Intramolecular Reaction of (γ-Alkoxyallyl)stannane with Aldehyde: Origin of the Stereoselectivities

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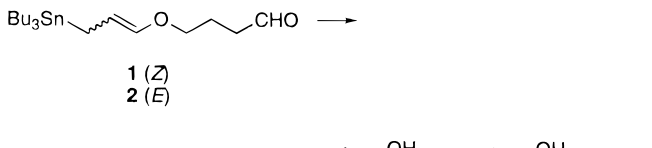
The intramolecular cyclization of simple acyclic (γ-alkoxyallyl)stannane aldehydes **1**, **2**, and **12**−**15** was investigated to elucidate the relationship between the geometry of the double bond of the allylstannanes, the ring size of cyclic ethers produced by the cyclization, and the procedures for promoting the cyclization. The Lewis acid-mediated cyclization of **1**-**2**, **12**-**13**, and **14**-**15** gave the *trans* cyclic ethers **3**, **39**, and **41**, respectively, either predominantly or exclusively irrespective of the geometry of the double bond and of the ring size of the cyclic ethers. The relationship in the thermal cyclization of **1** and **2**, which gave the 6-membered cyclic ethers **4** and **3**, was straightforward; the *Z* isomer **1** gave the *cis* product **4**, and the *E* isomer **2** afforded the *trans* product **3**. However, the relationship in the thermal cyclization of **12** and **13** which afforded the 5-membered cyclic ethers **39** and **40** was different from that expected from the cyclization *via* the well-accepted cyclic transition state, as observed in the case of **1** and **2**. Both the *Z* (**12**) and *E* (**13**) isomers gave the *cis* cyclic ether **40** either predominantly or exclusively. The protic acid-mediated (or -catalyzed) cyclization of **12**-**13** and **14**-**15** gave the *trans* cyclic ethers **39** and **41**, respectively, regardless of the geometry of the double bonds. On the other hand, the protic acid-promoted cyclization of **1** and **2** was very strange; the *Z* isomer **1** gave the *cis* isomer **4**, and the *E* isomer **2** afforded the *trans* isomer **3**. The mechanisms for these cyclization reactions are proposed.

Introduction

In recent years there has been an explosion of interest in biologically active natural products of marine origin.[1] Owing to their structural novelty and toxicity, polycyclic ethers are particularly attractive targets for synthetic chemists.[2] In view of the structural feature, synthetic approach requires an efficient method for the synthesis of β-hydroxy cyclic ether as a constituent unit. We developed a new strategy for the construction of cyclic ether *via* the intramolecular condensation of allylstannane with aldehyde.[3] As demonstrated by the total synthesis of hemibrevetoxin B[4] and related polycyclic ethers,[5] this route is efficient for the stereocontrolled construction of 7-membered cyclic ethers.

In addition, the formation of 6-membered cyclic ethers was studied by the intramolecular condensation method. The Lewis acid-mediated cyclization of **1** and **2** gave predominantly the *trans* isomer **3** regardless of the double-bond geometry (eq 1).[6] This stereoselectivity was



1 (*Z*)
2 (*E*)

3 (*trans*) **4** (*cis*) (1)

quite reasonable from the well-accepted theory for the Lewis acid-mediated allylic stannane−aldehyde condensation.[7] On the other hand, the protic acid-promoted reaction of **1** and **2** afforded **4** and **3**, respectively. Similar stereoselectivities were observed in the thermal cyclization. The stereoselectivities *via* the thermal cyclization were able to be explained by the well-accepted cyclic transition state,[7a,8] but those *via* the protic acid-promoted cyclization were very difficult to explain on the basis of the ordinary mechanisms. Accordingly, we proposed the push−pull mechanism.

During this study, a related cyclization was reported by Keck and co-workers.[9] The reaction of the *Z*-allylic stannane **5** in the presence of Lewis or protic acids afforded the *cis* product **8** predominantly. On the other

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(1) For recent reviews, see: (a) Shimizu, Y. *Chem. Rev.* **1993**, *93*, 1685−1698. (b) Yasumoto, T.; Murata, M. *Chem. Rev.* **1993**, *93*, 1897−1909.

(2) For recent review, see: Alvarez, E.; Candenas, M.-L.; Pérez, R.; Ravelo, J. L.; Martín, J. D. *Chem. Rev.* **1995**, *95*, 1953−1980 and references cited therein.

(3) (a) Yamamoto, Y.; Yamada, J.; Kadota, I. *Tetrahedron Lett.* **1991**, *32*, 7069−7072. (b) Yamamoto, Y.; Kadota, I. *Main Group Met. Chem.* **1994**, *17*, 269−289.

(4) (a) Kadota, I.; Park, J.-Y.; Koumura, N.; Pollaud, G.; Matsukawa, Y.; Yamamoto, Y. *Tetrahedron Lett.* **1995**, *36*, 5777−5780. (b) Kadota, I.; Yamamoto, Y. *Main Group Met. Chem.* **1996**, *19*, 361−366.

(5) (a) Suzuki, T.; Sato, O.; Hirama, M.; Yamamoto, Y.; Murata, M.; Yasumoto, T.; Harada, N. *Tetrahedron Lett.* **1991**, *32*, 4505−4508. (b) Ravelo, J. L.; Regueiro, A.; Martín, J. D. *Tetrahedron Lett.* **1992**, *33*, 3389−3392. (c) Alvarez, E.; Díaz, M. T.; Pérez, R.; Ravelo, J. L.; Regueiro, A.; Vera, J. A.; Zurita, D.; Martín, J. D. *J. Org. Chem.* **1994**, *59*, 2848−2870. (d) Kadota, I.; Matsukawa, Y.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1993**, 1638−1641. (e) Yamamoto, Y.; Kadota, I. *Bull. Soc. Chim. Belg.* **1994**, *103*, 619−629. (f) Alvarez, E.; Candenas, M.-L.; Pérez, R.; Ravelo, J. L.; Martín, J. D. *Chem. Rev.* **1995**, *95*, 1953−1980. (g) Oguri, H.; Hishiyama, S.; Oishi, T.; Hirama, M. *Synlett* **1995**, 1252−1254.

(6) Gevorgyan, V.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 1313−1316.

(7) For recent reviews, see: (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293. (b) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395−7426.

(8) For examples, see: (a) Marshall, J. A.; Dehoff, B. S.; Crooks, S. L. *Tetrahedron Lett.* **1987**, 527−530. (b) Hull, C.; Mortlock, S. V.; Thomas, E. J. *Tetrahedron Lett.* **1987**, 5343−5346.

(9) (a) Keck, G. E.; Dougherty, S. M.; Savin, K. A. *J. Am. Chem. Soc.* **1995**, *117*, 6210−6223. For a related work on intermolecular reactions, see: (b) Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889−7896.

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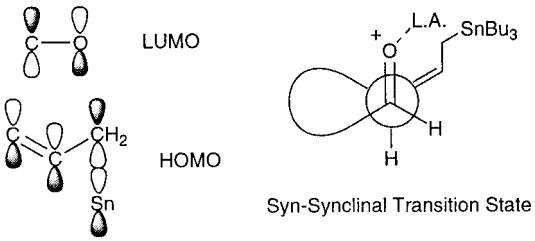
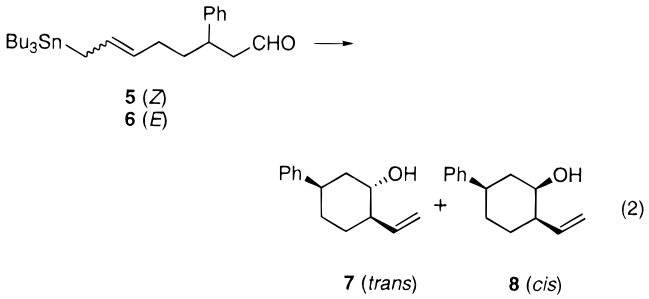
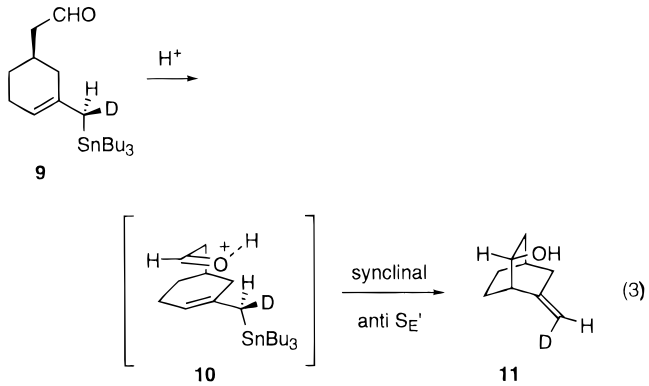


