C–H Activation

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Rhodium-Catalyzed Intramolecular C–H Silylation by Silacyclobutanes

*Qing-Wei Zhang[+], Kun An[+], Li-Chuan Liu, Shuangxi Guo, Chenran Jiang, Huifang Guo, and Wei He**

Abstract: *Silacyclobutane was discovered to be an efficient C–H bond silylation reagent. Under the catalysis of Rh^I/TMS-segphos, silacyclobutane undergoes sequential C–Si/C–H bond activations, affording a series of π-conjugated siloles in high yields and regioselectivities. The catalytic cycle was proposed to involve a rarely documented endocyclic β-hydride elimination of five-membered metallacycles, which after reductive elimination gave rise to a Si–Rh^I species that is capable of C–H activation.*

Silacyclobutanes (SCB) were first reported by Sommer and Baum over half a century ago.[1] Compared with other organosilicons, SCB is unique due to their high ring strain energy, as evidenced in ring opening polymerization,[2] aldol reactions of SCB[3] and retro-[2+2] reaction.[4] Also because of the high ring strain, low valent transition metals can facilely insert into the SCB to form 5-membered silametallacycles.[5] A signature reactivity of the resulting silametallacycles involves the migratory insertion of π systems into the M–Si bonds. Based on this reactivity, various fascinating formal cycloaddition reactions of SCB have been developed.[6] For example, reactions of alkynes or alkenes with SCB resulted in formal $[_\sigma2+_\pi2]$ cycloaddition[7] (Figure 1 a). Similarly, enones were shown to give formal $[_\sigma2+_\pi4]$ products.[8] Most recently, Murakami and co-workers discovered that electron-rich silapalladacycle is capable of oxidative insertion into an adjacent cyclobutanone, cultivated in an intriguing formal σ bond metathesis reaction.[9] Despite these advancements, SCB is not shown to react with C–H bonds.

In our continuing research in the Rh catalyzed construction of Si–C bonds,[10] we became curious if SCB could act as a C–H silylation reagent. If a 5-membered Rh silametallacycle is to be assumed, converting this Rh^{III} to catalytically active Si–Rh^I would be required, since only the latter is known to perform C–H activation.[11] Such a Si–Rh^I might be achieved by a two-step sequence: β-hydride elimination of the Rh silametallacycle followed with reductive elimination (Rh^{III} to Rh^I). However, these silametallacycles were proposed to be stable against β-H elimination.[12] In general, endocyclic β-H elimination of related metallacycles (especially that of 3- to 6-membered rings) are conceived to be extremely challenging.[13] A classic example is the alkene–alkyne coupling reaction reported by Trost, in which acyclic β-H elimination was shown to prevail.[14] Although DFT calculations suggested that endocyclic β-H elimination might be possible,[15] only a few examples were reported very recently.[16] Herein we reported that SCB is an efficient reagent for C–H bond silylation[17] under Rh catalysis in the presence of a hindered ligand, possibly enabled by endocyclic β-H elimination of Rh silametallacycles (Figure 1 b). This reaction produces various siloles in high yield with excellent regioselectivity.

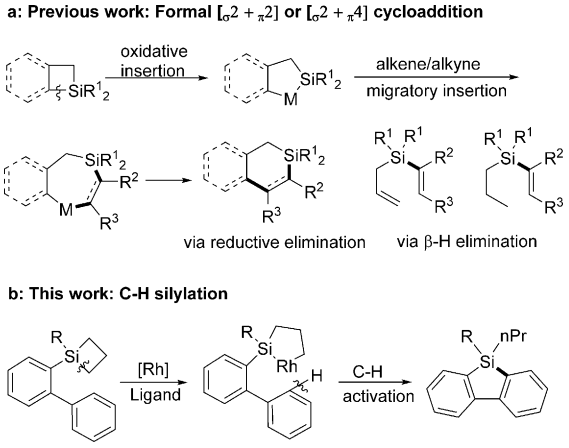

Figure 1. Silacyclobutanes as C–H silylation reagent.

