Synthetic Methods

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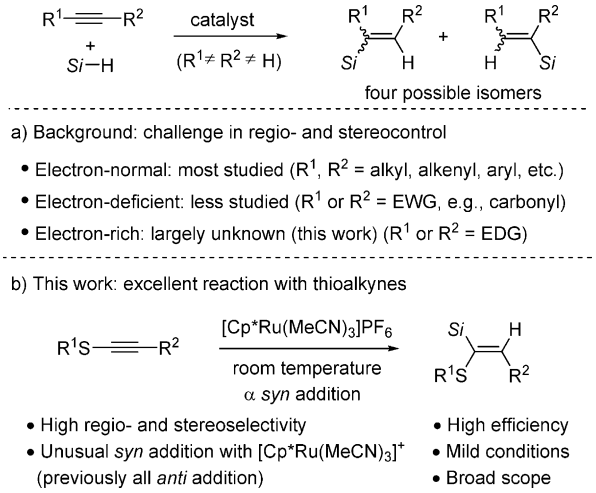
Highly Regio- and Stereoselective Hydrosilylation of Internal Thioalkynes under Mild Conditions**

Shengtao Ding, Li-Juan Song, Yong Wang, Xinhao Zhang, Lung Wa Chung,* Yun-Dong Wu,* and Jianwei Sun**

Abstract: *A general and mild hydrosilylation of thioalkynes is described. With the cationic catalyst $[Cp^*Ru(MeCN)_3]^+$ and the bulky silane $(TMSO)_3SiH$, a range of thioalkynes underwent smooth hydrosilylation at room temperature with excellent α regioselectivity and syn stereoselectivity. DFT calculations provided important insight into the mechanism, particularly the unusual syn selectivity with the $[Cp^*Ru(MeCN)_3]^+$ catalyst. The sulfenyl group in the substrates was found to provide important chelation stabilization to direct the reaction through a new mechanistic pathway.*

Vinyl silanes are valuable synthetic precursors to various useful small organic molecules and polymeric organosilicon materials.[1] Consequently, the hydrosilylation of alkynes, arguably the most direct and atom-economical route to vinyl silanes, has become an area of intense investigation in the past few decades.[2] However, despite the significant progress made, there still remain challenges (e.g., regio- and stereocontrol), particularly for unsymmetrical internal alkynes in intermolecular reactions (Scheme 1). Moreover, almost all previous studies on this topic have been focused on electron-normal[2,3] and electron-deficient[4] alkynes (Scheme 1 a). In contrast, the hydrosilylation of electron-rich alkynes (bearing an electron-donating group (EDG) at the triple bond) remains largely unknown.[5]



Scheme 1. Background to alkyne hydrosilylation. *Si* stands for a silyl group of the type R_3Si; EWG = electron-withdrawing group.

In continuation of our studies on transformations of electron-rich alkynes,[6] we report herein the first general, mild, and highly selective process of this type (Scheme 1 b). Specifically, we have developed an efficient ruthenium-catalyzed intermolecular hydrosilylation of internal thioalkynes with high regio- and stereoselectivity. In this study, we also observed unprecedented *syn* addition selectivity with $[Cp^*Ru(MeCN)_3]^+$ (Cp^* = pentamethylcyclopentadienyl), a well-known catalyst for *anti* addition reactions of alkynes.[7,8] The unusual *syn* selectivity was also rationalized by careful DFT studies.

In our initial study, we employed thioalkyne **1a** and triethoxysilane (**2a**) as model starting materials (Table 1). $[Cp^*Ru(MeCN)_3]PF_6$ was chosen for initial evaluation of the transformation in view of its demonstrated catalytic capability in a range of alkyne-functionalization reactions.[7] The reaction in CH_3CN proceeded smoothly to afford the desired vinyl silane at room temperature, albeit with only moderate regioselectivity (Table 1, entry 1). The excellent *syn* stereoselectivity observed stands in remarkable contrast to the uniform *anti* addition previously observed with this catalyst for the functionalization of alkynes.[8] The use of other solvents did not improve the overall efficiency and selectivity of the reaction. The smaller catalyst $[CpRu(MeCN)_3]PF_6$ resulted in almost no regioselectivity (Table 1, entry 2). Furthermore, previously reported Pt and Co complexes were found to be ineffective (Table 1, entries 3 and 4).[5]