Figure 1. Proposed secondary orbital overlap in the *syn*-synclinal transition state.[9]

hand, the *E* substrate **6** afforded the *trans* isomer **7** as a major product (eq 2). On the basis of these results, the



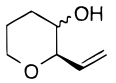
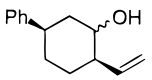
authors concluded that the stabilization by a secondary orbital overlap between the oxygen of the carbonyl and the stannyl methylene carbon is the most important factor for the determination of stereochemical outcome (Figure 1). The stereoselectivities observed in the cyclizations of **1**, **2**, **5**, and **6** are summarized in Table 1. Remarkable differences between our results and Keck's observations can be found in the Lewis acid-promoted cyclization of *Z* substrates (**1** and **5**) and the thermal cyclization of *E* substrates (**2** and **6**). More recently, Denmark et al. reported that the protic acid-promoted reaction of a conformationally rigid cyclic system (**9**) provided a bridged compound (**11**) with high stereoselectivity (eq 3).[10] It was concluded that the reaction



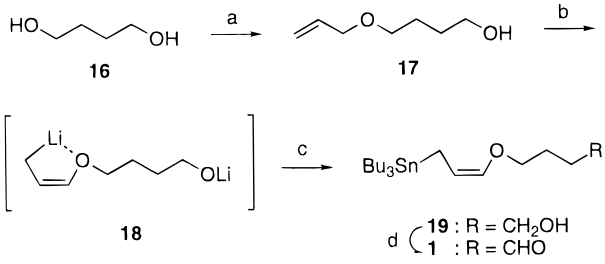
proceeded *via* an acyclic transition state (**10**) and there was no interaction between the tin atom and oxygen atom. Although the mechanisms proposed by Keck and Denmark are reasonable, at least in their own systems, and explain well their stereochemical results (eqs 2 and 3), it was difficult for us to explain the origin of the stereoselectivities in our cyclic ether synthesis based upon their mechanisms (Table 1). To elucidate the origin of the observed stereoselectivities in our previous studies, we examined the intramolecular cyclization of the simple

(10) Denmark, S. E.; Hosoi, S. *J. Org. Chem.* **1994**, *59*, 5133−5135.

Table 1. Summary of the Stereoselectivities in the Cyclization of 1, 2, 5, and 6

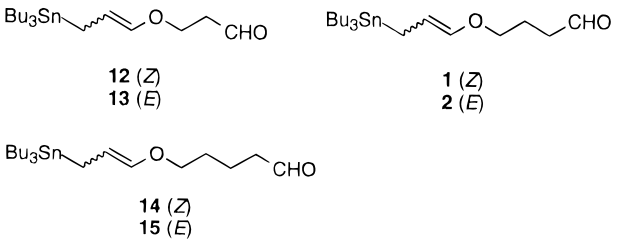
product	substrate	Lewis acid	protic acid	Δ
	**1** (*Z*)	*trans*	*cis*	*cis*
	2 (*E*)	*trans*	*trans*	*trans*
	**5** (*Z*)	*cis*	*cis*	*cis*
	6 (*E*)	*trans*	*trans*	*cis*

Scheme 1. Preparation of (*Z*)-(γ-Alkoxyallyl)stannane 1[a]



[a] (a) Allyl bromide, NaH, THF; (b) *s*-BuLi, TMEDA, THF; (c) *n*-Bu_3SnCl; (d) SO_3·py, DMSP, Et_3N, CH_2Cl_2.

acyclic substrates **1**, **2**, and **12**−**15** which would produce 5-, 6-, and 7-membered cyclic ethers.



Results

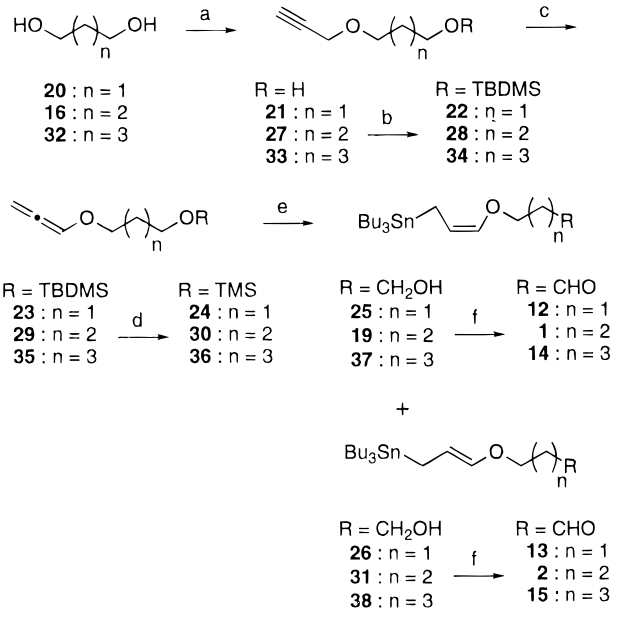
Preparation of the Substrates 1, 2, and 12−15. The (γ-alkoxyallyl)stannanes **1**, **2**, and **12**−**15**, having an aldehyde at the terminus of the carbon chain, were prepared as shown in Schemes 1 and 2. The *Z* isomer **1** was easily synthesized by the usual method (Scheme 1).[3] Selective monoallylation of 1,4-butanediol (**16**) with allyl bromide/NaH gave **17**. Treatment of **17** with 2.2 equiv of *s*-BuLi/TMEDA followed by trapping the resulting allylic anion **18** with *n*-Bu_3SnCl afforded **19** in 68% yield.[11] Oxidation of the alcohol **19** produced **1** in 66% yield. In contrast to preparation of (*Z*)-(γ-alkoxyallyl)-stannanes, there was great difficulty in the synthesis of the *E* isomers. The lithium anion−tin trapping method produced exclusively *Z*-allylic stannanes, as shown in Scheme 1, because a chelate (*Z*)-lithium derivative such as **18** is more stable than the corresponding *E* isomer. After several unfruitful attempts,[12] we found that the Pd^0-catalyzed hydrostannylation of allenyl ether provided an allowable route to the desired *E* isomers (Scheme 2).[13] The propargyl ether alcohol **21**, prepared from **20** and propargyl bromide/NaH, was converted into the TBDMS

(11) (a) Keck, G. E.; Abbott, D. E.; Wiley, M. R. *Tetrahedron Lett.* **1987**, *28*, 139−142. (b) Koreeda, M.; Tanaka, Y. *Tetrahedron Lett.* **1987**, *28*, 143−146.

(12) For example, hydrostannation of the corresponding propargyl ether gave an inseparable mixture of regioisomers.

(13) (a) Koerber, K.; Gore, K.; Vatele, J.-M. *Tetrahedron Lett.* **1991**, *32*, 1187−1190. (b) Gevorgyan, V.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2963−2967.

Scheme 2. Preparation of 1, 2, and 12−15[a]



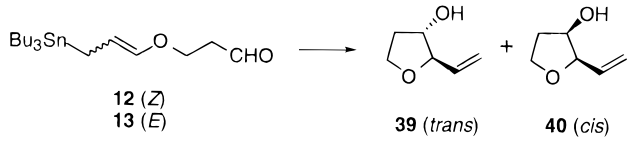
[a] (a) Propargyl bromide, NaH, THF; (b) TBDMSCl, imidazole, DMF; (c) *t*-BuOK; (d) (i) TBAF, THF, (ii) HMDS, TMSCl; (e) (i) *n*-Bu_3SnH, $Pd(PPh_3)_4$; (ii) K_2CO_3, MeOH; (f) SO_3·py, DMSO, Et_3N, CH_2Cl_2.

ether **22**. Isomerization of the propargyl ether **22** was performed by heating it in the presence of a catalytic amount of *t*-BuOK, affording the corresponding allenyl ether **23**.[14] Replacement of the TBDMS group of **23** with a TMS group by the traditional method gave **24**. Treatment of **24** with *n*-Bu_3SnH in the presence of a catalytic amount of $Pd(PPh_3)_4$ at 60 °C followed by desilylation gave a 5.5:1 mixture of **25** and **26** in 58% yield. The yield of the *E* isomer **26** was decreased at lower temperatures. Oxidation of each isomer afforded the aldehydes **12** and **13**, respectively. Other starting materials (**2**, **14**, and **15**) were prepared by the same procedure as above.[15]

Cyclization of 12 and 13. The results of the cyclization reactions of **12** and **13** are summarized in Table 2. The BF_3·OEt_2-mediated reaction gave the cyclized products **39** and **40** in good to very high yields, and high *trans* selectivity was obtained regardless of the geometry of the double bond of the starting materials (entries 1 and 4). Good *trans* selectivity was observed in the reaction in the presence of CF_3CO_2H (entries 3 and 6). The thermal cyclization of **12** proceeded with very high *cis* stereoselectivity, and the *cis* isomer **40** was obtained as the sole product (entry 2). The *cis* selectivity was decreased when **13** was used as a substrate (entry 5). In all cases, the cyclization products were obtained in good to nearly quantitative yields.

