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Palladium-Catalyzed Synthesis of Benzosilolo[2,3-*b*]indoles via Cleavage of a C(sp^3)−Si Bond and Consequent Intramolecular C(sp^2)−Si Coupling

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Supporting Information

ABSTRACT: An efficient process involving Pd-catalyzed selective cleavage of a C(sp^3)−Si bond and consequent intramolecular C(sp^2)−Si coupling has been developed, affording benzosilolo[2,3-*b*]indoles as a new type of silicon-bridged polyheteroarene in excellent yields. Aldehyde was found for the first time to be able to promote the efficiency of the catalytic process remarkably.

The cleavage of carbon−silicon bonds is an important process in synthetic chemistry because it allows the construction of new C−C or C−X bonds, thus leading to new functional molecules.[1] Most of the transition-metal-catalyzed reactions involving cleavage of C−Si bonds have focused on C(sp^2)−Si and C(sp)−Si bonds.[2,3] Trialkylsilyl groups such R^1R^2MeSi are in fact among the most frequently encountered C−Si bonds. However, for the cleavage of C(sp^3)−Si bonds, classic methods usually apply a stoichiometric amount of either an organomagnesium[4] or organolithium reagent[5] under extremely vigorous conditions that do not tolerate many functional groups, thus limiting the synthetic application of these approaches. Although transition-metal-catalyzed cleavage of C(sp^3)−Si bonds would be ideal for overcoming the limitation, only a few special cases involving either small silacycles[1c,6] or activated silyl groups (e.g., Me_3SiCF_3,[7] allyl- or benzylsilanes[8]) have been reported. As for transition-metal-catalyzed cleavage of normal alkyl C(sp^3)−Si bonds, only two reports are present in the literature. Rauf and Brown[9] reported cleavage of a methyl C(sp^3)−Si bond in a $SiMe_3$ group by palladium-catalyzed oxidative methylation of olefins using the $SiMe_3$ group as a methyl source. In this reaction, the presence of an amide group at an appropriate position was essential. Chatani and co-workers[10] developed a rhodium-catalyzed coupling of 2-trimethylsilylphenylboronic acids with alkynes via cleavage of the methyl C(sp^3)−Si bond. Benzosilole derivatives were obtained in high yields. Since trialkyl C(sp^3)−Si bonds are frequently encountered, their efficient selective cleavage and further synthetic applications would be very attractive for both mechanistic study and synthetic chemistry. Herein we report a novel process involving Pd-catalyzed selective cleavage of the C(sp^3)−Si bond in a trialkyl group and consequent intramolecular C(sp^2)−Si bond formation (Scheme 1), which results in the first efficient synthesis of benzosilolo[2,3-*b*] indoles, a new type of silicon-bridged polyheteroarene.[11,12] In addition, for the first time, aldehyde has been found to be able to promote the efficiency of the catalytic process remarkably.

We have recently been studying the preparation and synthetic applications of polyfunctional conjugated compounds such as polyhalo compounds, aiming at utilizing the cooperative effect among functional groups on the conjugated systems.[13] During our studies of the Pd-catalyzed reaction of polyhalo compounds with amines, we found that when **1a** was treated with *p*-toluidine (Scheme 2), the indole derivative **2a** was obtained in 87% isolated yield.[14] Surprisingly, the benzosilolo[2,3-*b*] indole derivative **3a** was also obtained in 7% isolated yield, and its structure was confirmed by X-ray structural analysis (Figure 1). We assumed that **3a** might be the result of continuous intramolecular coupling of **2a** under the Pd-catalyzed reaction conditions. To test this hypothesis, we investigated the Pd-catalyzed intramolecular coupling of (2′-bromobiphen-2-yl)trimethylsilane (**4a**) as a model compound (Scheme 3). Gratifyingly, screening of various reaction conditions [see the Supporting Information (SI) for details] revealed the optimal reaction conditions, and the expected dibenzosilole **5a** was obtained in 82% isolated yield (Scheme 3). LiO*t*-Bu was found to be the most effective base in this reaction. Other bases (e.g., Cs_2CO_3, CsF, K_2CO_3, NaOAc, KO*t*-Bu, and LiOMe) afforded either low yields or mixtures of products. To our surprise, we found that the addition of an aldehyde could remarkably increase the yields of the products (see the SI for details).

Since such a selective cleavage of the C(sp^3)−Si bond and the consequent intramolecular C(sp^2)−Si coupling process was unprecedented, we next investigated the effect of substituents on the silicon center, expecting the chemoselective cleavage of a C(sp^3)−Si bond.[5,10] As summarized in Scheme 3, the C(Me)−Si bond was always selectively cleaved in the cases of $SiMe_2Et$, $SiMe_2$*i*-Pr, and $SiMe_2Ph$, probably because of steric effects. The reaction of **4e** ($SiEt_3$), which afforded **5e** in a much lower yield, also suggested the role of steric effects.

