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<th>Title</th>
<th>Rhodium-Catalyzed Dehydrogenative Borylation of Aliphatic Terminal Alkenes with Pinacolborane.</th>
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<tr>
<td>Author(s)</td>
<td>Morimoto, Masao; Miura, Tomoya; Murakami, Masahiro</td>
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Textversion  | author         |

Kyoto University
Abstract: Aliphatic terminal alkenes react with pinacolborane at ambient temperature to afford dehydrogenative borylation compounds as the major product when Pr-Foxap is used as the ligand of a cationic rhodium(I) in the presence of norbornene, which acts as the sacrificial hydrogen acceptor. The reaction is applied to the one-pot syntheses of aldehydes and homoallylic alcohols from aliphatic terminal alkenes.

The hydroboration of alkenes with borane reagents giving the corresponding alkylboranes is a fundamental textbook reaction. The use of transition metal catalysts makes it possible to use dialkoxyborane reagents [HB(OR)2] for the hydroboration under mild conditions.[1] A variety of transition metal complexes such as rhodium(I),[2] iridium(I),[3] ruthenium(II),[4] iron(0),[5] and cobalt(I)[6] catalyze the hydroboration of terminal alkenes with pinacolboronate, showing that a half of styrene was used as the sacrificial hydrogen acceptor. The reaction is applied to the stereoselective preparation of (E)-alkenyl pinacolboronates.[11] Even (Z)-isomers have become accessible by hydroboration of terminal alkenes.[12] Sometimes, over-reduction of the alkyne to give saturated diborates compounds,[13] along with issues of regioselectivity, complicates this route. The attractiveness of the dehydrogenative borylation is the use of readily available terminal alkenes as starting materials instead of terminal alkynes.

Initially, 4-phenylbut-1-ene (1a, 1.0 equiv) was subjected to the reaction with HBpin (2, 1.7 equiv) in the presence of [Rh(cod)2]BF4,[2c] and norbornene (nbe, 2.3 equiv) as the sacrificial hydrogen acceptor.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Rh]</th>
<th>Ligand</th>
<th>Conversion of 1a [%]</th>
<th>Total Yield [%][b]</th>
<th>3a(E/Z):4a:5a[c]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Rh(cod)2]BF4</td>
<td>none</td>
<td>&gt;95</td>
<td>20</td>
<td>15(&gt;95/5):5:80</td>
</tr>
<tr>
<td>3</td>
<td>[Rh(cod)2]BF4</td>
<td>dppe</td>
<td>50</td>
<td>49</td>
<td>0.0:100</td>
</tr>
<tr>
<td>4</td>
<td>[Rh(cod)2]BF4</td>
<td>L1</td>
<td>63</td>
<td>50</td>
<td>40(87/13):2:58</td>
</tr>
<tr>
<td>5</td>
<td>[Rh(cod)2]BF4</td>
<td>Pr-Foxap</td>
<td>&gt;95</td>
<td>92(86)</td>
<td>91(85/15):3:6</td>
</tr>
<tr>
<td>6</td>
<td>[Rh(cod)2]BF4</td>
<td>Pr-Foxap</td>
<td>95</td>
<td>90(78)</td>
<td>93(83/17):3:4</td>
</tr>
<tr>
<td>7</td>
<td>[Rh(cod)2]BF4</td>
<td>Pr-Foxap</td>
<td>79</td>
<td>58</td>
<td>28(81/19):3:69</td>
</tr>
<tr>
<td>8</td>
<td>[Rh(cod)2]BF4</td>
<td>Pr-Foxap</td>
<td>93</td>
<td>82(76)</td>
<td>77(83/17):3:20</td>
</tr>
<tr>
<td>9f</td>
<td>[Rh(cod)2]BF4</td>
<td>Pr-Foxap</td>
<td>22</td>
<td>19</td>
<td>21(71/29):5:74</td>
</tr>
<tr>
<td>10c</td>
<td>[Rh(cod)2]BF4</td>
<td>Pr-Foxap</td>
<td>72</td>
<td>26</td>
<td>73(82/18):4:23</td>
</tr>
</tbody>
</table>

