## FULL PAPERS

DOI: 10.1002/adsc.201200200

## **Copper-Catalyzed Highly Selective Semihydrogenation of Non-Polar Carbon-Carbon Multiple Bonds using a Silane and an Alcohol**

Kazuhiko Semba,<sup>a</sup> Tetsuaki Fujihara,<sup>a</sup> Tinghua Xu,<sup>a</sup> Jun Terao,<sup>a</sup> and Yasushi Tsuji<sup>a,\*</sup>

<sup>a</sup> Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 615-8510, Japan

Fax: (+81)-75-383-2514; phone: (+81)-75-383-2515; e-mail: ytsuji@scl.kyoto-u.ac.jp

Received: March 12, 2012; Published online: May 15, 2012

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201200200.

Abstract: A copper catalyst bearing a suitable Xantphos derivative or NHC ligand was found to be highly efficient for the selective semihydrogenation of non-polar unsaturated compounds using a mixture of a silane and an alcohol as reducing agent. The catalytic system was useful for the selective semihydrogenation of internal alkynes to (Z)-alkenes with sup-

## Introduction

Copper compounds are highly valuable reagents in organic synthesis.<sup>[1]</sup> Among them, copper hydrides, typi-cally [CuH(PPh<sub>3</sub>)]<sub>6</sub>,<sup>[2a,b]</sup> are powerful tools for 1,4-reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds.<sup>[2b,c]</sup> These reductions also can be carried out catalytically using various reducing reagents.<sup>[2d,e,3]</sup> Especially, silanes are widely applied in the catalytic reduction of polar unsaturated bonds such as C=O, C=N, and C=C conjugated with polar functionalities (viz., Michael acceptors).<sup>[3]</sup> However, it is quite surprising and frustrating that reduction of non-polar carbon-carbon multiple bonds such as simple alkynes cannot be carried out catalytically with copper complexes. To date, there have been six precedents<sup>[4]</sup> using an excess amount of copper reagents in the reduction of alkynes. However, such an important class of transformations<sup>[5]</sup> should be performed catalytically.

Semihydrogenation of internal alkynes is a crucial methodology to provide (*Z*)-alkenes which are often found in many biologically active compounds.<sup>[6]</sup> Various heterogeneous catalysts are effective in this transformation.<sup>[7]</sup> Especially, the Lindlar catalyst<sup>[8]</sup> is best known and most efficient, but it often suffers from Z/E isomerization, low chemoselectivity, and poor reproducibility. In the catalytic reactions, hydrogen

pression of overreduction to the corresponding alkanes. Furthermore, semihydrogenations of terminal alkyne, 1,2-diene, 1,3-diene, 1,3-enyne and 1,3-diyne systems were also achieved selectively.

**Keywords:** alkynes; copper; homogeneous catalysis; reduction

uptake may be strictly monitored to prevent the overreduction to undesired alkanes. On the other hand, several homogeneous catalysts showed good selectivity in the semihydrogenation of alkynes.<sup>[9,10,11]</sup> Recently, homogeneous palladium catalysts were intensively developed.<sup>[9]</sup> During the course of our studies on copper-catalyzed hydrosilylation of bulky ketones<sup>[12a]</sup>, hydrocarboxylation of alkynes using carbon dioxide<sup>[12b]</sup> and hydroboration of alkynes<sup>[12c]</sup> we found that *non-polar* carbon-carbon multiple bonds were efficiently semihydrogenated by a homogeneous copper catalyst. As reported herein, a copper complex bearing a suitable bidentate phosphane or N-heterocyclic carbene (NHC) ligand shows high catalytic activity and excellent selectivity by using a mixture of a silane and an alcohol as a reducing agent.

### **Results and Discussion**

#### **Optimization of the Reaction Conditions**

The semihydrogenation of 1-phenyl-1-propyne (1a) was carried out at room temperature (Table 1). As a reducing reagent, a mixture of polymethylhydrosiloxane (PMHS) and *t*-BuOH was employed. Using  $Cu(OAc)_2 \cdot H_2O$  as a catalyst precursor without any

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Table 1. Semihydrogenation of 1-phenyl-1-propyne (1a) with various catalysts<sup>[a]</sup>



Entry	Cu catalyst	Ligand $(P/Cu = 4.0)$	Yield [%] <sup>[b]</sup>	
			(Z)-2a	3a
1	Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O	none	2	0
2	$Cu(OAc)_2 \cdot H_2O$	PPh <sub>3</sub>	6	0
3	$Cu(OAc)_2 \cdot H_2O$	PCy <sub>3</sub>	9	0
4	$Cu(OAc)_2 \cdot H_2O$	dppe	2	0
5	$Cu(OAc)_2 \cdot H_2O$	dppp	3	0
6	$Cu(OAc)_2 \cdot H_2O$	rac-BINAP	8	0
7	$Cu(OAc)_2 \cdot H_2O$	dppbz	4	0
8	$Cu(OAc)_2 \cdot H_2O$	Xan	34	1
9 <sup>[c]</sup>	$Cu(OAc)_2 \cdot H_2O$	Xan	75	9
10	$Cu(OAc)_2 \cdot H_2O$	CF <sub>3</sub> Ar-Xan	99	<1
11	$Cu(OAc)_2 \cdot H_2O$	MeAr-Xan	80	10
12	$Cu(OAc)_2 \cdot H_2O$	t-Bu-Xan	2	0
13 <sup>[d]</sup>	$Cu(OAc)_2 \cdot H_2O$	CF <sub>3</sub> Ar-Xan	0	0
14 <sup>[e]</sup>	$Cu(OAc)_2 \cdot H_2O$	CF <sub>3</sub> Ar-Xan	10	0
15	CuCl/t-BuONa <sup>[f]</sup>	CF <sub>3</sub> Ar-Xan	43	0
16	$CuF(PPh_3)_3$	CF <sub>3</sub> Ar-Xan	54	0

