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Regio-selective and stereo-selective hydrosilylation of internal alkynes catalyzed by ruthenium complexes†

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In this study, ruthenium(II)-catalyzed direct hydrosilylation of internal alkynes with high regio-selectivity and stereo-selectivity is reported. This title transformation led to various vinylsilanes in good to excellent yields. This approach features mild reaction conditions, low catalyst loading, air-stability, and good functional group tolerance. Furthermore, gram-scale preparation and some transformations of vinylsilanes were carried out, which further underscored its synthetic utility and applicability.

Introduction

Vinyl-metal reagents play a key role in organic synthesis. Among the available vinyl-metal reagents, silicon-based reagents are increasingly important. Vinylsilanes are versatile synthetic building blocks, because of their minimal toxicity, low cost, ease of handling, and tendency to undergo different kinds of transformation.[1] Among the available methods for preparation of vinylsilanes, the hydrosilylation of alkynes is the most powerful strategy because it is direct and atom-economical, and it offers the potential to control the regio-selectivity and stereo-selectivity.[2–4] Although there are many methods for the hydrosilylation of terminal alkynes, particularly for the preparation of *cis*- and *trans*-β-vinylsilanes, the regio-selective and stereo-selective hydrosilylation of internal alkynes still remains a great challenge due to their low reactivity and close similarity in terms of electronic and steric properties to the acetylenic substituents.[5–7] Non-selective hydrosilylation of internal alkynes would potentially give four isomeric addition products (Fig. 1).

To address the difficulty of regiocontrol in the hydrosilylation of unsymmetrical (internal) alkynes, a directing group (DG) was introduced into an unsymmetrical alkyne to control their regio-selectivity of the hydrosilylation. Zakarian[6d] and co-workers developed the silylation of internal alkyne and sequential iododesilylation with high

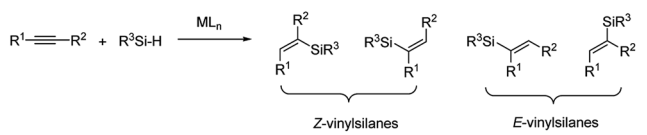
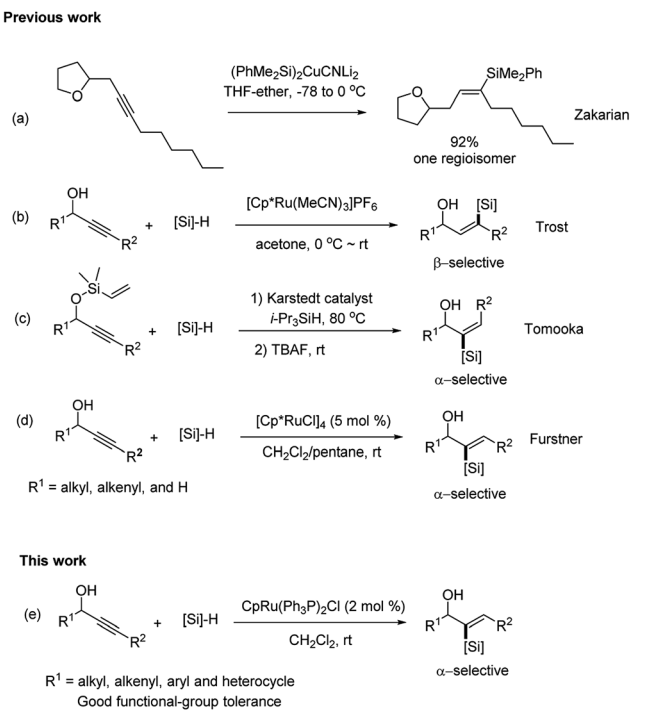


Fig. 1 Four isomeric addition products.



Scheme 1 Directed hydrosilylation of internal alkynes.

