JOC Article

1,2-Silyl-Migrative Cyclization of Vinylsilanes Bearing a Hydroxy Group: Stereoselective Synthesis of Multisubstituted Tetrahydropyrans and Tetrahydrofurans[1]

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Acid-catalyzed intramolecular addition of a hydroxy group to α-alkylated vinylsilanes has been studied. Treatment of (*Z*)-5-alkyl-5-silyl-4-penten-1-ols **1** (R = alkyl) with 5 mol % $TiCl_4$ in $CHCl_3$ gave *trans*-2-alkyl-3-silyltetrahydropyrans **2** exclusively (*trans*/*cis* = >99/1 to 97/3). The cyclization efficiency and rate strongly depended on the geometry of the C−C double bond and the silyl group. The use of (*E*)-vinylsilanes resulted in lower yields with poor *cis*-selectivity. In the cyclization of (*Z*)-**1** (R = Bu), the silyl group used, the reaction time, and the yield of **2** were as follows: $SiMe_2Ph$, 9.5 h, 75%; $SiMe_3$, 7.5 h, 66%; $SiMePh_2$, 24 h, 58%; $SiMe_2$-*t*-Bu, 0.75 h, 85%; $SiMe_2Bn$, 1.5 h, 78%. This 1,2-silyl-migrative cyclization could be applied to stereoselective synthesis of trisubstituted tetrahydropyrans. The acid-catalyzed reaction of 1-, 2-, or 3-substituted (*Z*)-5-silyl-4-nonen-1-ols **8** gave *r*-2,*t*-3,*c*-6-, *r*-2,*t*-3,*t*-5-, or *r*-2,*t*-3,*c*-4-trisubstituted tetrahydropyrans with high diastereoselectivity, respectively. (*Z*)-4-Alkyl-4-silyl-3-buten-1-ols **5** as well as **1** underwent the 1,2-silyl-migrative cyclization to give 2-alkyl-3-silyltetrahydrofurans **6** with high *trans*-selectivity. This silicon-directed cyclization was also available for the stereoselective synthesis of tri- and tetrasubstituted tetrahydrofurans.

Introduction

It is well recognized that triorganosilyl groups strongly stabilize β-carbenium ions by σ−π orbital interaction.[2] The β-effect is considerably valuable for regio- and stereocontrolled C−X (X = C, H, or heteroatom) bond formation. In particular, electrophilic substitution reactions with allylsilanes and vinylsilanes have been extensively utilized as highly selective allylation and vinylation methods.[3] Because of the β-effect, electrophiles react with the γ-carbon in allylsilanes or the α-carbon in vinylsilanes so as to form saturated β-silylcarbenium ions (e.g., $R_3Si-CHR^1-C^+HR^2$) in both cases. The cationic intermediates, which are thermodynamically stable, rapidly undergo β-elimination of the silyl group by nucleophilic attack of a counteranion or a solvent molecule to afford allylation and vinylation products. On the basis of this fact, the active carbon species had been considered not to be useful for C−X bond formation, with some exceptions.[4−6]

In the past decade, however, it has turned out that internal carbon and heteroatom nucleophiles add to saturated β-silylcarbenium ions efficiently, and this process serves for the stereoselective construction of carbocycles and heterocycles.[7−9] In the reactions involving such a bond-forming process, the Lewis acid promoted [2 + 2] and [3 + 2] cycloadditions of allylsilanes to electron-deficient unsaturated bonds (C=Y) have been intensively studied by several research groups because they provide powerful methods for highly stereoselective

(1) Organosilicon Chemistry. 157. For part 156, see: Miura, K.; Ootsuka, K.; Suda, S.; Nishikori, H.; Hosomi, A. *Synlett* **2002**, 313.

(2) (a) Lambert, J. B. *Tetrahedron* **1990**, *46*, 2677. (b) Bassindale, A. R.; Taylor, P. G. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Ed.; Wiley: Chichester, 1989; Part 2, p 893.

(3) (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (b) Panek, J. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 1, p 579. (c) Fleming, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 563. (d) Fleming, I.; Dunoguñì, J.; Smithers, R. *Org. React.* **1989**, *37*, 57. (e) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200. (f) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworth: London, 1981.

(4) The use of unsaturated β-silylcarbenium ions (e.g., $R_3Si-CR^1=C^+R^2$ or $R^1CH=C^+-CHR^2(SiR_3)$) arising from allenylsilanes and propargylsilanes for C−C, C.-O, or C−N bond formation was reported in the 1980s. (a) Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604. (b) Pornet, J.; Miginiac, L.; Jaworski, K.; Randrianoelina, B. *Organometallics* **1985**, *4*, 333. See also ref 3b.

(5) Nucleophilic addition of halide ions to β-silylcarbenium ions generated from allylsilanes and vinylsilanes: (a) Sommer, L. H.; Tyler, L. J.; Whitmore, F. C. *J. Am. Chem. Soc.* **1948**, *70*, 2872. (b) Sommer, L. H.; Bailey, D. L.; Goldberg, G. M.; Buck, C. E.; Bye, T. S.; Evans, F. J.; Whitmore, F. C. *J. Am. Chem. Soc.* **1954**, *76*, 1613. (c) Koenig, K. E.; Weber, W. P. *Tetrahedron Lett.* **1973**, 2533. (d) Miller, R. B.; McGarvey, G. *J. Org. Chem.* **1978**, *43*, 4424.

(6) [2 + 2] Cycloadditions of allylsilanes to highly activated unsaturated bonds was reported in the 1970s. These reactions may proceed via saturated β-silylcarbenium ions. (a) Au-Yeung, B. W.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1977**, 81. (b) Abel, E. W.; Rowley, R. J. *J. Organomet. Chem.* **1975**, *84*, 199. (c) Déléris, G.; Dunoguñì, J.; Calas, R. *J. Organomet. Chem.* **1976**, *116*, C45.

(7) Reviews: (a) Knölker, H.-J. *J. Prakt. Chem.* **1997**, *339*, 304. (b) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293.

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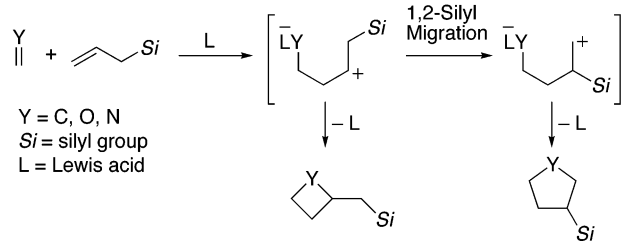
SCHEME 1



construction of four- and five-membered rings. The silicon-directed cycloadditions are believed to proceed via a stepwise mechanism shown in Scheme 1. The first step is nucleophilic addition of an allylsilane to an electron-deficient unsaturated bond activated by a Lewis acid. The β-silylcarbenium ion intermediate formed is directly cyclized to a four-membered ring by intramolecular nucleophilic addition; otherwise, it is converted to another β-silylcarbenium ion by 1,2-silyl migration, then cyclized to a five-membered ring.

A number of the bond-forming reactions of β-silylcarbenium ions arising from allylsilanes have been reported,[5–9] while similar reactions utilizing the reactivity of vinylsilanes remain to be unexplored.[5,10] Previously, we have reported that, in the presence of an acid catalyst, vinylsilanes **1** (R = H) bearing a hydroxy group are smoothly converted into tetrahydrofurans **3** via β-silylcarbenium ions generated by protonation of the α-carbon (path a in Scheme 2).[11,12] The silicon-directed cyclization can be successfully utilized for the stereoselective synthesis of disubstituted tetrahydrofurans. The intramolecular addition of a hydroxy group to vinylsilanes proceeds in a stereospecific *syn* mode. Thus, we next directed our efforts to the stereocontrolled introduction of a side chain into the 2-position of the tetrahydrofuran ring with α-alkylated vinylsilanes **1**. Unexpectedly, the acid-catalyzed cyclization of **1** (R = alkyl) exclusively formed tetrahydropyrans **2** without **3**. Similar to the Lewis acid promoted [3 + 2] cycloaddition of allylsilanes, the formation of **2** would proceed via 1,2-silyl migration of the initially formed β-silylcarbenium ion intermediate (path b). We herein report the scope and mechanistic aspects of this 1,2-silyl-migrative cyclization and its application to the stereoselective synthesis of multisubstituted tetrahydropyrans and tetrahydrofurans.[13,14]

