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Chirality transfer from silicon to carbon via diastereoselective Simmons–Smith cyclopropanation of chiral alkenylsilanols

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Abstract—Simmons–Smith cyclopropanation of a chiral alkenylsilanol with CH_2I_2–Et_2Zn proceeds diastereoselectively to give the corresponding cyclopropylsilanol product. Chirality transfer from silicon to the alkenyl carbons of the silicon substituent is observed. The stereochemistry of the obtained cyclopropylsilanol is confirmed by converting to cyclopropanol via Tamao oxidation. © 2002 Elsevier Science Ltd. All rights reserved.

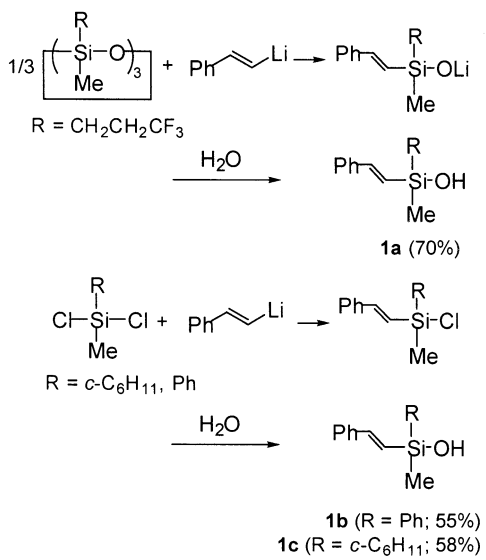
Silicon-centered stereogenicity attracts much attention but has been less well studied compared with the extensive works on the analogous carbon centres.[1] Accordingly, chirality transfer from silicon to neighboring carbon atoms has seldom been investigated to date.[2] However, the development of such highly efficient transfer reactions involving stereogenic silicon atoms could possibly open up a new area of stereochemical studies in organic synthesis.

We recently reported the synthesis of silanols with a stereogenic silicon center and their resolution via HPLC with a chiral column.[3] Hence, our continuing interest in the chemistry of silanols[4] has turned to chirality transfer of these chiral silanols by diastereoselective reaction to a functional group on one of the silicon substituents.

On the other hand, Simmons–Smith cyclopropanation with CH_2I_2–Et_2Zn to non-chiral alkenylsilanols was shown to be accelerated by the hydroxy group to afford cyclopropylsilanols.[5] In such a reaction, the chirality of silicon might be efficiently transferred to carbons when the reaction proceeds in a highly diastereoselective manner, as observed in that of allylic alcohols.[6] Herein, we report such a diastereoselective Simmons–Smith cyclopropanation of chiral non-racemic alkenylsilanols.

The diastereoselective reaction was first examined with several racemic silanols **1a**–**c** under the standard conditions for the Simmons–Smith cyclopropanation reported previously.[5] The synthesis of **1** was carried out by the following methods, as shown in Scheme 1. (a) The cleavage of cyclic siloxane with alkenyllithium followed by hydrolysis of the formed lithium silanolate to give **1** in 70% yield, and (b) alkenylation of a dichlorosilane with the corresponding organolithium reagent followed by careful hydrolysis of the obtained chlorosilane (55–58% yield).

Cyclopropanation of the obtained alkenylsilanols was carried out using diethylzinc and diiodomethane (1:2), a system that is considered to generate $(ICH_2)_2Zn$.[7] When



Scheme 1.