- <sup>[a]</sup> 1-Phenyl-1-propyne (1a, 0.50 mmol), Cu cat. (0.010 mmol, 2.0 mol%), ligand (P/Cu=4.0), PMHS (2.0 mmol as the Si-H unit, 4.0 equiv.), *t*-BuOH (1.0 mmol, 2.0 equiv.), THF (0.50 mL), hexane (0.50 mL), at room temperature, for 17 h.
- <sup>[b]</sup> GC yields by the internal standard method.
- <sup>[c]</sup> At 65 °C.
- <sup>[d]</sup> Without PMHS.
- <sup>[e]</sup> Without *t*-BuOH.
- <sup>[f]</sup> CuCl (0.010 mmol) and *t*-BuONa (0.060 mmol).

added ligands resulted in very low conversion of 1a (entry 1). With added monodentate phosphanes (P/ Cu = 4.0) such as PPh<sub>3</sub> and PCy<sub>3</sub>,<sup>[13]</sup> the conversions were also low and the corresponding (Z)-alkene [(Z)-2a] was formed only in 6% and 9% yields, respectively (entries 2 and 3). Bidentate phosphanes such as dppe, dppp, *rac*-BINAP and dppbz<sup>[13]</sup> were not effective in the reaction (entries 4-7). In contrast, Xantphos<sup>[13]</sup> (Xan) as a ligand afforded the product in 34% yield (entry 8). When the reaction temperature was raised to 65 °C with Xan, the yield of (Z)-2a increased to 75%, but the undesired alkane (3a) via the overreduction was formed in considerable amounts (9% yield, entry 9). Gratifyingly, a Xantphos derivative bearing 3,5-bis(trifluoromethyl)phenyl moieties on the phosphorus atoms (CF<sub>3</sub>Ar-Xan<sup>[14]</sup>, Figure 1) was found to be much more effective, giving (Z)-2a in 99% vield without the formation of (E)-2a (entry 10). This excellent (Z)-selectivity is noteworthy because such selective semihydrogenation of aromatic alkynes was often difficult owing to Z/E isomerization and



Figure 1. The structures of Xantphos derivatives.

overreduction to alkanes.<sup>[15]</sup> With a Xantphos derivative bearing 3,5-xylyl moieties (MeAr-Xan<sup>[16]</sup>), (Z)-2a was obtained in 80% yield with considerable formation of 3a in 10% yield (entry 11). A Xantphos derivative bearing t-Bu on the phosphorus atoms (t-Bu-Xan) was not effective at all (entry 12). Thus, the electron-deficient aryl moieties on the phosphorus atoms would be preferable. Both PMHS and t-BuOH are indispensable components in the reducing agent. When PMHS was removed from the reaction mixture, no hydrogenation occurred (entry 13). Removing t-BuOH from the system decreased the yield of (Z)-2a to 10% (entry 14). PMHS is a by-product of the silicon industry, and a cheap, easy-to-handle, and environmentally friendly reducing agent.<sup>[17]</sup> In place of PMHS in entry 10, other silanes such as (EtO)<sub>3</sub>SiH, Ph<sub>2</sub>SiH<sub>2</sub>, (EtO)<sub>2</sub>MeSiH, PhMe<sub>2</sub>SiH, and Et<sub>3</sub>SiH afforded (Z)-2a in 93%, 82%, 61%, 55%, and 0% yields, respectively. t-BuOH can be replaced with i-PrOH and MeOH in entry 10, and (Z)-2a was obtained in 99% and 94% yields, respectively. As for catalyst precursors, CuCl/t-BuONa and CuF(PPh<sub>3</sub>)<sub>3</sub> were not so effective (entries 15 and 16).

To confirm the coordination ability of CF<sub>3</sub>-ArXan to copper, we successfully isolated the chlorocopper(I) complex with  $CF_3$ -ArXan as a ligand and the structures of copper(I) chloride complexes with Xan and CF<sub>3</sub>-ArXan were determined by X-ray crystallography. The complex bearing a CF<sub>3</sub>-ArXan was obtained as a dimeric form (Figure 2x, a). The copper atom has a distorted tetrahedral geometry with two phosphorus atoms and two chlorine atom. Two copper atoms were bridged by two chlorine atoms. In contrast, the complex bearing Xan was obtained as a monomeric form (Figure 2, b). The copper atom has a trigonal-planar coordination geometry with two phosphorus atoms and chlorine atom. Generally, a bulkier ligand supresses the formation of mutinuclear complexes.<sup>[18]</sup> However, the present results are interesting since the bulkier CF<sub>3</sub>-ArXan gives a dinuclear complex. Electron-deficiency of the ligand would favor formation of the dimeric structure.



