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Palladium(0)-catalyzed $C(sp^3)$–Si bond formation *via* formal carbene insertion into a Si–H bond†

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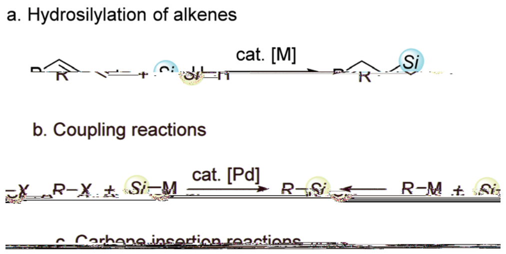
Pd(0)-Catalyzed formal carbene insertion into Si–H bonds has been achieved as an efficient method for $C(sp^3)$–Si bond formation. The reaction, which uses readily available *N*-tosylhydrazones as the diazo precursors, is highly efficient and shows a wide substrate scope. Rh(II) and Cu(I) salts, which are the widely used catalysts for carbene insertion reactions, have been proved to be ineffective for the current reaction. A Pd(II) carbene migratory insertion/reductive elimination mechanism is proposed.

Organosilicon compounds play vital roles in various fields such as organic synthesis, material sciences and life sciences.[1] Therefore, methods for constructing C–Si bonds are highly demanded. For $C(sp^3)$–Si bond formation, hydrosilylation of alkenes represents one of the most important methods, which has found applications both in research laboratories and in industry (Scheme 1a).[2] However, this powerful method still suffers drawbacks of low efficiency and poor regioselectivity with hindered alkenes.[3] Another effective way to construct $C(sp^3)$–Si bonds is the reaction of organometallic species with silicon electrophiles.[4] Besides, the coupling of silicon nucleophiles (Zn and B-based silicon nucleophiles) with alkyl electrophiles has been reported by Fu and Oestreich (Scheme 1b).[5]



Scheme 1 Construction of a $C(sp^3)$–Si bond.

On the other hand, transition-metal-catalyzed carbene insertion into Si–H bonds represents a unique route for $C(sp^3)$–Si bond formation (Scheme 1c).[6] A series of transition metals, including Rh(II), Rh(I), Cu(II), Cu(I), Ir(III), Ag(I), Ru(II) and Fe(II), are effective for this transformation. Rh(II) and Cu(I) salts are among the most frequently used catalysts for this reaction. Mechanistic studies indicate that the Si–H insertion occurs through a concerted three-membered cyclic transition state, similar to the Rh(II) or Cu(I)-catalyzed C–H bond insertions.[7] It is worth mentioning that for those carbene Si–H bond insertions, the relatively stable diazocarbonyl compounds have been applied as the carbene precursor in most cases. Thus, the carbene Si–H insertion method is limited to the introduction of a C–Si bond to the α-position of an electron-withdrawing group. The diazo substrates without an electron-withdrawing substituent are unstable, but they can be generated *in situ* from *N*-tosylhydrazones *via* Bamford–Stevens reaction.[8] Therefore, *N*-tosylhydrazones have recently been extensively explored in transition-metal-catalyzed carbene transfer reactions as well as in cross-coupling reactions.[9]

We have recently reported a Pd(0)-catalyzed formal carbene insertion into Si–Si and Sn–Sn bonds with *N*-tosylhydrazones as the carbene precursors.[10] The reaction is proposed to follow a reaction sequence consisting of oxidative addition of σ-bonds to Pd(0), Pd(II) carbene formation, migratory insertion and finally reductive elimination. As the continuation of our interest in this type of σ-bond insertion reaction, herein we report our study on the Pd(0)-catalyzed carbene insertion into Si–H bonds with

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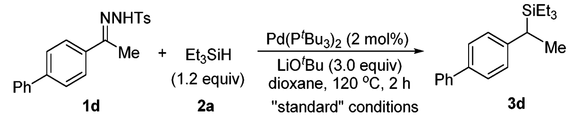
Table 1 Investigation of the reaction parameters[a]



