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A Facile Stereoselective Synthesis of (2*E*)-3-Silylallylic Alcohols by Hydromagnesiation of 1-Aryl-2-silylacetylenes

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Hydromagnesiation of 1-aryl-2-silylacetylenes **1** in diethyl ether gave (1*E*)-2-silylvinyl Grignard reagents **2**, which reacted with aldehydes or ketones **3** to afford stereoselectively (2*E*)-3-silylallylic alcohols **4** in good to high yields.

Introduction

Allylic alcohols are among the most versatile intermediates in organic synthesis and are pervasive in natural products and commercially important pharmaceuticals.[1] Thus, the stereocontrolled synthesis of allylic alcohols is of considerable interest in organic chemistry.[2] Although substantial progress has been made in the synthesis of (2*E*)-di- and (2*E*)-trisubstituted allylic alcohols,[3–7] the direct synthesis of (2*E*)-2,3-disubstituted allylic alcohols remains a formidable challenge.[8] The stereocontrolled synthesis of allylic alcohols containing metal or heteroatom functional groups is also of considerable interest in organic synthesis because many useful functional-group transformations can be achieved by introduction and removal of metal or heteroatom functions. Lee et al. reported the efficient preparation of enantiomerically pure (3*E*)-4-(tributylstannyl)but-3-en-2-ol by lipase-mediated resolution.[9] The stereoselective synthesis of (2*Z*)-2-(butylseleno)allylic alcohols,[10] (2*Z*)-2-(alkylthio)allylic alcohols,[11] (2*Z*)-2-silylallylic alcohols,[12] and (2*E*)-2-sulfonylallylic alcohols[13] has also been described in the literature. Recently, Huang et al. reported an efficient synthesis of (2*Z*)-2,3-difunctionalized allylic alcohols by stereoselective Michael/aldol tandem reaction of phenylselenomagnesium bromide with acetylenic sulfones and aldehydes.[14] However, to the best of our knowledge, there is no report on the stereoselective synthesis of (2*E*)-3-silylallylic alcohols. Hydromagnesiation has emerged as a unique hydrometallation with some attractive features such as the high regioselectivity and stereoselectivity observed with 1-aryl-2-silylacetylenes and alkynylsilanes.[15] Herein we wish to report that (2*E*)-3-silylallylic alcohols could be conveniently synthesized by hydromagnesiation of 1-aryl-2-silylacetylenes, followed by a reaction with aldehydes or ketones.

Results and Discussion

1-Aryl-2-silylacetylenes **1** were prepared according to a literature procedure.[16] Hydromagnesiation of 1-aryl-2-silylacetylenes is known to proceed with high regio- and stereoselectivity to generate (1*E*)-1-aryl-2-silylvinyl Grignard reagents (Scheme 1).[15] We observed that the hydromagnesiation of 1-aryl-2-silylacetylenes **1** at 25 °C in diethyl ether for 6 h gave (1*E*)-1-aryl-2-silylvinylmagnesium bromides **2**, which reacted with aldehydes or ketones **3** to afford stereoselectively the desired (2*E*)-3-silylallylic alcohols **4** (Scheme 1). Typical results are summarized in Table 1 which shows that both aldehydes and ketones could react rapidly with the intermediates **2** under mild conditions to give the corresponding (2*E*)-3-silylallylic alcohols **4** in good to high yields. To examine the scope for this methodology, the hydromagnesiation reactions of 1-heteroaryl-2-silylacetylenes, such as 1-(2-pyridyl)-2-(trimethylsilyl)acetylene and 1-(2-furyl)-2-(trimethylsilyl)acetylene, were also investigated. It was found that no desired (2*E*)-3-silylallylic alcohol was formed under the same reaction conditions since the hydromagnesiation reactions did not occur at all. The hydromagnesiation of 1-alkyl-2-silylacetylenes could proceed highly regio- and stereoselectively under the same conditions to give the (1*Z*)-1-silylvinyl Grignard reagents,[15] but it was not suitable for the preparation of (2*E*)-3-silylallylic alcohols. This is the current limitation of the method.