**Figure 2.** The crystal structures of (a)  $[(CF_3-ArXan)CuCl]_2$  and (b) (Xan)CuCl.

Table 2. Semihydrogenation of various internal alkynes.<sup>[a]</sup>

#### Semihydrogenation of Various Internal Alkynes

The scope of the catalytic reaction was examined using various internal alkynes (1b-x), and the corresponding (Z)-alkenes [(Z)-2b-x] were isolated in high yields [Eq. (1) and Table 2]. In the reaction of 1-

$$R \xrightarrow{\text{Cu(OAc)}_{2} \cdot H_{2}O(2.0 \text{ mol}\%)}_{\text{CF}_{3}Ar-Xan(4.0 \text{ mol}\%)} \xrightarrow{\text{R}} \xrightarrow{\text{R}'}_{\text{H}} (1)$$

$$1b-x \xrightarrow{\text{H}}_{\text{N}} \xrightarrow{\text{Cu(OAc)}_{2} \cdot H_{2}O(2.0 \text{ mol}\%)}_{\text{CF}_{3}Ar-Xan(4.0 \text{ mol}\%)} \xrightarrow{\text{R}} \xrightarrow{\text{R}'}_{\text{H}} \xrightarrow{\text{R}'}_{\text{H}} (1)$$

$$\xrightarrow{\text{H}}_{\text{N}} \xrightarrow{\text{Cu(OAc)}_{2} \cdot H_{2}O(2.0 \text{ mol}\%)}_{\text{H}} \xrightarrow{\text{R}'}_{\text{H}} \xrightarrow{\text{R}'}_{\text{H}} (1)$$

$$\xrightarrow{\text{H}}_{\text{H}} \xrightarrow{\text{C}}_{\text{H}} \xrightarrow{\text{C}} \xrightarrow{\text{C}}_{\text{H}} \xrightarrow{\text{C}}_{\text{H}} \xrightarrow{\text{C}}_{\text{H}} \xrightarrow{\text{C}} \xrightarrow{\text{C}}_{\text{H}} \xrightarrow{\text{C}} \xrightarrow{\text{C}$$

phenyl-1-hexyne (1b), the (Z)-alkene [(Z)-2b] was isolated in 92% yield with concomitant overreduction to hexylbenzene in 2% yield (entry 1). Fortunately, however, in all the other reactions in Table 2 (entries 2-24), the overreduction to undesired alkanes (3) did not occur at all. Various functionalities such as hyphthalimido droxy (entry 2), siloxy (entry 3), (entry 4), chloro (entry 5), cyano (entry 6) and vinylsilane (entry 7) were tolerated in the reactions. An alkyne bearing a thienyl moiety also afforded the corresponding (Z)-alkene  $[(Z)-2\mathbf{i}]$  exclusively (entry 8). Diaromatic internal alkynes also afforded the corresponding (Z)-alkenes stereoselectively without the formation of alkanes. Diphenylacetylene (1j) was reduced to stilbene (2j, Z/E = 98/2) in 93% isolated vield without formation of bibenzyl (entry 9), while the conventional Lindlar catalyst afforded a considerable amount of the alkane: selectivity of (Z)-2j/(E)-2j/bibenzyl = 93/2/5.<sup>[7d]</sup> It is noteworthy that even 0.10 mol% catalyst loading afforded a satisfactory result at 50°C after 79 h (entry 10). Both electron-rich (entries 12 and 13) and electron-poor (entries 14–19)

Entry	2: Product	Temp. [°C]	Yield $[\%]^{[b]}$ (Z/E ratio)	Entry	2: Product	Temp. [°C]	Yield $[\%]^{[b]}$ (Z/E ratio)
1 <sup>[c]</sup>	2b:	65	92 (100/0)	13	2m: Me	50	86 (100/0)
2	2c: OH	65	>99 (100/0)	14	2n: BuOOC	r.t.	94 (>99/1)
3	2d: OSiMe <sub>2</sub> (t-Bu)	65	98 (100/0)	15	<b>20</b> : Bu <sub>2</sub> NOC	65	98 (100/0)

Entry	2: Product	Temp. [°C]	Yield $[\%]^{[b]}$ (Z/E ratio)	Entry	2: Product	Temp. [°C]	Yield $[\%]^{[b]}$ (Z/E ratio)
4 <sup>[d]</sup>	2e:	65	96 (100/0)	16 <sup>[d]</sup>	2p':	65	90 (100/0)
5 <sup>[e]</sup>	2f:	65	90 (100/0)	17	2q:	r.t.	86 (100/0)
6	2g: 2	65	99 (100/0)	18	2r:	r.t.	97 (100/0)
7 <sup>[f]</sup>	2h: SiMe <sub>3</sub>	65	72 (95/5)	19 <sup>[i]</sup>	2s:	65	86 (100/0)
8	2i: (5) (1) 4	50	88 (100/0)	20	2t: Br	65	98 (100/0)
9 <sup>[g]</sup>	2j:	r.t.	93 (98/2)	21	2u: 1	65	98 (100/0)
10 <sup>[g,h]</sup>	2j:	50	96 (98/2)	22 <sup>[e,j]</sup>	2v:	65	78 (100/0)
11	2k:	65	94 (100/0)	23 <sup>[k]</sup>	2w:	65	87 (100/0)
12	2I: MeO	50	98 (>99/1)	24 <sup>L]</sup>	2x:	65	83 (100/0)

#### Table 2. (Continued)

[a] Internal alkyne (0.50 mmol), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.010 mmol, 2.0 mol%), CF<sub>3</sub>Ar-Xan (0.020 mmol, 4.0 mol%), PMHS (2.0 mmol as the Si-H unit, 4.0 equiv.), *t*-BuOH (1.0 mmol, 2.0 equiv.), solvent [1.0 mL, hexane:THF=1:1 (v/v)], for 20 h.
[b] Isolated yields. In the case of 1c and 1p, 2c and 2p' were isolated after hydrolysis by adding 1.0 M HCl/MeOH.

