Acid-Catalyzed Cyclization of Vinylsilanes Bearing a Hydroxy Group: A New Method for Stereoselective Synthesis of Disubstituted Tetrahydrofurans[1]

Katsukiyo Miura, Shigeo Okajima, Takeshi Hondo, Takahiro Nakagawa, Tatsuyuki Takahashi, and Akira Hosomi*

Contribution from the Department of Chemistry, Graduate School of Pure and Applied Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8571, Japan

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Abstract: In the presence of a catalytic amount of TsOH or $TiCl_4$, (*Z*)-5-silyl-4-penten-1-ols ((*Z*)-**1**) are smoothly cyclized to 2-silylmethyl-substituted tetrahydrofurans. This cyclization is applicable to the construction of a tetrahydropyran ring. The silyl group and the geometry of the C−C double bond strongly influence the cyclization rate. TBDMS and benzyldimethylsilyl groups considerably accelerate the cyclization in comparison with a dimethylphenylsilyl group, and (*E*)-vinylsilanes show much lower reactivity than the corresponding (*Z*)-isomers. The cyclization proceeds by stereospecific syn addition of the hydroxy group. Vinylsilanes **17**, **19**, and **21**, (*Z*)-5-silyl-4-penten-1-ols bearing a substituent on the methylene tether, smoothly undergo the acid-catalyzed cyclization to give *trans*-2,5-, *cis*-2,4-, and *trans*-2,3-disubstituted tetrahydrofurans, respectively, with moderate to high stereoselectivity. The silyl group of some cyclized products can be easily converted into a hydroxy group with stereochemical retention.

Introduction

The stereoselective synthesis of substituted cyclic ethers is an important and attractive subject in organic synthesis since cyclic ether units are frequently found in polyether antibiotics and other biologically active natural products.[2] Cyclization of alkenyl alcohols is a straightforward route to the cyclic skeletons. In general, a Brønsted acid or an electrophilic heteroatom reagent (e.g., Br_2, I_2, Pd(II) salts, etc.) is known to promote the process when the C−C double bond is not activated by an electron-withdrawing group.[3] The acid-catalyzed cyclization is rather limited in its applicability.[4] In contrast, the electrophile-initiated reaction provides a powerful method for the synthesis of highly functionalized cyclic ethers, although it is not necessarily effective for highly stereoselective synthesis. There is still a need for a new method realizing high levels of efficiency and stereoselectivity in the synthetic route to cyclic ethers from alkenyl alcohols.

The development of new synthetic methods utilizing nucleophilic addition to β-silylcarbenium ions is of considerable current interest.[5−14] Particularly, the Lewis acid-promoted [3 + 2] cycloadditions of allylsilanes and the related compounds to electrophilic unsaturated bonds are highly efficient in the stereoselective synthesis of carbocycles and heterocycles.[5,6] On the other hand, vinylsilanes have been rarely used as precursors of β-silylcarbenium ions for C−C and C−heteroatom bond

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Scheme 1

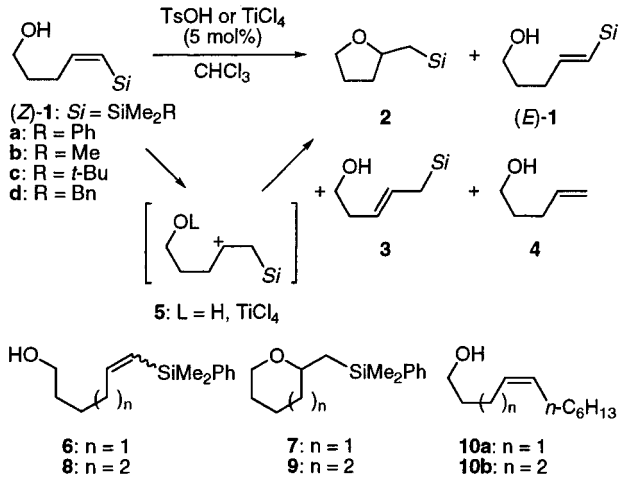

Table 1. Acid-Catalyzed Cyclization of Vinylsilanes **1**, **6**, and **8**[a]

entry	substrate	catalyst	temp/°C	time/h	product	yield/%
1	(*Z*)-**1a**	TsOH	60	10	**2a**	94
2	(*Z*)-**1b**	TsOH	60	5	**2b**	64[b] (92)[c]
3	(*Z*)-**1a**	$TiCl_4$	25	3	**2a**	92
4	(*Z*)-**1a**	AcCl	25	12	**2a**	86
5	(*Z*)-**1c**	$TiCl_4$	25	1.2	**2c**	85[b]
6	(*Z*)-**1d**	TsOH	60	2.75	**2d**	97
7	(*Z*)-**1d**	$TiCl_4$	25	0.75	**2d**	96
8	(*E*)-**1a**	TsOH	60	25	**2a**	91
9	(*E*)-**1a**	$TiCl_4$	25	25	**2a**	61
10	(*Z*)-**6**	TsOH	60	96	**7**	86
11	(*Z*)-**6**	$TiCl_4$	60	96	**7**	71
12	(*E*)-**6**	TsOH	60	96	**7**	64
13	(*E*)-**6**	$TiCl_4$	60	96	**7**	29
14	(*Z*)-**8**	TsOH	60	85	**9**	17

[a] All reactions were carried out with a substrate (1.0 mmol) and a catalyst (0.05 mmol) in $CHCl_3$ (5 mL). [b] The lower yield is due to volatility of the product. [c] The yield in parentheses was determined by ^1H NMR analysis of a crude product.

formation.[8,9] In the course of our studies on silicon-directed synthetic reactions,[10] we have found that vinylsilanes bearing a hydroxy group are easily cyclized to tetrahydrofurans and tetrahydropyrans in the presence of an acid catalyst.[11−13] A plausible mechanism for this cyclization involves the formation of a β-silylcarbenium ion intermediate by protonation of the sp^2 carbon α to the silyl group and the subsequent intramolecular attack of the hydroxy oxygen to the carbenium ion center. We report herein the scope and mechanistic aspects of the silicon-directed cyclization and its application to the stereoselective synthesis of disubstituted tetrahydrofurans.[11]

Results and Discussion

Acid-Catalyzed Cyclization of Vinylsilanes 1, 6, and 8. Treatment of dimethylphenylvinylsilane (*Z*)-**1a** (*Z*:*E* = >98:2) with a catalytic amount of $TsOH\cdot H_2O$ in $CHCl_3$ at 60 °C gave tetrahydrofuran **2a** in 94% yield, along with a mixture of (*Z*)-**1a** (3%), (*E*)-**1a** (0.3%), allylsilane **3** (0.9%), and 4-penten-1-ol (**4**, 0.3%) (Scheme 1 and entry 1 in Table 1). The formation of these products indicates that the acid-catalyzed reaction proceeds via β-silylcarbenium ion intermediate **5** generated by protonation of the C−C double bond. Trimethylvinylsilane (*Z*)-**1b** as well was efficiently cyclized to the corresponding tetrahydrofuran **2b** and hardly suffered desilylation to **4** (entry 2). Thus, the present cyclization does not require a bulky silyl group to achieve high efficiency, in contrast with the Lewis acid-promoted cycloaddition of allylsilanes.[14]

$TiCl_4$ served as an effective catalyst for this cyclization, even at 25 °C (entry 3). Other Lewis acids such as $SnCl_4$ and $BF_3\cdot OEt_2$ showed little catalytic ability because of fast desilylation to **4**. AcCl also induced the cyclization of (*Z*)-**1a** at 25 °C (entry 4). In this case, HCl generated by the reaction of AcCl with the hydroxy group would be the actual catalyst.[15] There is a possibility that $TiCl_4$ also works as a HCl source. However, $TiCl_4$ has a higher catalytic activity than AcCl. In addition, the $TiCl_4$-catalyzed cyclization in the presence of di-*tert*-butylpyridine (5 mol %) as a proton scavenger gave **2a** in 88% yield, although the reaction took a prolonged time (18 h) to reach completion. From these observations, it is probable that $TiCl_4$ itself is the actual catalyst.

The reaction rate is strongly dependent on the silyl group and the geometry of the C−C double bond. Introduction of a TBDMS or benzyldimethylsilyl (BnDMS) group effectively increased the cyclization rate (entries 5−7). The *Z*-isomer of **1a** is more reactive than its *E*-isomer in both catalyst systems with TsOH and $TiCl_4$ (entries 1, 3 vs 8, 9). In the initial period (within 3 h) of the TsOH-catalyzed cyclization, the yield of **2a** was directly proportional to the reaction time, and (*Z*)-**1a** was cyclized 2.7 times (k = slope, $k_Z/k_E = 2.7$) faster than (*E*)-**1a**. The rate difference with the $TiCl_4$ catalyst was remarkable compared to that with the TsOH catalyst, although the relationship between the yield and the reaction time was not in direct proportion (see Supporting Information).

Both isomers of vinylsilane **6** bearing a longer methylene tether by one carbon also underwent the acid-catalyzed cyclization to afford the corresponding tetrahydropyran **7**, although they showed lower reactivity than **1a** (entries 10−13). TsOH was superior to $TiCl_4$ in catalytic activity, which is quite different from the observation with **1a**. We also attempted to apply the present method to the construction of seven-membered cyclic ethers. However, the TsOH-catalyzed cyclization of vinylsilane **8** was rather slow and afforded oxepane **9** in poor yield (entry 14).

To confirm that the acid-catalyzed cyclization is directed by the silyl group, control experiments using alkenols **10** were carried out under the same conditions. As a result, no cyclized products were obtained, and the substrates were recovered intact.

Stereochemical Aspect. The stereochemistry of the present intramolecular addition of a hydroxy group was investigated with deuterium-labeled (*Z*)- and (*E*)-vinylsilanes **11** and **14** (98% D, *Z*:*E* or *E*:*Z* = >98:2, Table 2). Cyclization of (*Z*)- and (*E*)-**11** afforded diastereomeric mixtures of tetrahydrofurans **12** and **13** with inverse stereochemistry (entries 1−4).[16] This result indicates that syn addition of the hydroxy group to the C−C double bond is favored over anti addition. Both isomers of vinylsilane **14** were also cyclized to tetrahydropyrans **15** and **16** with high levels of syn addition (entries 5−8). The observed stereochemistry stands in sharp contrast to the stereospecific anti addition in electrophile-initiated cyclofunctionalization.[3b]

A plausible mechanism for the stereospecific syn addition is as follows (Scheme 2, X = D): (1) attachment of a proton or $TiCl_4$ to the hydroxy group of (*Z*)-**11** or (*Z*)-**14** forms oxonium

(13) Related work by other groups: (a) Akiyama, T.; Ishida, Y. *Synlett* **1998**, 1150; **1999**, 160 (Errata). (b) Adiwidjaja, G.; Flörke, H.; Kirschning, A.; Schaumann, E. *Liebigs Ann.* **1995**, 501.

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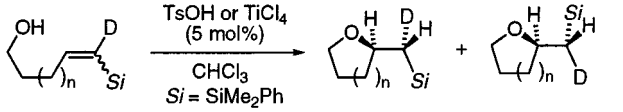
(15) We have reported that HCl gas as well as AcCl catalyzes the 1,2-silyl-migrative cyclization of vinylsilanes bearing a hydroxy group. See ref 12a.

(16) The relative configurations of **12**, **13**, **15**, and **16** were determined by comparison of their ^1H NMR spectra with the spectra of their authentic samples which were prepared by the stereodefined methods. See Supporting Information.

