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Copper-Catalyzed Enantioselective Coupling between Allylboronates and Phosphates with a Phenol-Carbene Chiral Ligand: Asymmetric Synthesis of Chiral Branched 1,5-Dienes

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INTRODUCTION AND BACKGROUND

Chiral 1,5-dienes with a stereogenic center at the allylic/homoallylic position are found in many important biologically active molecules such as FK-506, Plakotide E, and Chaetoglobosin A (Figure 1)[1], and also serve as useful building blocks in organic synthesis due to the versatility of the two alkene functionalities for further transformations. While several methods have been developed to produce chiral 1,5-dienes[2], enantioselective γ-substitution of allyl alcohol derivatives with organometal reagents (allyl-allyl coupling) using the chiral transition metal complexes as catalysts is the most straightforward because it uses readily available substrates.[3] In 2010, Morken and co-workers reported the pioneering example of catalytic asymmetric allyl-allyl coupling; Pd-catalyzed allyl-allyl coupling between substituted allylboronates[4] and (E)-allylic carbonates occurred with high regio- and enantioselectivity.[5] This protocol enabled access to chiral 1,5-dienes containing contiguous stereogenic centers with high diastereo- and enantioselectivity. More recently, Feringa’s group reported asymmetric cross-coupling between allyl Grignard reagents and (E)-allyl bromides using the copper-chiral monodentate phosphoramidite catalyst, but only moderate SN2’ regioselectivity was obtained.[6] In 2014, Carreira et al. developed Ir-catalyzed regio- and enantioselective allylic cross-coupling between allylsilanes and secondary aromatic allylic alcohols.[7] Despite these efforts, the allyl-allyl coupling was limited to use of acrylic (E)-allylic electrophiles.

Recently, the Cu-catalyzed enantioselective allyl-allyl coupling between allylboronates and allylic phosphates[8-11] using a new chiral N-heterocyclic carbene (NHC) ligand bearing a phenolic hydroxyl group[12,13] was reported. Reaction occurred with exceptional γ-regioselectivity and high enantioselectivity. Various functional groups were tolerated. The ability to use (Z)-aliphatic allylic substrates in the copper catalysis was complementary to Morken’s Pd system (in their reports, only primary (E)-allylic electrophiles were used).[5] The present report describes the details of further studies of this Cu-catalyzed enantioselective allyl-allyl coupling.[8]
For screening of the reaction conditions, commercially available allylboronic acid pinacol esters were used instead of the allyl-1-9-BBN reagents (Table 1). While investigating an effective achiral ligand that could selectively produce the racemic, branched 3-substitution product (3aa), a ring-saturated NHC/Cu complex prepared in situ from 1,3-bis(2,4,6-trimethylphenyl)imidazol-1-ylmethyl chloride (SIMes-HCl), CuCl, and KOME was produced in high yield (93%) with exclusive γ-regioselectivity (γ/α > 99:1) to form the branched coupling product 3aa from reaction between 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1a) and γ-monosubstituted primary (2)-allylic phosphate 2a in THF at −20 °C (entry 1). In contrast to the excellent performance of the ring-saturated NHC ligand SIMes, the corresponding unsaturated NHC ligand IMes, derived from 1,3-bis(2,4,6-trimethylphenyl)imidazol-1-ylmethyl chloride (IMes-HCl), gave a mixture of branched and linear products with a low γ-regioselectivity. These results indicated that the nearly racemic coupling product (99% ee) compared to the system using (93% ee) with greater enantioselectivity (85% ee) but yields were low (entries 8 and 9). Next, the allyl-9-BBN reagents (Table 1). While investigating an allylboronic acid pinacol esters were used instead of the imidazolinium salt [15], which has two effective imidazolinium salts. Chang CuCl to CuOTf·toluenesulfonamide afforded similar selectivity but a lower product yield. Use of MesCu and cationic Cu(MeCN)PF6 as effective as CuCl, and gave comparable results.

