

Iron Porphyrin-Catalyzed Insertion Reaction of *N*-Tosylhydrazone-Derived Carbenes into X-H (X = Si, Sn, Ge) Bonds

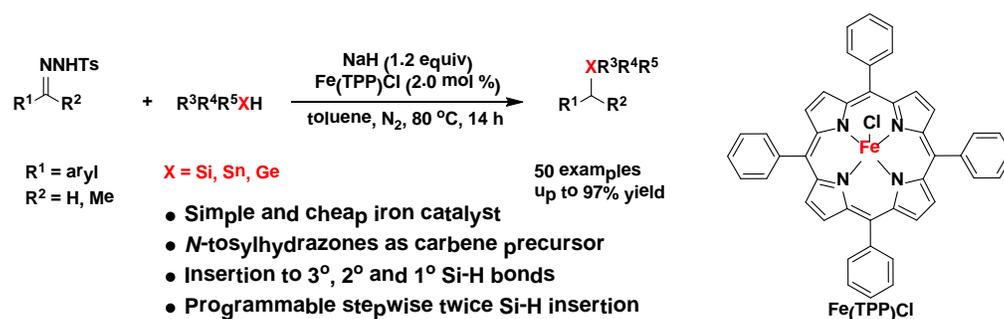
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Supporting Information Placeholder



ABSTRACT: An efficient Fe(TPP)Cl catalyzed insertion reaction of *in situ* generated benzylic carbenes from *N*-tosylhydrazones into X-H (X = Si, Sn, Ge) was developed. Silanes bearing 3°, 2° and 1° Si-H bonds all reacted well to afford insertion products in moderate to high yields (up to 97%) and the reaction time could be significantly shortened to 1 hour under microwave irradiation. A programmable stepwise twice insertion strategy was developed for the synthesis of unsymmetrical tetra-substituted silanes.

A transition metal catalyzed carbene insertion reaction to X-H bonds is a straightforward and appealing strategy for the construction of C-X bonds.¹ In particular, the metal catalyzed carbene insertion reaction into the Si-H bond of simple silanes has emerged as an efficient and convenient method for the preparation of functionalized organosilicon compounds.² Due to the versatile application of organosilicon compounds in organic synthesis,³ material science⁴ as well as the abundance of simple silanes, much effort has been devoted to metal complexes catalyzing selective carbene insertion reactions to Si-H bonds. Transition metals such as Rh⁵, Cu⁶, Ir⁷ and Ru⁸ have been reported to catalyze the decomposition of diazo compounds to generate carbene intermediates and insert to Si-H bonds in high efficiency. It is noteworthy that, recently, iron catalysts were also reported to catalyze the carbene insertion reaction of Si-H bonds with α -diazo compounds as the carbene source.⁹ Despite the fact that much progress has been achieved in transition metal catalyzed Si-H insertion reactions with diazo compounds as the carbene source, the toxicity and potential explosive character of diazo compounds restricts their

application in organic synthesis. In this regard, generation of diazo compounds *in situ* from a stable precursor such as *N*-sulfonylhydrazones would be beneficial.¹⁰ An elegant AgOTf prompted carbene insertion reaction into a tertiary Si-H bond was reported by Bi and coworkers in 2017.¹¹ *N*-tosylhydrazones derived from aldehydes and ketones were successfully used as the carbene precursor and the corresponding insertion products were isolated in moderate to high yields. Unfortunately, the more commonly used *N*-tosylhydrazone gave low yield under the same reaction conditions, and 30 mol % AgOTf was necessary for achieving a high yield of the insertion product. Recently, Xiao and Lin reported the iron porphyrin catalyzed insertion reaction into a tertiary Si-H bond with trifluoromethylcarbene and difluoromethylcarbene generated *in situ* from sulfonium salts, in which the fluorinated carbon chain was essential for the reaction.¹² Metal porphyrins are robust catalysts in carbene transfer reactions.^{9a,13} We have previously reported the isolation of reactive iron porphyrin carbene intermediates which may undergo C-H insertion,¹⁴ and found iridium porphyrin could efficiently catalyze asymmetric

