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Copper(II)-catalyzed allylation of propargylic and allylic alcohols by allylsilanes: a facile synthesis of 1,5-enynes

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Abstract

Propargylic alcohols undergo smooth deoxygenative allylation with allylsilanes in the presence of a solution of 10 mol % of copper(II) tetrafluoroborate in acetonitrile to afford the corresponding 1,5-enynes in good to high yields under mild and neutral conditions. Scandium triflate is also found to catalyze efficiently the nucleophilic substitution of propargylic alcohols with allylsilanes.

Keywords: Allylation; Propargylic alcohols; Allylic alcohols; 1,5-Enynes; Cu(II) reagents

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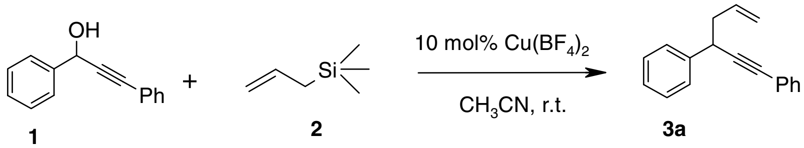
The Lewis acid catalyzed coupling of propargyl alcohols and halides with allylsilanes is an important transformation, as it provides a direct approach to synthetically valuable 1,5-enynes.[1–4] The Nicholas reaction has been widely used as a powerful tool for the substitution of propargylic alcohols.[5] However, this method generally requires a stoichiometric amount of $Co_2(CO)_8$ and several steps are necessary to obtain the propargylic product from propargylic alcohols through cationic propargylic complexes.[6–9] Subsequently, several transition metal catalyzed propargylic substitutions have been reported using ruthenium, rhenium(V), and gold(III) catalysts.[10–15] Recently, boron(III) and bismuth(III) reagents have also been used to accomplish this transformation.[16–19] In most cases, either a high reaction temperature or an additive is required to enhance the leaving ability of the hydroxyl group. Therefore, the direct catalytic substitution of alcohols with allylsilanes using a simple and efficient catalyst is highly desirable.

In this Letter, we report a direct and facile method for the nucleophilic substitution of propargylic alcohols with allylsilanes. Initially, we attempted the allylation of 1,3-diphenyl-2-propyn-1-ol (**1**) with allyltrimethylsilane (**2**) in the presence of 10 mol % of $Cu(BF_4)_2$. The reaction proceeded smoothly at room temperature in acetonitrile to give 1,5-enyne **3a** in 85% yield (Scheme 1).

This interesting catalytic activity of $Cu(BF_4)_2$ in acetonitrile provided the incentive for further study of reactions with different propargylic alcohols. A wide range of



Scheme 1. Preparation of **3a**.