The effect of solvent is shown in Table 2. Reaction with toluene gave only the racemic product in moderate yield (43%) and low regioselectivity (γ/α 64:36). Dichloromethane was ineffective in the reaction (26% yield, γ/α 71:29, 51% ee). No reaction occurred in MeCN or hexane.

Table 2. Effects of copper salts and solvents [e]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cu Salt</th>
<th>Solvent</th>
<th>Yield [%]</th>
<th>γ/α [%]</th>
<th>ee [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>CuCl</td>
<td>THF</td>
<td>83</td>
<td>&gt;99:1</td>
<td>92</td>
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<tr>
<td>2</td>
<td>Cu2OAc</td>
<td>THF</td>
<td>85</td>
<td>91:9</td>
<td>76</td>
</tr>
<tr>
<td>3</td>
<td>Cu(OAc)2</td>
<td>THF</td>
<td>68</td>
<td>73:27</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>CuOTf·toluenesulfonamide</td>
<td>THF</td>
<td>48</td>
<td>&gt;99:1</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>MesCu</td>
<td>THF</td>
<td>85</td>
<td>&gt;99:1</td>
<td>89</td>
</tr>
<tr>
<td>6</td>
<td>Cu(MeCN)PF6</td>
<td>THF</td>
<td>73</td>
<td>&gt;99:1</td>
<td>88</td>
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<tr>
<td>7</td>
<td>CuCl</td>
<td>toluene</td>
<td>43</td>
<td>64:36</td>
<td>0</td>
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<td>8</td>
<td>CuCl</td>
<td>DCM</td>
<td>26</td>
<td>72:19</td>
<td>51</td>
</tr>
<tr>
<td>9</td>
<td>MeCN</td>
<td></td>
<td>0</td>
<td></td>
<td>51</td>
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<tr>
<td>10</td>
<td>CuCl</td>
<td>hexane</td>
<td>0</td>
<td></td>
<td>51</td>
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</table>

[a] Conditions: 1a (0.24 mmol), (2) 2a (0.15 mmol), CuCl/ligand (10 mol%), KOME (0.18 mmol), THF (0.6 mL) for 20 h. (b) Yield of isolated product. (c) Determined by 1H NMR analysis of the crude product. (d) The ee was determined by HPLC. (e) Table 1, entry 11.

The effects of leaving groups and bases are summarized in Table 3. The use of allyl bromide or chloride as an allylic electrophile under the conditions described for Table 1, entry 11, decreased both regio- and enantioselectivity (entries 2 and 3).

Table 3. Use of NaOMe instead of KOME decreased regioselectivity (γ/α 89:11 and enantioselectivity (74% ee) (entry 4). No reaction occurred with LiOMe, due to the greater

**Table 1.** Ligand effects for reaction between 1a and 2a [e]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Temp (°C)</th>
<th>Yield [%]</th>
<th>γ/α [%]</th>
<th>ee [%]</th>
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<tr>
<td>1</td>
<td>SIMes·HCl</td>
<td>−20</td>
<td>93</td>
<td>&gt;99:1</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>IMes·HCl</td>
<td>−20</td>
<td>65</td>
<td>62:38</td>
<td>51</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
<td>−20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Phen</td>
<td>−20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

[a] Data are taken from ref 8. Conditions: 1a (0.24 mmol), (2) 2a (0.15 mmol), CuCl/ligand (10 mol%), KOME (0.18 mmol), THF (0.6 mL) for 20 h. (b) Yield of isolated product. (c) Determined by 1H NMR analysis of the crude product. (d) The ee was determined by HPLC. (e) Table 1, entry 11.
solubility of LiCl or LiOP(O)(OEt)₂, which may form inactive Cu species through ionic interactions. (entry 5). The structure of the alkoxide moiety of the base also had a strong impact on yield, regioselectivity, and enantioselectivity. Thus, when KOMe was changed to a sterically more demanding base, K0Bu product yield was moderate and both regioselectivity and enantioselectivity decreased significantly (entry 6). This result suggests that the trialkoxyboron ROBpin may participate in the reaction because Lewis acids activate the phosphate leaving group (see Figure 4). Coupling reaction with K2CO3 did not occur (entry 7).