- <sup>[c]</sup> Hexylbenzene was afforded in 2% yield.
- <sup>[d]</sup> Hexane:THF=1:2 (v/v).
- [e] Hexane:THF = 10:1 (v/v).
- <sup>[f]</sup> Hexane (1.0 mL).
- <sup>[g]</sup> THF (1.0 mL).
- <sup>[h]</sup> Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.50  $\mu$ mol, 0.10 mol%), CF<sub>3</sub>Ar-Xan (1.0  $\mu$ mol, 0.20 mol%), for 79 h.
- [i] Hexane:THF=3:1 (v/v).
- <sup>[j]</sup> Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.020 mmol, 4.0 mol%), CF<sub>3</sub>Ar-Xan (0.040 mmol, 8.0 mol%).
- <sup>[k]</sup> **2w** (1.0 mmol), (<sup>CI</sup>IPr)CuCl (0.040 mmol, 4.0 mol%), *t*-BuONa (0.12 mmol, 12 mol%), PMHS (4.0 mmol as the Si-H unit, 4.0 equiv.), *t*-BuOH (2.0 mmol, 2.0 equiv.), hexane (2.0 mL).
- <sup>[1]</sup> **2x** (1.0 mmol), (<sup>CI</sup>IPr)CuCl (0.060 mmol, 6.0 mol%) and *t*-BuONa (0.18 mmol, 18 mol%), PMHS (4.0 mmol as the Si-H unit, 4.0 equiv.), *t*-BuOH (2.0 mmol, 2.0 equiv.), hexane (2.0 mL).

diaromatic alkynes afforded the (Z)-alkenes selectively. Functionalities on the phenyl rings such as ester

(entry 14) and amide (entry 15) were intact after the reaction, while the acetyl moiety of 4-

Adv. Synth. Catal. 2012, 354, 1542-1550

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim asc.wiley-vch.de

$Ph \longrightarrow Ph + Bu \longrightarrow Bu$ 1j $1y0.5$ mms	catalytic system A or B ───►	Ph_Ph + 2j	Bu_Bu 2y
catalytic system	yield of <b>2j</b>	yield of <b>2y</b>	
A: Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O (2 mol%), Xan (4 mo (4.0 equiv.), <i>t</i> -BuOH (2.0 equiv.), TI	99%	0%	
B: Lindlar cat. (5 mol%), H <sub>2</sub> (balloon), 4 28 °C, 6 h	37%	62%	

Scheme 1. Competitive reaction of diphenylacetylene (1j) and 5-decyne (1y) employing copper catalysts or the Lindlar catalyst.

 $CH_3CO-C_6H_4C \equiv CC_6H_5$  (1p) was reduced to the corresponding hydroxy moiety (2p', entry 16). To our delight, bromo and iodo moieties on the aromatic ring remained intact (2t and 2u, entries 20 and 21), which must undergo the oxidative addition reaction with most low-valent transition metal catalyst centers such as Pd(0).<sup>[9]</sup> 6-Dodecyne (1v) was smoothly converted to the corresponding (Z)-alkene [(Z)-2v] in good yield with perfect selectivity (entry 22). However, other internal aliphatic alkynes such as 1w and 1x were not converted completely with the Cu(OAc)<sub>2</sub>·H<sub>2</sub>O/CF<sub>3</sub>Ar-Xan catalyst system which was highly efficient in most entries in Table 2. In these cases, (<sup>CI</sup>IPr)CuCl/t-BuONa catalyst system (for <sup>CI</sup>IPr, see Figure 2) was much more effective, and (Z)-2w and (Z)-2x were isolated in high yields with perfect selectivities (entries 23 and 24).

One of the remarkable features of the present copper-catalyzed semihydrogenation is that diaromatic alkynes can be more easily reduced than dialkylalkynes (entries 9 vs. 22 in Table 2). Such preferential reduction was confirmed in a competitive reaction with an equimolar mixture of diphenylacetylene (1j) and 5-decyne (1y) (Scheme 1). Notabely, 1j was selectively reduced to 2j in the presence of 1y. In sharp contrast, employing the Lindlar catalyst, non-selective reduction was observed.

#### Semihydrogenation of Terminal Alkynes

Selective semihydrogenation of terminal alkynes is known to be difficult due to the overreduction to the corresponding alkanes.<sup>[7b,9e]</sup> The Cu(OAc)<sub>2</sub>·H<sub>2</sub>O/ CF<sub>3</sub>Ar-Xan catalyst system, which was efficient for internal alkynes (Table 2), was not active enough to realize complete conversion of terminal alkynes. Actually, phenylacetylene (**3a**) afforded styrene (**4a**) only in 13% yield with the Cu(OAc)<sub>2</sub>·H<sub>2</sub>O/CF<sub>3</sub>Ar-Xan catalyst system (entry 1, Table 3), even overreduction to ethylbenzene did not occur at all. For terminal alkynes, NHC ligands such as IPr, <sup>Me</sup>IPr, and <sup>CI</sup>IPr (Figure 3) were more effective than the Xan de-

Table 3. Semihydrogenation of various terminal alkynes.<sup>[a]</sup>



- [a] Terminal alkyne (0.50 mmol), (<sup>CI</sup>IPr)CuCl (0.010 mmol, 2.0 mol%), *t*-BuONa (0.060 mmol, 12 mol%), PMHS (2.0 mmol as the Si-H unit, 4.0 equiv.), *t*-BuOH (1.0 mmol, 2.0 equiv-), THF (0.50 mL), hexane (0.50 mL), at 40 °C, for 20 h.
- <sup>[b]</sup> Isolated yields. The numbers in the parentheses show GC yields determined by the internal standard method.
- <sup>[c]</sup> Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.010 mmol, 2.0 mol%) and CF<sub>3</sub>Ar-Xan (0.020 mmol, 4.0 mol%) as the catalyst.
- <sup>[d]</sup> (IPr)CuCl in place of (<sup>CI</sup>IPr)CuCl.
- <sup>[e]</sup> (<sup>Me</sup>IPr)CuCl in place of (<sup>Cl</sup>IPr)CuCl.
- <sup>[f]</sup> At 50 °C.
- <sup>[g]</sup> (<sup>Me</sup>IPr)CuCl (0.020 mmol, 4.0 mol%), *t*-BuONa (0.12 mmol, 24 mol%), THF (1.0 mL), hexane (1.0 mL).



