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Versatile Dehydrogenative Alcohol Silylation Catalyzed by Cu(I)–Phosphine Complex

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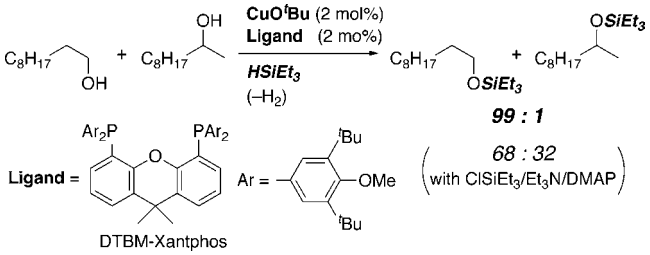
ABSTRACT



Cu(I) complexes of xanthane-based diphosphines were versatile catalysts for dehydrogenative alcohol silylation, exhibiting high activity and broad substrate scope. Highly selective silylation of 1-decanol over 2-decanol is possible even with a silylating reagent of small steric demand such as $HSiMe_2Ph$ or $HSiEt_3$.

Development of environmentally benign chemical processes is a challenge in modern synthetic organic chemistry. Substituting a process that employs an organic halide for a halogen-free process should have an impact. Silyl ether formation is not only a fundamental process in the synthesis of functional organosilicon compounds but also an important technique for protection of reactive hydroxy groups during multistep organic syntheses.[1] From the standpoint of "green chemistry", this transformation should be conducted through catalytic dehydrogenative silylation with a hydrosilane rather than through electrophilic silylation with a silyl electrophile (R_3Si-X) in combination with a stoichiometric base.[2−6] The former forms H_2 as the sole byproduct instead of a HX·base in the latter. Here, we report that copper complexes of xanthene-based diphosphines (Figure 1, **1a**, **1b**)[7] are highly efficient catalysts for dehydrogenative alcohol silylation, which provides an unprecedented broad substrate scope and a high level of chemoselectivity.

Various transition metal complexes have been reported as catalysts for dehydrogenative silylation.[2−5] Because of poor activity, however, most are applicable only with a limited range of substrate sets. Moreover, some possess C=C hydrosilylation, hydrogenation, and isomerization activities. Therefore, unsaturated alcohols cannot be utilized. While $[(Ph_3P)CuH]_6$ is a chemoselective catalyst for the dehydrogenative alcohol silylation of unsaturated alcohols, its low activity prevents its use in practical syntheses.[4]

To find an efficient and versatile catalyst for dehydrogenative silylation, we screened various copper salt−ligand

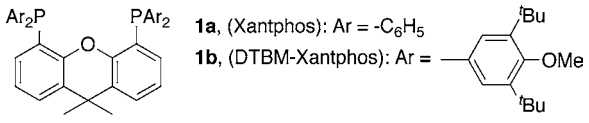


Figure 1. Xanthene-based ligands.

(1) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley & Sons: New York, 1999.

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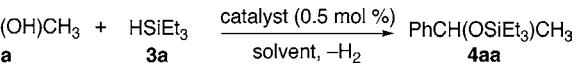
combinations for reaction of 1-phenylethanol (**2a**) with $HSiEt_3$ (**3a**) and found that the copper complex generated in situ from *t*-BuOCu and Xantphos (**1a**) possessed high catalytic activity (Table 1, entry 1). With 0.5 mol % catalyst loading, the reaction was complete in 1 h at 24 °C, while almost no reaction occurred with $[(Ph_3P)CuH]_6$ under the same conditions (entry 2). Replacing Xantphos with other phosphine ligands such as PPh_3, dppe, dppp, dppf, and (*R*)-BINAP resulted in a drastic decrease in activity (1−34% conversion at 2 h, entries 3−7). The superior activity of the *t*-BuOCu−Xantphos system compared to previously reported silylation catalysts such as $RhCl(PPh_3)_3$,[3a] $Rh_2(OCOC_4F_7)_4$,[3b] $RuCl_2(p\text{-cymene})_2$,[3d] and $Ru_3(CO)_{12}$,[3c] is apparent as shown in Table 1 (<6% conversion at 2 h, entries 8−11).[3]