[a] On a 0.50 mmol scale. [b] Total yield of 3, 4, and 5 determined by GC. In parentheses, total yield after chromatographic purification. [c] Product ratio determined by GC. [d] Using PPh3 (6 mol %). [e] Using [Rh(cod)2]BF4 (1 mol %). [f] Using norbornadiene (2.3 equiv) instead of nbe. [g] Using styrene (2.3 equiv) instead of nbe.
sacrificial hydrogen acceptor (Table 1, entry 1). After the reaction mixture was stirred at 28 °C for 9 hours, a mixture of the dehydrogenative borylation products 3a and 4a, and the hydroboration product 5a was formed in a ratio of 3a:4a:5a = 15:5:80, albeit in 20% total yield. The hydroboration of 1a also occurred as a side reaction. Next, various ligands were examined using [Rh(cod)]2BF4 as the catalyst precursor. Whereas the use of simple phosphine ligands such as PPh3 and dppe yielded preferentially the hydroboration product 5a (entries 2 and 3), P-N bidentate ligand (L1) gave a better product selectivity for 3a (3a:4a:5a = 40:2:58) (entry 4). A commercially available P-N bidentate ligand, Pr-Foxap,[15] exhibited a dramatic effect to favor the formation of 3a.[16] After chromatographic purification, the product 3a was obtained as a mixture with 4a and 5a (3a:4a:5a = 91:3:6) in 86% total yield (entry 5).[17] The E/Z ratio of 3a was 85:15. The counterions of [RhCl(cod)]2 is known as the effective precursor for the dehydrogenative borylation of styrene,[15a,c] it gave a result inferior to [Rh(cod)]2BF4 in terms of both yield and product selectivity (entry 6). While the neutral complex [RhCl(cod)]2 resulted in a lower product selectivity (3a:4a:5a = 28:3:69) (entries 6 and 7). While the neutral complex [RhCl(cod)]2 is known as the effective precursor for the dehydrogenative borylation of styrene,[15a,c] it gave a result inferior to [Rh(cod)]2BF4 in terms of both yield and product selectivity (entry 8). Furthermore, the choice of hydrogen acceptor was important. When norbornadiene or styrene was used as the hydrogen acceptor, the yield of 3a markedly decreased (entries 9 and 10).[16]

Although it is difficult to explain the reaction pathway leading to alkanyl boronate 3 from aliphatic terminal alkene 1 and HBpin (2), a possible mechanism is depicted in Scheme 1. It is similar to the one proposed by Hartwig et al. for the iridium(I)-catalyzed dehydrogenative silylation using norbornene as the hydrogen acceptor.[17] Oxidative addition of the B–H bond of 2 onto rhodium(I) affords the boryl(hydride)rhodium species A. Subsequent insertion of the alkene 1 into the Rh–B bond of A takes place to give the alkyl-rhodium intermediate B. The initial conformer undergoes rotation along the C–C bond axis to form the other conformer C. Then, syn β-hydride elimination furnishes the (E)-isomer of alkanyl boronate 3. Dihydride/rhodium species D reacts with norbornene to generate an active rhodium(I) species together with norbornene.[17,20] The strained structure of norbornene enhances the reactivity toward D.[18] Therefore, hydroboration of norbornene is preferred over the alkyl pinacolboronate 3a.

The following experiments were carried out in order to obtain mechanistic insights into the stereoselectivity. First, the rhodium(I)-catalyzed reaction of 4-phenylbut-1-ene (1a) with HBpin (2) was monitored by GC after 20 min (Eq 1). The E/Z ratio of 3a was 74:26 at 18% conversion of 1a. Thus, the E/Z ratio of 3a changed during the reaction (vs. 9 hours; Table 1, entry 5).

\[
\begin{align*}
\text{Ph} & \text{ H} \text{Bpin (2, 1.7 equiv)} \\
\text{[Rh(cod)2]BF4 (2 mol %)} & \text{Pr-Foxap (3 mol %)} \quad \text{nbe (2.3 equiv)} \\
\text{THF, 28 °C, 20 min} & \quad \text{Ph} \text{ Bpin} + \text{1a} \quad \text{3a 10% GC} \\
\text{E/Z = 74:26} & \quad \text{82% GC}
\end{align*}
\]

Secondly, the purified (Z)-isomer of 3a was subjected to the standard reaction conditions using oct-1-ene (1c) as a substrate (Eq 2). The E/Z isomerization of 3a took place to give an E/Z = 57:43 mixture. Based on these results, the stereoselectivity seems to be subject to thermodynamics rather than kinetics.

