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$B(C_6F_5)_3$-Catalyzed Cyclization of alkynes: Direct Synthesis of 3-Silyl Hetero Cyclic Compounds

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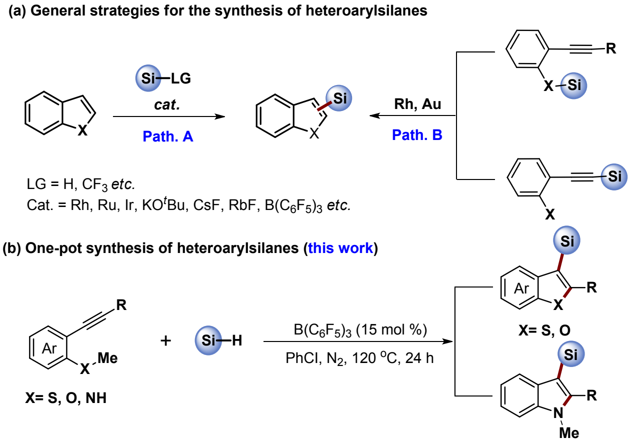
Mengxing Li, Ting Wang, Zhenyu An, Rulong Yan*

An efficient one-pot strategy for easy access to 3-silyl hetero cyclic compounds has been developed via a $B(C_6F_5)_3$-catalyzed cycloaddition reaction of *o*-(1-alkynyl)(thio)anisoles or *o*-(1-alkynyl)-*N*-methylaniline. In this reaction, benzenethiophene, benzofuran or indole skeleton can be constructed by the intermolecular cycliazation with diphenylsilane. This protocol features moderate to good yields with metal-free reaction systems.

Heteroarylsilanes are stable and find widespread use in medical imaging applications, polymer synthesis, and drug discovery.[1] As a consequence, the exploitation of efficient methods to construct heteroarylsilanes has become one of the hot-topic areas in modern organic synthesis. Reports to today, many researches have been reported for the synthesis of substituted heteroarylsilanes.[2, 3] As depicted in Scheme 1， these synthetic strategies can be divided into two pathways: (a) direct silylation of heterocyclic compounds catalyzed by the Rh, Ru , Ir etc,[4] and (b) construction of heteroarylsilanes by the cyclizations from the aryne precursors containing the silicon groups.[5] In the developing pathway B, the obvious features of the substrates were already containing the silicon groups, and suffering the tedious and difficult synthesis operation. Therefore, the intermolecular strategy to construct the hetero cyclic compounds with silanes to afford heteroarylsilanes is still highly desirable for its simple and easy operation.

The C-Si bond formation has constantly attracted tremendous interest in the organic and material chemistry.[6] Recently, the $B(C_6F_5)_3$ have often been served as powerful metal-free catalyst for the C-Si bond formation. Several studies on the $B(C_6F_5)_3$-catalyzed the C-Si bond formation have been developed.[7,8] The group of Piers reported the $B(C_6F_5)_3$-catalyzed reactions between hydrosilane and the aromatic aldehydes, ketones, and esters.[8a] In 2016, Hou's group reported the effective C-H silylation of a series of electron-rich aromatic compounds such as *N,N*-disubstituted anilines with a variety of hydrosilanes using $B(C_6F_5)_3$ as a catalyst.[8b] Later, Zhang and co-workers showed that $B(C_6F_5)_3$ -catalyzed convergent disproportionation reaction of indoles with hydrosilanes.[8c] On the other hand, 2-alkynylthioanisoles have been widely used in cyclization process for the construction of benzothiophenes owing to the very stable and readily available properties.[9] In order to develop the method of intermolecular cyclization and silylation to achieve silyl hetero cyclic compounds, herein, we envisaged the feasibility of using $B(C_6F_5)_3$ as a catalyst to generate silylbenzo[*b*]thiophenes with 2-alkynylthioanisoles and diphenylsilane.



Scheme 1 Approaches for the synthesis of heteroarylsilanes

Initially, methyl(2-alkynylphenyl)sulfanes (**1a**) and diphenylsilane were chose as starting materials to explore the reaction conditions. The product (**2a**) was successfully obtained in 34% yield with $B(C_6F_5)_3$ (5 mol %) in toluene at 120°C under nitrogen atmosphere (Table 1, entry 1). Among the various solvents examined, chlorobenzene was superior than toluene, dimethylformamide (DMF), ethanol, and 1,2-dichloromethane (DCM) (Table 1, entries 2-5). When the reaction was carried out under air, a slightly lower yield was obtained (Table 1, entry 6). The amount of $B(C_6F_5)_3$ was also evaluated and 15 mol % of $B(C_6F_5)_3$ showed the best catalytic