Table 2. Cyclization of Deuterated Vinylsilanes **11** and **14**[a]

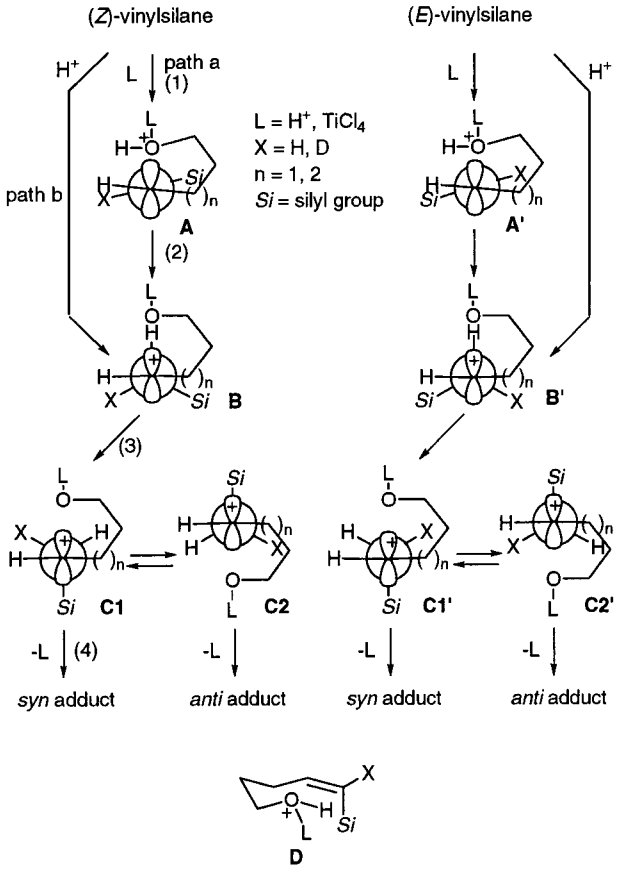


11: n = 1 **14**: n = 2 **12**: n = 1 **15**: n = 2 **13**: n = 1 **16**: n = 2

entry	substrate	catalyst	temp/°C	time/h	yield/%	**12**:**13** or **15**:**16**[b]
1	(*Z*)-**11**	TsOH	60	10	94	83:17
2	(*Z*)-**11**	$TiCl_4$	25	4	94	91:9
3	(*E*)-**11**	TsOH	60	25	92	13:87
4	(*E*)-**11**	$TiCl_4$	25	25	60	12:88
5	(*Z*)-**14**	TsOH	60	96	81	94:6
6	(*Z*)-**14**	$TiCl_4$	60	96	68	92:8
7	(*E*)-**14**	TsOH	60	96	69	12:88
8	(*E*)-**14**	$TiCl_4$	60	96	30	16:84

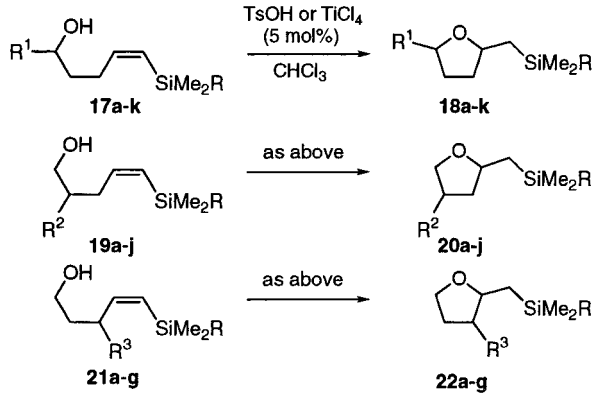
[a] See footnote *a* in Table 1. [b] The ratio was determined by ^{1}H NMR analysis. See ref 16 for the stereochemical assignment.

Scheme 2



ion **A**; (2) the proton on the oxygen atom shifts to the α-carbon; (3) the resultant β-silylcarbenium ion **B** immediately turns to its rotamer **C1**, stabilized by σ−π conjugation at the least motion;[17] (4) intramolecular attack of the hydroxy oxygen from the side opposite to the silyl group gives syn adduct **12** or **15** and regenerates the acid catalyst. Similarly, the reaction of (*E*)-**11** or (*E*)-**14** proceeds through **A**′, **B**′, and **C1**′ to give syn adduct **13** or **16**. Minor anti adduct would be formed by cyclization of another stabilized rotamer **C2** (**C2**′) arising from **C1** (**C1**′). Since

Scheme 3



rotamers **C1** and **C2** are enantiomers of **C2**′ and **C1**′, respectively, the rotation of **C1**′ to **C2**′ (**C1** to **C2**) is equivalent to that of **C2** to **C1** (**C2**′ to **C1**′). Accordingly, the formation of anti adducts from *Z*- and *E*-substrates suggests the presence of the rotation interconverting **C1** and **C2** (**C1**′ and **C2**′) as a minor reaction path. Intermolecular protonation (path b) directly forming **B** (**B**′) is also possible. However, the path including steps 1 and 2 (path a) provides a reasonable explanation for the low reactivity of **6** and the stereochemical outcomes in the diastereoselective cyclization (vide infra).

To obtain an insight into the reversibility of the protonation step (from **A** to **C1**), the TsOH-catalyzed cyclization of (*Z*)-**11** (98% D) was stopped before it reached completion (2 h, 67% conversion of (*Z*)-**11**, 61% yield of **12** and **13**, **12**:**13** = 85:15). The recovered substrate retained almost all the deuterium label as well as the (*Z*)-configuration (97% D, *Z*:*E* = >98:2). This observation shows that β-silylcarbenium ion **C2** is hardly converted into dedeuterated (*Z*)-vinylsilane; therefore, the reversion of **C1** to (*Z*)-**11** is also unlikely. The configurational retention discloses that the formation of anti adduct **13** is not due to the cyclization of (*E*)-**11** generated by the acid-catalyzed isomerization of (*Z*)-**11**.

The rate difference between *Z*- and *E*-isomers suggests that step 2 is the rate-determining step,[12] because steps 1 and 4 should not be influenced by the geometry of substrates, and step 3 would be much faster than the other steps. The enhanced cyclization rate with **1c** and **1d** is probably a result of the fact that the electron-donating ability of the TBDMS and BnDMS groups facilitates step 2 by raising the HOMO level of the C−C double bond.[18] The high reactivity of the *Z*-isomer is attributable to steric repulsion between the silyl group and the methylene tether, which would also accelerate step 2. Another possible explanation, particularly in the cyclization of (*Z*)-**1**, is that allylic 1,3-strain caused by the silyl group induces **A** ($n = 1$) to take chairlike conformation **D** that is requisite for step 2.[19] The lower reactivity of **6** compared with that of **1** would arise from the difficulty of intramolecular protonation of **A** ($n = 2$) with a longer methylene tether.

Stereoselective Synthesis of Disubstituted Tetrahydrofurans. The present silicon-directed cyclization is considerably efficient in the construction of tetrahydrofurans. Therefore, our efforts were directed toward the stereoselective synthesis of disubstituted tetrahydrofurans using (*Z*)-vinylsilanes **17**, **19**, and **21** (Scheme 3).

(17) There is a long-standing dispute over the structure of β-silyl carbenium ions, which can take a hyperconjugatively stabilized open form or a bridged form. Although the open forms (**C1**, **C2**, **C1**′, and **C2**′) are employed in Scheme 2, they can be easily displaced to the bridged forms. Lambert, J. B.; Zhao, Y. *J. Am. Chem. Soc.* **1996**, *118*, 7867 and references cited therein.

(18) For the difference between TBDMS and phenyldimethylsilyl (PDMS) groups in electronic effect, see: Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938.

(19) For acceleration of an intramolecular reaction by the increase of strain energy, see: Beckwith, A. L. J.; Zimmermann, J. *J. Org. Chem.* **1991**, *56*, 5791 and references therein.

Table 3. Cyclization of (*Z*)-1-Substituted 5-Silyl-4-penten-1-ols **17**[a]

	substrate			TsOH at 60 °C			$TiCl_4$ at room temperature		
entry	R	R^1		time/h	yield/%	trans:cis[b]	time/h	yield/%	trans:cis[b]
1	Ph	Ph	**17a**	8	92	83:17	7	89	90:10
2	Ph	*n*-C_6H_{13}	**17b**	7	95	83:17	7	89	86:14
3	Ph	*i*-Pr	**17c**	6	95	89:11	6	92	92:8
4	Me	Ph	**17d**	7	90	83:17	7	88	86:14
5	Me	Ph	(*E*)-**17d**	16	90	60:40	25	82	66:34
6	Me	*n*-C_6H_{13}	**17e**	8	93	81:19	7	86	82:18
7	Me	*i*-Pr	**17f**	7	89	85:15	7	73	87:13
8	H	Ph	**17g**	9	76	90:10	7	84	96:4
9	H	*n*-C_6H_{13}	**17h**	6	66	89:11	7	82	91:9
10	H	*i*-Pr	**17i**	11	66	91:9	7	68	93:7
11	*t*-Bu	*i*-Pr	**17j**	2	93	83:17	0.3	98	88:12
12	Bn	Ph	**17k**	1.3	94	85:15	0.7	89	88:12
13	Bn	Ph	**17k**				23[c]	89	95:5

[a] All reactions were carried out with a vinylsilane (1.00 mmol) and $TsOH \cdot H_2O$ (10 mg, 0.05 mmol) or $TiCl_4$ (1.0 M in CH_2Cl_2, 50 μL, 0.05 mmol) in $CHCl_3$ (5 mL). [b] Determined by ^1H NMR analysis. [c] At −20 °C.

Table 4. Cyclization of (*Z*)-2-Substituted 5-Silyl-4-penten-1-ols **19**[a]

	substrate			TsOH at 60 °C			$TiCl_4$ at room temperature		
entry	R	R^2		time/h	yield/%	trans:cis[b]	time/h	yield/%	trans:cis[b]
1	Ph	Ph	**19a**	11	80	18:82	11	97	14:86
2	Ph	*n*-C_6H_{13}	**19b**	8	97	21:79	9	98	15:85
3	Ph	*i*-Pr	**19c**	8	96	17:83	9	97	10:90
4	Me	Ph	**19d**	11	95	18:82	8	94	13:87
5	Me	*n*-C_6H_{13}	**19e**	10	96	23:77	7	93	16:84
6	Me	*i*-Pr	**19f**	10	83	16:84	7	82	12:88
7	H	Ph	**19g**	11	84	16:84	14	85	9:91
8	H	*n*-C_6H_{13}	**19h**	7	78	19:81	7	82	12:88
9	H	*i*-Pr	**19i**	7	79	14:86	8	72	9:91
10	Bn	Ph	**19j**	1.5	90	17:83	0.7	94	16:84
11	Bn	Ph	**19j**				10[c]	93	10:90

[a,b,c] See footnotes *a*, *b*, and *c* in Table 3, respectively.

Table 5. Cyclization of (*Z*)-3-Substituted 5-Silyl-4-penten-1-ols **21**[a]

	substrate			TsOH at 60 °C			$TiCl_4$ at room temperature		
entry	R	R^3		time/h	yield/%	trans:cis[b]	time/h	yield/%	trans:cis[b]
1	Ph	Ph	**21a**	20	80	>99:1	20	70	>99:1
2	Ph	*n*-C_5H_{11}	**21b**	14	87	>99:1	5	93	>99:1
3	Me	Ph	**21c**	8	79	>99:1	8	86	>99:1
4	Me	*n*-C_5H_{11}	**21d**	9	89	>99:1	5	90	>99:1
5	H	Ph	**21e**	14	47	>99:1	12	65 (84)[c]	>99:1
6	H	*n*-C_5H_{11}	**21f**	6	34	>99:1	5	81	>99:1
7	Bn	Ph	**21g**	8.5	96	>99:1[d]	7	93	98:2[d]

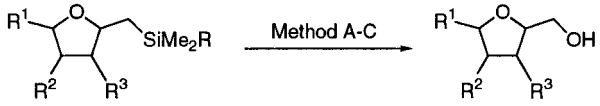
[a] See footnote *a* in Table 3. [b] Determined by ^1H NMR analysis. The ratio >99:1 means that no cis isomer is detected by ^1H NMR analysis. [c] The yield with 10 mol % of $TiCl_4$. [d] Determined by GC analysis.

