

A general approach to difunctionalised 1,3-dienes containing silicon and halogen via hydrozirconation of (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne

Xinglin Ye^{a,b}, Pingping Wang^b and Mingzhong Cai^{a*}

^aDepartment of Chemistry, Jiangxi Normal University, Nanchang 330022, P. R. China

^bDepartment of Chemistry, Jiujiang University, Jiujiang 332000, P. R. China

Sonogashira coupling of (*E*)- α -iodovinylsilanes **1** with (trimethylsilyl)acetylene gave (*Z*)-1,3-bis(trimethylsilyl)alk-3-en-1-yne **2**, which underwent a desilylation reaction to afford (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3** in high yields. (1*E*,3*Z*)-1-Halo-3-(trimethylsilyl)-substituted 1,3-dienes **5** could be synthesised stereoselectively via hydrozirconation of (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3**, followed by trapping with iodine or *N*-bromosuccinimide.

Keywords: difunctionalised 1,3-diene, Sonogashira coupling, hydrozirconation, vinylsilane, vinylic iodide

The stereocontrolled synthesis of 1,3-dienes containing metal or heteroatom functional groups has been of considerable interest in organic synthesis because many useful functional group transformations can be achieved by the introduction and removal of metal or heteroatom functionalities. The stereoselective synthesis of 1,3-dienyl sulfides,¹ 1,3-dienyl selenides,² 1,3-dienylsilanes³ and 1,3-dienylstannanes⁴ has already been described in the literature. Recently, the synthesis of difunctionalised 1,3-dienes has also attracted much attention since such dienes may find use as synthetic building blocks.⁵ In addition, difunctionalised 1,3-dienes containing heteroatom can control both regio- and stereoselectivity and play a very important role in cycloadditions.⁶ Jin and co-workers reported the stereoselective synthesis of 2-alkoxy-3-alkyl(aryl)thiobuta-1,3-dienes by Negishi coupling between α -alkyl(aryl)thio vinyl zinc chloride and α -bromo vinyl ether.⁷ Coleman and Walczak reported the stereoselective synthesis of (*E,E*)-1-tributylstannyl-4-borylbuta-1,3-diene and its use as an orthogonal Stille and Suzuki–Miyaura coupling partner.⁸ The stereoselective synthesis of 1,4-dihalo-1,3-dienes has also been described.⁹ Very recently, we have described the stereoselective synthesis of (*Z,Z*)-2-silyl-3-stannyl-substituted 1,3-dienes via the hydromagnesiation of alkynylsilanes, followed by the cross-coupling reaction with (*E*)- α -iodovinylstannanes in the presence of Pd(PPh₃)₄ catalyst.¹⁰ However, to the best of our knowledge, there is no well-established method for the preparation of stereoselectively difunctionalised 1,3-dienes containing silicon and halogen. Herein, we report that (1*E*,3*Z*)-1-halo-3-(trimethylsilyl)-substituted 1,3-dienes can be conveniently synthesised via hydrozirconation of (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne, followed by trapping with iodine or *N*-bromosuccinimide (NBS).

There has been a lively interest in terminal conjugated enynes, alk-3-en-1-yne, due to their synthetic utility; the acetylenic hydrogen can be converted into various functionalities as well as undergo carbon-carbon bond formation. Furthermore, the terminal conjugated enyne is a useful building block for the synthesis of natural products because the terminal conjugated enyne unit occurs in natural products such as laurenān,¹¹ dactylene,¹² quinolizidine,¹³

and histrionicotoxin.¹⁴ Very recently, Hoshi *et al.*¹⁵ reported the synthesis of terminal conjugated enynes via Cu-mediated Suzuki–Miyaura cross-coupling reactions of alkenyldialkylboranes with (trimethylsilyl)ethynyl bromide. Our methodology involves the preparation and the reactions of the building block (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3** which can be conveniently prepared according to Scheme 1.

Sonogashira coupling of alkenyl iodides with terminal alkynes provides a simple and general route for the synthesis of conjugated enynes.¹⁶ We observed that, when the coupling reactions of (*E*)- α -iodovinylsilanes **1** with (trimethylsilyl)acetylene were performed in piperidine at room temperature using Pd(PPh₃)₄ and CuI as co-catalysts, fairly rapid reactions occurred affording stereoselectively the desired (*Z*)-1,3-bis(trimethylsilyl)alk-3-en-1-yne **2** in high yields, the typical results are summarised in Table 1. Kusumoto *et al.*¹⁷ reported that the desilylation reaction of (*E*)-1,2,4-tri(trimethylsilyl)but-1-en-3-yne with KF in methanol afforded (*E*)-1,2-bis(trimethylsilyl)but-1-en-3-yne, the desilylation reaction occurring selectively at the acetylenic carbon atom. We investigated the desilylation reaction of (*Z*)-1,3-bis(trimethylsilyl)alk-3-en-1-yne **2** with KF in methanol in order to prepare (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3**. We found that the desilylation reaction of

