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Direct synthesis of Stryker's reagent from a Cu(II) salt

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Abstract—A convenient, one-pot procedure for the preparation of $[(PPh_3)CuH]_6$ from a Cu(II) precursor, $Cu(OAc)_2$ in the presence of organosilanes as the reducing agent is described. This method provides a simple route to Stryker's reagent without the necessity of preparing and purifying reagents in additional steps.

Copper(I) hydride complexes have been the subject of considerable interest as mild and selective reducing agents both in stoichiometric reactions and in copper-catalyzed reductions.[1] The best studied of these, is the hexameric $[(PPh_3)CuH]_6$ cluster,[2] known as Stryker's reagent. This well-characterized copper(I) hydride reagent is a good source of hydride for the chemoselective conjugate reduction of α,β-unsaturated carbonyl compounds,[3] and continues to be sold commercially. The conjugate reduction can be performed either stoichiometrically or catalytically in the presence of reducing agents, and the reaction intermediates can be used for further C–C bond formations.[4] However, the quality of the commercially available Stryker's reagent varies considerably due to its sensitivity to air, showing only limited activity in reductions depending on samples.[4b] For optimum activity, preparing the reagent in the laboratory has been suggested.

Among the published procedures for the preparation of $[(PPh_3)CuH]_6$, the Stryker's protocol[5] employing sodium or potassium *t*-butoxide, triphenylphosphine, and copper(I) chloride under pressure (1 atm) of hydrogen proved to be practical and convenient. Recently, using organosilanes instead of hydrogen as the reducing agent for the preparation of Stryker's reagent was also reported.[6] Although the above procedures have operational advantages and afford reproducibly good quality of the reagent, a simpler and more convenient synthetic method is still required. For example, in both procedures, copper(I) chloride and sodium/potassium *t*-butoxide are used to generate copper(I) *t*-butoxide in situ, and sodium/potassium chloride produced as a side-product is needed to be removed at a later stage of the preparation (Scheme 1). Furthermore, copper(I) chloride is often prepared from copper(II) chloride by the reduction with sodium sulfite in a separate step before use because copper(I) chloride itself is sensitive to moisture and air and converted to a mixture of copper(II) impurities.[7]

Recently, we reported that the combination of catalytic amounts of copper(II) acetate or copper(II) acetate monohydrate in the presence of organosilanes without an alkoxide base generated an active copper catalytic species for the reduction of ketones.[8] We postulated that σ-bond metathesis between copper(II) acetate and an organosilane took place, generating a copper hydride species. However, we were not sure whether the active catalytic species was a copper(I) hydride or copper(II) hydride, and presumed that copper(I) hydride might be generated from the copper(II) sources, as judged by the fact that the same levels of enantioselectivity were obtained with both copper(I) and copper(II) precursors. Therefore, we set out to synthesize the thermally stable copper(I) hydride cluster $[(PPh_3)CuH]_6$ to investigate the nature of a catalytic species generated from copper(II) acetate. As a result, we report here a direct and expedient synthesis of $[(PPh_3)CuH]_6$ from a copper(II) salt in the presence of an organosilane.

In initial experiments, we set up a small-scale reaction by mixing $Cu(OAc)_2$, PPh_3, and Ph_2SiH_2 in a NMR tube to see if a characteristic signal of the hydride of $[(PPh_3)CuH]_6$ would appear near 3.52 ppm.[4b,9] The

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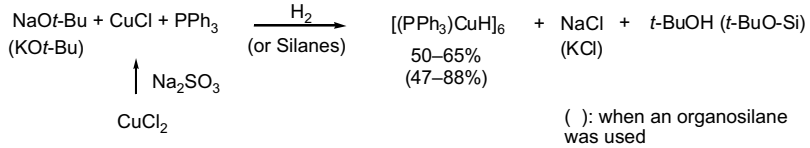
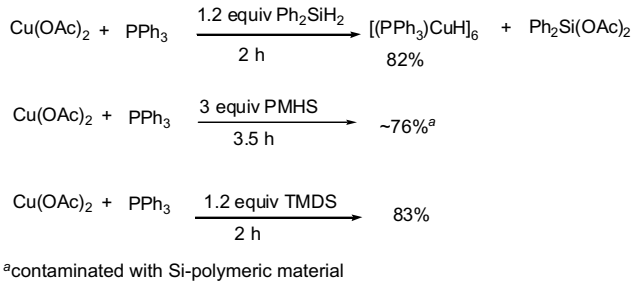


