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Regio- and Stereoselective Synthesis of Multisubstituted Vinylsilanes via Zirconacycles†

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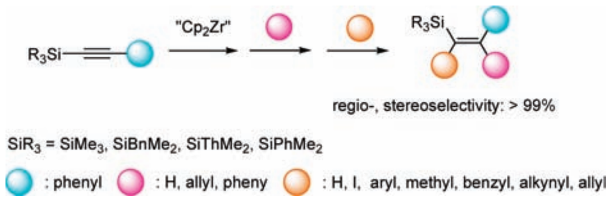
ABSTRACT



A series of novel multisubstituted vinylsilanes are prepared regio- and stereoselectively by carbozirconation of various alkynylsilanes through zirconacycles such as zirconacyclopropenes and zirconacyclopentenes and the subsequent transformation of the formed alkenylzirconocene complexes.

Carbon−carbon double bonds are essential structural constituents in organic molecules and controlling the regio- and stereoselectivity of the multisubstituted olefins has been one of the central issues in synthetic organic chemistry.[1] Along this line, we have succeeded in synthesizing various multisubstituted olefins in regio- and stereoselective manners via Suzuki−Miyaura coupling for vinylboronates derived from alkynylboronates and a low-valent ziroconocene complex.[2]

On the other hand, vinylsilanes[3] have received increased attention due to the lower toxicity of organosilicon compounds that are suitable for Hiyama coupling.[4] Originally, heteroatom-functionalized vinylsilanes such as halosilanes,[5] oxysilanes,[6] silanols,[7] cyclic silyl ethers,[8] and polysiloxanes[9] were necessary owing to efficient reactivity.[10] However, these vinylsilanes in general are difficult to handle from the standpoint of their chemical stability. Recently, several disclosures have demonstrated the synthetic potential of more stable, all-carbon-substituted silyl groups for Hiyama coupling, including methylsilacyclobutanes,[11] dimethylphenyl-,[12] benzyldimethyl-,[13] 2-dimethyl-

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[†] This work is dedicated to Prof. John M. Birmingham on the occasion of his 80th birthday.

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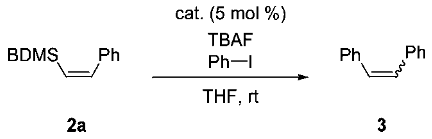
Table 1. Effect of Reaction Parameters on Hiyama Coupling of the Benzyldimethylsilyl-Substituted Vinylsilane **2a**[a]



run	catalyst	**2a** (equiv)	PhI (equiv)	TBAF (equiv)	time/h	yield/%[b]	*E*/*Z*[c]
1	$Pd(dba)_2$	1.0	1.5	2.2	24	76	16:84
2	$Pd(dba)_2$	1.5	1.0	3.3	1	66	0:100
3	$Pd(dba)_2$	1.5	1.0	2.2	1	77	0:100
4	$Pd(dba)_2$	1.2	1.0	1.2	1	94	0:100
5	$Pd(PPh_3)_4$	1.0	1.5	2.2	24	<1	n/a
6	$Pd(dba)_2/2\ P^tBu_3$	1.0	1.5	2.2	1	<1	n/a
7	CpPd(π-ally)	1.5	1.0	1.5	24	59	97:3
8[d]	$Pd(acac)_2$	1.0	1.5	2.2	24	33	100:0
9[d]	$Ni(acac)_2$	1.0	1.5	2.2	24	<1	n/a

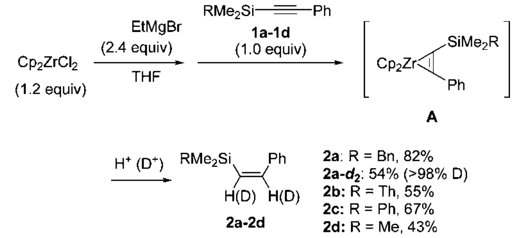
[a] All reactions employed vinylsilane **2a** (0.1 mmol) and 1.0−1.5 equiv of iodobenzene in THF (0.5 mL, 0.2 M) at 0 °C. TBAF (1.2−3.3 equiv) was added, and the mixture was stirred for 10 min followed by addition of 5 mol % of the catalyst. The mixture was then stirred at room temperature. [b] GC yields (combined for both isomers of **3**). [c] Determined by GC−MS with internal standard of (*E*)- and (*Z*)-stilbenes and/or ^{1}H NMR of the crude reaction mixture. [d] Reaction was conducted at 50 °C.