As shown in Table 3, cyclization of **17** afforded 2,5-disubstituted tetrahydrofurans in good to high yields with moderate to high trans selectivity. The $TiCl_4$-catalyzed system at room temperature exhibited slightly higher diastereoselectivity than the TsOH-catalyzed system at 60 °C. The higher selectivity is probably due to the lower reaction temperature because the TsOH-catalyzed cyclization of **17d** at room temperature for 114 h achieved higher selectivity (88%, trans:cis = 85:15) than that at 60 °C (entry 4). The use of (*E*)-**17d** revealed that the *E*-configuration markedly diminished not only reactivity but also trans selectivity (entry 5). Introduction of a bulky substituent (Ph or *i*-Pr) as R^1 is effective in improving the proportion of the trans isomer. The silyl group also affected the stereoselectivity to some extent. Vinylsilanes **17g**−**i** bearing a dimethylsilyl group gave the best results in stereoselectivity under the same reaction conditions (entries 8−10). Unfortunately, the cyclization of **17g**−**i** resulted in lower yields than that of **17a**−**c** because of competitive desilylation and Si−H bond cleavage of the product. The TBDMS and BnDMS groups strongly accelerated the cyclization, in accordance with the results of (*Z*)-**1c** and (*Z*)-**1d**, while they were not effective in improving the diastereoselectivity (entries 11, 12). However, the high reactivity of **17k** enabled the cyclization at −20 °C to effect high trans selectivity (entry 13).

Vinylsilanes **19** bearing a homoallylic substituent (R^2) were cyclized to 2,4-disubstituted tetrahydrofurans **20** with moderate to high cis selectivity (Table 4). The influence of the reaction conditions and the substituents R and R^2 on the stereoselectivity is similar to that observed with **17**. The $TiCl_4$-catalyzed cyclization at 25 °C exhibited better syn selectivity than the TsOH-catalyzed cyclization at 60 °C. The use of hydrogen as R or a bulky group as R^2 slightly improved the syn selectivity. In this case also, a BnDMS group effectively raised the cyclization rate, and the cyclization of **19j** at −20 °C achieved high efficiency and stereoselectivity (entries 10, 11).

In most cases, vinylsilanes **21** formed only *trans*-**22** irrespective of the reaction conditions and the substituents R and R^3 unlike **17** and **19** (Table 5). When R^3 was a phenyl group, the yield of **22** was not so high under both reaction conditions except for the case with **21g** (entries 1, 3, 5, and 7). Thus, the BnDMS group proved to be an effective promoter for the cyclization of **21** as well.

Table 6. Oxidative Cleavage of the Silicon−Carbon Bond of 2-(Silylmethyl)Tetrahydrofurans[a]



23-25

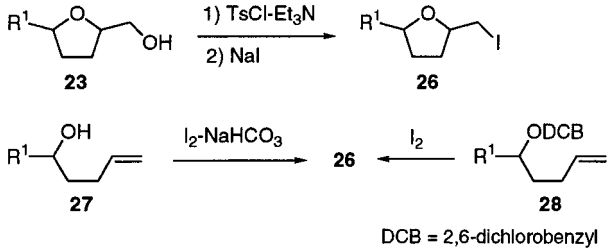
	substrate							product		
entry	R	R^1	R^2	R^3		trans:cis[b]	method		yield/%	trans:cis[b]
1	H	Ph	H	H	**18g**	96:4	A	**23a**	93	96:4
2	H	*n*-C_6H_{13}	H	H	**18h**	86:14	A	**23b**	85	87:13[c]
3	H	*i*-Pr	H	H	**18i**	93:7	A	**23c**	83	93:7[c]
4	H	H	Ph	H	**20g**	12:88	A	**24**	90	13:87
5	H	H	H	Ph	**22e**	>99:1	A	**25a**	91	>99:1
6	H	H	H	*n*-C_5H_{11}	**22f**	>99:1	A	**25b**	89	>99:1
7	Ph	Ph	H	H	**18a**	92:8	B	**23a**	59	90:10
8	Bn	Ph	H	H	**18k**	88:12	C	**23a**	93	88:12
9	Bn	H	Ph	H	**20j**	15:85	C	**24**	96	15:85
10	Bn	H	H	Ph	**22g**	98:2[d]	C	**25a**	55	95:5[d]

[a] For methods A−C, see the text and the Experimental Section. [b] Determined by ^{1}H NMR analysis. [c] Determined by ^{1}H NMR analysis of iodides **26** derived from **23**. See Table 7. [d] Determined by GC analysis.

Oxidative Cleavage of the Silicon−Carbon Bond. It is well known that some silyl groups are useful as hydroxy surrogates.[20] To enhance the synthetic utility of the present cyclization, oxidative cleavage of the silicon−carbon bond of the cyclized products was next attempted. As shown in Table 6, each dimethylsilyl group of **18g**−**i**, **20g**, and **22e**,**f** could be easily converted to a hydroxy group by treatment of H_2O_2−$KHCO_3$/THF−MeOH (method A, Tamao's method)[21] with retention of the stereochemistry (entries 1−6). The conversion of **18a**, bearing a dimethylphenylsilyl group, to alcohol **23a** was achieved by a two-step procedure including pretreatment with *t*-BuOK/DMSO and subsequent oxidation with TBAF−H_2O_2−$KHCO_3$/MeOH−THF (method B, entry 7).[22] In contrast, the cyclized products **18k**, **20j**, and **22g** bearing a BnDMS group were smoothly oxidized to the corresponding alcohols by a one-step procedure using only the latter set of reagents without the pretreatment (method C, entries 8−10).[12b,c] Accordingly, the BnDMS group is considerably valuable as not only a promoter of the present cyclization but also a latent hydroxy group.

Stereochemical Assignment. The relative configuration of 2,5-disubstituted tetrahydrofurans can be determined on the basis of the chemical shifts for the protons at the 2- and 5-positions.[23] Due to a 1,3-deshielding effect of an alkyl substituent on the γ-proton, the signals of H-2 and H-5 of the trans isomers appear at lower fields than those of the corresponding cis isomers.[24] On the basis of this criterion, the major isomers of **18** were assigned to the trans configuration. This assignment was ascertained by derivatization of **18**. Namely, **18g**−**i** were converted to iodides **26** with stereochemical retention by oxidative cleavage of the Si−C bond, tosylation of the resulting alcohols **23**, and subsequent iodination with NaI (Table 7). Bartlett et al. have reported that iodocyclization of 4-alkenyl alcohols **27** gives **26** with moderate trans selectivity, while the reaction of 4-alkenyl 2,6-dichlorobenzyl ethers **28** shows high cis selectivity.[25] The major isomers of iodides **26** derived from **18g**−**i** were identical with those from **27**. The observation proves the major isomers of **18g**−**i** to be trans.

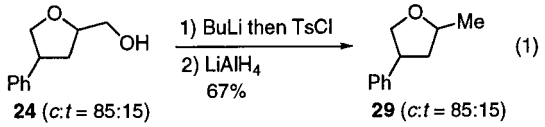
Table 7. Derivatization of **23** and Iodocyclization of **27** and **28**



	yield of **26**/% (trans:cis)[a]		
R^1	from **23**[b]	from **27**	from **28**
a: Ph	89 (96:4)	61 (74:26)	*c*
b: *n*-C_6H_{13}	79 (87:13)	68 (69:31)	83 (<5:95)
c: *i*-Pr	82 (93:7)	66 (81:19)	90 (5:95)

[a] Determined by ^{1}H NMR analysis. [b] Derived from **18h** (trans:cis = 96:4), **18i** (trans:cis = 86:14), and **18j** (trans:cis = 93:7). See entries 1−3 in Table 6. [c] The reaction resulted in a complex mixture of products, including a small amount of **26a**.

According to Eliel et al., ring carbon atoms C-2, C-3, and C-4 of the cis isomers of 2,4-disubstituted tetrahydrofurans show a downfield shift, while the signal of C-5 appears at higher field compared to that of the trans isomer.[26] On the basis of these criteria, the major isomers of **20** were determined to possess a cis configuration. This assignment was ascertained by NOE experiments of the major isomer of **20j**. Irradiation of one proton on C-3 showed considerable enhancements of protons on C-2 (7.3%) and C-4 (7.9%). In contrast, these protons were not so enhanced upon irradiation of another proton on C-3 (1.8% in both cases). These observations clearly support the above assignment. In addition, alcohol **24** derived from **20j** was converted into the deoxygenated form **29** (eq 1), whose major isomer was found to be identical with the authentic sample of



24 (*c*:*t* = 85:15) **29** (*c*:*t* = 85:15)

(20) Reviews: (a) Colvin, E. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 7, p 641. (b) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

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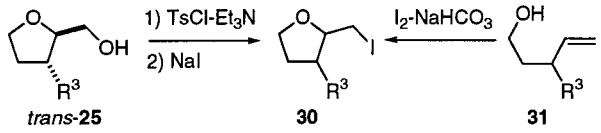
Table 8. Derivatization of **25** and Iodocyclization of **31**



	yield of **30**/% (trans:cis)[a]	
R^3	from *trans*-**25**	from **31**
a: Ph	82 (>99:1)	77 (64:36)
b: n-C_5H_{11}	63 (>99:1)	90 (57:43)

[a] Determined by ^{1}H NMR analysis.

cis-**29** prepared from methyl phenylacetate (see Supporting Information).

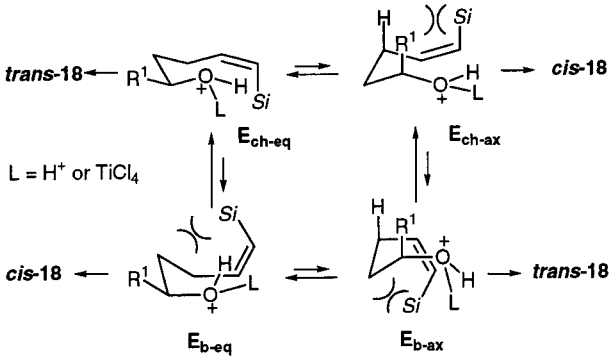
For configurational assignment of **22**, derivatization of alcohols **25** to the corresponding iodides **30** and the preparation of both isomers of **30** from alkenyl alcohols **31** were performed as described in Table 8. In *trans*-2,3-disubstituted tetrahydrofurans, H-2 and H-3 on the ring are shielded by the vicinal C−C bond, and their signals are observed at higher field than those of the cis isomers. For the same reason, the 2,3-*cis* configuration induces an upfield shift of the alkyl protons of the substituents.[23,24] Additionally, nonbonding interaction arising from the cis configuration brings C-2, C-3, and α-carbons of the substituents to higher field.[27] Judging from these criteria, the ^{1}H and ^{13}C NMR data for **30** prepared from **25** and **31** show that the major isomers of **22** have the trans configuration.

Origin of Stereoselectivity. The present cyclization proceeds by stereospecific syn addition of a hydroxy group, as mentioned above. This result means that proton transfer (step 2) and nucleophilic attack of the hydroxy oxygen (step 4) take place on the same side of the π-face, as shown in Scheme 2. Accordingly, the relative configuration of products would depend mainly on diastereoface selection of the proton transfer. In other words, the observed diastereoselectivity would be attributed to diastereoface-selective protonation. Considering that the protonation site is away from the stereogenic center in vinylsilanes **17** and **19**, it is difficult to explain the diastereoface-selective protonation through intermolecular path b (Scheme 2). Conversely, intramolecular path a, via an oxonium ion intermediate such as **A**, can easily rationalize the diastereoface-selection.

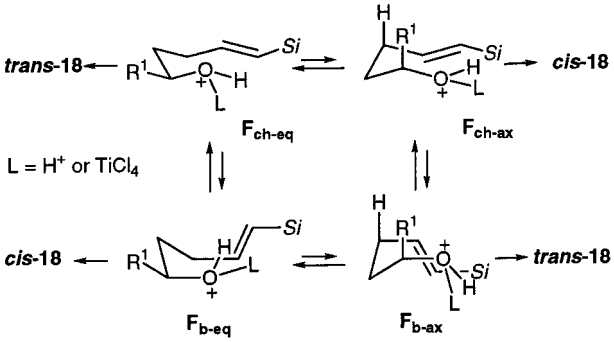
In intramolecular protonation of **17**, two transition states arising from chairlike conformers $\mathbf{E}_{ch-eq}$ and $\mathbf{E}_{ch-ax}$ are plausible, while boatlike conformers $\mathbf{E}_{b-eq}$ and $\mathbf{E}_{b-ax}$ are strictly inhibited by an allylic 1,3-strain between the methylene tether and the silyl group (Scheme 4).[28,29] Conformer $\mathbf{E}_{ch-ax}$ has a repulsive nonbonding interaction between R^1 and the silyl group, which makes $\mathbf{E}_{ch-ax}$ an energetically unfavorable conformer. Consequently, the proton transfer would proceed exclusively via conformer $\mathbf{E}_{ch-eq}$ to achieve high levels of diastereoface selection. The subsequent nucleophilic attack of the hydroxy oxygen on the same side as the protonation gives *trans*-**18**, in agreement with the present observation.