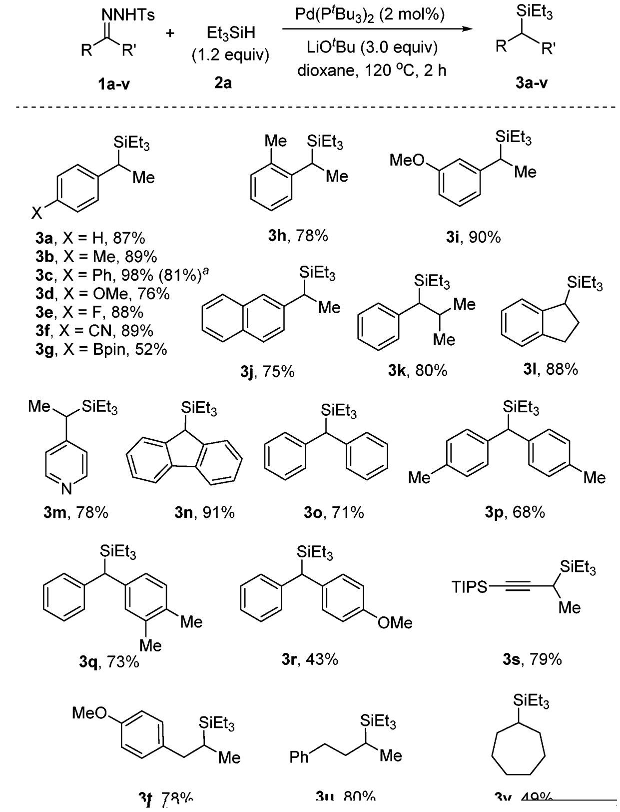
Entry	Variation from the ''standard'' conditions	Yield[b] (%)
1	None	98
2	Without $Pd(P^tBu_3)_2$	Trace
3	With $Rh_2(OAc)_4$ (2 mol%), instead of $Pd(P^tBu_3)_2$	Trace
4	With CuCl (5 mol%) instead of $Pd(P^tBu_3)_2$	Trace
5	With $Cu(OTf)_2$ (5 mol%) instead of $Pd(P^tBu_3)_2$	Trace
6	With $Pd(OAc)_2$ (5 mol%) instead of $Pd(P^tBu_3)_2$	Trace
7	With $Pd(PPh_3)_4$ (5 mol%) instead of $Pd(P^tBu_3)_2$	Trace
8	With $Pd_2(dba)_3$ (2.5 mol%)/$P^tBu_3{\cdot}HBF_4$ (10 mol%) instead of $Pd(P^tBu_3)_2$	40
9	At 100 °C instead of 120 °C	78

[a] All reactions were conducted at a 0.1 mmol scale. [b] Yields of isolated products with silica gel column chromatography.

N-tosylhydrazones as the carbene precursors (Scheme 1d).[11] To the best of our knowledge, this reaction represents the first example of formal Si–H bond carbene insertion with a palladium catalyst.

As benzylsilane, especially secondary benzylsilane, cannot be easily accessed by hydrosilylation of alkenes or coupling reactions, we chose *N*-tosylhydrazone **1d** and commercially available triethylsilane **2a** as the substrates (Table 1).[12] Upon some initial experiments, we determined that 2 mol% $Pd(P^tBu_3)_2$ with 3.0 equiv. LiO^tBu in dioxane at 120 °C were ''standard'' conditions, furnishing the target compound **3d** in 98% yield (Table 1, entry 1). The $Pd(P^tBu_3)_2$ turned out to be necessary (Table 1, entry 2). $Rh_2(OAc)_4$, CuCl and $Cu(OTf)_2$, which are widely-used catalysts for carbene insertion into Si–H bonds, failed to catalyse the current reaction (Table 1, entries 3–5). This indicates that the Pd(0)-catalyzed reaction is mechanistically different from the classic Rh(II)- or Cu(I)-catalyzed carbene Si–H bond insertion. Further experiments showed that $Pd(OAc)_2$ and $Pd(PPh_3)_4$ could not catalyse the reaction, while the reaction with $Pd_2(dba)_3$/$P^tBu_3{\cdot}HBF_4$ gave the product in 40% yield (Table 1, entries 6–8). This suggests that the electron-rich phosphine ligand is essential, presumably for the effective oxidative addition of Si–H bond to Pd(0) (*vide infra*). It was also observed that high temperature is beneficial for the insertion reaction as the yield dropped to 78% when the reaction was carried out at 100 °C (Table 1, entry 9).