2-thienyl-,[14] 2-pyridyldimethyl-,[15] allyldimethyl-,[16] and reusable [2-(hydroxymethyl)phenyl]dimethylsilanes.[17] Although di- or trisubstituted vinylsilanes have been utilized for Hiyama coupling, few examples are shown to synthesize the stereodefined multisubstituted vinylsilanes. Herein, we report the extension of our vinylboronate synthesis using a zirconocene complex to a new, versatile procedure for the regio- and stereospecific one-pot formation of a variety of multisubstituted vinylsilanes.

The starting alkynylsilanes **1a**−**d** were prepared by the reaction of phenylacetylene with EtMgBr, followed by addition of various chlorosilanes in good to excellent yields.[18]

Addition of benzyldimethylsilyl (BDMS)-substituted alkynylsilane **1a** to $Cp_2ZrCl_2/2EtMgBr$ (Takahashi's reagent)[19] afforded (*Z*)-benzyldimethyl(2-phenylethenyl)silane (**2a**), upon hydrolysis, in 82% yield with a perfect stereoselectivity as shown in Scheme 1. Deuterium labeling of the intermediate zirconacycle by DCl/D_2O workup of the reaction mixture showed the presence of two deuterium atoms (>95% incorporation) in **2a-*d*$_2$**, indicative of the formation of zirconacyclopropene **A** bearing two zirconium−carbon bonds. To the best of our knowledge, zirconacyclopropenes as the intermediate species are believed to be fleeting and difficult to observe,[20] although related complexes are known.[21] Similarly, analogous vinylsilanes **2b**−**d** were obtained in a stereoselective (*Z*)-manner. The perfect control of the stereochemistry of (*Z*)-vinylsilanes **2** by hydrosilylation of terminal alkynes has been known to be difficult.[22] Obtained (*Z*)-vinylsilanes **2** are fully characterized by GC−MS, ^{1}H, and ^{13}C NMR spectra as well as elemental analyses.

Scheme 1. Zirconocene-Mediated Synthesis of (*Z*)-Vinylsilanes **2a**−**d** with Different Silyl Groups



With access to the stereodefined (*Z*)-vinylsilane **2a** in hand, we turned to Hiyama coupling, expecting retention of the stereochemistry of the coupled products. The results from our survey of catalysts, an amount of tetrabutylammonium

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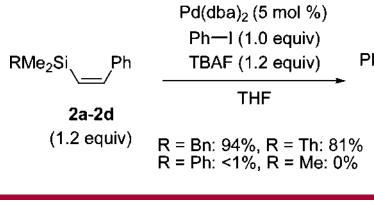
fluoride (TBAF), and temperatures are collected in Table 1. We first conducted the reaction **2a** with iodobenzene under Denmark's reaction conditions, e.g., TBAF/Pd(dba)$_2$/THF,[23] yielding stilbenes **3** in 76% yield with a mixture of *E*/*Z* isomers (84:16 ratio) (run 1). We found that various ratios of **2a** and iodobenzene, TBAF provided the predominant formation of (*Z*)-**3** with a shorter reaction time (1 h) in up to 94% yield (runs 2−4). The mild reaction conditions would lead to a general process that retains the stereochemistry of **3**. When Pd(dba)$_2$ was replaced with other palladium catalysts, almost no product was formed (runs 5 and 6). Interestingly, if the Pd(II) precursors such as CpPd(π-allyl) and Pd(acac)$_2$ were employed, **3** was formed in moderate yields, albeit mostly (*E*)-isomers (runs 7 and 8). Other fluoride sources such as KF and CsF did not show improvement over TBAF at all.