In the cyclization of (*E*)-**17**, four conformers leading to transition states of intramolecular protonation are conceivable (Scheme 5). Boatlike conformers $\mathbf{F}_{b-eq}$ and $\mathbf{F}_{b-ax}$ do not have a severe allylic 1,3-strain as shown in $\mathbf{E}_{b-eq}$ and $\mathbf{E}_{b-ax}$; therefore,

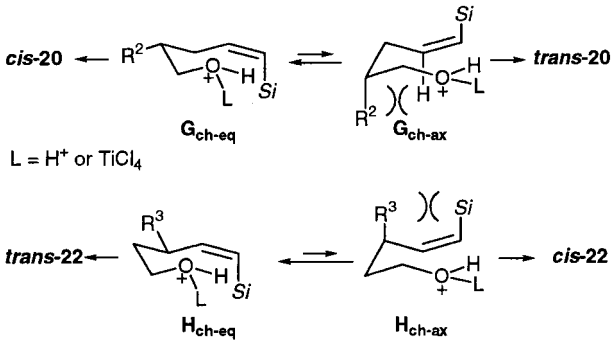
Scheme 4



Scheme 5



Scheme 6



the energy difference between $\mathbf{F}_{ch-eq}$ and $\mathbf{F}_{b-eq}$ is much smaller than that between $\mathbf{E}_{ch-eq}$ and $\mathbf{E}_{b-eq}$. In addition, the energy difference between $\mathbf{F}_{ch-eq}$ and $\mathbf{F}_{ch-ax}$ is not as large as that between $\mathbf{E}_{ch-eq}$ and $\mathbf{E}_{ch-ax}$ because of the absence of a steric repulsion between R^1 and the silyl group. These decreases in energy difference would cause low diastereoselectivity to (*E*)-**17d** (entry 5 in Table 3).

The stereochemical outcome with **19** can be explained by considering two conformers, $\mathbf{G}_{ch-eq}$ and $\mathbf{G}_{ch-ax}$, in the protonation step (Scheme 6). Since $\mathbf{G}_{ch-ax}$ exhibits nonbonding interactions of R^2 with the olefinic hydrogen and lone electron pair of the hydroxy oxygen, the cyclization of **19** would proceed mainly via the energetically more favored conformer $\mathbf{G}_{ch-eq}$ to afford *cis*-**20** selectively. Similarly, the high trans selectivity with **21** is probably due to a large energy difference between $\mathbf{H}_{ch-eq}$ and $\mathbf{H}_{ch-ax}$. The latter conformer has a severe allylic 1,3-strain between R^3 and the silyl group, which would strictly suppress the cyclization to *cis*-**22** via $\mathbf{H}_{ch-ax}$.

As shown in Table 2, the present cyclization includes anti addition of a hydroxy group as a minor path. The formation of a minor diastereomer in the cyclization of **17**, **19**, and **21** is attributable to anti addition via the chair-equatorial conformer of an oxonium ion intermediate as well as syn addition via the

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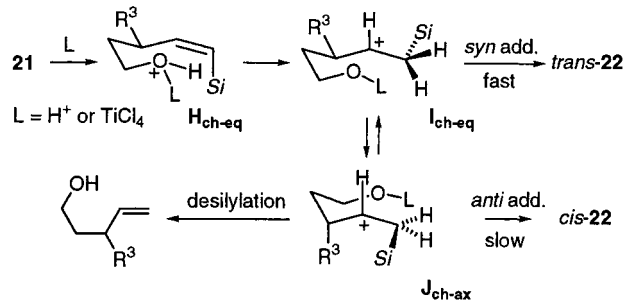
Scheme 7



other conformers. The selectivities of (*Z*)-**11** toward syn addition are 83% with TsOH at 60 °C and 91% with $TiCl_4$ at room temperature (entries 1 and 2 in Table 2). On the assumption that the substituent on the methylene tether (R^1, R^2, or R^3) has no influence on the selectivities, **17a**−**c**, **19a**−**c**, and **21a**,**b** are expected to show less than 83% (TsOH, 60 °C) or 91% ($TiCl_4$, room temperature) diastereoselectivity. However, some observed stereoselectivities are higher than these values (entry 3 in Table 3; entries 1 and 2 in Table 5). This inconsistency indicates that the above assumption is not reasonable and there is a secondary factor controlling the diastereoselectivity, other than the diastereoface-selective intramolecular proton transfer.

Based on the mechanism shown in Scheme 2, the reaction path from **21** to *trans*- and *cis*-**22** would include oxonium ion **H**, β-silylcarbenium ion **I**, and its rotamer **J** as intermediates (Scheme 7). An equilibrium between **I** and **J** is also conceivable, although it is not as fast as the ring closure of **I**. The intermediates **I** and **J** should take chairlike conformations $\mathbf{I}_{ch-eq}$ and $\mathbf{J}_{ch-ax}$ for the ring closure, forming *trans*- and *cis*-**22**, respectively. In this situation, the ring closure of **J** is expected to be much slower than that of **I** because of the pseudoaxial substituent R^3 in $\mathbf{J}_{ch-ax}$. The decreased cyclization rate, which can cause isomerization of **J** to **I** and desilylation of **J**, would be a secondary reason for the high trans selectivity with **21**. A similar explanation is applicable for the stereochemical outcomes with **17** and **19**.

Conclusion

We have found that vinylsilanes **1** and **6** smoothly undergo acid-catalyzed cyclization by stereospecific syn addition of the hydroxy group to give 2-silylmethyl-substituted cyclic ethers. This silicon-directed reaction proceeds with a catalytic amount of an acid in high efficiency, even when the substrate has a relatively small silyl group such as a TMS group. A plausible mechanism for the present cyclization includes intramolecular protonation, forming a β-silylcarbenium ion intermediate, and the subsequent nucleophilic attack of the hydroxy oxygen to the carbenium ion center. The β-effect of the silyl group not only accelerates the protonation step but also holds the conformation of the carbenium ion intermediate to realize the stereospecific syn addition. The cyclization rate, enhanced by an electron-donating silyl group and the (*Z*)-geometry of the C−C double bond, shows that the intramolecular protonation is the rate-determining step. Vinylsilanes **17**, **19**, and **21** are cyclized to *trans*-2,5-, *cis*-2,4-, and *trans*-2,3-disubstituted tetrahydrofurans, respectively, with moderate to high levels of stereoselectivity. The stereochemical outcomes are rationalized by diastereoface-selective intramolecular proton transfer via a chairlike conformation bearing an equatorial substituent. The cyclized products can be converted to the corresponding alcohols by oxidative cleavage of the Si−C bond. In particular, a BnDMS group works as a good hydroxy surrogate as well as an effective promoter. In conclusion, we have demonstrated that the present cyclization followed by oxidative cleavage of the Si−C bond is effective for the stereoselective synthesis of a variety of disubstituted tetrahydrofurans.

Experimental Section

General Method. Unless otherwise noted, all reactions and the following distillations were carried out under N_2. Solvents were dried by distillation from sodium metal/benzophenone ketyl (THF, Et_2O), $CaCl_2$−$NaHCO_3$ ($CHCl_3$), and CaH_2 (DMSO, CH_2Cl_2). AcCl was distilled from *N*,*N*-dimethylaniline. $TiCl_4$, BF_3·OEt_2, and $SnCl_4$ were simply distilled and stored as a CH_2Cl_2 solution (1.0 M). All other commercial reagents were used as received. Na_2SO_4 was used as the drying agent for aqueous workup. Boiling points (air-bath temperature) were determined with Kugelrohr distillation apparatus. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 270 and 67.7 MHz, respectively. The chemical shifts (δ) are referenced to 0.00 ppm (Me_4Si) or 7.26 ppm ($CHCl_3$) for the proton and to 77.00 ppm (centered on the signal of $CDCl_3$) for the carbon. ^{13}C NMR data of minor isomers are shown only for well-resolved signals.

Acid-Catalyzed Cyclization of Vinylsilanes (Typical Procedure). Vinylsilane (*Z*)-**1a** (220 mg, 1.00 mmol) was added to TsOH·H_2O (10 mg, 0.05 mmol) in $CHCl_3$ (5 mL), and then the mixture was heated to 60 °C. After being stirred for 10 h, the resultant solution was poured into saturated aqueous $NaHCO_3$ (20 mL). The extract with CH_2Cl_2 (2 × 20 mL) was dried and evaporated. Purification by column chromatography (SiO_2, hexane−AcOEt 10:1) gave 2-(dimethylphenylsilylmethyl)tetrahydrofuran (**2a**, 208 mg, 94%) along with a mixture of (*E*)-5-dimethylphenylsilyl-3-penten-1-ol (**3**, 0.9%), **4** (0.3%), and both isomers of **1a** (3.3%, *Z*:*E* = 10:1). In the $TiCl_4$-catalyzed cyclization, a CH_2Cl_2 solution of $TiCl_4$ (0.05 mL, 0.05 mmol) was added to **1a** (220 mg, 1.00 mmol) in $CHCl_3$ (5 mL). After completion of the reaction, the same workup and purification gave **2a** (202 mg, 92%).

2a: bp 90 °C (1.0 Torr); IR (neat) 2960, 1249, 1112, 1077, 832, 700 cm^{-1}; ^1H NMR δ 0.316 (s, 3H), 0.322 (s, 3H), 1.06 (dd, J = 14.2, 8.6 Hz, 1H), 1.23−1.38 (m, 2H), 1.74−1.94 (m, 3H), 3.58−3.67 (m, 1H), 3.80−3.93 (m, 2H), 7.32−7.36 (m, 3H), 7.49−7.54 (m, 2H); ^{13}C NMR δ −2.46 (CH_3), −2.19 (CH_3), 23.41 (CH_2), 25.88 (CH_2), 33.81 (CH_2), 66.86 (CH_2), 77.05 (CH), 127.66 (CH × 2), 128.79 (CH), 133.45 (CH × 2), 139.07 (C); MS *m*/*z* (relative intensity) 220 (M^+, 0.3), 137 (100). Anal. Calcd for $C_{13}H_{20}OSi$: C, 70.68; H, 8.72. Found: C, 70.68; H, 9.08.

3: IR (neat) 3394 (br), 2922, 1427, 1257, 1049 cm^{-1}; ^1H NMR δ 0.28 (s, 6H), 1.25 (br s, 1H), 1.71 (d, J = 7.9 Hz, 2H), 2.21 (dt, J = 7.3, 6.6 Hz, 2H), 3.52 (br s, 2H), 5.18 (dt, J = 15.2, 7.3 Hz, 1H), 5.50 (dt, J = 15.2, 7.9 Hz, 1H), 7.30−7.37 (m, 3H), 7.47−7.54 (m, 2H); ^{13}C NMR δ −3.39 (CH_3 × 2), 22.07 (CH_2), 36.17 (CH_2), 62.16 (CH_2), 124.98 (CH), 127.78 (CH × 2), 129.04 (CH), 129.60 (CH), 133.59 (CH × 2), 138.54 (C); MS *m*/*z* (relative intensity) 205 (M^+ − Me, 0.9), 135 (100); HRMS calcd for $C_{13}H_{20}OSi$ 220.1283, found 220.1279.

2-(Trimethylsilylmethyl)tetrahydrofuran (2b): bp 75 °C (84 Torr); IR (neat) 2935, 1248, 1112, 860, 835 cm^{-1}; ^1H NMR δ 0.03 (s, 9H), 0.81 (dd, J = 14.3, 8.9 Hz, 1H), 1.09 (dd, J = 14.3, 5.6 Hz, 1H), 1.29−1.43 (m, 1H), 1.83−2.02 (m, 3H), 3.65 (ddd, J = 8.0, 8.0, 6.2 Hz, 1H), 3.82−3.94 (m, 2H); ^{13}C NMR δ −0.914 (CH_3 × 3), 24.28 (CH_2), 26.04 (CH_2), 33.82 (CH_2), 66.92 (CH_2), 77.49 (CH); MS *m*/*z* (relative intensity) 157 (M^+ − H, 1.9), 175 (100). Anal. Calcd for $C_8H_{18}OSi$: C, 60.69; H, 11.46. Found: C, 60.57; H, 11.17.

