Copper-catalyzed α-selective hydrostannylation of alkynes for synthesis of branched alkenylstannanes

A variety of branched alkenylstannanes can directly be synthesized depending upon the α-selective hydrostannylation of terminal alkynes by use of a distannane or a silylstannane under copper catalysis.

Copper-catalyzed \( \alpha \)-selective hydrostannylation of alkenes for the synthesis of branched alkenylstannanes†

H. Yoshida, a b A. Shinke, a Y. Kawano a and K. Takaki a

A variety of branched alkenylstannanes can directly be synthesized with excellent \( \alpha \)-selectivity by the copper-catalyzed hydrostannylation using a distannane or a silylstannane, irrespective of the electronic and steric characteristics of terminal alkynes employed. Synthetic utility of the resulting branched alkenylstannane has been demonstrated by the total synthesis of bexarotene.

In view of the high synthetic versatility of alkenylstannanes, especially in carbon–carbon bond-forming processes via Migita–Kosugi–Stille coupling, tin–lithium exchange reaction, etc., the development of potent methods for making alkenylstannanes with defined structures in a regio- and stereoselective manner has continued to be a key subject in modern synthetic organic chemistry.1 One of the most popular and straightforward routes to alkenylstannanes would be hydrostannylation of alkynes,2 and three isomers, namely the \( \alpha \)-adduct and the (\( E/Z \))-\( \beta \)-adduct, can be generated in the case of terminal alkynes (eqn (1)).3 Hence the regio- and stereocontrol of hydrostannylation is a pivotal issue, and (\( Z \))- or (\( E \))-linear alkenylstannanes have successfully been synthesized with high \( \beta \)-selectivity under radical conditions,4 Lewis acid5 or transition metal catalysis.6 Although selective access to branched alkenylstannanes has also been achieved in some cases depending upon direct addition of a tin hydride7–9 or a stannylation–protonation sequence,10 the existing methods are still not versatile, owing to limited substrate scope of alkynes in every reaction and the use of an excess amount of a stannylation reagent in the latter case (Scheme 1). Therefore the development of a universal system for \( \alpha \)-selective hydrostannylation of terminal alkynes, which gives direct and efficacious access to pharmacologically important 1,1-disubstituted alkenes such as bexarotene11 and isoombretastatin A-4,12 has been a long-awaited goal.

We have recently riveted our attention on potential copper catalysis for metallation reactions of unsaturated carbon–carbon bonds, and have already disclosed that distannylation13 as well as various borylations14 of alkynes and alkenes facilely occur to afford organostannanes and -boranes with structural diversity by employing a distannane and a diboron as a metallating reagent. The distannylation of alkynes was found to proceed through intermediary formation of a \( \beta \)-stannyalkenylcopper species with enough nucleophilicity, which was finally converted into vic-distannylalkenes by capturing a tin electrophile. Therefore, we envisioned that a copper catalyst would also promote

![Scheme 1](https://example.com/scheme1.png)

**Scheme 1** Reported \( \alpha \)-selective hydrostannylation of terminal alkynes.
Table 1  Cu-catalyzed hydrostannylation with a distannane

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>2:3'</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>nC12H23 (1a)</td>
<td>1.5</td>
<td>75</td>
<td>98:2</td>
<td>2a,2'a</td>
</tr>
<tr>
<td>2</td>
<td>nC10H18 (1b)</td>
<td>2</td>
<td>89</td>
<td>97:3</td>
<td>2b,2'b</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>1.5</td>
<td></td>
<td>97:3</td>
<td>2c,2'c</td>
</tr>
<tr>
<td>4</td>
<td>THPO(CH2)6 (1d)</td>
<td>1</td>
<td>84</td>
<td>94:6</td>
<td>2d,2'd</td>
</tr>
<tr>
<td>5</td>
<td>TBSO(CH2)2 (1e)</td>
<td>1.5</td>
<td>85</td>
<td>96:4</td>
<td>2e,2'e</td>
</tr>
<tr>
<td>6</td>
<td>BN(CH2)2 (1f)</td>
<td>1</td>
<td>76</td>
<td>97:3</td>
<td>2f,2'f</td>
</tr>
<tr>
<td>7</td>
<td>HO(CH2)6 (1g)</td>
<td>3</td>
<td>76</td>
<td>&gt;99:1</td>
<td>2g</td>
</tr>
<tr>
<td>8</td>
<td>Br(CH2)6 (1h)</td>
<td>24</td>
<td>43</td>
<td>89:11</td>
<td>2h,2'h</td>
</tr>
<tr>
<td>9</td>
<td>nC3H7 (1i)</td>
<td>8</td>
<td>63</td>
<td>&gt;99:1</td>
<td>2i</td>
</tr>
<tr>
<td>10</td>
<td>BnOCH2 (1j)</td>
<td>6</td>
<td>37</td>
<td>92:8</td>
<td>2j,2'j</td>
</tr>
<tr>
<td>11</td>
<td>2-Pyridyl (1k)</td>
<td>5.5</td>
<td>68</td>
<td>&gt;99:1</td>
<td>2k</td>
</tr>
<tr>
<td>12</td>
<td>MeOCH2 (1l)</td>
<td>6</td>
<td>68</td>
<td>86:14</td>
<td>2l,2'l</td>
</tr>
<tr>
<td>13</td>
<td>4-nBuC6H4 (1m)</td>
<td>24</td>
<td>61</td>
<td>&gt;99:1</td>
<td>2m</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>2</td>
<td>80</td>
<td>&gt;99:1</td>
<td>2n</td>
</tr>
</tbody>
</table>