Table 3. Effect of leaving group and base (a)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Leaving group</th>
<th>Base</th>
<th>Yield (%)</th>
<th>(\gamma / \alpha)</th>
<th>ee (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>OP(O)(OEt)₂</td>
<td>KOMe</td>
<td>83</td>
<td>&gt;99:1</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>Cl</td>
<td>KOMe</td>
<td>89</td>
<td>94:6</td>
<td>64</td>
</tr>
<tr>
<td>3</td>
<td>Br</td>
<td>KOMe</td>
<td>85</td>
<td>82:18</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>OP(O)(OEt)₂</td>
<td>NaOMe</td>
<td>91</td>
<td>89:11</td>
<td>74</td>
</tr>
<tr>
<td>5</td>
<td>OP(O)(OEt)₂</td>
<td>LiOMe</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>OP(O)(OEt)₂</td>
<td>KOBu</td>
<td>67</td>
<td>82:18</td>
<td>50</td>
</tr>
</tbody>
</table>

[a] Data are taken from ref 8. Conditions: \(\gamma\)-alkyl CuL₅ catalyst (0.15 mmol), CuCl (5.9 mmol, 2.0 g) afforded only the branched coupling product in 73% yield (0.98 g, 4.3 mmol) with 92% ee.

Substrate Scopes. (2)-Allylic phosphates with various aliphatic substituents were reacted with 1a in the Cu-L₅ catalyst system (Table 4). When the 2-phenylethyl group of 2a was replaced with a benzy or ocyt group, coupling proceeded with excellent \(\gamma\)-selectivity and preservation of enantioselectivity (entries 1 and 3). A sterically more demanding \(\gamma\)-substituent, such as a cyclohexyl group, was also tolerated and produced a high level of enantioselectivity (80% ee) (entry 4). Notably, the enantioselective reaction with 2-buten-1,4-diol derivatives, which have two potential leaving groups at different allylic positions, occurred with the allylic C–O bonds in the ether or carboxylic ester leaving groups untouched (entries 5–12 and 15).

The reaction has a great functional group compatibility (entries 2 and 5–12, 15–17). For example, an allylic phosphate (2) bearing a 1,3-benzodioxole (2c), THF ether (2f), benzy ether (2g), allyl ether (2h, q),[17] pivalate (2i), carboxylic ester (2p) or \(\rho\)-toluenesulfonate (2r) group as the aliphatic \(\gamma\)-substituent, reacted with 1a to produce the corresponding 1,5-diene derivatives in good yields with high enantioselectivities (85–97% ee) (entries 2, 5–8, 15–17). Methoxy, trifluoromethyl bromo, or dimethylamino substituents were tolerated in the aromatic ring of the benzoate groups (entries 9–12). However, no reaction occurred with the allylic phosphate bearing a nitro (2n) or cyano (2o) group (entries 13 and 14).

The potential for scaling up the enantioselective allyl–allyl coupling was examined on a preparative scale (Eq. 1). Reaction between allylboronate 1a (9.4 mmol, 1.5 g) and allylic phosphate 2h (5.9 mmol, 2.0 g) afforded only the branched coupling product in 73% yield (0.98 g, 4.3 mmol) with 92% ee.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phosphate</th>
<th>Product</th>
<th>Temp (°C)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>2b</td>
<td>3ba</td>
<td>-50</td>
<td>62</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>2c</td>
<td>3ca</td>
<td>-30</td>
<td>97</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>2d</td>
<td>3da</td>
<td>30</td>
<td>85</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td>3ea</td>
<td>-50</td>
<td>59</td>
<td>80</td>
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</table>

[a] Data are taken from ref 8. Conditions: 1a (0.24 mmol), 2a (0.15 mmol), CuCl (1.5 g), HBF₄ (10 mol%), THF (0.6 mL), –20 °C for 20 h. [b] Yield of isolated product. [c] Determined by \(^1\)H NMR of crude product. [d] The ee was determined by HPLC.
Reactions of β-substituted allylboronate derivatives using the Cu-L5 catalyst system were investigated (Table 5). Methylboronate 1b and 2-ethyl-2-propen-1-ylboronate 1c reacted with (Z)-2a with excellent γ-selectivity (γ/α = 20:1) and high enantioselectivity (95% and 80% ee, respectively) (entries 1 and 2). An allylboronate with a hexyl benzyl or phenyl group at the β-position (1d-f) underwent reaction to afford the coupling products with enantiomeric excesses greater than 80%, while the regioselectivities were moderate (entries 3–5). The allylboronate with a chloro group at the β-position did not react (entry 6). In addition, no reaction occurred with γ-substituted allylboronates such as trans- or cis-crotlyboronates.

