Highly Stereoselective Intramolecular Addition of a Hydroxyl Group to Vinylsilanes via 1,2-Silyl Migration[1]

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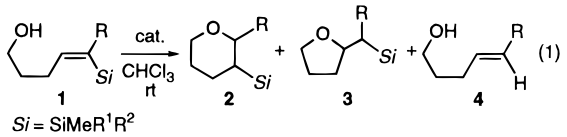
The development of new synthetic methods utilizing the 1,2-silyl migration of β-silyl carbenium ions is of considerable current interest.[2−4] Previously, we have reported the acid-catalyzed cyclization of the vinylsilanes **1** (R = H) to the tetrahydrofurans **3** via a β-silyl carbenium ion intermediate (eq 1).[5] We first report herein that the acid-catalyzed cyclization of **1** (R = alkyl) gives the tetrahydropyrans **2** with high *trans*-selectivity, but not **3**, and also describe the mechanistic aspects of this novel cyclization via 1,2-silyl migration.



Treatment of the (*Z*)-vinylsilane **1a** with a catalytic amount of $TiCl_4$ (5 mol %) in $CHCl_3$ stereoselectively gave the 2,3-disubstituted tetrahydropyran **2a** (trans/cis = >99/<1)[6] along with a desilylated product, (*E*)-4-nonen-1-ol (**4a**) (entry 1 in Table 1). While HCl gas and AcCl (5 mol %) as well as $TiCl_4$ were good catalysts (HCl, 24 h, 67%; AcCl, 30 h, 67%), CH_3CO_2H, $SnCl_4$, BF_3•OEt_2, and $Sc(OTf)_3$ hardly induced the cyclization. AcCl would serve as a source of HCl by the reaction with the hydroxyl group because the presence of 2,6-di-*tert*-butylpyridine (DTBP, 5 mol %), a proton scavenger, prevented the AcCl-catalyzed cyclization of **1a**. Similarly, in the $TiCl_4$-catalyzed system, there is a possibility that HCl generated from $TiCl_4$ is an actual catalyst. However, $TiCl_4$ exhibited a higher catalytic activity than HCl gas and AcCl, and the $TiCl_4$-catalyzed cyclization in the presence of DTBP gave **2a** in 80% yield although it took a longer reaction time (72 h). These results strongly support that $TiCl_4$ functions as the actual catalyst rather than HCl.

The change in the geometry of **1a** resulted in a marked decrease in both the reactivity and stereoselectivity.[5] Under the standard conditions shown in Table 1, the (*E*)-isomer of **1a** was cyclized to **2a** in 17% yield (*trans*/*cis* = 41/59) after being stirred for 4 days. The substituent on silicon also affected the reactivity of **1** (entries 1−7). The vinylsilane **1b**, bearing a trimethylsilyl group, was more sensitive to protiodesilylation than **1a**. To suppress the desilylation, a more sterically bulky silyl group (*Si*) such as $SiMePh_2$ or $SiMe_2$-*t*-Bu was employed.[3h] Contrary to our expectation, **1c** underwent desilylation to a significant extent, and the reactivity of **1c** was lower than that of **1a**. On the other hand, the cyclization of **1d** effected not only a high yield of **2d** but also fast reaction rate,[7] although it exhibited a lower *trans*-selectivity (trans/cis = 95/5) in addition to the formation of **3d** as a minor product at room temperature. However, the stereoselectivity (trans/cis = 97/3) was improved by the lowering of the reaction temperature to 0 °C, and the direct cyclization to **3d** and the protiodesilylation of **1d** were restrained. We further conducted the cyclization of the vinylsilanes **1e**−**g** to investigate the electronic effects of the substituent R^1 on the reactivity. As a result, it turned out that electron-donating *p*-tolyl and *p*-anisyl groups accelerated the protiodesilylation while the electron-withdrawing *p*-trifluoromethylphenyl group considerably diminished the reactivity of the carbon−carbon double bond to prevent the conversion of **1g**. The latter result implies that proton addition to the α-carbon is the rate-determining step in the present cyclization (vide infra).

The $TiCl_4$-catalyzed reaction tolerated polar functionalities such as ether and ester groups (entries 9 and 10). However, the vinylsilane **1k** (R = Ph) underwent no cyclization because of fast desilylation (entry 11). In the case of **1l** (R = $SiMe_3$), the 1,2-silyl migration did not occur at all, and **3l** was exclusively obtained as a ca. 1:1 diastereomeric mixture (entry 12).