Figure 3. The structures of IPr derivatives.





- <sup>[a]</sup> Substrate (0.50 mmol), Cat. A or B, PMHS (2.0 mmol as the Si-H unit, 4.0 equiv.), *t*-BuOH (1.0 mmol, 2.0 equiv.), THF (0.50 mL), hexane (0.50 mL) for 20 h.
- <sup>[b]</sup> Cat. A: Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.010 mmol, 2.0 mol%), CF<sub>3</sub>Ar-Xan (0.020 mmol, 4.0 mol%). Cat. B: (<sup>CI</sup>IPr)CuCl (0.010 mmol, 2.0 mol%), *t*-BuONa (0.060 mmol, 12 mol%).
- <sup>[e]</sup> Isolated yields. The numbers in the parentheses show GC yields determined by the internal standard method.
- <sup>[d]</sup> PMHS (1.0 mmol as the Si-H unit, 2.0 equiv.), for 18 h.

rivatives (entries 2–4). Especially, the (<sup>CI</sup>IPr)CuCl/*t*-BuONa catalyst system was highly effective to afford **4a** in 92% yield without the formation of ethylbenzene (entry 4). With the conventional Lindlar catalyst, considerable overreduction occurred (selectivity: **4a**/ ethylbenzene = 89/11).<sup>[8a]</sup> Other aromatic and aliphatic terminal alkynes were also selectively semihydrogenated using (<sup>CI</sup>IPr)CuCl/*t*-BuONa (entries 5–9) or (<sup>Me</sup>IPr)CuCl/*t*-BuONa (entries 10 and 11) catalyst system without the overreduction to the corresponding alkanes.

# Semihydrogenation of Conjugated Carbon-Carbon Unsaturated Compounds

Besides simple alkynes, conjugated non-polar carboncarbon unsaturated compounds such as 1,2-diene, 1,3diene, 1,3-envne and 1,3-divne systems were selectively semihydrogenated to products (6a-e) in high yields (Table 4). No overreductions occurred in all the cases in Table 4. From a 1,2-diene (5a), the terminal alkene (6a) was selectively afforded in 81% yield (entry 1). 1-Phenyl-1,3-butadiene (5b) provided the corresponding (Z)-alkene [(Z)-6b] exclusively (entry 2).<sup>[19]</sup> Often semihydrogenation of 1,3-envnes was not so selective. As for 5c, considerable overreduction occurred with the Lindlar catalyst (selectivity: 5c/6c/ethylcyclohex $ene = 6/86/8)^{[8c]}$  or a complex mixture of various isomers was obtained in transfer semihydrogenation with an NHC Pd(0) catalyst.<sup>[9d]</sup> In the present reaction, 5c and 5d were semihydrogenated to the corresponding 1,3-dienes (6c and 6d) in high selectivities (entries 3 and 4). 1,3-Divnes are also known to be difficult substrates in selective semihydrogenation.<sup>[9d]</sup> However, with the Cu(OAc)<sub>2</sub>/CF<sub>3</sub>Ar-Xan catalyst system, a 1,3diyne (5e) was reduced to the corresponding 1,3enyne [(Z)-6e] exclusively (entry 5).

#### **Reaction Mechanisms**

To gain insights into the reaction mechanism, a deuterium labeling experiment was carried out [Eq. (2)]. Employing non-deuterated PMHS and t-BuOD (98 atom% D) in the semihydrogenation of diphenylacetylene (1j), a monodeuterated stilbene (2j- $d_1$ , Z/E =98/2) was selectively formed, and dideuterated stilbene  $(2j-d_2)$  was not detected at all, which was confirmed by <sup>1</sup>H NMR (see Figure S1 in Supporting Information) and GC-MS. Furthermore, several stoichiometric reactions relevant to each step in the catalytic cycle were carried out (Scheme 2). In the reactions of (<sup>CI</sup>IPr)CuCl with *t*-BuONa<sup>[20]</sup> and successively with PMHS,<sup>[21]</sup> <sup>1</sup>H resonances of the reaction mixtures (see Figure S2 in Supporting Information) indicated that the reactions were very clean and the corresponding copper hydride, (CIPr)CuH, was afforded quantitatively as shown by the diagnostic <sup>1</sup>H resonance of Cu-H at 2.4 ppm<sup>[12b]</sup> (step i in Scheme 2). The resulting (<sup>CI</sup>IPr)CuH easily underwent syn-addition<sup>[22]</sup> to C<sub>6</sub>H<sub>5</sub>C $\equiv$ C(*t*-Bu) (**1**z) at room temperature to afford the corresponding alkenyl copper complex (7),





© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

asc.wiley-vch.de



Scheme 2. Stoichiometric reactions relevant to the mechanism.



which was isolated in pure form in 70% yield<sup>[12b]</sup> (step ii). The isolated **7** smoothly and cleanly reacted with *t*-BuOH at room temperature for 1 h and the corresponding (*Z*)-alkene (**2**z) was quantitatively afforded (step iii) as judged by <sup>1</sup>H NMR (see Figure S3 in the Supporting Information) and GC-MS analysis.