2-(*tert*-Butyldimethylsilylmethyl)tetrahydrofuran (2c): IR (neat) 2935, 1462, 1360, 1249, 1078, 827 cm^{-1}; ^1H NMR δ −0.02 (s, 3H), −0.01 (s, 3H), 0.79 (dd, J = 14.0, 9.1 Hz, 1H), 0.86 (s, 9H), 1.12 (dd, J = 14.0, 4.4 Hz, 1H), 1.23−1.43 (m, 1H), 1.79−2.06 (m, 3H), 3.65 (dt, J = 6.6, 6.3 Hz, 1H), 3.82−3.95 (m, 2H); ^{13}C NMR δ −5.70 (CH_3), −5.34 (CH_3), 16.42 (C), 19.91 (CH_2), 26.08 (CH_2), 26.37 (CH_3 × 3), 33.95 (CH_2), 66.90 (CH_2), 77.61 (CH); MS *m*/*z* (relative intensity) 200 (M^+, 0.1), 185 (0.2), 75 (100). Anal. Calcd for $C_{11}H_{24}OSi$: C, 65.92; H, 12.07. Found: C, 65.74; H, 12.16.

2-(Benzyldimethylsilylmethyl)tetrahydrofuran (2d): bp 70 °C (0.17 Torr); IR (neat) 2955, 1591, 1491, 1249 cm^{-1}; ^1H NMR δ 0.004 (s, 3H), 0.02 (s, 3H), 0.82 (dd, J = 14.2, 7.9 Hz, 1H), 1.08 (dd, J = 14.2, 5.9 Hz, 1H), 1.26−1.43 (m, 1H), 1.78−2.03 (m, 3H), 2.12 (s,

2H), 3.66 (td, $J = 7.9$, 6.6 Hz, 1H), 3.82−3.95 (m, 2H), 6.98−7.09 (m, 3H), 7.17−7.24 (m, 2H);^{13}C NMR δ −2.91 (CH_3), −2.82 (CH_3), 22.43 (CH_2), 25.97 (CH_2), 26.13 (CH_2), 34.07 (CH_2), 67.03 (CH_2), 77.14 (CH), 123.94 (CH), 128.14 (CH × 4), 140.09 (C); MS *m*/*z* (relative intensity) 219 (M^+ − Me, 0.1), 75 (100). Anal. Calcd for $C_{14}H_{22}OSi$: C, 71.73; H, 9.46. Found: C, 71.82; H, 9.19.

2-(Dimethylphenylsilylmethyl)tetrahydropyran (7): bp 95 °C (0.30 Torr); IR (neat) 2960, 1246, 1112, 1086, 820, 700 cm^{-1}; ^{1}H NMR δ 0.30 (s, 3H), 0.32 (s, 3H), 0.99 (dd, $J = 14.4$, 6.3 Hz, 1H), 1.14 (dd, $J = 14.5$, 7.6 Hz, 1H), 1.22−1.57 (m, 5H), 1.70−1.78 (m, 1H), 3.28−3.40 (m, 2H), 3.90−3.96 (m, 1H), 7.32−7.36 (m, 3H), 7.49−7.55 (m, 2H); ^{13}C NMR δ −2.36 (CH_3), −1.78 (CH_3), 23.78 (CH_2), 24.61 (CH_2), 25.79 (CH_2), 35.05 (CH_2), 68.29 (CH_2), 75.88 (CH), 127.63 (CH × 2), 128.69 (CH), 133.55 (CH × 2), 139.60 (C); MS *m*/*z* (relative intensity) 234 (M^+, 0.4), 219 (M^+ − Me, 58), 137 (100), 135 (100). Anal. Calcd for $C_{14}H_{22}OSi$: C, 71.73; H, 9.46. Found: C, 71.53; H, 9.48.

2-(Dimethylphenylsilylmethyl)oxepane (9): IR (neat) 2925, 1247, 1116, 836, 699 cm^{-1}; ^{1}H NMR δ 0.30 (s, 3H), 0.32 (s, 3H), 0.99 (dd, $J = 14.8$, 5.6 Hz, 1H), 1.17 (dd, $J = 14.8$, 8.6 Hz, 1H), 1.40−1.82 (m, 8H), 3.38 (ddd, $J = 12.2$, 7.6, 4.0 Hz, 1H), 3.60 (dddd, $J = 9.2$, 8.6, 5.6, 3.6 Hz, 1H), 3.76 (ddd, $J = 12.2$, 5.6, 5.0 Hz, 1H), 7.32−7.37 (m, 3H), 7.50−7.55 (m, 2H); ^{13}C NMR δ −2.46 (CH_3), −1.82 (CH_3), 25.15 (CH_2), 25.81 (CH_2), 26.64 (CH_2), 30.94 (CH_2), 39.69 (CH_2), 67.84 (CH_2), 77.67 (CH), 127.65 (CH × 2), 128.67 (CH), 133.57 (CH × 2), 139.80 (C); MS *m*/*z* (relative intensity) 248 (M^+, 0.1), 233 (M^+ − Me, 50), 135 (100). Anal. Calcd for $C_{15}H_{24}OSi$: C, 72.52; H, 9.74. Found: C, 72.25; H, 9.91.

(2*R,1′*S**)-2-[Deuterio(dimethylphenylsilyl)methyl]tetrahydrofuran (12)**: bp 70 °C (0.30 Torr); IR (neat) 2960, 1249, 1112, 1077, 832, 700 cm^{-1}; ^{1}H NMR δ 0.317 (s, 3H), 0.321 (s, 3H), 1.04 (d, $J = 8.6$ Hz, 1H), 1.21−1.40 (m, 1H), 1.75−1.94 (m, 3H), 3.59−3.67 (m, 1H), 3.80−3.92 (m, 2H), 7.33−7.36 (m, 3H), 7.50−7.55 (m, 2H); ^{13}C NMR δ −2.39 (CH_3), −2.14 (CH_3), 23.08 (CHD, t, $J_{C-D} = 18.0$ Hz), 25.97 (CH_2), 33.79 (CH_2), 66.96 (CH_2), 77.11 (CH), 127.74 (CH × 2), 128.89 (CH), 133.55 (CH × 2), 139.17 (C); MS *m*/*z* (relative intensity) 206 (M^+ − Me, 26), 43 (100). Anal. Calcd for $C_{13}H_{19}DOSi$: C, 70.53; H, 8.65; D, 0.91. Found: C, 70.68; H, 8.72; D, 0.92.

(2*R,1′*R**)-2-[Deuterio(dimethylphenylsilyl)methyl]tetrahydrofuran (13)**: IR (neat) 2935, 1250, 1106, 831 cm^{-1}; ^{1}H NMR δ 0.317 (s, 3H), 0.321 (s, 3H), 1.22−1.39 (m, 2H), 1.71−1.94 (m, 3H), 3.58−3.67 (m, 1H), 3.81−3.92 (m, 2H), 7.33−7.37 (m, 3H), 7.50−7.55 (m, 2H); ^{13}C NMR δ −2.53 (CH_3), −2.24 (CH_3), 22.93 (CHD, t, $J_{C-D} = 18.3$ Hz), 25.81 (CH_2), 33.69 (CH_2), 66.78 (CH_2), 76.93 (CH), 127.58 (CH × 2), 128.72 (CH), 133.39 (CH × 2), 138.96 (C); MS *m*/*z* (relative intensity) 206 (M^+ − Me, 32), 135 (100). Anal. Calcd for $C_{13}H_{19}DOSi$: C, 70.53; H, 8.65; D, 0.91. Found: C, 70.46; H, 8.90; D, 0.94.

(2*R,1′*S**)-2-[Deuterio(dimethylphenylsilyl)methyl]tetrahydropyran (15)**: IR (neat) 2930, 1246, 1109, 1083, 838, 698 cm^{-1}; ^{1}H NMR δ 0.30 (s, 3H), 0.31 (s, 3H), 0.97 (dt, $J = 6.3$, 2.0 Hz, 1H), 1.17−1.60 (m, 5H), 1.70−1.77 (m, 1H), 3.30−3.39 (m, 2H), 3.89−3.96 (m, 1H), 7.32−7.37 (m, 3H), 7.49−7.55 (m, 2H); ^{13}C NMR δ −2.37 (CH_3), −1.80 (CH_3), 23.78 (CH_2), 24.21 (CHD, t, $J_{C-D} = 18.3$ Hz), 25.79 (CH_2), 34.97 (CH_2), 68.32 (CH_2), 75.85 (CH), 127.64 (CH × 2), 128.72 (CH), 133.57 (CH × 2), 139.59 (C); MS *m*/*z* (relative intensity) 235 (M^+, 0.1), 220 (M^+ − Me, 43), 135 (100). Anal. Calcd for $C_{14}H_{21}DOSi$: C, 71.43; H, 8.99; D, 0.86. Found: C, 71.32; H, 8.99; D, 0.86.

(2*R,1′*R**)-2-[Deuterio(dimethylphenylsilyl)methyl]tetrahydropyran (16)**: IR (neat) 2930, 1246, 1110, 1084, 837, 698 cm^{-1}; ^{1}H NMR δ 0.30 (s, 3H), 0.32 (s, 3H), 1.11 (dt, $J = 7.6$, 2.0 Hz, 1 H), 1.18−1.56 (m, 5H), 1.70−1.79 (m, 1H), 3.30−3.40 (m, 2H), 3.90−3.96 (m, 1H), 7.32−7.37 (m, 3H), 7.49−7.55 (m, 2H); ^{13}C NMR δ −2.37 (CH_3), −1.80 (CH_3), 23.76 (CH_2), 24.20 (CHD, t, $J_{C-D} = 17.7$ Hz), 25.79 (CH_2), 34.99 (CH_2), 68.30 (CH_2), 75.83 (CH), 127.62 (CH × 2), 128.70 (CH), 133.55 (CH × 2), 139.57 (C); MS *m*/*z* (relative intensity) 235 (M^+, 0.1), 220 (M^+ − Me, 45), 135 (99), 43 (100). Anal. Calcd for $C_{14}H_{21}DOSi$: C, 71.43; H, 8.99; D, 0.86. Found: C, 71.23; H, 9.00; D, 0.86.

2-Dimethylphenylsilylmethyl-5-phenyltetrahydrofuran (18a, trans:cis = 85:15): bp 180 °C (0.50 Torr); IR (neat) 1248, 1112, 836, 824, 697 cm^{-1}; ^{1}H NMR δ 0.32−0.33 (s × 3, 6H), 1.09−1.22 (m, 1H) including 1.13 (dd, $J = 14.2$, 8.3 Hz), 1.35−1.58 (m, 2H), 1.70−1.84 (m, 1H), 1.88−2.07 (m, 1H), 2.17−2.38 (m, 1H), 4.02−4.12 (m, 0.15H), 4.27 (tt, $J = 8.3$, 5.9 Hz, 0.85H), 4.77 (dd, $J = 7.3$, 6.9 Hz, 0.15H), 4.96 (dd, $J = 8.4$, 6.4 Hz, 0.85H), 7.15−7.37 (m, 8H), 7.49−7.55 (m, 2H); ^{13}C NMR for major isomer δ −2.35 (CH_3), −2.01 (CH_3), 24.12 (CH_2), 35.35 (CH_2), 35.71 (CH_2), 77.74 (CH), 79.46 (CH), 125.43 (CH × 2), 126.83 (CH), 127.73 (CH × 2), 128.19 (CH × 2), 128.88 (CH), 133.57 (CH × 2), 139.12 (C), 144.29 (C), for minor isomer δ −2.01 (CH_3), 23.91 (CH_2), 33.77 (CH_2), 34.76 (CH_2), 77.20 (CH), 77.81 (CH), 125.71 (CH × 2), 128.00 (CH), 128.12 (CH × 2), 128.57 (CH), 143.68 (C); MS *m*/*z* (relative intensity) 296 (M^+, 0.8), 281 (M^+ − Me, 4), 135 (100). Anal. Calcd for $C_{19}H_{24}OSi$: C, 76.97; H, 8.16. Found: C, 77.13; H, 8.20.

