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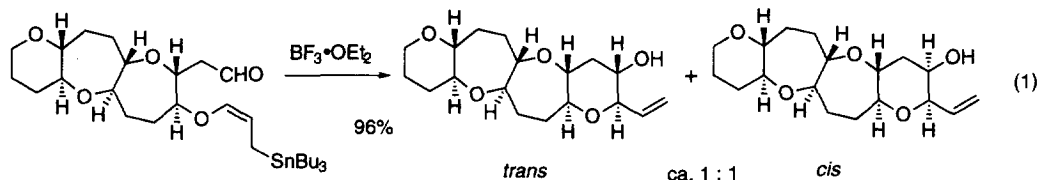
Intramolecular Reaction of Oxo-Substituted Allenyl- and Propargylstannane with Aldehyde

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Abstract: The Lewis acid mediated reactions of allenylstannanes **1** and **13** gave *trans* cyclic ethers **3a** and **14**, respectively, with high stereoselectivities. The cyclization of **7** gave *trans* cyclic ether **9a**. The treatment of propargylstannanes **2** and **8** with Lewis acids such as SnCl₄, BuSnCl₃, and ZnCl₂•OEt₂ induced isomerization to allenylmetal species, which underwent cyclization to the corresponding 6- and 5-membered cyclic ethers **3** and **9**, respectively. The stereoselectivities depended upon the ring size and Lewis acid utilized. Copyright © 1996 Elsevier Science Ltd

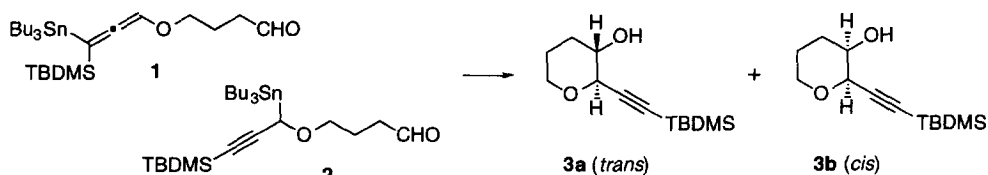
Recently, we developed a novel method for the synthesis of cyclic ethers *via* the intramolecular reaction of γ -alkoxyallylstannane with aldehyde.¹ As demonstrated by the total synthesis of hemibrevetoxin B² and related polycyclic ethers,³ this route is efficient for the stereocontrolled construction of seven membered cyclic ethers. However, six membered ring formation proceeded with low stereoselectivity, especially in polycyclic system (eq 1).^{1a,c} This problem prompted us to develop a new method for the construction of medium sized cyclic ethers. We now report the intramolecular cyclization of allenyl- and propargylstannanes having aldehyde.^{4,5}



The results of the cyclization of allenyl- and propargylstannane **1** and **2**, are summarized in Table 1. In all cases of the Lewis acid mediated reactions of **1**, as expected, *trans* cyclic ether **3a** was obtained with high stereoselectivities in good yields (entries 1-5). The thermal cyclization also proceeded smoothly to give *cis* cyclic ether **3b** as a major product, although the level of the stereoselectivity is moderate (entry 6). On the other hand, the reaction of **2** in the presence of BF₃•OEt₂ gave an unexpected product, α,β -unsaturated aldehyde **5** in 50% yield (entry 7). Perhaps, the direct S_E2' cyclization of **2** would afford strained cyclic enol ether **4** which would be hydrolyzed to **5** under acidic condition (Scheme 1). Although the use of TiCl₄ caused decomposition of the substrate (entry 8), interestingly, the reaction of **2** in the presence of SnCl₄ afforded cyclized products **3a**

and **3b** in allowable yields (entries 9 and 10). These results suggest that SnCl_4 promotes conversion of propargylstannane **2** to allenyl derivative **6**, which produces **3a** and **3b** via cyclization (Scheme 2).⁶ Furthermore, **2** gave **3** upon treatment with Bu_3SnCl_3 and $\text{ZnCl}_2\cdot\text{OEt}_2$ (entries 11-13), indicating that the isomerization of **2** to allenyl derivative was induced also by these Lewis acids.^{5d,6} It is interesting that not only the stannyl Lewis acids but also $\text{ZnCl}_2\cdot\text{OEt}_2$ induces the isomerization although the diastereoselectivity is not high.