Cyclization of 1 and 2. The results on the reaction of **1** and **2** are summarized in Table 3. Both substrates cyclized in the presence of Lewis acids to give the *trans* isomer **3** predominantly in good to very high yields (entries 1, 2, 13, and 14). On the other hand, the

Table 2. Cyclizations of 12 and 13[a]

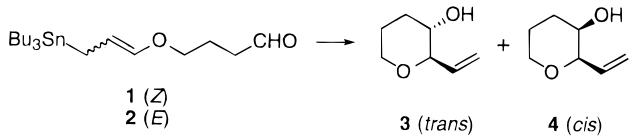


12 (*Z*)
13 (*E*)
39 (*trans*) **40** (*cis*)

entry	substrate	reagent	equiv	time (min)	temp (°C)	ratio (**39**:**40**)[b]	yield (%)[b]
1	**12**	BF_3·OEt_2	1.2	30	−78	90:10	>95
2		*c*		120	100	2:98<[d]	>95
3		CF_3CO_2H	2.0	10	−78	71:29	>95
4	**13**	BF_3·OEt_2	1.2	30	−78	93:7	79
5		*c*		120	100	30:70	>95
6		CF_3CO_2H	2.0	10	−78	83:17	87

[a] All reactions were carried out with 0.1 M substrate in CH_2Cl_2 under the conditions indicated in the table and quenched with Et_3N at the reaction temperature. [b] Ratios and yields were determined by capillary GLC analyses. Propiophenone was used as an internal standard. [c] Benzene was used as a solvent. [d] *Trans* isomer **39** was not detected.

Table 3. Cyclizations of 1 and 2[a]



1 (*Z*)
2 (*E*)
3 (*trans*) **4** (*cis*)

entry	substrate	reagent	equiv	time (min)	temp (°C)	ratio (**3**:**4**)[b]	yield (%)[b]
1	**1**	$TiCl_4$	2.0	30	−70	83:17	86
2		BF_3·OEt_2	2.0	30	−70	68:32	80
3		*c*		60	120	2:98<	78
4		CF_3SO_3H	2.0	5	−70	13:87	>95
5		CF_3SO_3H	*d*	15	−70	11:89	>95
6		CF_3SO_3H	*d*	15	−90	7:93	94
7		CF_3SO_3H	0.1	30	−70	20:80	>95
8		CF_3CO_2H	2.0	5	−70	10:90	>95
9		CCl_3CO_2H	2.0	5	−70	11:89	>95
10		CH_2ClCO_2H	2.0	600	0	25:75	>95
11		CH_3CO_2H	2.0	3600	25	29:71	66
12		HCl	2.0	5	−70	18:82	90
13	**2**	$TiCl_4$	2.0	30	−70	84:16	>95
14		BF_3·OEt_2	2.0	30	−70	87:13	>95
15		*c*		60	120	98:2	>95
16		CF_3SO_3H	2.0	5	−70	>98:2	>95
17		CF_3CO_2H	2.0	5	−70	97:3	>95
18		HCl	2.0	5	−70	97:3	86

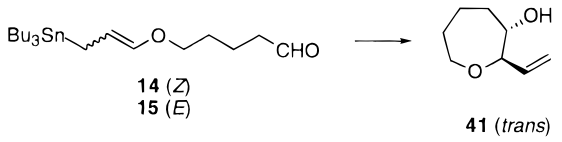
[a] All reactions were carried out with 0.1 M substrate in CH_2Cl_2 under the conditions indicated in the table and quenched with aqueous satd $NaHCO_3$ at the reaction temperature. [b] Ratios and yields were determined by capillary GLC analyses. Tetradecane was used as an internal standard. [c] Toluene was used as a solvent. [d] The substrate was added very slowly to the reagent, and thus at the initial stage of the reaction [CF_3SO_3H]:[**1**] >> 2:1. The final ratio was 2:1.

stereoselectivity of the thermal reaction strongly depended upon the substrate geometry, i.e., the reaction of the *Z* isomer **1** gave *cis* product **4** exclusively, whereas that of the *E* isomer **2** afforded **3** exclusively (entries 3 and 15). In each case, only one stereoisomer was detected. Notable stereoselectivities were observed in the protic acid-promoted cyclization. The reaction of **1** in the presence of CF_3SO_3H, CF_3CO_2H, and other protic acids proceeded smoothly to give **3** with good to high diastereoselectivities, the stereoselectivity being similar to that of the reaction *via* the Lewis acids (entries 4−12). However, the treatment of **2** with the protic acids afforded **4** either predominantly or exclusively (entries 16−18). The mode of the stereoselectivity in the protic acid-mediated reaction agrees with that in the thermal cyclization and is not in accord with that in the Lewis acid-mediated reaction. Interestingly, the use of a cata-

(14) Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acetylenes, Allenes and Cumulenes, a Laboratory Manual*; Elsevier: New York, 1981; pp 92−93.

(15) Although most of the early stage starting materials prepared according with known procedures[11,12] were characterized by IR and ^{1}H-NMR spectroscopic analyses only, the *Z*- and *E*-allylic stannanes **12**, **13**, **21**, **27**, **28**, **39**, and **40** were fully characterized by IR, ^{1}H-NMR, and elemental analyses or high-resolution mass spectra. Because of their low stability, the aldehydes **14**−**17** could not be fully characterized. See the Experimental Section.

Table 4. Cyclizations of 14 and 15[a]



14 (*Z*)
15 (*E*)

41 (*trans*)

entry	substrate	reagent	equiv	time (min)	temp (°C)	yield (%)[b]
1	**14**	BF_3·OEt_2	1.2	40	−78	45
2		$TiCl_4$	2.0	40	−78	28
3		*c*		1200	150	trace
4		CF_3SO_3H	2.0	40	−78	trace
5		CF_3CO_2H	2.0	30	−78	27
6		CCl_3CO_2H	2.0	900	25	0[d]
7		HCl	2.0	210	−78	12
8	**15**	BF_3·OEt_2	1.2	30	−78	79
9		*c*		1200	150	trace
10		CF_3SO_3H	2.0	40	−78	trace
11		CF_3CO_2H	2.0	30	−78	3
12		CCl_3CO_2H	2.0	900	25	0[d]
13		HCl	2.0	210	−78	trace

[a] All reactions were carried out with 0.1 M substrate in CH_2Cl_2 under the conditions indicated in the table and quenched with Et_3N at the reaction temperature. [b] Yields were determined by capillary GLC analyses. Propiophenone was used as an internal standard. No *cis* isomer was detected. [c] Benzene was used as a solvent. [d] Total decomposition of the starting material was observed.

42 (*trans*, J_{ab} = 2.5 Hz) **43** (*cis*, J_{ab} = 4.0 Hz)

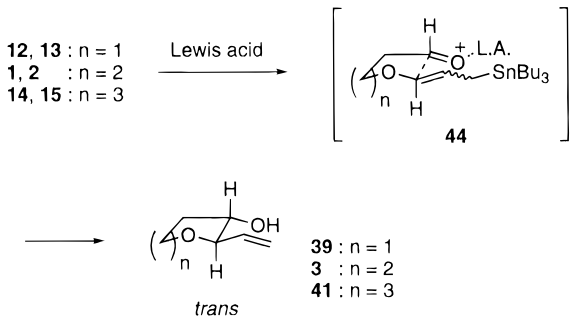
Figure 2. Comparison of the coupling constants of **42** and **43**.

lytic amount of CF_3SO_3H led to complete conversion of the substrate **1**, giving a 20:80 mixture of **3** and **4** in an essentially quantitative yield (entry 7).