Table 1. Dehydrogenative Silylation with Various Catalysts[a]



entry	catalyst	solvent	temp (°C)	time (h)	yield[b] (%)
1	*t*-BuOCu, **1a**	toluene	24	1	99
2	$[(Ph_3P)CuH]_6$[c]	toluene	23	2	trace
3	*t*-BuOCu, PPh_3	toluene	24	2	1
4	*t*-BuOCu, dppe	toluene	23	2	2
5	*t*-BuOCu, dppp	toluene	22	2	34[d]
6	*t*-BuOCu, dppf	toluene	23	2	12
7	*t*-BuOCu, (*R*)-BINAP	toluene	23	2	5
8	$RhCl(PPh_3)_3$	toluene	22	2	trace
9	$Rh_2(OCOC_4F_7)_4$	CH_2Cl_2	23	2	3
10	$RuCl_2(p\text{-cymene})_2$	neat	25	2	6
11	$Ru_3(CO)_{12}$	neat	26	2	trace

[a] **2a**, 0.5 mmol; **3a**, 1.0 mmol; solvent, 1.0 mL unless otherwise noted. [b] Determined by GC. [c] Performed with 0.5 mol % for Cu(I). [d] After 24 h, yield = 40%.

The scope and limitations of the present Cu-catalyzed silylation are summarized in Table 2. Simple primary and secondary alkanols (**2b**, **2c**) also were silylated with Et_3SiH (**3a**) at 23 and 24 °C, but this catalyst was not effective for tertiary alcohol **2d** (entries 1−3). $HSiMe_2t$-Bu (**3b**) underwent silylation with primary alcohol **2b** at room temperature and with secondary alcohol **2e** at 50 °C (entries 4 and 5). Even $HSiPh_2t$-Bu (**3c**) and $HSiPh_3$ (**3d**), which are more hindered than **3a** and **3b**, reacted smoothly with primary and secondary alcohols (**2f**, **2a**) (entries 6−9). Only a trace of the product was detected in the reaction of $HSi(i\text{-}Pr)_3$ (**3e**) even with primary alcohol **2f** after 24 h at 70 °C (entry 10). Silyl ethers of 9-decen-1-ol (**2g**) and 3-hexyn-1-ol (**2h**) were obtained in good yields with unsaturated bonds intact (entries 11 and 12). No carbonyl hydrosilylation was observed in the alcohol silylation of 5-hydroxy-2-pentanone (**2i**) (entry 13). The β-alkoxy group, which is a potential coordination site for the metal center, exerted virtually no influence on reactivity (entry 14). Entry 15 in Table 2 demonstrates the practical advantage of this method in large-scale preparation (see, Supporting Information for experimental procedures).

It is an additional characteristic feature of the present catalytic silylation that the selective silylation of a sterically less congested hydroxy group over a more congested one is possible with rather small silyl groups such as $PhMe_2Si$ and Et_3Si groups. Such silylation is generally difficult with the conventional electrophilic silylation.[8] Results for the selective silylation of primary alcohol 1-decanol (**2b**) in the presence of secondary alcohol 2-decanol (**2c**) are summarized in Table 3. The electrophilic method using chlorosilanes in combination with Et_3N and DMAP (method A) required the bulkiness of the *t*-$BuMe_2Si$ group to obtain a reasonably high selectivity; **4bx**:**4cx** = 51:49 ($ClSiMe_2Ph$, **5f**), 68:32 ($ClSiEt_3$, **5a**), 95:5 ($ClSiMe_2t$-Bu, **5b**) (entries 1−3). In sharp contrast, dehydrogenative silylation with Cu(I)−Xantphos (**1a**) catalyst (method B) exhibited selectivity for the primary alcohol as high as 90:10, even with $HSiMe_2Ph$ (**3f**) (entry 4). Higher selectivities were obtained with sterically more demanding hydrosilanes $HSiEt_3$ (**3a**) (93:7) and $HSiMe_2t$-Bu (**3b**) (96:4) (entries 5, 6). Use of a new xanthene-based ligand **1b** with larger steric demand (method C) further improved