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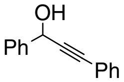
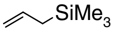
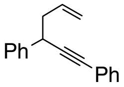
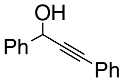
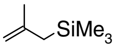
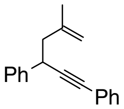
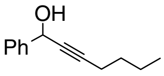
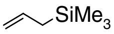
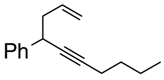
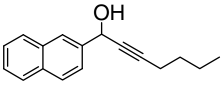
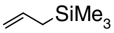
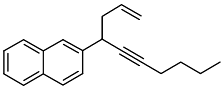
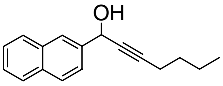
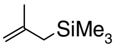
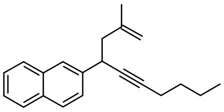
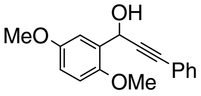
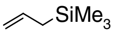
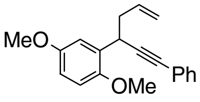
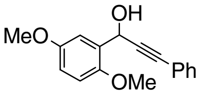
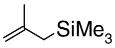
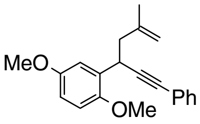
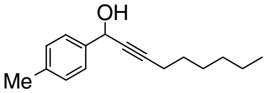
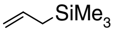
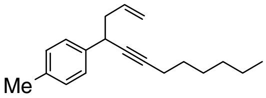
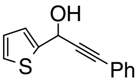
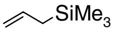
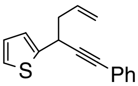
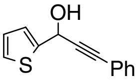
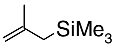
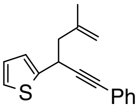
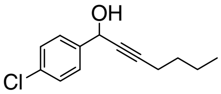
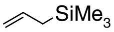
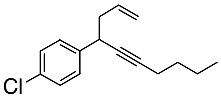
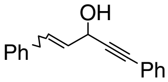
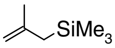
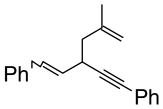
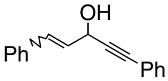
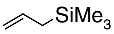
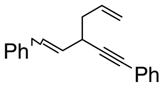
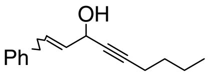
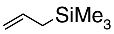
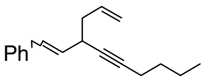
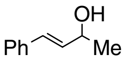
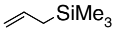
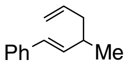
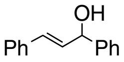
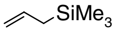
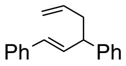
Table 1
$Cu(BF_4)_2$-catalyzed allylation of propargyl alcohols with allylsilanes

Entry	Propargyl alcohol	Allylsilane	Product[a]	Time (h)	Yield[b] (%)
a				4.0	85
b				4.0	86
c				4.5	78
d				3.5	86
e				4.0	85
f				3.5	88
g				3.5	86
h				5.5	78
i				3.0	85
j				3.0	84
k				6.0	86
l				4.0	84
m				4.0	88
n				4.5	85

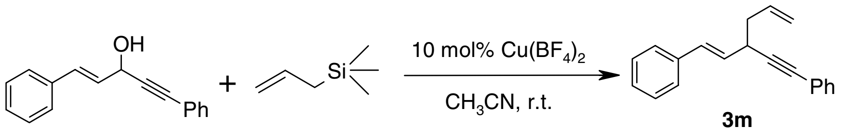
(continued on next page)

Table 1 (*continued*)

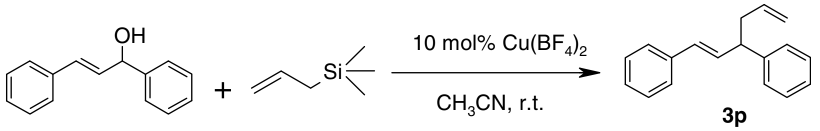
Entry	Propargyl alcohol	Allylsilane	Product[a]	Time (h)	Yield[b] (%)
o				2.0	88
p				3.0	86

[a] All products were characterized by NMR, IR, and mass spectrometry.

[b] Yield refers to pure products after chromatography.



Scheme 2. Preparation of **3m**.



Scheme 3. Preparation of **3p**.

propargylic alcohols underwent smooth allylation with allylsilanes to afford the corresponding 1,5-enynes in high yields (Table 1, entries **b**–**k**). In all cases, the reactions proceeded smoothly at room temperature under the influence of 10 mol % of $Cu(BF_4)_2$. In addition, doubly activated (*E*)-1,5-diphenyl-1-penten-4-yn-3-ol underwent facile nucleophilic substitution with allylsilanes to furnish the respective 3-allylpent-1-en-4-yne derivatives (Scheme 2, Table 1, entries **l**, **m**, and **n**).

Likewise, doubly activated allylic alcohols reacted rapidly with allyltrimethylsilane to furnish 1,5-dienes in excellent yields (Table 1, entries **o**–**p**, Scheme 3).