We next examined a range of silanes (Table 2). Most of them gave the product either in moderate yield or with moderate selectivity; however, tris(trimethylsiloxy)silane

[*] L.-J. Song,[+] Prof. X. Zhang, Prof. Y.-D. Wu
Laboratory of Computational Chemistry and Drug Design
Laboratory of Chemical Genomics
Peking University Shenzhen Graduate School
Shenzhen 518055 (China)
E-mail: zhangxh@pkusz.edu.cn
wuyd@pkusz.edu.cn
S. Ding,[+] Y. Wang, Prof. J. Sun
Department of Chemistry
The Hong Kong University of Science and Technology
Clear Water Bay, Kowloon, Hong Kong SAR (China)
E-mail: sunjw@ust.hk
Prof. L. W. Chung
Department of Chemistry
South University of Science and Technology of China
Shenzhen 518055 (China)
E-mail: oscarchung@sustc.edu.cn
[+] These authors contributed equally to this work.

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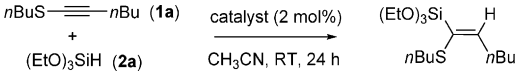
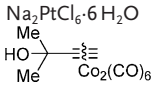
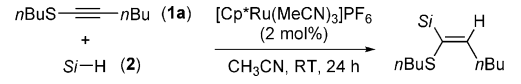
Table 1: Catalyst evaluation.



Entry	Catalyst	Yield [%][a]	α/β[b]	Z/E[b]
1	$[Cp^*Ru(MeCN)_3]PF_6$	82	5.6:1	>30:1
2	$[CpRu(MeCN)_3]PF_6$	63	1:1	1.4:1
3	$Na_2PtCl_6 \cdot 6H_2O$	<5[c]	–	–
4		<5[c]	–	–

[a] The yield was determined by GC. [b] The ratio of α/β addition and the *E*/*Z* ratio of the product were determined by ^{1}H NMR spectroscopy of the crude product. [c] Almost no conversion was observed.

Table 2: Evaluation of silanes for the hydrosilylation of thioalkynes.



Entry	Silane (2)	Yield [%][a]	α/β[b]	Z/E[b]
1	$(MeO)_3SiH$ (**2b**)	54	3.6:1	>50:1
2	$(EtO)_2MeSiH$ (**2c**)	84	8.4:1	5.9:1
3	$(EtO)Me_2SiH$ (**2d**)	87	14.7:1	1.1:1
4	Et_3SiH (**2e**)	53	>20:1	25:1
5	$PhMe_2SiH$ (**2f**)	91	>20:1	1.3:1
6	$BnMe_2SiH$ (**2g**)	75	>20:1	4.5:1
7	$(TMSO)_3SiH$ (**2h**)	99	>50:1	25:1
8	$(TMS)_3SiH$ (**2i**)	0	–	–
9[c]	Me_2SiClH (**2j**)	79	2.1:1	–

[a] Yield of the isolated product. [b] The ratio of α/β addition and the *E*/*Z* ratio of the product were determined by ^{1}H NMR spectroscopy of the crude product. [c] MeOH (5.0 equiv) and Et_3N were added to trap the chlorosilane product. Bn = benzyl, TMS = trimethylsilyl.

(**2h**) provided the product in quantitative yield with excellent selectivity (Table 2, entry 7). Notably, no reaction was observed with tris(trimethylsilyl)silane (**2i**).

Under the optimized conditions, a wide range of thioalkynes participated in the hydrosilylation with excellent efficiency as well as high regio- and stereoselectivity (Table 3). The mild conditions tolerate a variety of functional groups, such as acetals (THP-protected alcohols), esters, ethers, and even free alcohols.

