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Synthesis of Silicon Substituted Cyclopropylmethyl Alcohols in Optically Active Form *via* Asymmetric Simmons-Smith Reaction of γ-Silicon Substituted Allylic Alcohols

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Optically active silicon substituted cyclopropylmethyl alcohols were synthesized through asymmetric Simmons-Smith reaction; that is, the reaction of γ-silicon substituted allylic alcohols with diethylzinc and diiodomethane utilizing (+)-diethyl tartrate as a chiral auxiliary was found to afford the corresponding silicon substituted cyclopropylmethyl alcohols with high stereoselectivity up to 92% ee.

Recently enantioselective Simmons-Smith reaction of allylic alcohols with diethylzinc and diiodomethane utilizing (+)-(*R*,*R*)-diethyl tartrate (DET) as a chiral auxiliary was developed to give the corresponding optically active cyclopropylmethyl alcohols through methylene addition from *re*-face corresponding to C_2 carbon in allylic alcohols.[1-3] With these results in hand, we were interested in the synthesis of optically active silicon substituted cyclopropanes, which are versatile synthetic intermediates for various types of chemicals.[4] In this paper, we wish to describe the enantioselective synthesis of silicon functionalized cyclopropylmethyl alcohols by asymmetric Simmons-Smith reaction of γ-silicon substituted allylic alcohols[5] using (+)-DET as a chiral auxiliary.[6]

Firstly the cyclopropanation reaction of (*E*)-3-(dimethylphenylsilyl)-2-propen-1-ol (**1a**) in CH_2Cl_2 was carried out; that is, **1a** was treated with diethylzinc (1 equiv.) at 0 °C under a nitrogen atmosphere and (+)-DET (1 equiv.) was added after 10 min. At this stage, zinc-bridging intermediate **2** was presumed to be formed. Another diethylzinc (3 equiv.) was added to the mixture 1 h later, followed by the addition of diiodomethane (3 equiv.) after 10 min. After being stirred for 4 h at 0 °C, the reaction mixture was treated with sat. aq NH_4Cl and the crude products were purified by TLC on silica gel to give the corresponding cyclopropane **3a** in 69% yield. As shown in the Table 1, enantiomeric excess of the product was determined to be 63% ee by ^1H NMR analysis in the presence of $Eu(hfc)_3$ (Entry 1). For this cyclopropanation reaction, using $ClCH_2CH_2Cl$ as a solvent lowered the stereoselectivity compared with the reaction in CH_2Cl_2 (Entry 2).

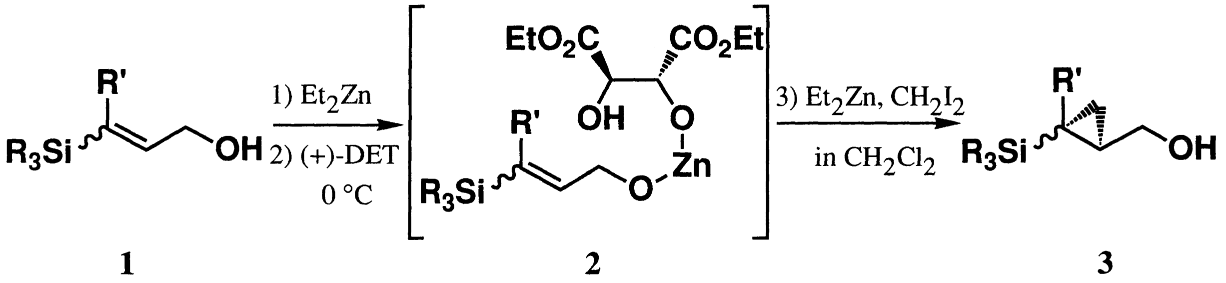
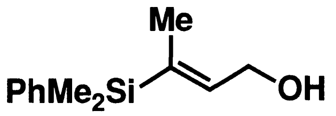
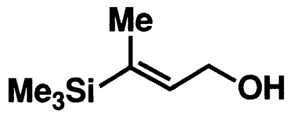
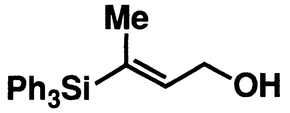
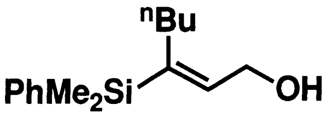
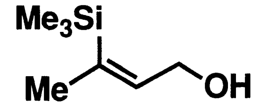
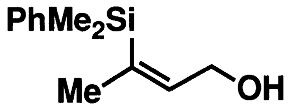
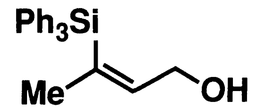
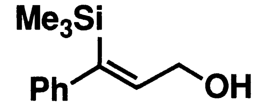
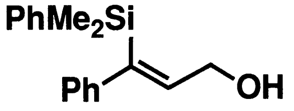


