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Palladium-Catalyzed *Ortho*-Silylation of Aryl Iodides with Concomitant Arylsilylation of Oxanorbornadiene: Accessing Functionalized (*Z*)-β-Substituted Vinylsilanes and Their Analogues

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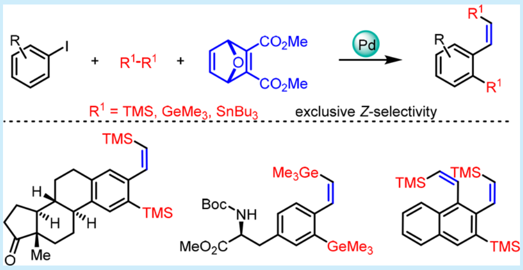
Supporting Information

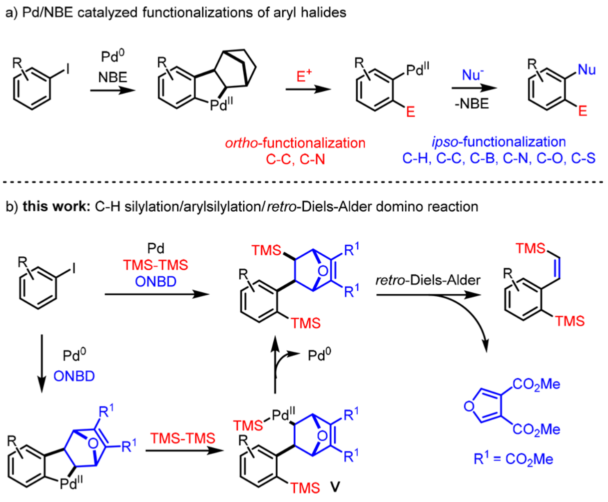
ABSTRACT: A palladium-catalyzed *ortho*-silylation of aryl iodides/arylsilylation of oxanorbornadiene/retro-Diels−Alder domino reaction was developed. Such a transformation provides access to various functionalized (*Z*)-β-substituted vinylsilanes with exclusive selectivity using hexamethyldisilane as a bis-silylation reagent and 2,3-dicarbomethoxy-7-oxanorbornadiene (ONBD) as an *ortho*-C−H activator and ethylene surrogate. A variety of (*Z*)-β-substituted vinylgermanes and (*Z*)-β-substituted vinylstannanes were also obtained under mild reaction conditions. This atom-economical, stereoselective, and scalable approach is compatible with a diverse range of readily available functionalized aryl iodides.



Vinylsilanes are valuable synthetic intermediates in organic synthesis.[1] Thus, methods for the synthesis of vinylsilanes in a practical, efficient, and divergent manner have been attracting significant interest. Indeed, numerous transition-metal-catalyzed reactions have been developed for the preparation of (*E*)-β-substituted vinylsilanes.[2] In contrast, only a few reports on the selective synthesis of thermodynamically less stable (*Z*)-β-isomers have appeared to date. Current methods to access (*Z*)-β-substituted vinylsilanes include the alkyne hydrosilylation[3] and direct dehydrogenative silylation of alkenes;[4] both of the methods carry significant drawbacks, including the requirement of sophisticated transition-metal complexes as catalysts and the formation of the (*E*)-β-isomers as byproducts. The generation of the (*Z*)-β-isomers using simple transition-metal catalysts with exclusive selectivity is regarded as a long-standing challenge.

On the other hand, transition-metal-catalyzed domino reactions that form complex molecules from simple starting materials in a single operation without the isolation of intermediates are of great significance in organic syntheses.[5] Noteworthy among them is the Pd/norbornene (NBE)-based *ortho*-functionalization with *ipso*-termination of aryl iodides leading to highly substituted arenes.[6] The reaction was first reported by Catellani's group[7] and further developed by several groups, including those of Lautens,[8] Dong,[9] Gu,[10] and others.[11−14] A variety of nucleophiles or olefins were used as terminal reagents via C−H, C−C, C−B, C−N, C−O, and C−S bond formations at the *ipso*-position in the past decades (Scheme 1a). However, the chemical bonds constructed at the *ortho*-position via this approach have been restricted to C−C and C−N bonds. To the best of our knowledge, the compatibility of the Catellani reaction with silylation, germanylation, or stannylation has not yet been demonstrated to date. Inspired by recent innovative research on Pd-catalyzed C(sp^2)−H and C(sp^3)−H silylation reactions,[15] we envisioned that hexamethyldisilane may be qualified as a silylating reagent to facilitate the installation of a TMS group at the *ortho*-position of aryl iodides. The resulting intermediate (**V**) could undergo reductive elimination to give disilanes bearing an NBE fragment. Then (*Z*)-β-substituted vinylsilanes may be formed via a retro-Diels−Alder reaction (Scheme 1b). Herein, we report our observation that the bis-silylation reaction of aryl iodides,

