

Copper-Catalyzed Vinylsilane Allylation

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Soft reaction conditions, particularly important in total synthesis, have dragged many researchers into the field of silylated organic compounds. Hereby, we describe a new copper-catalyzed vinylsilane transformation. Various vinylsilanes were allylated by using a copper(I) salt, and this led to the formation of polysubstituted 1,4-dienes bearing sensitive moieties such as halogens, ketones, and aldehydes.

Introduction

Functional-group compatibility and soft reaction conditions are of utmost importance in organic synthesis. Allowing sensitive groups to remain unprotected usually leads to much shorter and efficient synthetic pathways. Organosilicon compounds have been shown to be perfect candidates to meet these criteria, as they are stable under various conditions.^[1] Supported by the recent development of highly efficient hydrosilylation and silylcupration catalysts (Scheme 1),^[2] vinylsilanes have proven to be reagents of choice for the introduction of unsaturation into complex organic frameworks. Although the more common way to synthesize β -(E)-vinylsilanes uses platinum-catalyzed hydrosilvlation of alkynes,^[3] cross-metathesis with the use of ruthenium catalysts^[4] might be used as well; β -(Z)- and α vinylsilanes can be obtained by iridium-[5] and rutheniumcatalyzed^[6] hydrosilylation, respectively.



R = alkyl, aryl, alkoxy

Scheme 1. Formation of different vinylsilanes by using transitionmetal catalysis.

The lack of reactivity induced by the stable nature of vinylsilanes has been overcome by the use of transition

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metals. Although palladium cross-coupling methodologies have been used for decades,^[7] copper-catalyzed vinylsilane transformations have also recently started to emerge as powerful tools. Takeda showed that a Brook rearrangement might be used to promote the formation of a vinylcopper species, which could be captured by various electrophiles.^[8] Shibasaki et al. reported the (diphosphine)copper(I)-catalyzed enantioselective transfer of vinylsilanes to aldehydes for the straightforward preparation of enantiomerically enriched allylic alcohols.^[9] Chiral N-heterocyclic carbenes have also been used to promote the conjugated addition of vinylsilanes onto α , β -unsaturated carbonyl compounds with high enantioselectivities, as recently shown by Hoveyda et al.^[10]

Over the past few years, copper-catalyzed allylic substitution has emerged as a powerful strategy to insert various nucleophiles into a carbon backbone.^[11] Among others, it is nowadays possible to graft magnesium-,^[12] lithium-,^[13] zinc-,^[14] boron-,^[15] and silylboronate-containing^[16] nucleophiles enantioselectively. Copper-catalyzed allylation reactions of a vinyl moiety to form 1,4-dienes from vinylaluminum^[17] and vinylboron^[18] reagents have also recently been developed. The resulting 1,4-diene fragments are useful intermediates and are also present in several natural-product structures.^[19]

Herein we wish to describe our first results regarding a new and robust methodology that uses simple copper salts as efficient catalysts for the allylation of various vinylsilanes by using allyl bromides as electrophilic partners. β -(*E*)-Vinylsilanes, easily available from the corresponding alkynes, were used as models for the initial optimizations. These β -(*E*)-vinylsilanes bear different base- and nucleophile-sensitive moieties, including halogens, esters, and ketones.

Results and Discussion

We started our experiments with model vinylsilane **1a** bearing a triethoxysilane group acting as an activated sili-

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SHORT COMMUNICATION

con moiety (Table 1). The initial idea was to promote transmetalation between the silicon atom and the copper(I) source to generate a vinylcopper(I) intermediate that should then be easily captured by the electrophile. We found that without any activating agent, no reaction was observed (Table 1, Entry 1). Several nucleophilic bases were tested to activate the silane and facilitate the migration of the vinylic fragment to the copper atom. Both cesium fluoride and sodium *tert*-butoxide did not promote the reaction (Table 1, Entries 2 and 3), and this left the vinylsilane unchanged. The use of tetrabutylammonium fluoride (TBAF) as a fluoride source gave only the protodesilylated products, as this reagent always contains various amounts of water.^[20]

Table 1. Initial optimization of the coupling reaction to afford 2a.