Table 1. Asymmetric Simmons-Smith Reaction of γ-Silicon Substituted Allylic Alcohols **1**

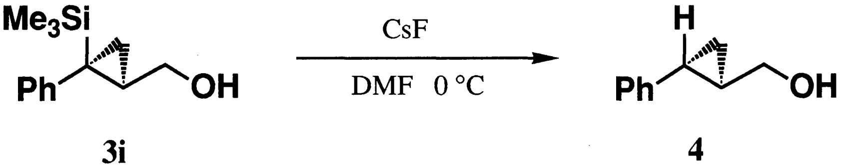
Entry	Substrates **1**		Temp/°Ca)	Time/h	Yield of **3**b)/%	ee/%	$[\alpha]_D^{25}$ c)
1		**1a**	0	4	69	63d)	
2e)			0	5	62	47d)	
3			-22	6	42f)	77d)	-19°
4		**1b**	0	21	78	78d)	
5			-20	8	93	89d)	
6			-30	5	88	92d)	-17°
7		**1c**	-30	7	53	87d)	-11°
8		**1d**	0	10	82	90d)	-22°
9		**1e**	-30	5	84	87d)	-8°
10		**1f**	0	13	50	46d)	-19°
11		**1g**	0	5	83	62g)	
12			-30	9	72h)	74g)	+5°
13		**1h**	0	15	84	34d)	+9°
14		**1i**	0	20	84	80d)	-20°
15		**1j**	0	10	70	58d)	-22°

a) The addition of diiodomethane and the subsequent stirring of the reaction mixture were performed at the indicated temperature. b) All the products gave spectral data in full accord with the assigned structure. c) Specific rotations were measured in MeOH (c 0.2-0.8). d) Optical yield was determined by ^{1}H NMR analysis in the presence of Eu(hfc)$_3$. e) ClCH$_2$CH$_2$Cl was used as a solvent instead of CH$_2$Cl$_2$. f) The allylic alcohol **1a** was recovered in 27% yield. g) Optical yield was determined by HPLC analysis (Daicel Chiralcel OD-H). h) The allylic alcohol **1g** was recovered in 11% yield.

When the reaction was performed at lower temperature -22 °C, the cyclopropane **3a** was obtained with enhanced optical purity (Entry 3). A trisubstituted allylic alcohol **1b** was found to be more reactive and the stereoselectivity was increased compared with the disubstituted allyic alcohol **1a** (Entry 4). Even when the reaction temperature was lowered to -20 °C, the Simmons-Smith reaction readily proceeded to give the silicon functionalized cyclopropane **3b** in 93% yield with higher stereoselectivity (Entry 5). In this reaction, the methyl ether and/or the formaldehyde acetal of the produced alcohol, which were obtained as by-products in the asymmetric Simmons-Smith reaction of non-silicon substituted allylic alcohols,[1] were not detected. The excellent stereoselectivity was achieved in the reaction at -30 °C to afford the cyclopropane **3b** in 92% ee (Entry 6). The influence on the stereoselectivity by the kind of silicon substituent was also investigated using 2-buten-1-ol derivatives. Trimethylsilyl derivative **1c** also reacted even at -30 °C to give the cyclopropane **3c** with high selectivity (Entry 7). Cyclopropanation reaction of triphenylsilyl substituted allylic alcohol **1d** did not proceed below 0 °C, but at 0 °C furnished the corresponding cyclopropane **3d** in an excellent optical yield (Entry 8). Furthermore, asymmetric Simmons-Smith reaction of (*E*)-dimethylphenylsilyl substituted 2-hepten-1-ol derivative **1e** was examined at -30 °C and the corresponding cyclopropane **3e** was produced in a high stereoselective manner (Entry 9).