Scheme 1. Palladium/NBE-Based *Ipso*- and *Ortho*-Dual Functionalizations of Aryl Iodides



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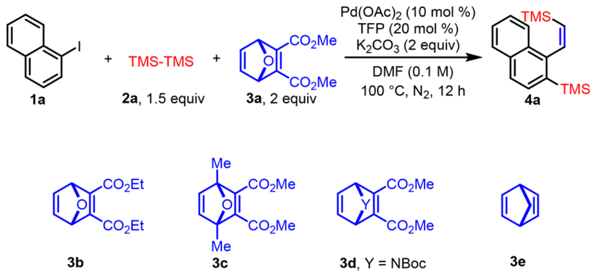
hexamethyldisilane, and ONBD afforded functionalized (*Z*)-*β*-substituted vinylsilanes chemo-, regio-, and stereoselectively with high efficiency.

Initially, we began the studies with 1-iodonaphthalene (**1a**), hexamethyldisilane (**2a**), and ONBD (**3a**) to explore the reaction conditions (see the Supporting Information for details). After systematic screening of the reaction conditions, the optimal conditions were achieved to be $Pd(OAc)_2$ (10 mol %), tri(2-furyl)phosphane (TFP, 20 mol %), and K_2CO_3 (2 equiv) in DMF under N_2 at 100 °C to yield the desired (*Z*)-*β*-substituted vinylsilane product (**4a**) in 84% yield (Table 1, entry 1). A similar result was obtained using **3b** as the mediator (entry 2). Only 12% yield was obtained when the sterically hindered **3c** was used (entry 3). Azanorbornadiene **3d** could also be employed uner the reaction conditions, giving 20% yield of **4a** (entry 4). However, interestingly, no desired product was detected when norbornadiene (NBD, **3e**) was used in lieu of **3a** (entry 5).

Table 1. Screening of Norbornadiene Derivatives[a]

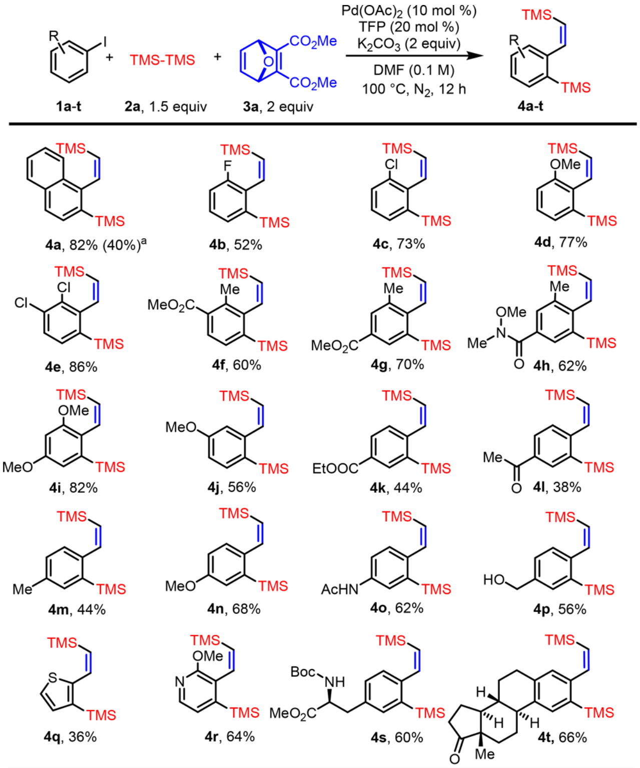


entry	deviation from standard conditions	yield[b] (%)
1	none	84
2	**3b** instead of **3a**	83
3	**3c** instead of **3a**	12
4	**3d** instead of **3a**	20
5	**3e** instead of **3a**	0

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), **3** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), TFP (20 mol %), and K_2CO_3 (0.2 mmol) in DMF (1 mL) under nitrogen atmosphere for 12 h. [b]Determined by ^1H NMR analysis of the crude products using CH_2Br_2 as an internal standard. DMF = *N*,*N*-dimethylformamide.

