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Journal of Organometallic Chemistry 624 (2001) 367–371

Journal of Organo metallic Chemistry

www.elsevier.nl/locate/jorganchem

Communication

Hydrosilylation of aldehydes and ketones catalyzed by $[Ph_3P(CuH)]_6$

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Received 6 October 2000; accepted 22 November 2000

Dedicated with warmest regards to Professor Jean Normant on the occasion of his 65th birthday

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Abstract

Exposure of an aldehyde or ketone to ≤ 5 mol% (in copper) of Stryker's reagent $[Ph_3P(CuH)]_6$ in the presence of one of several silanes affords the corresponding protected alcohol in high yields. Aldehydes can be cleanly reduced in the presence of ketones.

Keywords: Copper hydride; Hydrosilylation; Silyl ethers; Selective reductions

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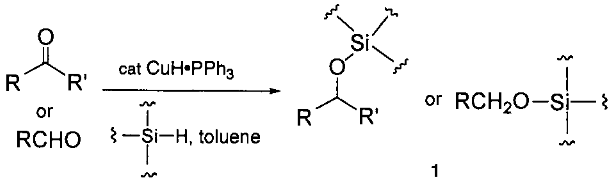
1. Introduction

Reduction of a non-conjugated aldehyde or ketone to the corresponding alcohol is among the most fundamental transformations in organic chemistry. The presence of the resulting hydroxyl group in a molecule oftentimes necessitates its masking during a synthetic sequence, and thus enormous literature has also been amassed over the years dedicated to providing alternatives for protection of the alcohol function. This conversion is most commonly viewed as a two-step/two-pot sequence, notwithstanding extensive literature on hydrosilylation chemistry [1]. Although an impressive array of protecting groups for the newly generated alcohols has been developed [2], it would not be unreasonable to suggest that silyl ethers play a leading role. In this report we describe a new, especially mild and efficient method which is catalytic in Cu(I) for the direct one-pot conversion of aldehydes and ketones to their (selected) silyl ether (or alcohol) derivatives (Eq. (1)).



(1)

2. Results and discussion

The procedure developed derives from our earlier observation of the ease with which an enolate bearing a presumed copper–oxygen bond undergoes transmetalation with one of several arylsilanes [3]. Treatment of an aldehydic substrate with catalytic amounts of Stryker's reagent (the hexamer of $CuH \cdot Ph_3P$) [4] in toluene at 0°C to room temperature in the presence of an aryl silane (e.g. $PhMe_2SiH$) [5] leads to the silylated alcohol essentially quantitatively. Since $CuH \cdot PPh_3$ alone appears to be sufficiently reactive to reduce an aldehyde [6], which is not true for the silane, the former species is the likely reductant. The intermediate copper alkoxide then undergoes transmetalation (perhaps via the four-centered species **2**) to arrive at product **1** with regeneration of the catalyst (Scheme 1) [7]. Replacement of

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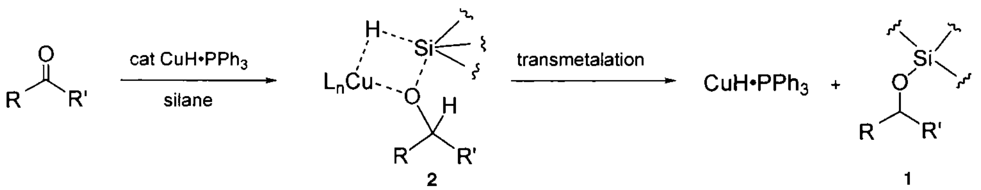
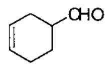
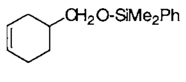
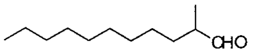
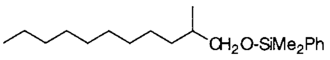
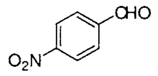
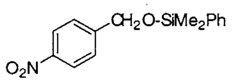
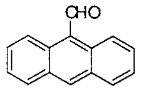
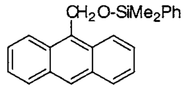
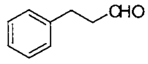
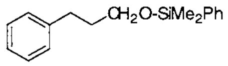
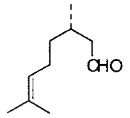
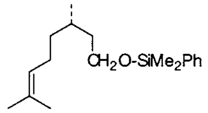
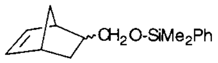
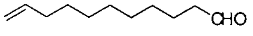
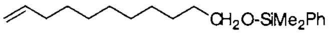
PII: S0022-328X(00)00903-7



Scheme 1. Regeneration of CuH·PPh$_3$ via transmetalation.