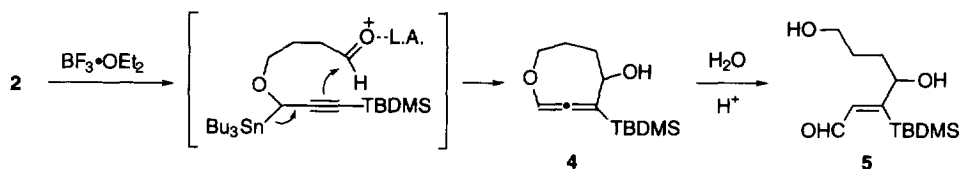
Table 1. Cyclization of **1** and **2**^a



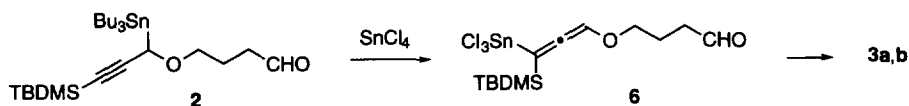
entry	substrate	Lewis acid (equiv)	temp (°C)	time (min)	ratio (3a:3b) ^b	yield (%) ^c
1	1	$\text{BF}_3\cdot\text{OEt}_2$ (2.0)	-78	60	91:9	87
2		TiCl_4 (2.0)	-78	20	89:11	70
3		SnCl_4 (2.0)	-78	60	90:10	44
4		AlCl_3 (2.0)	-78	55	83:17	66
5		$\text{ZnCl}_2\cdot\text{OEt}_2$ (2.0)	-78	90	94:6	77
6		- ^d	110	2580	40:60	76
7	2	$\text{BF}_3\cdot\text{OEt}_2$ (2.0)	-78	30	-	(50) ^e
8		TiCl_4 (2.0)	-78		decomposition	
9		SnCl_4 (2.0)	-78	25	89:11	38
10		SnCl_4 (1.0)	-78	60	67:33	52
11		Bu_3SnCl_3 (2.0)	-78, rt	120, 240	52:48	53
12		$\text{ZnCl}_2\cdot\text{OEt}_2$ (2.0)	-78, rt	120, 180	31:69	71
13		$\text{ZnCl}_2\cdot\text{OEt}_2$ (1.0)	-78, rt	30, 1440	26:74	61

^aThe reactions were carried out with 0.02 M substrate in CH_2Cl_2 under the conditions indicated in the table, and quenched with aqueous saturated NaHCO_3 at the reaction temperature. ^bRatios were determined by a capillary GC analysis. ^cIsolated yields. ^dToluene was used as a solvent. ^eYield of **5**.

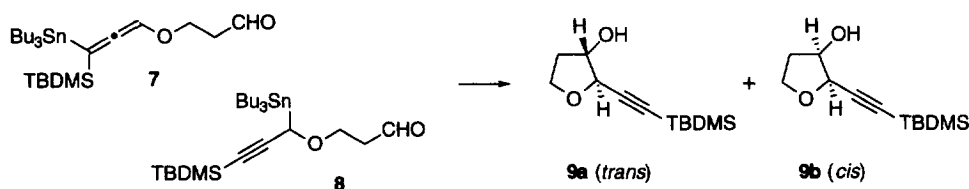
Scheme 1



Scheme 2



We next examined the synthesis of tetrahydrofuran derivatives **9a** and **9b** (Table 2). Owing to its high reactivity, allenylstannane **7** underwent cyclization to **9** at room temperature during its preparation process; it was intended to prepare **7** by the oxidation of the corresponding alcohol using $\text{SO}_3\cdot\text{py}/\text{DMSO}/\text{Et}_3\text{N}$ or $^i\text{PrOMgBr}/1,1'$ -(azodicarbonyl)dipiperidine^{1a,c,7}, but **7** could not be isolated, instead only cyclic ethers **9a** and **9b** were obtained (entries 1 and 2). The *trans* isomer **9a** was obtained as a major product in ratios of 87:13 and 92:8. Although the *trans/cis* ratios in entries 1 and 2 are slightly different, the reason for this difference and for high level of *trans* selectivities are not clear; it is not clear whether this difference is due to either kinetic or thermodynamic origin. The reaction of **8** in the presence of $\text{BF}_3\cdot\text{OEt}_2$ and TiCl_4 gave no cyclized products (entries 3 and 4). Interestingly, the treatment of **8** with SnCl_4 afforded **9b** as a sole product regardless of the amount of the Lewis acid (entries 5 and 6). The *cis* selectivity was decreased to a ratio of 2:3 in the reaction mediated by $\text{ZnCl}_2\cdot\text{OEt}_2$ (entry 7). A proposed reaction pathway of **8** is illustrated in Scheme 3. Allenylmetal species, **10a** and **10b** would be generated from the reaction of **8** with SnCl_4 and $\text{ZnCl}_2\cdot\text{OEt}_2$, respectively. Because of its strong Lewis acidity, allenyltrichlorostannane **10a** would undergo cyclization to **9b** via cyclic transition state **11**; *trans*-fusion in a 5-5 ring system such as **11** is impossible. On the other hand, lower Lewis acidity of $\text{ZnCl}_2\cdot\text{OEt}_2$ would allow the intervention of acyclic transition state **12** which leads to **9a**. Accordingly, the *cis* selectivity decreased by using $\text{ZnCl}_2\cdot\text{OEt}_2$.