Our investigation started with the intramolecular silylation reaction of SCB **1 a.** Since our previous work showed that the steric hindrance of diphosphine ligands has a profound influence[10b] on the C–H bond silylation reaction, we screened a large panel of ligands (Table 1). No reaction took place in the absence of a ligand (entry 1). Similar to our previous observations,[10b] ligands with different dihedral angles showed dramatically different reactivity. The less hindered ligand spirophos and BINAP were ineffective (entries 2–3). DTBM-MeO-Biphep, which possesses a wider dihedral angle and more hindered 3, 5-di-*t*-Bu-4-MeO-phenyl substituent, gave the silole product[18] **2 a** in 15% yield (entry 4). A systematic screening of ligands with segphos backbone that possess wider dihedral angles[19] was then conducted (entries 5–8). Among these ligands, TMS-segphos[20] gave the best result (52% yield, entry 7). Further increasing the bulkiness, either by using larger 3, 5-di-triethylsilylphenyl (TES)[21] or by employing C1-tunephos[22]

[*] Dr. Q.-W. Zhang,[+] K. An,[+] L.-C. Liu, S. Guo, C. Jiang, Dr. H. Guo, Prof. Dr. W. He
School of Pharmaceutical Sciences, Tsinghua University
Beijing, 100084 (China)
E-mail: whe@mail.tsinghua.edu.cn
Homepage: http://www.med.tsinghua.edu.cn/index.php/en/research/faculty/item/he-wei
[+] These authors contributed equally to this work.
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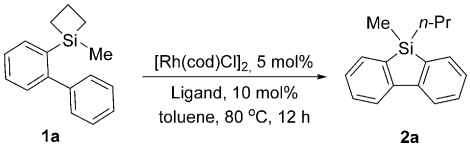
Table 1: Screening of the reaction parameters.[a]



1a 2a

Entry	Ligand	Yield[b]
1	–	n.r.
2	spirophos	n.r.
3	BINAP	trace
4	DTBM-MeO-Biphep	15%
5	segphos	n.r
6	DTBM-segphos	10%
7	TMS-segphos	52%
8	TES-segphos	trace
9	DTBM-C1-tunephos	trace
10[c]	TMS-segphos	trace
11[d]	TMS-segphos	trace
12[e]	TMS-segphos	84%

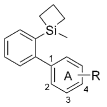
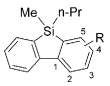
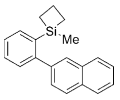
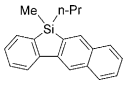
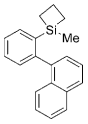
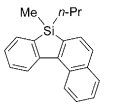
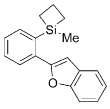
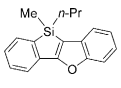
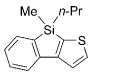
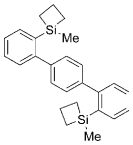
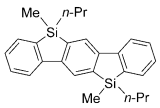
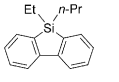
[a] Conditions: 0.1 mmol substrate, catalyst (10 mol%), ligand (10 mol%) and toluene (1 mL) were dissolved in the glove box. [b] Isolated yield. [c] Catalyst is $[Rh(cod)_2]BF_4$. [d] Catalyst is [Rh(cod)](acac). [e] 48 h.

with narrower dihedral angle backbone, resulted in loss of activity (entries 8 and 9). This nonlinear dependence of catalyst performance on the steric hindrance of the ligands is in line with our previous C–H silylation study.[10b] Catalysts with other counterions, such as $[Rh(cod)_2]BF_4$ and [Rh(cod)](acac), were also inactive (entries 10 and 11). Gratifyingly, when the reaction time was extended to 48 h, the desired product **2a** was isolated in 84% yield (entry 8 vs. 12).