SCHEME 2

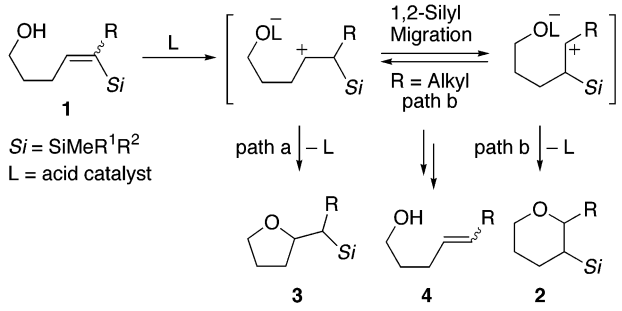
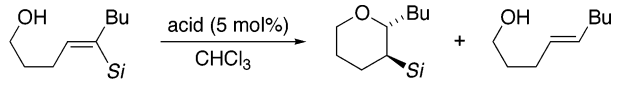


TABLE 1. Screening of Acid Catalysts Using (*Z*)-1a[a]



entry	catalyst	temp (°C)	time (h)	yield (%) *trans*-**2a**	(*E*)-**4a**[b]	**1a**[b]
1	$TiCl_4$	25	9.5	75	15	6
2	$TiCl_2(O\text{-}i\text{-}Pr)_2$	25	50	48	3	32
3	$TsOH{\cdot}H_2O$	60	24	30	61	0
4	HCl gas	25	24	67	10	14
5	AcCl	25	30 (4.5)[c]	67 (83)	5 (5)	25 (6)

[a] All reactions were performed with **1a** (0.50 mmol), an acid (0.025 mmol), and $CHCl_3$ (2.5 mL) unless otherwise noted. [b] Desilylated product and unreacted substrate were obtained as a mixture. Their yields were estimated by ^1H NMR analysis. The recovered substrate included its *E*-isomer as a minor component. [c] The values in parentheses are the results using 20 mol % AcCl.

Results and Discussion

Cyclization of Vinylsilanes 1 and 5. For the screening of acid catalysts, (*Z*)-**1a** was initially selected as a substrate (Table 1). Treatment of (*Z*)-**1a** with 5 mol % $TiCl_4$ in $CHCl_3$ at room temperature gave *trans*-2,3-disubstituted tetrahydropyran **2a** in 75% yield along with desilylated product (*E*)-**4a** (entry 1). The *cis*-isomer of **2a**

(8) [3 + 2] and [2 + 2] cycloadditions of allylsilanes to unsaturated bonds: (a) Knölker, H.-J.; Jones, P. G.; Pannek, J.-B. *Synlett* **1990**, 429. (b) Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868. (c) Danheiser, R. L.; Dixon, B. R.; Gleason, R. W. *J. Org. Chem.* **1992**, *57*, 6094. (d) Audran, G.; Monti, H.; Léandri, G.; Monti, J.-P. *Tetrahedron Lett.* **1993**, *34*, 3417. More recent reports: (e) Peng, Z.-H.; Woerpel K. A. *Org. Lett.* **2001**, *3*, 675. (f) Akiyama, T.; Sugano, M.; Kagoshima, H. *Tetrahedron Lett.* **2001**, *42*, 3889. (g) Panek, J. S.; Liu, P. *J. Am. Chem. Soc.* **2000**, *122*, 11090. (h) Peng, Z.-H.; Woerpel K. A. *Org. Lett.* **2000**, *2*, 1379. (i) Roberson, C. W.; Woerpel, K. A. *J. Org. Chem.* **1999**, *64*, 1434. (j) Isaka, M.; Williard, P. G.; Nakamura, E. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2115. (k) Knölker, H.-J.; Jones, P. G.; Wanzl, G. *Synlett* **1998**, 613. (l) Akiyama, T.; Hoshi, E.; Fujiyoshi, S. *J. Chem. Soc., Perkin Trans 1* **1998**, 2121. (m) Akiyama, T.; Yamanaka, M. *Tetrahedron Lett.* **1998**, *39*, 7885. (n) Groaning, M. D.; Brengel, G. P.; Meyers, A. I. *J. Org. Chem.* **1998**, *63*, 5517.

(9) Other types of nucleophilic addition to β-silylcarbenium ions generated from allylsilanes: (a) Sugimura, H. *Tetrahedron Lett.* **1990**, *31*, 5909. (b) Kiyooka, S.; Shiomi, Y.; Kira, H.; Kaneko, Y.; Tanimori, S. *J. Org. Chem.* **1994**, *59*, 1958. (c) Adiwidjaja, G.; Flörke, H.; Kirschning, A.; Schaumann, E. *Liebigs Ann.* **1995**, 501. (d) Akiyama, T.; Nakano, M.; Kanatani, J.; Ozaki, S. *Chem. Lett.* **1997**, 385. (e) Brocherieux-Lanoy, S.; Dhimane, H.; Poupon, J.-C.; Vanucci, C.; Lhommet, G. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2163. (f) Monti, H.; Rizzotto, D.; Léandri, G. *Tetrahedron* **1998**, *54*, 6725. (g) Akiyama, T.; Asayama, K.; Fujiyoshi, S. *J. Chem. Soc., Perkin Trans 1* **1998**, 3655. (h) Akiyama, T.; Ishida, Y. *Synlett* **1998**, 1150. **1999**, 160. (i) Akiyama, T.; Ishida, Y.; Kagoshima, H. *Tetrahedron Lett.* **1999**, *40*, 4219. (j) Sugita, Y.; Kimura, Y.; Yokoe, I. *Tetrahedron Lett.* **1999**, *40*, 5877. (k) Angle, S. R.; El-Said, N. A. *J. Am. Chem. Soc.* **1999**, *121*, 10211.

(10) (a) Brook, M. A.; Sebastian, T.; Jueschke, R.; Dallaire, C. *J. Org. Chem.* **1991**, *56*, 2273. (b) Brook, M. A.; Henry, C.; Jueschke, R.; Modi, P. *Synlett* **1993**, 97. (c) Yamazaki, S.; Tanaka, M.; Yamabe, S. *J. Org. Chem.* **1996**, *61*, 4046.

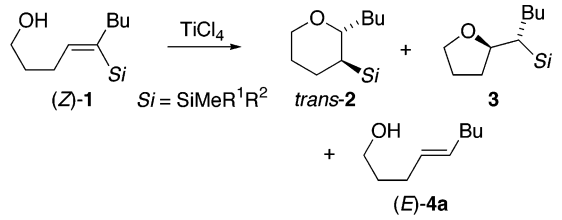
(11) (a) Miura, K.; Okajima, S.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. *J. Am. Chem. Soc.* **2000**, *122*, 11348. (b) Miura, K.; Okajima, S.; Hondo, T.; Hosomi, A. *Tetrahedron Lett.* **1995**, *36*, 1483. (c) Miura, K.; Hondo, T.; Okajima, S.; Hosomi, A. *Tetrahedron Lett.* **1996**, *37*, 487.

(12) Schaumann et al. also reported a similar type of cyclization in 1995. See ref 9c.

(13) For 1,2-silyl-migrative cycloadditions forming tetrahydrofurans, see: (a) Panek, J. S.; Beresis, R. *J. Org. Chem.* **1993**, *58*, 809. (b) Akiyama, T.; Ishikawa, K.; Ozaki, S. *Chem. Lett.* **1994**, 627. (c) Schinzer, D.; Panke, G. *J. Org. Chem.* **1996**, *61*, 4496. See also ref 8b,g,h.

(14) For preliminary papers on this work, see: (a) Miura, K.; Hondo, T.; Saito, H.; Ito, H.; Hosomi, A. *J. Org. Chem.* **1997**, *62*, 8292. (b) Miura, K.; Hondo, T.; Takahashi, T.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 2129.