Si-H insertion with a donor-acceptor diazo compound as the carbene source.^{7b} Herein, we would like to report our work on iron porphyrin catalyzed selective carbene insertion into X-H bonds with readily available *N*-tosylhydrazones as the carbene source. Not only tertiary, but also secondary and primary Si-H bonds could be efficiently inserted under mild reaction conditions. Consequently, a programmable stepwise insertion sequence was developed, through which unsymmetrical tetra-substituted silanes could be easily accessed. In addition, the insertion reaction of Sn-H and Ge-H bonds could also be efficiently catalyzed to afford the insertion products in high yields.

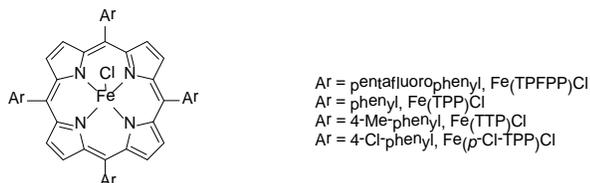


Figure 1. Structure of iron porphyrin catalysts

The catalytic carbene insertion reaction into a Si-H bond was initially investigated using triethylsilane **1a** as the model substrate and *N*-tosylhydrazone **2a** as the carbene source, in the presence of various catalysts including iron porphyrins (Figure 1) with K₂CO₃ as base in toluene at 80 °C. The reactions catalyzed by copper salts were complicated and the desired Si-H insertion product **3a** was formed in only 16-25% yields (entries 1-4, Table S1 in the Supporting Information). Subsequently, some rhodium and cobalt porphyrins were investigated as the catalyst in the reaction (entries 5-10, Table S1), and Rh(TPP)Cl showed higher activity to afford **3a** in 50% yield (entry 6, Table S1). To our delight, when various iron porphyrin (Fig. 1) were employed as the catalyst (entries 11-15, Table S1), the readily available iron porphyrin Fe(TPP)Cl sufficiently promoted the Si-H insertion reaction to afford **3a** in a much higher yield of 62% (entry 12, Table S1). Extension of the reaction time to 14 hour further improved the reaction and **3a** was isolated in 76% yield (entry 15, Table S1).

With Fe(TPP)Cl as the catalyst, the reaction conditions were further optimized (Table 1). The reaction was tolerant to a number of common solvents such as DCM, CHCl₃, DCE, THF and 1,4-dioxane, and **3a** was obtained in moderate to good yields. Toluene and DCE led to highest yield of 76% (Table 1, entries 1-6). Either lowering or raising the reaction temperature led to lower yield of **3a**, which may due to the insufficient conversion of *N*-tosylhydrazones to the diazo compound at 60 °C and more competitive side reactions at 110 °C (Table 1, entries 7-8). It is noteworthy that the base played an important role for achieving high yield of **3a**. Organic bases such as Et₃N and DBU were not strong enough to convert *N*-tosylhydrazones **2a** to the corresponding diazo compound and only a trace amount of **3a** was formed (Table 1, entries 9-10). Stronger inorganic bases gave better results and NaH proved to be the best to afford **3a** in 90% yield (Table 1, entries 11-13). Lowering the catalyst loading to 1 mol % and 0.5 mol % led to slightly lower yields of 85% and 75%, respectively (Table 1, entries 14-15). While increasing the catalyst loading to 5 mol % didn't improve the reaction (Table 1, entry 16). And

increasing the amount of Et₃SiH to 4 equiv slightly improved the yield (Table 1, entry 17).