This new C–H silylation reaction is applicable to a wide scope of SCB substrates (Table 2). First, substituents on aryl ring A were examined. Methyl substituent at either 3-position (**1b**) or 4-position (**1c**) gave comparable yields to that of **1a** (entries 2 and 3 vs. entry 1). Only one of the two possible regioisomeric products was obtained from substrate **1b**: the silylation occurred exclusively at the less hindered 6-position (entry 2). Alkyl substitution at the 4-position (**1c** and **1d**) did not interfere with the reaction. With the bulky 4-*t*-Butyl group (**1d**), the reaction yield increased to 93% (entry 4). Electron withdrawing groups such as Cl, F, and keto (**1e**, **1f** and **1g**) at the 4 position were well tolerated and the desired products (**2e**, **2f** and **2g**) were isolated in 84%, 86% and 78% yields, respectively (entries 5–7). It is worth noting that for substrate **1g**, possible cycloaddition to the C=O bond was not observed, neither was the transfer hydrogenation of the C=O bond. This might suggest that the C–H activation is kinetically favored and the Rh was not scramble to other parts of the reactant during the reaction. Substrate **1e** with the electron-rich methoxyl group was also amenable to the protocol, giving the desired product **2e** in 83% yield (entry 8).

Other types of aryl ring A were also tested (entries 9–12). Both 2-naphthyl (**1i**) and 1-naphthyl (**1j**) substrates afforded π-extended conjugated silole products **2i**, **2j** in respectively 90% and 78% yield (entries 9 and 10). In the case of **1i,** the C–H silylation occurred exclusively at the less hindered position. Heterocyclic siloles are promising optoelectronic

Table 2: Substrate scope.[a]

Entry	Substrate	Product	Yield[b]
			
1	R = H, **1a**	**2a**	84
2	*R* = 3-Me, **1b**	**2b**	89[d]
3	*R* = 4-Me, **1c**	**2c**	90
4	*R* = 4-*t*-Bu, **1d**	**2d**	93
5	*R* = 4-Cl, **1e**	**2e**	84
6	*R* = 4-F, **1f**	**2f**	86
7[c]	*R* = 4-C(O)$(CH_2)_3CH_3$, **1g**	**2g**	78
8	*R* = 4-OMe, **1h**	**2h**	83
			
9	**1i**	**2i**	90
			
10	**1j**	**2j**	78
			
11	**1k**	**2k**	85
			
12	**1l**	**2l**	84[d]
			
13	**1m**	**2m**	91
			
14[c]	**1n**	**2n**	57

[a] Conditions: 0.1 mmol substrate, $[Rh(cod)Cl]_2$ (5 mol%), TMS-segphos (10 mol%) and toluene (1 mL) were dissolved in the glove box. [b] Isolated yield. [c] 72 h. [d] other possible regioisomeric products were not detected.

materials,[18] but their syntheses are more challenging than siloles. Using this SCB method, both benzofuran and thiophene fused siloles **2k** and **2l** were rapidly obtained in 85% and 84% yields, respectively (entries 11 and 12). Again, the C–H bond silylation of **1l** occurred exclusively at the *ortho* position of the sulfur atom (entry 12). Double C–H silylation is possible: the fused bis-silole product **2m** was obtained in an excellent yield (91%) (entry 13). Although the

stereo center generated from the first C–H silylation is far away from the second silicon atom, excellent stereoselectivity of the second C–H silylation was observed, affording only one diastereomeric product. Substrate **1n** with ethyl substituent on the silicon atom gave product **2n** in a lower yield (entry 14), confirming that the reaction is very sensitive to steric effect.