A variety of terminal alkenes 1 were subjected to the dehydrogenative borylation with HBpin (2) by using a combination of [Rh(cod)]2BF4/Pr-Foxap and norbornene (Table 2). Mono-substituted alkenes 1b–f readily reacted with 2 to afford the corresponding alkylpinacolboronates 3b–f with good yields, product selectivities, and E/Z ratios (entries 1–5), whereas the reactions of 3-tert-butylprop-1-ene (1g) and cyclohexylmethene (1h) were rather sluggish, probably owing to the steric hindrance (entries 6 and 7). Functional groups such as siloxy, chloro, methoxycarbonyl, and epoxy groups were tolerated in the alkyl chain under the reaction conditions (entries 8–13). The reaction of 1,1-, 1,2-disubstituted alkenes such as 1,1-diethylethenyl and cyclohexene failed to give the desired alkylpinacolboronates.[21] Therefore, in the case of 2-methylhexa-1,5-diene (1o) including 1,1-disubstituted alkene moiety, only the terminal mono-substituted alkene moiety underwent the dehydrogenative borylation to afford mono-borylated product 3o (entries 14). Similarly, 4,8-dimethylnona-1,7-diene (1p) produces selectively mono-borylated product 3p (entry 15). 1,1-Dimethylbuta-1,3-diene (1q) was also a suitable substrate to give the corresponding dienylboronate 3q with high product selectivity and E/Z ratio (entry 16). Allyltriphenylsilane (1r) and 4-methoxystyrene (1s) successfully participated in this reaction (entries 17 and 18). The (E)-isomer was exclusively formed with 3s.
Table 2: Rh\textsuperscript{I}-catalyzed dehydrogenative borylation of various terminal alkenes 1 with HBpin (2).\textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>Product 3</th>
<th>Total Yield [%]\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>3b</td>
<td>79\textsuperscript{[d]}</td>
</tr>
<tr>
<td>2</td>
<td>1c</td>
<td>3c</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>1d</td>
<td>3d</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>1e</td>
<td>3e</td>
<td>78\textsuperscript{[e]}</td>
</tr>
<tr>
<td>5</td>
<td>1f</td>
<td>3f</td>
<td>71</td>
</tr>
<tr>
<td>6</td>
<td>1g</td>
<td>3g</td>
<td>66</td>
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<tr>
<td>7</td>
<td>1h</td>
<td>3h</td>
<td>52\textsuperscript{[e]}</td>
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<tr>
<td>8</td>
<td>1i</td>
<td>3i</td>
<td>83</td>
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<tr>
<td>9</td>
<td>1j</td>
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<td>11</td>
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<tr>
<td>12</td>
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<td>3m</td>
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<td>14</td>
<td>1o</td>
<td>3o</td>
<td>71\textsuperscript{[h]}</td>
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<td>15</td>
<td>1p</td>
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<tr>
<td>17</td>
<td>1r</td>
<td>3r</td>
<td>82\textsuperscript{[d]}</td>
</tr>
<tr>
<td>18</td>
<td>1s</td>
<td>3s</td>
<td>76\textsuperscript{[g]}</td>
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</table>

\textsuperscript{[a]} On a 0.50 mmol scale. \textsuperscript{[b]} Total yield of 3, 4, and 5 after chromatographic purification. \textsuperscript{[c]} Product ratio determined by \textsuperscript{[1]}H NMR analysis. \textsuperscript{[d]} NMR yield. \textsuperscript{[e]} Using nbe (2.3 equiv). \textsuperscript{[f]} Containing 2-cinnamyl-Bpin (4\%). \textsuperscript{[g]} Using nbe (1.7 equiv). \textsuperscript{[h]} Using nbe (2.5 equiv). \textsuperscript{[i]} Containing 1-(4-methoxyphenyl)ethyl-Bpin (2\%).