BzO	Si(OEt) ₃		Cu ^l activating agent		BzO	~~/
	1a ₊ ∕/Br		solvent r.t., 16 h		2a	
	(2.0)	equiv.)				
Entry	Solvent	Cu ^I salt (equiv.)		Activating agent (equiv.)		Yield [%] ^[a]
1	MeCN	CuI (1.1)		_		_
2	MeCN	CuI (1.1)		CsF (1.2)		_
3	MeCN	CuCl (1.1)		NaOtBu (1.2)		_
4	MeCN	CuI (1.1)		TBAT (1.2)		60
5	MeCN	CuI (1.1)		TBAT (2.4)		87
6	MeCN	CuI (0.2)		TBAT (2.4)		86 (84 ^[b])
7	MeCN	CuI (0.1)		TBAT (2.4)		53
8	THF	CuI (0.2)		TBAT (2.4)		56 ^[c]
9	DMF	CuI (0.2)		TBAT (2.4)		74
10	MeCN			TBAT (2.4)		_

[a] Determined by analysis of the crude reaction mixture by ${}^{1}H$ NMR spectroscopy by using an internal standard. [b] Yield of the isolated product. [c] Conversion [%].

However, the use of tetrabutylammonium difluorotriphenylsilicate (TBAT) as an anhydrous fluorine source with a stoichiometric amount of copper(I) iodide allowed us to observe the formation of desired allylated product 2a in a modest 60% yield (Table 1, Entry 4). This could be improved to 87% yield (Table 1, Entry 5) if 2.4 equiv. of TBAT was used under the same reaction conditions. To evaluate the capacity of the copper(I) reagent to act as a catalyst, the loading of copper(I) iodide was evaluated. The use of 20 mol-% of CuI (Table 1, Entry 6) allowed us to keep a satisfactory 86% yield. However, reducing the catalytic loading to 10 mol-% led to a decreased 53% yield (Table 1, Entry 7). THF, used as a less-coordinating solvent, was tested, and this resulted in a poor 56% conversion (Table 1, Entry 8), which indicates that relatively strong stabilization was required. DMF, in contrast, acting as a much stronger coordinating solvent, did not give better results than acetonitrile, and the product was obtained in only 74% yield (Table 1, Entry 9). A control reaction was also performed without added copper and did not lead to any substrate conversion (Table 1, Entry 10). The use of 0.2 equiv. of CuI in acetonitrile (Table 1, Entry 6) was chosen as optimal with 86% yield.

Although model substrate **1a** was considered to be quite sensitive because of the presence of a carbonyl group and because of the leaving ability of the benzoyl moiety, it was important to test the limits of the functional-group compatibility. Using the optimal conditions (Table 1, Entry 6), six other vinylsilanes were allylated by using allyl bromide (Figure 1). A change from the benzoyl group to a more robust benzyl group led to better results, and product 2b was isolated in 98% yield. Shortening the tether between the olefin and the functional group did not influence the reactivity, as shown with tosylamine 2c. A highly hindered and chelating vinylsilane also reacted accordingly, as revealed by diethyl malonate 2d, which was obtained in 89% yield. The presence of an aryl bromide was tolerated and gave corresponding diene 2e in 80% yield. A vinylsilane bearing a more polar phthalimide group was easily allylated to give 2f in 85% yield. Interestingly, the presence of a ketone was fully tolerated as shown by the formation of 2g in 86% yield.



Figure 1. Substrate scope of the vinylsilane allylation. Yields of isolated products are given in parentheses.

