Functional Group Tolerable Synthesis of Allylsilanes through Copper-Catalyzed γ-Selective Allyl–Alkyl Coupling between Allylic Phosphates and Alkylboranes

Kazunori Nagao, Hirohisa Ohmiya,* and Masaya Sawamura*

Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060-0810, Japan; Fax: +81-11-706-3749; E-mail: ohmiya@sci.hokudai.ac.jp; sawamura@sci.hokudai.ac.jp

Abstract: A copper-catalyzed γ-selective allyl–alkyl coupling between γ-silylated allylic phosphates and alkylboron compounds (alkyl-9-BBN, prepared by hydroboration of alkenes with 9-BBN-H) produced allylsilanes. The reaction tolerated various functional groups in both the alkylboranes and the allylic phosphates, and afforded functionalized allylsilanes.

Key words: allylsilane, copper, allylic substitution, alkylborane, regioselectivity

Allylsilanes are versatile synthetic intermediates in organic synthesis.1 The development of facile and efficient methods for the synthesis of allylsilanes is important. Among the available methods for accessing to allylsilanes,2–14 two types of the S N2′ displacement strategies, γ-substitutions of γ-silylated allylic alcohol derivatives with organocuprate reagents15,16 and silylations of allylic alcohol derivatives with silylcuprate reagents17,18 are particularly useful because the substrates and the reagents are readily available and the reactions are highly reliable in terms of product yield and selectivity.

Previously we developed the copper-catalyzed allyl–alkyl coupling reaction between allylic phosphates and alkylboranes (alkyl-9-BBN) that proceeds with excellent γ- and E-selectivities.19 Herein, we report that this copper-catalyzed protocol is applicable to the reaction between γ-silylated allylic phosphates and alkylboranes (alkyl-9-BBN), which appeared to be a straightforward, functional group-tolerable approach to allylsilanes.19–22 The wide availability of alkylboranes via the established alkene hydroboration reaction is an attractive feature of this transformation.

Scheme 1.

Alkylborane 2a (0.32 mmol), which was prepared via hydroboration of styrene (1a) with 9-borabicyclo[3.3.1]nonane (9-BBN-H) dimer, and γ-trimethylsilyl allylic substrates 3a (0.2 mmol) bearing a cyclic phosphate leaving group were subjected to the standard reaction conditions for the copper-catalyzed allyl–alkyl coupling (2a/3a/CuOAc/t-BuOK, 1:6:1:0.1:1.5, THF, 60 °C) (Scheme 1).23 The reaction afforded allylsilane 4aa in 89% yield (based on 3a; 100% convn of 3a) with complete γ- and E-selectivities. The use of a diethyl phosphate as a leaving group gave a slightly decreased product yield compared to the cyclic phosphate (80% yield). The reaction of (E)-3a proceeded with significantly decreased E-selectivity (E/Z 71:29) (data not shown).23

The hydroboration–coupling one-pot protocol affords a variety of allylsilanes (Table 1). Allylic phosphates 3b–d with other silyl substituents such as PhMe2Si, Ph2MeSi and BnMe2Si instead of Me3Si at the γ-position were also converted to the corresponding allylsilanes derivatives 4ab, ac, ad in high yields (entries 1–3). The reaction tolerates a variety of functional groups including ester, methoxy, silyl ethyl, phthalimide, acetal, thiophene, bromo and amide moieties in alkenes and allylic phosphates (entries 4–13).

The tolerance of the reaction toward steric demand in both the alkylboranes (2) and allylic phosphates (3) is also shown in Table 1. The sterically more demanding alkylborane 2b, which was derived from a alkene (1b) bearing a tertiary alkyl substituent, served as a substrate to afford the corresponding allylsilanes 4ba in high yield (entry 4). The reaction of the β-branched alkylborane (2i), which was prepared from α-methylstyrene (1i), was also successful to give 4ia as a 1:1 diastereomeric mixture (entry 12). Unfortunately, however, the use of secondary alkylborane reagents prepared from internal alkenes resulted in no reaction (data not shown). The allylic phosphate 3e with a CH2CH2OTIPS group instead of a Me group at the α-position underwent the reaction (entry 13). A sterically more demanding α-substituent such as an Pr group was also tolerated (entry 14).

