained by the slow diffusion of pentane into a concentrated CH_2Cl_2 solution of catalyst **1**. A representation of the X-ray structure is shown in Fig. 1, with selected bond lengths and bond angles.§ The Cu–$C_{carbene}$ distance of 1.942(4) Å confirms the absence of π-character in the bond.[13] The Cu–O distance for the bound carboxylate oxygen (1.941(3) Å) is shorter than those in three- or four-coordinate copper(I) bis(triphenylphosphine)carboxylates,[14] and longer than those in two-coordinate linear copper carboxylates.[15] A relatively strong interaction exists between the Cu and the distal oxygen O(2) (2.259(3) Å). This



Scheme 1 Synthesis of $(IPr)Cu^{II}(OAc)_2$.

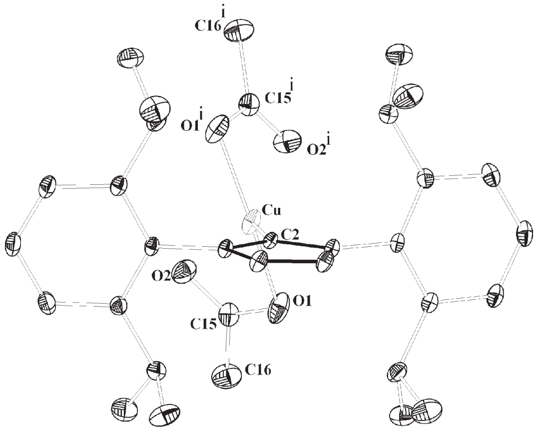


Fig. 1 X-Ray structure of **1**. Thermal ellipsoids are shown at their 30% values. Symmetry code: (i) $-x, y, 0.5 - z$. Selected bond distances (Å) and angles (°): Cu–C(2) = 1.942(4), Cu–O(1), (Cu–O(1)^{i}) = 1.941(3), Cu–O(2), (Cu–O(2)^{i}) = 2.259(3), O(1)–Cu–O(1)^{i} = 160.36(19), O(1)–Cu–C(2), (O(1)^{i}–Cu–C(2)) = 99.82(9).

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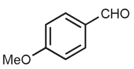
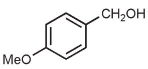
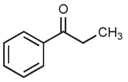
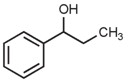
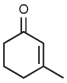
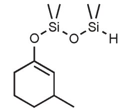
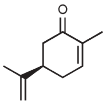
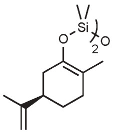
Table 1 1,2-/1,4-Reductions catalyzed by **1** *vs.* Stryker's reagent

			Catalyst **1** (1 mol%)		Stryker's reagent (3 mol%)	
Substrate	Product	Silane (equiv.)	Time/h[a]	Yield (%)	Time/h[a]	Yield (%)
		PMHS (2.5)	<0.1	97	3 3	98 94[b]
		PMHS (2.5)	0.3	96	10	97[b]
		TMDS (1.5)	0.5	79[c]	24	85[b,d]
		TMDS (0.55)	6	93	14	91[b,d]

[a] Time needed for complete conversion. [b] Taken from ref. 3 and 17. [c] Combined yields of monomeric and dimeric products. [d] 5 mol% Stryker's reagent was used.

complex is air stable and storable at ambient temperature without any special precautions for months, but decomposes at temperatures above 180 °C.

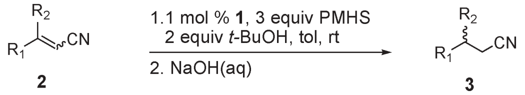
The activation of precatalyst **1** was tested in the presence of various hydrosilanes in toluene. Diphenylsilane and polymethylhydrosiloxane (PMHS) instantly activate **1** upon mixing. Activation is indicated by the color change of the solution from blue to yellow. The activation of **1** by tetramethyldisiloxane (TMDS) was slow in comparison to diphenylsilane and PMHS.[16] In order to compare the catalytic activity of **1** with that of Stryker's reagent in hydrosilylation reactions, a few examples of 1,2-/1,4-reductions were carried out. As shown in Table 1, **1** performs better than Stryker's reagent both in the 1,2-reduction of aldehydes and ketones[17] and in the conjugate reduction of enones.[3] The conjugate reduction of α,β-, β,β-disubstituted enones was completed at faster reaction rates with lower catalyst loading (1 mol%) of **1** than with Stryker's reagent (5 mol%).

Next, we applied this catalyst system to the conjugate reduction of α,β-unsaturated nitriles. α,β-Unsaturated nitriles are a class of compounds that react very slowly compared to other related unsaturated carbonyl compounds. Even stoichiometric amounts of Stryker's reagent cannot complete the conjugate reduction of β-monosubstituted unsaturated nitriles,[18] and our previous reduction system based on Cu–H with a chelating Xantphos-type ligand[19] is not effective for the reduction of highly sterically demanding nitriles.[5] As shown in Table 2, 1 mol% **1** is sufficient to effect 1,4-reductions of a series of α,β-unsaturated nitriles.[20] In general, reactions catalyzed by **1** require smaller amounts of catalyst, hydrosilane, and *t*-BuOH and shorter reaction times than our previous system. For example, β-monosubstituted unsaturated nitriles, **2a** and **2b**, were reduced to the corresponding saturated nitriles in less than 20 min. with 1 mol% **1**, which previously took 1 h with 3 mol% Cu(II)–Xantphos. β,β-Disubstituted unsaturated nitriles (**2c–2e**) were successfully reduced in shorter reaction times as well. It is noteworthy that the present catalytic system is quite tolerant to steric hindrance at the β-carbon and reduces even bulkier nitrile substrates (**2f, 2g**) that were not reactive under our previous reduction conditions employing the Cu–Xantphos-type ligand.