Scheme 1.

color of the solution changed to green and gradually, to red during the reaction and the characteristic peak was observed. Large scale reactions were run with 1.2 equiv of Ph_2SiH_2 as the reducing agent, maintaining the optimum ratio (1:2) of copper to PPh_3, as described in the original Stryker's protocol.[5] Without the necessity of filtering, the homogeneous reaction mixture was concentrated and crystallized to afford pure Stryker's reagent as dark red crystals in 82% yield (Scheme 2). The ^1H NMR spectrum of this reagent in C_6D_6 was of high purity without impurities.[10]

Inexpensive organosilanes other than Ph_2SiH_2 were employed for the synthesis of Stryker's reagent. Polymethylhydrosiloxane (PMHS) was less efficient than Ph_2SiH_2 for generating copper hydride; a color change to dark red was observed rather slowly. Furthermore, Stryker's reagent prepared using PMHS contained silylated polymeric impurities as indicated by broad upfield signals in ^1H NMR. Tetramethyldisiloxane (TMDS) was effective for the reduction to give a dark red solution in 1 h, but in this case the reaction did not become homogeneous completely and some material precipitated; filtration of the precipitated material was necessary. However, Stryker's reagent was obtained in 83% yield after crystallization with no problem.

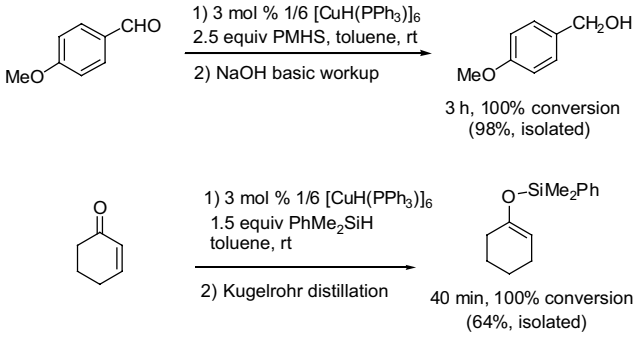
In order to ensure complete reduction, a slight excess amount of organosilanes was used than the amount of theoretically required (Si–H to Cu(II) = 2:1 in ratio). The amount of silanes used in our experiment is comparable to the amount used in the reduction of Cu(I) precursor to guarantee high yields (~80%) of the product in the previous procedure.[6] It is not certain whether the copper(I) hydride complex formed via a copper(II) dihydride species or other copper hydride species during the process. Nonetheless, we have found that the copper(I) hydride complex is generated from copper(II) acetate in the presence of organosilanes, and copper(I) hydride is the active catalytic species in our previous ketone reduction. 1,2 and 1,4-Hydrosilylations were briefly examined with the Stryker's reagent prepared and the results are shown in Scheme 3. The rates of reduction were comparable to those published previously.[4b,11]



Scheme 2. Synthesis of Stryker's reagent from copper(II) acetate.

In summary, we have developed an alternative, simple, and efficient procedure for the preparation of Stryker's reagent using a copper(II) precursor. This procedure is experimentally straightforward to give pure Stryker's reagent in high yield directly from copper(II) acetate in one pot. In particular, when Ph_2SiH_2 is used as the reducing agent, the product can be isolated by crystallization without further workup of the reaction mixture. The simplicity of this protocol will facilitate the preparation and applications of Stryker's reagent in organic synthesis.