Table 1. Optimization of the reaction conditions^a

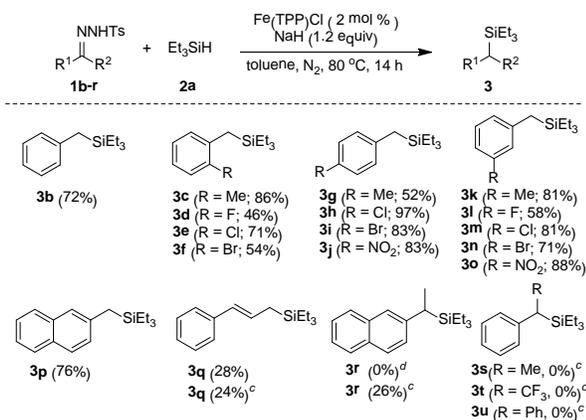
entry	solvent	base	temp (°C)	yield ^b (%)
1	toluene	K ₂ CO ₃	80	76
2	DCM	K ₂ CO ₃	80	69
3	CHCl ₃	K ₂ CO ₃	80	42
4	DCE	K ₂ CO ₃	80	76
5	THF	K ₂ CO ₃	80	51
6	1,4-dioxane	K ₂ CO ₃	80	60
7	toluene	K ₂ CO ₃	60	NP
8	toluene	K ₂ CO ₃	110	38
9	toluene	Et ₃ N	80	5
10	toluene	DBU	80	4
11	toluene	KH ₂ PO ₄	80	34
12	toluene	Na ₂ CO ₃	80	2
13 ^c	toluene	NaH	80	90
14 ^{c,d}	toluene	NaH	80	85
15 ^{c,e}	toluene	NaH	80	75
16 ^{c,f}	toluene	NaH	80	90
17 ^{c,g}	toluene	NaH	80	92

^aUnless otherwise specified, reaction conditions were: **1a** (0.2 mmol), **2a** (0.4 mmol, 2 equiv), cat. (2 mol %) and corresponding base (0.4 mmol, 2 equiv) were reacted in specified solvent (2 mL) at the specified temperature for 14 hours. ^bIsolated yield. ^c1.2 equiv of NaH were used. ^d1 mol % cat. ^e0.5 mol % cat. ^f5 mol % cat. ^g4 equiv of Et₃SiH were used.

With the optimized reaction conditions and employing 2 mol % Fe(TPP)Cl as catalyst, the insertion reaction of various *N*-tosylhydrazones into Et₃SiH was investigated; the corresponding products are depicted in Scheme 1. A series of *N*-tosylhydrazones derived from different substituted benzaldehydes were well tolerant of the optimized reaction conditions. The insertion products were generally obtained in moderate to excellent yields, regardless of the electronic nature and position of the substituents in the phenyl ring (**3b-o**). *N*-Tosylhydrazone **1p** derived from β-naphthaldehyde also underwent the reaction well to afford the insertion product **3p** in 76% yield. The α,β-unsaturated aldehyde derived *N*-tosylhydrazone **1q** could also be converted to the corresponding insertion product **3q** in 28% yield. *N*-Tosylhydrazones derived from ketones were subsequently investigated. When the *N*-tosylhydrazone derived from 2-acetonaphthone **1r** was treated in the optimized reaction conditions, 42% of 2-naphthylethylene derived from 1,2-hydride migration was formed instead of the desired insertion product **3r**. Changing the base from NaH to K₂CO₃ improved the reaction and **3r** was afforded in 26% yield. When benzophenone derived *N*-

tosylhydrazone **1s** was employed as the substrate, 1,2-hydride migration dominated and **3s** was not detected. When *N*-tosylhydrazone **1s** and **1t** derived from ketones without an α -hydride were attempted, alkenes derived from the dimerization side reaction dominated and no desired insertion products were detected.