Hydrostannylation of alkenes in the presence of a suitable protic reagent for trapping the β-stannylationintermediate.13

Herein we report that the hydrostannylation of terminal alkynes smoothly takes place under the copper catalysis by use of water as a protic reagent, and that the universal system allows a variety of branched alkenylstannanes to be synthesized with excellent 3:selectivity, irrespective of the electronic and steric characteristics of terminal alkynes.

![ChemComm](https://www.chemcomm.org/content/51/67/10617)

The 3:selective hydrostannylation has proven to be feasible to provide a branched (2a) and a linear (2a') alkenylstannane with 75% yield (2a:2'a = 98:2), when we treated 1-tetradecyne (1a) with hexamethyldistannane and water in toluene at 110 °C in the presence of the Cu(OAc)2-PbBu3 catalyst (Table 1, entry 1).16,17

The reaction was also applicable to 1-dodecyne (1b) and a monosubstituted alkyne (1c), giving 2b and 2c with high degrees of 3:selectivity in excellent yield (entries 2 and 3), and furthermore functionalized aliphatic alkynes bearing an acetoxymethylsilylethyl (1d), a silyloxyalkyl (1e) or a benzyl ether (1f) smoothly underwent the 3:selective hydrostannylation, leaving these reactive moieties intact (entries 4–6).

The high functional group compatibility was also demonstrated by the reaction of a hydroxyl- (1g) or a bromo-substituted alkyne (1h), and propargyl-functionalized alkynes (1i and 1j), although the yields became moderate in some cases (entries 7–10). The regioselective installation of a stannyl group into an internal carbon of aromatic terminal alkynes was achieved under the present conditions as well, and thus pyridyl (1k), naphthyl (1l) and phenyl (1m and 1n) acetylenes were efficiently transformed into the respective branched alkenylstannanes (2k–2n) (entries 11–14).

An internal alkyne, diphenylacetylene (1o), could participate in the reaction to furnish (E)-trimethylstannylstilbene (2o) as the sole product (eqn (2)), showing that hydrostannylation proceeds in a cis fashion.18

With the successful synthesis of diverse branched alkenylstannanes having a trimethylstannyl moiety, we next investigated 3:selective installation of a tributyldistannylmoy. Although the reaction of 1-octyne (1p) with hexabutyldistannane in the presence of the Cu(OAc)2-PCy3 catalyst19 led to regioselective formation of a branched alkenylstannane (3p) in moderate yield (Table 2, entry 1), a silylstannane, tributyl(trimethylstannyl)stannane, turned out to serve as a more effective and reactive stannylation reagent to afford a 74% yield of 3p and 3p' (3p:3p' = 86:14) (entry 2).22 It should be noted that a silyl moiety was not incorporated into an alkyne as in the reaction of all the silylstannane, which is in marked contrast to the copper-catalyzed selective silyl incorporation reactions into unsaturated hydrocarbons with a silylborane.20

Hydrostannylation using a silylstannane also took place smoothly with 1-decyne (1q), 1-hexyne (1r) and branched aliphatic terminal alkynes (1s and 1t) to provide 3q–3t with high 3:selectivity (entries 3–6), and furthermore functionalized terminal alkynes bearing a cyano (1u), a chloro (1v) or a benzoxo moiety (1w), and 3-phenyl-1-propanol (1w) were transformed into the respective branched alkenylstannanes (entries 7–10).21

Since water can serve as a proton source in hydrostannylation, we expected that the present system may be extended to deuterostannylation by use of deuterium oxide. Surprisingly, the