Optimization experiments including varying the Cu^I source led us to choose copper(I) thiophenecarboxylate (CuTC) to explore the electrophile scope. Although no major difference was observed, CuTC provided the best γ/α selectivity over CuI and various other copper(I) sources. Providing the best results in the first stage of the substrate exemplification (Figure 1), vinylsilane **1b** was also used for the electrophile screening (Figure 2). Cinnamyl bromide led to the formation of **3a** in 93% yield with $\gamma/\alpha = 84:16$. Replacing the aryl group by an alkyl group such as cyclohexyl gave **3b** in a good 89% yield with only a slight decrease in selectivity.

Aryl moieties bearing halogen substituents led to the formation of aryl bromide **3c** and aryl chloride **3d** in 86 and 76% yield, respectively, and no major change in the γ/α selectivity. An electron-rich substituent such as a thiophene induced a decrease in the yield to a moderate 67% for **3e** and a slight increase in selectivity. Surprisingly, the presence of an aldehyde in the aryl moiety allowed the formation of



Figure 2. Electrophile scope of the vinylsilane allylation. Yields of isolated products are given in parentheses.

desired product **3f** in 79% yield, which is very satisfactory considering the sensitive nature of such an electrophile. The selectivity was still within standards with $\gamma/\alpha = 82$:18, and the aldehyde group remained intact. No 1,4- to 1,3-diene isomerization was observed during any workup and chromatographic separation.

As α -olefins are important building blocks in organic synthesis, it was interesting to know whether or not α -vinylsilanes would react under our standard conditions. Both **4a** and **4b** were synthesized from the corresponding alkynes according to the Trost and Ball method^[6] with $\alpha/\beta(E+Z) =$ 90:10 and 92:8, respectively. The mixture of isomers was allylated under the previous optimal conditions (Figure 3). Benzoyl-bearing vinylsilane **4a** was successfully allylated to α -olefin **5a** in 90% yield. Benzyl-functionalized vinylsilane **4b** smoothly afforded **5b** in 97% yield (Figure 3). In both cases, the $\alpha/\beta(E+Z)$ ratio remained unchanged, and no isomerization took place.



Figure 3. α -Vinylsilane allylation reactions. Yields of isolated products are given in parentheses.

Using internal alkynes to perform the ruthenium-based hydrosilylation led to the formation of trisubstituted β -(Z)-vinylsilanes such as α , β -unsaturated ketone **6** (Figure 4).

The mixture of isomers was allylated under our standard conditions to provide desired polysubstituted diene 7 in a satisfactory 73% yield. Notably, no 1,4- or 1,2-addition onto the carbonyl group was observed.



Figure 4. Trisubstituted alkene synthesis.

Conclusions

An efficient catalytic method to functionalize vinylsilanes with allylic electrophiles has been developed. Broad functional-group compatibility was possible by using a copper(I) reagent and allyl bromides. The allylation reactions proceeded even in the presence of esters, ketones, and aldehydes with yields up to 98%. α -Vinylsilanes showed interesting reactivity, as they delivered the corresponding α -olefins in good yields. Finally, the use of a trisubstituted vinylsilane showed the extent of this method, which led to the construction of polysubstituted 1,4-dienes. Further studies concerning the copper-catalyzed functionalization and applications of vinylsilanes are ongoing and will be reported in due time.

Experimental Section

General Method: To a solution of the vinylsilane (0.20 mmol, 1.0 equiv.) in MeCN (2 mL) was added the allylic bromide (0.40 mmol, 2.0 equiv.) and the copper(I) salt (0.04 mmol, 0.2 equiv.). TBAT (0.48 mmol, 2.4 equiv.) was added, and the resulting mixture was stirred at room temperature for 16 h. The solvent was removed in vacuo to afford a dark brown oil. This oil was diluted with a minimum amount of CH_2Cl_2 (0.5 mL), filtered through a short pad of silica, and eluted with diethyl ether (25 mL). The ethereal solution was concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography by using CH_2Cl_2 in petroleum ether to afford the desired olefin.

Supporting Information (see footnote on the first page of this article): Experimental details, characterization data, and copies of the ¹H and ¹³C NMR spectra of all key intermediates and final products.

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SHORT COMMUNICATION

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