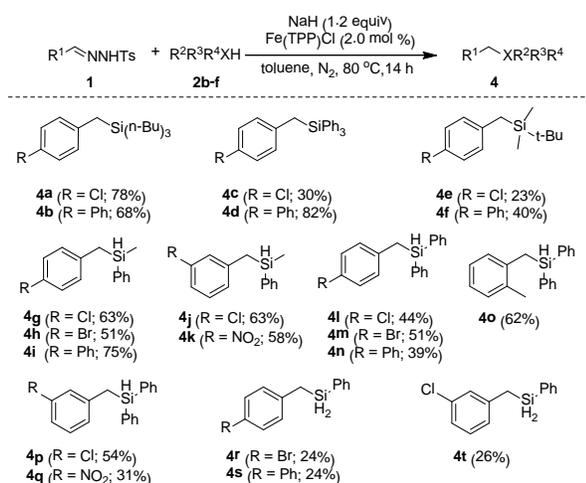
Scheme 1. Scope of *N*-tosylhydrazones^{a,b}



^aReaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $\text{Fe}(\text{TPP})\text{Cl}$ (2 mol %) and NaH (0.24 mmol) were reacted in toluene (2 mL) at 80 °C for 14 hours. ^bIsolated yield. ^c K_2CO_3 (2 equiv) was used. ^d42% 2-naphthylethylene was formed.

Subsequently we explored the scope of silanes and the results are summarized in Scheme 2. Tributyl silane and triphenyl silane afforded the corresponding insertion products **4a-4d** in moderate to good yields. *Tert*-butyldimethylsilane was also a suitable substrate for this reaction albeit with relatively low yield, presumably due to the steric hindrance of *tert*-butyl group. To our delight, silanes with secondary Si-H bonds could also be employed in the reaction. The insertion reaction of both methylphenylsilane and diphenylsilane underwent smoothly with a variety of different substituted *N*-tosylhydrazones under the optimized reaction conditions and the insertion products **4g-4q** were obtained in moderate to good yields. It is noteworthy that the insertion into the primary Si-H bond of phenylsilane was also applicable to give the corresponding insertion products **4r-4t** in relatively low yield.

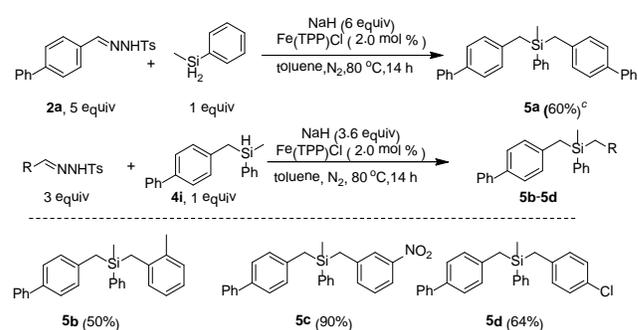
Scheme 2. Scope of silanes^{a,b}



^aReaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $\text{Fe}(\text{TPP})\text{Cl}$ (2 mol %) and NaH (0.24 mmol) were reacted in toluene (2 mL) at 80 °C for 14 hours. ^bIsolated yield.

As insertion into secondary Si-H bonds could be efficiently catalyzed by $\text{Fe}(\text{TPP})\text{Cl}$, a novel method for the preparation of tetra-substituted silanes was further developed (Scheme 3). When methylphenylsilane was treated with excess **2a** (5 equiv), the one-pot double Si-H insertion reaction occurred to afford the desired tetra-substituted silane **5a** in 60% yield, and the mono Si-H insertion product **4i** was obtained in 38% yield. Alternatively, when mono Si-H insertion product **4i** was treated with an excess of different *N*-tosylhydrazones with the optimized reaction conditions, unsymmetrical tetra-substituted silanes **5b-5d** were obtained in moderate to good yields, thus providing an efficient programmable method for the preparation of tetra-substituted silanes.

