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ACID-CATALYZED INTRAMOLECULAR ADDITION OF A HYDROXY GROUP TO VINYLGERMANES

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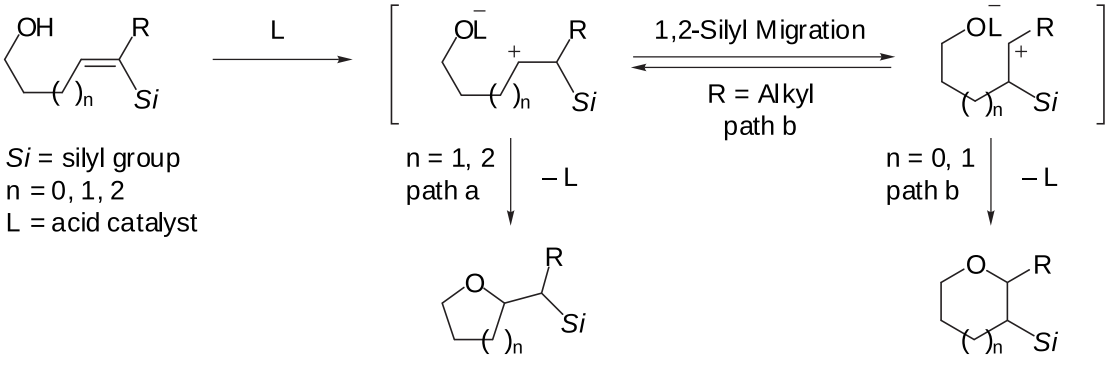
Abstract-Vinylgermanes (**1**), bearing a hydroxy group, were efficiently cyclized to 2-(germylmethyl)tetrahydrofurans (**2**) in the presence of an acid catalyst. The intramolecular addition of the hydroxy group proceeded in a stereospecific *syn* mode. The acid-catalyzed cyclization of α-alkyl-substituted vinylgermanes (**8**) gave 1,2-germyl-migration products (**9**).

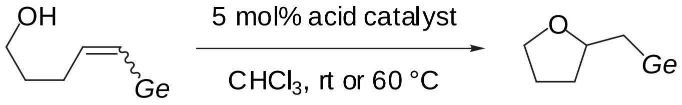
Triorganogermyl groups as well as triorganosilyl groups are known to stabilize β-carbenium ions effectively.[1] Application of the β-effect of triorganosilyl groups to organic synthesis has been extensively studied, and a number of synthetically useful organic reactions have been developed for the last few decades.[2] In contrast, the directing effect of triorganogermyl groups has been little utilized for organic synthesis except that allylgermanes are available for allylation of carbon electrophiles.[3] Previously, we have reported that vinylsilanes bearing a hydroxy group are smoothly cyclized to tetrahydrofurans (THFs) and tetrahydropyrans (THPs) by the action of an acid catalyst (path a in Scheme 1).[4] 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. Thus the β-effect of triorganogermyl groups induced us to examine the acid-catalyzed cyclization of vinylgermanes bearing a hydroxy group. We herein report a new method for the synthesis of THFs and THPs utilizing the reactivity of vinylgermanes.

Scheme 1



Treatment of *Z*-rich 5-tributylgermyl-4-penten-1-ol (**1a**, *Z*:*E* = 93:7) with 5 mol% of $TiCl_4$ gave 2-(tributylgermylmethyl)tetrahydrofuran (**2a**) in 79% yield (Entry 1 in Table 1). As predicted from our previous results,[4] the reactivity of vinylgermane (**1**) was affected by the geometry of the C-C double bond and the substituent on germanium atom. Under the same reaction conditions, the use of *E*-rich **1a** resulted in a lower yield of **2a** because of slow conversion of (*E*)-**1a** (Entry 2). Benzyldimethylvinylgermane ((*Z*)-**1b**) was cyclized faster than (*Z*)-**1a**, while introduction of a phenyl group into the germyl group markedly decreased the reactivity of the substrate (Entries 3 and 6). $TsOH•H_2O$ and $TiCl_2(O\textit{i}\text{-}Pr)_2$ could be used as acid catalysts although they showed lower catalytic activities (Entries 4 and 5). The present cyclization was applicable to the construction of a THP ring as shown in Eq. 1.

