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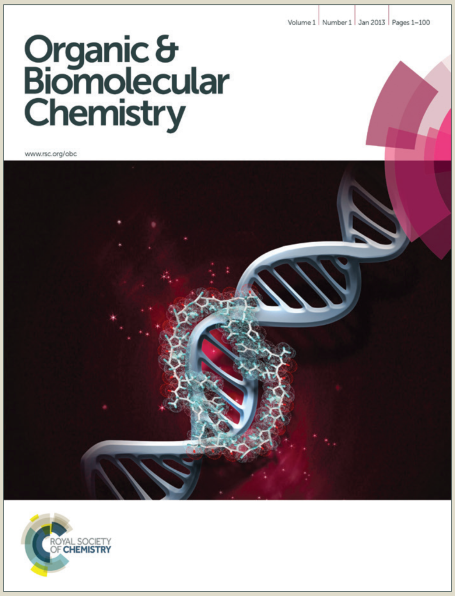

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Copper(II)-Catalyzed Highly Regio- and Stereo-selective Hydrosilylation of Unactivated Internal Alkynes with Silylborate in Water

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The highly regio- and stereoselective hydrosilylation of internal alkynes with silylborate catalyzed by $Cu(OTf)_2$ with 1,10-phenanthroline as ligand in the presence of Cs_2CO_3 in water was developed. This protocol was applied efficiently in the aqueous synthesis of multi-substituted vinylsilanes.

Vinylmetal species are extremely important building blocks in organic synthesis. Among them, vinylsilanes are becoming more and more attractive due to their stability, low toxicity, and easy of handling.[1] Hydrosilylation of alkynes is the most straightforward method to access vinylsilanes.[2] Although Fe-,[3] Co-[4] and Ni-[5] complexes have been used as catalysts for the hydrosilylation of alkynes with silanes, the more widely employed were high-cost noble metal catalysts. Moreover, when unactivated internal alkynes underwent the hydrosilylations with silanes, it usually gave inferior regio- and stereosectivity.[6] Due to the difficulty 0f control in the regio- and stereoselectivity, few examples of efficient and highly stereo- and regioselective hydrosilylation of unactivated internal alkynes were reported.

Recently, on the basis of the environmental concern, aqueous organic reactions catalyzed by transition-metals have made great progresses.[7] However, there were few examples of the hydrosilylation of alkynes with silanes in water.[8] Li, de Jesús, E. and Terennas. respectively reported the synthesis of vinylsilanes by hydrosilylations of terminal alkynes with silanes in water. Unfortunately, when internal alkyne, 1-phenyl-propyne, was treated with triethylsilane in the presence of catalyst $RuCl(PPh)_3$ (5 mol%) in water,[8a] we only got complicated mixtures. Thus, the development of highly regio- and stereoselective method for the hydrosilylation of internal alkynes in water is still a challenge task. It is necessary to search for novel catalytic system, efficient catalyst and silylation reagent, for aqueous hydrosilylation of unactivated internal alkynes.

Commercially available $Me_2PhSiBpin$ is a powerful and efficient silylation reagent.[9] The electronegativity difference between boron and silicon allows the chemoselective activation of the Si-B bond. It has been applied broadly in the formation of C-Si bond.[10] Loh and Oestreich reported copper(I)-catalyzed hydrosilylation of alkynes and allenes with silylborate.[11] Tsuji and co-workers reported the copper-catalyzed silylcarboxylation of internal alkynes by employing carbon dioxide and silylborates to give the silylactone in high yield with excellent selectivity.[12] As for the aqueous C-Si bond formation by employing silylborate, most recently, Santos[13] and Lipshutz,[14] respectively developed copper-catalyzed silylation of conjugated alkynes with carbonyl or carboxyl moiety in water through a conjugated addition process. Until now, there was no report on the hydrosilylation of unactivated internal alkynes with silylborate in water.

Herein, we like to report the $Cu(OTf)_2$-catalyzed highly stereo- and regioselective synthesis of multi-substituted vinylsilanes in water with unactivated internalkynes by employing $Me_2PhSiBpin$ as an efficient silylation reagent.

Initially, we examined the reaction of 1-phenyl-propyne (**1a**) with $Me_2PhSiBpin$ (**2**) in the presence of $Cu(OTf)_2$ (2.5 mol%) and Cs_2CO_3 (10 mol%) in water under N_2 atmosphere. When no ligand was used, a trace amount of product of **3a** (β**- +** α-isomer**)** could be detected (Table 1, entry 1).