(2) For selected references, see: (a) Sommer, L. H.; Lyons, J. E. *J. Am. Chem. Soc.* **1969**, *91*, 7061−7067. (b) Chalk, A. J. *J. Chem. Soc., Chem. Commun.* **1970**, 847−848. (c) Oehmichen, U.; Singer, H. *J. Organomet. Chem.* **1983**, *243*, 199−204. (d) Lukevics, E.; Dzintara, M. *J. Organomet. Chem.* **1985**, *295*, 265−315. (e) Luo, X. L.; Crabtree, R. H. *J. Am. Chem. Soc.* **1989**, *111*, 2527−2535. (f) Yamamoto, K.; Takemae, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2111−2113. (g) Gregg, B. T.; Cutler, A. R. *Organometallics* **1994**, *13*, 1039−1043. (h) Chung, M. K.; Ferguson, G.; Robertson, V.; Schlaf, M. *Can. J. Chem.* **2001**, *79*, 949−957. (i) Chung, M. K.; Orlova, G.; Goddard, J. D.; Schlaf, M.; Harris, R.; Beveridge, T. J.; White, G.; Hallett, F. R. *J. Am. Chem. Soc.* **2002**, *124*, 10508−10518. (j) Maifeld, S. V.; Miller, R. L.; Lee, D. *Tetrahedron Lett.* **2002**, *43*, 6363−6366. (k) Field, L. D.; Messerle, B. A.; Rehr, M.; Soler, L. P.; Hambley, T. W. *Organometallics* **2003**, *22*, 2387−2395. (l) Schmidt, D. R.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 1190−1191. (m) Biffis, A.; Braga, M.; Basato, M. *Adv. Synth. Catal.* **2004**, *346*, 451−458.

(3) (a) Ojima, I.; Kogure, T.; Nihonyanagi, M.; Kono, H.; Inaba, S. *Chem. Lett.* **1973**, 501−504. (b) Doyle, M. P.; High, K. G.; Bagheri, V.; Pieters, R. J.; Lewis, P. J.; Pearson, M. M. *J. Org. Chem.* **1990**, *55*, 6082−6086. (c) Funatsu, A.; Kubota, T.; Endo, M. (Shin-Etsu Chemical Industry Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP2001-114788, 2001. (d) Miller, R. L.; Maifeld, S. V.; Lee, D. *Org. Lett.* **2004**, *6*, 2773−2776.

(4) (a) Lorenz, C.; Schubert, U. *Chem. Ber.* **1995**, *128*, 1267−1269. (b) Mahoney, W. S.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 8818−8823. For the synthesis of optically active silanes by asymmetric silane alcoholysis catalyzed by a chiral Cu(I)−complex, see ref 2l.

(5) $[IrH_2(THF)_2(PPh_3)_2]SbF_6$ was reported as the most active catalyst for Et_3SiH. However, this complex also promotes isomerization of C−C double bonds and slow hydrosilylation of ketones. See ref 2e.

(6) For Lewis acid and base catalysts, see: (a) Tanabe, Y.; Okumura, H.; Maeda, A.; Murakami, M. *Tetrahedron Lett.* **1994**, *35*, 8413−8414. (b) Blackwell, J. M.; Foster, K. L.; Beck, V. H.; Piers, W. E. *J. Org. Chem.* **1999**, *64*, 4887−4892. See also ref 2d.

(7) **1b** is a new compound. For **1a**, see: (a) Kranenburg, M.; Vanderburgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081−3089. (b) Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Acc. Chem. Res.* **2001**, *34*, 895−904.