**Table 5. Scope of allylboronates**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Allylboronate</th>
<th>Phosphate</th>
<th>Product</th>
<th>Yield (%)</th>
<th>γ/α (%)</th>
<th>ε (%)</th>
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<tr>
<td>1</td>
<td>1b</td>
<td>OP(O)(OEt)</td>
<td>3aa</td>
<td>77</td>
<td>&gt;20:1</td>
<td>95</td>
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<tr>
<td>2</td>
<td>1c</td>
<td>OP(O)(OEt)</td>
<td>3aa</td>
<td>50</td>
<td>&gt;20:1</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>1d</td>
<td>OP(O)(OEt)</td>
<td>3aa</td>
<td>87</td>
<td>84:16</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>1e</td>
<td>OP(O)(OEt)</td>
<td>3aa</td>
<td>59</td>
<td>87:13</td>
<td>82</td>
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<tr>
<td>5</td>
<td>1f</td>
<td>OP(O)(OEt)</td>
<td>3aa</td>
<td>89</td>
<td>78:22</td>
<td>83</td>
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<tr>
<td>6</td>
<td>2a</td>
<td>OP(O)(OEt)</td>
<td>3aa</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

[a] Data are taken from ref 8 for entries 1–5. Conditions: 1 (0.24 mmol), (Z)-2 (0.15 mmol), CuCl/L5–LHBF4 (10 mol%), KOMe (0.18 mmol), THF (0.6 mL), –50 °C (entry 1) or –30 °C (entries 2–6) for 48 h. [b] Yield of isolated product. [c] Determined by 1H NMR of crude product. [d] The ee was determined by HPLC.

**Mechanistic Study and Proposed Reaction Pathway.**

The alkene geometry of the allylic phosphates influenced both regio- and enantioselectivity. Thus, reaction between 1a and (E)-2a under the conditions described in Table 1, entry 11 gave the linear α-substitution product (E)-4aa preferentially with minor formation of (S)-3aa (71% ee), the antipode of the product derived from (Z)-2a (Eq. 5). This α-selectivity appeared to occur via allylic 1,3-migration of Cu in the allylcopper(III) species. To gain insight into the nature of the postulated allylcopper(III) species, secondary allylic phosphate 2a', a constitutional isomer of (Z)-2a, was reacted under the same conditions (Eq. 6). Interestingly, this reaction gave results similar to reaction with (E)-2a. The convergence observed in the regioselectivity and stereochemistry suggests that (E)-2a and 2a' led to a common equilibrium mixture of the allylcopper(III) species prior to reductive elimination to form the product mixture (Figure 3).

**Figure 3. Allylcopper(III) species**

Based on the assumption that γ-selective reaction of (Z)-2 also occurs via allylcopper(III) intermediates, a catalytic cycle was proposed for the enantioselective allyl-allyl coupling catalyzed by the Cu-L5 system, as shown in Figure 4. An allylcopper(I) complex (A) was formed from reaction between CuCl, L5·HBF4 and KOMe. For this complex, the chiral NHC ligand coordinated to Cu as an anionic C,O-bidentate ligand. Then, transmetalation between A and an allylborate (B)[21] afforded the potassium phenoxo(allyl)cuprate (C). Compound C formed a π-complex (D) with the allylic phosphate 2, in which the Cu was anti to the phosphate leaving group. The MeOBpin may activate the phosphate group as a Lewis acid.[14] Subsequently, oxidative addition produced (π-en-α-yl)copper(III) complex E1 with a secondary sp2-carbon atom bound to Cu. Facile reductive elimination of E1, which was faster than allylic 1,3-Cu-migration to form E2, produced the
branched $\gamma$-substitution product 3 and regenerated alkoxy copper(I) complex A (Figs. 5 and 6 for enantio-discrimination models).