Then, various ligands (Fig. 1) were screened. In the presence of **L1** and **L2**, only trace product was detected (Table 1, entries 2 and 3). However, when pyridine **L3** was added as the ligand in the absence of additional base, product **3a** was obtained in 22% yield. To our delight, the addition of Cs_2CO_3 (10 mol%) as additional base increased the yield to 66%, and the regioisomeric ratio (β/α)[15] was raised from 83 : 17 to 92 : 8 (Table1, entries 4 and 5). Thus, both additional base and ligand are crucial for copper catalyzed reaction of internal alkyne with silylboronate in water. When pyridine derived ligands **L4-L6** were employed in the aqueous reaction of **1a** with **2** catalyzed by $Cu(OTf)_2$, excellent yields of **3a** were obtained,

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but with slightly less regioselectivities (entries 6~8). On the contrary, 4-hydroxymethyl-pyridine **L7** gave relatively lower yield (80%) with high regioselectivity (β/α = 92 : 8) (entry 9). 2,2'-bipyridine ligand **L8** gave moderate yield and regioselectivity (Table 1, entry 10). To our delight, 1,10-phenanthroline **L9**, which has more rigid structure than **L8**, afforded both high yield (97%) and excellent regioselectivety (β/α = 94 : 6) (Table 1, entry 11). However, when the loading of **L9** was increased from 3 mol% to 6 mol%, the reaction of **1a** with **2** did not proceed at all (entry 16). It could be assumed that the inactivated intermediate of Cu(II) with 1,10-phenanthroline was formed (Fig. 2),[16] which could not go through the subsequent transmetalation process.

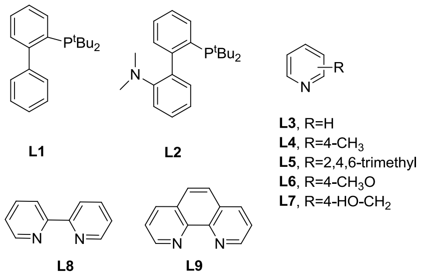
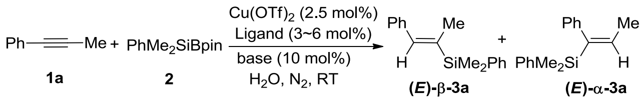


Figure 1. Ligands for Cu(II)-catalyzed reaction of **1a** with **2** in water.

Table 1. Cu(II)-Catalyzed Hydrosilylation of **1a** with **2** in Water.[a]



Entry	Ligand (mol%)	Base	Yield of **3a** (%)[b] (β/α)[c]
1[d]	---	Cs_2CO_3	trace[e]
2	**L1** (6)	Cs_2CO_3	trace[e]
3	**L2** (6)	Cs_2CO_3	trace[e]
4 [f]	**L3** (6)	---	22 (83/17)
5	**L3** (6)	Cs_2CO_3	66 (92/8)
6	**L4** (6)	Cs_2CO_3	99 (87/13)
7	**L5** (6)	Cs_2CO_3	99 (88/12)
8	**L6** (6)	Cs_2CO_3	91 (87/13)
9	**L7** (6)	Cs_2CO_3	80 (92/8)
10	**L8** (3)	Cs_2CO_3	70 (84/16)
11	**L9** (3)	Cs_2CO_3	97 (94/6)
12	**L9** (3)	K_2CO_3	26 (81/19)
13	**L9** (3)	Na_2CO_3	34 (81/19)
14	**L9** (3)	KOAc	trace[e]
15	**L9** (3)	KOH	16 (81/19)
16	**L9** (6)	Cs_2CO_3	NR

[a] General procedure: A mixture of **1a** (1.0 equiv), **2** (1.5 equiv), ligand (3~6 mol%), base (10 mol%) and $Cu(OTf)_2$ (2.5 mol%) in water (1 mL) was stirred under N_2 at room temperature. [b] The yields of **3a** were determined by ^1H NMR analysis. [c] The ratio (β/α) was determined by ^1H NMR analysis. [d] Without the use of ligand. [e] the ratio was not detected. [f] Without the use of base.

Additional base affected the yield and regioselectivity significantly. Among the screened bases, Cs_2CO_3 could provide the best result (entry 11 vs 12~15). It is noteworthy that the use of KOH as a base gave poor yield and regioselectivity (entry 15). Therefore, for aqueous reaction of **1a** with **2**, *t*-BuOK is not an optimal base as it is prone to hydrolysis to KOH in water. In summary, the best conditions for the reaction of internal alkynes with silylboronate in water included that: $Cu(OTf)_2$ (2.5 mol%) with 1,10-phenanthroline **L9** (3 mol%) as the ligand and additional base Cs_2CO_3 (10 mol%) under N_2 atmosphere at room temperature. The protocol showed preference *syn*-addition leading to excellent β-selectivity with the absolute (*E*)-configuration of formed double bond.