On the basis of our previous and present results,[5,8] a plausible mechanism for the formation of *trans*-**2** is shown in Scheme 1. It consists of the following five steps: (1) the attachment of a proton or $TiCl_4$ to the hydroxyl group of **1** forms the oxonium ion **5**, (2) the proton on the oxygen atom in **5** shifts to the α-carbon, (3) the resultant β-silyl carbenium ion **6** turns to its conformer **7** stabilized by $\sigma-\pi$ conjugation,[9,10] (4) a 1,2-silyl migration converts **7** into another β-silyl carbenium ion **8**,[11] and (5) intramolecular attack of the oxygen from the side opposite to the silyl group gives *trans*-**2** and regenerates the proton or $TiCl_4$. The presence of an alkyl group as R is essential to the 1,2-silyl migration in step 4. This is probably reasonable because the alkyl group

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(5) (a) Miura, K; Okajima, S.; Hondo, T.; Hosomi, A. *Tetrahedron Lett.* **1995**, *36*, 1483. (b) Miura, K; Hondo, T.; Okajima, S.; Hosomi, A. *Tetrahedron Lett.* **1996**, *37*, 487.

(6) No cis isomer was detected at all within the limitation of 270 MHz ^{1}H NMR analysis.

(7) The high reactivity of **1d** is probably due to electron-donating ability of the *tert*-butyl group, which accelerates proton addition to the α-carbon (step 2 in Scheme 1). The phenyl group of **1a** or **1c** would rather act as an electron-withdrawing substituent and reduce the reactivity of the double bond toward protonation. Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938.

(8) We have shown that the cyclization of **1** (R = H) to **3** proceeds in a syn addition mode of the hydroxyl group and proposed the oxonium ion intermediate from the stereochemical outcome. See ref 5.

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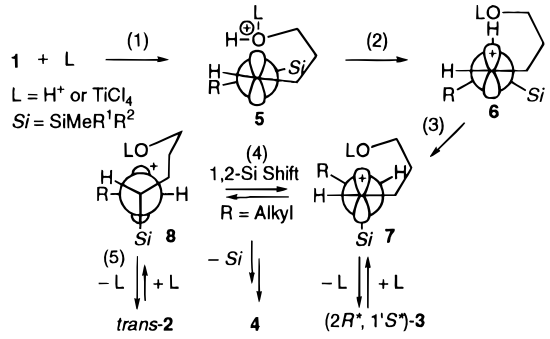
Table 1. $TiCl_4$-Catalyzed Cyclization of Vinylsilanes 1[a]

	substrate (**1**)					yield/%			
entry	R	R^1	R^2		time/h	**2**[b] (*trans*/*cis*)[c]	**3**	**4**[d,e]	**1**[d] (*Z*/*E*)[c]
1	Bu	Ph	Me	**1a**	9.5	75 (>99/<1)	0	15	6 (83/17)
2	Bu	Me	Me	**1b**	7.5	66 (>99/<1)	0	26	0
3	Bu	Ph	Ph	**1c**	24	58 (>99/<1)	0	13	25 (92/8)
4[f]	Bu	*t*-Bu	Me	**1d**	2.3	93 (97/3)[g]	3[g]	0	0
5	Bu	*p*-MeC_6H_4	Me	**1e**	9.5	57 (>99/<1)	0	20	12 (>99/<1)
6	Bu	*p*-$MeOC_6H_4$	Me	**1f**	9.5	53 (>99/<1)	0	28	15 (>99/<1)
7	Bu	*p*-$CF_3C_6H_4$	Me	**1g**	9.5	39 (>99/<1)	0	6	49 (>99/<1)
8	Me	Ph	Me	**1h**	15	76 (>99/<1)	0	10	3 (81/19)
9	$-(CH_2)_3OBn$	Ph	Me	**1i**	15	72 (>99/<1)	0	27	0
10	$-(CH_2)_3OAc$	Ph	Me	**1j**	47	72 (>99/<1)	0	20	4 (>99/<1)
11	Ph	Ph	Me	**1k**	24	0	0	29[h]	30 (82/18)
12	$SiMe_3$	Ph	Me	**1l**	13	0	67[i]	8[j]	4 (>99/<1)