The effect of substituents on aryl ring B was then investigated (Figure 2). Overall, this class of substrates is less reactive, such that longer reaction time (72 h) was

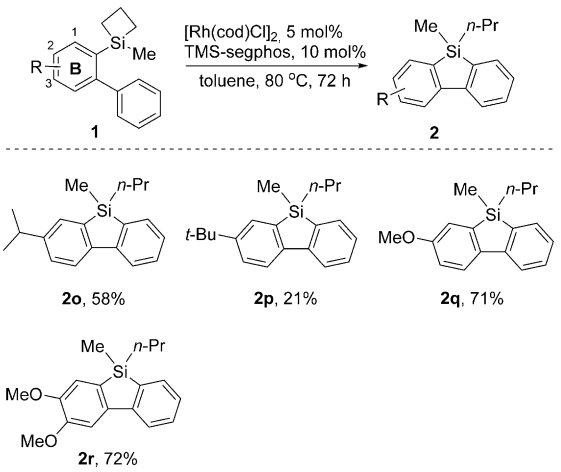


Figure 2. Substituents on aryl ring B

required for complete conversion. The reaction yields range from moderate to good. 3-Isopropyl substituted substrate **1o** gave a 58% yield. When this same position was substituted with a *tert*-butyl group (**1q**), the yield dropped to 21%. This result again suggested that the steric hindrance, even seemingly remote from the Si center, has a dramatic influence on the reaction (c.f. **1m**). In line with this observation, less hindered aryl ring B is beneficial. For example, 3-methoxyl substituted **2q** and 3,4-dimethoxyl substituted substrate **2r** furnished the desired products in good yields.

During the screening, we discovered that C(sp^3)–H bonds could also be silylated (Figure 3).[23] 2,6-Dimethyl substituted substrates **1s** and **1t** reacted smoothly under the standard conditions to afford the six-member silacycles **3a** and **3b** in

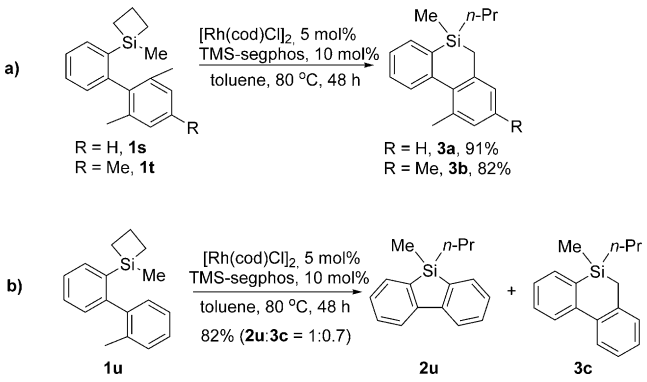
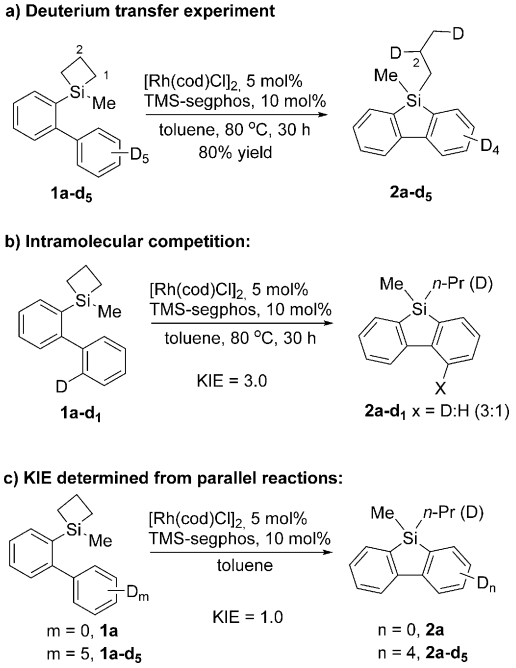


Figure 3. C(sp^2)–H vs. C(sp^3)–H silylation.

high yields (Figure 3a). When there is a competing C(sp^2)–H bond such as in substrate **1u**, silyation of both types of C–H bonds were observed and the C(sp^2)–H bond silylation product is slightly favoured (Figure 3b).