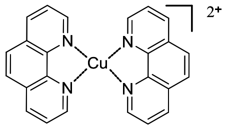


Figure 2. Unactive complex of Cu(II) with 1,10-phenanthroline

Methanol has been employed widely as proton donor and solvent in the reactions of $Me_2PhSiBpin$.[11] However, in the reaction of **1a** with **2** under the catalysis of $Cu(OTf)_2$/1,10-phenanthroline, the amount of water in co-solvent (CH_3OH/H_2O) affected the yields of products **3a** (β- + α-) strongly (Table 2). When the ratio of methanol to water in co-solvent was 1 : 4, the reaction system became heterogeneous, the yield of **3a** increased to 76% with high β-selectivity (Table 2, entry 3). Interestingly, it was found that for the reaction of **1a** with **2**, the results obtained in heterogeneous system were better than that in homogeneous system (Table 2, entries 3, 4 vs 1, 2)

Table 2. Cu(II)-Catalyzed Hydrosilylation of **1a** with **2** in Water.[a]

Entry	Solvent	Yield (%)[b] (β/α)[c]
1	CH_3OH (homogenous)	28 (90/10)
2	CH_3OH/H_2O(1:1) (homogeneous)	56 (90/10)
3	CH_3OH/H_2O(1:4) (heterogeneous)	76 (92/8)
4	H_2O (heterogeneous)	97 (92/8)

[a] General procedure: A mixture of **1a** (1.0 equiv), **2** (1.5 equiv), **L9** (3 mol%), Cs_2CO_3 (10 mol%) and $Cu(OTf)_2$ (2.5 mol%) in water (1 mL) was stirred under N_2 at room temperature. [b] The yields of **3a**(α+β) were determined by ^1H NMR analysis. [c] The ratio of (β/α) was determined by ^1H NMR analysis.

With optimized conditions in hand, the substrate-scope of the reaction of internal alkynes with $Me_2PhSiBpin$ in water was investigated (Table 3). Substrates possessing both electron-donating and electron-withdrawing groups on the phenyl ring could react efficiently, giving highly regio- and stereospecific vinylsilanes. A wide range of functional groups in the phenyl ring, including halide, cyano, ester groups, were tolerant to the reaction conditions.

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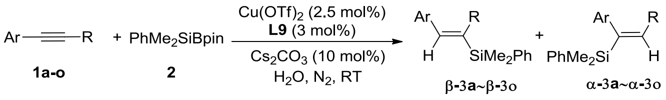
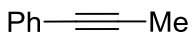
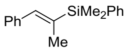
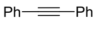
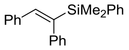
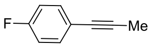
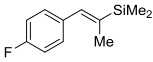
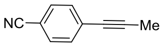
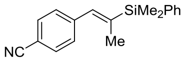
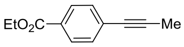
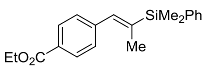
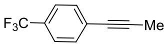
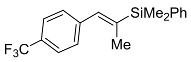
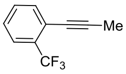
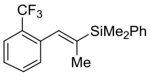
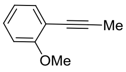
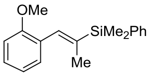
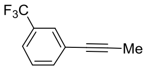
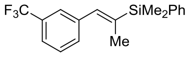
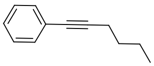
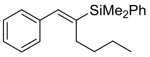
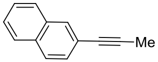
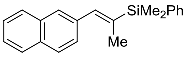
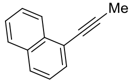
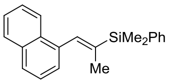
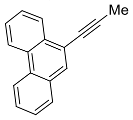
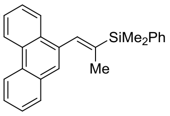
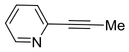
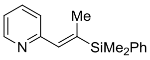
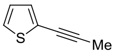
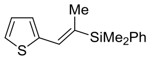
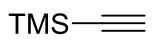
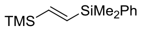
Even the ester group was not hydrolyzed in such aqueous basic media. The substrate with long alkyl chain (**1j**) gave lower yield of (*E*)-**3j** (65%), but with the high regioselectivity (β/α = 90 : 10) (Table 3, entry 10). It was noteworthy that the internal alkynes bearing pyridinyl (**1n**) and thiophenyl (**1o**) gave high yields and excellent regioselectivities (Table 3, entries 14 and 15). Especially, for **1n**, it gave β-**3n** as a sole isomer. It was suggested that the nitrogen atom of the pyridine ring might coordinate with vinyl copper complex to enhance the β-regioselectivity. When trimethylsilylacetylene (**1p**) was used in the reaction with **2** in water, the β-regioselective product **3p** was obtained with exclusively *E*- configuration in 95% yield (entry 16), while under the Pt(DVDS)-P catalysis, the stereoselectivity of the hydrosilylation of **1o** with triethylsilane was poor (*E*/*Z* = 35 : 65).[8a]