Cyclization of 14 and 15. The results on the cyclization of **14** and **15** are summarized in Table 4. Very interestingly, in all cases the *trans* isomer **41** was obtained as the sole product regardless of the geometry of the substrates and the type of the reagents used. The use of BF_3·OEt_2 gave **41** in reasonable to good yields (entries 1 and 8). The use of $TiCl_4$ or protic acids gave **41** in an allowable to very low yields. In particular, the thermal reactions of **14** and **15** did not afford the cyclized product at all (entries 5 and 9). It was rather surprising for us to observe the inefficient thermal cyclization of the acyclic systems **14** and **15**, since the cyclization to a 7-membered ring in the cyclic systems proceeded very well in respect to the chemical yield and stereoselectivity.[3−5] Perhaps, in contrast to 6-membered ring formation, the cyclization to a 7-membered ring requires a certain constrained system in order to bring the γ-carbon of allylic stannane close to the aldehyde.

Structural Assignments of the Products. Because of the volatility of **39** and **40**, the stereochemistries of these products were confirmed by ^{1}H-NMR analyses of the benzoate derivatives **42** and **43**, prepared from **39** and **40** by the usual benzoylation method (Figure 2). The *trans* relationship between H_a and H_b of **42** was determined by the coupling constant of J_{ab} = 2.5 Hz, and the *cis* stereochemistry of **43** was confirmed by that of J_{ab} = 4.0 Hz.[16,17] The stereochemistries of the other compounds (**3**, **4**, and **41**) were determined by the comparison of their ^{1}H-NMR spectra with those of authentic materials.[18]

Scheme 3. Acyclic Transition State Model



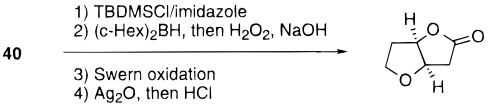
Transition State Structures and Origin of the Stereoselectivities. 1. Lewis Acid-Promoted Cyclization. It is widely accepted that the Lewis acid-mediated reaction of allylic stannanes with aldehydes proceeds *via* an acyclic transition state.[7] The Lewis acid-promoted cyclization of **1**, **2**, and **12**−**15** gave the *trans* isomers either predominantly or exclusively, regardless of the geometry of the double bond of the allylic stannanes. The *trans* preference can be explained by the well-accepted acyclic transition state model (Scheme 3).[7] To avoid the 1,3-diaxial repulsion, the allylic stannane moiety and the carbonyl oxygen of the substrates are oriented to a *pseudo*equatorial position as depicted by the synclinal transition state **44**, which leads to the *trans* cyclic ethers **3**, **39**, and **41** regardless of the double-bond geometry and of the size of the rings produced.

2. Thermal Reaction. The substrates **14** and **15** gave only trace amounts of cyclized products under the thermal conditions, and therefore the stereochemical discussion on the thermal reaction of **14** and **15** can not be made at the present time. The thermal reaction of **1**, **2**, **12**, and **13** proceeded smoothly to afford the desired cyclic ethers. As expected from the cyclic transition state models proposed for the thermal condensation, the stereochemical outcome of the products was strongly dependent upon the double-bond geometry of the substrates.[7a,8] As shown in Scheme 4, the (*Z*)-allylstannane **12** was converted to the *cis* isomer **40** with very high stereoselectivity *via* a *cis*-fused cyclic transition state (**45**). The (*E*)-allylstannane **13** gave also the *cis* isomer **40** predominantly, but the *cis* stereoselectivity in the cyclization of **13** was lower than that for **12**. Perhaps the reaction of **13** proceeds mainly through a *cis*-fused cyclic transition state (**46**), but a *trans*-fused cyclic transition state (**47**) intervenes to a cetain extent, giving the minor *trans* isomer **39** along with the major product **40**. In the case of the *Z*-allylic stannane **12**, a *cis*-fused one (**45**) is the only possible transition state, since the interaction

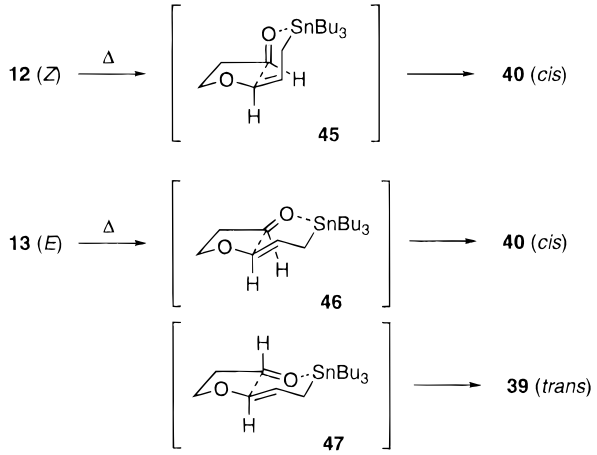
(16) (a) Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 5330−5334. (b) Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989**, *111*, 5335−5340.

(17) Gaudemer, A. In *Stereochemistry*; Kagan, H. B., Ed.; Georg Thieme Publishers: Stuttgart, 1977; Vol. 1, p 90.

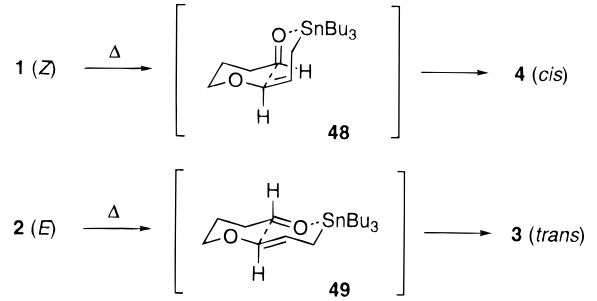
(18) To comfirm the stereochemical assignment, the *cis* isomer **40** was converted to a bicyclic lactone by four steps in good yield. In contrast, the *trans* isomer **39** did not give any cyclized product under the same conditions because of the steric problem of the *trans*-fused 5-5 ring system.



Scheme 4. Cyclic Transition State Model for the Thermal Cyclizations of 12 and 13



Scheme 5. Cyclic Transition State Model for the Thermal Cyclizations of 1 and 2

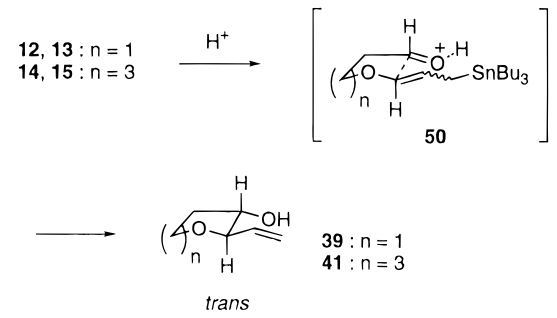


between Sn and the carbonyl oxygen atom is required. However, in the case of the *E* isomer **13**, both *cis*- and *trans*-fused models **46** and **47** are conceivable for the cyclic transition states. The preference of **46** over **47** may be due to the stability of the *cis*-fused 5-6 ring system in the transition state. As mentioned below, a *trans*-fused model (**49**) is preferable (as was expected) for the case of the 6-membered ring system.

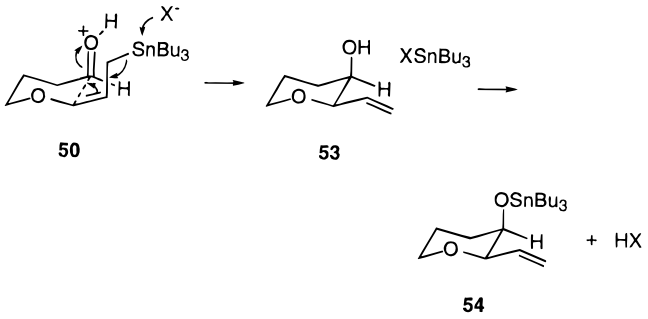
The high stereoselectivities observed in the thermal reaction of **1** and **2** can be explained clearly by the cyclic transition state model (Scheme 5). The reaction of **1** gave exclusively the *cis* cyclic ether **4** *via* a *cis*-fused model (**48**). The transition state model **48** is very similar to the model **45**; only a *cis*-fused structure is allowable for each case. The *E*-allylic stannane **2** gave the *trans* isomer **3** with very high stereoselectivity *via* the *trans*-fused 6-6 system **49**.