The obtained trisubstituted vinyl silane products can be readily transformed into other useful compounds [Eq. (1); TBAF = tetrabutylammonium fluoride]. The oxidation of **3k** with *m*-chloroperbenzoic acid (*m*CPBA) afforded the stereodefined α-silyl vinyl sulfone **4** with high efficiency. Vinyl sulfones are versatile species in organic synthesis and medicinal chemistry.[9] Furthermore, protodesilylation and Hiyama cross-coupling efficiently furnished vinyl sulfides **5** and **6**, respectively. Our method provides an attractive alternative route to these molecules.[10]

Previously, we established a new mechanism to rationalize generally observed *anti*-selective hydrosilylation with the catalyst $[Cp^*Ru(MeCN)_3]^+$.[11] The mechanism involves the direct formation of a ruthenacyclopropene intermediate, followed by silyl migration;[12] in this process the hydrogen atom and the silyl group of the silane are arranged on opposite sides of the ruthenacyclopropene plane.[13] The

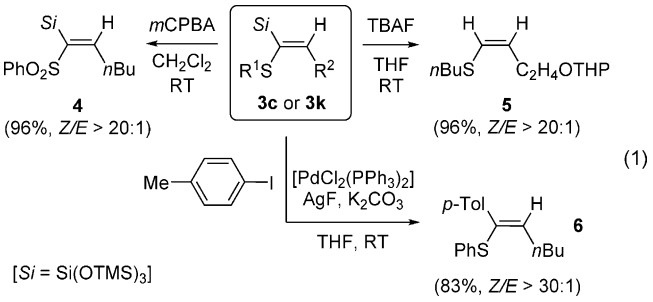
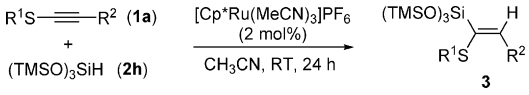


Table 3: Scope of the hydrosilylation of thioalkynes with $(TMSO)_3SiH$.



Entry	R^1	R^2	Product	Yield [%][a]
1	*n*Bu	*n*Bu	**3a**	99
2	*n*Bu	cyclopropyl	**3b**	91
3	*n*Bu	C_2H_4OTHP	**3c**	97
4	*n*Bu	C_2H_4OAc	**3d**	92
5	*n*Bu	C_2H_4OBn	**3e**	87
6	*n*Bu	C_2H_4OH	**3f**	74
7	*n*Bu	Ph	**3g**	91[b]
8	Me	*n*Bu	**3h**	95
9	*i*Pr	*n*Bu	**3i**	75
10	Bn	*n*Bu	**3j**	93
11	Ph	*n*Bu	**3k**	86
12	Ph	*n*-Oct	**3l**	99
13	Ph	cyclopropyl	**3m**	92
14	Ph	C_2H_4OTHP	**3n**	96
15	Ph	C_2H_4OAc	**3o**	84
16	Ph	C_2H_4OH	**3p**	94
17	Ph	Ph	**3q**	96
18	*p*-$OMeC_6H_4$	*n*Bu	**3r**	98
19	*p*-ClC_6H_4	*n*Bu	**3s**	60
20	*p*-MeC_6H_4	*n*Bu	**3t**	97

[a] Yield of the isolated product. In all cases except for entry 7, α/β > 20:1, *Z*/*E* > 20:1. [b] α/β = 5:1, *Z*/*E* > 20:1. THP = 2-tetrahydropyranyl.

observed *anti* addition in the hydrogermylation, hydrostannation, hydrogenation, and hydroboration of alkynes under the catalysis of $[Cp^*Ru(MeCN)_3]^+$ has also been suggested to follow this mechanism.[14]

Interestingly, the presence of a sulfenyl substituent leads to α selectivity and the unusual *syn* addition. Our DFT calculations suggest that the hydrometalation is the rate- and regioselectivity-determining step, and that **TS1-A** is more stable than **TS1-B** by about 2.9 kcal mol^{-1} (Figure 1; see also Figures S1 and S3 in the Supporting Information).[15] Also, the ruthenacyclopropene intermediate **2A** is more stable than **2B** by 5.2 kcal mol^{-1} because the proton-like hydrogen atom[11] preferentially attacks the more electron-rich C_β atom with the strongly π donating sulfenyl group. Moreover, the sulfenyl group stabilizes the electrophilic carbene ligand in **2A** through a conjugation effect (see resonance structure $\mathbf{2A_1}$, Figure 1; see also Figure S2a).