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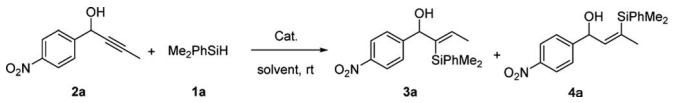
Table 1 Optimization of reaction conditions[a]

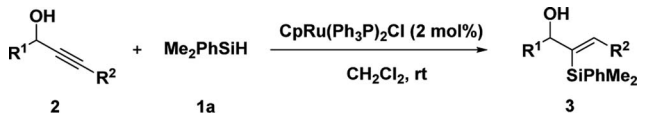


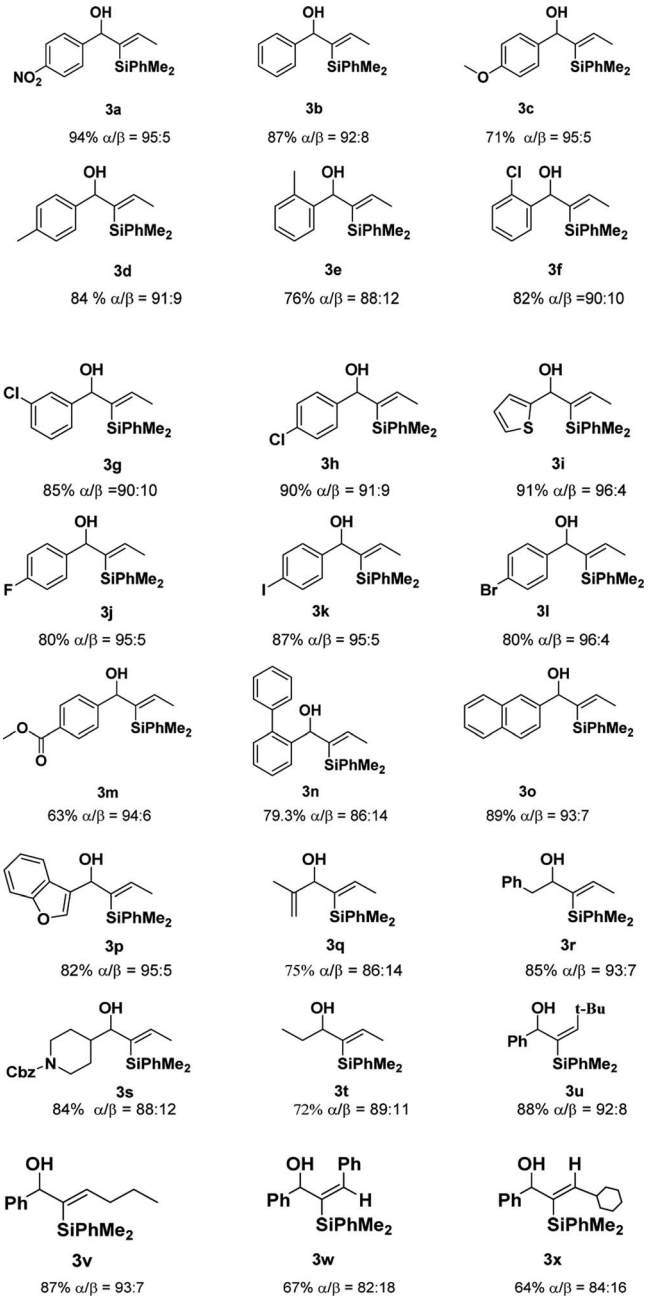
Entry	Catalyst (mol%)	Solvent	α : β ratio[b]	Yield[c] (%)
1	$CpRu(Ph_3P)_2Cl$ (5)	THF	82 : 18	68
2	$CpRu(Ph_3P)_2Cl$ (5)	Toluene	94 : 6	59
3	$CpRu(Ph_3P)_2Cl$ (5)	Acetone	79 : 21	65
4	$CpRu(Ph_3P)_2Cl$ (5)	CH_2Cl_2	95 : 5	94
5	$[\{RuCl_2(p\text{-cymene})\}_2]$ (5)	CH_2Cl_2	—	—[d]
6	$[Cp^*RuCl]_4$ (5)	CH_2Cl_2	92 : 8	83
7	$CpRu(Ph_3P)_2Cl$ (2)	CH_2Cl_2	95 : 5	94 (94)
8	$CpRu(Ph_3P)_2Cl$ (1)	CH_2Cl_2	95 : 5	89
9	$CpRu(Ph_3P)_2Cl$ (2)	CH_2Cl_2	91 : 9	86[e]
10	$[CpRu(Ph_3P)(tht)]BF_4$(5)	CH_2Cl_2	22 : 78	18