3. Protic Acid-Promoted Cyclization. The protic acid-mediated reaction of **12** and **13** gave the *trans* cyclic ether **39** predominantly, regardless of the double-bond geometry of the starting allylic stannanes. Although the yields were very low, only the *trans* cyclic ether **41** was obtained in the reactions of **14** and **15**. These results can be explained by the usual acyclic transition state model as depicted in Scheme 6; instead of Lewis acid, the proton would coordinate to the carbonyl oxygen of **12**−**15**, and the cyclization would proceed through an acyclic transition state (**50**). On the other hand, it was interesting to find that the stereoselectivities of the reactions of **1** and **2** were strongly dependent upon the double-bond geometry of the starting materal, as was observed in the thermal cyclization. Thus, the reaction of **1** or **2** gave **4** or **3**, respectively, with very high to good stereoselectivities.

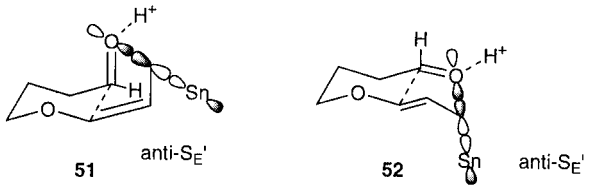
Scheme 6. Acyclic Transition State Model



Scheme 7. Cyclization with Catalytic Amounts of Protic Acids (HX)



The remarkable stereoselectivities observed for the cyclization of **1** and **2** may be explained by the size of protic acids; similar discussions have been made by Keck[9] and Denmark.[10] Proton as the smallest Lewis acid would coordinate to an aldehyde oxygen in an *anti* manner, and the reaction of **1** would proceed through a *syn*-synclinal transition state (**51**) in which Bu_3Sn is replaced in an *anti*-S_E' manner and the secondary orbital overlap between the LUMO of the cabonyl and the HOMO of the allylstannane is possible. Therefore, the protic acid-promoted cyclization of **1** gives the *cis* isomer **4**. Quite similarly, the reaction of **2** would proceed *via* a *syn*-synclinal transition state (**52**), which produces the *trans* isomer **3**. Perhaps, protic acid (HX) could be regenerated



by the exchange reaction between $^+SnBu_3$ and O-H (Scheme 7, **54**), and thus, even the use of a catalytic amount of HX could promote and complete the cyclization reaction (Table 3, entry 7). The *syn*-synclinal type transition state models such as **51** and **52** would be allowable only in the case of very small Lewis acids. In contrast, sterically demanding Lewis acids such as $BF_3{\cdot}OEt_2$ and $TiCl_4$ would prevent bringing the carbonyl oxygen close to the CH_2 carbon of the allylstannane (**53**).[19]

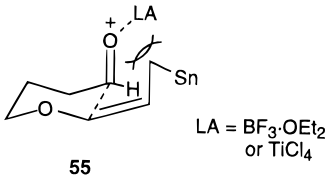
How can we explain by the *syn*-synclinal model the stereoselectivities observed in the protic acid-promoted processes to 5-membered (**12** and **13**) and 7-membered (**14** and **15**) formation? Compared with the 6-membered ring systems **51** and **52**, the distance between the carbonyl oxygen and the CH_2-Sn in the *syn*-synclinal

(19) Even in the case of $BF_3{\cdot}OEt_2$ and $TiCl_4$, the reaction *via* **51** and **52** may be involved to a certain extent.

Table 5. Summary of the Stereoselectivities in the Cyclization of 1, 2, and 12−15

product	5-membered ring		6-membered ring		7-membered ring	
substrate	**12** (*Z*)	**13** (*E*)	**1** (*Z*)	**2** (*E*)	**14** (*Z*)	**15** (*E*)
Lewis acid	*trans*	*trans*	*trans*	*trans*	*trans*	*trans*
Δ	*cis*	*cis*	*cis*	*trans*		
protic acid	*trans*	*trans*	*cis*	*trans*	*trans*	*trans*

model (**56**) of **12** becomes longer, whereas that in the *syn*-synclinal model (**57**) of **14** becomes shorter. Similar argument can be made for **13** and **15**. These changes in the transition states might prevent them from taking the *syn*-synclinal geometries, and thus the usual acyclic transition states such as **50** would become favorable. Therefore, the *syn*-synclinal models are applicable for very limited stereostructures among the allylstannane−aldehyde substrates (see also footnote 21a of ref 9).



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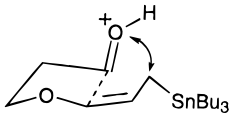

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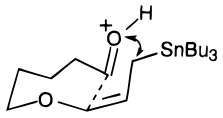

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Conclusion

The relationship between the substrate geometries and the stereochemistries of the cyclic ethers is summarized in Table 5. The noticeable stereoselectivities, which were strongly dependent upon the double-bond geometry, were observed in the protic acid-mediated cyclization of **1** and **2**. In contrast, Keck *et al.* observed that even in the BF_3·OEt_2-mediated reaction of the acyclic systems **5** and **6** the diastereoselectivity of the cyclization could depend upon the geometry of the double bond (Table 1). Perhaps, in the case of allylstannanes **1** and **2**, the oxygen atom at the γ-position may decrease the secondary orbital overlap interaction. Therefore, the reaction mediated by a sterically demanding Lewis acid such as BF_3·OEt_2 or $TiCl_4$ would proceed *via* the acyclic transition state **44**. The *syn*-synclinal transition states **51** and **52** would be allowable only in the case of proton as the smallest Lewis acid.

Experimental Section

General Procedures. ^{1}H- and ^{119}Sn-NMR spectra were recorded on JEOL GSX-270 spectrometers. Chemical shifts are reported in delta (δ) units, in part per million (ppm) downfield from tetramethylsilane or tetramethylstannane or in ppm relative to the singlet at 7.26 ppm for chloroform. Coupling constants are reported in hertz (Hz). IR spectra (cm^{-1}) were measured on neat compounds with a Hitach 260-10 or Shimadzu FTIR8200A infrared spectrophotometer. High-resolution mass spectra were obtained with a JEOL JMS-HX110 spectrometer. Capillary GC analyses were performed on a Shimadzu GC-14A instrument equiped with a flame ionization detector and CPB1-M25-025 column. All reactions were monitored by thin layer chromatography using Merck precoated aluminum plates (Kieselgel 60 F_{254}, 0.2 mm). Column chromatography was done on Merck silica gel 60 (70−230 mesh ASTM), and for flash chromatography, Merck silica gel 60 (230−400 mesh ASTM) was employed.

All solvents were dried immediately before use. Ether and THF were distilled from sodium/benzophenone ketyl; dichloromethane, hexane, benzene, triethylamine, pyridine, DMF, DMSO, and TMEDA were distilled from CaH_2; methanol was distilled from $Mg(OMe)_2$. All reactions involving air- and/or moisture-sensitive materials were carried out in an argon atmosphere. On workup, extracts were dried over $MgSO_4$.

4-(Allyloxy)-1-butanol (17). To a stirred suspension of NaH (12 g of a 60% suspension in mineral oil, 0.3 mol, prewashed with hexane) in THF (150 mL) at 0 °C was added dropwise a solution of 1,4-butanediol (**16**) (110 mL, 1.25 mol) in THF (80 mL). After 1 h, allyl bromide (21.7 mL, 0.25 mol) was added dropwise, and the mixture was refluxed for 2 h. The reaction was quenched with water (200 mL). Most of the organic solvent was evaporated, and the aqueous residue was extracted with ether (500 mL). The organic layer was washed with water (200 mL × 2) and concentrated. The crude product was purified by distillation to give **17** (25.2 g, 80% based on allyl bromide): colorless oil; bp 67−70 °C/2.0 mmHg; R_f = 0.39 (hexane/AcOEt, 1:1); IR (neat) 3600−3100, 3090, 2940, 2860, 1645, 1420, 1345, 1100, 1060, 1000, 930 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.92 (dddd, *J* = 17.0, 10.5, 5.5, 5.5 Hz, 1H), 5.28 (dddd, *J* = 17.0, 1.5, 1.5, 1.5 Hz, 1H), 5.19 (dddd, *J* = 10.5, 1.5, 1.5, 1.5 Hz, 1H), 3.99 (ddd, *J* = 5.5, 1.5, 1.5 Hz, 2H), 3.65 (t, *J* = 6.0 Hz, 2H), 3.49 (t, *J* = 6.0 Hz, 2H), 2.10 (brs, 1H), 1.70−1.50 (m, 4H).

