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Palladium-catalyzed synthesis of benzosilacyclobutenes *via* position-selective C(sp³)–H arylation[†]

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A palladium-catalyzed synthesis of benzosilacyclobutenes has been developed *via* position-selective $C(sp^3)$ -H bond activation, including those having substituents at the methylene carbon on the 4-membered silacycle. The obtained products could be engaged in the palladium- or nickel-catalyzed ring-expansion reactions to give compounds possessing 6-membered silacycles.

4-Membered silacycles, silacyclobutanes and related compounds, belong to a synthetically useful class of compounds and a variety of transformations have been developed based on their ring strain and Lewis acidity.^{1,2} Among them, arene-fused derivatives, benzosilacyclobutenes and their analogs, have been actively utilized as synthetic intermediates of more complex organosilanes,³ but their available preparation methods are very limited. In fact, other than a recent report by Petit and coworkers where they utilized a niobium-catalyzed [2+2+2] cycloaddition,⁴ most of the reported compounds are prepared from 2-bromobenzyl halides and dichlorosilanes using more than a stoichiometric amount of magnesium metal.^{1,5} In addition, the synthesis of benzosilacyclobutenes having substituents at the methylene carbon on the 4-membered ring has been even less explored and essentially limited to brominationmetalation-nucleophilic substitution of pre-formed unsubstituted benzosilacyclobutenes (Scheme 1a).^{5b,6}

As a new synthetic strategy of the 4-membered carbo- or heterocycles, the reactions involving a transition-metalcatalyzed intramolecular C–H bond activation can be a powerful alternative to the conventional approaches, and several effective methods have been reported to date for the synthesis of benzocyclobutenes and their analogs.^{7,8} However, most of

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them rely on the activation of methyl C–H bonds, and only a few reports have been made on the 4-membered ring formations through the activation of methylene C–H bonds.^{7d–f} In this context, herein we describe the development of a palladium-catalyzed 4-membered ring-forming intramolecular $C(sp^3)$ –H bond arylation of 2-(alkylsilyl)aryl triflates,^{8a–d} enabling the synthesis of substituted benzosilacyclobutenes at the methylene carbon of the silacycle (Scheme 1b).

Initially, we conducted a reaction of 2-naphthyl triflate **1a** having butyldicyclohexylsilyl group at 1-position in the presence of a catalytic amount of $Pd(OAc)_2/PPh_3$ with Et₂NH as the base in DMF at 80 °C. Under these conditions, desired naphthosilacyclobutene **2a** was obtained in a moderate yield of 40% along with some uncyclized butenyldicyclohexyl(1-naphthyl) silanes (Table 1, entry 1). The change of ligand to PCy₃ led to a significant improvement to give compound **2a** in 74% yield (entry 2), while the use of bulkier P(*t*Bu)₃ led to a decrease of the reaction efficiency (entry 3). On the other hand, no desired product **2a** was observed by using binap as the ligand (entry 4), and the ferrocene-based bisphosphine ligands such as dppf and dtbpf were found to be similarly ineffective as P(*t*Bu)₃ (entries 5 and 6).⁹

Under the conditions in Table 1, entry 2, several alkyl groups were installed at the alkyl carbon on the silacycle of compounds 2 by changing the R group of substrates 1 (Scheme 2). For example, in addition to propyl group, naphthosilacyclobutenes having isobutyl group or alkyl groups containing aryl, silyloxy,



Scheme 1 (a) Conventional and (b) new synthesis of benzosilacyclobutenes having substituents at the carbon on the 4-membered ring.

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Table 1 Palladium-catalyzed reaction of 1a to give 2a: Ligand effect



^{*a*} Determined by ¹H NMR against internal standard. ^{*b*} PR₃·HBF₄/Et₂NH was used. ^{*c*} 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl. ^{*d*} 1,1'-Bis(diphenylphosphino)ferrocene. ^{*e*} 1,1'-Bis(di-*tert*-butylphosphino)ferrocene.