Next, the cyclopropanation reaction of (*Z*)-silicon substituted allylic alcohols was investigated. In the reaction of 2-buten-1-ol derivatives, the stereoselectivity was not so high as that in the reaction of (*E*)-silicon substituted 2-buten-1-ol derivatives (Entries 10-13). Among trimethylsilyl, dimethylphenylsilyl, and triphenylsilyl substituted allylic alcohols **1f-h**, dimethylphenylsilyl substituted allylic alcohol **1g** still realized good stereoselectivity at -30 °C (Entry 12). In the reaction of cinnamyl alcohol derivatives, the cyclopropanation reaction of trimethylsilyl substituted allylic alcohol **1i** was found to proceed with better stereoselectivity than the reaction of dimethylphenylsilyl substituted allylic alcohol **1j** to give the cyclopropane **3i** in 80% ee (Entries 14 and 15).

The obtained cyclopropane **3i** (67% ee) was desilylated by the treatment with cesium fluoride[7] to the optically active *trans*-cyclopropane **4** (58%) accompanied with the corresponding *cis*-isomer (20%). The absolute configuration of **4** was determined to be *R*,*R* by the comparison of its specific rotation ($[\alpha]_D^{25}$ -51° (c 0.1, EtOH)) with the reported data (lit[3a] $[\alpha]_D^{21}$ -56.2° (c 0.60, EtOH) for 75% ee, lit[8] $[\alpha]_D^{12}$ -46.6° (c 2.640, EtOH) for 51.3% ee). Therefore, the absolute configuration of **3i** was confirmed to be *S*,*S* form. The stereochemical courses of the attachment of methylene group in the reactions of **1a-h**, **j** were also assumed to be from back side of the olefins in the allylic alcohols when they were depicted like **1a-h**, **j** in the Table 1.



As described above, the present method provides a useful example for the stereoselective preparation of optically active silicon functionalized cyclopropanes. Furthermore, easy availability of (+)- and (-)-DET has now realized the facile preparation of both enantiomers of silicon functionalized cyclopropanes.

References

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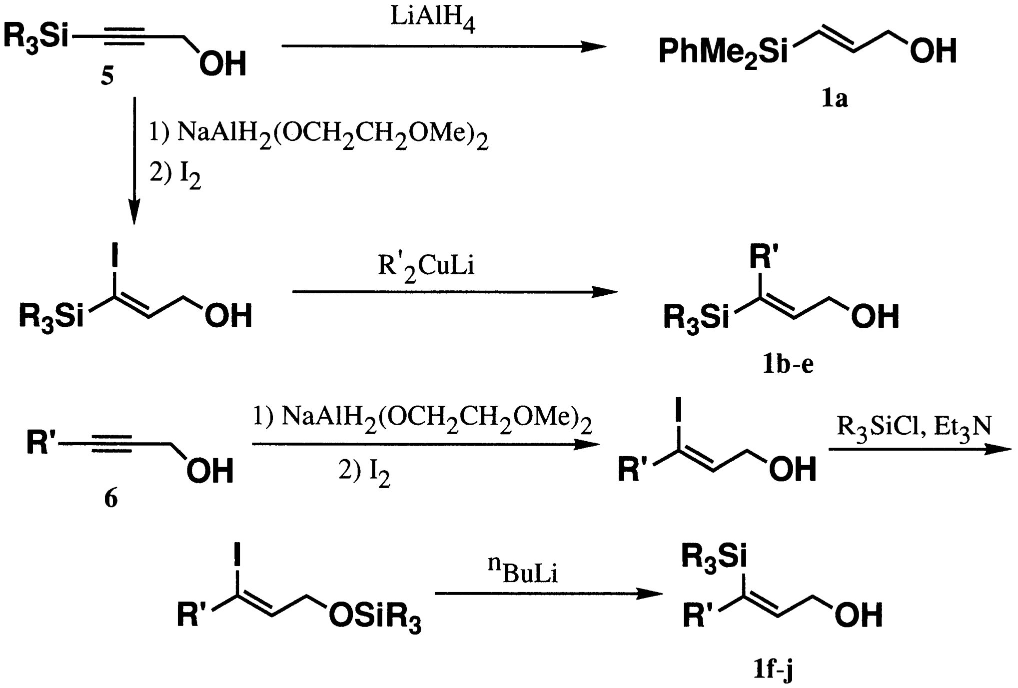
5) (*E*)- and (*Z*)-γ-silicon substituted allylic alcohols **1a**-**j** were prepared from propargyl alcohols **5** and **6**, respectively, according to the following scheme in good to moderate yields.



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