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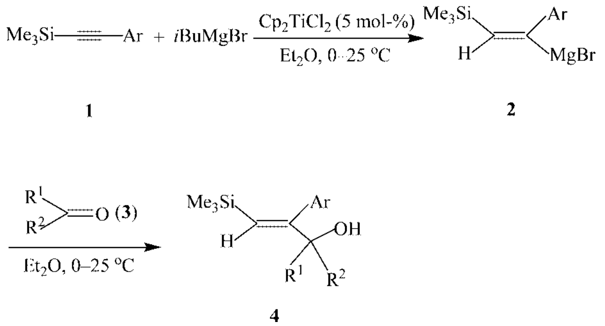

Scheme 1.

Table 1. Synthesis of (2*E*)-3-silylallylic alcohols **4a**–**j**.

Entry	Ar	R^1	R^2	Product	Yield[a] (%)
1	Ph	CH_3	CH_3	**4a**	82
2	Ph	Ph	H	**4b**	85
3	Ph	Ph	CH_3	**4c**	79
4	Ph	*n*-C_6H_{13}	H	**4d**	80
5	Ph	3,4-$CH_2O_2C_6H_3$	H	**4e**	83
6	4-ClC_6H_4	CH_3	CH_3	**4f**	89
7	4-ClC_6H_4	Ph	H	**4g**	84
8	4-ClC_6H_4	3,4-$CH_2O_2C_6H_3$	H	**4h**	81
9	4-$CH_3OC_6H_4$	Ph	CH_3	**4i**	78
10	4-$CH_3OC_6H_4$	CH_3	CH_3	**4j**	90

[a] Isolated yield based on the aldehyde or ketone **3** used.

Investigations of the crude products **4** by ^{1}H NMR spectroscopy (400 MHz) showed their isomeric purities to be $> 97\%$. One olefinic proton signal of compounds **4a**–**j** appears as a singlet at $\delta = 5.83$–6.16 ppm, which indicates that the hydromagnesiation of 1-aryl-2-silylacetylenes **1** had taken place with strong preference for the addition of the magnesium atom at the carbon atom adjacent to the aryl group.

Conclusion

A convenient synthetic method for (2*E*)-3-silylallylic alcohols has been developed by the hydromagnesiation of 1-aryl-2-silylacetylenes, followed by a reaction with aldehydes or ketones. The present method has the advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions and high yields.

Experimental Section

General: Diethyl ether was distilled from sodium immediately prior to use. IR spectra were obtained with a Perkin–Elmer 683 instrument as neat films. ^{1}H NMR spectra were recorded with a Bruker AC-400 (400 MHz) spectrometer using $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded with a Bruker AC-400 (100 MHz) spectrometer using $CDCl_3$ as solvent. Mass spectra were determined with a Finnigan 8230 mass spectrometer. Microanalyses were measured with a Yanaco MT-3 CHN micro-elemental analyzer.

General Procedure for the Synthesis of (2*E*)-3-Silylallylic Alcohols 4a–j: To a solution of isobutylmagnesium bromide (4.5 mmol) in diethyl ether (7 mL) was added Cp_2TiCl_2 (50 mg, 0.2 mmol) at 0 °C under Ar, and the mixture was stirred at that temperature for 30 min. To this solution was added 1-aryl-2-silylacetylene **1** (4.0 mmol), and the mixture was stirred at 25 °C for 6 h. After being cooled to 0 °C, aldehyde or ketone **3** (3.5 mmol) was added and the mixture was stirred at 25 °C for 2 h, quenched with satd. aq. NH_4Cl solution (25 mL), and extracted with Et_2O (2×30 mL). The combined organic layers were washed with satd. aq. NH_4Cl solution (20 mL) and water (3×20 mL) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave an oil, which was purified by column chromatography on silica gel (eluent: light petroleum ether/EtOAc, 12:1).

Supporting Information (for details see the footnote on the first page of this article): Characterization data (IR, ^{1}H NMR, ^{13}C NMR, mass spectra, and elemental analyses) of (2*E*)-3-silylallylic alcohols **4a**–**j**.

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