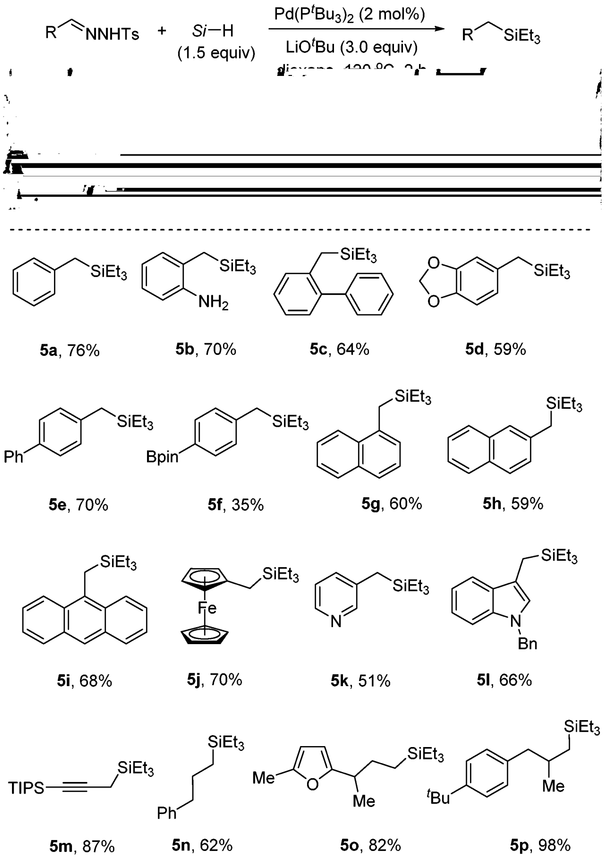
Next, we proceeded to explore the substrate scope of the reaction. As shown in Scheme 2, a series of *N*-tosylhydrazones worked well under the current conditions, affording the desired products efficiently. For mono-substituted aromatic ketone derived *N*-tosylhydrazones, the substrates bearing substituents on the *para*-, *meta*-, and *ortho*-positions with different electronic properties all proceeded well in the reaction (**3a–i**). Interestingly, the Bpin substituent could be tolerated under the current conditions (**3g**). Substrates bearing naphthyl-, indanyl- and sterically bulky isopropyl substituents also reacted smoothly to give the corresponding products in good yields (**3j–l**). Pyridine-containing *N*-tosylhydrazone was also a suitable substrate for the reaction (**3m**). *N*-Tosylhydrazone derived from diaryl ketones could be used in the reaction and the corresponding products were obtained in moderate to good yields (**3n–r**). Besides, *N*-tosylhydrazone derived from alkynyl ketone also worked well (**3s**). It is noteworthy that the TIPS substituent is essential in this case, otherwise the *N*-tosylhydrazone undergoes an intramolecular cyclization reaction. Apart from the preparation of benzylsilanes, tetra-alkyl silanes could also be obtained using this reaction (**3t–v**).



Scheme 2 Scope of the reaction with *N*-tosylhydrazones derived from ketones. All the reactions were carried out at a 0.3 mmol scale. All the yields refer to the isolated products with silica gel column chromatography. [a] The yield in the bracket refers to a gram-scale reaction (1.08 g of **3c** obtained).

The *N*-tosylhydrazones derived from aldehydes were then examined. The reaction was found to be similarly efficient and the substrate scope is wide (Scheme 3). For *N*-tosylhydrazones derived from aromatic aldehydes, the yields ranged from moderate to good (**5a–i**). Notably, a NH_2 group and Bpin could be tolerated (**5b**, **5f**). The reaction substrate could also be expanded to ferrocene-carboxaldehyde and heteroaromatic aldehyde derived *N*-tosylhydrazones (**5j–l**). *N*-Tosylhydrazones derived from alkynyl and alkyl aldehydes also worked well (**5m–q**). Bis-*N*-tosylhydrazones could also be used in the reaction, affording the corresponding bis-silylation products in moderate yields (**5r**). Apart from triethylsilane, dimethyl(phenyl)silane reacted similarly with *N*-tosylhydrazone **4e** and gave the product **5s** in 71% yield.