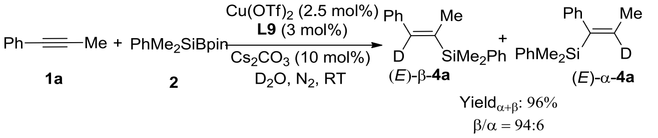
Table 3. The aqueous synthesis of multisubstituted vinylsilanes [a]



Entry		Alkyne		Product[b]	Yield(%)[c] (β/α)[d]
1	1a		β-3a		95 (96:4)
2	1b		β-3b		93
3	1c		β-3c		85 (98:2)
4	1d		β-3d		95 (88:12)
5	1e		β-3e		90 (91:9)
6	1f		β-3f		76 (96:4)
7	1g		β-3g		78 (90:10)
8	1h		β-3h		85 (90:10)
9	1i		β-3i		87 (94:6)
10	1j		β-3j		65 (90:10)
11	1k		β-3k		92 (96:4)
12	1l		β-3l		89 (92:8)
13	1m		β-3m		91 (98:2)
14	1n		β-3n		87 (100:0)
15	1o		β-3o		94 (93:7)
16	1p		β-3p		95

[a] General procedure: A mixture of alkynes (1.0 equiv), 2 (1.5 equiv), L9 (3 mol%), Cs_2CO_3 (10 mol%) and $Cu(OTf)_2$ (2.5 mol%) in 1 ml water was stirred under N_2 at room temperature, [b] determined by NOESY, [c] isolated yield, [d] the ratio (β/α) was determined by ^1H NMR analysis.

We also conducted the reaction of internal alkynes **1a** with **2** in D_2O (Scheme 1). The reaction could afford deuterated (*E*)- vinylsilanes stereospcifically in high yield (β-4a+α-4a) (96%) with excellent regioselectivity (β/α = 94 : 6).



Scheme 1. The reaction was carried out in D_2O.

Santos proposed that Cu(II)-catalyst could activate Si-B bond through transmetalation to form Cu-Si intermediate,[17] which undergoes Michael addition with α,β-unsaturated carbonyl substrates. Thus we assume that the silylcupration of internal alkynes also proceeds through transmetalation process. $LCu(OTf)_2$ can be converted to more activated $LCu(OH)_2$ assisted by Cs_2CO_3 in water. Then $LCu(OH)_2$ undergoes σ-bound metathesis with $Me_2PhSiBpin$, generating intermediate I. The intermediate I can be coordinated with alkyne, forming intermediate II. Subsequently, the C-C triple bond inserts into the Cu-Si bond, giving intermediate III. Finally the vinyl copper species undergoes hydrolysis to afford vinylsilanes and $LCu(OH)_2$ is regenerated.

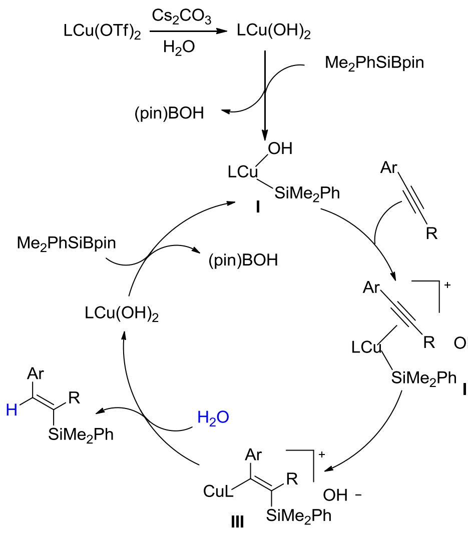


Figure 3. The proposed mechanism of the silylcupration of internal alkynes

Conclusions

In conclusion, we have developed an efficient system for the synthesis of multisubstituted vinylsilanes via silylcupration of unactivated internal alkynes. The reactions were conducted in water which was environmentally friendly. The aqueous

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hydrosilylation exhibited high efficiency and excellent regio- and stereoselectivity. This method, using low cost Cu(OTf)$_2$ as catalyst with 1,10-phenanthroline (**L9**) as ligand, and water as solvent and proton source, provided a convenient and practical route to multisubstituted vinylsilanes.

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