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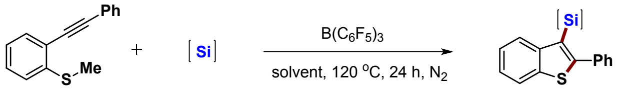
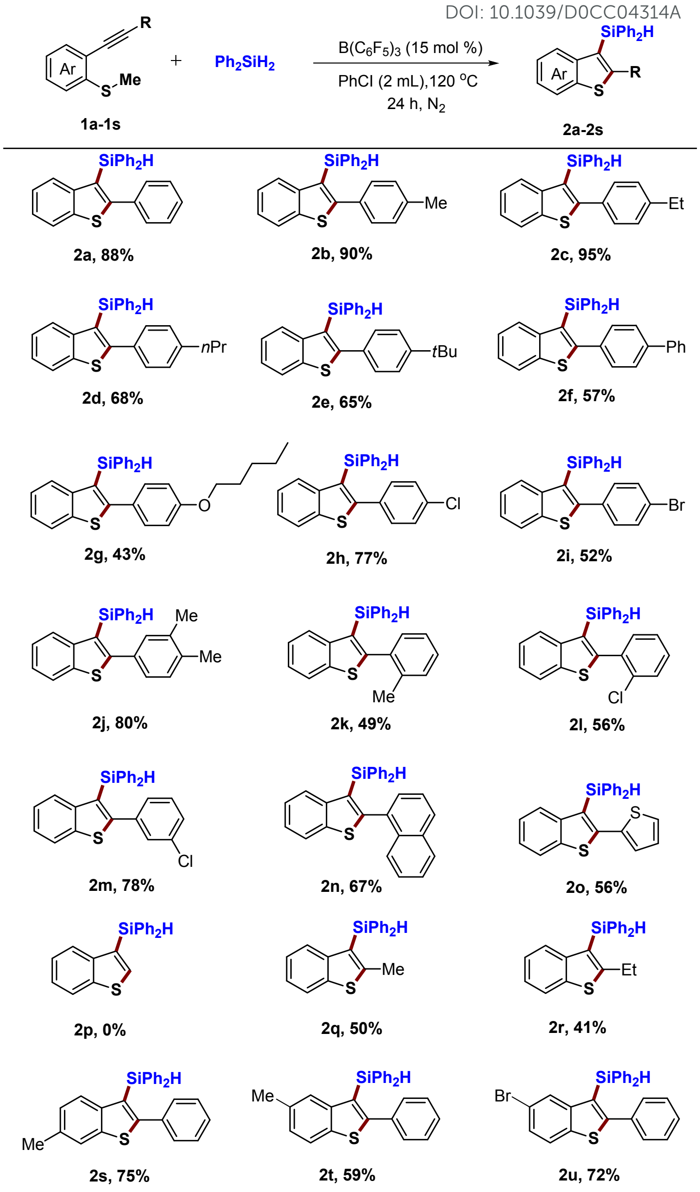
Table 1 Optimization of the reaction conditions [a]



Entry	Silicon sources	Catalyst (mol %)	Solvent	Yield (%)
1	Ph_2SiH_2	5	Toluene	34
2	Ph_2SiH_2	5	PhCl	62
3	Ph_2SiH_2	5	DMF	n.d.
4	Ph_2SiH_2	5	EtOH	n.d.
5	Ph_2SiH_2	5	DCM	25
6[c]	Ph_2SiH_2	5	PhCl	55
7	Ph_2SiH_2	10	PhCl	70
8	**Ph_2SiH_2**	**15**	**PhCl**	**88**
9	Ph_2SiH_2	0	PhCl	n.d.
10[b]	HMD	15	PhCl	n.d.
11	Ph_3SiH	15	PhCl	n.d.
12	$PhSiH_3$	15	PhCl	68
13	Et_3SiH	15	PhCl	44
14	Ph_2MeSiH	15	PhCl	trace

[a] Reaction conditions: **1a** (0.2 mmol), Ph_2SiH_2 (0.4 mmol), $B(C_6F_5)_3$, solvent (2 mL), 120 °C, N_2, 24 h. Isolated yield based on **1a**. [b] HMD = Hexamethyldisilane. [c] Under air.

Table 2 Scope of 3-silylbenzo[*b*]thiophenes [a]



[a] Reaction conditions: **1** (0.2 mmol), Ph_2SiH_2 (0.4 mmol), $B(C_6F_5)_3$ (15 mol %), solvent (2 mL), 120 °C, N_2, 24 h.

efficiency, giving the desired product **2a** in 88% yield (Table 1, entries 7-9). Other silicon sources were also investigated and no corresponding products were detected when hexamethyldisilane(HMD) and triphenylsilane served as silicon sources (Table 1, entries 10-11). Phenylsilane and triethylsilane were employed for this reaction system, giving the corresponding desired products **5** and **6** in 68% and 44% yields respectively (Table 1, entries 12-13). But Ph_2MeSiH only gave a trace amount of the desired product (Table 1, entry 14).