(8) Moderate selectivity between primary and secondary alcohols was reported for the $Rh_2(OCOC_4F_7)_4$-catalyzed silylation with $HSiEt_3$; 1-butanol: 2-butanol = 79:21, see ref 3b.

(9) Observed ligand effect is in sharp contrast to that in the Cu-catalyzed (asymmetric) 1,2-hydrosilylation of ketones and 1,4-hydrosilylation of α,β-unsaturated carbonyl compounds. It has been reported that the hydrosilylations were remarkably accelerated by some diphosphines of *normal* bite angles. To the contrary, we observed that Xantphos was less effective than the normal diphosphines for the hydrosilylations, see: (a) Lipshutz, B. H.; Noson, K.; Chrisman, W. *J. Am. Chem. Soc.* **2001**, *123*, 12917−12918. (b) Lipshutz, B. H.; Caires, C. C.; Kuipers, P.; Chrisman, W. *Org. Lett.* **2003**, *5*, 3085−3088. (c) Moritani, Y.; Appella, D. H.; Jurkauskas, V.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 6797−6798. (d) Chen, J. X.; Daeuble, J. F.; Stryker, J. M. *Tetrahedron* **2000**, *56*, 2789−2798. (e) Chen, J. X.; Daeuble, J. F.; Brestensky, D. M.; Stryker, J. M. *Tetrahedron* **2000**, *56*, 2153−2166.

Table 2. Dehydrogenative Silylation with Cu(I)−**1a** Catalyst[a]

ROH (**2b-k**) + $HSiR^1R^2R^3$ (**3a-e**) —cat. CuO*t*-Bu, **1a**, toluene, $-H_2$→ $ROSiR^1R^2R^3$ (**4**)

entry	alcohol	hydrosilane	product	catalyst (mol %)	temp (°C)	time (h)	yield[b] (%)
1	$CH_3(CH_2)_8CH_2OH$ (**2b**)	$HSiEt_3$ (**3a**)	**4ba**	0.5	23	1	91
2	$CH_3(CH_2)_7CH(OH)CH_3$ (**2c**)	**3a**	**4ca**	1.0	24	4	97
3	$(CH_3)_3COH$ (**2d**)	**3a**	**4da**	0.5	50	22	7
4	$CH_3(CH_2)_8CH_2OH$ (**2b**)	$HSiMe_2{}^t$Bu (**3b**)	**4bb**	1.0	25	4	99
5	*cyclo*-$C_6H_{11}OH$ (**2e**)	**3b**	**4eb**	0.5	50	5	95
6	$PhCH_2CH_2OH$ (**2f**)	$HSiPh_2{}^t$Bu (**3c**)	**4fc**	1.0	24	3	94
7	$PhCH(OH)CH_3$ (**2a**)	**3c**	**4ac**	5.0	50	3	94
8	$PhCH_2CH_2OH$ (**2f**)	$HSiPh_3$ (**3d**)	**4fd**	1.0	23	2	94
9	$PhCH(OH)CH_3$ (**2a**)	**3d**	**4ad**	2.0	23	1	96
10	$PhCH_2CH_2OH$ (**2f**)	$HSi(^iPr)_3$ (**3e**)	**4fe**	0.5	70	24	trace
11	$CH_2{=}CH(CH_2)_7CH_2OH$ (**2g**)	**3a**	**4ga**	0.5	25	2	95
12	$EtC{\equiv}CCH_2CH_2OH$ (**2h**)	**3a**	**4ha**	0.5	26	2	95
13	$CH_3CO(CH_2)_2CH_2OH$ (**2i**)	**3a**	**4ia**	2.0	24	5	84
14	$CH_3OCH_2CH_2OH$ (**2j**)	**3b**	**4jb**	0.5	23	1	89
15	geraniol (**2k**)[c]	**3a**	**4ka**	0.1	24	1	97

[a] **2**, 0.5 mmol; **3**, 1.0 mmol; solvent, 1.0 mL unless otherwise noted. [b] Isolated yield. [c] **2k**, 50 mmol; **3a**, 55 mmol, no solvent.

the selectivity, and very high selectivities were achieved irrespective of the silyl group structures; **4bx**:**4cx** = 98:2 ($HSiMe_2Ph$), 99:1 ($HSiEt_3$), 99:1 ($HSiMe_2t$-Bu) (entries 7−9).