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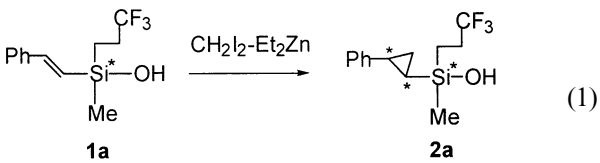
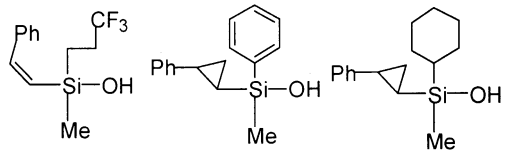
the reaction of **1a** was performed with 3 mol equiv. of diethylzinc and 6 mol equiv. of diiodomethane in diethyl ether at room temperature for 3 h, most of **1a** was consumed (as confirmed by ^{1}H NMR analysis) and the corresponding cyclopropylsilanol **2a** was isolated in 80% yield after purification by column chromatography on silica gel (Eq. (1)). The diastereoselectivity was tentatively estimated by ^{1}H NMR analysis via the relative integration of the isomeric methylsilane signals, which appeared at $\delta = 0.162$ (minor) and 0.166 (major) ppm, respectively. As summarized in Table 1, the diastereoselectivity was consistently in the range 78–84% when **1a** was employed irrespective of the reaction temperature. In addition, the combined use of $(ICH_2)_2Zn$ and a Lewis acid (Et_2AlCl or $TiCl_4$) at lower temperature, previously shown to be an efficient system to enhance the reaction rate in the Simmons–Smith reaction of allylic alcohols,[8] had little effect upon the diastereoselectivity. Although the diastereoselectivity of the Simmons–Smith reaction for (*Z*)-allylic alcohols is known to be higher relative to the (*E*)-isomer,[7] in this case the reaction with the (*Z*)-isomer **3a** (Chart 1) occurred with lower diastereoselectivity (entry 7, 68:32).



1a **2a** (1)

We next examined the effect of a silanol substituent on the stereochemical course of the reaction. When a phenyl group was employed instead of a 3,3,3-trifluoropropyl group, the selectivity for the reaction of silanol **1b** was found to be much lower although the reaction proceeded smoothly. In contrast, higher selectivity was achieved in the reaction of **1c**, bearing a cyclohexyl substituent and a single diastereomer was observed by measurement of the ^{1}H NMR, $\delta = 0.04$ ppm ($CDCl_3$). The results suggest that introduction of a sterically encumbered substituent on the silicon atom is necessary to improve the diastereoselectivity (chart 1).



3a **2b** **2c**

Chart 1.

The stereochemistry of cyclopropylsilanol **2** was determined by conversion into cyclopropanol **4** via Tamao oxidation.[9] The cyclopropanation of (−)-**1a** (the latter enantiomerically enriched; 92% e.e.), which was obtained by separation with HPLC using chiral stationary phase column as reported previously,[3] was carried out to afford cyclopropylsilanol **2a**, whose diastereoselectivity was confirmed to be 84:16 (68% d.e.) by ^{1}H NMR analysis. Tamao oxidation with 3-chloroperbenzoic acid (*m*-CPBA) in DMF at room temperature over 3 h furnished the cyclopropanol (+)-**4** in 31% yield. The absolute configuration of **4** was confirmed to be (1*S*,2*R*) by comparison with the literature.[10] HPLC analysis of the cyclopropanol after transformation to its benzoate revealed it to have e.e. of 58%, suggesting that the stereochemistry was retained through the oxidation. Alkenylsilanol (+)-**1a** (80% e.e.), the antipode of (−)-**1a**, was also subjected to a similar protocol (66% d.e. in the Simmons–Smith reaction) to give (1*R*,2*S*)-2-phenyl-1-cyclopropanol of 55% e.e.[11]

Separation of (±)-**1c** was also successful by HPLC with a chiral column (Daicel AD) to afford (+)-**1c** and (−)-**1c**, each with e.e. of 98% and the cyclopropanation of each enantiomer was conducted in a similar manner to afford the corresponding cyclopropylsilanol as a single diastereomer. The Tamao oxidation of **2c** with *m*-CPBA in the presence of KHF_2 at room temperature in DMF gave (−)-**4** and (+)-**4**, each with 97% e.e., which was also confirmed by HPLC analyses of the benzoate derivatives. (Eq. (2))