Thus, the crucial dependence of regioselectivity on the E/Z geometry of the allylic substrate (Z) can be explained by the greater instability of the allylcopper(III) intermediate $E_2$ compared to the corresponding Cu(III) species ($E_1$) produced from the E substrate, due to larger steric repulsion in the allyl moiety derived from the Z substrate (Fig. 3). Similar consideration may be applicable to the corresponding transition states that determine the E/Z-isomeric product distribution.

Figure 4. Postulated catalytic reaction pathway.

Reactions of $E$- and $Z$-isomers of 2a gave the antipodes of 3aa, (Table 1, entry 11 vs. Eq. 5), and the products from (Z)-2a were produced with greater enantioselectivity. This led to the proposal of the enantioselcetion models shown in Figs. 5 and 6. In the $\pi$-complex D (Fig. 4), the chiral copper center adopted a tetrahedral coordination geometry including the C,O-bidentate chelation. The $K^+$ ion bridged the phenoxide oxygen and MeO-Bpin, which interacted with the phosphate leaving group as a Lewis acid. These assumptions suggest four possible $\pi$-complexes ($D_1$ and $D_2$ for the major enantiomer; $D_3$ and $D_4$ for the minor enantiomer) (Fig. 5). Complex $D_1$ is the most favorable, because it results in the fewest steric repulsions between catalyst and allylic phosphate. Complexes $D_2$, $D_3$, and $D_4$ appear to be destabilized by the steric repulsions between the $\gamma$-substituent (R) and nonhydroxylated $N$-aryl group or one of the phenyl groups on the imidazolidine ring. These conclusions are consistent with the experimental observations that the enantioselcetivity is influenced by the steric nature of the $\gamma$-substituent (R) (Table 4, entries 3 and 4) or the nonhydroxylated $N$-aryl group in the phenolic NHC ligands (Table 1, entries 10 and 11).

CONCLUSIONS

In conclusion, a versatile method was developed for Cu-catalyzed enantioselective allyl-allyl coupling between allylboronates and (Z)-acyclic and cyclic allylic phosphates to form various chiral 1,5-diene derivatives. Catalysis of a Cu(I) complex with a new phenol-NHC chiral ligand enabled the reaction, demonstrating the utility of this class of chiral ligands for enantioselcetive copper catalysis with organoboron compounds.[12] This Cu-catalyzed protocol provides efficient access to functionalized, enantio-enriched chiral 1,5-dienes with a stereogenic carbon center at the allylic/homoallyl position. The broad functional group compatibility and the use of earth-abundant and relatively low-toxic Cu as a metal are attractive features of this protocol. A functional role for the phenolic
hydroxy group in the chiral NHC ligand was suggested by the results.

**EXPERIMENTAL SECTION**

**Instrumentation and Chemicals**

NMR spectra were recorded on a JEOL ECX-400, operating at 400 MHz for $^1$H NMR, 100.5 MHz for $^{13}$C NMR and 128 MHz for $^{2}$H NMR. Chemical shift values for $^1$H and $^{13}$C are referenced to Me$_3$Si and the residual solvent resonances, respectively. Chemical shifts are reported in ppm.

Mass spectra were obtained with Thermo Fisher Scientific Exactive, JEOL JMS-T100LP or JEOL JMS-700TZ at the Instrumental Analysis Division, Global Facility Center, Creative Research Institution, Hokkaido University. HPLC analyses were conducted on a HITACHI ELITE LaChrom system with a HITACHI L-2450 diode array detector. Optical rotations were measured on a JASCO P-2200. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F254. Chromaster with a HITACHI 5430 diode array detector.