Table 1. Synthesis of Allylsilanesa

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene</th>
<th>phosphate</th>
<th>product</th>
<th>yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>3a</td>
<td>4aa</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>3b</td>
<td>4bb</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>3c</td>
<td>4bc</td>
<td>94</td>
</tr>
</tbody>
</table>

a) The reaction conditions for the copper-catalyzed allyl–alkyl coupling (2a/3a/CuOAc/t-BuOK, 1:6:1:0.1:1.5, THF, 60 °C) (Scheme 1).
In conclusion, we have developed a versatile, functional group-tolerable approach to allylsilanes through a copper-catalyzed γ-selective cross-coupling reaction between γ-silylated allylic phosphates and alkylboranes.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. t-BuOK (1.0 M THF solution) and CuOAc were purchased from Aldrich Chemical Co., stored under nitrogen, and used as it is. Tetrahydrofuran (THF) was purchased from Kanto Chemical Co., stored under nitrogen, and used as it is. 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphinane 2-oxide (3a) was prepared in THF at 60 °C for 6 h. Alkylborane was prepared in advance by hydroboration of 1 with 9-BBN dimer in THF at 60 °C for 1 h and used without purification. Isolated yield based on 3. Isomeric ratios (γα >99:1, E/Z >99:1). Determined by 1H NMR or GC of the crude product. Diasteremeric ratio (1:1).

Preparation of γ-Silylated Allylic Phosphates 3a–d

THP-protection of commercially available 3-butyne-2-ol followed by silylations gave γ-silylated propargylic alcohol derivatives. Next, DIBAL-H reduction followed by deprotection afforded γ-silylated allylic alcohols. Finally, allylic phosphates 3a–d were prepared by the phosphorylation of the γ-silylated allylic alcohols (vide infra for the product yield of the phosphorylation).

The phosphorylation of (Z)-4-(dimethylphenylsilyl)-3-buten-2-ol to 3b is representative. To a solution of (Z)-4-(dimethylphenylsilyl)-3-buten-2-ol (413 mg, 2.0 mmol) in THF (16.0 mL) and TMEDA (4.0 mL), t-BuLi (1.3 mL, 1.63 M, 2.1 mmol) was added at –78 °C. After being stirred at –78 °C for 45 min, 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphinane 2-oxide (Aldrich Chemical Co., 480 mg, 2.6 mmol) was added to the reaction mixture. The reaction mixture was stirred for an additional 5 minutes at –78 °C, then warmed to room temperature, and stirred for 3 hours. The resulting solution was quenched with saturated NH4Cl aq. Aqueous layer was extracted with ethyl acetate. The organic layers were combined and washed with brine, dried over MgSO4, filtered, and concentrated under vacuum to leave an oil. After passing through a short plug of aluminum oxide with diethyl ether, an eluent was concentrated, and the residue was purified with GPC to provide 3b in 73% yield (517 mg, 1.46 mmol).

(Z)-5,5-Dimethyl-2-[(4-(trimethylsilyl)-3-buten-2-yl)oxy]-1,3,2-dioxaphosphinane 2-Oxide (3a)

White solid; yield: 345 mg (59%); mp 45.6–45.8 °C.

1H NMR (300 MHz, CDCl3) δ 0.17 (s, 9H), 0.87 (s, 3H), 1.25 (s, 3H), 1.44 (d, J = 5.1 Hz, 3H), 3.78–4.11 (m, 4H), 5.13 (dd, J = 9.0, 5.1 Hz, 1H), 5.71 (dd, J = 14.1, 1H), 6.29 (dd, J = 14.1, 9.0 Hz, 1H).

13C NMR (75.4 MHz, CDCl3) δ 21.55, 22.59 (d, J = 4.6 Hz, 1H), 31.91 (d, J = 5.7 Hz, 75.14 (d, J = 5.1 Hz), 77.36 (d, J = 6.8 Hz), 77.75 (d, J = 6.8 Hz), 132.39, 146.26 (d, J = 5.7 Hz).

(Z)-2-[(4-Dimethylphenylsilyle)-3-buten-2-yl]oxy]-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxide (3b)

Colorless oil; yield: 517 mg (73%).

1H NMR (300 MHz, CDCl 3) δ 0.44 (s, 3H), 0.48 (s, 3H), 0.84 (s, 3H), 1.23 (s, 3H), 1.28 (d, J = 6.3 Hz, 3H), 3.69–4.04 (m, 4H), 5.04 (dq, J = 9.0, 6.3 Hz, 1H), 5.86 (d, J = 14.2 Hz, 1H), 6.38 (dd, J = 14.2, 9.0 Hz, 1H), 7.26–7.56 (m, 3H), 7.54–7.56 (m, 2H).