Having optimized the reaction conditions in hand, we explored the generality of this cycloadditions reaction for the generation of 3-silylbenzo[*b*]thiophenes with methyl(2-alkynylphenyl)sulfanes and diphenylsilane as substrates. The results were summarized in table 2. It was found that reactions of methyl(2-alkynylphenyl)sulfanes with various groups work smoothly to provide the corresponding products in moderate to good yields. With electron-donating substituents on the aromatic ring at the terminal alkyne, such as methyl, ethyl, propyl, tertiary butyl, pentyloxy, and phenyl groups, desired products were obtained in 43-95% yields. Electron-withdrawing groups such as chloro and bromo were also tolerated with the optimized reaction conditions, affording the corresponding products in moderate yields (**2h**, **2i**, **2l**, **2m**). The substrate **2k** with substituent at the *ortho* position of the phenyl ring slightly lowered the reactivity may cause by the steric hindrance. Additionally, the substrates with **R** as the naphthyl group (**1n**) and thienyl group (**1o**) were employed for this reaction system, giving the desired products in 67% and 56% yields, respectively. Notably, no desired product **2p** was obtained and starting material **1p** almost all was recovered in this reaction system, this result demonstrated that the terminal active hydrogen of acetylene affected this transformation severely. Moreover, the reaction system is also

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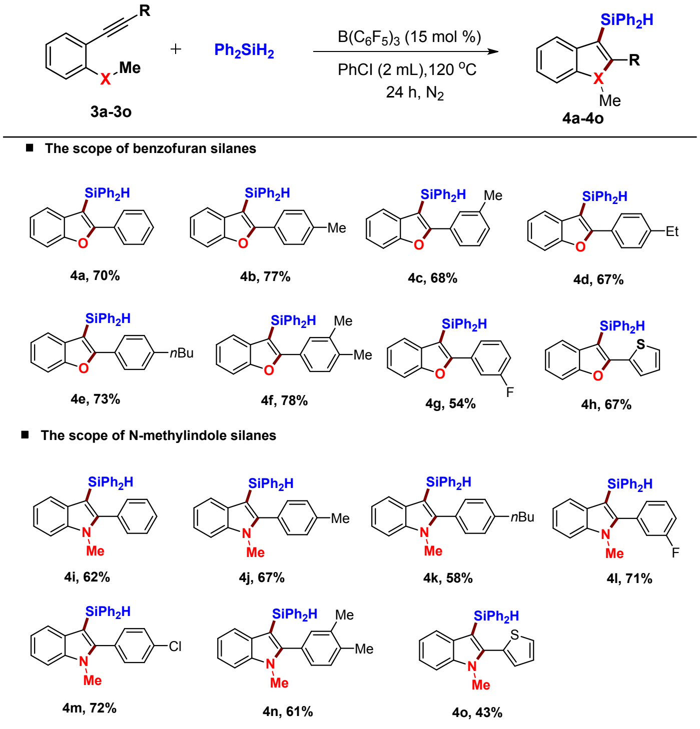
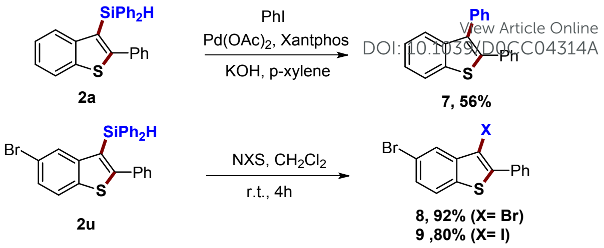
Table 3 Scope of 3-silylbenzo[*b*]furans and 3-silylindoles [a]



[a] Reaction conditions: **3** (0.2 mmol), Ph_2SiH_2 (0.4 mmol), $B(C_6F_5)_3$ (15 mol%), solvent (2 mL), 120 °C, N_2, 24 h.

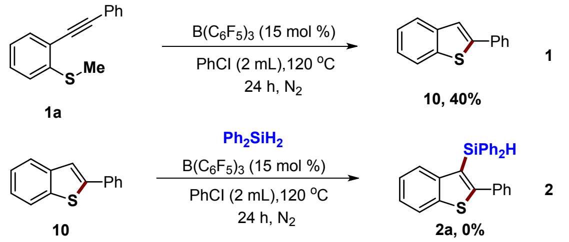
suitable for the more challenging substrates carrying alkyl group on the terminal alkyne (**2q-2r**). Furthermore, the substrates with methyl or bromo group on the aromatic ring also generated the corresponding products **2s, 2t** and **2u** in moderate yields.