A mechanism for Cu-catalyzed silylation is proposed in Scheme 1. Mixing *t*-BuOCu, the diphosphine, and $HSiR'_3$ generates phosphine-chelated Cu(I) hydride **A** as an active species, which is in equilibrium with less active or inactive dimer **B** or higher aggregates **C**. Hydride **A** reacts with ROH through σ-bond metathesis to produce alkoxocopper(I) **D** and H_2. Subsequent metathesis between **D** and $HSiR'_3$ affords $ROSiR'_3$ and **A**. According to this mechanism, the high reactivity of Xantphos catalyst is attributable at least in part to the larger contribution of the monomeric hydride **A** in the aggregation equilibria. However, this alone cannot explain the unique superiority of the Xantphos ligand compared to other chelating diphosphines. A large P−Cu−P bite angle expected for Xantphos should exert some salient effect on the acceleration of σ-bond metathesis between **A** and the alcohol.[9]

Scheme 1. Proposed Mechanism for Cu(I)-Catalyzed Silylation

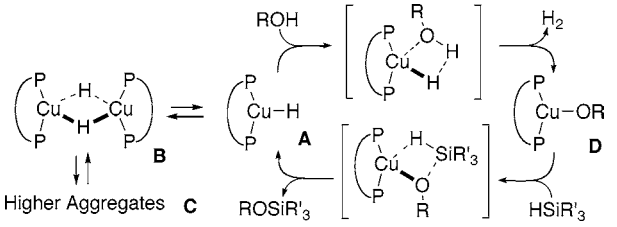


Table 3. Selective Silylation of a Primary Alcohol in the Presence of a Secondary Alcohol

n-Oct(OH) **2b** + *n*-Oct(OH) **2c** —silyl reagent (**3** or **5**), (**2b**:**2c**:**3** or **5** = 1:1:1)→ *n*-Oct($OSiR_3$) **4bx** + *n*-Oct($OSiR_3$) **4cx**

entry	silyl reagent	method[a]	temp (°C)	time (h)	yield (%)[b] **4bx** + **4cx**	ratio[c] **4bx**:**4cx**
1	$ClSiMe_2Ph$ (**5f**)	A	24	13	94	51:49
2	$ClSiEt_3$ (**5a**)	A	24	2	95	68:32
3	$ClSiMe_2{}^t$Bu (**5b**)	A	23	1	94	95:5
4	$HSiMe_2Ph$ (**3f**)	B	25	1	91	90:10
5	$HSiEt_3$ (**3a**)	B	22	2	93	93:7
6	$HSiMe_2{}^t$Bu (**3b**)	B	23	3	88	96:4
7	$HSiMe_2Ph$ (**3f**)	C	22	7	92	98:2
8	$HSiEt_3$ (**3a**)	C	22	19	95	99:1
9	$HSiMe_2{}^t$Bu (**3b**)	C[d]	22	24	85	99:1

[a] Method A: **2b**, 0.5 mmol; CH_2Cl_2, 1.0 mL; **2b**:**2c**:**5**:Et_3N:DMAP = 1:1:1:1.2:0.04. Method B (C): **2b**, 0.5 mmol; toluene, 1.0 mL; **2b**:**2c**:**3**:*t*-BuOCu:**1a** (**1b** for method C) = 1:1:1:0.02:0.02. [b] Isolated yield. [c] Determined by GC. [d] **2b**:**2c**:**3b**:*t*-BuOCu:**1b** = 1:1:1:0.05:0.05.

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Supporting Information Available: Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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