Table 1
Hydrosilylations of aldehydes with cat CuH·PPh$_3$/PhMe$_2$SiH [a]

Aldehyde	Product[b]	Yield(%)[c]
		95
		92
		89
		96
		90
		93
		98
		95

[a] All reactions were run using 3 mol % CuH(PPh$_3$) and 1.3 equiv PhMe$_2$SiH in toluene at rt over 2 h.
[b] Fully characterized by IR, NMR, MS, and HRMS data. [c] Isolated, purified material.

CuH·PPh$_3$ with a copper halide (e.g. CuCl/LiCl; 1:1) led to no detectable reaction, not unexpected in light of Hosomi's observations where the CuCl/PhMe$_2$SiH combination requires heating in dimethylimidazolone (DMI) to generate 'CuH' [8]. Table 1 offers a sampling of aldehydes that have been converted directly to their silyl ethers. Under the conditions used, several functional groups (e.g. esters, alkenes, alkynes, bromides, nitro groups, etc.)[1] are unaffected.

Other silanes, which lead to hydrolytically more robust derivatives [2], could also be employed as sources of hydride. Thus, MePh$_2$SiH[2] and even (t-Bu)Ph$_2$SiH [9] give the corresponding silyl ethers (cf. Table 2 and Eq. (2), respectively). Reactions with the latter reagents require slight heating (ca. 40–45°C), although net efficiency of the process is not compromised[3,4]. More reactive PMHS [10], the least expensive silane of this group, likewise gives an intermediate (polymeric) silyl ether, which upon basic workup affords alcohols in good yields. Table 3 highlights representative examples. Levels of catalyst as low as 0.1 mol% are sufficient in the case of aldehydes to arrive at similar results (Scheme 2).

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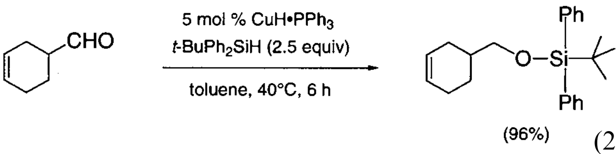
[1] Control experiments involving exposure of these functional groups to our standard conditions for hydrosilylation in the absence of a substrate indicated no reduction had occurred in any case.

[2] Available from Gelest Chemicals; catalog number SID44555.0.

[3] Excess silane could be recovered via Kugelrohr distillation (b.p. 210–215°C at 1.5 mmHg) and reused.

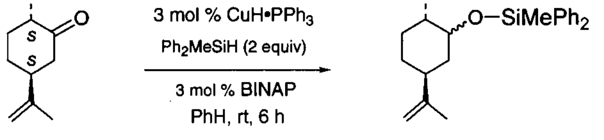
[4] Triphenylsilane (Ph$_3$SiH) also reacts under similar conditions, as expected, to afford a silylated alcohol in excellent yield (e.g. as in the case of an aldehyde; Table 1, entry 7: yield = 94%).



(2)

Differences in reactivity between aldehydes and ketones could be exploited to selectively reduce the former in the presence of the latter. As illustrated in Scheme 3, a 1:1 mix of aldehyde **3** and ketone **4** led to products **5** and **6** in a 98.6:1.4 (GC) ratio; with alcohol **5** being isolated in 94% yield after basic workup and column chromatography. The same experiment conducted on acyclic ketone **7** showed even greater chemoselectivity, as **3** was fully reduced without a trace of alcohol **8** being noted by capillary GC analysis of the crude reaction mixture. Moreover, ketone **7** was recovered to the extent of 96%. While several other reagents exist for the selective reduction of an aldehyde over a ketone (e.g. Raney Ni [11a], $KBPh_4$ [11b], $Bu_3SnH/Ti(0)$ [11c], etc.), the catalytic $CuH{\cdot}PPh_3$/silane combination is one of the mildest and most economically attractive.