Encouraged by the above selective cleavage of the C(sp^3)−Si bond and the consequent intramolecular C(sp^2)−Si coupling process, we then turned our attention to the synthesis of

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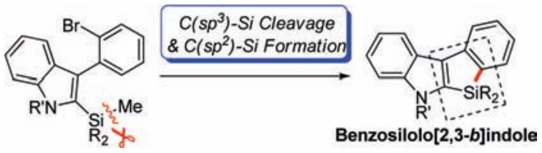
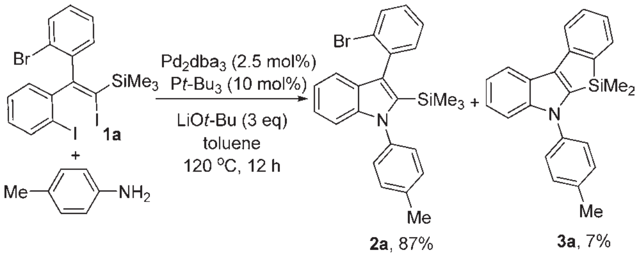
Scheme 1



Scheme 2



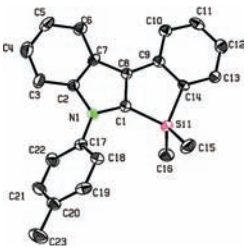
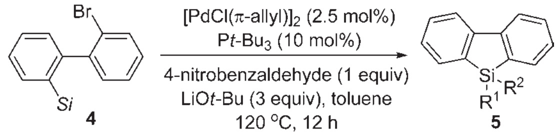


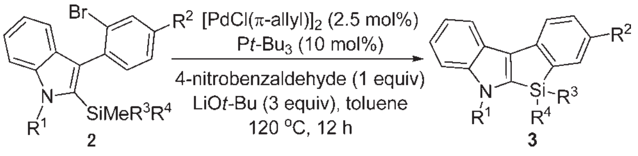
Figure 1. ORTEP drawing of **3a** with 30% thermal ellipsoids. Hydrogen atoms have been omitted for clarity.

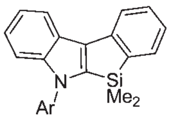
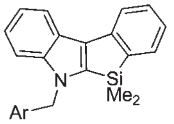
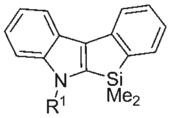
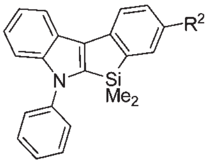
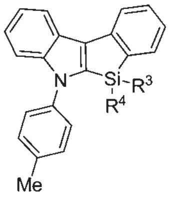
Scheme 3



Si = SiMe$_3$ (**4a**)	R^1 = R^2 = Me	82% (**5a**)
SiMe$_2$Et (**4b**)	R^1 = Me, R^2 = Et	66% (**5b**)
SiMe$_2$(*i*-Pr) (**4c**)	R^1 = Me, R^2 = *i*-Pr	73% (**5c**)
SiMe$_2$Ph (**4d**)	R^1 = Me, R^2 = Ph	70% (**5d**)
SiEt$_3$ (**4e**)	R^1 = R^2 = Et	30% (**5e**)

Table 1. Formation of Various Benzosilolo[2,3-*b*]indoles[a,b]



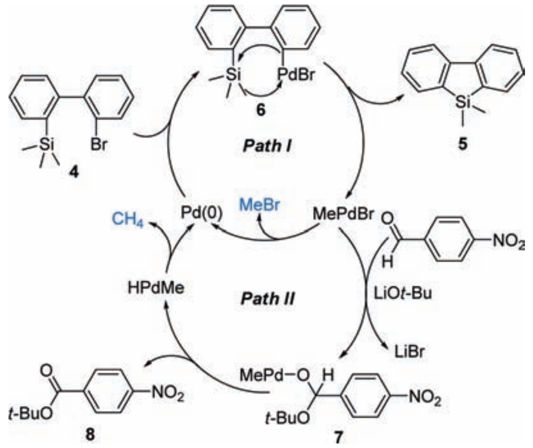
Type I		**3a**: Ar = 4-Me-Ph, 97% (62%)[c] **3b**: Ar = Ph, 95% **3c**: Ar = 2-MeO-Ph, 95% **3d**: Ar = 3,5-(MeO)$_2$-Ph, 99% **3e**: Ar = 4-NO$_2$-Ph, 59% **3f**: Ar = 4-CN-Ph, 65%
Type II		**3g**: Ar = Ph, 93% **3h**: Ar = 2,4-dichloro-Ph, 88% **3i**: Ar = 4-MeO-Ph, 58%
Type III		**3j**: R^1 = Hex, 93% **3k**: R^1 =*s*-Bu, 96% **3l**: R^1 = Cy, 76%
Type IV		**3m**: R^2 = F, 98% **3n**: R^2 = Cl, 92% **3o**: R^2 = Me, 90%
Type V		**3p**: R^3 = Me, R^4 = Et, 73%[d] **3q**: R^3 = Me, R^4 = *i*-Pr, 72%[e]