13C NMR (75.4 MHz, CDCl 3) δ −1.54, −1.27, 20.26 (d, J = 4.0 Hz), 21.58, 22.19 (d, J = 4.0 Hz), 31.92 (d, J = 5.7 Hz), 75.18 (d, J = 5.1 Hz), 77.35 (d, J = 6.8 Hz), 77.73 (d, J = 6.8 Hz), 128.00, 129.24, 130.37, 133.75, 138.54, 147.67 (d, J = 5.7 Hz).


(Z)-5,5-Dimethyl-2-[(4-methyldiphenylsilyle)-3-buten-2-yl]oxy]-1,3,2-dioxaphosphinane 2-Oxide (3c)

Colorless oil; yield: 687 mg (83%).

1H NMR (300 MHz, CDCl 3) δ 0.78 (s, 3H), 0.81 (s, 3H), 1.19 (d, J = 6.3 Hz, 3H), 1.21 (s, 3H), 3.66–3.98 (m, 4H), 4.93 (dq, J = 9.0, 6.3 Hz, 1H), 6.08 (d, J = 14.4 Hz, 1H), 6.53 (dd, J = 14.4, 9.0 Hz, 1H), 7.33–7.39 (m, 6H), 7.53–7.58 (m, 4H).

13C NMR (75.4 MHz, CDCl 3) δ −2.57, 20.26 (d, J = 1.1 Hz), 21.53, 21.88 (d, J = 4.0 Hz), 31.88 (d, J = 5.7 Hz), 75.20 (d, J = 5.1 Hz), 77.34 (d, J = 6.8 Hz), 77.64 (d, J = 6.8 Hz), 128.04, 128.10, 128.14, 129.49, 129.60, 134.61, 134.75, 136.30, 136.68, 149.30 (d, J = 6.3 Hz).


(Z)-2-[(4-Benzylmethyldisilyl)-3-buten-2-yl]oxy]-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxide (3d)

Colorless oil; yield: 667 mg (91%).

1H NMR (300 MHz, CDCl 3) δ 0.16 (s, 3H), 0.17 (s, 3H), 0.87 (s, 3H), 1.24 (s, 3H), 1.37 (d, J = 6.3 Hz, 3H), 2.19 (s, 2H), 3.76–4.09 (m, 4H), 5.08 (dq, J = 9.0, 6.3 Hz, 1H), 5.68 (d, J = 14.4 Hz, 1H), 6.32 (dd, J = 14.4, 9.0 Hz, 1H), 7.00–7.10 (m, 3H), 7.19–7.24 (m, 2H).

13C NMR (75.4 MHz, CDCl 3) δ −2.05, −2.00, 20.25, 21.55, 22.51 (d, J = 4.6 Hz), 26.17, 31.94 (d, J = 5.7 Hz), 75.20 (d, J = 5.1 Hz), 77.38 (d, J = 6.8 Hz), 77.75 (d, J = 6.8 Hz), 124.19, 128.22, 128.28, 130.46, 139.51, 147.16 (d, J = 5.7 Hz).


(Z)-5,5-Dimethyl-2-[(5-trisopropyllysiloxy)-1-(trimethylsilyl)-1-penten-3-yl]oxy]-1,3,2-dioxaphosphinane 2-Oxide (3e)

THP-protection of 5-[(trisopropylsilyle)oxy]-1-pentyn-3-ol followed by silylation gave γ-silylated propargylic alcohol derivative. Next, DIBAL-H reduction followed by deprotection afforded γ-silylated allylic alcohol. Finally, the phosphorylation of the γ-silylated allylic alcohol (2.0 mmol) provided allylic phosphate 3e in 50% (171 mg, 1.0 mmol).

Colorless oil.
**(E)-Methyldiphenyl(1-phenyl-4-hexen-3-yl)silane (4ac)**

Colorless oil; yield: 65.6 mg (92%).

1H NMR (300 MHz, CDCl$_3$) $\delta$ 0.05 (s, 9H), 1.40–1.46 (m, 1H), 1.52–1.78 (m, 2H), 1.71 (d, $J = 4.8$ Hz, 3H), 2.43 (ddd, $J = 13.5$, 9.6, 6.9 Hz, 1H), 2.77 (ddd, $J = 13.5$, 9.3, 4.5 Hz, 1H), 5.23 (dd, $J = 15.0$, 7.8 Hz, 1H), 5.30 (dq, $J = 15.0$, 4.8 Hz, 1H), 7.15–7.19 (m, 3H), 7.25–7.30 (m, 2H).

13C NMR (75.4 MHz, CDCl$_3$) $\delta$ 31.31, 35.41, 123.91, 123.93, 125.67, 128.20, 128.27, 128.33, 123.16, 125.60, 128.29, 128.59, 132.17, 143.18.