4-[(*Z*)-[3-(Tributylstannyl)-1-propenyl]oxy]-1-butanol (19). To a solution of **17** (2.60 g, 20 mmol) and TMEDA (6.6 mL, 44 mmol) in THF (100 mL) at −78 °C was added *s*-BuLi (44 mL of a 1.1 M solution in cyclohexane, 44 mmol), and the resulting mixture was stirred for 1 h. To this yellow solution was added *n*-Bu_3SnCl (6.5 mL, 24 mmol), and the mixture was allowed to warm to rt. The reaction was quenched with water (30 mL), then most of the organic solvents were evaporated, and the aqueous residue was extracted with ether (250 mL). The organic layer was washed with brine (100 mL). Concentration and column chromatography gave **19** (5.72 g, 68%): colorless oil; R_f = 0.22 (CH_2Cl_2); IR (neat) 3600−3100, 3030, 2960, 2920, 2870, 1650, 1461, 1417, 1360, 1250, 1180, 1153, 1100, 1068, 958, 870, 768, 730, 680, 655 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.78 (ddd, *J* = 6.0, 1.2, 1.2 Hz, 1H), 4.52 (ddd, *J* = 8.9, 8.9, 6.0 Hz, 1H), 3.76−3.65 (m, 4H), 1.80−1.20 (m, 16H), 0.96−0.80 (m, 15H); HRMS *m*/*z* calcd for $C_{19}H_{40}O_2Sn$ 420.2048, found 420.2057.

4-[(*Z*)-[3-(Tributylstannyl)-1-propenyl]oxy]butanal (1). To a stirred mixture of **19** (5.72 g, 16.6 mmol), Et_3N (13 mL, 95 mmol), and DMSO (15 mL) in CH_2Cl_2 (30 mL) at 0 °C was added SO_3·py (8.66 g, 54.4 mmol). After 2 h, the reaction mixture was diluted with ether (200 mL) and washed with water (100 mL) and brine (100 mL). Concentration and column chromatography gave **1** (4.59 g, 66%): colorless oil; R_f = 0.67 (hexane/AcOEt, 3:1); IR (neat) 3040, 2960, 2930, 1730, 1650, 1460, 1100, 960, 870 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 9.81 (t, *J* = 1.4 Hz, 1H), 5.75 (ddd, *J* = 6.0, 1.3, 1.3 Hz, 1H), 4.53 (ddd, *J* = 8.9, 6.0, 6.0 Hz, 1H), 3.72 (t, *J* = 6.0 Hz, 2H), 2.58 (ddd, *J* = 7.1, 7.1, 1.4 Hz, 2H), 2.00−1.90 (m, 2H), 1.50−1.20 (m, 12H), 1.00−0.80 (m, 15H).

3-(2-Propynyloxy)-1-propanol (21). To a stirred suspension of NaH (8.3 g of a 60% suspension in mineral oil, 0.21 mol, prewashed with hexane) in THF (200 mL) at 0 °C was added dropwise a solution of 1,3-propanediol (**20**) (57 mL, 0.79 mol) in THF (40 mL). After 1 h, propargyl bromide (18 mL, 0.2 mol) was added dropwise, and the mixture was stirred at rt for 14 h. The reaction was quenched with water (150 mL). Most of the organic solvent was evaporated, and the residue was extracted with ether (400 mL). The organic layer was washed with water (150 mL × 2) and concentrated. The crude product was purified by distillation to give **21** (9.1 g, 40% based on propargyl bromide): colorless oil; bp 53−54 °C/1.5 mmHg; R_f = 0.28 (hexane/AcOEt, 1:1); IR (neat) 3650−3050, 3280, 2940, 2870, 2100, 1474, 1439, 1356, 1268, 1092, 1049, 1019, 962, 922, 900 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.17 (d, *J* =

2.4 Hz, 2H), 3.78 (t, J = 5.8 Hz, 2H), 3.71 (t, J = 5.8 Hz, 2H), 2.45 (t, J = 2.4 Hz, 1H), 1.99 (br, 1H), 1.87 (quint, J = 5.8 Hz, 2H).

1-[(*tert*-Butyldimethylsilyl)oxy]-3-(2-propynyloxy)propane (22). To a solution of **21** (8.5 g, 74.5 mmol) and imidazole (7.7 g, 113 mmol) in DMF (450 mL) at 0 °C was added TBDMSCl (13.1 g, 90.4 mmol), and the mixture was stirred at rt for 1 h. The mixture was diluted with ether (700 mL) and washed with water (300 mL), saturated aqueous $NaHCO_3$ (200 mL), and brine (200 mL). Concentration and column chromatography gave **22** (16.3 g, 96%): colorless oil; R_f = 0.34 (hexane/AcOEt, 20:1); IR (neat) 3320, 2960, 2940, 2870, 2120, 1475, 1465, 1443, 1394, 1365, 1258, 1192, 1100, 1009, 942, 911, 882, 845, 786, 720, 665 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.13 (d, J = 2.4 Hz, 2H), 3.70 (t, J = 6.2 Hz, 2H), 3.60 (t, J = 6.4 Hz, 2H), 2.44 (d, J = 2.4 Hz, 1H), 1.84 (quint, J = 6.2 Hz, 2H), 0.90 (s, 9H), 0.06 (s, 6H). Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 62.86; H, 10.55.

1-(Allenyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]propane (23). A mixture of **22** (16.0 g, 70.0 mmol) and *t*-BuOK (790 mg, 7 mmol) was stirred at 70 °C for 2 h. (The reaction was monitored by ^{1}H-NMR.) The mixture was diluted with ether (70 mL) and washed with water (50 mL). The organic layer was filtered through a silica gel pad, and the filtrate was concentrated under reduced pressure (below 30 °C). The crude product was purified by flash distillation to give **23** (9.4 g, 59%): colorless oil; bp 68 °C/1.0 mmHg; IR (neat) 3050, 2970, 2940, 2870, 1960, 1477, 1450, 1396, 1370, 1356, 1261, 1206, 1108, 1043, 1012, 948, 896, 840, 785, 670 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.71 (t, J = 5.8 Hz, 1H), 5.43 (d, J = 5.8 Hz, 2H), 3.71 (t, J = 6.3 Hz, 2H), 3.65 (t, J = 6.3 Hz, 2H), 1.84 (quint, J = 6.3 Hz, 2H), 0.89 (s, 9H), 0.05 (s, 6H).

1-(Allenyloxy)-3-[(trimethylsilyl)oxy]propane (24). A mixture of **23** (9.25 g, 40.5 mmol) and TBAF (49 mL of a 1 M solution in THF, 49 mmol) was stirred at rt for 1.5 h. The mixture was diluted with ether (100 mL), washed with water (50 mL) and brine (50 mL), and concentrated. The crude product was directly used for the next reaction.

A mixture of the alcohol obtained, HMDS (17.0 mL, 81 mmol), and TMSCl (1 drop) was stirred at 100 °C for 1 h. Fractional distillation of the reaction mixture afforded **24** (6.66 g, 88%): colorless oil; bp 50 °C/2.0 mmHg; R_f = 0.38 (hexane/AcOEt, 20:1); IR (neat) 3060, 3030, 2950, 2740, 1956, 1474, 1448, 1396, 1356, 1300, 1260, 1210, 1190, 1060, 946, 790, 760, 723, 688 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.71 (t, J = 5.9 Hz, 1H), 5.43 (d, J = 5.9 Hz, 2H), 3.68 (t, J = 6.2 Hz, 2H), 3.63 (t, J = 6.2 Hz, 2H), 1.85 (quint, J = 6.2 Hz, 2H), 0.11 (s, 9H).