TABLE 2. Effects of Silyl Group on Reactivity[a]

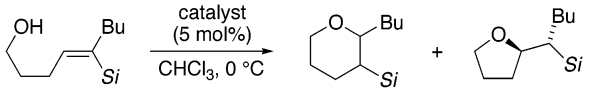


entry	vinylsilane **1** R[1]	R[2]		time (h)	yield (%) *trans*-**2**	**3**	(*E*)-**4a**[b]	**1**[b,c]
1	Ph	Me	(*Z*)-**1a**	9.5	75	0	15	6
2	Me	Me	(*Z*)-**1b**	7.5	66	0	26	0
3	Ph	Ph	(*Z*)-**1c**	24	58	0	13	25
4	*t*-Bu	Me	(*Z*)-**1d**	0.8	85[d]	5[e,f]	8	0
5	Bn	Me	(*Z*)-**1e**	1.5	78[d]	1[e,f]	17	4
6	*p*-MeC$_6$H$_4$	Me	(*Z*)-**1f**	9.5	57	0	20	12
7	*p*-MeOC$_6$H$_4$	Me	(*Z*)-**1g**	9.5	53	0	28	15
8	*p*-CF$_3$C$_6$H$_4$	Me	(*Z*)-**1h**	9.5	39	0	6	49

[a] All reactions were performed with a vinylsilane (0.50 mmol), $TiCl_4$ (0.025 mmol), and $CHCl_3$ (2.5 mL) at room temperature (method A). [b] Desilylated product and unreacted substrate were obtained as a mixture. Their yields were estimated by ^{1}H NMR analysis. [c] *Z*/*E* ratios of **1**: 83/17 (entry 1), 92/8 (entry 3), 61/39 (entry 5), >99/1 (entries 6−8). [d] The formation of *cis*-**2** was observed. The *trans*/*cis* ratios were 95/5 in both cases. [e] The cyclized products **2** and **3** were obtained as a mixture. The yields and isomeric ratio were determined by GC analysis. [f] (2*R**,1′*S**)-Isomer was formed predominantly.

was not detected by ^{1}H NMR (270 Hz) analysis. $TiCl_2$(O-*i*-Pr)$_2$ also promoted the cyclization with less catalytic activity (entry 2). The use of TsOH·H_2O at 60 °C, which was effective in the cyclization of α-unsubstituted (*Z*)-vinylsilanes **1** (R = H) (path a in Scheme 2),[11] markedly reduced the yield of *trans*-**2a**, and a considerable amount of (*E*)-**4a** was formed (entry 3). Acetic acid, $SnCl_4$, BF_3·OEt_2, Sc(OTf)$_3$, and Sn(OTf)$_2$ hardly induced the cyclization. HCl gas and AcCl as well as $TiCl_4$ were good catalysts for this cyclization (entries 4 and 5). An increased amount of AcCl (20 mol %) provided *trans*-**2a** in 83% yield. AcCl would serve as a source of HCl by the reaction with the hydroxy group of (*Z*)-**1a** or EtOH included in the solvent as a stabilizer (0.4−0.8% EtOH in $CHCl_3$), because 2,6-di-*tert*-butylpyridine (DTBP, 5 mol %), a proton scavenger,[15] prevented the AcCl-catalyzed cyclization. Similarly, in the $TiCl_4$-catalyzed system, there is a possibility that HCl generated from $TiCl_4$ is the actual catalyst. As shown in Table 1, $TiCl_4$ exhibited higher catalytic activity than HCl gas and AcCl; however, addition of DTBP (5 mol %) decelerated the $TiCl_4$-catalyzed cyclization of (*Z*)-**1a** although the yield of *trans*-**2a** was still good (5 mol % $TiCl_4$, 72 h, 80%). A part of $TiCl_4$ may work as a source of HCl.

The silyl group of (*Z*)-**1** strongly affected the cyclization efficiency and rate (Table 2). The $TiCl_4$-catalyzed reaction of vinylsilane (*Z*)-**1b** (Si = TMS) resulted in slightly lower yield of **2b** because (*Z*)-**1b** was more sensitive to protiodesilylation than (*Z*)-**1a** (entries 1 and 2). To suppress the desilylation, a more bulky silyl group such as SiMePh$_2$ and TBDMS was employed.[16] Contrary to our expectation, (*Z*)-**1c** (*Si* = SiMePh$_2$) suffered considerable desilylation and exhibited much lower reactivity than (*Z*)-**1a** (entry 3). On the other hand, the cyclization of (*Z*)-**1d** (*Si* = TBDMS) effected not only high yield of **2d** but also fast reaction rate (entry 4). A similar high reactivity was observed in the case with (*Z*)-**1e** (*Si* = SiMe$_2$Bn (BnDMS), entry 5). However, these substrates led to lower *trans*-selectivity of **2** (*trans*/*cis* = 95/5) in addition to the formation of tetrahydrofurans (2*R**,1′*S**)-**3**. As shown in eq 1, lowering the reaction temperature to 0 °C improved



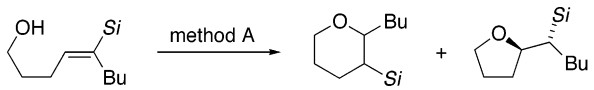
(1)

(*Z*)-**1d**	$TiCl_4$, 2.3 h	90% (*t*/*c* = 97/3)	3%
(*Z*)-**1d**	$TiCl_2$(O-*i*-Pr)$_2$, 24 h	93% (*t*/*c* = 98/2)	0%
(*Z*)-**1e**	$TiCl_2$(O-*i*-Pr)$_2$, 40 h	89% (*t*/*c* = 99/1)	3%

the yield and *trans*-selectivity of **2d** (90%, *trans*/*cis* = 97/3) with the inhibition of direct cyclization to **3d** and protiodesilylation to (*E*)-**4a**. The use of $TiCl_2$(O-*i*-Pr)$_2$ as catalyst completely suppressed the formation of **3d** to bring about a better yield of *trans*-**2d**. The $TiCl_2$(O-*i*-Pr)$_2$-catalyzed system at 0 °C was also effective in the stereoselective cyclization of (*Z*)-**1e**, although it could not suppress the formation of **3e**.

The electronic effect of substituent R[1] on the reactivity was investigated by the cyclization of (*Z*)-**1f**−**h** (Table 2). As a result, it turned out that electron-donating *p*-tolyl and *p*-anisyl groups accelerated the protiodesilylation to (*E*)-**4a** (entries 6 and 7), while the electron-withdrawing *p*-trifluoromethylphenyl group considerably diminished the reactivity of the C−C double bond to prevent the conversion of (*Z*)-**1h** (entry 8). The latter result implies that protonation of the sp^2 carbon α to the silyl group is the rate-determining step of the present cyclization (vide infra).

The change in the geometry of **1** resulted in a marked decrease in both the reactivity and stereoselectivity (eq 2). Under the standard reaction conditions (method A)



(2)

(*E*)-**1a**	100 h (54% conv.)	17% (*t*/*c* = 41/59)	-
(*E*)-**1d**	50 h	74% (*t*/*c* = 21/79)	8%
(*E*)-**1e**	26 h (78% conv.)	31% (*t*/*c* = 36/64)	-

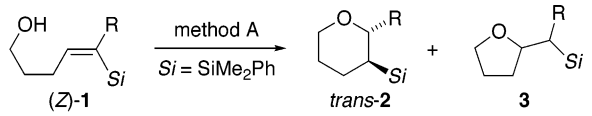
shown in Table 2, (*E*)-**1a** was converted into **2a** in only 17% yield with low *cis*-selectivity. Similarly, the reaction of (*E*)-**1e** gave a disappointing result. The cyclization of (*E*)-**1d** was much faster than that of (*E*)-**1a**, affording **2d** in a good yield with higher *cis*-selectivity. In this case, (2*R**,1′*R**)-**3d** was obtained as a byproduct in 8% yield. Thus, the results of Table 2 and eq 2 indicate that both the 1,2-silyl-migrative and direct cyclizations proceed in a stereospecific manner.

To examine the applicability in terms of the α-substituent R, the $TiCl_4$-catalyzed reactions of vinylsilanes

(15) Kostikov, R. R. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, S. Ed.; Wiley: Chichester, 1995; Vol. 3, p 1623.

(16) It is well-known that the use of a sterically demanding silyl group suppresses desilylation of β-silylcarbenium ion intermediates. Knölker, H.-J.; Foitzik, N.; Goesmann, H.; Graf, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1081.

TABLE 3. Effects of α-Substituent on Reactivity

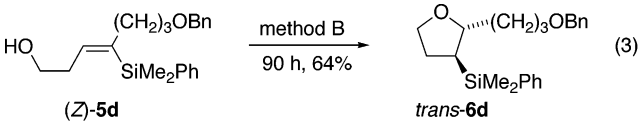


entry	vinylsilane 1 R		time (h)	yield (%) trans-2	3
1	Bu	(*Z*)-**1a**	9.5	75	0
2	Me	(*Z*)-**1i**	15	76	0
3	$(CH_2)_3OBn$	(*Z*)-**1j**	15	72	0
4	$(CH_2)_3OAc$	(*Z*)-**1k**	47	72	0
5	Ph	(*Z*)-**1l**	24	0[a]	0
6	Br	(*E*)-**1m**	24	0[b]	0
7	$SiMe_3$	(*Z*)-**1n**	13	0	67 (1/1)[c]

[a] Desilylated product **4l** was obtained in 29% yield. The substrate was recovered in 30% yield. [b] See the text. [c] Isomeric ratio of **3n**.

