Kazuhiko Semba a,*
Ryohei Kameyama a
Yoshiaki Nakao a,b

a Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-Ku, Kyoto 615-8510, Japan
semba.kazuhiko.5n@kyoto-u.ac.jp
nakao.yoshiaki.8n@kyoto-u.ac.jp
b CREST, Japan Science and Technology Agency (JST), 4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan

Received: 16.12.2014
Accepted after revision: 20.01.2015
Published online: 26.01.2015

Abstract
Copper-catalyzed semihydrogenation of internal alkynes has been developed. The reaction proceeds under an atmosphere of hydrogen (5 atm) at 100 °C in the presence of a readily available [(PPh₃)CuCl]₄ catalyst to give various Z-alkenes stereoselectively.

Key words
alkynes, alkenes, catalysis, copper, hydrogenation

Semihydrogenation of internal alkynes is an efficient method to prepare Z-alkenes, which are versatile building blocks in organic synthesis and often found in biologically active compounds. A variety of heterogeneous catalysts have been developed for this transformation. Especially, the Lindlar catalyst is a well-established and effective catalyst for semihydrogenation of alkynes. Nevertheless, it often suffers from Z/E isomerization, shift of double bonds, and overhydrogenation to give alkanes. Thus, uptake of H₂ must be accurately monitored to control the hydrogenation. To overcome such difficulties, homogeneous catalysts such as rhodium, chromium, palladium, ruthenium, vanadium, and niobium have been developed. Here, we report that [(PPh₃)CuCl]₄, a readily available copper complex, efficiently catalyzes semihydrogenation of internal alkynes to give Z-alkenes in a highly stereoselective manner under an atmosphere of H₂ (5 atm).

First, we optimized the reaction conditions employing 1-phenyl-1-hexyne (1a) as a model substrate (Table 1). After screening a variety of reaction parameters, semihydrogenation of 1a gave (Z)-1-phenyl-1-hexene [(Z)-2a] selectively in high yield without formation of (E)-1-phenyl-1-hexene [(E)-2a] and hexylbenzene (3a) under the standard conditions: [(PPh₃)CuCl]₄ (2.0 mol%/Cu), LiO-t-Bu (50 mol%), and i-PrOH (1.0 mmol) in toluene at 100 °C for 3 hours under an atmosphere of H₂ (5 atm) (Table 1, entry 1).

Table 1 Semihydrogenation of 1a with Various Copper Catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Variation from the standard conditions</th>
<th>Conv. of 1a (%)</th>
<th>Yield of (Z)-2a + (E)-2a + 3a (%)</th>
<th>Ratio of (Z)-2a/(E)-2a/3a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>&gt;99</td>
<td>99 (80)</td>
<td>99:1:1</td>
</tr>
<tr>
<td>2</td>
<td>run for 12 h</td>
<td>&gt;99</td>
<td>95</td>
<td>94:2:4</td>
</tr>
<tr>
<td>3</td>
<td>CuCl/PPh₃ instead of [(PPh₃)CuCl]₄</td>
<td>&gt;99</td>
<td>95</td>
<td>99:1:1</td>
</tr>
<tr>
<td>4</td>
<td>CuCl/P(o-tol)₃ instead of [(PPh₃)CuCl]₄</td>
<td>&lt;5</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
Notably, the selectivity is better than that reported using the Lindlar catalyst [(Z)-2a + (E)-2a + 3a] = 91\% \text{.}^{6 \text{d}} Compound (Z)-2a was isolated in 80\% yield after medium-pressure column chromatography on silica gel (Table 1, entry 1). Prolonging the reaction time to 12 hours slightly decreased the selectivity (Table 1, entry 2). [(PPh3)CuCl]4 generated in situ from CuCl and Ph3P showed reactivity comparable to an isolated one (Table 1, entry 3). CuBr was similarly effective as CuCl. In contrast, other copper(I) salts such as CuI, CuOAc, and CuCN showed activity far less than CuCl. The effects of phosphine ligands are summarized in entries 4–6 (Table 1). Without [(PPh3)CuCl]4, LiO-tBu, or i-PrOH, no products were obtained (Table 1, entries 7–9). The reaction did not proceed under an N2 atmosphere instead of H2 (Table 1, entry 10), indicating that i-PrOH did not act as a hydride source. Under an atmosphere of H2 (1.0 atm), the products were not formed (Table 1, entry 11). Cu2O, which was reported to serve as a catalyst for semihydrogenation of terminal alkenes,\textsuperscript{4} was ineffective under the present reaction conditions (Table 1, entry 12). Even in the presence of Ph3P, LiO-tBu, and i-PrOH, Cu2O was not a good catalyst.

