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Preparation of 2-trimethylsilylmethyl-1-alkene; cross-coupling and protodesilylation sequence from 1,1-dibromo-1-alkene

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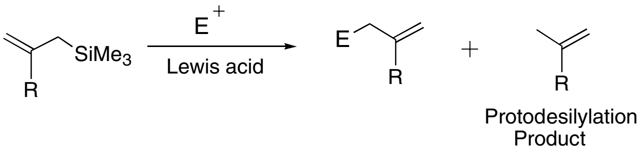
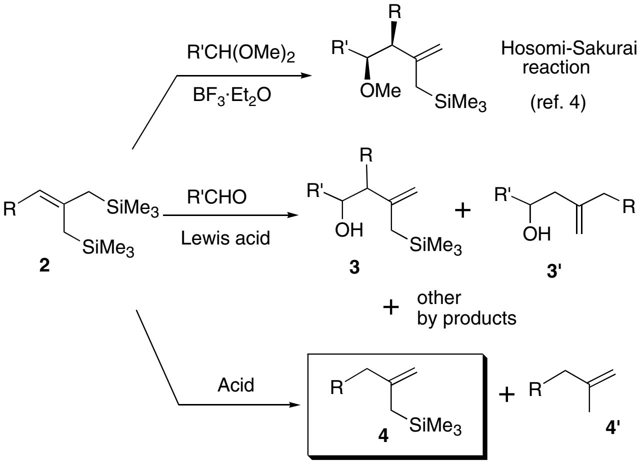
Abstract—A new method for the preparation of exomethylene type allylsilane is described. Selective mono-protodesilylation of 1-trimethylsilyl-2-trimethylsilylmethyl-2-alkenes **2** with PPTS afforded 2-trimethylsilylmethyl-1-alkenes **4** in excellent yields. Since the resulting allylsilanes **4** possess an exomethylene unit, the reactions of **4** with carbonyl compounds in the presence of Lewis acids gave the corresponding product **7** having an exomethylene unit in excellent yields.

Allylsilane is one of the most useful functional groups for carbon–carbon bond forming reactions.[1] Allylsilanes can be conventionally prepared and reacted with aldehyde, ketone, enone and other electrophiles in the presence of Lewis acid. However, protodesilylation sometimes occurs as an undesirable side reaction in Lewis acid promoted carbon–carbon bond formation reactions (Scheme 1).[2,3]



Scheme 1.

We have recently reported the synthesis of 1-trimethylsilyl-2-trimethylsilylmethyl-2-alkene **2** from 1,1-dibromo-1-alkene **1** by tandem Pd-catalyzed cross-coupling reaction with silylmethyl Grignard reagents.[4] Although Lewis-acid promoted reactions of **2** with dimethyl acetal using $BF_3 \cdot Et_2O$ provided the corresponding homoallylic alcohol methyl ether in good yields, those with an aldehyde gave complex mixtures including two kinds of homoallylic alcohols **3** and **3′** with other by-products. Compound **3** is the result of **2** subjected to the Hosomi–Sakurai reaction. The formation of **3′** resulted from the Hosomi–Sakurai reaction of exomethylene type allylsilane **4** with aldehyde (Scheme 2). Apparently, **4** was generated in the reaction mixture by the acid promoted protodesilylation of **2**. The acid treatment of **2** gave a mixture of **4** and the further protodesilylated product **4′**. We considered that if the protodesilylation of **2** could be controlled at the stage of mono-protodesilylation giving **4** selectively, then it would become a nice 3-step sequence for the preparation of exomethylene-type allylsilane **4**[5] from aldehyde via 1,1-dibromo-1-alkene and **2**, as shown in Scheme 3. In fact, we have used this procedure for the total synthesis of (−)-laulimalide.[6] However, its generality and versatility have not been revealed.



Scheme 2.

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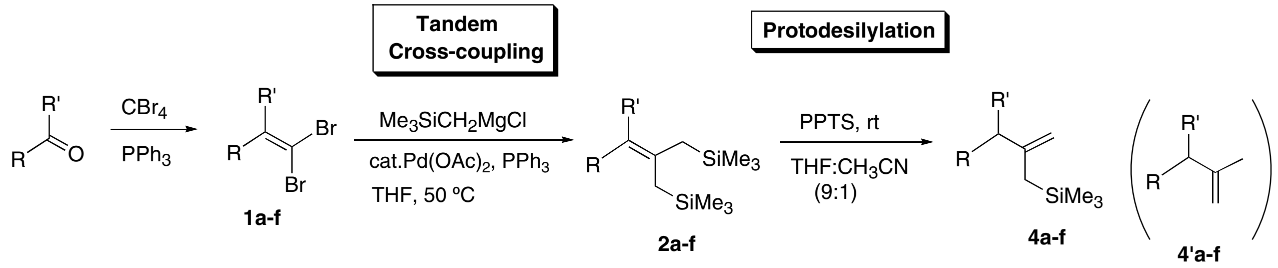