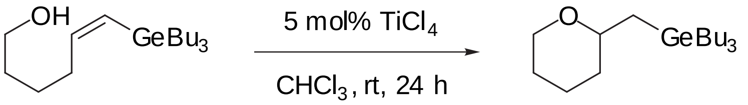
Table 1. Acid-Catalyzed Cyclization of Vinygermanes (**1a-c**)[a]



1a-c **2a-c**

Entry	Vinylgermane			Catalyst	Temp	Time	Yield
	Ge = germyl group		*Z*:*E*			/ h	/ %
1	$GeBu_3$	**1a**	93:7	$TiCl_4$	rt	9	79
2		**1a**	6:94	$TiCl_4$	rt	9	58
3	$GeMe_2Bn$	**1b**	99:<1	$TiCl_4$	rt	4	83
4		**1b**	99:<1	$TsOH•H_2O$	60 °C	24	78
5		**1b**	99:<1	$TiCl_2(O\textit{i}\text{-}Pr)_2$	rt	36	83
6	$GeMe_2Ph$	**1c**	93:7	$TiCl_4$	rt	48	65

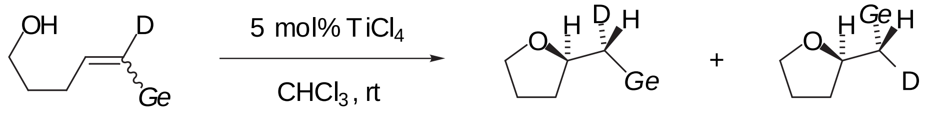
[a]All reactions were carried out with 0.50 mmol of **1** in $CHCl_3$ (2.5 mL).



(1)

3, *Z*:*E* = 97:3 **4**, 80%

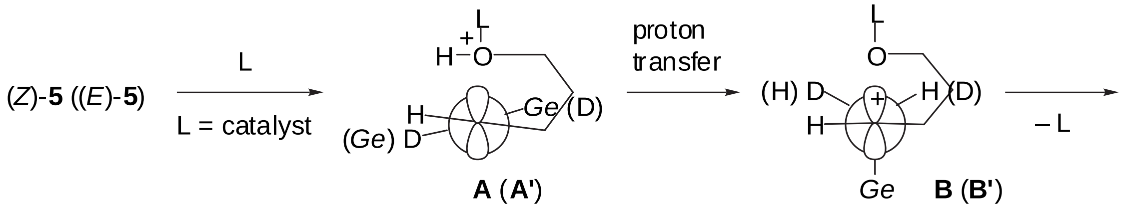
To examine the stereochemistry of the intramolecular addition of a hydroxy group, the $TiCl_4$-catalyzed cyclizations of α-deuterated (*Z*)- and (*E*)-vinylgermanes (**5**) were attempted (Eq. 2). As a result, it was found that these cyclizations showed inverse stereochemistry, and the intramolecular addition of a hydroxy group proceeded in a stereospecific *syn* mode. Similar to the case of the intramolecular addition to vinylsilanes,[4] the *syn* addition can be rationalized by the following mechanism (Eq. 3): (1) attachment of $TiCl_4$ or a proton[5] to the hydroxy group of (*Z*)-**5** or (*E*)-**5** forms oxonium ion (**A** or **A'**), (2) intramolecular proton transfer to the sp^2 carbon α to the silyl group followed by rotation at the least motion turns **A** or **A'** into β-germylcarbenium ion (**B** or **B'**), stabilized by σ-π conjugation,[1] and (3) intramolecular attack of the hydroxy oxygen from the side opposite to the germyl group gives *syn* adduct (**6** or **7**) and regenerates the acid catalyst.