1i−**m** were carried out (Table 3). The present cyclization tolerated polar functionalities such as ether and ester groups (entries 3 and 4). Vinylsilane (*Z*)-**1l** (R = Ph) was not cyclized at all because of fast desilylation (entry 5). In the case where R is a bromine atom, the substrate (*E*)-**1m** was recovered quantitatively (entry 6). The insensitivity of (*E*)-**1m** is presumably a result of the inductive effect of the electron-negative bromine atom, which would lower electron density of the C−C double bond to prevent the initial protonation step of the present cyclization. Interestingly, the use of (*Z*)-**1n** (R = $SiMe_3$) gave only the direct cyclization product **3n** as a 1:1 diastereomeric mixture (entry 7).

Vinylsilanes **5**, whose methylene tether is shorter than that of **1** by one carbon, also underwent the acid-catalyzed 1,2-silyl-migrative cyclization to afford 2,3-disubstituted tetrahydrofurans **6** (Table 4). Treatment of (*Z*)-**5a** with 5 mol % $TiCl_4$ at room temperature for 49 h gave *trans*-**6a** in a moderate yield (entry 1). Thus, (*Z*)-**5a** was much less reactive than (*Z*)-**1a**. AcCl was not suitable for this cyclization (102 h, 37%). However, the use of TsOH·H_2O at 60 °C (method B) improved the yield of **6a** to some extent (entry 2). Similar to the case with (*Z*)-**1**, the introduction of TBDMS or BnDMS as a silyl group remarkably increased both the cyclization efficiency and rate (entries 3−6). Vinylsilane (*Z*)-**5d**, bearing an ether functionality, also could be converted into *trans*-**6d** in 64% yield, although it took prolonged reaction time (eq 3). In both catalytic systems, the cyclization of

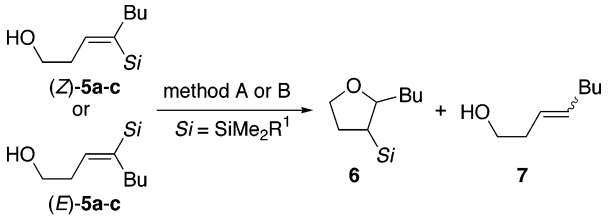


(3)

(*E*)-**5a** resulted in low efficiency, but it exhibited *cis*-selectivity higher than that of (*E*)-**1a** (entries 7 and 8). The TsOH-catalyzed cyclization of (*E*)-**5b**,**c** brought about much better yield and *cis*-selectivity (entries 10 and 12).

Mechanistic Aspect of Cyclization of Vinylsilanes 1 and 5. On the basis of the previous and present results,[11] a plausible mechanism for the *trans*-selective cyclization of (*Z*)-**1** and (*Z*)-**5** is shown in Scheme 3. The mechanism consists of the following five steps: (1) The attachment of a proton or a Lewis acid to the hydroxy

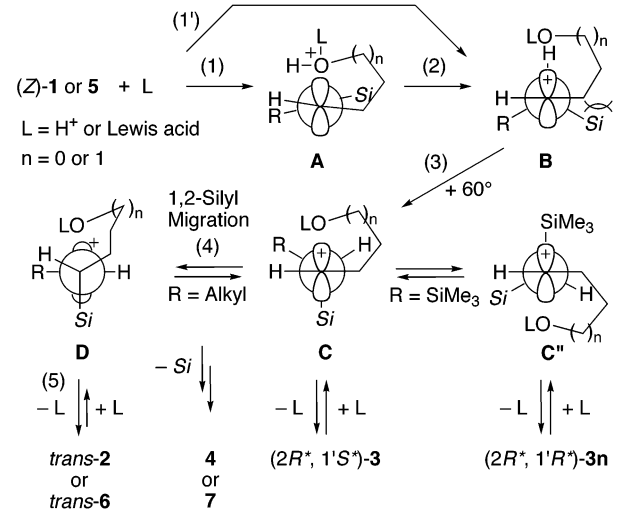
TABLE 4. Cyclization of (*Z*)- and (*E*)-Vinylsilanes 5[a]



entry	vinylsilane 5 R1	config		method[a]	time (h)	yield (%) 6 (t/c)[b]	7[c]	5[c,d]
1	Ph	Z	**5a**	A	49	46 (>99/1)	8	37
2	Ph	Z	**5a**	B	36	63 (>99/1)	16	16
3	*t*-Bu	Z	**5b**	A	4	89 (96/4)	0	6
4	*t*-Bu	Z	**5b**	B	14	95 (>99/1)	0	4
5	Bn	Z	**5c**	A	13	90 (99/1)	*e*	*e*
6	Bn	Z	**5c**	B	19	91 (99/1)	*e*	*e*
7	Ph	E	**5a**	A	50	15 (9/91)	11	66
8	Ph	E	**5a**	B	50	14 (21/79)	20	6
9	*t*-Bu	E	**5b**	A	98	27 (9/91)	9	45
10	*t*-Bu	E	**5b**	B	41	88 (4/96)	4	2
11	Bn	E	**5c**	A	22	33 (5/95)	9	52
12	Bn	E	**5c**	B	13	66 (2/98)	13	14

[a] Method B: TsOH·H_2O (5 mol %) was used as catalyst at 60 °C. Other conditions are similar to those in method A. [b] The isomeric ratio was determined by GC analysis. [c] Byproduct **7** and substrate **5** were obtained as a mixture. The yields were estimated by ^1H NMR analysis. The recovered **5** included another isomer as a minor component. [d] Desilylation of (*Z*)-**5** and (*E*)-**5** gave (*E*)-**7** and (*Z*)-**7**, respectively. [e] Not determined.

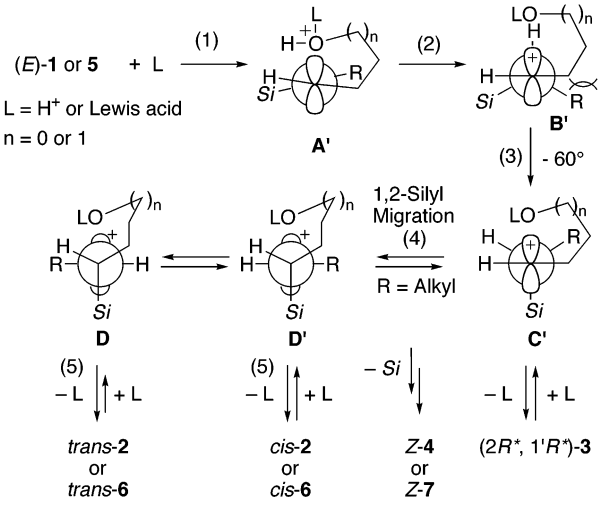
SCHEME 3



group of (*Z*)-**1** or (*Z*)-**5** forms oxonium ion **A**. (2) The proton on the oxygen atom adds to the α-carbon. (3) The resultant *β*-silyl carbenium ion **B**, which may be a transition state, turns to its conformer **C** stabilized by *σ*−*π* conjugation at the least motion.[17] (4) **C** is converted into another *β*-silyl carbenium ion **D** by 1,2-silyl migration.[18] (5) Intramolecular attack of the oxygen from the opposite side to the silyl group gives *trans*-**2** or *trans*-**6** and regenerates the proton or the Lewis acid. The direct

(17) As mentioned by Koenig and Weber, simultaneously with protonation to the double bond, rotation would occur about the developing carbon−carbon single bond in the direction to permit the silyl group to continuously stabilize the incipient *β*-silylcarbenium ion **B** by hyperconjugation of the Si−C bond. Koenig, K. E.; Weber, W. P. *J. Am. Chem. Soc.* **1973**, *95*, 3416.

SCHEME 4



cyclization of **C** (n = 1) without 1,2-silyl migration and the desilylation of **C** and **D** give (*2R**,1′*S**)-**3** and (*E*)-**4** or (*E*)-**7**, respectively. The route to *trans*-**2** may involve initial formation of (*2R**,1′*S**)-**3** followed by acid-catalyzed isomerization via **C** and **D** (vide infra).