With these results obtained in Eq. (2) and Scheme 2, a possible catalytic cycle for the present copper-catalyzed semihydrogenation of alkynes is shown in Scheme 3. A copper(I) hydride species (**A**) is generated by the reaction of the catalyst precursors with a silane. Addition of **A** to alkynes (**1**) must be much faster than to alkenes, and affords a copper alkenyl intermediate (**B**) stereoselectively *via syn*-addition<sup>[22]</sup> (step a). Successively, protonation of **B** with *t*-BuOH provides (*Z*)-alkenes (**2**) selectively with the concomitant formation of LCuO(*t*-Bu) (**C**) (step b). Finally,  $\sigma$ -bond metathesis between **C** and a silane regenerates **A** and the catalytic cycle is closed (step c).<sup>[21]</sup>

#### Conclusions

Non-polar unsaturated compounds such as internal alkyne, terminal alkyne, 1,2-diene, 1,3-diene, 1,3enyne, and 1,3-diyne systems were semihydrogenated selectively. A copper catalyst bearing a suitable Xantphos derivative or an NHC ligand was highly efficient in the semihydrogenation. Especially, the present catalytic system was useful for the semihydrogenation of

Scheme 3. A possible catalytic cycle.

internal alkynes to the corresponding (Z)-alkenes with suppression of both Z/E isomerization and over-reduction to alkanes.

### **Experimental Section**

#### General Procedure for Copper-Catalyzed Semihydrogenation of 1a (Table 1)

Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (2.0 mg, 0.010 mmol, 2.0 mol%) and a ligand (P/Cu=4.0) were placed in an oven-dried, 20-mL Schlenk flask. The vessel was evacuated and backfilled with argon three times. THF (0.50 mL) and hexane (0.50 mL) were added, and the mixture was stirred for 15 min at room temperature under an argon atmosphere. To the resulting solution, **1a** (63  $\mu$ L, 0.50 mmol), PMHS (130  $\mu$ L, 2.0 mmol as the Si–H unit, 4.0 equiv.) and *t*-BuOH (96  $\mu$ L, 1.0 mmol, 2.0 equiv.) were added and the mixture was stirred at room temperature for 17 h. After the reaction, the yield of the product was determined by GC analysis relative to an internal standard (tridecane).

#### General Procedure for Copper-Catalyzed Semihydrogenation of Internal Alkynes (Table 2) – Cu(OAc)<sub>2</sub>·H<sub>2</sub>O/CF<sub>3</sub>Ar-Xan as Catalyst

 $Cu(OAc)_2 \cdot H_2O$  (2.0 mg, 0.010 mmol, 2.0 mol%) and  $CF_3Ar-Xan$  (22 mg, 0.040 mmol, 4.0 mol%) were placed in an ovendried, 20-mL Schlenk flask. The vessel was evacuated and backfilled with argon three times. THF and hexane were

added, and the mixture was stirred for 15 min at room temperature under an argon atmosphere. Alkyne (0.50 mmol), PMHS (130  $\mu$ L, 2.0 mmol as the Si–H unit, 4.0 equiv.) and *t*-BuOH (96  $\mu$ L, 1.0 mmol, 2.0 equiv.) were added, and the mixture was stirred at indicated temperature for 20 h. After the reaction, isolated yields were determined after purification by silica gel column chromatography typically with a mixture of pentane and CH<sub>2</sub>Cl<sub>2</sub> as eluent.

# Using (<sup>CI</sup>IPr)CuCl/*t*-BuONa as Catalyst (entry 23, Table 2)

(<sup>CI</sup>IPr)CuCl (22 mg, 0.040 mmol, 4.0 mol%) and *t*-BuONa (12 mg, 0.12 mmol, 12 mol%) were placed in an oven-dried, 20-mL Schlenk flask. The vessel was evacuated and backfilled with argon three times. Hexane (2.0 mL) was added and the mixture was stirred for 15 min at room temperature under an argon atmosphere. The alkyne (**1w**, 190  $\mu$ L, 1.0 mmol), PMHS (260  $\mu$ L, 4.0 mmol as the Si–H unit, 4.0 equiv.) and *t*-BuOH (190  $\mu$ L, 2.0 mmol, 2.0 equiv.) were added, and the resulting mixture was stirred at 65°C for 20 h. After the reaction, (*Z*)-**2w** was isolated by silica gel column chromatography with pentane as an eluent; yield: 150 mg (0.87 mmol, 87%).

#### General Procedure for Copper-Catalyzed Semihydrogenation of Terminal Alkynes (Table 3)

(<sup>CI</sup>IPr)CuCl (5.6 mg, 0.010 mmol, 2.0 mol%) and *t*-BuONa (5.8 mg, 0.060 mmol, 12 mol%) were placed in an ovendried, 20-mL Schlenk flask. The vessel was evacuated and backfilled with argon three times. THF (0.50 mL) and hexane (0.50 mL) were added, and the mixture was stirred for 15 min at room temperature under an argon atmosphere. Alkyne (0.50 mmol), PMHS (130  $\mu$ L, 2.0 mmol as the Si–H unit, 4.0 equiv.) and *t*-BuOH (96  $\mu$ L, 1.0 mmol, 2.0 equiv.) were added, and the resulting mixture was stirred at the indicated temperature for 20 h. After the reaction, isolated yields were determined after the purification by silica gel column chromatography with a mixture of pentane and CH<sub>2</sub>Cl<sub>2</sub> as eluent or Kugelrohr distillation.

### Acknowledgements

This work was supported by Grant-in-Aid for Scientific Research on Innovative Areas ("Organic synthesis based on reaction integration" and "Molecular activation directed toward straightforward synthesis") from MEXT, Japan, and in part by the Mitsubishi Foundation. K. S. is grateful to a Research Fellowship of JSPS for Young Scientists. T. F. acknowledges The Naito Foundation Natural Science Scholarship.