A detailed experimental procedure for the synthesis of Stryker's reagent using diphenylsilane is given in the following;[12] Copper(II) acetate (0.182 g, 1 mmol) and triphenylphosphine (0.525 g, 2 mmol) were weighed into an oven-dried round bottomed flask in a nitrogen-filled glovebox. Benzene (2 mL) was added, followed by diphenylsilane (0.22 mL, 1.2 mmol). The reaction mixture turned from a blue suspension to a green solution within 5 min. The color of the reaction further changed from green to dark red in 1 h. The resulting homogeneous solution was stirred for another 1 h and concentrated under vacuum to approximately one-third of its volume. Anhydrous acetonitrile (4 mL) was slowly layered onto the benzene solution to promote crystallization of the product. After standing overnight, the red crystals were collected by filtration, washed with acetonitrile (3 × 5 mL), and dried under vacuum. Stryker's reagent was obtained as dark red crystals in 82% (0.267 g) yield. ^1H NMR (400 MHz, C_6D_6) δ 7.67 (t, J = 8.1 Hz, 36H), 6.95 (t, J = 7.3 Hz, 18H), 6.74 (t, J = 7.5 Hz, 36H), 3.53 (br s, 6H).



Scheme 3. 1,2/1,4-Reductions using cat. $[CuH(PPh_3)]_6$.

Acknowledgements

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References and notes

1. For examples, see: (a) Chen, J.-X.; Daeuble, J. F.; Brestensky, D. M.; Stryker, J. M. *Tetrahedron* **2000**, *56*, 2153–2166; (b) Appella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9473–9474; For a recent review, see: (c) Lipshutz, B. H. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley–VCH: Weinheim, 2002; pp 167–187.
2. Bezman, S. A.; Churchill, M. R.; Osborn, J. A.; Wormald, J. *J. Am. Chem. Soc.* **1971**, *93*, 2063–2065.
3. (a) Mahoney, W. S.; Brestensky, D. M.; Stryker, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 291–293; (b) Koenig, T. M.; Daeuble, J. F.; Brestensky, D. M.; Stryker, J. M. *Tetrahedron Lett.* **1990**, *31*, 3237–3240.
4. (a) Chiu, P.; Szeto, C.-P.; Geng, Z.; Cheng, K.-F. *Org. Lett.* **2001**, *3*, 1901–1903; (b) Lipshutz, B. H.; Chrisman, W.; Noson, K.; Papa, P.; Sclafani, J. A.; Vivian, R. W.; Keith, J. M. *Tetrahedron* **2000**, *56*, 2779–2788; (c) Chae, J.; Yun, J.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 4809–4812.
5. Brestensky, D. M.; Huseland, D. E.; McGettigan, C.; Stryker, J. M. *Tetrahedron Lett.* **1988**, *29*, 3749–3752.
6. Chiu, P.; Li, Z.; Fung, K. C. M. *Tetrahedron Lett.* **2003**, *44*, 455–457.
7. Keller, R. N.; Wycoff, H. D. In *Inorganic Syntheses*; Fernelius, W. C., Ed.; McGraw-Hill: New York, 1946; pp 1–4.
8. Lee, D.; Yun, J. *Tetrahedron Lett.* **2004**, *45*, 5415–5417.
9. For more chemical shifts of hydrides (or deuterides) in phosphine supported copper complexes, see: (a) Goeden, G. V.; Caulton, K. G. *J. Am. Chem. Soc.* **1981**, *103*, 7354–7355; (b) Goeden, G. V.; Huffman, J. C.; Caulton, K. G. *Inorg. Chem.* **1986**, *25*, 2484–2485; (c) Lemmen, T. H.; Folting, K.; Huffman, J. C.; Caulton, K. G. *J. Am. Chem. Soc.* **1985**, *107*, 7774–7775; In a carbene copper hydride complex: (d) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369–3371.
10. It was reported that an unknown impurity that showed broad signals at 7.4 and 7.0 ppm in the ^{1}H NMR spectrum in C_6D_6 were usually present in all batches of the product prepared by following the Stryker's protocol, depending upon the care taken in the crystallization step. See Refs. 4b and 5.
11. Lipshutz, B. H.; Chrisman, W.; Noson, K. *J. Orgnomet. Chem.* **2001**, *624*, 367–371.
12. General methods: benzene was distilled from sodium benzophenone ketyl under nitrogen and degassed for 30 min. Copper(II) acetate, diphenylsilane, polymethylhydrosiloxane (PMHS), tetramethyldisiloxane (TMDS), and triphenylphosphine were purchased from Aldrich, stored in an nitrogen-filled glovebox, and used without further purification.