Anal. Calcd for C$_{23}$H$_{28}$Si: C, 81.75; H, 9.15%. Found: C, 81.53; H, 9.76%.

**(E)-Benzyldimethyl(1-phenyl-4-hexen-3-yl)silane (4ad)**

Colorless oil; yield: 58.0 mg (94%).

1H NMR (300 MHz, CDCl$_3$) $\delta$ 0.12 (s, 3H), 0.10 (s, 3H), 1.48–1.80 (m, 3H), 1.72 (d, $J = 5.1$ Hz, 3H), 2.06 (s, 2H), 2.42 (ddd, $J = 13.5$, 9.0, 7.2 Hz, 1H), 2.77 (ddd, $J = 13.5$, 9.6, 4.2 Hz, 1H), 5.25 (dd, $J = 16.2$, 8.4 Hz, 1H), 5.31 (dq, $J = 16.2$, 5.1 Hz, 1H), 6.93–6.95 (m, 2H), 7.03–7.08 (m, 1H), 7.15–7.21 (m, 5H), 7.26–7.31 (m, 2H).

13C NMR (75.4 MHz, CDCl$_3$) $\delta$ 3.28, 35.10, 55.68, 55.83, 111.09, 111.68, 120.12, 123.37, 127.60, 128.86, 131.77, 134.12, 135.63, 138.33, 146.99, 148.75.

Anal. Calcd for C$_{23}$H$_{32}$O$_2$Si: C, 74.95; H, 8.75%. Found: C, 75.11; H, 8.77%.

**(E)-2-[6-(Trimethylsilyl)-7-non en-1-yl]isoindoline-1,3-dione (4da)**

Colorless oil; yield: 67.5 mg (87%).

1H NMR (300 MHz, CDCl$_3$) $\delta$ 0.22 (s, 3H), 0.24 (s, 3H), 1.28–1.70 (m, 5H), 1.64 (d, $J = 4.8$ Hz, 3H), 2.38 (ddd, $J = 14.4$, 8.4, 6.0 Hz, 1H), 2.51 (ddd, $J = 14.4$, 9.3, 4.5 Hz, 1H), 3.84 (s, 3H), 3.85 (s, 3H), 5.18 (dd, $J = 15.3$, 7.5 Hz, 1H), 5.22 (dq, $J = 15.3$, 4.8 Hz, 1H), 6.63–6.66 (m, 2H), 6.74–6.77 (m, 1H), 7.30–7.38 (m, 3H), 7.38–7.49 (m, 2H).

13C NMR (75.4 MHz, CDCl$_3$) $\delta$ 3.32, 11.90, 17.92, 18.02, 25.56, 28.81, 29.08, 32.88, 32.89, 63.50, 122.35, 132.63. HRMS–APCI (m/z): [M]$^+$ calcd for C$_{23}$H$_{24}$O$_4$Si$_2$: 370.3087; found, 370.3083.

**(E)-[9-(1,3-Dioxan-2-yl)-2-non en-4-yl](benzyl)dimethylsilane (4df)**

Colorless oil; yield: 57.0 mg (79%).

1H NMR (300 MHz, CDCl$_3$) $\delta$ 0.06 (s, 9H), 1.26–1.54 (m, 4H), 1.65 (d, $J = 4.8$ Hz, 3H), 1.71–1.78 (m, 1H), 2.46 (ddd, $J = 15.0$, 8.1, 6.6 Hz, 1H), 2.58 (ddd, $J = 15.0$, 9.6, 5.1 Hz, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 5.17 (dd, $J = 15.3$, 7.2 Hz, 1H), 5.24 (dq, $J = 15.3$, 4.8 Hz, 1H), 6.70–6.72 (m, 2H), 6.77–6.80 (m, 1H).

13C NMR (75.4 MHz, CDCl$_3$) $\delta$ 3.34, 18.01, 28.42, 31.34, 32.75, 35.23, 55.68, 55.82, 111.08, 111.69, 120.14, 122.59, 132.34, 135.69, 146.99, 148.75.

Anal. Calcd for C$_{23}$H$_{30}$NO$_2$Si: C, 70.53; H, 8.97%. Found: C, 70.52; H, 10.02%.
\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta \) -0.11 (s, 3H), -0.10 (s, 3H), 1.16–1.63 (m, 12H), 1.66 (d, \(J = 4.8\) Hz, 3H), 2.02–2.16 (m, 1H), 2.06 (s, 2H), 3.76 (dd, \(J = 12.3, 2.1\) Hz, 2H), 4.10 (dd, \(J = 10.8, 5.1\) Hz, 2H), 4.50 (t, \(J = 5.1\) Hz, 1H), 5.16 (dd, \(J = 15.3, 7.8\) Hz, 1H), 5.21 (dq, \(J = 15.3, 4.8\) Hz, 1H), 6.97–7.00 (m, 2H), 7.03–7.08 (m, 1H), 7.18–7.23 (m, 2H).