With the optimal conditions in hand, the bis-silylation reaction was extended to a variety of aryl iodides by using **2a** and **3a** as coupling partners (Scheme 2). In general, the reaction process can be extended to various *ortho*-, *meta*-, *para*-, as well as disubstituted iodobenzenes, thus giving the corresponding (*Z*)-*β*-substituted vinylsilanes (**4a**−**t**) in 36−86% yields. Various valuable functional groups were tolerated, including halogen, ester, Weinreb amide, acetamide, as well as hydroxyl. For *meta*-substituted iodobenzenes (**4j**), the C−H silylation occurred regioselectively at the sterically less hindered position. Importantly, the acetamide directing group did not prevent the **3a**-mediated C−H activation, and the desired product (**4o**) was obtained in 62% yield. Notably, benzyl alcohol substrate was also compatible with the reaction conditions (**4p**). 2-Iodothiophene was found to be an applicable substrate, albeit giving lower yield (**4q**, 36%). It is noted that the reaction with the more coordinative pyridyl iodide gave the corresponding product (**4r**) in 64% yield. The phenylalanine substrate was successfully converted into the corresponding (*Z*)-*β*-substituted vinylsilane (**4s**) in 60% yield. Notably, estrone derivative was modified by this protocol without obstacles (**4t**). 1-Bromonaphthalene was also subjected to the reaction conditions, giving **4a** in 40% yield. It should be noted that exclusive (*Z*)-isomers were formed in all cases of the aforementioned bis-silylation reactions, as indicated by the X-ray structure of **4t**.

Scheme 2. Scope of Aryl Iodides



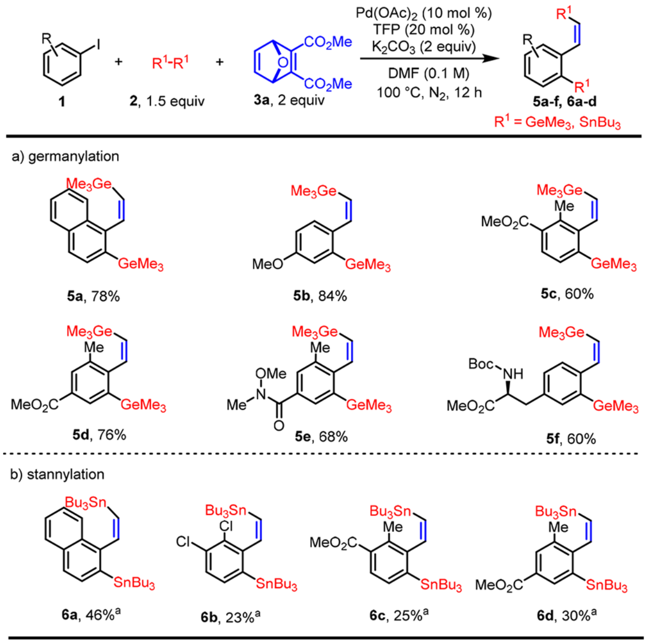
[a]1-Bromonaphthalene was used as substrate.

Encouraged by the successful Si−Si bond-cleavage reaction, we proceed to explore this strategy for other similar types of bonds. The Ge−Ge bond has been applied in palladium-catalyzed C−H functionalization as an Si−Si bond.[15b,g] Thus, we conceived that the (*Z*)-*β*-substituted vinylgermane products might also be formed by using hexamethyldigermane (**2b**) instead of hexamethyldisilane under similar reaction conditions, and this indeed proved to be the case. For a series of aryl iodides, the palladium-catalyzed domino reactions with **2b** and **3a** afforded the corresponding (*Z*)-*β*-substituted vinylgermanes (**5a**−**f**) in moderate to good yields (Scheme 3a).