To further explore the scope of this protocol, we turned our attention to synthesize of various 3-silylbenzofurans and 3-silylindoles. As shown in table 3, a series of 1-methoxy-2-(phenylethynyl)benzenes underwent efficiently through cyclization to produce the desired 3-silylbenzofurans successfully with satisfactory yields. When the substrates with alkyl on the aromatic ring at the terminal alkyne (**3a-3f**), the reaction worked well, delivering the desired products (**4a-4f**) in 67-77% yields. In the case of substrates with strong electron-withdrawing F group (**3g**), lower yields of the desired products were afforded. In addition, we find that the substrate with thienyl group (**3h**) was also worked smoothly through this transformation. Similarly, the 3-silylindoles were also can be synthesized from *N*-methyl-2(phenylethynyl)anilines with this reaction system. With this transformation, a variety of different substituted 3-silylindoles were furnished in acceptable yields. Various substitutions on the aromatic ring at the terminal alkyne were well tolerated with the reaction conditions and the expected products were obtained in moderate yields (**4i-4m**). As expected, the substrate with a thienyl group at the terminal alkyne also reacted with diphenylsilane to give the product **4o** in 43% yield.



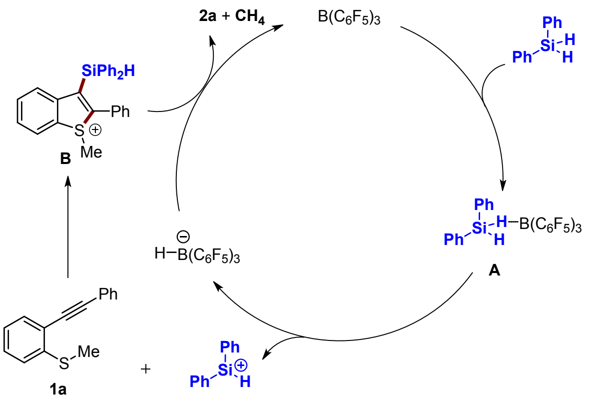
Scheme 2 Further transformation of the heteroarylsilanes

To demonstrate the synthetic value of this method, we investigated the further derivation potential to form diverse heterocyclic compounds by the 3-silylbenzo[*b*]thiophenes. For example, the silylated compound **2a** reacted with PhI to produce compound **7** in 56% yield through the Pd-catalyzed cross-coupling process.[10a] Similarly, the corresponding halogenated products **8** and **9** were obtained in high yields when the compound **2u** was employed as substrate through the bromination and iodination under mild conditions [8b] (Scheme 2).



Scheme 3 Control experiments

To gain insight into the reaction mechanism, several mechanistic experiments were carried out. First, we performed the reaction with **1a** in the absence of diphenylsilane and the benzothiophene **10** was obtained in 40% yield. (Scheme 3, entry 1). The benzothiophene **10** and diphenylsilane were also subjected to the standard conditions and no corresponding desired product **2a** was obtained (Scheme 3, entry 2). This result could rule out that the reaction is proceeded by the sequence of formation of heterocycles and C3 site C-H silylation.



Scheme 4 Proposed mechanism

A plausible reaction mechanism for the present $B(C_6F_5)_3$-catalyzed silylation is depicted in Scheme 4 on the basis of these experimental results and previous reports [7,8,11] Initially, the hydrosilane could be activated by $B(C_6F_5)_3$ through a B-H

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interaction to form the weak adduct **A**. Subsequently, the resulting cationic Ph_2SiH^+ species selectively attacks the triple bond of methyl(2-alkynylphenyl)sulfanes **1a** to generate the intermediate **B** with the forming of C-S bond. Finally, demethylation provides 3-silylbenzo[*b*]thiophene **2a**, along with the $B^-(C_6F_5)_3H$ converting to $B(C_6F_5)_3$.

In summary, we have developed a metal-free electrophilic silylation and cyclization of alkynes. The electrophilic silylation reagent diphenylsilane with $B(C_6F_5)_3$ catalyst proceeds smoothly cycloaddition reaction with alkynes to form various silylation heterocyclic compounds.

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Conflicts of interest

There are no conflicts to declare.

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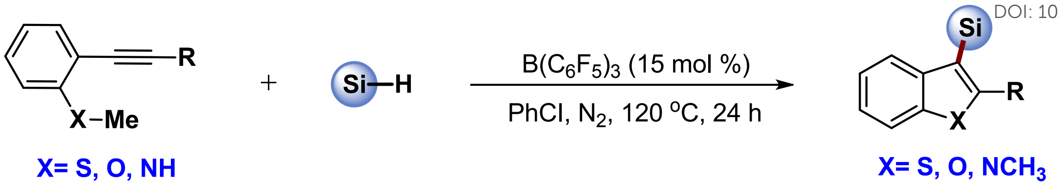

- **One-pot synthesis**
- **High chemoselectivity (C3 position)**
- **High functional group compatibility**
- **Transition-Metal free conditions**