The method is compatible with halides, aryl alkyl ethers, alkynes, and alkenes present in the molecule. Similarly, 2-methylallylsilane also reacted well with propargylic alcohols to provide methyl substituted 1,5-enynes (Table 1, entries **b**, **e**, **g**, **j**, and **l**). It should be noted that the allylation of all substrates led exclusively to the formation of propargylic products and no traces of allenic side products were detected. However, in the absence of catalyst, the reaction did not proceed even after a long reaction time. The scope and generality of this process is illustrated in Table 1.[20]

Furthermore, alkyl substituted propargylic alcohols failed to undergo allylation under the present reaction conditions. As solvent, acetonitrile gave the best results. All products were characterized by ^1H, ^{13}C NMR, IR, and mass spectrometry. No additives or activators were required for activation of the –OH group. The effects of various copper(II) salts such as $Cu(BF_4)_2$, $Cu(OTf)_2$, $Cu(acac)_2$, and $Cu(ClO_4)_2$ were screened for this conversion. Of these catalysts, $Cu(BF_4)_2$ was found to be most effective in

Table 2
$Sc(OTf)_3$-catalyzed allylation of propargyl alcohols with allylsilanes

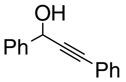
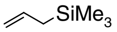
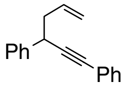
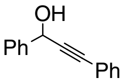
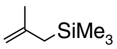
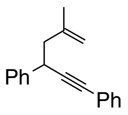
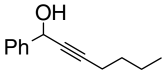
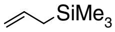
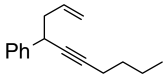
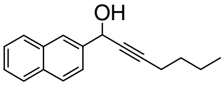
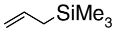
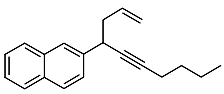
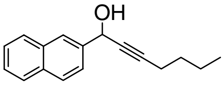
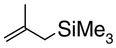
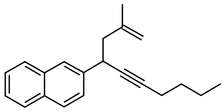
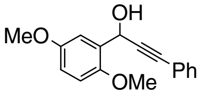
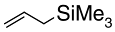
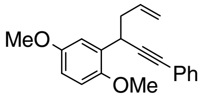
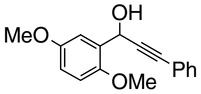
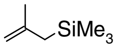
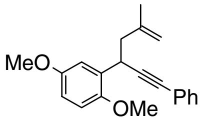
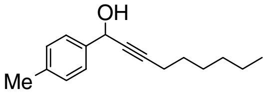
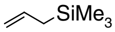
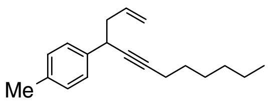
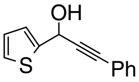
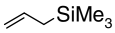
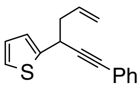
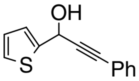
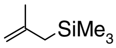
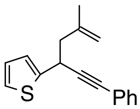
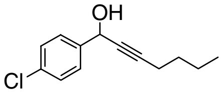
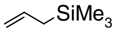
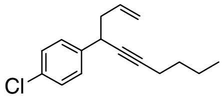
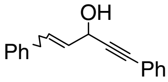
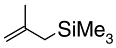
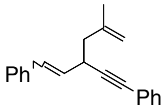
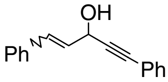
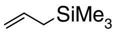
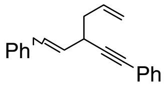
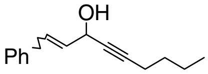
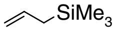
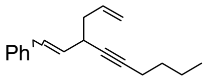
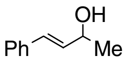
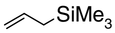
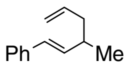
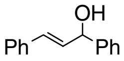
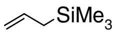
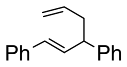
Entry	Propargyl alcohol	Allylsilane	Product[a]	Time (h)	Yield[b] (%)
a				1.0	84
b				1.0	80