 $\label{eq:scheme 2} \mbox{ Palladium-catalyzed synthesis of 2 from 1 with R \neq H.}$

and carbozolyl groups could be obtained in reasonably high yields (**2b–2g**). Regarding the 'spectator' groups on silicon, sterically demanding aryl groups could also be employed instead of cyclohexyl group as shown for the synthesis of compound **2h**, but simple phenyl group was more reactive toward C-H bond activation over an alkyl group for substrate **1x** to give the corresponding benzonaphthosilole preferentially instead of the desired naphthosilacyclobutene (data not shown).¹⁰ In addition to naphthosilacyclobutenes, substituted benzosilacyclobutenes could also be synthesized by using phenyl triflate derivatives in the present catalysis. Thus, although 3-unsubstituted aryl triflates such as **1y** did not undergo this reaction, various 3-substituted substrates **1** could be employed to give corresponding benzosilacyclobutenes **2** in moderate to



high yields (2i-2o). 4-Silyl-5-indolyl triflate **1p** could also be converted to product **2p** albeit with lower efficiency, but substrate **1z** having trifluoromethyl group at 3-position was not applicable. The structures of **2g** and **2p** were unambiguously confirmed by X-ray crystallographic analysis.¹¹

The present catalysis was further extended to the synthesis of compounds 2 with no substituents at the carbon on the 4membered ring by employing substrates having methyl group on silicon. Although the use of PCy3 as the ligand gave almost no desired product 2q for the reaction of 2-naphthyl triflate 1q having dicyclohexyl(methyl)silyl group at 1-position, a high vield of 85% was realized by employing dtbpf, a ferrocenebased bulky bisphosphine ligand (Scheme 3). Under these conditions, the product yields were found to be higher for substrates having bulkier substituents on silicon, and a gradual decrease in the yield was observed by changing the substituents from dicyclohexyl (2q) to diisopropyl (2r) and to (tert-butyl) (methyl) (2s). It is worth noting that a C-H bond of methyl group was selectively activated over a methylene C-H bond or a methyl C-H bond of ethyl group on silicon as demonstrated for the synthesis of 2t. In addition to naphthosilacyclobutenes, benzosilacyclobutenes 2u and 2v could also be synthesized with similar tendency.

With a series of naphtho- and benzosilacyclobutenes in hand, we briefly examined their reactivity by applying them to some reported transformations. For example, the reaction of naphthosilacyclobutene 2a with dimethyl acetylenedicarboxylate (3a) in the presence of Pd(PPh₃)₄ (5 mol%) proceeded via selective C(aryl)-Si bond cleavage to give ring-expanded naphthosilacyclohexadiene 4aa in 53% yield (Scheme 4a).^{3b} A similar result was obtained with benzosilacyclobutene 2i to give benzosilacyclohexadiene 4ia in 52% yield. On the other hand, compound 2q having no substituent at the alkyl carbon on the 4-membered ring showed a higher reactivity to give product 4ga in a nearly quantitative yield. The reaction of 2q with diethyl acetylenedicarboxylate (3b) also gave 4qb in a high yield, but the use of methyl propiolate (3c) resulted in a lower yield of 4qc as expected from the literature precedent.^{3b} Furthermore, these could be employed in a nickel-catalyzed ring-expansion reaction with aldehydes as well.^{3e,i} The reaction of 2a or 2i with



Scheme 4 Ring-expansion of **2** with (a) alkynes and (b) aldehydes.

benzaldehyde (**5a**) proceeded with relatively high diastereoselectivity (89/11–95/5) to give corresponding dihydronaphthoor dihydrobenzooxasiline **6aa** or **6ia** through the cleavage of a C(aryl)–Si bond (Scheme 4b). The relative configuration of the major diastereomer was determined to be *cis* by X-ray crystallographic analysis for both **6aa** and **6ia**.¹¹ A higher yield of 87% was achieved for the reaction of unsubstituted **2q** to give ringexpanded product **6qa**. *E*-Cinnamaldehyde (**5b**) could also be used for the reaction of **2q** to give compound **6qb** in 82% yield.