## References

 a) Modern Organocopper Chemistry, (Ed.: N. Krause), Wiley-VCH, Weinheim, 2002; b) Comprehensive Organometallic Chemistry III, (Eds.: P. J. Pérez, M. M. Díaz-Requejo), Elsevier, Amsterdam, 2007, Vols. 9–11.

- [2] a) S. A. Bezman, M. R. Churchill, J. A. Osborn, J. Wormald, J. Am. Chem. Soc. 1971, 93, 2063–2065; b) W. S. Mahoney, D. M. Brestensky, J. M. Stryker, J. Am. Chem. Soc. 1988, 110, 291–293; c) T. M. Koenig, J. F. Daeuble, D. M. Brestensky, J. M. Stryker, Tetrahedron Lett. 1990, 31, 3237–3240; d) W. S. Mahoney, J. M. Stryker, J. Am. Chem. Soc. 1989, 111, 8818–8823; e) B. H. Lipshutz, J. Keith, P. Papa, R. Vivian, Tetrahedron Lett. 1998, 39, 4627–4630.
- [3] a) S. Díez-González, S. P. Nolan, Acc. Chem. Rev. 2008, 41, 349–358; b) S. Rendler, M. Oestreich, Angew. Chem. 2007, 119, 504–510; Angew. Chem. Int. Ed. 2007, 46, 498–504; c) C. Deutsch, N. Krause, B. H. Lipshutz, Chem. Rev. 2008, 108, 2916–2927; d) B. H. Lipshutz, Synlett 2009, 509–524.
- [4] a) J. F. Daeuble, C. McGettigan, J. M. Stryker, *Tetrahedron Lett.* 1990, *31*, 2397–2400; b) I. Ryu, N. Kusumoto, A. Ogawa, N. Kambe, N. Sonoda, *Organometallics* 1989, *8*, 2279–2281; c) D. Masure, P. Coutrot, J. F. Normant, *J. Organomet. Chem.* 1982, 226, C55-C58; d) E. C. Ashby, J. J. Lin, A. B. Goel, *J. Org. Chem.* 1978, *43*, 757–759; e) J. K. Crandall, F. Collonges, *J. Org. Chem.* 1976, *41*, 4089–4092; f) T. Yoshida, E. Negishi, *J. Chem. Soc. Chem. Commun.* 1974, 762–763.
- [5] a) R. C. Larock, Comprehensive Organic Transformations, 2nd edn.; Wiley-VCH, New York, 1999, pp 6–29;
  b) Modern Reduction Methods, (Eds.: P. G. Andersson, Ian J. Munslow), Wiley-VCH, Weinheim, 2008;
  c) Handbook of Homogeneous Hydrogenation, (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, 2007.
- [6] a) C. A. Hecrick, *Tetrahedron* 1977, 33, 1845–1889;
  b) G. C. Tron, T. Pirali, G. Sorba, F. Pagliai, S. Busacca, A. A. Genazzani, *J. Med. Chem.* 2006, 49, 3033–3044;
  c) T. Brown, H., Jr. Holt, M. Lee, *Top. Heterocycl. Chem.* 2006, 2, 1–51.
- [7] a) B. M. Choudary, G. V. M. Sharma, P. Bharathi, Angew. Chem. 1989, 101, 506–507; Angew. Chem. Int. Ed. 1989, 28, 465–466; b) F. Alonso, I. Osante, M. Yus, Tetrahedron 2007, 63, 93–102; c) J. C. Choi, N. M. Yoon, Tetrahedron Lett. 1996, 37, 1057–1060; d) J. Brunet, P. Caubere, J. Org. Chem. 1984, 49, 4058–4060; e) J. Brunet, P. Gallois, P. Caubere, J. Org. Chem. 1980, 45, 1937–1945; f) C. A. Brown, V. K. Ahuja, J. Org. Chem. 1973, 38, 2226–2230.
- [8] a) J. Rajaram, A. P. S. Narula, H. P. S. Chawla, S. Dev, *Tetrahedron* 1983, 39, 2315–2322; b) E. N. Marvell, T. Li, *Synthesis* 1973, 457–468; c) E. N. Marvell, J. Tashiro, *J. Org. Chem.* 1965, 30, 3991–3993; d) H. Lindlar, R. Dubuis, *Org. Synth.* 1966, 46, 89–91; e) H. Lindlar, *Helv. Chim. Acta* 1952, 35, 446–450.
- [9] Pd-catalyzed semihydrogenation of alkynes, see: a) R. Shen, T. Chen, Y. Zhao, R. Qiu, Y. Zhou, S. Yin, W. Wang, M. Goto, L.-B. Han, J. Am. Chem. Soc. 2011, 133, 17037–17044; b) P. Hauwert, R. Boerleider, S. Warsink, J. J. Weigand, C. J. Elsevier, J. Am. Chem. Soc. 2010, 132, 16900–16910; c) J. Li, R. Hua, T. Liu, J. Org. Chem. 2010, 75, 2966–2970; d) P. Hauwert, G. Maestri, J. W. Sprengers, M. Catellani, C. J. Elsevier, Angew. Chem. 2008, 120, 3267–3270; Angew. Chem. Int. Ed. 2008, 47, 3223–3226; e) H. Sajiki, S. Mori, T. Ohkubo, T. Ikawa, A. Kume, T. Maegawa, Y. Monguchi, Chem.