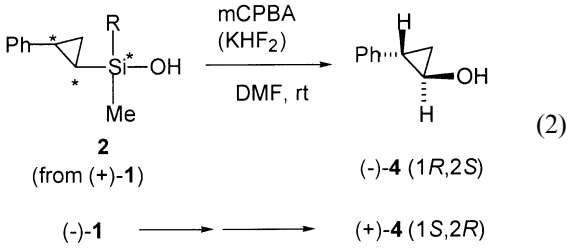
Table 1. Diastereoselective Simmons–Smith cyclopropanation of alkenylsilanols **1a–c** and **3a**[a]

Entry	Substrate	Additive	Temp (°C)	Time (h)	Yield (%)	Selectivity[b]
1	**1a**	None	Rt	3	80	84:16
2		None	−20	3	32	83:17
3		$TiCl_4$	−20	3	7	–
4		$TiCl_4$	−20	25	55	81:19
5		Et_2AlCl	−20	3	58	78:22
6		Et_2AlCl	−40	9	49	81:19
7	**3a**	None	Rt	3	92	68:32[c]
8	**1b**	None	Rt	3	88	55:45
9	**1c**	None	Rt	3	84	>99:1

[a] The reaction was carried out in diethyl ether (entries 1, 2, and 7–9) or dichloromethane (entries 3–6) using 3 mol amounts of Et_2Zn and 6 mol amounts of CH_2I_2.

[b] The selectivity was estimated by a ^{1}H NMR spectrum of the methyl signal on the silanol.

[c] Deduced from the results on the reaction of **1a**.



(2)

In conclusion, the absolute configurations of cyclopropylsilanols **2** were confirmed to be (1*R*,2*S*) when (+)-**1** was employed, whilst (1*S*,2*R*)-isomers were furnished from (−)-**1**, although the absolute configuration of the silicon atom is not yet known. The stereogenicity of the silicon center was successfully transferred to carbon via Simmons–Smith cyclopropanation. When a practical and preparative method to give chiral non-racemic **1** is in hand, the present chirality transfer would be a powerful tool for the synthesis of a variety of chiral organic molecules.

Typical experimental procedure: To a solution of (+)-**1c** (170 mg, 0.69 mmol) in diethyl ether (2.1 mL) were added diethylzinc (1 M hexane solution, 2.07 mL, 2.07 mmol) and diiodomethane (0.34 mL, 4.14 mmol) at 0°C. The mixture was stirred at room temperature for 3 h and poured into sat. NH_4Cl (20 mL) and diethyl ether (10 mL). The aqueous phase was extracted with diethyl ether (2×20 mL) and the combined organic layer was dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure left a crude oil, which was separated by column chromatography on silica gel (hexane–ethyl acetate = 85:15) to yield **2c** (152 mg, 84%). $[\alpha]_D^{23} = -58.4$ (*c* 1.11, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.09 (m, 1H), 0.78 (brs 1H), 0.98–1.06 (m, 2H), 1.12–1.33 (m, 5H), 1.61–1.56 (m, 5H), 1.86 (m, 1H), 7.07–7.16 (m, 3H), 7.23–7.28 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ −3.73, 26.62, 26.65, 26.75, 26.78, 27.72, 125.5, 126.5, 128.2, 128.5, 137.9, 145.6; IR (neat) 3300 br, 2921, 2847, 1605, 1499, 1447, 1252, 1102, 911, 849 cm^{-1}; HRMS: found 260.1594, calcd for $C_{16}H_{24}OSi$: 260.1595.

Acknowledgements

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10. $[\alpha]_D^{26} = -27.2$ (*c* 1.5, EtOH) for **4** from (+)-**1a**; $[\alpha]_D^{26} = +48.4$ (*c* 1.5, EtOH) for **4** from (−)-**1a**. Lit. $[\alpha]_D^{24} = -62.2$ (*c* 0.629, EtOH) for (1*R*,2*S*)-isomer of 73% e.e.; Imai, T.; Mineta, H.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 4986.
11. The e.e. values of **2** can be estimated to be 63% (92% e.e.×68% d.e.) from (−)-**1** and 55% (80% e.e.×66% d.e.).