**Optical rotations in the literature.**[8, 12a] (mL)/acetone (790 g/L)

**Preparation of Allylic Phosphate (5)-2s**

(5)-3-Butyn-2-ol (99% ee) (1.2 mL, 15 mmol) and imidazole (2.0 g, 30 mmol) were dissolved in DCM (30 mL) at 0 °C. Then, TBDMSCI (3.4 g, 22 mmol) was added to the mixture, and the solution was stirred at rt for 8 h. The reaction was quenched with H$_2$O and extracted with DCM (15 mL × 3). The combined organic layer was dried over MgSO$_4$, filtered, and evaporated under reduced pressure. The residue was purified through flash chromatography on silica gel (90–45% EtOAc/hexane) to provide (5)-3-Butyn-2-ol (790 g/L), maleic anhydride (2a) (3.6 mmol), and then the reaction mixture was stirred at room temperature for 30 min. Next, 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1a) was obtained from commercial suppliers. Allylboronates 1g were prepared according to the reported procedures.[22] Allylboronates 1b-f aliphatic phosphates 2a-r, 21-v, 2a’ and NHC ligands 2-L7 were reported in the literature.[12a] (E)-4aa are found in the literature.[20]

**Characterization Data for Allylic Phosphate**

<table>
<thead>
<tr>
<th>Phosphorus Compound</th>
<th>Data</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allylic Phosphate (5)-2s</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

**Procedure for the Copper-Catalyzed Enantioselective Allyl-Alkyne Coupling**

The reaction in Table 4, entry 1 is representative. CuCl (1.5 mg, 0.015 mmol), L5-IIBF$_4$ (9.8 mg, 0.015 mmol) and KOMe (12.6 mg, 0.18 mmol) were placed in a vial containing a magnetic stirring bar. The vial was sealed with a Teflon-coated silicon rubber septum, and then the vial was evacuated and filled with argon. THF (0.6 mL) was added to the vial, and then the mixture was stirred at room temperature for 30 min. Next, 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1a) (45.3 μL, 0.24 mmol) was added. Finally, allyl phosphate 2b (42.6 mg, 0.15 mmol) was added at −50°C. After 48 h stirring at −50°C, the reaction was quenched with saturated NH$_4$Cl aq. and extracted with diethyl ether (1 mL × 3). The combined organic layer was dried over MgSO$_4$. Then, the drying agent was removed by filtration, and the resulting solution was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane) to give 3ab.

**Characterization Data for Allyl-Alkyne Coupling Products**

**Full details for compounds** 3aa-am, 3ap-ar, 3ba-ea, 3f and 3au-av can be found in our previous report.[9]

**Conclusion**

The product 3aa was purified by flash chromatography on silica gel (hexane) (178.9 mg, 0.96 mmol, 80% isolated yield from (Z)-2a).

The product 3ab was purified by flash chromatography on silica gel (hexane) (15.9 mg, 0.09 mmol, 62% isolated yield from 2b).

The product 3ac was purified by flash chromatography on silica gel (hexane) (874 mg, 4.0 mmol, 80% isolated yield from (Z)-2a).
The product 3ac was purified by flash chromatography on silica gel (5% EtOAc/hexane) (31.5 mg, 0.14 mmol, 97% isolated yield from 2c).

(R)-4-Vinyl-1-dodecene (3ad)
The product 3ad was purified by flash chromatography on silica gel (hexane) (24.7 mg, 0.12 mmol, 85% isolated yield from 2d).

(R)-Hexa-1,5-dien-3-yloctahexane (3ae)
The product 3ae was purified by flash chromatography on silica gel (pentane) (14.6 mg, 0.09 mmol, 59% isolated yield from 2e).

(R)-2-[(2-Vinyl-4-penten-1-yl)oxy]tetrahydro-2H-pyran (3af) (Diastereomeric ratio 1:1)
The product 3af was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (22.8 mg, 0.11 mmol, 75% isolated yield from 2g).

(R)-[(2-Vinyl-4-penten-1-yl)oxy]methyl]benzene (3ag)
The product 3ag was purified by flash chromatography on silica gel (0–1% EtOAc/hexane) (26.6 mg, 0.12 mmol, 83% isolated yield from 2h).