Organostannanes are important compounds because of their application in Stille coupling reaction.[16] The syntheses of these organostannanes usually require expensive functionalized precursors.[17] The direct construction of the C−Sn bond through catalytic C−H bond activation reactions is highly desirable. We are pleased to find that C−Sn bond could be formed via our approach using hexabutyldistannane as Sn source (**6a**−**d**). However, efforts on further improving this reaction efficiency are still needed (Scheme 3b).[18]

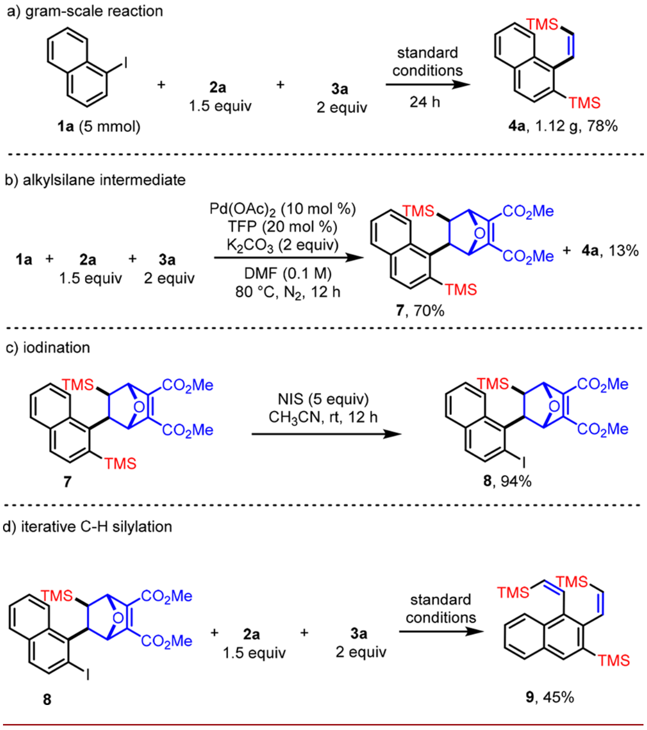
To further demonstrate the utility of this chemistry, the reaction was conducted on a 5 mmol scale. The reaction of **1a**, **2a**, and **3a** was complete within 24 h, generating the desired products (**4a**) in 78% yield (Scheme 4a). Importantly, we found that disilane **7** could be successfully isolated in 70% yield at lower temperature (Scheme 4b). It is worth mentioning that aryl silanes are versatile synthetic intermediates and could be selectively converted into various compounds with retention

Scheme 3. Scope of Aryl Iodides



^{a}K$_3$PO$_4$ was used instead of K$_2$CO$_3$.

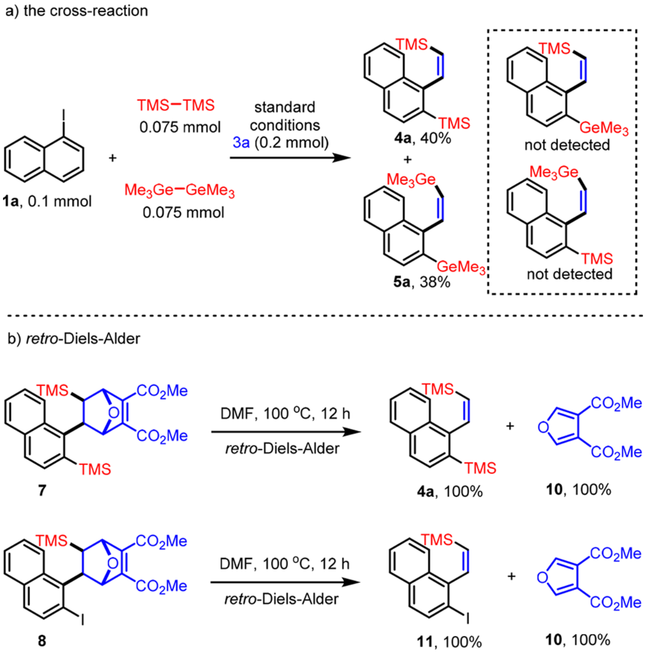
Scheme 4. Derivatization Reactions



of the alkyl TMS group. For example, when the trimethylsilyl entity was used as a transformable group, the C−I bond was formed (Scheme 4c). We then sought to explore the possibility of performing iterative bis-silylation, wherein the newly synthesized aryl iodide (**8**) would serve as the starting material for an additional bis-silylation. Gratifyingly, the trisilylated product (**9**) was obtained in 45% yield (Scheme 4d).