The lack of stereoselectivity observed in runs 1, 7, and 8 probably results from the isomerization of the vinylsilanol and/or vinylsiloxane intermediates derived from **2a** under the coupling conditions. Isomerization of the product (*Z*)-**3** was excluded because no isomerization of (*Z*)-**3** into (*E*)-**3** was observed by GC−MS when the once isolated (*Z*)-**3** was refluxed in THF in the presence of with Pd(dba)$_2$ and/or TBAF. We found that 1.2 equiv of TBAF was enough for complete conversion of **2a**, which was then used throughout. Since BDMS-vinylsilane **2a** was found to undergo Hiyama coupling with retention of stereochemistry in the presence of TBAF, couplings of other synthesized vinylsilanes **2b**−**d** with iodobenzene were performed under optimized reaction conditions.

The results are shown in Scheme 2. (*Z*)-Dimethyl(2-phenylethenyl)-2-thienylsilane (**2b**) provided **3** stereoselectively in 81% yield, whereas **2c** (R = Ph) and **2d** (R = Me) were unreacted. The usage of another activator KOSiMe$_3$[23,24] did not improve the yield of **3**.

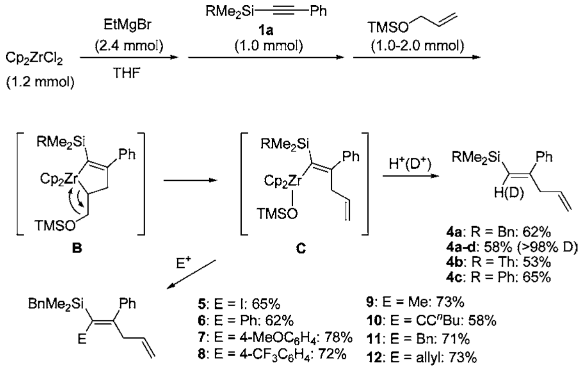
Scheme 2. Hiyama Coupling of (*Z*)-Vinylsilanes **2a**−**d** with Iodobenzene



This is the first example to show the comparison of the effect of the all-carbon-substituted silyl groups of a class of (*Z*)-vinylsilanes for Hiyama coupling.[25] Among four types of (*Z*)-vinylsilanes, the BDMS group is found to be most reactive under the present conditions because it can undergo debenzylation smoothly at 0 °C by activation of TBAF to form vinylsilanol in situ in the presence of the contaminating water.[26] Then, the generated silanols can form a reactive fluorosilicate with the assistance of a fluoride ion.[27] Thus, our investigations were focused on the regio- and stereoselective preparation of multisubstituted vinylsilanes with the most active BDMS group, expecting synthesis of multisubstituted olefins by a simple Hiyama coupling.

To achieve a one-pot synthesis of trisubstituted vinylsilanes directly from alkynylsilanes without isolation of zirconacycles, we chose the zircono-allylation reaction.[28] Starting from Takahashi protocol in the presence of alkynylsilanes, the added allyloxytrimethylsilane rapidly reacted with the intermediate zirconacyclopropene to form the transient zirconacylopentene **B**. It is well-known that a trimethylsilyl group direct zirconocene-mediated oxidative couplings such that it adopt the α-positions.[29] The following β-siloxy abstraction proceeds to form the alkenylzirconocene intermediate **C**, in which hydrolysis (or deuterolysis) of the remaining Zr−C bond can afford trisubstituted vinylsilanes **4a**−**c** in moderate yields (Scheme 3). It is noteworthy that this protocol does not need any additive running the reaction owing to the selective formation of zirconacyclopropene, although the original zircono-allylation reaction required the addition of PMe$_3$ to stabilize the zirconacyclopropene intermediate.