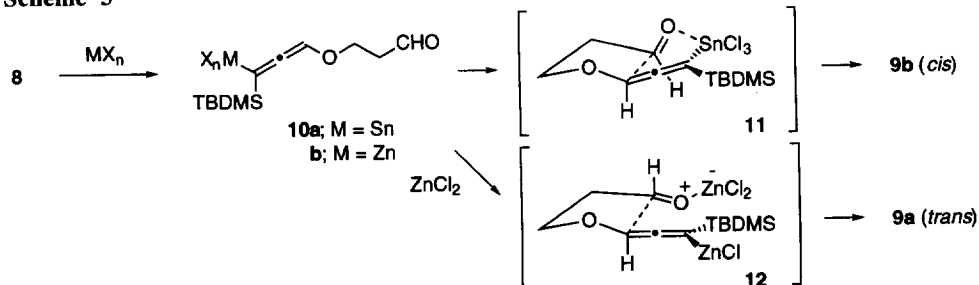
Table 2. Cyclization of **7** and **8**^a

entry	substrate	Lewis acid (equiv)	temp (°C)	time (min)	ratio (9a : 9b) ^b	yield (%) ^c
1	7	- ^d	rt	60	87:13	77
2	7	- ^e	rt	180	92:8	55
3	8	$\text{BF}_3\cdot\text{OEt}_2$ (2.0)	-78		decomposition	
4	8	TiCl_4 (2.0)	-78		decomposition	
5	8	SnCl_4 (2.0)	-78	45	2:98<	64
6	8	SnCl_4 (1.0)	-78	45	2:98<	63
7	8	$\text{ZnCl}_2\cdot\text{OEt}_2$ (2.0)	rt	120	40:60	73

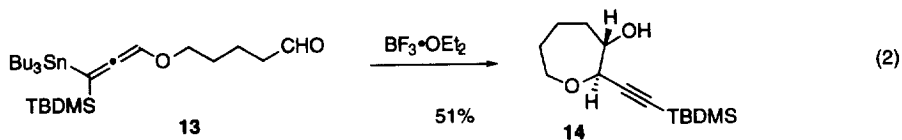
^aThe reactions were carried out with 0.02 M substrate in CH_2Cl_2 under the conditions indicated in the table, and quenched with aqueous saturated NaHCO_3 at the reaction temperature. ^bRatios were determined by a capillary GC analysis.

^cIsolated yields. ^dThe alcohol precursor of **7** was oxidized with $\text{SO}_3\cdot\text{py}$, DMSO, and Et_3N . ^eThe alcohol precursor of **7** was oxidized with $^i\text{PrOMgBr}$ and 1,1'-(azodicarbonyl)dipiperidine.

Scheme 3



The usefulness of this methodology is demonstrated by the synthesis of seven membered cyclic ether **14** as shown in eq 2. The treatment of allenylstannane **13** with $BF_3 \cdot OEt_2$ gave **14** as sole product in 51% yield. No *cis* isomer was detected in this reaction. We are now in a position to accomplish the stereocontrolled synthesis of not only 6-membered cyclic ethers but also 5- and 7-membered ring systems. Application of this methodology to the synthesis of natural polycyclic ethers is in progress.



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References

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- (a) Yamamoto, Y.; Yamada, J.; Kadota, I. *Tetrahedron Lett.* **1991**, *32*, 7069-7072. (b) Gevorgyan, V.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 1313-1316. (c) Yamamoto, Y.; Kadota, I. *Main Group Met. Chem.* **1994**, *17*, 269-289.
 - Kadota, I.; Park, J.-Y.; Koumura, N.; Pollaud, G.; Matsukawa, Y.; Yamamoto, Y. *Tetrahedron Lett.* **1995**, *36*, 5777-5780.
 - (a) Suzuki, T.; Sato, O.; Hiram, 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.; Canden, M.-L.; Pérez, R.; Ravelo, J. L.; Martín, J. D. *Chem. Rev.* **1995**, *95*, 1953-1980. (g) Oguri, H.; Hishiyama, S.; Oishi, T.; Hiram, M. *Synlett* **1995**, 1252-1254.
 - For reviews on the chemistry of allenyl and propargyl organometallics, see: (a) Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 2, p 81-98. (b) Kleinman, E. F.; Volkmann, R. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 2, p 975-1006.
 - For recent examples of the intermolecular reaction of allenyl- and propargylstannanes with aldehydes; see: (a) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1990**, *55*, 6246-6250. (b) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1992**, *57*, 1242-1252. (c) Marshall, J. A.; Perkins, J. *J. Org. Chem.* **1994**, *59*, 3509-3511. (d) Marshall, J. A.; Yu, R. H.; Perkins, J. F. *J. Org. Chem.* **1995**, *60*, 5550-5555. (e) Marshall, J. A.; Perkins, J. F.; Wolf, M. A. *J. Org. Chem.* **1995**, *60*, 5556-5559.
 - The conversion of allenylstannane to propargylstannane mediated by $SnCl_4$ and $BuSnCl_3$ has been reported; see ref 5c and d.
 - Narasaka, K.; Morikawa, A.; Saigo, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2773-2776.

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