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SIMPLIFIED, "ONE-POT" PROCEDURE FOR THE SYNTHESIS OF $[(Ph_3P)CuH]_6$, A STABLE COPPER HYDRIDE FOR CONJUGATE REDUCTIONS

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Summary: A convenient, inexpensive method for the preparation of $[(Ph_3P)CuH]_6$, a versatile reagent for the conjugate reduction of α,β-unsaturated carbonyl compounds, has been developed. This procedure is performed on the bench-top without specialized equipment and without the necessity of preparing and purifying species which are difficult to handle.

The thermally stable copper(I) hydride cluster $[(Ph_3P)CuH]_6$, a red crystalline solid, is a practical and convenient reagent for the regiospecific and stereoselective conjugate hydride reduction of α,β-unsaturated carbonyl compounds in high yield.[1] The reaction can be carried out in the presence of trialkylsilyl halides to give silyl enol ethers, the product of overall reductive silylation. This reaction is general for α,β-unsaturated ketones and esters, and has been extended both to unsaturated nitriles and, significantly, to the regiospecific conjugate reduction of α,β-unsaturated aldehydes.[2] Furthermore, because the proposed copper(I) enolate intermediate in this reduction reacts with molecular hydrogen, this reagent holds considerable promise for the development of hydride-mediated reduction chemistry which is catalytic in hydride.[1]

Published procedures for the preparation of $[(Ph_3P)CuH]_6$ suffer from serious economic or operational drawbacks. In the earliest procedures, the complex is prepared from $[(Ph_3P)CuCl]_4$ by halide metathesis using $NaB(OMe)_3H$ (20% yield, requiring "absolutely fresh" hydride reagent)[3a] or $LiAlH_4$ (52% yield provided the stoichiometry is carefully controlled).[3b] An improved procedure (71% yield), requiring excess $Li(BEt_3)H$ (Super-Hydride®), has been developed, but remains unpublished.[4] While the yield in this latter procedure is reasonably attractive, this route is quite expensive for large-scale synthesis. Caulton and Goeden[5] have published an alternative synthesis, involving low pressure hydrogenolysis of $(CuO^tBu)_4$ in the presence of excess triphenylphosphine This procedure obviates the need for expensive reducing agents, but requires the isolation and purification by vacuum sublimation of $(CuO^tBu)_4$, an extremely air and moisture sensitive complex Because the technology necessary to prepare and handle this material is beyond that commonly available to synthetic organic chemists, we have developed a simplified procedure based on the Caulton synthesis in which the copper alkoxide is prepared *in situ* and which *does not require the use of a glovebox*

The published procedure for the synthesis of $(CuO^tBu)_4$ involves reaction of LiO^tBu with CuCl in tetrahydrofuran [6] Attempts to incorporate this procedure into an *in situ* synthesis were unsuccessful formation of the hydride hexamer is inhibited in the presence of lithium salts [7] The use of either the sodium or potassium alkoxide was more promising, and has led to an experimentally straightforward and inexpensive preparation of relatively large batches of $[(Ph_3P)CuH]_6$ as indicated in Eq 1 A

$$NaO^tBu + CuCl + PPh_3 \xrightarrow[\text{Toluene}/C_6H_6,\ \text{rt}]{1\ \text{atm}\ H_2}$$

$$[(Ph_3P)CuH]_6 + {}^tBuOH + NaCl \qquad \text{(Eq. 1)}$$

detailed experimental procedure is given below

General All solvents were dried over the indicated reagent and distilled and stored under nitrogen Acetonitrile was dried over CaH_2, benzene and toluene were dried over sodium benzophenone ketyl *Tert*-butanol was dried over CaH_2 and distilled under nitrogen Triphenylphosphine, copper(II) chloride, and sodium sulfite were purchased from commercial vendors and used as received Copper(I) chloride was prepared by the reduction of copper(II) chloride with sodium sulfite [8] The following procedures were performed using a standard double manifold vacuum line and Schlenk techniques