2-Dimethylphenylsilylmethyl-5-hexyltetrahydrofuran (18b, trans:cis = 86:14): IR (neat) 2920, 1248, 1109, 838, 822, 727, 699 cm^{-1}; ^{1}H NMR δ 0.307 (s, 3H), 0.314 (s, 3H), 0.88 (t, $J = 6.6$ Hz, 3H), 1.00−1.10 (m, 1H) including 1.04 (dd, $J = 14.2$, 8.6 Hz), 1.25−1.57 (m, 13H), 1.80−2.05 (m, 2H), 3.63−3.73 (m, 0.14H), 3.82−3.95 (m, 1H), 4.05 (tt, $J = 8.3$, 5.9 Hz, 0.86H), 7.32−7.36 (m, 3H), 7.49−7.56 (m, 2H); ^{13}C NMR for major isomer δ −2.39 (CH_3), −2.12 (CH_3), 14.09 (CH_3), 22.61 (CH_2), 23.94 (CH_2), 26.29 (CH_2), 29.40 (CH_2), 31.84 (CH_2), 32.62 (CH_2), 34.88 (CH_2), 36.32 (CH_2), 76.10 (CH), 77.99 (CH), 127.69 (CH × 2), 128.82 (CH), 133.55 (CH × 2), 139.26 (C), for minor isomer δ −2.32 (CH_3), −1.99 (CH_3), 31.52 (CH_2), 31.57 (CH_2), 76.91 (CH), 78.76 (CH); MS *m*/*z* (relative intensity) 304 (M^+, 0.2), 289 (M^+ − Me, 8.7), 135 (100). Anal. Calcd for $C_{19}H_{32}OSi$: C, 74.93; H, 10.59. Found: C, 74.89; H, 10.55.

2-Dimethylphenylsilylmethyl-5-isopropyltetrahydrofuran (18c, trans:cis = 89:11): bp 100 °C (0.30 Torr); IR (neat) 2920, 1248, 1109, 838, 822, 727, 699 cm^{-1}; ^{1}H NMR δ 0.31 (s, 3H), 0.32 (s, 3H), 0.81−0.86 (m, 3H) including 0.82 (d, $J = 6.6$ Hz), 0.92−0.96 (m, 3H) including 0.93 (d, $J = 6.6$ Hz), 1.00−1.09 (m, 1H), 1.25−1.67 (m, 4H), 1.75−1.96 (m, 2H), 3.40 (q, $J = 6.9$ Hz, 0.11H), 3.59 (ddd, $J = 8.3$, 7.3, 5.6 Hz, 0.89H), 3.82−3.93 (m, 0.11H), 4.00 (tdd, $J = 7.9$, 6.6, 5.0 Hz, 0.89H), 7.32−7.36 (m, 3H), 7.50−7.54 (m, 2H); ^{13}C NMR for major isomer δ −2.39 (CH_3), −2.03 (CH_3), 18.40 (CH_3), 19.42 (CH_3), 23.94 (CH_2), 30.24 (CH_2), 33.52 (CH), 35.42 (CH_2), 76.53 (CH), 83.62 (CH), 127.68 (CH × 2), 128.78 (CH), 133.59 (CH × 2), 139.44 (C), for minor isomer δ −2.32 (CH_3), 18.61 (CH_3), 29.03 (CH_2), 33.32 (CH), 33.93 (CH_2), 76.80 (CH), 84.27 (CH); MS *m*/*z* (relative intensity) 262 (M^+, 0.2), 247 (M^+ − Me, 6), 75 (100). Anal. Calcd for $C_{16}H_{26}OSi$: C, 73.22; H, 9.98. Found: C, 73.24; H, 9.77.

2-Dimethylphenylsilylmethyl-4-phenyltetrahydrofuran (20a, trans:cis = 11:89): bp 150 °C (0.30 Torr); IR (neat) 1250, 1110, 836, 698 cm^{-1}; ^{1}H NMR δ 0.34 (s, 6H), 1.09−1.24 (m, 1H) including 1.20 (dd, $J = 14.2$, 8.7 Hz), 1.35−1.59 (m, 1.89H) including 1.46 (dd, $J = 14.2$, 5.8 Hz), 1.83−2.10 (m, 0.22H), 2.35 (ddd, $J = 12.2$, 7.9, 5.3 Hz, 0.89H), 3.33−3.46 (m, 1H), 3.60 (dd, $J = 8.5$, 8.2, 0.11H), 3.79 (dd, $J = 8.3$, 7.9 Hz, 0.89H), 4.03−4.14 (m, 1.78H), 4.18−4.28 (m, 0.22H), 7.17−7.38 (m, 8H), 7.51−7.55 (m, 2H); ^{13}C NMR for major isomer δ −2.28 (CH_3), −2.17 (CH_3), 23.54 (CH_2), 43.76 (CH_2), 46.00 (CH), 73.73 (CH_2), 78.15 (CH), 126.29 (CH), 127.08 (CH × 2), 127.73 (CH × 2), 128.43 (CH × 2), 128.90 (CH), 133.48 (CH × 2), 138.81 (C), 143.11 (C), for minor isomer δ 24.14 (CH_2), 42.37 (CH_2), 44.85 (CH), 74.25 (CH_2), 77.47 (CH), 127.19 (CH × 2), 138.92 (C), 142.93 (C); MS *m*/*z* (relative intensity) 296 (M^+, 0.1), 281 (M^+ − Me, 8.0), 135 (100). Anal. Calcd for $C_{19}H_{24}OSi$: C, 76.97; H, 8.16. Found: C, 77.02; H, 8.17.

2-Dimethylphenylsilylmethyl-4-hexyltetrahydrofuran (20b, trans:cis = 15:85): bp 160 °C (0.30 Torr); IR (neat) 2920, 1248, 1113, 835, 727, 698 cm^{-1}; ^{1}H NMR δ 0.31 (s, 6H), 0.85−1.56 (m, 16H), 1.97−2.24 (m, 2H), 3.20 (dd, $J = 8.3$, 7.9 Hz, 0.15H), 3.41 (dd, $J = 7.9$, 7.6 Hz, 0.85H), 3.79 (t, $J = 7.9$ Hz, 0.85H), 3.86−4.04 (m, 1.15H), 7.32−7.37 (m, 3H), 7.48−7.54 (m, 2H); ^{13}C NMR for major isomer δ −2.28 (CH_3), −2.17 (CH_3), 14.07 (CH_3), 22.59 (CH_2), 23.79 (CH_2), 28.48 (CH_2), 29.38 (CH_2), 31.75 (CH_2), 34.11 (CH_2), 40.47 (CH), 41.62 (CH_2), 72.47 (CH_2), 77.65 (CH), 127.73 (CH × 2), 128.88 (CH), 133.53 (CH × 2), 139.08 (C), for minor isomer δ 23.97 (CH_2), 28.36 (CH_2), 33.75 (CH_2), 39.18 (CH), 40.38 (CH_2), 72.99 (CH_2), 77.20 (CH); MS

m/*z* (relative intensity) 289 (M^+ − Me, 11), 135 (100). Anal. Calcd for $C_{19}H_{32}OSi$: C, 74.93; H, 10.59. Found: C, 75.06; H, 10.59.

2-Dimethylphenylsilylmethyl-4-isopropyltetrahydrofuran (20c, trans:cis = 10:90): bp 90 °C (0.30 Torr); IR (neat) 2955, 1248, 1113, 836, 728, 698 cm^{-1}; ^1H NMR δ 0.31 (s, 6H), 0.81−0.87 (m, 6H) including 0.83 (d, J = 5.9 Hz) and 0.85 (d, J = 5.9 Hz), 0.95−1.12 (m, 2H) including 1.07 (dd, J = 14.2, 8.9 Hz), 1.24−1.65 (m, 2.1H) including 1.35 (dd, J = 14.2, 5.4 Hz), 1.82−2.01 (m, 1.9H), 3.25 (t, J = 8.9 Hz, 0.1H), 3.48 (dd, J = 8.2, 7.6 Hz, 0.9H), 3.81 (t, J = 8.2 Hz, 0.9H), 3.87−4.01 (m, 1.1H), 7.32−7.37 (m, 3H), 7.48−7.54 (m, 2H); ^{13}C NMR for major isomer δ −2.30 (CH_3), −2.16 (CH_3), 21.33 (CH_3), 21.46 (CH_3), 23.67 (CH_2), 32.27 (CH), 40.05 (CH_2), 48.09 (CH), 71.13 (CH_2), 77.86 (CH), 127.70 (CH × 2), 128.85 (CH), 133.52 (CH × 2), 139.11 (C), for minor isomer δ 21.21 (CH_3), 24.19 (CH_2), 31.72 (CH), 38.56 (CH_2), 46.64 (CH), 71.65 (CH_2), 77.00 (CH); MS *m*/*z* (relative intensity) 262 (M^+, 0.3) 247 (M^+ − Me, 11), 75 (100). Anal. Calcd for $C_{16}H_{26}OSi$: C, 73.22; H, 9.98. Found: C, 73.22; H, 10.03.

***trans*-2-Dimethylphenylsilylmethyl-3-phenyltetrahydrofuran (*trans*-22a)**: bp 180 °C (0.50 Torr); IR (neat) 1247, 1112, 836, 819, 698 cm^{-1}; ^1H NMR δ 0.27 (s, 3H), 0.29 (s, 3H), 1.06 (dd, J = 14.8, 8.6 Hz, 1H), 1.10 (dd, J = 14.8, 5.0 Hz, 1H), 2.02 (dtd, J = 12.5, 8.6, 7.3 Hz, 1H), 2.30−2.42 (m, 1H), 2.81 (dt, J = 8.6, 8.3 Hz, 1H), 3.86−4.05 (m, 3H), 7.13−7.33 (m, 8H), 7.43−7.49 (m, 2H); ^{13}C NMR δ −2.57 (CH_3), −1.74 (CH_3), 21.30 (CH_2), 35.33 (CH_2), 54.39 (CH), 66.99 (CH_2), 83.98 (CH), 126.46 (CH), 127.65 (CH × 4), 128.53 (CH × 2), 128.71 (CH), 133.62 (CH × 2), 139.62 (C), 142.14 (C); MS *m*/*z* (relative intensity) 281 (M^+ − Me, 2.1), 118 (100). Anal. Calcd for $C_{19}H_{24}OSi$: C, 76.97; H, 8.16. Found: C, 77.17; H, 8.31.

***trans*-2-Dimethylphenylsilylmethyl-3-pentyltetrahydrofuran (*trans*-22b)**: bp 135 °C (0.30 Torr); IR (neat) 2920, 1246, 1112, 837, 820, 698 cm^{-1}; ^1H NMR δ 0.33 (s, 3H), 0.34 (s, 3H), 0.87 (t, J = 6.8 Hz, 3H), 0.98−1.65 (m, 12H) including 1.03 (dd, J = 14.5, 8.6 Hz) and 1.14 (dd, J = 14.5, 4.6 Hz), 2.03 (dtd, J = 11.9, 7.6, 5.3 Hz, 1H), 3.50 (ddd, J = 8.6, 6.9, 4.6 Hz, 1H), 3.70 (td, J = 8.3, 5.6 Hz, 1H), 3.81 (ddd, J = 8.3, 7.5, 6.6 Hz, 1H), 7.31−7.36 (m, 3H), 7.51−7.57 (m, 2H); ^{13}C NMR δ −2.48 (CH_3), −1.70 (CH_3), 14.05 (CH_3), 22.21 (CH_2), 22.57 (CH_2), 28.09 (CH_2), 32.01 (CH_2), 32.29 (CH_2), 32.74 (CH_2), 47.78 (CH), 66.33 (CH_2), 82.28 (CH), 127.66 (CH × 2), 128.70 (CH), 133.59 (CH × 2), 139.82 (C); MS *m*/*z* (relative intensity) 290 (M^+, 0.2), 275 (M^+ − Me, 6.7), 135 (100). Anal. Calcd for $C_{18}H_{30}OSi$: C, 74.42; H, 10.41. Found: C, 74.50; H, 10.53.