Hydrostannylation of 24. To a stirred mixture of **24** (6.3 g, 34 mmol) and $Pd(PPh_3)_4$ (400 mg, 0.35 mmol) was added *n*-Bu_3SnH (18.5 mL, 68 mmol) dropwise. During this addition an exothermic reaction started, and the temperature was maintained between 50 and 60 °C with a cooling bath if necessary. Stirring at rt was continued for 1 h, then the crude product was diluted with MeOH (50 mL), and K_2CO_3 (2 g) was added to the mixture. After the mixture was stirred at rt for 5 h, the solvent was removed. Flash column chromatography gave **25** (6.8 g, 49%) and **26** (1.2 g, 8.7%).

3-[(*Z*)-[3-(Tributylstannyl)-1-propenyl]oxy]-1-propanol (25): colorless oil; R_f = 0.25 (CH_2Cl_2); IR (neat) 3650−3100, 3050, 2970, 2930, 2880, 1650, 1460, 1416, 1370, 1295, 1260, 1192, 1180, 1155, 1100, 1000, 960, 930, 873, 735, 686, 660 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.58−5.46 (m, 1H), 4.28 (ddd, J = 9.2, 9.2, 6.2 Hz, 1H), 3.62−3.50 (m, 4H), 1.95−1.20 (m, 16H), 1.00−0.90 (m, 15H). Anal. Calcd for $C_{18}H_{38}O_2Sn$: C, 53.35; H, 9.45. Found: C, 53.17; H, 9.39.

3-[(*E*)-[3-(Tributylstannyl)-1-propenyl]oxy]-1-propanol (26): colorless oil; R_f = 0.14 (CH_2Cl_2); IR (neat) 3600−3100, 2970, 2930, 2880, 2860, 1530, 1662, 1644, 1466, 1420, 1380, 1343, 1296, 1251, 1191, 1128, 1075, 1074, 964, 620, 874, 714, 660 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.09 (m, 1H), 5.00 (ddd, J = 8.7, 8.7, 13 Hz, 1H), 3.80−3.70 (m, 4H), 1.95−1.20 (m, 16H), 1.00−0.80 (m, 15H); HRMS m/z calcd for $C_{18}H_{38}O_2Sn$ 406.1894, found 406.1892.

3-[(*Z*)-[3-(Tributylstannyl)-1-propenyl]oxy]propanal (12): colorless oil; R_f = 0.36 (hexane/AcOEt, 10:1); IR (neat) 3020, 2940, 2910, 2860, 2835, 2715, 1720, 1642, 1456, 1408, 1369, 1355, 1248, 1146, 990, 952, 866, 760, 720, 676, 650 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 9.82 (t, J = 1.8 Hz, 1H), 5.78 (ddd, J = 6.0, 1.8, 1.8 Hz, 1H), 4.58 (ddd, J = 9.1, 9.1, 6.0 Hz, 1H), 4.03 (t, J = 6.3 Hz, 2H), 2.72 (ddd, J = 6.3, 6.3, 1.8 Hz, 2H), 1.68−1.20 (m, 16H), 1.00−0.80 (m, 15H); ^{119}Sn-NMR ($CDCl_3$) δ −15.70; HRMS m/z calcd for $C_{18}H_{36}O_2Sn$ 404.1737, found 404.1748.

3-[(*E*)-[3-(Tributylstannyl)-1-propenyl]oxy]propanal (13): colorless oil; R_f = 0.67 (hexane/AcOEt, 3:1); IR (neat) 3050, 3020, 2950, 2920, 2850, 2725, 1728, 1658, 1642, 1461, 1417, 1377, 1338, 1293, 1182, 1123, 1070, 1020, 1000, 960, 920, 874, 802, 772, 714, 685 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 9.80 (t, J = 1.6 Hz, 1H), 6.10 (ddd, J = 12, 1.5, 1.5 Hz, 1H), 5.01 (ddd, J = 8.7, 8.7, 12 Hz, 1H), 3.94 (t, J = 6.2 Hz, 2H), 2.72 (ddd, J = 6.2, 6.2, 1.6 Hz, 2H), 1.65−1.20 (m, 16H), 1.98−1.78 (m, 15H); ^{119}Sn-NMR ($CDCl_3$) δ −18.23. Anal. Calcd for $C_{18}H_{36}O_2Sn$: C, 53.62; H, 9.00. Found: C, 53.34; H, 8.83.

4-(2-Propynyloxy)-1-butanol (27): colorless oil; R_f = 0.47 (hexane/AcOEt, 1:1); IR (neat) 3600−3200, 2950, 2860, 2220, 1440, 1360, 1100, 940 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.14 (d, J = 2.8 Hz, 2H), 3.65 (t, J = 6.0 Hz, 2H), 3.56 (t, J = 6.0 Hz, 2H), 2.42 (t, J = 2.8 Hz, 1H), 1.95 (s, 1H), 1.76−1.60 (m, 4H).

1-[(*tert*-Butyldimethylsilyl)oxy]-4-(2-propynyloxy)butane (28): colorless oil; R_f = 0.40 (hexane/AcOEt, 10:1); IR (neat) 3320, 2970, 2940, 2870, 2165, 2120, 1476, 1468, 1448, 1393, 1364, 1260, 1100, 1035, 1010, 980, 940, 840, 816, 783, 668 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.13 (d, J = 2.5 Hz, 2H), 3.63 (t, J = 6.2 Hz, 2H), 3.53 (t, J = 6.2 Hz, 2H), 2.41 (t, J = 2.5 Hz, 1H), 1.72−1.50 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H). Anal. Calcd for $C_{13}H_{26}O_2Si$: C, 64.41; H, 10.81. Found: C, 64.03; H, 10.83.

1-(Allenyloxy)-4-[(*tert*-butyldimethylsilyl)oxy]butane (29): colorless oil; R_f = 0.33 (hexane/AcOEt, 10:1); IR (neat) 3060, 2980, 2950, 2880, 1957, 1738, 1476, 1450, 1392, 1360, 1260, 1206, 1104, 1051, 1012, 986, 944, 894, 841, 780, 720, 665 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.72 (t, J = 5.8 Hz, 1H), 5.42 (d, J = 5.8 Hz, 2H), 3.63 (t, J = 6.2 Hz, 1H), 3.57 (t, J = 6.2 Hz, 1H), 1.78−1.52 (m, 4H), 0.90 (s, 9H), 0.05 (s, 6H).

1-(Allenyloxy)-4-[(trimethylsilyl)oxy]butane (30): colorless oil; IR (neat) 2970, 2870, 1950, 1730, 1252, 1200, 1100, 840, 778 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.71 (t, J = 5.7 Hz, 1H), 5.41 (d, J = 5.7 Hz, 2H), 3.58 (ddd, J = 8.6, 6.3, 6.1 Hz, 4H), 1.75−1.53 (m, 4H), 0.09 (s, 9H). Anal. Calcd for $C_{10}H_{20}O_2Si$: C, 59.95; H, 10.06. Found: C, 59.87; H, 10.06.

4-[(*E*)-[3-(Tributylstannyl)-1-propenyl]oxy]-1-butanol (31): colorless oil; R_f = 0.13 (CH_2Cl_2); IR (neat) 3600−3100, 2970, 2935, 2885, 2870, 1660, 1645, 1462, 1380, 1194, 1127, 1074, 963, 924, 872, 660 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.10, (ddd, J = 12.4, 1.4, 1.4 Hz, 1H), 4.98 (ddd, J = 12.4, 8.5, 8.5 Hz, 1H), 3.64 (m, 4H), 1.80−1.20 (m, 18H), 0.90−0.80 (m, 15H); HRMS m/z calcd for $C_{19}H_{40}O_2Sn$ 420.2048, found 420.2037.

4-[(*E*)-[3-(Tributylstannyl)-1-propenyl]oxy]butanal (2): colorless oil; IR (neat) 1730, 1645 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 9.79 (t, J = 1.4 Hz, 1H), 6.08 (ddd, J = 12.1, 1.3, 1.3 Hz, 1H), 4.95 (ddd, J = 12.1, 8.6, 8.6 Hz, 1H), 3.63 (t, J = 6.1 Hz, 2H), 2.55 (ddd, J = 7.7, 7.7, 1.4 Hz, 2H), 1.95 (m, 2H), 2.00−0.80 (m, 27H).

