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Tetrabutylammonium Bifluoride as an Efficient Activating Agent for Copper-Catalyzed Vinylsilane Cross-Coupling Reactions

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R : allyl and alkynyl electrophiles

E-, *Z*-, and 1,1'-alkenes 44–96% yield 14 examples

scalable

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Abstract Vinylsilanes are versatile and efficient nucleophiles in crosscoupling reactions. Herein is described the use of tetrabutylammonium bifluoride as a mild, cheap and scalable activating agent in several copper-catalyzed vinylsilane cross-couplings.

Key words vinylsilane, copper, cross-coupling, activating agent, catalysis

Organosilicon compounds are ubiquitous building blocks in organic chemistry.¹ Their readily availability, low cost, and low toxicity led to the early development of many efficient transition-metal-catalyzed cross-coupling reactions.² Copper-catalyzed transformations started to arise recently.³ Both aryl- and vinylsilanes are now efficiently used as nucleophiles, whereas aryl, alkyl, and allyl halides can be employed as electrophiles.⁴

Over the past few years, our group developed efficient copper-catalyzed vinylsilane cross-coupling reactions. Various *cis-*, *trans-*, and 1,1'-disubstituted vinylsiloxanes could be efficiently coupled with allyl⁵ and benzyl⁶ bromides, as well as bromoalkynes.⁷ The use of tetrabutylammonium difluorotriphenylsilicate (TBAT) as an activating agent in these reactions was the main limitation as it brought several drawbacks such as relatively high cost and poor atomeconomy.

Herein is described the use of commercially available tetrabutylammonium bifluoride (TBAHF₂) ⁸ as a mild, cheap, and scalable activating agent for the coppercatalyzed cross-coupling of vinylsilanes with brominated electrophiles (Scheme 1).⁹

We started our experiment using model vinylsilane **1a** as a nucleophile and phenylethynyl bromide as an electrophile (Table 1). The formation of **2a** was studied using a



Scheme 1 TBAHF₂ as a mild and efficient activating agent in coppercatalyzed transformations

large number of different activating agents,¹⁰ and showed TBAHF₂ as the most efficient. Both one equivalent (Table 1, entry 1) and two equivalents (Table 1, entry 2) were not sufficient to fully promote the desired reaction. It was found that 2.5 equivalents were appropriate, resulting in an excellent 94% yield (Table 1, entry 3). This result is similar to the one obtained with TBAT (Table 1, entry 4), albeit without any of its drawbacks.⁷ The need of five equivalents of fluoride per silicon atom suggests that the reaction goes through a penta- or hexa-coordinated silicate intermediate.¹¹ A smooth transmetalation with copper(I) and then an addition onto the electrophile leads to the formation of the desired cross-coupling product. Surprisingly, the formation of ethanol after fluorination of the triethoxysilane with TBAHF₂was not a problem and only traces of the protodesilylated compound were observed.¹²

With optimal conditions in hand, we evaluated the functional-group compatibility (Scheme 2). In light of this, various vinylsiloxanes and several brominated electrophiles were used in this cross-coupling reaction.

The first few examples were obtained by using β -(*E*)-vinylsilanes.¹³ Nitrogen-containing enyne **2b** could be synthesized in excellent yield. Once again, the results were as good as previously described with TBAT as an activating agent.⁷ Allylic bromides as electrophiles were perfectly tolerated, as shown with phthalimide **2c** and no isomerization of the 1,4-diene was observed. The presence of a leaving

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В

1

2

3

4



yields are given in parentheses

group on the nucleophilic precursor was allowed, as shown with chlorine-containing 2d. Moderate yield was observed with benzyl-protected 2e, although the deprotected alcohol was not observed. Acrylic compound 2f could be easily synthesized, no matter its instability. Once again, no isomerization of the desired product was observed, emphasizing the very mild nature of this reaction. Complex enyne-ene structures, present in several natural products,¹⁴ could be obtained in good yields, as shown by 2g and 2h.

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^a Determined by ¹H NMR spectroscopy vs. CHBr₃ as an internal standard.

1,1'-Disubstituted vinylsilanes¹⁵ were synthesized and employed as a mixture of α/β isomers, providing their corresponding cross-coupling products in moderate yields with the same ratio of isomers. This is the result of the high hindrance of such nucleophiles, lowering their reactivity. It should, however, be noted that ester 2i and more specially aldehyde 2j remained untouched during the reaction. Compound **2k** bearing an acidic hydrogen could also be synthesized.

 β -(*Z*)-Vinylsilanes¹⁶ could be efficiently synthesized and engaged in this cross-coupling reaction as well. Full retention of stereochemistry was observed in all cases. 1,4-Diene **21** could be synthesized in almost quantitative yield. Very challenging acrylic ester **2m** could also be isolated in excellent yield, no matter its instability and promptness to polymerize.

This cross-coupling reaction could easily be scaled-up to gram quantities (Scheme 3). An important decrease of the initial temperature was required because of the exothermicity of the reaction. The preparation of enyne 2a was



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carried out on several grams of the starting silane **1a** without any loss in isolated yield, emphasizing the user-friendly character of this method.

In conclusion, an efficient, mild, cheap, and scalable copper-catalyzed vinylsilane cross-coupling reaction was presented. This methodology uses TBAHF₂ as an activating agent and allows the synthesis of many challenging *trans*-, *cis*-, and 1,1'-disubstituted alkenes.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1588504.

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(9) Vinylsilane Cross-Couplings: Typical Procedure

To a mixture of (*E*)-2-[4-(triethoxysilyl)but-3-enyl]isoindoline-1,3-dione (1a, 0.20 mmol, 1.0 equiv) and (bromoethynyl)benzene (0.30 mmol, 1.5 equiv) in an oven-dried vial was added TBAHF₂ (0.5 mmol, 2.5 equiv, 25 wt% solution in MeCN). Cu[MeCN]₄PF₆ (0.01 mmol, 0.05 equiv) was added, and the resulting mixture was stirred at 40 °C in an oil bath for 16 h. The solution was diluted with Et₂O (5 mL), filtered through a short pad of silica and eluted with Et₂O (25 mL). The solution was evaporated under reduced pressure to afford the crude product. The crude product (94% NMR yield using CHBr₃ as an internal standard) could be purified by flash chromatography using 20% EtOAc in PE to afford **2a** as a pale orange solid. $R_f = 0.68$ (95%) CH₂Cl₂ in PE). IR (thin film): 1771, 1497, 1394, 1364, 1340, 1219, 1055, 959, 870, 754, 719, 689 cm⁻¹. ¹H NMR (300 MHz, $CDCl_3$): δ = 7.85 (dd, J = 5.4, 3.1 Hz, 2 H), 7.71 (dd, J = 5.4, 3.1 Hz, 2 H), 7.45-7.35 (m, 2 H), 7.34-7.22 (m, 3 H), 6.19 (dt, J = 15.4, 7.2 Hz, 1 H), 5.77 (d, J = 15.8 Hz, 1 H), 3.80 (t, J = 7.1 Hz, 2 H), 2.68–2.49 (m, 2 H). ¹³C NMR (75 MHz, CDCl₃): δ = 168.16, 139.56, 133.94, 131.96, 131.42, 128.20 (br), 128.01, 123.25, 112.51, 88.85, 87.56, 36.95, 32.21. ESI-HRMS: m/z calcd for $C_{20}H_{16}O_2N_1[MH^+]$ 302.1176; found: 302.1174.

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