Oxidative Cleavage of Si−C Bond (Typical Procedure). Method A.[21] H_2O_2 (30% in water, 2.3 mL, 20 mmol) was added to a mixture of **18g** (352 mg, 1.60 mmol), $KHCO_3$ (160 mg, 1.60 mmol), MeOH (3.9 mL), and THF (3.9 mL), and then the mixture was stirred for 2 h at 60 °C. The reaction mixture was poured into water (50 mL) and extracted with Et_2O (2 × 30 mL). The combined organic layer was washed with 10% aqueous $NaHSO_3$ (30 mL) and saturated aqueous $NaHCO_3$ (30 mL), dried, and evaporated. Purification by column chromatography (SiO_2, hexane−AcOEt 1:1) gave 2-hydroxymethyl-5-phenyltetrahydrofuran (**23a**, 276 mg, 97%, trans:cis = 96:4).

23a: bp 145 °C (0.41 Torr); IR (neat) 3420 (br), 1044, 700 cm^{-1}; ^1H NMR δ 1.61 (br s, 1H), 1.76−1.96 (m, 2H), 2.03−2.16 (m, 2H), 2.28−2.43 (m, 1H), 3.55−3.85 (m, 2H) including 3.74 (ddd, J = 11.5, 6.9, 3.3 Hz), 4.17−4.25 (m, 0.04H), 4.33−4.42 (m, 0.96H), 4.93 (dd, J = 7.8, 6.4 Hz, 0.04H), 5.01 (dd, J = 7.9, 5.9 Hz, 0.96H), 7.23−7.36 (m, 5H); ^{13}C NMR for major isomer δ 27.83 (CH_2), 35.35 (CH_2), 65.09 (CH_2), 80.13 (CH), 80.87 (CH), 125.56 (CH × 2), 127.29 (CH), 128.33 (CH × 2), 142.86 (C); MS *m*/*z* (relative intensity) 178 (M^+, 7.3), 91 (100). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92%. Found: C, 74.22; H, 8.04%.

Method B.[22] *t*-BuOK (40 mg, 0.32 mmol) was added to a solution of **18a** (85.0 mg, 0.287 mmol, trans:cis = 92:8) in DMSO (0.7 mL). The mixture was stirred for 6 h at room temperature and then diluted with phosphate buffer solution (pH 7, 10 mL). The extract with ether (2 × 10 mL) was evaporated. MeOH (1 mL), $KHCO_3$ (63 mg, 0.63 mmol), TBAF (1M in THF, 1.1 mL, 1.1 mmol), and H_2O_2 (30% in water, 0.40 mL, 3.5 mmol) were added to the residue. The mixture was stirred for 14 h at 40 °C and then poured into 10% aqueous $Na_2S_2O_3$ (20 mL). The extract with Et_2O (2 × 10 mL) was dried and evaporated. Purification by column chromatography (SiO_2, hexane−AcOEt 1:1) gave **23a** (30.1 mg, 59%, trans:cis = 90:10).

Method C. TBAF (1.0 M in THF, 1.5 mL, 1.5 mmol), MeOH (1.5 mL), $KHCO_3$ (83 mg, 0.83 mmol), and H_2O_2 (30% in water, 0.45 mL, 4.0 mmol) were added to **18k** (126 mg, 0.406 mmol, trans:cis = 88:12). The mixture was stirred for 11 h at 40 °C. The same workup and purification as described for method B gave **23a** (67 mg, 93%, trans:cis = 88:12).

2-Hydroxymethyl-5-hexyltetrahydrofuran (23b, trans:cis = 87:13): bp 110 °C (0.31 Torr); IR (neat) 3430 (br), 2930, 1044 cm^{-1}; ^1H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.28−1.73 (m, 12H), 1.83−2.08 (m, 3H), 3.43−3.53 (m, 1H), 3.59−3.74 (m, 1H) including 3.63 (ddd, J = 11.6, 6.9, 3.3 Hz), 3.82−4.15 (m, 2H); ^{13}C NMR for major isomer δ 14.04 (CH_3), 22.57 (CH_2), 26.13 (CH_2), 27.53 (CH_2), 29.36 (CH_2), 31.79 (CH_2), 32.02 (CH_2), 35.73 (CH_2), 65.03 (CH_2), 78.83 (CH), 79.50 (CH), for minor isomer δ 27.03 (CH_2), 31.38 (CH_2), 35.90 (CH_2), 65.28 (CH_2), 79.16 (CH), 80.20 (CH); MS *m*/*z* (relative intensity) 155 (M^+ − CH_2OH, 45), 41 (100). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.59; H, 11.90.

2-Hydroxymethyl-5-isopropyltetrahydrofuran (23c, trans:cis = 93:7): bp 160 °C (38 Torr); IR (neat) 3425 (br), 2965, 1045 cm^{-1}; ^1H NMR δ 0.85−0.89 (m, 3H) including 0.87 (d, J = 6.9 Hz), 0.95−0.99 (m, 3H) including 0.96 (d, J = 6.6 Hz), 1.52−1.75 (m, 3H), 1.87−2.02 (m, 3H), 3.44−3.67 (m, 3H), 3.98−4.12 (m, 1H); ^{13}C NMR for major isomer δ 18.09 (CH_3), 19.19 (CH_3), 27.68 (CH_2), 29.20 (CH_2), 32.89 (CH), 64.82 (CH_2), 79.32 (CH), 84.76 (CH), for minor isomer δ 18.27 (CH_3), 27.13 (CH_2), 28.46 (CH_2), 65.16 (CH_2), 79.18 (CH), 85.42 (CH); MS *m*/*z* (relative intensity) 113 (M^+ − CH_2OH, 23), 57 (100). Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.70; H, 11.03.

2-Hydroxymethyl-4-phenyltetrahydrofuran (24, trans:cis = 15:85): bp 120 °C (0.55 Torr); IR (neat) 3420 (br), 2925, 1602, 1495, 1454 cm^{-1}; ^1H NMR δ 1.82−1.95 (m, 0.85H), 2.05−2.24 (m, 1.30H), 2.35 (ddd, J = 12.5, 7.6, 6.3 Hz, 0.85H), 3.41−3.83 (m, 4H), 4.18−4.34 (m, 2H), 7.19−7.35 (m, 5H); ^{13}C NMR for major isomer δ 35.73 (CH_2), 45.49 (CH), 64.76 (CH_2), 74.34 (CH_2), 80.46 (CH), 126.69 (CH), 127.20 (CH × 2), 128.58 (CH × 2), 141.22 (C), for minor isomer δ 35.66 (CH_2), 44.96 (CH), 65.16 (CH_2), 74.77 (CH_2), 79.50 (CH), 126.60 (CH), 141.96 (C); MS *m*/*z* (relative intensity) 178 (M^+, 3.1), 41 (100). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.02; H, 7.88.

***trans*-2-Hydroxymethyl-3-phenyltetrahydrofuran (*trans*-25a)**: bp 145 °C (0.59 Torr); IR (neat) 3415 (br), 3025, 1050, 756, 701 cm^{-1}; ^1H NMR δ 1.87 (br s, 1H), 2.18 (ddt, J = 12.5, 9.6, 8.3 Hz, 1H), 2.39 (dddd, J = 12.5, 8.3, 6.9, 4.3 Hz, 1H), 3.20 (dt, J = 9.6, 8.3 Hz, 1H), 3.54 (dd, J = 11.6, 5.0 Hz, 1H), 3.75 (dd, J = 11.6, 3.0 Hz, 1H), 3.94 (ddd, J = 8.3, 5.0, 3.0 Hz, 1H), 4.01 (td, J = 8.3, 6.9 Hz, 1H), 4.12 (td, J = 8.3, 4.3 Hz, 1H), 7.20−7.36 (5H); ^{13}C NMR δ 35.40 (CH_2), 46.08 (CH), 62.77 (CH_2), 68.25 (CH_2), 86.29 (CH), 126.77 (CH), 127.60 (CH × 2), 128.70 (CH × 2), 141.15 (C); MS *m*/*z* (relative intensity) 178 (M^+, 2.3), 147 (100). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.74; H, 8.05.

***trans*-2-Hydroxymethyl-3-pentyltetrahydrofuran (*trans*-25b)**: IR (neat) 3400 (br), 2905, 1449, 1042 cm^{-1}; ^1H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.25−1.50 (m, 8H), 1.58 (dq, J = 11.9, 7.9 Hz, 1H), 1.66−2.00 (m, 2H), 2.09 (dddd, J = 11.9, 7.6, 6.6, 4.6 Hz, 1H), 3.51 (dd, J = 11.2, 5.9 Hz, 1H), 3.54−3.61 (m, 1H), 3.71 (dd, J = 11.2, 2.6 Hz, 1H), 3.80 (td, J = 8.3, 6.6 Hz, 1H), 3.88 (td, J = 8.3, 4.6 Hz, 1H); ^{13}C NMR δ 13.95 (CH_3), 22.48 (CH_2), 27.93 (CH_2), 31.86 (CH_2), 32.98 (CH_2), 33.01 (CH_2), 40.15 (CH), 63.99 (CH_2), 67.46 (CH_2), 85.05 (CH); MS *m*/*z* (relative intensity) 141 (M^+ − CH_2OH, 65), 55 (100). HRMS calcd for $C_9H_{17}O$ (M^+ − CH_2OH): 141.1279. Found: 141.1277.

Conversion of Alcohols to Iodides (Typical Procedure). A solution of **23a** (178 mg, 1.00 mmol, trans:cis = 96:4) in CH_2Cl_2 (2 mL) was added to a mixture of TsCl (286 mg, 1.50 mmol), Et_3N (0.42 mL, 3.0 mmol), and CH_2Cl_2 (1 mL) at room temperature. After 15 h the reaction mixture was poured into saturated aqueous $NaHCO_3$ (20 mL). The extract with Et_2O (3 × 20 mL) was dried and evaporated. The residual oil was treated with NaI (900 mg, 6.00 mmol) in acetone (3 mL) at 60 °C for 23 h. The resultant mixture was subjected to the same workup as described for the above tosylation. Purification by column chroma-

tography (SiO_2, hexane−AcOEt 20:1) gave 2-iodomethyl-5-phenyltetrahydrofuran (**26a**, 258 mg, 89%, trans:cis = 96:4).

26a (trans:cis = 96:4): bp 140 °C (0.31 Torr); IR (neat) 1047, 697 cm^{-1}; ^1H NMR δ 1.77−2.00 (m, 2H), 2.25−2.47 (m, 2H), 3.25−3.41 (m, 2H) including 3.29 (dd, J = 9.9, 7.3 Hz) and 3.37 (dd, J = 9.9, 4.6 Hz), 4.12−4.21 (m, 0.04H), 4.28−4.37 (m, 0.96H), 4.96 (dd, J = 7.6, 6.6 Hz, 0.04H), 5.12 (dd, J = 7.9, 6.3 Hz, 0.96H), 7.21−7.37 (m, 5H); ^{13}C NMR for major isomer δ 10.95 (CH_2), 32.78 (CH_2), 35.35 (CH_2), 78.85 (CH), 81.46 (CH), 125.43 (CH × 2), 127.23 (CH), 128.24 (CH × 2), 142.64 (C), for minor isomer δ 10.59 (CH_2), 31.77 (CH_2), 34.25 (CH_2), 78.55 (CH), 82.09 (CH), 125.74 (CH); MS *m*/*z* (relative intensity) 288 (M^+, 43), 147 ($M^+ - CH_2I$, 78), 55 (100). Anal. Calcd for $C_{11}H_{13}IO$: C, 45.85; H, 4.55. Found: C, 45.59; H, 4.40.