Scheme 3. Regio- and Stereoselective Synthesis of Tri- and Tetrasubstituted Vinylsilanes **4**−**12**



The regioselectivity in vinylsilanes **4a**−**c** was determined by NMR data. In ^{1}H NMR spectra, the presence of a singlet in the double-bond region (around 5.8 ppm) is indicative that the vinyl hydrogen located in the α-position of the silyl groups. The successful transformation of the transient alkenylzirconocene species into trisubstituted vinylsilanes

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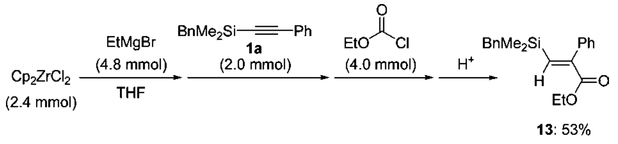
encouraged us to investigate the one-pot synthesis of tetrasubstituted vinylsilanes. The transient **C** could be converted into functionalized tetrasubstituted vinylsilanes by couplings with various electrophiles. The various reactions are also summarized in Scheme 3. The reaction with various aryl iodides in the presence of CuCl and a catalytic amount of Pd(PPh_3)$_4$[30] gave the corresponding cross-coupled products **6−8** in good yields. The reaction with iodomethane,[31] alkynyl iodide,[32] and benzyl chloride afforded the corresponding products **9−11** in 73, 58, and 71% yield, respectively. When **C** was treated with additional allyl chloride in the presence of CuCl,[33] double allylation of alkynylsilane **1a** was accomplished to give **12** in 73% yield. The stereochemistry of tetrasubstituted vinylsilanes **5−12** was determined by a comparison of spectroscopic data of **9** with those of the analogous TMS-containing vinylsilane.[34]

Scheme 4. Zircono-esterification of Alkynylsilane **1a**

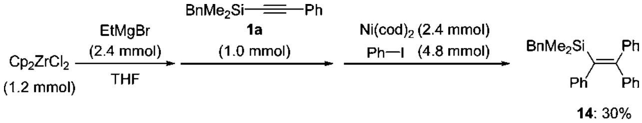


Since the cross-coupling of sterically hindered trisubstituted benzyldimethylvinylsilanes is known to proceed,[13,23] we attempted a Hiyama coupling of the synthesized trisubstituted vinylsilanes **4a** with iodobenzene. Unfortunately the reaction did not proceed at all under the conditions described in Table 1. Several trials to realize the successful Hiyama coupling of tri- or tetrasubstituted vinylsilanes have been failed.

Zirconocene-mediated transformations for alkynes are versatile methods to tolerate a wide range of functional groups such as the ester group.[35] The reaction of alkynylsilane **1a** with Takahashi's reagent and chloroformate, followed by hydrolysis resulted in the formation of hydroesterification product **13** in 53% yield in a single step (Scheme 4).

Since zirconacyclopropene has two Zr−C bonds, one might consider that it may be utilized as an intermediate for the double arylation reaction. The formed in situ zirconacyclopropene was treated with 2 molar equiv of iodobenzene in the presence of a stoichiometric amount of Ni(cod)$_2$ to give the desired products **14**, albeit in low yield (Scheme 5).[36]

Scheme 5. Nickel-Mediated Double Arylation of Alkynylsilane **1a**



In summary, we have developed a direct, regio- and stereoselective synthesis of tri- and tetrasubstituted vinylsilanes by a one-pot zirconocene-mediated carbometalation of alkynylsilanes and the subsequent transformation with various electrophiles. This method is potentially applicable to the regio- and stereoselective synthesis of multisubstituted olefins. Current efforts to expand the scope of coupling partners on zirconacycles as well as to elucidate the Hiyama coupling of the produced tri- and tetrasubstituted vinylsilanes are in progress.

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Supporting Information Available: Experimental procedures as well as characterization data for all vinylsilanes. This material is available free of charge via the Internet at http://pubs.acs.org.

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