We are at present uncertain of the exact nature of the active copper hydride species. Currently, we assume that an NHC–Cu(I)H is the active catalytic species and the silane effects the generation of the Cu(I)–H from the Cu(II) precursor.[21] The active copper hydride species reacts with α,β-unsaturated nitrile forming a new organocopper species and the intermediate undergoes rapid deprotonation by *t*-BuOH to yield the protonated product and a copper alkoxide. The latter then regenerates the active catalyst Cu–H with PMHS.

In conclusion, a robust and highly effective copper(II) precatalyst for 1,2- and 1,4-hydrosilylations has been prepared and isolated in good yield. This well-defined and easily-handled precatalyst is effectively activated by hydrosilanes and displays great reactivity in reduction. Considering the convenience and efficiency offered by **1**, this precatalyst can be a good alternative to the widely-used Stryker's reagent under hydrosilylation conditions.

Table 2 Conjugate reduction of α,β-unsaturated nitriles using **1**



2 **3**

Entry	Substrate	R	R′	Time/h	Yield (%)[a]
1	**2a**	Ph	H	<0.3	91
2	**2b**	Furanyl	H	<0.3	87
3	**2c**	$CH_3(CH_2)_5$	CH_3	1.5	88
4	**2d**	Ph	CH_3	3	88
5	**2e**	*p*-CNC_6H_4	CH_3	4.5	94
6	**2f**	1,2,3,4-Tetrahydronaphthyl		1.5	87
7	**2g**	*t*-Bu	CH_3	1.5	82

[a] Isolated yield.

Studies aimed at investigating the scope and mechanism of this catalyst system and devising more efficient NHC–Cu(II) acetate complexes are currently ongoing in our laboratories.

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Notes and references

‡ Synthesis of **1**: $Cu(OAc)_2$ (90.8 mg, 0.5 mmol) and IPr (214.8 mg, 0.55 mmol) were placed in a Schlenk flask and 3 mL of toluene were added. The reaction mixture was stirred at room temperature for 12 h and a blue precipitate formed. The resulting precipitate was isolated by filtration, washed with toluene, and dried *in vacuo* to afford $[Cu(IPr)(OAc)_2]$ as a blue solid (229 mg, 80%). Crystals suitable for X-ray diffraction studies were obtained by slow diffusion of pentane to a concentrated CH_2Cl_2 solution of the complex. (Found: C, 65.34; H, 7.48; N, 4.98%. Calc. for $C_{31}H_{42}CuN_2O_4$: C, 65.30; H, 7.42; N, 4.91%.)

§ Crystal structure data for **1**, $C_{31}H_{42}CuN_2O_4$, $M_r = 570.22$, monoclinic, space group $C2/c$, $a = 22.863(3)$ Å, $b = 8.680(4)$ Å, $c = 17.977(5)$ Å, $\beta = 119.275(15)°$, $V = 3111.8(16)$ Å^3, $T = 150(1)$ K, $Z = 4$, $\rho_{calc} = 1.217$ Mg m^{-3}, $F(000) = 1212$, crystal dimensions 0.10 × 0.10 × 0.10 mm^3, μ(MoKα) = 0.737 mm^{-1}, MoKα radiation ($\lambda = 0.7107$ Å). Of 14788 reflections collected in the 2θ range 3.0°–55.0° using an ω scan on a Rigaku R-axis rapid diffractometer, 3554 were unique reflections ($R_{int} = 0.109$). The structure was solved and refined against F^2 using SHELXS[22] and SHELXL97[23], 164 variables, w$R2 = 0.1450$ (the 3554 unique reflections), $R1 = 0.0618$ (the 1667 reflections having $F_o^2 > 2\sigma(F_o^2)$), GOF = 1.008, and max/min residual electron density 0.336/−0.267 e Å^{-3}. CCDC 274568. See http://dx.doi.org/10.1039/b509964a for crystallographic data in CIF or other electronic format.

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13 A Cu–C_{sp^3} single bond distance (1.90–1.96 Å) is expected if the carbene binds through a pure σ-lone pair. See ref. 7*c*.

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16 The following order of silane reactivity was observed $PhSiH_3 > Ph_2SiH_2 \sim$ PMHS > TMDS >>$PhMe_2SiH$; when TMDS was employed, the reaction mixture was stirred for 20–30 min for catalyst activation before the addition of substrate. The activation of **1** with $PhMe_2SiH$ failed and no reduction occurred with $PhMe_2SiH$ as the stoichiometric reducing agent.

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19 DPEphos = bis(2-diphenylphosphinophenyl)ether, Xantphos = 9,9-dimethyl-4,6-bis(diphenylphosphino)xanthene.

20 General procedure for the conjugate reduction of α,β-unsaturated nitriles: **1** (5.7 mg, 0.010 mmol) was placed in an oven-dried Schlenk tube and PMHS (0.18 mL, 3.0 mmol) and toluene (0.50 mL) were added under N_2. The reaction mixture was stirred for 5 min at room temperature and then, α,β-unsaturated nitrile (1.0 mmol) was added, followed by *t*-BuOH (0.18 mL, 2.0 mmol). The reaction tube was washed with toluene (0.50 mL), sealed, and stirred until no starting nitrile was detected by TLC or GC. The reaction mixture was quenched with water and transferred to a round-bottom flask with the aid of Et_2O (10 mL), and NaOH (2.5 M, 1.2 mL) was added. The biphasic mixture was stirred vigorously for 0.5 h. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The product was purified by Kugelrohr distillation or silica gel chromatography.

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