A proposed catalytic cycle of the present catalysis toward benzosilacyclobutenes is illustrated in Scheme 5a. Oxidative addition of aryl triflate of **1** to palladium(0) gives arylpalladium species **A**. This then undergoes C–H bond activation of the alkyl carbon adjacent to silicon to give 5-membered palladacycle **B**.¹² Carbon–carbon bond-forming reductive elimination leads to the formation of product **2** along with regeneration of palladium(0) species. As shown in Table 1, side products for the reaction of **1a** are butenyldicyclohexyl(1-naphthyl)silanes, and the formation of these compounds can be explained by the pathways shown in Scheme 5b. Instead of reductive elimination from **A**-**a** gives alkylpalladium species **C**-**a** or **D**-**a**,¹³ and subsequent β -hydrogen elimination would lead to the observed side products.

To gain insights into the reaction mechanism of the present catalysis, we conducted some control experiments. When the reaction of **1s-d**₃ having *tert*-butyl(methyl)(methyl- d_3)silyl group was conducted under the conditions in Scheme 3, C–H bond



Scheme 5 (a) A proposed catalytic cycle for the synthesis of 2 from 1, (b) proposed pathways toward alkene side products from 1a, and (c) substituent effect on the formation and reactivity of intermediate B.

activated product $2s \cdot d_3$ and C–D bond activated product $2s \cdot d_2$ were obtained in the ratio of 7.5/1 (Scheme 6a). We also carried out a competition between 1q and $1q \cdot d_3$ to determine their relative reactivity, and found that C–H bond activated product 2q and C–D bond activated product $2q \cdot d_2$ were obtained in the ratio of 1.2/1 at an early stage of the reaction (Scheme 6b). These results indicate that the C–H(D) bond activation step ($A \rightarrow B$ in Scheme 5a) is not the turnover-limiting step and occurs after the irreversible oxidative addition step.¹⁴ Although we have not been able to determine the turnover-limiting step by kinetic experiments due to the existence of an induction period at the beginning of the reaction, 4-membered ringforming reductive elimination step could be the turnoverlimiting step, considering that this step generates a significant



Scheme 6 (a) Intramolecular and (b) intermolecular KIE experiments.

ring strain.^{7d,f} It is also worth noting that the substituent effects observed in Scheme 2 could be explained by the difficulty of the 4-membered ring formation. As illustrated in Scheme 5c, the methyl group at 3-position of **1i** would facilitate the reductive elimination from intermediate **B-i** to reduce the steric repulsion between the methyl group and the silyl group. On the other hand, 3-unsubstituted **1y** does not have this effect in intermediate **B-y**. Along this line, the lack of reactivity of **1z** having trifluoromethyl group at 3-position might be due to the favorable interaction between the fluorine atoms and the silicon atom, which could retard the formation and/or subsequent reductive elimination of palladacycle **B-z**. Furthermore, the decrease of the product yield by reducing the steric bulk of the silicon substituents in Scheme 3 is also consistent with these explanations.

In summary, we developed a palladium-catalyzed synthesis of benzosilacyclobutenes from 2-(alkylsilyl)aryl triflates *via* position-selective $C(sp^3)$ –H bond activation. Although the applicable substrates need to meet the steric requirement, various benzosilacyclobutenes could be synthesized including those substituted at the methylene carbon on the 4-membered silacycle. The obtained products could be employed in the palladium- or nickel-catalyzed ring-expansion reactions to give benzosilacyclohexadienes or dihydrobenzooxasilines possessing 6-membered silacycles. Future studies will be directed toward further expansion of this process for the synthesis of various functional organosilicon compounds.

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Conflicts of interest

There are no conflicts to declare.

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