[a] Reaction conditions: **1a** (0.24 mmol), **2a** (0.2 mmol), in 2 mL solvent at room temperature, Ar atmosphere for 12 h. [b] Determined by ^{1}H NMR analysis of the crude reaction mixtures. [c] NMR yields using CH_2Br_2 as an internal standard, isolated yields in parenthesis. [d] This entry's major product is α-selective *cis*- hydrosilylation (see NOE analysis in SI). [e] **1a** (0.24 mmol), **2a** (0.2 mmol), in 2 mL solvent at room temperature under air atmosphere for 12 h.

regioselectivity. The regioselectivity is guided by coordination of the silylcupration reagent to hydroxy or alkoxy groups in the substrate (Scheme 1a). In the early 2000s, Trost[8] and co-workers reported the regio-selective *trans*-hydrosilylation of propargylic alcohols catalyzed by the cationic complex $[Cp^*Ru(MeCN)_3]PF_6$, which resulted in β-selective silylation at the alkyne carbon (Scheme 1b). The introduction of a hydroxyl group at the propargylic position is crucial to control the regioselectivity of hydrosilylation. In addition, a carbonyl group has been also shown to direct hydrosilylation of internal alkynes to provide α-vinylsilanes. While, the regio-selectivity largely depends on the electronic effect.[7d] On the contrary, the examples of α-selective hydrosilylation of unbiased unsymmetrical internal alkynes are very limited,[7c,7e,9] especially for the propargylic alcohol substrates. To date, selective hydrosilylation on the α-carbon of propargylic alcohols are rarely reported. In 2011, Tomooka's group[7c] described Pt-catalyzed α-selective hydrosilylation of unsymmetrical alkynes using a dimethylvinylsilyl (DMVS) group as the directing group (Scheme 1c). However, the substrate scope of this method was limited for the primary alcohols. More recently, Fürstner[9a,9b,9c] and co-workers disclosed that $[Cp^*RuCl]_4$ also catalyzed the hydrosilylation of propargylic alcohols to form α-vinylsilanes with a high degree of regioselectivity (Scheme 1d). While, the R^1 part of propargylic alcohols was alkyl, alkenyl and H. In view of the importance of the broad synthetic utility of vinylsilanes, we are interested in developing another efficient catalyst for α-selective hydrosilylation of propargylic alcohols. Herein, we describe a new method for the hydrosilylation of differentially propargyl alcohols with a new ruthenium complex under mild conditions (Scheme 1e). The transformation is highly

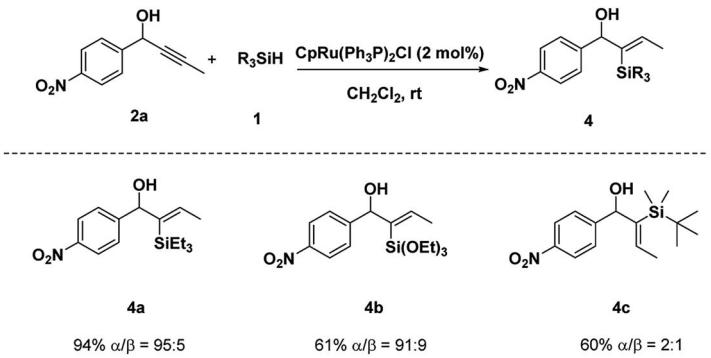
Table 2 Propargylic alcohol scope.[a,b,c]





[a] Reaction conditions: **1a** (0.24 mmol), **2** (0.2 mmol), $CpRu(Ph_3P)_2Cl$ (2 mol%), in anhydrous CH_2Cl_2 (2 mL) under Ar at room temperature for 12 h. [b] Isolated yields. [c] Determined by ^{1}H NMR analysis of the crude reaction mixtures.