[a] Conditions: **2** (0.3 mmol), [PdCl(π-allyl)]$_2$ (2.5 mol %), P*t*-Bu$_3$ (10 mol %), LiO*t*-Bu (0.9 mmol), 4-nitrobenzaldehyde (0.3 mmol), toluene (2 mL), 120 °C, 12 h. [b] Isolated yields are shown. [c] The yield in parentheses was obtained without 4-nitrobenzaldehyde. [d] From SiMe$_2$Et, **3a** was also formed as the minor product (**3q**:**3a** = 2.7:1). [e] From SiMe$_2$(*i*-Pr).

benzosilolo[2,3-*b*] indoles **3**, which represent a new type of silicon-bridged polyheteroarene.[11,12] As shown in Table 1, a variety of benzosilolo[2,3-*b*]indoles (types **I**−**V**) could be obtained from the corresponding 3-(2-bromoaryl)-2-(trialkylsilyl)-1*H*-indoles **2** under the optimal reaction conditions. The substituent of the indole moiety (R^1) could be aryl (types **I**, **IV**, and **V**), benzyl (type **II**), or alkyl (type **III**). For type **I** (R^1 = Ar), the phenyl ring could be substituted with either electron-donating groups such as OMe or Me (**3a**−**d**) or electron-withdrawing groups such as NO$_2$ and CN (**3e** and **3f**). In the absence of 4-nitrobenzaldehyde as the promoting reagent, the isolated yield of **3a** decreased to 62% (from 97% with 4-nitrobenzaldehyde). In most cases, in the presence of an aldehyde, the yield of the product could be increased by 10−40%. These results again showed that the addition of an aldehyde could obviously promote the efficiency of this synthetic method. Similarly, *N*-benzylbenzosilolo[2,3-*b*] indoles **3g**−**i** (type **II**) could be obtained in good to high isolated yields. For type **III** (R^1 = alkyl), *N*-alkylindoles with linear-chain (**3j**), branched-chain (**3k**), and cycloalkyl (**3l**) groups could all be obtained in excellent yields. For type **IV** (R^1 = Ph), the indole derivatives **3m** (R^2 = F), **3n** (R^2 = Cl), and **3o** (R^2 = Me) were obtained in isolated yields of 98, 92, and 90%, respectively. This result showed that the R^2 substituent did not remarkably affect the reaction. Finally, we investigated the selective cleavage of the substituents on the silicon moiety. The products are shown as type **V**. The results again showed that the C(Me)−Si bond was more easily cleaved than the C(Et)−Si and C(*i*-Pr)−Si bonds.[5,10] All of these benzosilolo[2,3-*b*]indole derivatives **3** showed fluorescence with blue emission under excitation using UV light. Detailed studies of their optoelectronic properties will be published in due course.

Several experiments were carried out to investigate the reaction mechanism. (1) In the absence of 4-nitrobenzaldehyde, MeBr was obviously observed by using GC analysis (see the SI

Scheme 4



for details). (2) When 4-nitrobenzaldehyde was added, the reaction did not generate any MeBr. Instead, GC analysis clearly showed the formation of CH_4 (see the SI for details). In addition, *tert*-butyl 4-nitrobenzoate (**8**) was obtained in 55% isolated yield. (3) Formation of MeO*t*-Bu was not observed either with or without the aldehyde.

On the basis of the above experimental observations, a possible mechanism for the selective cleavage of the C(Me)−Si bond and the consequent intramolecular C(sp^2)−Si coupling is given in Scheme 4. First, oxidative addition of Pd(0) to the C−Br bond of substrates **4** (or **2**) would generate intermediate **6**. Next, though the detailed mechanism is not clear yet, nucleophilic attack by the C−Pd bond at the silicon center would generate product silole **5** (or **3**) along with elimination of the MePdBr species via cleavage of the Me−Si bond.[9,10,15] Reductive elimination of the MePdBr would then release MeBr (observed) and regenerate the active Pd(0) species for the catalytic cycle via path I. When 4-nitrobenzaldehyde is added, an addition reaction of the in situ-generated MePdBr with 4-nitrobenzaldehyde and LiO*t*-Bu would form intermediate **7** and LiBr, as shown in path II.[16] β-Hydrogen elimination from **7** would then generate **8** (observed) along with the MePdH species.[17] Reductive elimination from the MePdH species would then release CH_4 (observed) and regenerate the active Pd(0) species for the catalytic cycle via path II. As a consequence of the fact that reductive elimination of MePdH occurs more readily than that of MePdBr,[17,18] the yields of products are remarkably increased.

In summary, a novel process involving Pd-catalyzed selective cleavage of the C(sp^3)−Si bond in a trialkyl group and consequent intramolecular C(sp^2)−Si bond forming process has been developed. This reaction provides the first efficient synthesis of benzosilolo[2,3-*b*] indoles, which represent a new type of silicon-bridged polyheteroarene. In addition, for the first time, aldehyde has been found to be able to promote the efficiency of the catalytic process remarkably. This finding opens a new method for selective cleavage of the C(sp^3)−Si bond in a trialkyl group and its synthetic applications.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Experimental details, X-ray data for **3a** (CIF), and scanned NMR spectra of all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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