Manifested in the case of dihydrocarvone (**9**) is yet another feature of this system (Eq. (3)). This substrate was chosen to examine the integrity of an adjacent stereogenic center upon ketone reduction. Catalytic $CuH{\cdot}PPh_3$ in the presence of $PhMe_2P$ and *t*-BuOH under an atmosphere of hydrogen has been reported to epimerize these sites, presumably a consequence of strongly basic conditions by virtue of the copper alkoxide generated in situ [6b]. While alkoxide intermediates of this type may be at some point in our sequence obligatory, their lifetime is minimized due to rapid transmetalation with the silane present in solution. Thus, conversion of **9** to its diphenylmethylsilyl ether **10** occurred cleanly, favoring axial attack, to afford only the expected two diastereomers in a combined yield of 94%. Interestingly, the presence of bidentate phosphine ligands, such as DPPF and racemic BINAP, in amounts equal to that of $CuH{\cdot}PPh_3$, had a dramatic effect on accelerating the rates of these hydrosilylations, an observation which is now being pursued further.



9

10 (94%; 2 : 1 ratio, α : β)

(3)

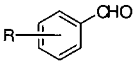
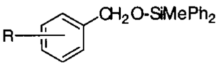
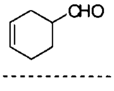
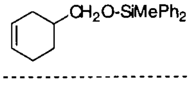
In summary, a new method for hydrosilylation of aldehydes and ketones has been uncovered which can be used to arrive at silylated alcohols bearing any of several commonly used silicon protecting groups. Conditions are very mild, reagents are inexpensive, and the amount of transition metal required can be as little as 0.1 mol% in the case of aldehydes. Future efforts directed at the asymmetric version of this copper(I)-mediated process as applied to unsymmetrically substituted ketones [12] are in progress and will be reported in due course.

3. Experimental

3.1. Representative 1,2-reduction/silylation of an aldehyde ((2-bromobenzyloxy)-diphenylmethylsilane; Table 2, entry 1)

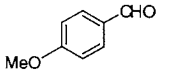
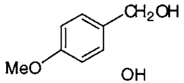
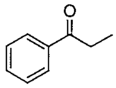
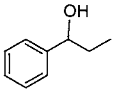
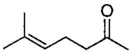
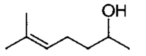
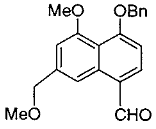
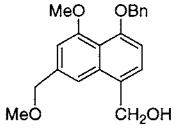
A dried 25 ml flask with a rubber septum top was flushed with argon and charged with $[PPh_3(CuH)]_6$ (53 mg, 0.162 mmol) as a red solid. Toluene (5.4 ml) followed by neat diphenylmethylsilane (1.4 ml, 7.0 mmol) were added resulting in a homogeneous red solution. In a second dry argon flushed vessel (10 ml) with a rubber septum top 2-bromobenzaldehyde (0.63

Table 2
Hydrosilylations using cat $CuH{\cdot}PPh_3/MePh_2SiH$ [a]

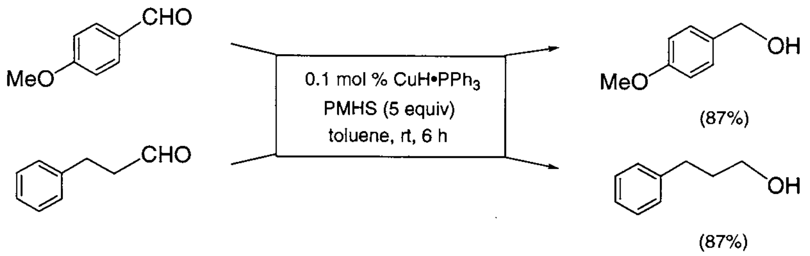
Aldehyde	Time (min)	Product[b]	Yield(%)
			
R = *ortho*-Br	30		95
R = *para*-Br	45		98
R = *para*-NO_2	30		89[c]
R = *para*-OMe	120		92
R = *para* -OTs	60		89
R = *meta*-OBn	120		97
	120		98

[a] All reactions were run at 0.5 M using 3% CuH•PPh3 and 1.3 - 2.5 equiv Ph2MeSiH. See legend for Table 1.
[b] Isolated, purified material. [c] Coversion was 96% by GCMS analysis of the crude reaction mixture.