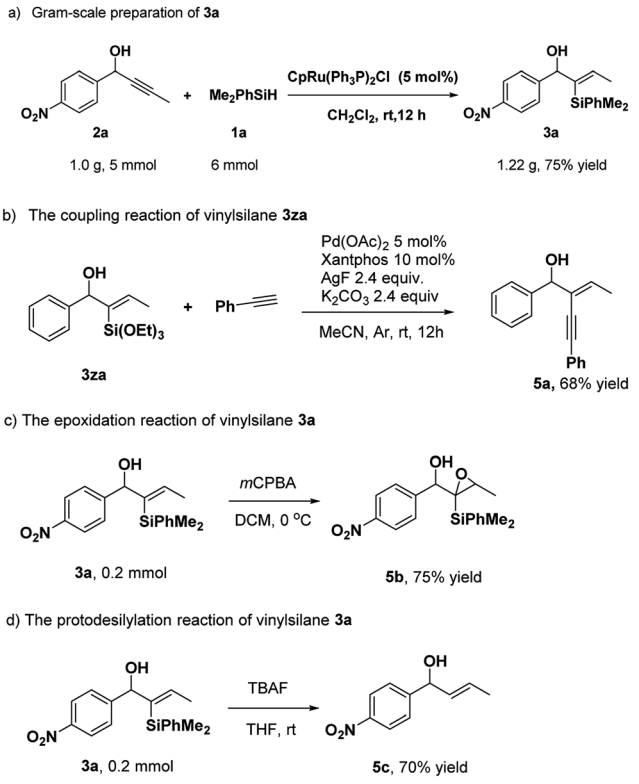
regio-selective and stereo-selective for the preparation of α-vinylsilanes from unbiased and unsymmetrical internal alkynes.



Scheme 2 Alternative silane scope.

Results and discussion

We initiated our studies with the hydrosilylation reaction of 1-(4-nitrophenyl) but-2-yn-1-ol **2a** and the easily available $PhMe_2SiH$ **1a** in the presence of a Ru complex. Interestingly, when the reaction was carried out with $CpRu(Ph_3P)_2Cl$ (5 mol%) in THF for 12 h, **3a** was obtained in 68% yield with good regioselectivity (α/β = 82 : 18) (Table 1, entry1). Then solvent screening was conducted, when the reaction was conducted in CH_2Cl_2, the best result was obtained (94% yield with excellent regioselectivity (α/β = 95 : 5)) (entries 2–4). Other catalysts, such as $[\{RuCl_2(p\text{-cymene})\}_2]$, $[Cp^*RuCl]_4$, reduced the yield of **3a** with poor regioselectivity compared to $CpRu(Ph_3P)_2Cl$ (entries 5 and 6). To further improve the reaction efficiency, the loading amount of the catalyst was investigated. When we reduced the loading amount of the $CpRu(Ph_3P)_2Cl$ from 5 mol% to 2 mol%, the reaction also produced **3a** in excellent yield (94%) and excellent regioselectivity (α/β = 95 : 5) (entry 7). However, when 1 mol% $CpRu(Ph_3P)_2Cl$ was used in the hydrosilylation reaction, the yield of **3a** was slightly decreased (entry 8). Then this reaction was carried out in air atmosphere, the yield and regioselectivity slightly decreased (entry 9). When 5 mol% $[CpRu(Ph_3P)(tht)]BF_4$ was applied, we got the poor regioselectivity (α/β = 22 : 78) (entry 10), it showed the Cl ligand played a crucial role. Briefly, the optimal results could be obtained when 1-(4-nitrophenyl) but-2-yn-1-ol **2a** (0.2 mmol) and $PhMe_2SiH$ **1a** (0.24 mmol, 1.2 equiv.) were treated with 2 mol% $CpRu(Ph_3P)_2Cl$ in CH_2Cl_2 at room temperature for 12 h.