(R)-2-Vinyl-4-penten-1-yl Pivalate (3ai)
The product 3ai was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (20.6 mg, 0.11 mmol, 70% isolated yield from 2i).

(R)-2-Vinyl-4-penten-1-yl 4-Methoxybenzoate (3aj)
The product 3aj was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (31.2 mg, 0.13 mmol, 85% isolated yield from 2j).

(R)-2-Vinyl-4-penten-1-yl 4-(Trifluoromethyl)benzoate (3ak)
The product 3ak was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (25.9 mg, 0.09 mmol, 61% isolated yield from 2k).

(R)-2-Vinyl-4-penten-1-yl 4-Bromobenzoate (3al)
The product 3al was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (28.8 mg, 0.10 mmol, 65% isolated yield from 2l).

(R)-2-Vinyl-4-penten-1-yl 4-(Dimethylamino)benzoate (3am)
The product 3am was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (34.0 mg, 0.13 mmol, 87% isolated yield from 2m).

(R)-1-Benzyl 4-(2-Vinyl-4-penten-1-yl)piperidine-1,4-dicarboxylate (3ap)
The product 3ap was purified by flash chromatography on silica gel (5–10% EtOAc/hexane) (43.0 mg, 0.12 mmol, 80% isolated yield from 2p).

(R)-tert-Butyldimethyl[4-(vinyl-6-hepten-1-yl)oxy]silane (3aq)
The product 3aq was purified by flash chromatography on silica gel (0–1% EtOAc/hexane) (29.8 mg, 0.12 mmol, 78% isolated yield from 2q).

(R)-4-Vinyl-6-hepten-1-yl 4-Methylbenzenesulphonate (3ar)
The product 3ar was purified by flash chromatography on silica gel (0–5% EtOAc/hexane) (38.7 mg, 0.13 mmol, 88% isolated yield from 2r).

tert-Butyldimethyl[15(3S,3S)-3-vinyl-5-hexen-2-yl]oxy]silane (3as)
The product 3as was purified by flash chromatography on silica gel (0–2% EtOAc/hexane) (22.2 mg, 0.09 mmol, 61% isolated yield from 2s). Colorless Oil. IR (neat) 664, 772, 830, 910, 994, 1072, 1254, 1361, 1374, 1463, 1472, 1641, 2858, 2887, 2930, 2957, 3078 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl3) δ 6.05 (s, 6H), 0.89 (s, 9H), 1.08 (d, $J$ = 6.4 Hz, 3H), 1.98–2.12 (m, 2H), 2.34 (m, 1H), 3.70 (quintet, $J$ = 6.4 Hz, 1H), 4.95–5.08 (m, 4H), 5.59–5.88 (m, 2H). $^{13}$C NMR (100 MHz, CDCl3) δ –4.8, –4.3, 17.9, 20.8, 25.7, 34.5, 51.7, 70.5, 115.2, 115.8, 137.4, 139.1. HRMS–APCI (m/z): [M+H]$^+$ calcld for C24H40O5Si, 388.2411; found, 388.2480. $[α]_D^{20}$ +34 ($c$ 0.37, CHCl3). The d.r. (90:10) was determined by $^1$H NMR analysis of the crude product. The absolute configuration of 3as was assigned by consideration of the stereochemical pathway.

(R)-[5-Methyl-3-vinyl-5-hexen-1-yl]benzene (3ba)
The product 3ba was purified by flash chromatography on silica gel (hexane) (23.1 mg, 0.12 mmol, 77% isolated yield from (Z)-2a).

(R)-[5-Methylene-3-vinylheptyl]benzene (3ca)
The product 3ca was purified by flash chromatography on silica gel (hexane) (16.1 mg, 0.07 mmol, 50% isolated yield from (Z)-2a).

(R)-[5-Methylene-3-vinylundecyl]benzene (3da)
The product 3da was purified by flash chromatography on silica gel (hexane) (35.3 mg, 0.13 mmol, 87% isolated yield from (Z)-2a).