Sodium *tert*-butoxide.[9] Toluene (150 mL) was added via cannula to a dry, nitrogen-flushed 500-mL Schlenk flask equipped with a Claisen head, a condenser topped with a gas inlet, and a 50-mL pressure-equalizing addition funnel Under positive pressure of nitrogen, sodium (3 52 g, 0 153 mol, cut in thin slices) was added. The toluene was heated with an oil bath to 70-80 °C [10] *Tert-*

butanol (45 0 mL, 35 4 g, 0 477 mol) was delivered dropwise The vigorously-stirred mixture was heated until all of the sodium had reacted (12-24 h). Under positive nitrogen flush, the condenser was replaced with a rubber septum, and for ease of subsequent cannula transfer of the resultant suspension, large clumps of the alkoxide which may be present were broken up with a glass rod

[(Ph$_3$P)CuH]$_6$. Triphenylphosphine (100 3 g, 0 3825 mol) and copper(I) chloride (15 14 g, 0 1529 mol) were added to a dry, septum-capped 2 L Schlenk flask and placed under nitrogen Benzene (approximately 800 mL) was added via cannula, and the resultant suspension was stirred [11] The NaO^{t}Bu/toluene suspension was transferred via a wide-bore cannula to the reaction flask, washing if necessary with additional toluene or benzene, and the yellow nearly homogeneous mixture was placed under positive pressure (1 atm) of hydrogen and stirred vigorously for 15-24 h During this period the residual solids dissolved, the solution turned red, typically within one hour, then dark red, and some gray or brown material precipitated The reaction mixture was transferred under nitrogen pressure through a wide-bore Teflon cannula to a large Schlenk filter containing several layers of sand and Celite [12] The reaction flask was rinsed with several portions of benzene, which were then passed through the filter The very dark red solution was concentrated under vacuum to approximately one-third of its volume and acetonitrile (300 mL) was layered onto the benzene, promoting crystallization of the product The yellow-brown supernatant was removed via cannula, and the product was washed several times with acetonitrile and dried under high vacuum to give 25 0-32 5 g (50-65%) of bright red to dark-red crystals [13]

The degree of crystallinity and purity of the product varies somewhat with the degree of care exerted in the crystallization procedure The major impurity present in the product is observed in the ^{1}H NMR as two broad resonances at approximately δ 7 6 and 6 8 ppm, and has not been identified Small amounts of this byproduct have no perceptible effect on subsequent reduction chemistry Crystallization of the product can also be induced by addition of hexane or pentane with no effect on product purity or yield The yields obtained by this procedure are roughly comparable to those obtained starting directly with purified (CuO^{t}Bu)$_4$ and one atmosphere of hydrogen, although higher yields (ca 80 %) are reported under 1500 psi hydrogen pressure [5] The hydride hexamer has appreciable air stability in the solid state and can be handled briefly in the atmosphere without significant decomposition,[3a] however, the material is air sensitive in solution.[14]

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References and Notes

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6. Tsuda, T.; Hashimoto, T.; Saegusa, T. *J. Am. Chem. Soc.* **1972**, 94, 658.
7. Addition of PPh_3 and hydrogen to a benzene solution of the $(CuO^tBu)_4$ so obtained results in reaction; however, no red color characteristic of the hydride hexamer developed, and the product(s) of this reaction could not be identified.
8. Keller, R. N.; Wycoff, H. D. *Inorg. Synth.* **1946**, 2, 1. It is simpler and more efficient to prepare pure cuprous chloride by reduction of cupric chloride than it is to purify the commercially available cuprous salt.
9. Both NaO^tBu and KO^tBu are commercially available; commercial KO^tBu (Aldrich) has been used successfully in this procedure without special purification. Preparation of NaO^tBu as described, however, avoids potential variation in the quality of commercial reagent on storage.
10. Above this temperature, the product NaO^tBu tends to aggregate, making subsequent cannula transfer of the suspension more difficult.
11. Most of the solids do not dissolve initially; use of lesser solvent volume results in a suspension which is not easily stirred.
12. In the absence of the sand/Celite layers, the muddy dark material will clog the frit. Filtration through the layers normally proceeds slowly but without complication.
13. Rapid addition of acetonitrile affords a light red powder, slightly less pure than the crystalline material obtained by layering. Highly crystalline hydride hexamer dissolves significantly more slowly in benzene or toluene than amorphous or microcrystalline material.
14. The material should be stored under nitrogen, and is indefinitely stable at room temperature under these conditions.

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