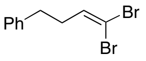
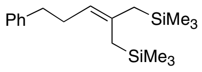
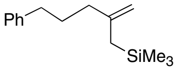
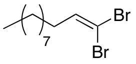
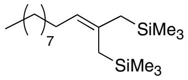
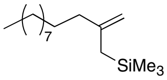
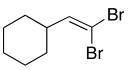
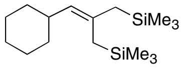
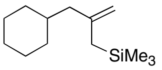
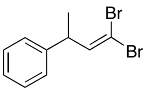
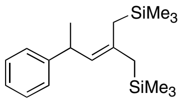
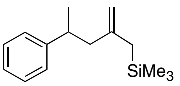
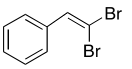
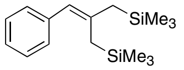
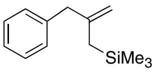
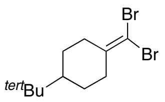
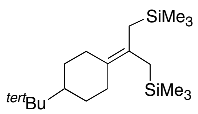
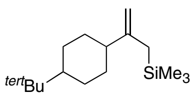
a, R = phenethyl, R' = H
b, R = $nC_{10}H_{21}$, R' = H
c, R = cyclohexyl, R' = H
d, R = 1-phenethy, R' = H
e, R = phenyl, R' = H
f, R = R' = $-(CH_2)_2-CH^tBu-(CH_2)_2-$

Scheme 3.

In this Letter, we report an acid-promoted protodesilylation of bisallylsilanes **2** for the general preparation of 2-trimethylsilylmethyl-1-alkenes **4** and synthetic utilities of the allylsilanes for efficient coupling with some electrophiles, giving compounds **7** that have an exomethylene.

A 1,1-dibromo-1-alkene **1** can be derived from the corresponding aldehyde or ketone with carbon tetrabromide and triphenylphosphine.[7] The Pd-catalyzed tandem Kumada–Tamao–Corriu cross-coupling reaction of **1a**–**d** with an excess of trimethysilylmethyl Grignard reagent gave **2a**–**d** in good to excellent yields,[8] though undesired reactions occurred partially in the cases of **2e** and **2f** (Table 1). Protodesilylated products **4** or **4′** were obtained not only by Lewis acid but also by Brönsted acid promoted electrophilic reactions. Protodesilylation of **2a** with aq HCl in THF gave a mixture of **2a**, **4a** and **4′a**. The reaction was conducted in a mixture of acetic acid/THF/H_2O = 3:2:1 ratio for 2.5 h at room temperature and gave a mixture of **4a** and **4′a** in a 2:1 ratio. The use of $ZnCl_2$ in CH_2Cl_2 for 30 min at room temperature gave them in a 26:2:1 ratio, and IR-400 resin in CH_2Cl_2 gave a recovery of **2a**. However, when 1 equiv of PPTS was used in THF for 4 h at room temperature, the reaction gave a 1:5:0 ratio of **2a**:**4a**:**4′a**.

Table 1. Preparation of 2-trimethylsilylmethyl-1-alkene from aldehydes and ketones

Entry	1,1-Dibromo-1-alkene 1		Yield[a] (%)	Bisallylsilane 2		Yield[a] (%)	Allylsilane 3		Yield[a] (%)
1		1a	88		2a	93		4a	97
2		1b	95		2b	94		4b	Quant.
3		1c	92		2c	85		4c	Quant.
4		1d	96		2d	79		4d	96
5		1e	98		2e	43[b]		4e	85[c]
6		1f	95		2f	21[d]		4f	26

[a] Isolated yield.

[b] Polymer was formed.

[c] 2 days.

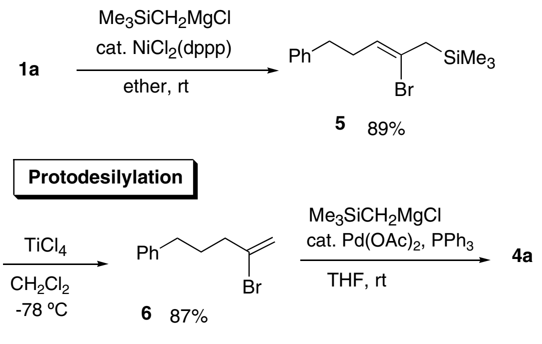
[d] 4-*tert*-Butyl-1-(2-trimethylsilylvinyl)cyclohexane was a major by-product.

The reaction in CH_3CN and MeOH is faster than that in THF. Eventually, when the reaction was performed in a 9:1 mixture of THF:CH_3CN, **4a** was obtained exclusively in a 97% yield.[9] An addition of MeOH, CH_3CN or CH_2Cl_2 to THF accelerates the reaction.