(R)-[2-Methylene-4-vinylhexane-1,6-diyldibenzene (3ea)
The product 3ea was purified by flash chromatography on silica gel (0–1% EtO2/hexane) (24.7 mg, 0.08 mmol, 59% isolated yield from (Z)-2a).

(R)-[4-Methyl-1,5-hexadien-2-yl]benzene (3fb)
The product 3fb was purified by flash chromatography on silica gel (hexane) (23.0 mg, 0.13 mmol, 89% isolated yield from 2o). The isolated branched product (3ft) was contaminated with a trace amount of the linear product.

(1R,2R)-2-Allyl-3-cyclopenten-1-yl Diethyl Phosphate (3au)
The product 3au was purified by flash chromatography on silica gel (20–50% EtOAc/hexane) (25.1 mg, 0.10 mmol, 64% isolated yield from 2u).

(1R,2R)-2-Allyl-3-cyclohexen-1-yl Diethyl Phosphate (3av)
The product 3av was purified by flash chromatography on silica gel (20–50% EtOAc/hexane) (21.3 mg, 0.08 mmol, 52% isolated yield from 2v).

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Supporting Information
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References


[15] The use of allyl-9-BBN reagent instead of 1a under the conditions for Table 1, entry 12 resulted in decreases in both enantioselectivity (87% ee) and product yield (30%) but with the exclusive regioselectivity ($\gamma/\alpha$)-unchanged.


[17] The absolute configurations of 3ae and 3ah were determined by comparison of the specific rotations with the values reported previously. See ref 5a. The absolute configuration of 3ae was determined by the Mosher’s NMR spectroscopic method. Absolute configurations of the other products were assigned by consideration of the stereochemical pathway. See ref 8.

[18] The linear $\alpha$-substitution product was $\delta$-isomer.

[19] Data are taken from ref 8 for Eq. 3-6.

[20] Nakamura conducted DFT calculations on the mechanism of the reaction between [MeCu(CN)Li] and allyl acetate to form a square planar four-coordinate ($\gamma\sigma$-enyl)copper(III) species. The asymmetric nature of MeCuCN–. Our proposed mechanism is in accord with the Nakamura’s mechanism, in which the ($\gamma\sigma$-enyl)copper(III) species is not in equilibrium with the corresponding ($\epsilon\eta$-aryl)copper(III) species; the regioselectivity is determined at the oxidative addition step as a consequence of the asymmetric nature of MeCuCN. Our proposed mechanism is in accord with the Nakamura’s mechanism in that the reaction proceeds through oxidative addition of a cuprate to form the ($\gamma\sigma$-enyl)copper(III) species followed by reductive elimination. However, the coordination number of Cu in the allylcopper(III) complex is different by virtue of bidentate coordination of the anionic phenol-NHC chiral ligand (I). The strongly electron-donating NHC coordination should render the $\epsilon\eta$-coordination weaker, making the allylic 1.3-Cu-migration in the allylcopper(III) complex more feasible. See: a) Yoshikai, N.; Zhang, S.-L.; Nakamura, E. J. Am. Chem. Soc. 2008, 130, 12862. For the effect of a $\sigma$-donor ligand, see: b) Yamakawa, M.; Kato, S.; Nakamura, E. J. Am. Chem. Soc. 2004, 126, 6287. For Table 1, entry 12 resulted in decreases in both enantioselectivity (87% ee) and product yield (30%) but with the exclusive regioselectivity ($\gamma/\alpha$)-unchanged.

[21] Rapid formation of a tetravalent borate (B) was confirmed by $^1$B NMR spectroscopy. See ref 8.

Biosketches

Yuto Yasuda graduated from Hokkaido University in 2014. He received his M. Sc in 2016 from Hokkaido University under the supervision of Professor Masaya Sawamura. Currently, he is working on his Ph. D. thesis on the development of copper-catalyzed asymmetric C–C bond formation reactions. He is a JSPS research fellow (DC1) since 2016. Awards: CSJ Student Presentation Award (2014), CSJ Student Presentation Award (2016), Poster Award in 1st Singapore Japan Germany Trilateral Symposium on Precision Synthesis & Catalysis (2017).

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