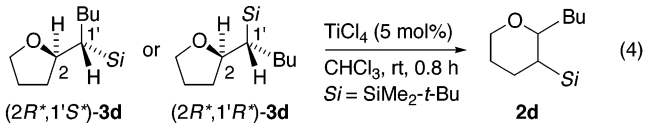
Intermolecular direct protonation of the substrate (step 1′) also is a possible process. However, the reaction path via **A** provides a reasonable explanation for the stereochemical outcomes in the stereoselective synthesis of trisubstituted tetrahydropyrans and tetrahydrofurans (vide infra). In our previous study on the cyclization of α-unsubstituted vinylsilanes **1** (R = H), we have proposed the intramolecular protonation via **A** to rationalize the observed asymmetric induction.[11]

The presence of an alkyl group as the α-substituent R is essential to the present 1,2-silyl-migrative cyclization. This fact suggests that the stabilization of carbenium ion **D** by the alkyl group induces the 1,2-silyl migration (step 4) as mentioned by Danheiser et al.[19] In the cyclization of **1n**, the lower stabilizing ability of the TMS group to α-carbenium ions would inhibit the 1,2-silyl migration of **C**.[2] The nonstereoselective formation of **3n** implies a rapid equilibrium between **C** (R = $SiMe_3$) and **C″**.

The *cis*-selective cyclization of (*E*)-**1** and (*E*)-**5** can be rationalized by a similar mechanism (Scheme 4), in which intramolecular protonation of oxonium ion **A′** forms β-silyl carbenium ion intermediate **C′** via **B′** and then **C′** undergoes 1,2-silyl migration and intramolecular addition of the oxygen nucleophile to give *cis*-**2** or *cis*-**6**. As shown above, the stereoselectivity with (*E*)-vinylsilanes is lower than that with the corresponding (*Z*)-isomers. This result may be due to the fast rotation of β-silylcarbenium ion **D′** to **D** assisted by the steric interaction between R and the methylene tether.

The cyclization rate of vinylsilanes **1** and **5** (R = alkyl) was effectively enhanced by the (*Z*)-geometry of the C−C double bond and an electron-donative silyl group such as TBDMS. Similar rate-accelerating effects have been observed in the cyclization of α-unsubstituted vinylsilanes **1** (R = H) to tetrahydrofurans **3**.[11] These observations can be properly rationalized by the rate-determining protonation of **A** (**A′**) to **C** (**C′**). The high reactivity of (*Z*)-isomers probably originates from the steric repulsion between the methylene tether and the silyl group in **A** and **B**, which would promote the protonation process from **A** to **C**. In contrast, the torsional interaction between the methylene tether and R would decelerate the process from **A′** to **C′**, resulting in the low cyclization rate of (*E*)-vinylsilanes. The rate-acceleration by a TBDMS group is attributable to its relatively electron-donative character,[20] which would facilitate the protonation process by enhancing the HOMO level of the C−C double bond.

Two possibilities can be considered for the origin of the preferred formation of **2** to **3**. One is the isomerization of **3** to **2** (thermodynamic control), and the other is that the cyclization of **D** or **D′** is faster than that of **C** or **C′** (kinetic control). To ascertain the former possibility, (*2R**, 1′*S**)-**3d** and its diastereomer were prepared from 4-pentyn-1-ol (see Supporting Information) and subjected to a catalytic amount of $TiCl_4$. Indeed, their isomerization to **2d** rapidly proceeded with inverse stereoselectivity (eq 4).[21] The stereospecific conversion agrees well with the



91% (*t*/*c* = 95/5) from (*2R**,1′*S**)-**3d**
85% (*t*/*c* = 2/98) from (*2R**,1′*R**)-**3d**

mechanism shown in Schemes 3 and 4. This result discloses that **2d** is a thermodynamically favored product. In addition, MM2 calculation of the steric energy indicates that *trans*-**2d** is more stable than (*2R**,1′*S**)-**3d** by 3.5 kcal/mol in their optimized structures.[22]

To examine which product (**2** or **3**) is kinetically favored, the $TiCl_4$- or $TiCl_2(O\text{-}i\text{-}Pr)_2$-catalyzed cyclization of (*Z*)-**1d** was carried out at 0 °C. As a result, the major product was *trans*-**2d** even at low conversion. However, this observation does not necessarily prove that *trans*-**2d** is kinetically favored because of the fast isomerization of (*2R**,1′*S**)-**3d** to *trans*-**2d**. Electrophilic heteroatom cyclization of 5-alkyl-4-penten-1-ols, which appears to proceed via a transition state similar to that proposed in the present cyclization, usually provides tetrahydrofurans (5-exo products) rather than tetrahydropyrans (6-endo products).[23] This fact implies that tetrahydrofurans **3** are kinetic products. As described below, we found an example that a tetrahydrofuran product was formed

(18) There is a long-standing dispute on the structure of β-silylcarbenium ions, which can take a hyperconjugatively stabilized open form or a bridged form. Although the open forms **C** and **D** are employed in Scheme 3, they can be displaced to one bridged form without any problems. (a) Lambert, J. B.; Zhao, Y. *J. Am. Chem. Soc.* **1996**, *118*, 7867. (b) Ibrahim, M. R.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1989**, *111*, 819. See also ref 2.

(19) Danheiser, R. L.; Takahashi. T.; Bertók, B.; Dixon, B. R. *Tetrahedron Lett.* **1993**, *34*, 3845.

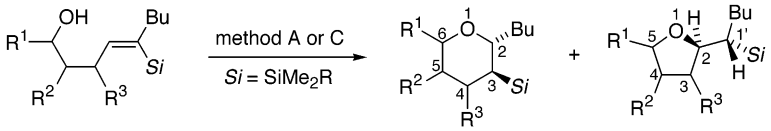
(20) (a) Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938. (b) Brengel, G. P.; Meyers, A. I. *J. Org. Chem.* **1996**, *61*, 3230.

(21) Ring contraction and enlargement via 1,2-silyl migration: (a) Hudrlik, P. F.; Hudrlik, A. M.; Nagendrappa, G.; Yimenu, T.; Zellers, E. T.; Chin, E. *J. Am. Chem. Soc.* **1980**, *102*, 6896; correction *J. Am. Chem. Soc.* **1982**, *104*, 1157. (b) Tanino, K.; Yoshitani, N.; Moriyama, F.; Kuwajima, I. *J. Org. Chem.* **1997**, *62*, 4206.

(22) The strain energy of tetrahydrofuran is higher than that of tetrahydropyran by 5.4 kcal/mol and lower than that of oxetane by 19.8 kcal/mol. Isaacs, N. S. *Physical Organic Chemistry*; Wiley: New York, 1987.

(23) Harding, K. E.; Tiner, T. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 4, p 363.

TABLE 5. Cyclization of (*Z*)-Vinylsilanes 8



8 **9** **10**

	(*Z*)-vinylsilane **8**							yield (%)	
entry	R	R^1	R^2	R^3		method[a]	time (h)	**9** (*t*/*c*)[b,c]	**10** (*t*/*c*)[b,d]
1	Ph	Ph	H	H	**8a**	A	28	59 (<1/99)	0
2	*t*-Bu	Ph	H	H	**8b**	A	2	91 (29/71)	0
3	Bn	Ph	H	H	**8c**	A	2	78 (9/91)	0
4	Ph	Me	H	H	**8d**	A	24	71 (16/84)	0
5[e]	Ph	Me	H	H	**8d**	C[f]	24	52 (3/97)	0
6[e]	Ph	*i*-Pr	H	H	**8e**	A	11	76 (7/93)	0
7	Ph	H	Ph	H	**8f**	A	24	70 (93/7)	0
8	Bn	H	Ph	H	**8g**	A	2	74 (85/15)[g]	0
9	Bn	H	Ph	H	**8g**	C	7.5	19 (>99/1)[g]	73 (19/81)[g]
10	Ph	H	Me	H	**8h**	A	9	66 (88/12)	0
11	Ph	H	Me	H	**8h**	C	27	90 (89/11)	0
12	Ph	H	*i*-Pr	H	**8i**	A	3	76 (96/4)	3 (<1/99)
13	Ph	H	*i*-Pr	H	**8i**	C	2.5	22 (>99/1)	72 (8/92)
14[e]	Ph	H	*i*-Pr	H	**8i**	C	0.5	2 (>99/1)	41 (6/94)
15[e]	Ph	H	H	Ph	**8j**	A	34	16 (<1/99)	12 (>99/1)
16[e]	Bn	H	H	Ph	**8k**	A	23	33 (<1/99)[g]	18 (>99/1)[g,h]
17[e]	Bn	H	H	Ph	**8k**	C	72	2 (<1/99)[g]	14 (>99/1)[g,h]
18	Ph	H	H	Pen[i]	**8l**	A	96	18 (<1/99)	42 (>99/1)
19	Ph	H	H	Pen[i]	**8l**	C[f]	76	2 (<1/99)	68 (>99/1)

[a] Method C: AcCl was used as catalyst. Other conditions were identical with those in method A. [b] The isomeric ratio was determined by 270 MHz ^{1}H NMR analysis. The ratios >99/1 and <1/99 mean that no isomer is detected by ^{1}H NMR analysis. In entries 9, 12−15, and 17−19, **9** and **10** were obtained as a mixture. Their yields were estimated by ^{1}H NMR analysis. [c] The ratio is concerned with the relative configuration between the butyl and R^1 (entries 1−6), R^2 (entries 7−14), or R^3 groups (entries 15−19). [d] The ratio is concerned with the relative configuration between the 1-silylpentyl and R^2 (entries 9 and 12−14) or R^3 groups (entries 15−19). [e] Recovery of the substrate (%): 20 (entry 5), 10 (entry 6), 55 (entry 14), 47 (entry 15), 17 (entry 16), 83 (entry 17). The recovered substrate included the *E*-isomer as a minor component. [f] With 20 mol % AcCl. [g] The ratio was determined by GC analysis. [h] (2*R**,3*S**,1′*S**)-**10k**/(2*R**,3*S**,1′*R**)-**10k** = 93/7 (entry 16) and 97/3 (entry 17). [i] Pen = pentyl.

predominantly and gradually isomerized to the corresponding tetrahydropyran by the action of an acid catalyst.