The scope of substrates was investigated under the optimized reaction conditions (Table 2).\textsuperscript{3} In the case of 1-phenyl-1-propyne (1b), (Z)-1-phenyl-1-propene [(Z)-2b] was obtained in high yield with a small amount of (E)-1-phenyl-1-propene [(E)-2b] and propylene [3b] (Table 2, entry 1). The reduction of 1-phenyl-2-trimethylsilylacetylene (1c) did not proceed (Table 2, entry 2). Diphenylacetylene derivatives 1d–g were efficiently semihydrogenated to give the corresponding Z-alkenes (Table 2, entries 3–6). Electron-donating and electron-withdrawing substituents on the phenyl group did not affect the yields and selectivities (Table 2, entries 4–6). The catalytic system was also effective for semihydrogenation of aliphatic alkynes 1h and 1i, giving the corresponding Z-alkenes (Z)-2h and (Z)-2i selectively (Table 2, entries 7 and 8). On the other hand, ynoate 1j and terminal alkyne 1k were not competent substrates. The reaction of 1j afforded a complex mixture (Table 2, entry 9), whereas 1k was not converted at all under the present conditions (Table 2, entry 10). With 5,7-dodecadiyne (1l), (Z)-5-dodecene was obtained selectively (Table 2, entry 11).

A plausible reaction mechanism is depicted in Scheme 1. Copper hydride 5 is generated from heterolytic cleavage of H2 by copper alkoxide 4 (step a).\textsuperscript{10} According to the literature, syn addition of 5 across an alkene gives alkylidenecopper 6 in a stereoselective manner (step b).\textsuperscript{11} Compound 6 is protonated by alcohol to afford (Z)-2 and regenerate 4 (step c).\textsuperscript{12} To gain insights into the proposed reaction mechanism, semihydrogenation of 1a was performed using i-PrOD
Table 2  Semihydrogenation of Various Alkynes 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkyne</th>
<th>Conv. of 1 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Yield of (Z)-2 + (E)-2 + 3 (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ratio of (Z)-2/(E)-2/3 (%)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph≡Me</td>
<td>&gt;99</td>
<td>(78)</td>
<td>96:2:2</td>
</tr>
<tr>
<td>2</td>
<td>Ph≡SiMe₃</td>
<td>&lt;5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3&lt;sup&gt;d&lt;/sup&gt;</td>
<td>R¹ = R² = H (1d)</td>
<td>&gt;99</td>
<td>91</td>
<td>96:3:1</td>
</tr>
<tr>
<td>4</td>
<td>R¹ = R² = Me (1e)</td>
<td>&gt;99</td>
<td>99</td>
<td>98:&lt;1;2</td>
</tr>
<tr>
<td>5</td>
<td>R¹ = R² = F (1f)</td>
<td>&gt;99</td>
<td>95</td>
<td>98:1:1</td>
</tr>
<tr>
<td>6&lt;sup&gt;f&lt;/sup&gt;</td>
<td>R¹ = C(O)O-i-Pr, R² = H (1g)</td>
<td>&gt;99</td>
<td>52 (95)</td>
<td>&gt;99:&lt;1:&lt;1</td>
</tr>
<tr>
<td>7</td>
<td>C₆H₁₃≡C₂H₁₁</td>
<td>&gt;99</td>
<td>76</td>
<td>&gt;99:&lt;1:&lt;1</td>
</tr>
<tr>
<td>8</td>
<td>Et≡Cl</td>
<td>&gt;99</td>
<td>(93)</td>
<td>&gt;99:&lt;1:&lt;1</td>
</tr>
<tr>
<td>9</td>
<td>C₂H₁₅≡C₂H₁₃OMe</td>
<td>&gt;99</td>
<td>complex mixture</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>C₆H₁₃≡H</td>
<td>&lt;5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>11&lt;sup&gt;f&lt;/sup&gt;</td>
<td>C₆H₁₃≡Bu</td>
<td>&gt;99</td>
<td>(78)&lt;sup&gt;h&lt;/sup&gt;</td>
<td>–</td>
</tr>
</tbody>
</table>

<sup>a</sup> Determined by GC analysis with n-tridecane as an internal standard.
<sup>b</sup> Isolated yield. Yields determined by ¹H NMR analysis with 1,3,5-trimethoxybenzene as an internal standard are given in parentheses.
<sup>c</sup> Determined by ¹H NMR analysis of a crude product.
<sup>d</sup> Run at 60 °C for 3 h.
<sup>e</sup> Run at 80 °C for 3 h.
<sup>f</sup> Run in 0.30 mmol scale.
<sup>g</sup> (Z)-5-Dodecene was obtained selectively.
(Scheme 2). Monodeuterated alkene (Z)-2a-d₁ was obtained regioselectively albeit with low deuterium incorporation. This result supports that i-ProH serves as a source of hydrogen and that the addition of copper hydride 5 across 1a (step b) proceeds regioselectively. Reversibility of step a should be responsible for contamination of i-ProOH under the reaction conditions of Scheme 2 and thus the observed low deuterium content in (Z)-2a-d₁.¹³

![Scheme 2](image)

In conclusion, we have established the copper-catalyzed semihydrogenation of internal alkynes. The present transformation is catalyzed by a readily available copper complex under an atmosphere of H₂ (5 atm), giving Z-alkenes in high yields and selectivities. This simple catalytic system employing inexpensive metal catalyst can be an alternative to known protocols using a noble-metal catalyst such as the Lindlar catalyst.