*Eur. J.* 2008, *14*, 5109–5111; f) J. W. Sprengers, J. Wassenaar, N. D. Clement, K. J. Cavell, C. J. Elsevier, *Angew. Chem.* 2005, *117*, 2062–2065; *Angew. Chem. Int. Ed.* 2005, *44*, 2026–2029; g) M. W. van Laren, C. J. Elsevier, *Angew. Chem.* 1999, *111*, 3926–3929; *Angew. Chem. Int. Ed.* 1999, *38*, 3715–3717; h) B. M. Trost, R. Braslau, *Tetrahedron. Lett.* 1989, *30*, 4657–4660.

- [10] Selected examples of Ru-catalyzed semihydrogenation of alkynes, see: a) J. Li, R. Hua, *Chem. Eur. J.* 2011, *17*, 8462–8465; b) C. Belger, N. M. Neisius, B. Plietker, *Chem. Eur. J.* 2010, *16*, 12214–12220; c) Y. Blum, D. Czarkie, Y. Raharmim, Y. Shvo, *Organometallics* 1985, *4*, 1459–1461; d) Y. Shvo, I. Goldverg, D. Czerkie, D. Reshef, Z. Stein, *Organometallics* 1997, *16*, 133–138.
- [11] Other metals such as Cr, Rh, V and Nb have catalyzed the semihydrogenation of alkynes, see: a) M. Sodeoka, M. Shibasaki, J. Org. Chem. 1985, 50, 1147–1149; b) R. R. Schrock, J. A. Osborn, J. Am. Chem. Soc. 1976, 98, 2143–2147; c) H. S. La Pierre, J. Arnold, F. D. Toste, Angew. Chem. 2011, 123, 3986–3989; Angew. Chem. Int. Ed. 2011, 50, 3900–3903; d) T. L. Gianetti, N. C. Tomson, J. Arnold, R. G. Bergman, J. Am. Chem. Soc. 2011, 133, 14904–14907.
- [12] a) T. Fujihara, K. Semba, J. Terao, Y. Tsuji, Angew. Chem. 2010, 122, 1514–1518; Angew. Chem. Int. Ed. 2010, 49, 1472–1476; b) T. Fujihara, T. Xu, K. Semba, J. Terao, Y. Tsuji, Angew. Chem. 2011, 123, 543–547; Angew. Chem. Int. Ed. 2011, 50, 523–527; c) K. Semba, T. Fujihara, J. Terao, Y. Tsuji, Chem. Eur. J. 2012, 18, 4179–4184.
- [13] Abbreviations: PCy<sub>3</sub>: tricyclohexylphosphane, Xantphos: 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, dppe: 1,2-bis(diphenylphosphino)ethane, dppp: 1,3-bis(diphenylphosphino)propane, *rac*-BINAP: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, dppbz: 1,2-diphenylphosphinobenzene.
- [14] A. G. Sergeev, G. A. Artamkina, I. P. Beletskaya, *Tetrahedron Lett.* 2003, 44, 4719–4723.
- [15] a) T. Mizugaki, M. Murata, S. Fukubayashi, T. Mitsudome, K. Jitsukawa, K. Kaneda, *Chem. Commun.* 2008, 241–243; b) K. Tani, N. Ono, S. Okamoto, F. Sato, *J. Chem. Soc. Chem. Commun.* 1993, 386–387.
- [16] H. Ito, T. Saito, T. Miyahara, C. Zhong, M. Sawamura, Organometallics 2009, 28, 4829–4840.

- [17] PMHS is commercially available from Lancaster. PMHS was used as a hydrogen source, see: a) O. Jacquet, C. D. N. Gomes, M. Ephritikhine, T. Cantat, J. Am. Chem. Soc. 2012, 134, 2934–2937; b) A. P. Dieskau, J.-M. Begouin, B. Plietker, Eur. J. Org. Chem. 2011, 5291–5296; c) X.-C. Zhang, F.-F. Wu, S. Li, J.-N. Zhou, J. Wu, N. Li, W. Fang, K. H. Lam, A. S. C. Chan, Adv. Synth. Catal. 2011, 353, 1457–1462.
- [18] The copper chloride complex bearing PPh<sub>3</sub> as a ligand was obtained in a tetrameric form ([(PPh<sub>3</sub>)CuCl]<sub>4</sub>). In contrast, a copper chloride complex bearing a bulkier ligand BSP was obtained in a dimeric form ([(BSP)CuCl]<sub>2</sub>), see: M. R. Churchill, K. Kalra, *Inorg. Chem.* **1974**, *13*, 1065–1071.



- [19] Selected examples of the semihydrogenation of 1,3dienes, see: a) C. Fehr, I. Magpantay, M. Vuagnoux, P. Dupau, *Chem. Eur. J.* 2011, 17, 1257–1260; b) S. Staines, U. Englert, B. Drießen-Hölscher, *Chem. Commun.* 2000, 217–218; c) M. Murata, Y. Tanaka, T. Mizugaki, K. Ebitani, K. Kaneda, *Chem. Lett.* 2005, 34, 272–273.
- [20] (IPr)CuCl reacted with *t*-BuONa to afford (IPr)CuO(*t*-Bu), see: a) N. P. Mankad, D. S. Laitar, J. P. Sadighi, *Organometallics* 2004, 23, 3369–3371; b) T. Ohishi, M. Nishimura, Z. Hou, *Angew. Chem.* 2008, 120, 5876–5879; *Angew. Chem. Int. Ed.* 2008, 47, 5792–5795.
- [21] (IPr)CuH was obtained by the reaction of (IPr)CuO(*t*-Bu) and (EtO)<sub>3</sub>SiH.<sup>[20a].</sup>
- [22] The stereoselective *syn*-addition of [(IPr)CuH]<sub>2</sub> to 3-hexyne was reported.<sup>[20a]</sup>

1550