A key new feature is the isomerization of **2A** to form a more stable sulfur-chelated σ-vinyl intermediate **3A**.[16]

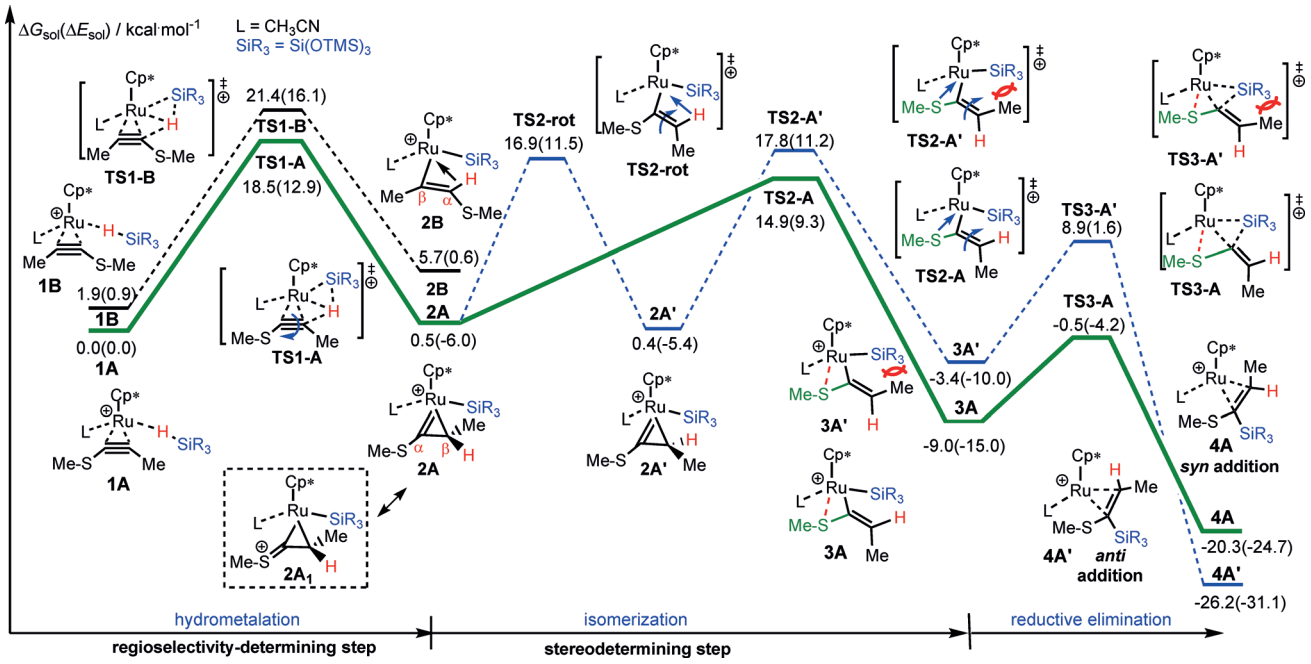


Figure 1. Energy profiles of the $[Cp^*Ru(MeCN)_3]^+$-catalyzed hydrosilylation of 1-methylthiopropyne. A resonance structure of **2A** is given in the dotted box.

Ring opening via **TS2-A** involves the clockwise rotation of the C_α–C_β bond to move the C_β–H bond inward with concomitant Ru–S bond formation to form the *syn* σ-vinyl intermediate **3A**. The transition state for counterclockwise rotation from **2A** to **3A′** could not be located owing to steric interactions between the methyl and bulky silyl groups. Intermediate **2A** can also undergo C_α–C_β rotation via **TS2-rot**[17] to form **2A′**. Then clockwise rotation of the C_α–C_β bond (via **TS2-A′**) can occur to move the C_β–Me group inward to form the *anti* σ-vinyl intermediate **3A′**. **TS2-A** is calculated to be more stable than **TS2-A′** by about 2.9 kcal mol^{-1}, in agreement with the observed *syn* selectivity. This difference in stability is attributed to the steric repulsion between the C_β–Me group and the bulky silyl group in **TS2-A′** (Figure 2; see also Figures S5 and S6). The vinyl moiety in **TS2-A′** is highly distorted by the steric repulsion, as reflected by the larger Ru-C_α-C_β and Si-Ru-C_α bond angles in **TS2-A′** than those in **TS2-A** (131.6 and 103.8 versus 123.1 and 99.8°, respectively). The distortion energy attributed to the vinyl moiety in **TS2-A′** is estimated to be about 2.4 kcal mol^{-1} higher than in **TS2-A**.[18] The steric repulsion in the *anti* form becomes more significant along the pathway, as indicated by the 5.6 kcal mol^{-1} preference for **3A** over **3A′**.