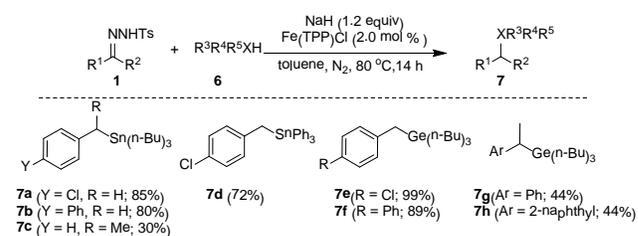
Scheme 3. Synthesis of tetra-substituted silanes^{a,b}



^aReactions were run with 0.2 mmol silane. ^bIsolated yield. ^cMono Si-H insertion product **4i** was isolated in 38% yield.

The insertion reaction of *N*-tosylhydrazones into Sn-H and Ge-H bonds were also explored with the same reaction conditions (Scheme 4). *N*-tosylhydrazones derived from both aldehydes and benzophenone reacted with tributylstannane hydride and triphenylstannane hydride to afford **7a-7d** in moderate to good yields. Similarly, the insertion into Ge-H bond was also applicable to afford **7e-7h** in moderate to high yields.

Scheme 4. Scope of $\text{Fe}(\text{TPP})\text{Cl}$ catalyzed carbene insertion into Sn/Ge-H bonds^{a,b}

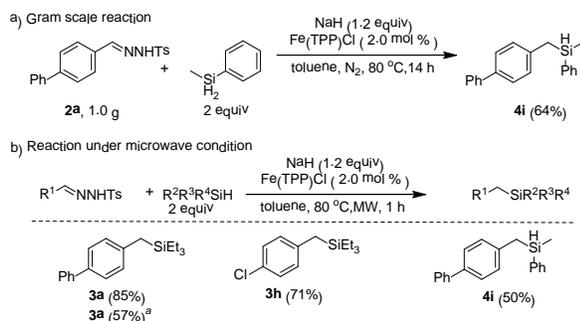


^aReaction conditions: **1** (0.2 mmol), **6** (0.4 mmol), $\text{Fe}(\text{TPP})\text{Cl}$ (2 mol %) and NaH (0.24 mmol) were reacted in toluene (2 mL) at 80 °C for 14 hours. ^bIsolated yield.

To demonstrate the utility of this novel iron porphyrin catalyzed insertion reaction, a gram-scale reaction of $\text{Fe}(\text{TPP})\text{Cl}$ catalyzed *N*-tosylhydrazone **2a**-derived carbene insertion into the secondary Si-H bond of methylphenylsilane was conducted, and the desired insertion product **4i** was isolated in 64% yield (Scheme 5, equation a). Moreover, the insertion

reaction could be carried out under microwave irradiation conditions at 80 °C and no precaution of moisture and oxygen was needed. The reaction time was greatly shortened to 1 hour and the corresponding insertion products were afforded in moderate to good yields. And the reaction even worked at 60 °C, albeit with lower yield. (Scheme 5, equation b).

Scheme 5. Gram-scale and microwave reaction



^aReaction was conducted at 60 °C for 1 h.

In conclusion, we successfully developed a practical and efficient iron porphyrin catalyzed carbene insertion into X-H (X = Si, Sn and Ge) bonds with readily available *N*-tosylhydrazones as the carbene source. With as low as 2 mol % Fe(PPP)Cl as the catalyst, a series of different substituted *N*-tosylhydrazones derived from benzaldehydes sufficiently reacted with silanes bearing tertiary, secondary and primary Si-H bonds under mild reaction conditions to afford the desired insertion products in moderate to high yields, and the reaction time could be significantly shortened to 1 hour under microwave irradiation. The insertion reaction could also be applied to Sn-H and Ge-H bonds to afford the insertion products in good to high yields. A programmable stepwise twice insertion strategy was developed for the synthesis of unsymmetrical tetra-substituted silanes, which further broaden the application of this iron porphyrin catalyzed Si-H insertion reaction. The detailed mechanism and application of this catalysis is currently underway in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

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Notes

The authors declared no competing financial interest.

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