In the cyclization of **5**, oxetane products were not formed at all. This observation is attributable to their intrinsic angle strain, which would retard the cyclization of β-silylcarbenium ion intermediates **C** (**C′**) ($n = 0$) to oxetanes or strongly accelerate the isomerization of oxetanes to tetrahydrofurans **6**.[24]

Stereoselective Synthesis of Highly Substituted Tetrahydropyrans and Tetrahydrofurans. Recently, much attention has been paid to the stereoselective synthesis of substituted oxygen-containing heterocycles since tetrahydropyran and tetrahydrofuran units are frequently found in polyether antibiotics and other biologically active natural products.[25] Therefore, we attempted to apply the present 1,2-silyl-migrative cyclization to the stereoselective synthesis of trisubstituted tetrahydropyrans and tetrahydrofurans using (*Z*)-5-silyl-4-nonen-1-ols and (*Z*)-4-silyl-3-octen-1-ols with a substituent on the methylene tether (**8** and **11**).

The cyclization of **8a**−**e** with a catalytic amount of $TiCl_4$ or AcCl gave *r*-2,*t*-3,*c*-6-trisubstituted tetrahydropyrans **9a**−**e** as major diastereomers along with their *r*-2,*t*-3,*t*-6-isomers (entries 1−6 in Table 5). Vinylsilane **8a** exhibited high 2,6-*cis*-selectivity, although the yield of **9a** was not so good as a result of protiodesilylation (entry 1). As expected, the introduction of a TBDMS or BnDMS group raised the cyclization rate and the yield of **9**, but the stereoselectivity dropped (entries 2 and 3). The use of AcCl as catalyst was effective in improving the 2,6-*cis*-selectivity with **8d** (entry 5).

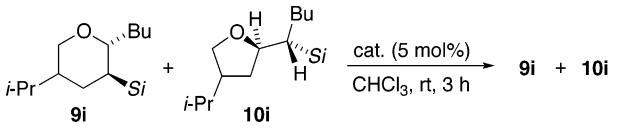
The $TiCl_4$-catalyzed reaction of **8f**−**i** formed 2,3,5-trisubstituted tetrahydropyrans **9f**−**i** with good to high 2,5-*trans*-selectivity (entries 7, 8, 10, and 12). Vinylsilane **8i**, bearing an isopropyl group as R^2, showed reactivity much higher than that of **8f** and **8h** (entry 12). The bulky substituent would accelerate the rate-determining protonation by raising the energy of the ground state relative to the transition state as in the *gem*-dimethyl effect.[26] The cyclization of **8i** also gave tetrahydrofuran **10i** as a byproduct. The AcCl-catalyzed system prevented protiodesilylation of **8h** to achieve a high yield of **9h** (entry 11). Interestingly, the AcCl-catalyzed reactions of **8g**,**i** gave **10g,i** in preference to **9g,i** (entries 9 and 13). The ratio of **10i** to **9i** at 45% conversion of **8i** (0.5 h) was higher than that at the complete conversion (entry 14). This fact indicates that **10i** is isomerized to **9i** under the reaction conditions. To confirm the isomerization, a mixture of **10i** (major component) and **9i** was treated with

(24) Akiyama et al. have reported that, in the cycloaddition of allylsilanes to ketones, the formation of oxetanes is a kinetically favored path. Akiyama, T.; Kirino, M. *Chem. Lett.* **1995**, 723.

(25) Reviews: (a) Boivin T. L. B. *Tetrahedron* **1987**, *43*, 3309. (b) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321. (c) Kotsuki, H. *Synlett* **1992**, 97. (d) Harmange, J. C.; Figadére, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711. (e) Koert, U. *Synthesis* **1995**, 115.

(26) (a) Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701. (b) Beckwith, A. L. J.; Zimmerman, J. *J. Org. Chem.* **1991**, *56*, 5791.

TABLE 6. Acid-Catalyzed Isomerization of Tetrahydrofuran 10i



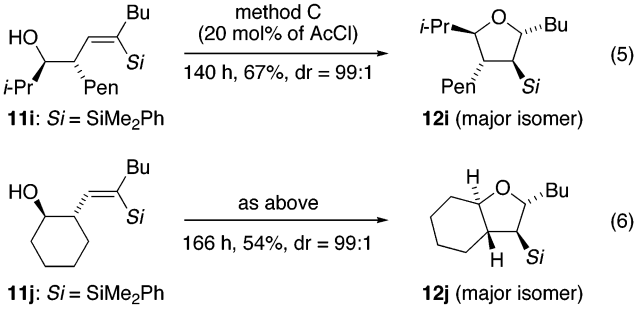
	2,5-*t*-**9i**/2,5-*c*-**9i**/*t*-**10i**/*c*-**10i**		
catalyst	substrate[a]	product[a]	yield (%)
AcCl	20/0/4/76	22/0/5/73	96
AcCl/1-hexanol (1:20)	9/0/6/85	37/0/5/58	99
$TiCl_4$	24/0/6/70	93/7/<1/<1	84

[a] Determined by ^1H NMR analysis.

AcCl (Table 6). As a result, AcCl itself hardly induced the isomerization; however, the combination of AcCl and 1-hexanol effected the partial conversion of **10i** into **9i**. This observation suggests that HCl generated from AcCl catalyzes not only the cyclization of **8i** but also the isomerization of **10i**. The slow isomerization with AcCl and 1-hexanol is consistent with the selective formation of **10i** in entry 13. As predicted from the result in entry 12, $TiCl_4$ smoothly isomerized **10i** to **9i** (the last line of Table 6). Thus, it is apparent that **9i** and **10i** are thermodynamic and kinetic products, respectively, in the AcCl-catalyzed system.

Vinylsilanes **8j**−**l**, bearing a substituent at the allylic position, were much less reactive toward the acid-catalyzed cyclization than other vinylsilanes (entries 15−19). The cyclization afforded a mixture of **9** and **10** in low to moderate yield, and each cyclized product was a single diastereomer with the exception of **10k**. Independently of the catalyst used, **8l** underwent the direct cyclization leading to **10l** selectively (entries 18 and 19).

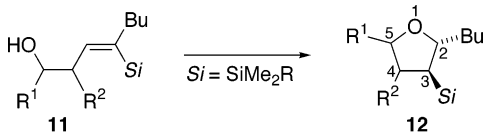
The TsOH-catalyzed cyclization of (*Z*)-vinylsilanes **11a**−**d** gave tetrahydrofurans **12a**−**d** in good to high yields (entries 2, 4, 5, and 7 in Table 7). Unfortunately, the diastereoselectivity with respect to the relative configuration between the 2- and 5-positions was rather low. Other acid catalysts, $TiCl_4$ and AcCl, were not so effective in improving the selectivity (entries 1, 3, 6, and 8). In contrast, the cyclization of (*Z*)-vinylsilanes **11e**−**h**, substituted at the allylic position, achieved high levels of 2,4-*cis*-selectivity, although the substrates showed low reactivity (entries 9−15). As shown in eqs 5 and 6, the present



cyclization was also applicable to the stereoselective synthesis of tetrasubstituted tetrahydrofurans.