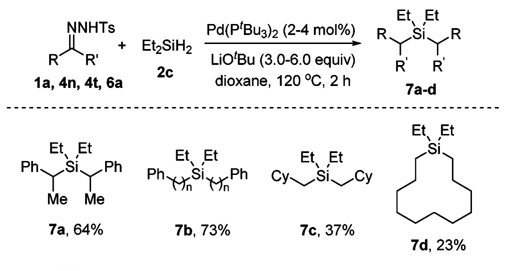
When Et_2SiH_2 was used as a reactant, two C–Si bonds can be formed in the reaction. As shown in Scheme 4, for the reactions of *N*-tosylhydrazones derived from ketone and aldehyde with Et_2SiH_2 (**2c**), double Si–H insertion products could be afforded in low to moderate yields (**7a–c**). When bis-*N*-tosylhydrazones were used, 12-membered silacycle could be obtained (**7d**).



Scheme 3 Scope of the reaction with *N*-tosylhydrazones derived from aldehydes. All the reactions were carried out at a 0.3 mmol scale. All the yields refer to the isolated products with silica gel column chromatography. [a]The amount of **4r** is 0.15 mmol, and the others are the same as above.

While the yield of silacycle was poor, the reaction demonstrates the possibility to access such type of silane compounds using this reaction.

Finally, we carried out the double Si–H insertions sequentially using two different *N*-tosylhydrazones in a one pot manner, obtaining the corresponding products (**8a**, and **b**) in moderate yields (Scheme 5).



Scheme 4 Pd(0)-Catalyzed cross-coupling of *N*-tosylhydrazones with Et_2SiH_2. Reaction conditions for **1a**, **4n**, and **4t** with **2c**: **1a**, **4n** or **4t** (0.3 mmol), **2c** (0.225 mmol), Pd(P^{t}Bu$_3$)$_2$ (0.006 mmol, 2 mol%), LiO^{t}Bu (0.9 mmol, 3.0 equiv.), dioxane (4.0 mL), 120 °C for 2 h. Reaction conditions for **6a** with **2c**: **6a** (0.15 mmol), **2c** (0.225 mmol), Pd(P^{t}Bu$_3$)$_2$ (0.006 mmol, 4 mol%), LiO^{t}Bu (0.9 mmol, 6.0 equiv.), dioxane (4.0 mL), 120 °C for 2 h. All the yields refer to the isolated products with silica gel column chromatography.

Based on the above results and our previous report,[10] we have proposed the reaction mechanism as shown in Scheme 6. The catalytic cycle starts with the oxidative addition of the Si–H bond to Pd(0) **A** to generate Pd(II) species **B**.[13] The Pd(II) species **B** then reacts with the *in situ* formed diazo substrate to generate Pd(II) carbene **C**. Subsequently, there are two possible pathways: (1) the hydride may migrate into carbenic carbon and form **D** (path a); or (2) silyl migratory insertion to give **C** (path b). Finally, reductive elimination occurs to complete the catalytic cycle and give the insertion products. Both paths are conceivable, and further rigorous investigation is required to unambiguously confirm the reaction mechanism.[14]

In summary, we have reported an efficient method for C(sp^3)–Si bond formation. Compared with the classic transition-metal-catalysed carbene Si–H bond insertions, the Pd(0)-catalysed reaction expands the reaction scope for more general C(sp^3)–Si bond formations. Moreover, the Pd(0)-catalyzed formal Si–H bond insertion is proposed to follow a stepwise mechanism involving oxidative addition, carbene migratory insertion and reductive elimination, which is fundamentally different from the classic carbene Si–H bond insertions. Further study toward enantioselective version of the reaction is currently under way in our laboratory.

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Conflicts of interest

There are no conflicts to declare.

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