Scheme 3 Gram-scale experiment and transformations of the products.

With the optimized conditions in hand, we examined the scope of different propargyl alcohols **2** in the hydrosilylation reaction with $PhMe_2SiH$ **1a** (Table 2). Substrates containing electron-withdrawing groups, such as nitro and halides, at the phenyl moiety of propargyl alcohols were well tolerated under the standard reaction conditions (**3a**, **3f–3h**, and **3j–3l**). A similar level of efficiency was observed when substrates having phenyl, *p*-tolyl, *o*-tolyl, and 1,1′-biphenyl groups (**3b**, **3d**, **3e**, and **3n**), while some other electron-rich substrates provided the desired products in decreased yields (**3c**). In addition, the desired products were obtained in higher yields and better regio-selectivity when substituents, such as methyl and chloride, were introduced at the *para* position of the phenyl moiety (**3d** *vs.* **3e**, and **3h** *vs.* **3f**). The tolerance of the reaction with active groups such as halides in the substrates meant that they could be further transformed into other functional groups. When an ester group was placed at the *para* position of phenyl ring, **3m** was obtained in 63% yield, and it seemed that the carbonyl may participate in coordination. Furthermore, substrates bearing other heteroaryl groups, such as thiophene and benzofuran, also could react with **1a** to produce the desired product in good yields with excellent regio-selectivity (**3i** and **3p**). Significantly, replacing the phenyl moiety of the propargyl alcohols with vinyl, benzyl, N-protected piperidyl and alkyl, the hydrosilylation reaction also underwent smoothly with satisfactory results (**3q–3t**). While the introduction of bulkier groups (such as *tert*-butyl and Ph) in the R_2 moiety of the substrates

provided the different stereo-selective products in good yields (**3u,3w**), which was different from Fürstner's work. [9a]

Moreover, when Et_3SiH was used, the hydrosilylation of **2a** proceeded with excellent result (α/β = 95 : 5, 94% yield) (Scheme 2). Given the poor reactivity of alkylsilanes toward a variety of synthetically transformations, we extended the method to more reactive and operationally convenient alkyoxysilanes. Hydrosilylation of **2a** with triethoxylsilane was performed under standard conditions and provided the desired product **4b** in 61% yield with excellent regioselectivity. However, hydrosilylation of **2a** with *t*-$BuMe_2SiH$ produced desired product **4c** in 60% yield with poor regio-selectivity.

To assess the efficiency and potential applications of this method, we carried out gram-scale preparation and transformations of the products (Scheme 3). When propargyl alcohol **2a** (1.0 g, 5 mmol) was used, the reaction afforded the corresponding product **3a** in 75% yield. Besides, there were few works about the transformation of α-hydroxy alkynylsilanes by coupling reactions to date.[9d] In our work, the coupling of vinylsilane **3za** and phenylacetylene could provide the product **5a** in good yield.[10] The epoxidation of **3a** with *m*CPBA resulted in product **5b**. Furthermore, vinylsilane **3a** could be converted to *trans*-olefin **5c** by tetrabutylammonium fluoride (TBAF) in 70% yield at room temperature (Scheme 3d).

Conclusions

In summary, we reported a mild and efficient ruthenium-catalyzed hydrosilylation of internal alkynes. This method enables the efficient preparation of vinylsilanes in good to excellent yields with highly regio-selectivity and stereo-selectivity. Its mild reaction conditions mean that this approach is also compatible with various functional groups. We also achieved the gram-scale production and some transformations of vinylsilanes, which further underscored the synthetic utility and versatile applicability of this method.

Conflicts of interest

There are no conflicts to declare.

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