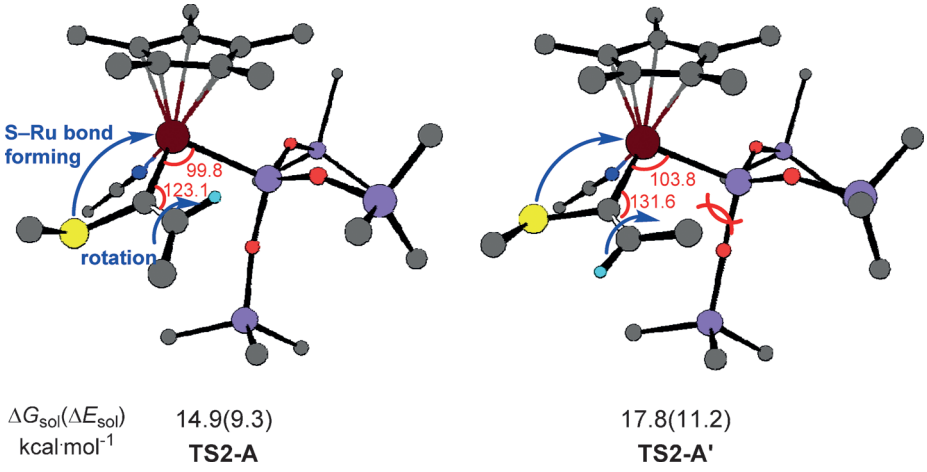


Figure 2. Optimized structures of the transition states of the stereodetermining isomerization (with key bond angles).

Finally, reductive elimination from **3A** involving sulfur chelation completes the reaction via **TS3-A**. The bulky silyl group approaches the less hindered side of the alkene in **TS3-A** (the *syn* form), and thus has a lower barrier of 8.5 kcal mol^{-1} to give the observed product of α *syn* addition, rather than the *anti*-addition product via **TS3-A′** (see Figure S7).[7,11] Overall, the *syn* addition stereoselectivity is determined in the ring-opening/isomerization process (the proposed catalytic cycle is summarized in Scheme S1 of the Supporting Information).[19] Notably, Ru–S chelation and steric effects play important roles in dictating the excellent and uncommon regio- and stereoselectivity.

In conclusion, we have developed the first general and mild hydrosilylation of thioalkynes. With $[Cp^*Ru(MeCN)_3]^+$ as the catalyst, a range of thioalkynes participated in the efficient hydrosilylation at room temperature with excellent regio- and stereoselectivity. The stereodefined vinyl sulfide

products are useful precursors to other valuable compounds. Particularly noteworthy is the unusual *syn* addition selectivity with the $[Cp^*Ru(MeCN)_3]^+$ catalyst. The unusual selectivity has been rationalized by DFT calculations. In the distinct mechanistic scenario, the sulfenyl group plays a key role by providing additional stabilization through S–Ru chelation. The bulky silane $(TMSO)_3SiH$ also contributes to the enhanced selectivity by a steric effect. Further studies of the highly selective functionalization of electron-rich alkynes are under way.

Keywords: electron-rich alkynes · homogeneous catalysis · hydrosilylation · ruthenium · stereoselectivity

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[17] Unlike **TS2-A**, **TS2-rot** does not involve the formation of a Ru–S bond.

[18] The difference in the distortion energy for the remaining parts of the transition state is 0.8 kcal mol^{-1}.

[19] The poor regioselectivity, stereoselectivity, or reactivity observed with various silanes (compounds **2b**,**d**,**i**) was mainly attributed to steric effects (see Tables S1–S3 and Figures S9–S11).

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