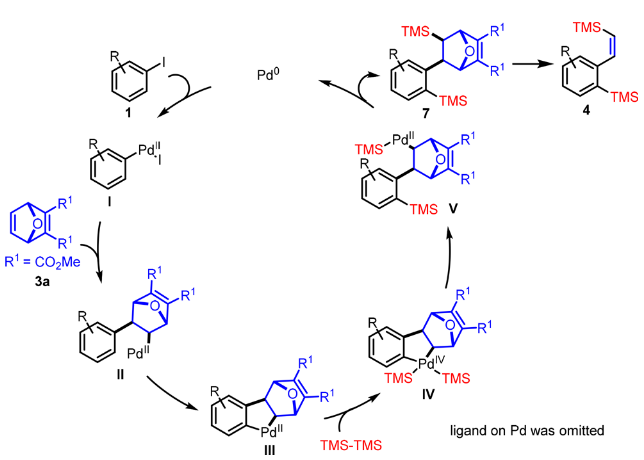
To further understand the reaction mechanism, we conducted a double-crossover experiment of **1a** and **3a** with hexamethyldisilane and hexamethyldigermane under the standard reaction conditions. The corresponding noncrossover products (**4a**) and (**5a**) were obtained in 40% and 38% yields, respectively. The crossover products were not observed, which indicated that both of the two TMS groups of **4a** are derived from one hexamethyldisilane molecule (Scheme 5a). Moreover, a solution of **7** in DMF was heated at 100 °C for 12 h, and both **4a** and 3,4-dicarbomethoxy furan (**10**) were obtained in quantitative yields (Scheme 5b). Iodide (**8**) could also be successfully converted into (*Z*)-*β*-substituted vinylsilane (**11**) via a retro-Diels−Alder reaction in quantitative yield. It is well-known that electron-deficient dienophiles are prone to form Diels−Alder adducts with electron-rich dienes. Thus, we proposed that the release of an electron-rich dienophile (**4a**) and an electron-deficient aromatic diene (**10**) may provide the driving force for the retro-Diels−Alder process.

Scheme 5. Control Experiments



On the basis of these results and the literature reports, we proposed that the reaction would proceed as shown in the Scheme 6. This reaction is initiated by Ar−I oxidative addition to Pd^0 and subsequent ONBD-mediated vicinal C−H activation

Scheme 6. Plausible Catalytic Cycle



to generate a palladacycle (**III**), which can react with hexamethyldisilane leading to the palladacycle (**IV**).[15b] Then palladacycle (**IV**) undergoes reductive elimination to give intermediate (**V**), which could further undergo a second reductive elimination to furnish the desired *exo*-product **7** and regenerate the Pd^0 catalyst. Finally, **7** could be converted into (*Z*)-*β*-substituted vinylsilane **4** via a retro-Diels–Alder reaction.

In conclusion, we have described the first palladium-catalyzed Catellani-type *ortho*-silylation of aryl rings with arylsilylation of oxanorbornadiene to form (*Z*)-*β*-substituted vinylsilanes, thus expanding the Catellani reaction beyond the construction of C–C and C–N bonds. A variety of functional groups are compatible with this method, which could be readily extended to the rapid preparation of (*Z*)-*β*-substituted vinylgermanes and (*Z*)-*β*-substituted vinylstannanes. We believed that the utility of 2,3-dicarbomethoxy-7-oxanorbornadiene as an *ortho*-C–H activator and ethylene synthon in Catellani-type reactions should have broad implications.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b02106.

General experimental procedures, characterization data, and ^1H and ^{13}C NMR spectra of new compounds (PDF)

Accession Codes

CCDC 1849591 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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