Acknowledgment

This work was supported by a Grant-in-Aid for Young Scientists (B) (26810058) from MEXT and the Japan Science and Technology Corporation (CREST, ‘Establishment of Molecular Technology towards the Creation of New Functions’ Area).

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1379896.

References and Notes


In a glove box, [(PPh₃)₂CuH]₄ (7.2 mg, 5.0 μmol), toluene (1.0 mL), LiO-Bu (40 mg, 0.50 mmol), and i-ProH (60 mg, 1.0 mmol) were added to a vial in this order. After being stirred for 1 min at r.t., alkyn L₁ (1.0 mmol) and toluene (2.0 mL) were added to the resulting mixture. The vial was placed in an autoclave, and the autoclave was taken out of the glove box. An N₂ atmosphere in the autoclave was purged by positive pressure of H₂. Then, the mixture was stirred at 100 °C for 3 h under H₂ (5 atm). After being cooled to r.t., H₂ was released, and the mixture was diluted with EtOAc. The conversion of alkynes was determined by GC analysis with n-tridecane as an internal standard. The resulting solution was filtered through a pad of silica gel, and the filtrate was concentrated. The residue was purified by medium-pressure column chromatography on silica gel to give (Z)-2.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

© Georg Thieme Verlag Stuttgart · New York — Synlett 2015, 26, 318–322
Representative data:

(\(Z\))-2d: The reaction of 1d (180 mg, 1.0 mmol) at 60 °C followed by purification by MPLC (16 g of silica gel and Biotage® SNAP Ultra 10 g; n-hexane) gave the corresponding product (160 mg, 0.91 mmol, 91%) as a mixture of (\(Z\))-2d,14a (\(E\))-2d,14b and 3d14c ([\(Z\)]-2d/\(E\)-2d/3d = 95:5:<1 determined by 1H NMR analysis] as a colorless oil; \(R_f\) = 0.53 (hexane). 1H NMR (CDCl3, 400 MHz): \(\delta\) = 7.28–7.16 (m, 10 H), 6.60 (s, 2 H); 13C NMR (CDCl3, 101 MHz): \(\delta\) = 137.2, 130.2, 128.8, 128.2, 127.1. All the resonances of 1H and 13C NMR spectra were consistent with reported values.14a

(\(Z\))-2g: The reaction of 1g (79 mg, 0.30 mmol) at 80 °C in toluene (0.80 mL) followed by purification by MPLC (16 g of silica gel and Biotage® SNAP Ultra 10 g; n-hexane–EtOAc, 99:1 to 93:7) gave the corresponding product (\(Z\))-2g (42 mg, 0.16 mmol, 52%) as a pale yellow oil; \(R_f\) = 0.35 (n-hexane–EtOAc, 95:5). 1H NMR (CDCl3, 400 MHz): \(\delta\) = 7.90 (d, \(J\) = 8.5 Hz, 2 H), 7.25–7.20 (m, 5 H), 6.71 (d, \(J\) = 12.2 Hz, 1 H), 6.61 (d, \(J\) = 12.2 Hz, 1 H), 5.24 (sept, \(J\) = 6.1 Hz, 1 H), 1.36 (d, \(J\) = 6.1 Hz, 6 H); 13C NMR (CDCl3, 101 MHz): \(\delta\) = 165.9, 141.8, 136.7, 132.1, 129.4, 129.31, 128.28, 128.8, 128.7, 128.3, 127.4, 68.3, 21.9. HRMS–APCI (+): \(m/z\) [M + H]+ calcld for C18H19O2: 267.1380; found: 267.1375

(10) [(PPh3)CuH]6 was synthesized from Cu(Ot-Bu) and Ph3P, see: (a) Goeden, G. V.; Caulton, K. G. J. Am. Chem. Soc. 1981, 103, 7354. For catalytic activation of H2 by copper salts, see (b) Halpern, J. J. Phys. Chem. 1959, 63, 398.


(12) For a reference on protonation of an alkenyl copper with an alcohol, see ref. 2a.

(13) H–D exchange between copper hydride and alcohols was reported, see ref. 2b and: Lipshutz, B. H.; Servesko, J. M.; Taft, B. R. J. Am. Chem. Soc. 2004, 126, 8352.