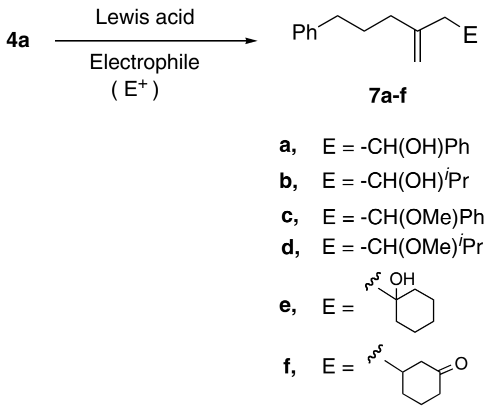
Other results for the synthesis of **4** from carbonyl compound in three steps are listed in Table 1. Protodesilylation of **2** takes place very nicely with PPTS in a mixed solvent of THF and CH_3CN or MeOH with the exception of **2f**.[10] In the case of ketone (entry 6), the formation of **2f** and its protodesilylation were both troublesome. The protodesilylation of **2f** was slow and the starting material was recovered along with decomposed products. The use of a stronger acid or harsh conditions gave disappointing results in the protodesilylation reaction.[11]

Although compounds **2** were yielded by the tandem Pd-catalyzed cross-coupling directly from **1**, Ni-catalyzed cross-coupling reaction of **1a** with $TMSCH_2MgCl$ in ether at room temperature gave 2-bromo-5-phenyl-1-trimethylsilyl-2-pentene **5** in an 89% yield (Scheme 4). Protodesilylation of **5** was performed with $TiCl_4$ in CH_2Cl_2 at −78 °C to give 2-bromo-5-phenyl-1-pentene **6** in an 87% yield. Vinylbromide **6** is known as a vinyl anion equivalent. Thus, after a metal–bromine exchange reaction, the corresponding vinyl-metal can react with various electrophiles to give coupling products that have an exomethylene unit. The introduction of a trimethylsilylmethyl group to **6** by Pd-catalyzed cross-coupling with $TMSCH_2MgCl$ gave **4a** in an 88% yield.

Next, allylsilane **4a** was subjected to further carbon–carbon bond formation with aromatic and aliphatic aldehyde, their acetals, cyclohexanone and cyclohexenone in the presence of Lewis acid. The results are shown in Scheme 5 and Table 2. In all cases, an exomethylene product **7** was obtained. The Hosomi–Sakurai reaction of **4a** with aldehydes and acetals was conducted using $InCl_3$ at 0 °C and using $BF_3{\cdot}OEt_2$ at −78 to 0 °C giving **7a–d** in good to excellent yields. $TiCl_4$ promoted addition with cyclohexanone gave **7e** in a 96% yield. On the other hand, the reaction of **4a** with cyclohexenone gave 1,4-adduct **7f** in a 69% yield.

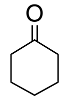
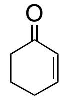


Scheme 4.



Scheme 5.

Table 2. Lewis-acid promoted reaction of **4a** with various electrophiles

Entry	Electrophile	Lewis acid	Product	Yield (%)
1	PhCHO	$InCl_3$[a]	**7a**	88
2	^{i}PrCHO	$InCl_3$	**7b**	80
3	$PhCHO(OMe)_2$	$BF_3{\cdot}OEt_2$[b]	**7c**	75
4	$^{i}PhCHO(OMe)_2$	$BF_3{\cdot}OEt_2$	**7c**	75
5		$TiCl_4$[c,d]	**7e**	96
6		$TiCl_4$[c,e]	**7f**	69 (1,4-adduct)

[a] 0.2 equiv in CH_2Cl_2 at 0 °C for 2.5 h.

[b] 1.2 equiv in CH_2Cl_2 at −78 °C to rt for 30 min.

[c] 1.2 equiv in toluene at −78 °C.

[d] 2 h.

[e] 5 min.

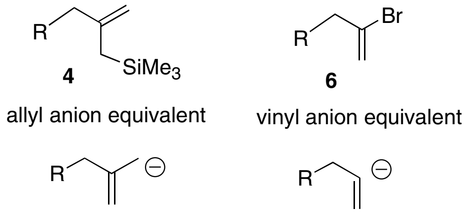


Figure 1.

In conclusion, a new preparation of allylsilanes **4** has been achieved by tandem cross-coupling of **1** and selective protodesilylation of **2**. Compounds **4** have an exomethylene unit regarded as *an allyl anion equivalent* that reacts with various electrophiles to produce addition products featuring an exomethylene unit (Fig. 1). Compound **4a** was also prepared from **1a** by stepwise cross-coupling through compounds **5** and **6**. Compound **6** is also useful as *a vinyl anion equivalent* for the synthesis of compounds possessing an exomethylene unit.

Acknowledgements

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COE Program from Ministry of Education, Culture, Sports, Science and Technology, Japan.

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9. Typical experiment: A mixture of **2** (1 mmol) and PPTS (1.5 mmol) was stirred in a mixture of THF (9 mL) and CH_3CN (1 mL) at room temperature overnight. Then the mixture was quenched with aq $NaHCO_3$ and extracted with hexane. The crude product was purified by column chromatography on silica gel to give **4**.
10. It should be noted that protodesilylation is a delicate reaction. Fine adjustment of reaction conditions for solvent and temperature are required in specific cases.
11. Over protodesilylation occurred.