2-Iodomethyl-5-hexyltetrahydrofuran (26b, trans:cis = 87:13): bp 100 °C (0.20 Torr); IR (neat) 2935, 1045 cm^{-1}; ^1H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.28−1.75 (m, 12H), 1.92−2.24 (m, 2H), 3.13−3.31 (m, 2H) including 3.17 (dd, J = 9.6, 7.6 Hz) and 3.27 (dd, J = 9.6, 4.6 Hz), 3.87−4.02 (m, 0.26H), 3.99−4.12 (m, 1.74H); ^{13}C NMR for major isomer δ 11.23 (CH_2), 14.06 (CH_3), 22.57 (CH_2), 25.97 (CH_2), 29.34 (CH_2), 31.77 (CH_2), 32.17 (CH_2), 32.56 (CH_2), 35.78 (CH_2), 77.90 (CH), 80.31 (CH), for minor isomer δ 10.93 (CH_2), 26.05 (CH_2), 30.96 (CH_2), 31.52 (CH_2), 36.09 (CH_2), 78.26 (CH), 80.96 (CH); MS *m*/*z* (relative intensity) 296 (M^+, 0.1), 55 (100). Anal. Calcd for $C_{11}H_{21}IO$: C, 44.61; H, 7.15. Found: C, 44.80; H, 7.33.

2-Iodomethyl-5-isopropyltetrahydrofuran (26c, trans:cis = 93:7) (CAS Registry No. [78631-56-8] for trans isomer, [78631−52−4] for cis isomer; registry numbers provided by the author):[25] ^1H NMR δ 0.84−0.98 (m, 6H) including 0.85 (d, J = 6.6 Hz) and 0.95 (d, J = 6.6 Hz), 1.61−1.74 (m, 3H), 1.95−2.24 (m, 2H), 3.12−3.32 (m, 2H) including 3.16 (dd, J = 9.9, 7.6 Hz) and 3.28 (dd, J = 9.6, 4.6 Hz), 3.59−3.68 (m, 0.07H), 3.72−3.80 (m, 0.93H), 3.94−4.10 (m, 1H).

***trans*-2-Iodomethyl-3-phenyltetrahydrofuran (*trans*-30a)**: bp 130 °C (0.60 Torr); IR (neat) 2873, 1601, 1493, 1047, 756 cm^{-1}; ^1H NMR δ 2.26 (ddt, J = 12.5, 9.5, 8.3 Hz, 1H), 2.40−2.53 (m, 1H), 3.07−3.17 (m, 1H), 3.21 (dd, J = 10.4, 5.4 Hz, 1H), 3.41 (dd, J = 10.4, 3.9 Hz, 1H), 3.73 (ddd, J = 9.2, 5.3, 3.9 Hz, 1H), 4.04−4.18 (m, 2H), 7.22−7.38 (m, 5H); ^{13}C NMR δ 9.62 (CH_2), 35.24 (CH_2), 50.98 (CH), 68.11 (CH_2), 84.28 (CH), 126.95 (CH), 127.44 (CH × 2), 128.73 (CH × 2), 140.43 (C); MS *m*/*z* (relative intensity) 288 (M^+, 6.0), 161 (100). Anal. Calcd for $C_{11}H_{13}IO$: C, 45.86; H, 4.55. Found: C, 45.89; H, 4.55.

***trans*-2-Iodomethyl-3-pentyltetrahydrofuran (*trans*-30b)**: IR (neat) 2925, 1460, 1049 cm^{-1}; ^1H NMR δ 0.87−0.93 (m, 3H), 1.21−1.56 (m, 8H), 1.64 (dq, J = 11.9, 7.7 Hz, 1H), 1.86−2.00 (m, 1H), 2.09−2.22 (m, 1H), 3.22 (dd, J = 10.4, 5.6 Hz, 1H), 3.36 (dd, J = 10.4, 4.8 Hz, 1H), 3.45−3.52 (m, 1H), 3.82−3.96 (m, 2H); ^{13}C NMR δ 10.51 (CH_2), 13.98 (CH_3), 22.50 (CH_2), 27.78 (CH_2), 31.83 (CH_2), 32.89 (CH_2), 33.10 (CH_2), 44.94 (CH), 67.64 (CH_2), 83.31 (CH); MS *m*/*z* (relative intensity) 282 (M^+, 0.6), 55 (100). HRMS calcd for $C_{10}H_{19}IO$: 282.0481. Found: 282.0470.

Iodocyclization of Alkenols (Typical Procedure).[25] A mixture of 1-phenyl-4-penten-1-ol (**27a**, 324 mg, 2.00 mmol) and $NaHCO_3$ (252 mg, 3.00 mmol) in CH_3CN (5 mL) was treated with I_2 (761 mg, 3.00 mmol) at 0 °C for 4.5 h. The reaction mixture was poured into 10% aqueous $Na_2S_2O_3$ (20 mL). The extract with Et_2O (3 × 15 mL) was dried and evaporated. Purification by column chromatography (SiO_2, hexane−AcOEt, 20:1) gave **26a** (351 mg, 61%, trans:cis = 74:26).

2-Iodomethyl-3-phenyltetrahydrofuran (30a, trans:cis = 64:36): bp 130 °C (0.60 Torr); IR (neat) 2970, 1601, 1493, 1047, 756 cm^{-1}; ^1H NMR δ 2.16−2.33 (m, 1H), 2.40−2.55 (m, 1H), 2.70 (dd, J = 10.1, 5.6 Hz, 0.36H), 2.89 (dd, J = 10.1, 8.0 Hz, 0.36H), 3.07−3.17 (m, 0.64H), 3.21 (dd, J = 10.4, 5.4 Hz, 0.64H), 3.41 (dd, J = 10.4, 3.9 Hz, 0.64H), 3.52 (ddd, J = 8.3, 5.6, 5.6 Hz, 0.36H), 3.73 (ddd, J = 9.2, 5.3, 3.9 Hz, 0.64H), 3.98 (ddd, J = 8.6, 8.6, 7.1 Hz, 0.36H), 4.04−4.18 (m, 1.28H), 4.21−4.33 (m, 0.72H), 7.19−7.38 (m, 5H); ^{13}C NMR (see *trans*-**30a** for trans isomer) for cis isomer δ 5.39 (CH_2), 33.07 (CH_2), 47.57 (CH), 67.26 (CH_2), 82.50 (CH), 126.70 (CH), 128.23 (CH × 2), 128.30 (CH × 2), 139.82 (C); MS *m*/*z* (relative intensity) for cis isomer 288 (M^+, 6.1), 117 (100). Anal. Calcd for $C_{11}H_{13}IO$: C, 45.86; H, 4.55. Found: C, 45.97; H, 4.66.

2-Iodomethyl-3-pentyltetrahydrofuran (30b, trans:cis = 57:43): bp 115 °C (0.70 Torr); IR (neat) 2925, 1458, 1178, 1049 cm^{-1}; ^1H NMR δ 0.90 (t, J = 6.5 Hz, 3H), 1.14−1.56 (m, 8H), 1.58−1.79 (m, 1H), 1.88−2.29 (m, 2H), 3.09−3.22 (m, 0.86H), 3.22 (dd, J = 10.4, 5.6 Hz, 0.57H), 3.36 (dd, J = 10.4, 4.8 Hz, 0.57H), 3.45−3.52 (m, 0.57H), 3.76−4.02 (m, 2H), 4.14 (ddd, J = 8.0, 6.2, 5.6 Hz, 0.43H); ^{13}C NMR (see *trans*-**30b** for trans isomer) for cis isomer δ 6.20 (CH_2), 14.04 (CH_3), 22.55 (CH_2), 27.94 (CH_2), 28.02 (CH_2), 28.89 (CH_2), 31.86 (CH_2), 41.94 (CH), 66.99 (CH_2), 81.28 (CH); MS *m*/*z* (relative intensity) for cis isomer 282 (M^+, 0.2), 55 (100). Anal. Calcd for $C_{10}H_{19}IO$: C, 42.57; H, 6.79. Found: C, 42.52; H, 7.00.

Iodocyclization of 2,6-Dichlorobenzyl Ethers (Typical Procedure).[25] A solution of 5-(2,6-dichlorobenzyloxy)-1-undecene (**28b**, 329 mg, 1.00 mmol) in CH_3CN (5 mL) was treated with I_2 (380 mg, 1.50 mmol) at 0 °C for 1 h. The reaction mixture was subjected to the same workup as iodocyclization of alkenols. Purification by column chromatography (SiO_2, hexane−AcOEt, 20:1) gave **26b** (247 mg, 83%, trans:cis = <2:98).

***cis*-26b**: bp 115 °C (0.53 Torr); IR (neat) 2910, 1451, 1085, 1040 cm^{-1}; ^1H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.19−1.79 (m, 12H), 1.91−2.13 (m, 2H), 3.16 (dd, J = 9.8, 6.8 Hz, 1H), 3.26 (dd, J = 9.8, 4.5 Hz, 1H), 3.86−4.02 (m, 2H); ^{13}C NMR δ 10.93 (CH_2), 14.05 (CH_3), 22.57 (CH_2), 26.06 (CH_2), 29.33 (CH_2), 30.95 (CH_2), 31.52 (CH_2), 31.77 (CH_2), 36.08 (CH_2), 78.26 (CH), 80.95 (CH); MS *m*/*z* (relative intensity) 211 ($M^+ - C_6H_{13}$, 0.2), 55 (100). Anal. Calcd for $C_{11}H_{21}IO$: C, 44.61; H, 7.15. Found: C, 44.91; H, 7.38.

Deoxygenation of Alcohol 24. BuLi (1.69 M in hexane, 0.74 mL, 1.25 mmol) was added dropwise to a solution of **24** (cis:trans = 85:15, 203 mg, 1.14 mmol) in THF (4 mL) at −78 °C. After 10 min, a THF (2 mL) solution of TsCl (238 mg, 1.25 mmol) was added to the mixture. After additional 10 min, the mixture was warmed to room temperature and stirred for 30 min. The resulting mixture was subjected to a usual aqueous workup. The crude product obtained (a white solid) was dissolved in THF (2 mL) and added to a suspension of $LiAlH_4$ (50 mg, 1.3 mmol) in THF (3 mL) at 0 °C. After being stirred at room temperature for 12 h, the resulting mixture was quenched with 20% aqueous potassium sodium tartrate (15 mL). The extract with *t*-BuOMe (2 × 20 mL) was dried and evaporated. Purification of the residual oil by column chromatography (SiO_2, hexane−AcOEt 10:1) gave 2-methyl-4-phenyltetrahydrofuran (**29**, 124 mg, 67%, cis:trans = 85:15).

29: bp 130 °C (26 Torr); IR (neat) 2968, 756, 700 cm^{-1}; ^1H NMR δ 1.30 (d, J = 6.1 Hz, 0.45H), 1.36 (d, J = 6.1 Hz, 2.55H), 1.62 (dt, J = 12.2, 10.0 Hz, 0.85H), 1.97 (ddd, J = 12.5, 9.1, 6.4 Hz, 0.15H), 2.15 (dt, J = 12.5, 7.2 Hz, 0.15H), 2.45 (ddd, J = 12.2, 7.6, 5.4 Hz, 0.85H), 3.40−3.53 (m, 1H), 3.70 (t, J = 8.3 Hz, 0.15H), 3.83 (dd, J = 8.2, 7.9 Hz, 0.85H), 4.08−4.34 (m, 2H), 7.17−7.34 (m, 5H); ^{13}C NMR for cis isomer δ 20.86 (CH_3), 42.86 (CH_2), 45.94 (CH), 74.34 (CH_2), 76.35 (CH), 126.44 (CH), 127.17 (CH × 2), 128.53 (CH × 2), 142.88 (C), for trans isomer δ 21.63 (CH_3), 41.37 (CH_2), 44.75 (CH), 74.74 (CH_2), 75.48 (CH), the signals of the phenyl group overlapped those of cis isomer; MS *m*/*z* (relative intensity) for cis isomer 162 (M^+, 21), 117 (100), for trans isomer 162 (M^+, 17), 117 (100).

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Supporting Information Available: Experimental procedures for the syntheses of vinylsilanes **1**, **6**, **8**, **11**, **14**, **17**, **19**, and **21**, alkenols **10**, **27**, and **31**, authentic samples of **12**, **13**, **15**, **16**, and *cis*-**29**, and dichlorobenzyl ethers **28**; spectral data for all substrates, their synthetic intermediates, and cyclized products **18d**−**k**, **20d**−**j**, and **22c**−**g**; and yield at each reaction time in the cyclization of (*Z*)-**1a** and (*E*)-**1a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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