The resulting alkenyl pinacolboronates were useful intermediates in organic synthesis.\textsuperscript{[15]} Thus, we examined one-pot two-step transformations via the formation of alkenyl boronates, saving time and solvents required for a workup/purification procedure. After volatile materials in the reaction mixture of aliphatic terminal alkenes 1a with HBpin (2) were removed under reduced pressure, aqueous THF solution of sodium perborate was directly added to the residue including alkenyl pinacolboronate 3a. Oxidation of 3a occurred to form the corresponding aldehyde 6 in 60\% isolated yield based on 1a (Scheme 2). Formally, this one-pot reaction achieved anti-Markovnikov oxidation of terminal alkenes at ambient temperature,\textsuperscript{[22]} complementing the Wacker-Tsuji oxidation by palladium catalyst. Furthermore, it avoids the need for two oxidation steps to convert a hydroboration product (alkyl boronate) of an alkenne into an aldehyde.

We have recently reported an enantioselective synthesis of anti-homoallylic alcohols from terminal alkynes, HBpin, and aldehydes via the formation of alkenyl pinacolboronates, which act as \(\gamma\)-substituted allylboron species.\textsuperscript{[23]} Thus, the residue including alkenyl pinacolboronate 3b was treated with benzaldehyde (7) in the presence of [(Ir(cod))\textsubscript{2}]BF\textsubscript{4}/PCy\textsubscript{3} and (R)-TRIP in 1,2-dichloroethane (DCE). Anti-homoallylic alcohol 8 was obtained with high diastereo- and enantioselectivities (Scheme 3). The above-mentioned reactions provide efficient methods to directly functionalize aliphatic terminal alkenes in one pot.

In summary, we have disclosed that a combined use of a cationic rhodium(I) complex, Pr-Foxap, and norbornene enables the facile preparation of alkenyl pinacolboronates from aliphatic terminal alkenes and HBpin at ambient temperature. Since terminal alkenes are more easily accessible and often more desirable starting materials than terminal alkynes, the reaction represents an interesting alternative to alkyne hydroboration. Based upon the dehydrogenative borylation reaction, the one-pot syntheses of aldehydes and homoallylic alcohols starting from terminal alkenes have also been realized. Further studies...
to elucidate the mechanism of this reaction and to expand its utility are in progress.

Keywords: alkenyl boronate • borylation • pinacolboronate • rhodium • terminal alkenes

[15] When the reaction of 1a with 2 was conducted using (rac)-2-(oxazolin-2-y1)]ferrocenyl]diarylphosphine (the Pr group of Pr-Foxap is lacking) in place of Pr-Foxap, the yield of 3a significantly decreased. The result suggests that the bulkiness of the Pr group would be one of the important factors.
[16] Norbornane (ca. 63%), 2-norbornyl pinacolboronate (ca. 46%), and butylbenzene (ca. 3%) were also formed (GC yield).
[17] When the reaction was conducted in the absence of norbornene, no alkenyl pinacolboronate 3a was formed. The hydroboration product 5a and the diboration product 9a were formed in 41% and 44% yields, respectively. These results indicate that norbornene plays a crucial role in inhibiting over-reduction of 3a. When cyclohexene was used in place of norbornene, it was too unreactive to act as the hydrogen acceptor, giving 5a and 9a as the major products.

\[
\text{HBpin} (2, 1.7 \text{ equiv}) \\
\quad [\text{Rh(cod)}_2\text{BF}_4 \quad \text{(Pr mol %)}] \\
\text{Pr-Foxap} \quad (3 \text{ mol %}) \\
\text{R} \\
\begin{align*}
\text{THF, 28 °C, 9 h} \\
9a & \quad 44\% \\
5a & \quad 41\% 
\end{align*}
\]
Aliphatic terminal alkenes react with pinacolborane at ambient temperature in the presence of $\text{[Rh(cod)$_2$]BF}_4/i\text{Pr-Foxap}$ and norbornene to produce dehydrogenative borylation compounds as the major product. The reaction is applied to the one-pot syntheses of aldehydes and homoallylic alcohols from aliphatic terminal alkenes.

M. Morimoto, T. Miura,* M. Murakami*

Rhodium-Catalyzed Dehydrogenative Borylation of Aliphatic Terminal Alkenes with Pinacolborane