Table 2 (*continued*)

Entry	Propargyl alcohol	Allylsilane	Product[a]	Time (h)	Yield[b] (%)
c				1.5	86
d				0.5	88
e				0.5	86
f				0.5	92
g				0.5	90
h				1.5	84
i				0.25	96
j				0.25	95
k				1.2	78
l				0.6	80
m				0.5	82
n				0.8	80
o				1.4	86
p				2.0	84

[a] All products were characterized by NMR, IR, and mass spectrometry.

[b] Yield refers to pure products after chromatography.

terms of conversion. A solution of 10 mol % of $LiBF_4$ in acetonitrile was not so effective for this reaction, albeit, acetonitrile can form the complex $CH_3CN^+–BF_3$ which acts as the catalytic species. The use of $Cu(BF_4)_2$ makes this procedure very mild, simple, and convenient. Alternatively, 5 mol % of scandium triflate was also found to be an equally effective catalyst for this conversion and comparative results are presented in Table 2.

In summary, a solution of 10 mol % of Cu(II) tetrafluoroborate in acetonitrile was shown to be a highly efficient and convenient catalytic medium for the preparation of 1,5-enynes via the allylation of propargylic and allylic alcohols with allylsilanes. In addition to its simplicity and mild reaction conditions, this method provides good yields of 1,5-enynes with high selectivity, which makes it a useful and attractive process.

Acknowledgment

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References and notes

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20. *General procedure*: To a stirred solution of the propargylic alcohol (1 mmol) and $Cu(BF_4)_2$ (10 mol %) or 5 mol % $Sc(OTf)_3$ in acetonitrile (10 mL), allyltrimethylsilane (1.5 mmol) was added slowly dropwise at 0 °C and the resulting mixture allowed to stir at room temperature for the appropriate time (Tables 1 and 2). After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with water and extracted with dichloromethane (2×10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. Removal of the solvent followed by purification on silica gel using ethyl acetate/*n*-hexane (1:9) as eluent afforded pure 1,5-enyne. Spectral data for selected products: Entry **d** (Table 1): IR (KBr): ν 3055, 2957, 2930, 2865, 1637, 1601, 1506, 1436, 1368, 1323, 1125, 914, 816, 746 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.77–7.72 (m, 4H), 7.45–7.35 (m, 3H), 5.90–5.76 (m, 1H), 5.06–4.98 (m, 2H), 3.77 (t, 1H, $J = 6.9$ Hz), 2.52, (t, 2H, $J = 6.9$ Hz), 2.25 (t, 2H, $J = 6.8$ Hz), 1.58–1.39 (m, 4H), 0.94 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.3, 135.8, 133.4, 132.2, 127.9, 127.7, 127.5, 125.9, 125.4, 116.7, 83.9, 81.0, 42.8, 38.1, 31.1, 21.9, 18.4, 13.5. Mass (ESI): 263 (M + H), 261 (M−H), 221 (M−41). Entry **f** (Table 1): IR (KBr): ν 2935, 2833, 1497, 1462, 1278, 1241, 1216, 1049, 915, 802, 756, 692 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 7.43–7.22 (m, 5H), 7.15 (d, $J = 2.2$ Hz,1H), 6.74–6.63 (m, 2H), 6.02–5.82 (m, 1H), 5.11–5.02 (m, 2H), 4.32 (t, 1H, $J = 6.9$ Hz), 3.78 (s, 3H), 3.74 (s, 3H), 2.63–2.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.4, 150.3, 135.7, 131.5, 130.7, 128.0, 127.6, 123.7, 116.6, 115.0, 111.7, 111.2, 91.1, 83.2, 55.8, 55.5, 40.7, 31.9; Mass (ESI): 292 (M + H), 251 (M−41).