Origin of Asymmetric Induction. In the $TiCl_4$-catalyzed reaction of (*Z*)-**1a** (entry 1 in Table 2), the yield and *Z*/*E* ratio of the recovered **1a** (6%, *Z*/*E* = 83/17) clearly show that the isomerization of (*Z*)-**1a** to (*E*)-**1a** is much slower than the 1,2-silyl-migrative cyclization to *trans*-**2a** and the protiodesilylation to (*E*)-**4a**. We have also reported a similar observation in the cyclization of α-unsubstituted (*Z*)-vinylsilane **1** (R = H, Si = $SiMe_2$-Ph).[11] Judging from the slow isomerization and the strong *β*-effect of silyl groups, the reversion of carbenium ion intermediates **C** and **D** to **A** hardly occurs as a result of the fast ring closure and desilylation. Accordingly, in the cyclization of (*Z*)-vinylsilanes bearing a chiral center (**8** and **11**), the relative configurations of the newly formed chiral centers should be determined in the protonation step. In other words, the asymmetric induction observed with **8** and **11** would originate from diastereoface-selective protonation. It is very difficult to explain the face-selective protonation with an intermolecular protonation process such as step 1′ in Scheme 3, while intramolecular protonation via an oxonium ion intermediate such as **A** easily rationalizes the origin of the present asymmetric induction. For instance, in the cyclization of **8f**−**i**, the intramolecular protonation would proceed via $\mathbf{E}_{ch-eq}$, a chairlike conformation with a pseudoequatorial substituent, because another chairlike conformation $\mathbf{E}_{ch-ax}$ is unfavored by the intrinsic nonbonding interactions arising from the pseudoaxial substituent (Scheme 5). Then *β*-silylcarbenium ions **F** and **G** formed from $\mathbf{E}_{ch-eq}$ are cyclized to *cis*-**10** and 2,5-*t*-**9**, respectively. Similarly, the stereochemical outcomes with **8a**−**e** and **8j**−**l** are attributable to the intramolecular protonation via chairlike conformations $\mathbf{H}_{ch-eq}$ and $\mathbf{I}_{ch-eq}$ (Scheme 6). The high diastereoselectivity with **8j**−**l** is probably because the allylic 1,3-strain between the substituent R^3 and the silyl group strictly forbids the oxonium ion intermediate to take conformation $\mathbf{I}_{ch-ax}$.[27] The origin of the low reactivity of **8j**−**l** is not clear.

TABLE 7. Cyclization of (*Z*)-Vinylsilanes 11

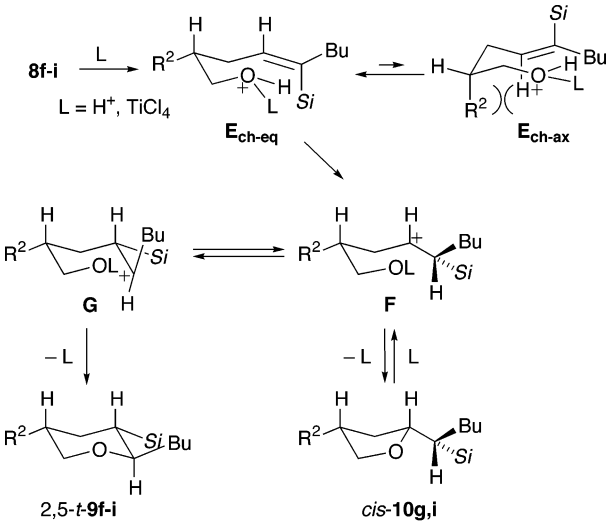


	vinylsilane **11**						yield (%)	
entry	R	R^1	R^2		method	time (h)	**12** (dr)[a]	**11**[b]
1	Ph	Ph	H	**11a**	A	48	37 (53/47)	55
2	Ph	Ph	H	**11a**	B	55	77 (51/49)	2
3	Bn	Ph	H	**11b**	A	6.5	78 (58/42)	13
4	Bn	Ph	H	**11b**	B	6.5	91 (55/45)	4
5	Ph	Hex	H	**11c**	B	58	87 (68/32)	4
6	Ph	*i*-Pr	H	**11d**	A	35	46 (74/26)	18
7	Ph	*i*-Pr	H	**11d**	B	22	93 (69/31)	0
8	Ph	*i*-Pr	H	**11d**	C	168	25 (77/23)	75
9	Ph	H	Ph	**11e**	A[c]	82	61 (4/96)	20
10	Ph	H	Ph	**11e**	B	124	68 (<1/99)	9
11	Bn	H	Ph	**11f**	A[c]	21	62 (<1/99)	0
12	Bn	H	Ph	**11f**	B	76	84 (<1/99)	5
13	Ph	H	Pen	**11g**	A[c]	38	65 (1/99)	8
14	Ph	H	Pen	**11g**	B	115	55 (6/94)	11
15	Ph	H	*c*-Hex	**11h**	B	72	34 (5/95)	16

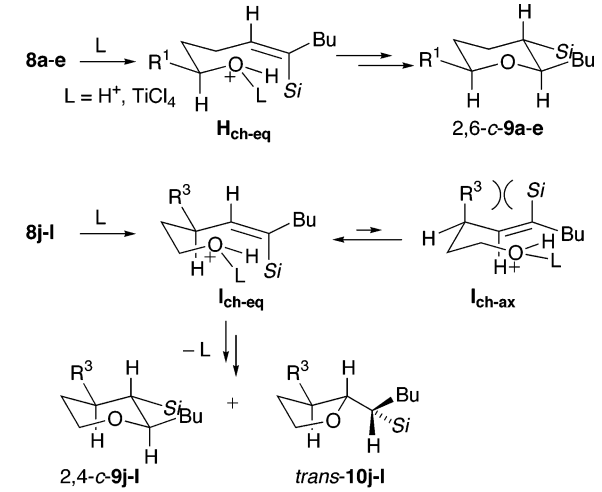
[a] The isomeric ratio was determined by GC analysis. The relative configurations of **12a**−**d** were not determined. The major isomers of **12e**−**h** were 2,4-*cis*. [b] Including *E*-isomer as a minor component. [c] With 20 mol % $TiCl_4$.

(27) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.

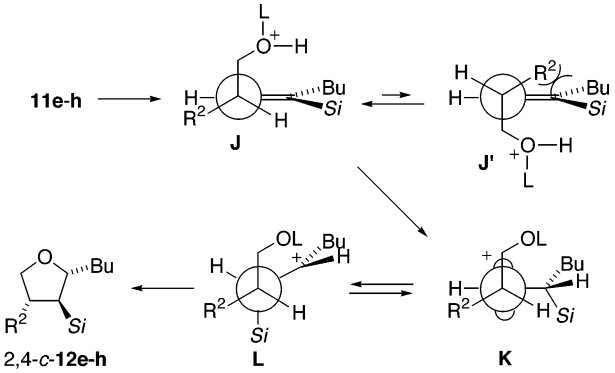
SCHEME 5



SCHEME 6



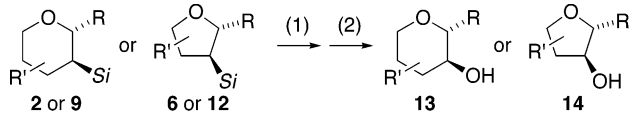
SCHEME 7



However, the low reactivity is likely to arise from the nonbonding interaction between R^3 and the silyl group in the transition state of intramolecular protonation. The repulsive interaction may also restrain the 1,2-silyl migration leading to 2,4-*c*-**9j**−**l**.

The 2,4-*cis*-selectivity with **11e**−**h** is explainable by intramolecular protonation via **J**, a conformer of the oxonium ion intermediate (Scheme 7). The protonation forms *β*-silylcarbenium ion **K**, which turns to 2,4-*c*-**12e**−**h** via **L**. Another conformer **J′** is energetically unfavorable as a result of the 1,3-allylic strain between R^2 and the silyl group.[27]

TABLE 8. Conversion of Silyl Group to Hydroxy Group[a]



entry	substrate	product	yield (%)
1	*trans*-**2a**	**13a**	88
2[b]	*trans*-**2e**	**13a**	82
3	*trans*-**2j**	**13b**	84
4	**9d** (2,6-*c*/*t* = 84/16)	**13c**	57 (2,6-*c*) + 7 (2,6-*t*)
5	2,5-*t*-**9f**	**13d**	86
6	**9i** (2,5-*t*/*c* = 96/4)	**13e**	53 (2,5-*t*/*c* = >95/5)
7	*trans*-**6a**	**14a**	89
8[b]	*trans*-**6c**	**14a**	87
9	2,4-*c*-**12g**	**14b**	72
10	2,4-*c*-**12j**	**14c**	93

[a] Reagents and conditions: (1) *t*-BuOK (1.2 equiv), DMSO, rt, 7 h; (2) H_2O_2 (10 equiv), TBAF (3.6 equiv), $KHCO_3$ (2 equiv), MeOH, THF, 40 °C, 24 h. See ref 29b. [b] The oxidation was performed without pretreatment using *t*-BuOK and DMSO.