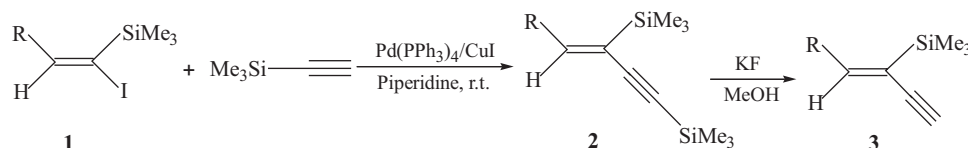
Table 1 Coupling reaction of **1** with (trimethylsilyl)acetylene^a and desilylation of **2**^b

Entry	R	Product	Yield/% ^c
1	<i>n</i> -Bu	2a	87
2	Ph	2b	90
3	CH ₃ OCH ₂	2c	85
4	<i>n</i> -C ₆ H ₁₃	2d	88
5	<i>n</i> -Bu	3a	86
6	Ph	3b	87
7	CH ₃ OCH ₂	3c	81
8	<i>n</i> -C ₆ H ₁₃	3d	84

^aThe reaction of **1** (2 mmol) with (trimethylsilyl)acetylene (3 mmol) was carried out using Pd(PPh₃)₄ (0.1 mmol), CuI (0.2 mmol) and piperidine (6 ml) at room temperature for 2 h.

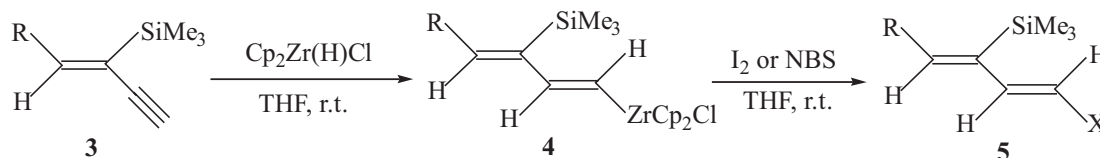
^bThe desilylation reaction of **2** (1 mmol) with KF (10 mmol) was performed in methanol (3 ml) at 70°C for 5 h.

^cIsolated yield of **2** based on the **1** used.



Scheme 1

* Correspondent. E-mail: caimzhong@163.com



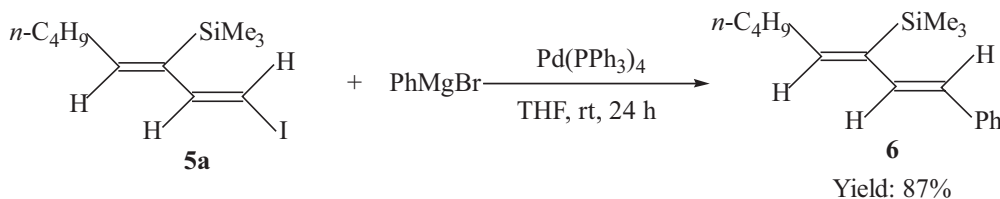
Scheme 2

(*Z*)-1,3-bis(trimethylsilyl)alk-3-en-1-yne **2** with KF proceeded smoothly in methanol at 70°C to give the desired (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3** in high yields. Typical results are also summarised in Table 1.

Hydrozirconation has emerged as a unique hydrometallation with some attractive features such as the high regioselectivity and stereoselectivity observed with alkynes¹⁸ and heteroatom-substituted alkynes.¹⁹ However, the hydrozirconation of terminal conjugated enynes has received less attention.²⁰ With a convenient route to (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3** established we decided to investigate the feasibility of using **3** in a hydrozirconation reaction with Cp₂Zr(H)Cl. We observed that, when the hydrozirconation of **3** with Cp₂Zr(H)Cl was performed in THF at room temperature, fairly rapid reactions occurred affording stereoselectively (*1E,3Z*)-3-(trimethylsilyl)-substituted 1,3-dienylzirconium(IV) complexes **4**. The intermediates **4** were then trapped with iodine or NBS to give stereoselectively (*1E,3Z*)-1-halo-3-(trimethylsilyl)-substituted 1,3-dienes **5** in good yields (Scheme 2). Typical results are summarised in Table 2. As shown in Table 2, a variety of (*1E,3Z*)-1-halo-3-(trimethylsilyl)-substituted 1,3-dienes **5** could be synthesised stereoselectively via hydrozirconation of (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3**, followed by trapping with iodine or NBS. The (*1E*)-configuration of compounds **5a–f** has been proved by their ¹H NMR spectra which show two doublets at δ = 6.03–7.47 with coupling constants of 13.6–15.2 Hz, and this also indicates that hydrozirconation of (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne **3** with Cp₂Zr(H)Cl occurs highly regio- and stereoselectively, affording intermediates **4**. In addition, the (*3Z*)-configuration of compound **5a** was confirmed by NOESY experiments. An enhancement of the allylic protons was observed as the vinylic proton (δ = 6.17 ppm) of **5a** was irradiated. There was a correlation between the allylic protons and the methyl protons of the trimethylsilyl. A correlation between the vinylic proton (δ = 6.17 ppm) and one other vinylic proton (δ = 6.03 ppm) was also observed. The NOE results indicate that **5a** has the expected (*1E,3Z*)-configuration.