\(^13\)C NMR (75.4 MHz, CDCl\(_3\)) \(\delta \) -5.32–5.28, 18.02, 23.75, 23.82, 25.74, 28.77, 29.08, 29.24, 31.70, 35.17, 66.86, 102.47, 123.09, 123.86, 124.18, 123.29, 140.49.

Anal. Calcd for C\(_{24}\)H\(_{32}\)O\(_8\)Si: C, 72.31; H, 10.06%. Found: C, 73.21; H, 10.33%.

\((E)-5\)-(Dimethylphenylsilyl)-1-[(thiopen-2-yl)-6-ocan-1-ylacetate (4gb)

Colorless oil; yield: 54.6 mg (73%).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta \) 0.22 (s, 3H), 0.23 (s, 3H), 1.07–1.50 (m, 5H), 1.62 (d, \(J = 4.8\) Hz, 1.5H), 1.63 (d, \(J = 4.8\) Hz, 1.5H), 1.79–1.93 (m, 2H), 2.02 (s, 2H), 5.94 (t, \(J = 7.2\) Hz, 0.5H), 5.95 (t, \(J = 7.2\) Hz, 0.5H), 6.92–6.98 (m, 2H), 7.23–7.26 (m, 1H), 7.34–7.35 (m, 3H), 7.44–7.48 (m, 2H).

\(^13\)C NMR (75.4 MHz, CDCl\(_3\)) \(\delta \) -5.46, -5.41, -4.46, -4.42, 17.97 (\(\times 2\)), 21.09 (\(\times 2\)), 24.87, 25.00, 28.29, 28.31, 32.02, 32.24, 35.68, 35.90, 71.09, 71.30, 123.56, 123.62, 125.11, 125.20, 125.77, 125.91, 126.50, 126.52, 127.67, 126.91, 131.43, 131.49, 134.09, 134.11, 138.15, 138.19, 143.64, 170.41, 170.44.

HRMS–ESI (m/z): [M+Na] \(^{+}\) calcd for C\(_{32}\)H\(_{51}\)NO\(_4\)Si\(_2\)Na, 626.40368; found, 626.40313.

\((E)-5\)-(Dimethyl-1-phenyl-4-hepten-3-yl)(phenylsilane (4af)

Colorless oil; yield: 59.4 mg (92%).

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta \) 0.22 (s, 3H), 0.24 (s, 3H), 0.96 (d, \(J = 6.6\) Hz, 3H), 0.98 (d, \(J = 6.6\) Hz, 3H), 1.50–1.78 (m, 5H), 2.67–2.76 (m, 1H), 5.15 (dd, \(J = 15.3, 7.8\) Hz, 1H), 5.22 (dd, \(J = 15.3, 6.0\) Hz, 1H), 7.08–7.10 (m, 2H), 7.13–7.18 (m, 1H), 7.22–7.27 (m, 2H), 7.30–7.34 (m, 3H), 7.42–7.45 (m, 2H).

\(^13\)C NMR (75.4 MHz, CDCl\(_3\)) \(\delta \) -5.34, -4.53, 22.87, 23.03, 30.81, 31.41, 31.70, 35.18, 125.58, 127.29, 127.60, 128.25, 128.63, 128.89, 134.18, 137.17, 138.07, 142.89.

HRMS–EI (m/z): [M\(^{+}\)] \(^{+}\) calcd for C\(_{26}\)H\(_{45}\)NO\(_2\)Si\(_2\)Na, 626.40313; found, 622.2115.

Acknowledgement

This work was supported by Grants-in-Aid for Scientific Research (B) and for Young Scientists (B), JSPS. We thank MEXT for financial support in the form of a Global COE grant (Project No. B01: Catalysis as the Basis for Innovation in Materials Science).

References and Notes


(21) For the synthesis of \( \alpha \)-arylated allylsilanes through Pd-catalyzed \( \gamma \)-selective and stereospecific allyl–aryl coupling between \( \gamma \)-silylated allylic esters and arylboronic acids, see: Li, D.; Tanaka, T.; Ohmiya, H.; Sawamura, M. Org. Lett. 2010, 12, 3344–3347.