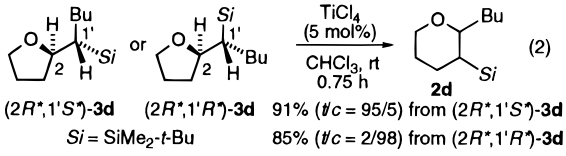
[a] All reactions were performed with **1** (0.50 mmol), $TiCl_4$ (0.025 mmol), and $CHCl_3$ (2.5 mL) at rt unless otherwise noted. [b] Isolated yield of a purified product except for entry 4. [c] Determined by ^1H NMR analysis. The ratio >99/<1 means that no isomer is detected by ^1H NMR analysis. [d] **4** and **1** were obtained as a mixture. The yields and the isomeric ratios of the recovered **1** were determined by ^1H NMR analysis. [e] *E*/*Z* = >99/<1. [f] At 0 °C. [g] The yields and ratio were estimated by GC analysis of a mixture of **2d** and (2*R**,1′*S**)-**3d**. The reaction at rt for 0.75 h afforded **2d**, **3d**, (*E*)-nonen-1-ol (**4a**), and **1d** in 85% (*trans*/*cis* = 95/5), 5%, 8%, and 0% yields, respectively. [h] A $PhMe_2Si$ ether of **4k** was also obtained in 22% yield. [i] A 51:49 diastereomeric mixture. [j] The total yield of (*E*)-5-(trimethylsilyl)-4-penten-1-ol (2%) and (*E*)-5-(dimethylphenylsilyl)-4-penten-1-ol (6%).

Scheme 1

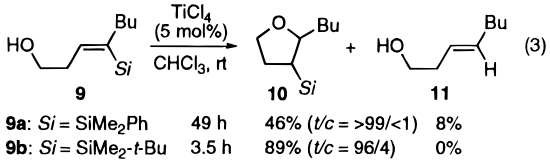


stabilizes the rearranged carbenium ion **8**.[3i] In the cyclization of **1l**, the lower stabilizing ability of the TMS group than that of ordinary alkyl groups[9] would inhibit the 1,2-silyl migration of **7**.

The preferred formation of **2** to **3** in entries 1−10 is attributable to acid-catalyzed isomerization of **3** to **2** by thermodynamic control.[12] Indeed, the isomerizations of (2*R**,1′*S**)-**3d** and (2*R**,1′*R**)-**3d** to **2d** rapidly proceeded with inverse stereoselectivity[13,14] (eq 2). The stereospecific conversion of (2*R**,1′*S**)-**3d** into *trans*-**2** well agrees with the mechanism shown in Scheme 1. We could also observe the partial isomerization of *trans*-**2d** to (2*R**,1′*S**)-**3d**. These results demonstrate that the present isomerization is reversible, and therefore, *trans*-**2d** is a thermodynamically favored product.[15]



We have further disclosed that the vinylsilanes **9** also undergo the present cyclization via 1,2-silyl migration to provide the 2,3-disubstituted tetrahydrofurans **10** with high *trans*-selectivity, although **9** was much less reactive than **1** (eq 3). Similar to the cyclization of **1**, the introduction of $SiMe_2$-*t*-Bu remarkably improved both the reaction rate and the yield of **10**.



Finally, we carried out oxidative removal of the silicon moiety of the cyclized products to enhance the synthetic utility of the present reaction. According to the reported procedure,[16] **2a** and **10a** could be converted to the corresponding alcohols in 88% and 89% yields, respectively, with stereochemical retention.[13]

We are now studying application of this method to the stereoselective synthesis of trisubstituted tetrahydropyrans and tetrahydrofurans, and the results will be reported in due course.

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Supporting Information Available: Experimental procedures and spectral data for the substrates and the products (15 pages).

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(11) There is a longstanding dispute on the structure of β-silyl carbenium ions, which can take a hyperconjugatively stabilized open form or a bridged form. Although the open forms **7** and **8** are employed in Scheme 1, when R is an alkyl group, they can be displaced to one bridged intermediate without any problems. Lambert, J. B.; Zhao, Y. *J. Am. Chem. Soc.* **1996**, *118*, 7867.

(12) Although the fast cyclization of **8** compared with **7**, that is, kinetic control, can be responsible for the exclusive formation of *trans*-**2d**, we do not have any reliable evidence that *trans*-**2d** is a kinetically favored product.

(13) See the Supporting Information.

(14) Recently, Kuwajima et al. have reported novel ring expansion reactions with the 1,2-silyl migration. See ref 4a.

(15) The MM2 calculation of the steric energy using the CAChe system (Sony/Tektronix Co. Ltd.) indicates that *trans*-**2d** is more stable by 3.5 kcal/mol than (2*R**,1′*S**)-**3d** in their optimized structures.

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