We have also carried out the palladium-catalysed cross-coupling reaction of compound **5a** with phenylmagnesium bromide in THF to afford iodine-free (*1Z,3E*)-2-(trimethylsilyl)-substituted 1,3-diene **6** in 87% yield (Scheme 3).

In summary, we have developed a highly stereoselective and general route to difunctionalised 1,3-dienes containing silicon and halogen by hydrozirconation of (*Z*)-3-(trimethylsilyl)alk-3-en-1-yne, followed by trapping with iodine or NBS. The present method has the advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions, high stereoselectivity and good yields.



Scheme 3

Table 2 Synthesis of (*1E,3Z*)-1-halo-3-(trimethylsilyl)-substituted 1,3-dienes **5**

Entry	R	X	Product	Yield ^a /%
1	<i>n</i> -C ₄ H ₉	I	5a	74
2	<i>n</i> -C ₄ H ₉	Br	5b	76
3	Ph	I	5c	78
4	Ph	Br	5d	80
5	<i>n</i> -C ₆ H ₁₃	I	5e	73
6	<i>n</i> -C ₆ H ₁₃	Br	5f	81

^aIsolated yield based on the **3** used.

Investigations into the synthetic applications of compounds **5** are currently in progress.

Experimental

¹H NMR spectra were recorded on a Bruker AC-P400 (400 MHz) spectrometer with TMS as an internal standard using CDCl₃ as the solvent. ¹³C NMR (100 MHz) spectra were recorded on a Bruker AC-P400 (400 MHz) spectrometer using CDCl₃ as the solvent. IR spectra were determined on an FTS-185 instrument as neat films. Mass spectra were obtained on a Finigan 8239 mass spectrometer. Microanalyses were measured using a Yanaco MT-3 CHN microelemental analyser. All reactions were carried out in pre-dried glassware (150°C, 4 h) and cooled under a stream of dry Ar. All solvents were dried, deoxygenated and freshly distilled before use. (*E*)- α -Iodovinylsilanes **1** were prepared from alkynylsilanes according to a literature procedure.²¹

General procedure for the synthesis of (*Z*)-1,3-bis(trimethylsilyl)alk-3-en-1-yne **2a–d**

(*E*)- α -Iodovinylsilane **1** (2.0 mmol), Pd(PPh₃)₄ (0.1 mmol), piperidine (6 ml), and CuI (0.2 mmol) were added to a flask under Ar, and the resulting mixture was stirred at room temperature for 5 min. To this solution was added (trimethylsilyl)acetylene (3.0 mmol), and the reaction mixture was stirred at room temperature for 2 h, quenched with sat. NH₄Cl aq. solution (10 ml) at 0°C and extracted with Et₂O (2 × 25 ml). The ethereal solution was washed with water (2 × 10 ml) and dried over MgSO₄. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel eluting with light petroleum ether (bp. 30–60°C).

(*Z*)-1,3-Bis(trimethylsilyl)oct-3-en-1-yne (**2a**): Oil. IR (film): ν (cm⁻¹) 2959, 2928, 2120, 1719, 1581, 1406, 1249, 841, 759; ¹H NMR (CDCl₃): δ 6.71 (t, *J* = 7.6 Hz, 1H), 2.22–2.14 (m, 2H), 1.39–1.28 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.22 (s, 9H), 0.17 (s, 9H); ¹³C NMR (CDCl₃): δ 156.0, 123.2, 109.0, 93.7, 32.3, 31.5, 22.5, 14.0, 0.2, -0.2; MS: *m/z* 252 (M⁺, 18), 73 (100), 57 (43); Anal. Calc. for C₁₄H₂₈Si₂: C, 66.58; H, 11.18. Found: C, 66.3; H, 11.0%.

(*Z*)-1,3-Bis(trimethylsilyl)-4-phenylbut-3-en-1-yne (**2b**): Oil. IR (film): ν (cm⁻¹) 3058, 3026, 2959, 2898, 2118, 1717, 1557, 1490, 1407, 1250, 840, 759, 698; ¹H NMR (CDCl₃): δ 7.76 (s, 1H), 7.31–7.21 (m, 5H), 0.22 (s, 9H), 0.09 (s, 9H); ¹³C NMR (CDCl₃): δ 152.4, 138.6, 128.4, 127.9, 127.0, 125.2, 109.3, 96.9, 0.2, -0.1; MS: *m/z* 272 (M⁺, 13), 91 (80), 78 (100), 77 (57), 73 (41); Anal. Calc. for C₁₆H₂₄Si₂: C, 70.51; H, 8.88. Found: C, 70.2; H, 8.6%.

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