A series of experiments were carried out to explore the reaction mechanism (Scheme 1). First, the fully deuterated



Scheme 1. Deuterium experiments.

substrate **1a**–$\mathbf{d_5}$ was subjected to the reaction conditions (Scheme 1a). The desired product **2a**–$\mathbf{d_5}$ was isolated in a comparable yield (80%) to that of **1a** (84%). The deuterium atom was observed to transfer to both C1 and C2 positions of the propyl group (the existence of D atom in C1 and C2 was confirmed by both ^{1}H and ^{2}H NMR, see the Supporting Information). This deuterium incorporation indicates that the SCB is the internal hydrogen acceptor and the re-hydrogenation step proceeded in a non-regioselective fashion. Moreover, while reaction of mono-deuterated substrate **1a**-$\mathbf{d_1}$ revealed a moderate kinetic isotope effect (KIE) (Scheme 1b), the parallel reactions between substrates **1a** and **1a**-$\mathbf{d_5}$ however did not show a similar effect (Scheme 1c). This pair of experiments suggested that the C–H bond activation is unlikely the rate limiting step.[24]

Based on our preliminary mechanistic study (Supporting Information) we proposed a plausible mechanism (Figure 4) using **1a** as an example. First, five-membered silametallacycle **I** is formed via reversible oxidative insertion of Rh^I complex into the SCB.[5,25] Subsequent β-H elimination of **I**, possibly enabled by the sterically hindered TMS-segphos ligand, would give the key hydrido-rhodium(III) **II**, in which the terminal alkene probably still coordinates to the Rh. Since only Rh^I is known to activate C–H bonds, reductive elimination of intermediate **II** is assumed to give Rh^I intermediated **III** along with HCl. The Si–Rh^I then undergoes reversible C–H bond activation,[11] affording Rh^{III} intermedi-

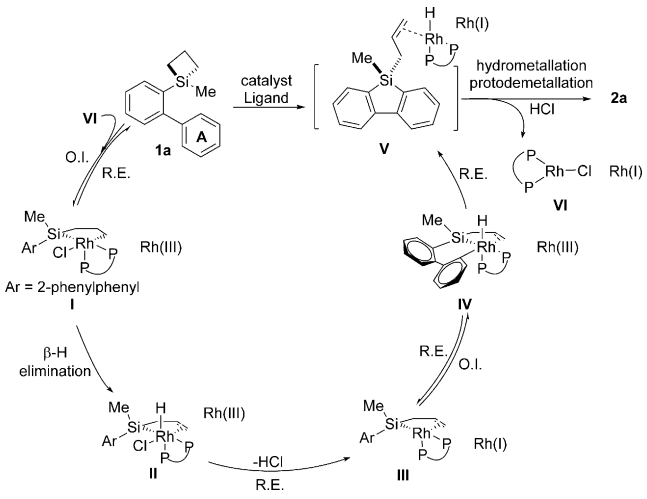


Figure 4. Proposed mechanism.

ate **IV**. A second reductive elimination would generate the silole precursor **V**. Hydrometallation of the terminal alkene and subsequent protodemetallation with HCl would produce the final product **2a** and regenerate Rh complex **VI**. In essence, the endocyclic β-H elimination not only leads to the formation of catalytic active Si–Rh^I, but also generates a pendant alkene as the internal hydrogen acceptor. Such a catalytic cycle is in good agreement with current experimental observations and is under active investigation.

In conclusion, we discovered that silacyclobutane is a new C–H silylation reagent under the catalysis of Rh^I, providing efficient and regioselective syntheses of functionalized siloles. This new reactivity of SCB can be attributed to a rarely documented endocyclic β-H elimination of five-membered metallacycles. We expect SCB to find applications in other C–H silylation reactions. Related studies along this line, as well as full mechanistic studies are being pursued and will be reported in due course.

Experimental Section

To a screw caped tube were added **1** (0.1 mmol), $[Rh(cod)Cl]_2$ (5 mol%, 2.5 mg), TMS-segphos (10 mol%, 12.0 mg) and degassed toluene (1 mL) in a N_2 flushed glove box. The tube was capped, removed from the glove box. The system was stirred at indicated temperature and concentrated under vacuum after completion. The residue was purified by silica gel chromatography to afford the desired product.

Acknowledgements

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Keywords: C–H activation · metallocycle · silole · silylation · β-hydrogen elimination

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