5-(2-Propynyloxy)-1-pentanol (33): colorless oil; R_f = 0.32 (hexane/AcOEt, 1:1); bp 89−91 °C/3 mmHg; IR (neat) 3600−3100, 3320, 3950, 2880, 3130, 1368, 1100 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.55 (brs, 1H), 4.14 (d, J = 2.5 Hz, 2H), 3.65 (t, J = 6.4 Hz, 2H), 3.53 (t, J = 6.4 Hz, 2H), 2.42 (t, J = 2.5 Hz, 1H), 1.70−1.40 (m, 6H).

1-[(*tert*-Butyldimethylsilyl)oxy]-5-(2-propynyloxy)pentane (34): colorless oil; R_f = 0.36 (hexane/AcOEt, 20:1); IR (neat) 3325, 2950, 2880, 2130, 1728, 1479, 1470, 1396, 1368, 1260, 1105, 1012, 862, 780, 669 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 4.13 (d, J = 2.2 Hz, 2H), 3.61 (t, J = 6.4 Hz, 2H), 3.51 (t, J = 6.5 Hz, 2H), 2.41 (t, J = 2.3 Hz, 1H), 1.70−1.30 (m, 6H), 0.89 (s, 9H), 0.06 (s, 6H).

1-(Allenyloxy)-5-[(*tert*-butyldimethylsilyl)oxy]pentane (35): colorless oil; bp 81−83 °C/0.8 mmHg; R_f = 0.83

(hexane/AcOEt, 3:1); IR (neat) 2980, 2910, 2370, 1968, 1483, 1473, 1458, 1399, 1360, 1263, 1218, 1112, 1058, 854, 792 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.72 (t, J = 6.0 Hz, 1H), 5.42 (d, J = 6.0 Hz, 2H), 3.61 (t, J = 6.4 Hz, 2H), 3.55 (t, J = 6.4 Hz, 2H), 1.70−1.30 (m, 6H), 0.89 (s, 9H), 0.04 (s, 6H).

1-(Allenyloxy)-5-[(trimethylsilyl)oxy]butane (36): colorless oil; bp 68−70 °C/1.5 mmHg; IR (neat) 3041, 3953, 2864, 1472, 1447, 1352, 1251, 1096, 1043, 840 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.72 (t, J = 6.0 Hz, 2H), 5.42 (d, J = 6.0 Hz, 2H), 3.58 (t, J = 6.3 Hz, 2H), 3.55 (t, J = 6.3 Hz, 2H), 1.70−1.30 (m, 6H), 0.11 (s, 9H).

5-[(*Z*)-[3-(Tributylstannyl)-1-propenyl]oxy]-1-pentanol (37): colorless oil; R_f = 0.30 (CH_2Cl_2); IR (neat) 3600−3200, 3050, 2950, 2850, 1660, 1470, 1370, 1260, 1169, 1120, 975, 890, 750, 680 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 5.77 (ddd, J = 6.2, 1.2, 1.2 Hz, 1H), 4.50 (ddd, J = 9.0, 9.0, 6.2 Hz, 1H), 3.72−3.62 (m, 4H), 1.70−1.20 (m, 18H), 1.00−0.90 (m, 15H). Anal. Calcd for $C_{20}H_{42}O_2Sn$: C, 55.44; H, 9.77. Found: C, 55.29; H, 9.75.

5-[(*E*)-[3-(Tributylstannyl)-1-propenyl]oxy]-1-pentanol (38): colorless oil; R_f = 0.18 (CH_2Cl_2); IR (neat) 3600−3100, 3050, 2950, 2850, 1658, 1640, 1450, 1370, 1330, 1280, 1190, 1120, 1070, 957, 920, 870, 712, 670 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 6.10 (ddd, J = 12, 1.2, 1.2 Hz, 1H), 4.95 (ddd, J = 8.4, 8.4, 12 Hz, 1H), 3.70−3.55 (m, 4H), 1.70−1.20 (m, 18H), 0.90−0.80 (m, 15H); HRMS m/z calcd for $C_{20}H_{42}O_2Sn$ 434.2205, found 434.2210.

5-[(*Z*)-[3-(Tributylstannyl)-1-propenyl]oxy]pentanal (14): colorless oil; R_f = 0.11 (hexane/AcOEt, 50:1); IR (neat) 3045, 2950, 2850, 1730, 1660, 1468, 1380, 1260, 1110, 963, 879, 742 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 9.77 (t, J = 1.6 Hz, 1H), 5.75 (ddd, J = 6.0, 1.2, 1.2 Hz, 1H), 4.51 (ddd, J = 9.1, 6.0, 6.0 Hz, 1H), 3.69 (t, J = 6.1 Hz, 2H), 2.48 (ddd, J = 7.3, 7.3, 1.6 Hz, 2H), 1.80−1.20 (m, 16H), 0.98−0.80 (m, 15H); ^{119}Sn-NMR ($CDCl_3$) δ −16.64.

5-[(*E*)-[3-(Tributylstannyl)-1-propenyl]oxy]pentanal (15): colorless oil; R_f = 0.08 (hexane/AcOEt, 50:1); IR (neat) 2960−2550, 1714, 1648, 1630, 1446, 1368, 1177, 1112, 909 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 9.76 (t, J = 1.8 Hz, 1H), 6.09 (brd, J = 12.6 Hz, 1H), 4.95 (ddd, J = 12.6, 8.6, 8.6 Hz, 1H), 3.60 (t, J = 5.9 Hz, 2H), 2.47 (ddd, J = 7.0, 7.0, 1.8 Hz, 2H), 1.80−1.20 (m, 16H), 0.98−0.70 (15H); ^{119}Sn-NMR ($CDCl_3$) δ −18.83.

General Procedure for the Cyclization of 1, 2, and 12−15. To a stirred solution of the substrate (0.025 mmol) in CH_2Cl_2 (0.1 mL) at −78 °C was added a Lewis or protic acid solution (1.0 M, in CH_2Cl_2). Thermal reactions were performed in toluene. Reaction times varied with conditions and reagents as shown in Tables 1−3. The reactions were quenched with Et_3N and the mixtures allowed to warm to room temperature. The mixtures were filtered through a silica gel column. The yields and isomer ratios were determined by capillary GC analysis.

(2*R,3*S**)-3-Benzoyl-2-vinyltetrahydrofuran (42):** colorless oil; R_f = 0.32 (hexane/AcOEt, 10:1); IR (neat) 3070, 2980, 2950, 2875, 1720, 1644, 1603, 1588, 1494, 1452, 1402, 1368, 1317, 1273, 1180, 1114, 1100, 1073, 1029, 989, 930, 712, 688 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 8.02−8.08 (m, 2H), 7.62−7.54 (m, 1H), 7.49−7.41 (m, 2H), 5.95 (ddd, J = 17.0, 10.4, 5.0 Hz, 1H), 5.41 (ddd, J = 17.0, 1.8, 1.8 Hz, 1H), 5.29 (ddd, J = 6.0, 2.2, 2.2 Hz, 1H), 5.22 (ddd, J = 10.3, 1.8, 1.8 Hz, 1H), 4.57−4.52 (m, 1H), 4.20−4.00 (m, 2H), 2.39−2.05 (m, 2H); HRMS m/z calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0922.

(2*R,3*R**)-3-Benzoyl-2-vinyltetrahydrofurane (43):** colorless oil; R_f = 0.21 (hexane/AcOEt, 10:1); IR (neat) 3080, 2980, 2950, 2890, 1735, 1650, 1605, 1584, 1490, 1450, 1375, 1354, 1313, 1270, 1178, 1113, 1068, 1027, 989, 927, 880, 805, 769, 709, 685 cm^{-1}; ^{1}H-NMR (270 MHz, $CDCl_3$) δ 8.06−8.00 (m, 2H), 7.60−7.52 (m, 1H), 7.48−7.40 (m, 2H), 5.94 (ddd, J = 17.3, 11.6, 6.2 Hz, 1H), 5.61 (ddd, J = 6.2, 4.6, 2.6 Hz, 1H), 5.42 (ddd, J = 17.3, 1.6, 1.6 Hz, 1H), 5.23 (ddd, J = 17.3, 1.7, 1.6 Hz, 1H), 4.43 (m, 1H), 4.16 (q, J = 7.8 Hz, 1H), 3.94 (ddd, J = 17.0, 17.0, 5.3 Hz, 1H), 2.50−2.35 (m, 1H), 2.25−2.15 (m, 1H); HRMS m/z calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0945.

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