Oxidative Cleavage of Silicon−**Carbon Bond.** Some silyl groups are known to be valuable as latent hydroxy groups for the stereocontrolled synthesis of alcohols.[28,29] To enhance the synthetic utility of the present cyclization, we examined oxidative cleavage of the C−Si bond in the cyclized products (Table 8). According to the reported two-step procedure,[29b] a variety of cyclic ethers having a dimethylphenylsilyl group could be converted to the corresponding alcohols in moderate to high yields. On the other hand, oxidative removal of a BnDMS group could be performed in one step (entries 2 and 8). Thus, a BnDMS group not only effectively accelerates the 1,2-silyl-migrative cyclization but also works as an efficient hydroxy surrogate.[14b]

Conclusion

We have found that the acid-catalyzed reaction of α-alkylated (*Z*)-vinylsilanes **1** and **5** gives *trans*-2-alkyl-3-silyl-disubstituted tetrahydropyrans **2** and tetrahydrofurans **6**, respectively, by intramolecular addition of the hydroxy group. This observation stands in sharp contrast to our previous observation that α-unsubstituted vinylsilanes **1** (R = H) are cyclized to tetrahydrofurans **3**.[11] The present cyclization is a novel type of 1,2-silyl migration reaction via *β*-silylcarbenium ion intermediates; most of the known 1,2-silyl migration reactions require more than an equimolar amount of an acid promoter and are usually utilized for the construction of five-membered carbocycles and heterocycles.[30] The 1,2-silyl-migrative cyclization is applicable to the stereoselective synthesis of highly substituted tetrahydropyrans and tetrahydro-

(28) Reviews: (a) Tamao K. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; JAI Press Inc.: Greenwich, 1996; Vol. 3, p 1. (b) Jones G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599. (c) Colvin, E. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 7, p 641.

(29) (a) Tamao, K.; Ishida, N. *J. Organomet. Chem.* **1984**, *269*, C37. (b) Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Andersson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487.

furans. The stereochemical outcomes can be well rationalized by the diastereoface-selective intramolecular protonation of oxonium ion intermediates. The cyclized products having a dimethylphenylsilyl or BnDMS group are readily accessible to the corresponding alcohols by oxidative removal of the silyl group. In conclusion, the present cyclization, a novel type of 1,2-silyl-migrative cyclization, provides a powerful method for the stereocontrolled synthesis of various tetrahydropyran and tetrahydrofuran derivatives.

Experimental Section

General Method. Unless otherwise noted, all reactions and distillations of solvents were carried out under N_2. Solvents were dried by distillation from sodium/benzophenone ketyl (THF, Et_2O), $CaCl_2-NaHCO_3$ ($CHCl_3$ containing 0.4−0.8% of ethanol), and CaH_2 (CH_2Cl_2). AcCl was distilled from *N*,*N*-dimethylaniline. $TiCl_4$, $BF_3{\cdot}OEt_2$, and $SnCl_4$ were simply distilled and stored as a CH_2Cl_2 solution (1.0 M). Boiling points indicated by air-bath temperature (bath temp) were determined with Kugelrohr distillation apparatus. ^1H and ^{13}C NMR were recorded in $CDCl_3$ at 270 and 67.7 MHz, respectively. The chemical shifts (δ) are reported with reference at 0.00 ppm (Me_4Si) or 7.26 ppm ($CHCl_3$) for the proton and at 77.00 ppm (centered on the signal of $CDCl_3$) for the carbon. The number of protons on each carbon atom was definitely determined by DEPT experiments.

Acid-Catalyzed Cyclization of Vinylsilanes (Typical Procedure). Method A. $TiCl_4$ (1.0 M in CH_2Cl_2, 25 μL, 0.025 mmol) was added to a solution of (*Z*)-**1a** (138 mg, 0.500 mmol) in $CHCl_3$ (2.5 mL) at room temperature. After being stirred for 9.5 h, the mixture was poured into saturated aqueous $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was dried over Na_2SO_4 and evaporated. The crude product was chromatographed on silica gel (hexane−AcOEt, 10:1) to give *trans*-2-butyl-3-dimethylphenylsilyltetrahydropyran (*trans*-**2a**, 103 mg, 75%) and a mixture of (*E*)-4-nonen-1-ol (**4**, 15%)[31] and **1a** (6%, *Z*/*E* = 83/17). *trans*-**2a**: bp 140 °C (0.30 Torr, bath temp); IR (neat) 2950, 1458, 1428, 1377, 1249, 1104, 731, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.28 (s, 3H), 0.31 (s, 3H), 0.78 (t, *J* = 6.9 Hz, 3H), 1.03−1.59 (m, 10H), 1.70−1.79 (m, 1H), 3.20 (ddd, *J* = 10.6, 7.9, 2.5 Hz, 1H), 3.36 (td, *J* = 10.9, 3.6 Hz, 1H), 3.92−4.00 (m, 1H), 7.32−7.38 (m, 3H), 7.44−7.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −3.66 (CH_3), −3.29 (CH_3), 13.98 (CH_3), 22.57 (CH_2), 25.93 (CH_2), 27.41 (CH_2 × 2), 30.05 (CH), 36.07 (CH_2), 68.38 (CH_2), 79.70 (CH), 127.71 (CH × 2), 128.84 (CH), 133.75 (CH × 2), 138.62 (C); MS *m*/*z* (relative intensity) 276 (M^+, 0.6), 135 (100). Anal. Calcd for $C_{17}H_{28}OSi$: C, 73.85; H, 10.21. Found: C, 73.63; H, 10.11. **Method B.** $TsOH{\cdot}H_2O$ (4.8 mg, 0.025 mmol) was charged to a reaction flask, and the flask was filled with N_2. $CHCl_3$ (2.5 mL) and (*Z*)-**5a** (132 mg, 0.501 mmol) were introduced to the flask, and then the mixture was heated to 60 °C. After being stirred for 10 h, the resultant solution was subjected to the same workup as in method A. The crude product was chromatographed on silica gel (hexane−AcOEt, 10:1) to give *trans*-2-butyl-3-dimethylphenylsilyltetrahydrofuran (*trans*-**6a**, 83 mg, 63%) and a mixture of (*E*)-3-octen-1-ol (**7**, 16%)[32] and (*Z*)-**5a** (16%). *trans*-**6a**: bp 80 °C (0.20 Torr, bath temp); IR (neat) 2955, 1426, 1249, 1111, 830, 733, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.32 (s, 3H), 0.33 (s, 3H), 0.83 (t, *J* = 7.1 Hz, 3H), 1.13−1.43 (m, 7H), 1.74 (ddt, *J* = 11.9, 10.6, 7.9 Hz, 1H), 1.93−2.06 (m, 1H), 3.64−3.75 (m, 3H), 7.30−7.40 (m, 3H), 7.47−7.52 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −4.26 (CH_3), −4.18 (CH_3), 13.98 (CH_3), 22.70 (CH_2), 28.72 (CH_2), 29.74 (CH_2), 31.61 (CH), 36.05 (CH_2), 67.32 (CH_2), 81.62 (CH), 127.82 (CH × 2), 129.15 (CH), 133.78 (CH × 2), 137.75 (C); MS *m*/*z* (rel intensity) 205 ($M^+ - C_4H_9$, 48), 135 (100). Anal. Calcd for $C_{16}H_{26}OSi$: C, 73.22; H, 9.98. Found: C, 73.01; H, 10.02. **Method C.** AcCl was used as catalyst, and other operations are identical with those of method A.

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Supporting Information Available: Experimental procedures for the synthesis of vinylsilanes and authentic samples (**3d**, **10i**, and **10l**), acid-catalyzed isomerization of 2-(silylmethyl)tetrahydrofurans, and oxidative cleavage of silicon−carbon bond; spectral data for all substrates, their synthetic intermediates, and products; stereochemical assignment of the cyclized products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026006J

(30) For the formation of six-membered rings via 1,2-silyl migration, see: (a) Danheiser, R. L.; Fink, D. M. *Tetrahedron Lett.* **1985**, *26*, 2513. (b) Angle, S. R.; Boyce, J. P. *Tetrahedron Lett.* **1994**, *35*, 6461. See also ref 21.

(31) Matsumoto, K.; Aoki, Y.; Oshima, K.; Utimoto, K. *Tetrahedron* **1993**, *49*, 8487.

(32) Vasil'ev, A. A.; Cherkaev, G. V.; Nikitina, M. A. *Zh. Org. Khim.* **1994**, *30*, 816.