Table 2  Cu-catalyzed hydrostannylation with a silylstannane

<table>
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<tr>
<th>Entry</th>
<th>R</th>
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<tr>
<td>1'</td>
<td>nC9H13 (1p)</td>
<td>43</td>
<td>43</td>
<td>&gt;99:1</td>
<td>3p</td>
</tr>
<tr>
<td>2</td>
<td>nC13H21 (1p)</td>
<td>4</td>
<td>73</td>
<td>86:14</td>
<td>3p,3'p</td>
</tr>
<tr>
<td>3</td>
<td>nC17H17 (1q)</td>
<td>2</td>
<td>74</td>
<td>88:12</td>
<td>3q,3'q</td>
</tr>
<tr>
<td>4</td>
<td>nBu (1r)</td>
<td>2</td>
<td>74</td>
<td>85:15</td>
<td>3r,3'r</td>
</tr>
<tr>
<td>5</td>
<td>tAmiyl (1s)</td>
<td>2.6</td>
<td>60</td>
<td>84:16</td>
<td>3s,3's</td>
</tr>
<tr>
<td>6</td>
<td>4-Bu (1t)</td>
<td>2</td>
<td>48</td>
<td>92:8</td>
<td>3t,3't</td>
</tr>
<tr>
<td>7</td>
<td>NC(CH3)2 (1u)</td>
<td>3</td>
<td>55</td>
<td>93:7</td>
<td>3u,3'u</td>
</tr>
<tr>
<td>8</td>
<td>Cl(C6H4)2 (1v)</td>
<td>2</td>
<td>44</td>
<td>92:8</td>
<td>3v,3'v</td>
</tr>
<tr>
<td>9</td>
<td>BnO(CH2)2 (1w)</td>
<td>2</td>
<td>55</td>
<td>88:12</td>
<td>3f,3'f</td>
</tr>
<tr>
<td>10</td>
<td>Bn (1w)</td>
<td>2</td>
<td>46</td>
<td>93:7</td>
<td>3w,3'w</td>
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Hydrostannylation using a silylstannane also took place smoothly with 1-decyne (1q), 1-hexyne (1r) and branched aliphatic terminal alkynes (1s and 1t) to provide 3q–3t with high 3:selectivity (entries 3–6), and furthermore functionalized terminal alkynes bearing a cyano (1u), a chloro (1v) or a benzoxo moiety (1w), and 3-phenyl-1-propanol (1w) were transformed into the respective branched alkenylstannanes (entries 7–10).21

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<td>4</td>
<td>73</td>
<td>86:14</td>
<td>3p,3'p</td>
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<td>Bn (1w)</td>
<td>2</td>
<td>46</td>
<td>93:7</td>
<td>3w,3'w</td>
</tr>
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copper-catalyzed reaction of 1-tetradecyne (1a) with hexamethyl-
distannane in the presence of deuterium oxide produced a
dideuterostannylation product (2a-d) predominantly (2a-d): 2a-
2b = 79:7:14, eqn (a), Scheme 2). The formation of 2a-d can be rationalized by considering the deuterostannylation of 1-
tetradecyne-d (1a-d), which should be generated in situ prior to
deuterostannylation. Actually, hydrogen–deuterium exchange
between 1a and deuterium oxide was demonstrated to occur smoothly under the copper catalysis (eqn (b), Scheme 2).

As depicted in Scheme 3, the branched alkenylstannane (2n)
was found to be facilely converted into 1,1-diarylalkene 4 by the
Migita–Kosugi–Stille coupling with ethyl 4-iodobenzoate. Hydrolysis
to deuterostannylation. Actually, hydrogen–deuterium exchange
between 1a and deuterium oxide was demonstrated to occur smoothly under the copper catalysis (eqn (b), Scheme 2).

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favored in a stoichiometric reaction of a stannylcopper species
with a terminal alkyne.24

In conclusion, we have developed a universal system for the
α-selective hydrostannylation of terminal alkynies by using a
distannane or a silylstannane as a stannylating reagent in the
presence of a copper-triallylphosphine catalyst, which leads to a
convenient and straightforward method for synthesizing diverse
branched alkenylstannanes, irrespective of the electronic and steric
nature of terminal alkynies employed. The resulting branched alkynyl-
stannane has been demonstrated to be facely transformed into
bexarotene of pharmacologically important via the cross-coupling
reaction. Further studies on copper-catalyzed stannylation reactions
using a distannane or a silylstannane are in progress.
COMMUNICATION