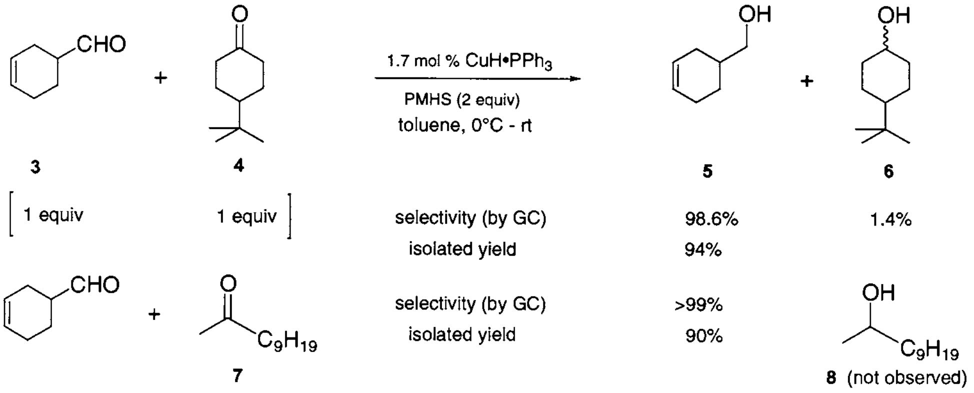
Table 3
Hydrosilylations using cat CuH·PPh$_3$/PMHS [a]/PMHSa followed by basic workup

Substrate	Time (h)	Product	Yield(%)
	3		**94**
	10		**97**
	22		**78**
	1.5		**85**[b]

[a] All reactions were run at 0.5 M using 3% CuH•PPh$_3$ and 2.5 equiv PMHS. See legend for Table 1.
[b] Reaction was run at 0.2 M.



Scheme 2. Hydrosilylations of aldehydes using only 0.1 mol% CuH·PPh$_3$.



Scheme 3. Selective 1,2-reductions with CuH·PPh$_3$.

ml, 5.4 mmol) and toluene (4 ml) were mixed, and the solution transferred via canula into the room temperature solution of copper and silane with stirring. The reaction mixture was monitored by TLC (elution with 5% diethyl ether/hexane, $R_f = 0.74$); the aldehyde was consumed after 30 min. The reaction was filtered through a pad of Celite/charcoal, washed with EtOAc (2 × 15 ml), and the filtrate concentrated in vacuo to an oil. Kugelrohr distillation (168°C, 0.2–0.3 Torr) yielded the title compound as a colorless oil (1.98 g, 95%). ^{1}H-NMR (400 MHz, CDCl$_3$) δ 0.70 (3H, s), 4.83 (2H, s), 7.11 (1H, m), 7.32 (1H, dt, 7.6, 1.2, 0.8 Hz), 7.40 (6H, m), 7.48 (1H, dd, 8.0, 1.2 Hz), 7.63 (5H, m). ^{13}C-NMR (100 MHz, CDCl$_3$) δ −2.94, 65.02, 121.46, 127.53, 128.08, 128.14, 128.54, 130.18, 132.28, 134.52, 135.76, 139.80. IR (neat) cm^{-1} 3069, 3047, 3022, 2953, 1957, 1888, 1820, 1770, 1590, 1569, 1429, 1255, 1203; LREIMS (*m*/*z*, rel. int.) 369(100), 339(9), 306(18), 289(8), 257(5), 245(7), 225(13), 211(17), 197(33), 183(37), 169(44), 149(33), 139(12), 121(8), 105(24), 90(33), 77(13), 57(10); HREIMS Calc. for $C_{20}H_{19}BrOSi$ 367.0154, Found 367.0152 $[M^+ - CH_3]$.

Acknowledgements

Financial support provided by the NSF (CHE 97-34813) and NIH (GM 56764) is warmly acknowledged with thanks.

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