(2)

5, *Ge* = $GeBu_3$
Z:*E* = 99:<1
Z:*E* = 8:92

6 **7**
12 h, 77% (**6**:**7** = 95:5)
120 h, 81% (**6**:**7** = 16:84)

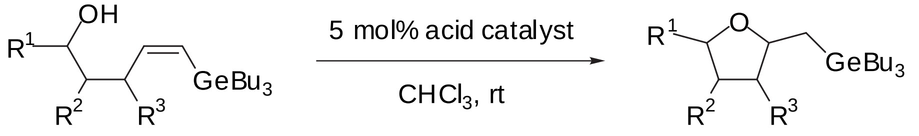


A (**A'**) **B** (**B'**)

(3)

We attempted the application of the present cyclization to the stereoselective synthesis of disubstituted THFs (Table 2). The $TiCl_4$-catalyzed cyclization of vinylgermane (**1d**), bearing a phenyl group at the position α to the hydroxy group, gave 2,5-disubstituted THF (**2d**) with low *trans*-selectivity (Entry 1). The use of $TiCl_2(Oi\text{-}Pr)_2$ as catalyst was not effective in improving the stereoselectivity (Entry 2). Vinylgermane (**1e**), substituted at the homoallylic position, was cyclized to 2,4-disubstituted THF (**2e**) with moderate *cis*-selectivity (Entries 3 and 4). In contrast to the results with **1d** and **1e**, the cyclization of vinylgermane (**1f**), substituted at the allylic position, achieved high *trans*-selectivity (Entries 5 and 6). The sense of diastereoselection in the cyclization of each vinylgermane is identical to that in the case with the corresponding vinylsilane.[4] However, the levels of diastereoselection with **1d** and **1e** are not as high as those with the corresponding vinylsilanes.

Table 2. Stereoselective Cyclization of Vinygermanes ((*Z*)-**1d-f**)[a]

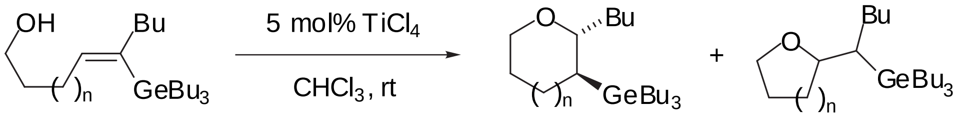


(*Z*)-**1d-f** **2d-f**

Entry	Vinylgermane (*Z*:*E* = ≥98:2)				Catalyst	Time	Yield	*trans*:*cis*[b]
	R^1	R^2	R^3			/ h	/ %	
1	Ph	H	H	**1d**	$TiCl_4$	24	81	63:37
2				**1d**	$TiCl_2(Oi\text{-}Pr)_2$	30	92	63:37
3	H	Ph	H	**1e**	$TiCl_4$	24	86	21:79
4				**1e**	$TiCl_2(Oi\text{-}Pr)_2$	24	95	18:82
5	H	H	Ph	**1f**	$TiCl_4$	24	83	99:<1
6				**1f**	$TiCl_2(Oi\text{-}Pr)_2$	50	55	99:<1

[a]See footnote a in Table 1. [b]Determined by 270 MHz ^1H NMR spectral analysis of the isolated product.

Previously, we have disclosed that the acid-catalyzed reaction of (*Z*)-5-alkyl-5-silyl-4-penten-1-ols gives *trans*-2-alkyl-3-silyltetrahydropyrans by 1,2-silyl-migrative cyclization (path b in Scheme 1).[6] A lot of synthetic reactions involving cationic 1,2-silyl rearrangement have been developed to date,[2,7] while similar reactions using organogermanes are little known.[8] Thus our attention was next focused on 1,2-germyl-migrative cyclization of α-alkyl-substituted vinylgermanes (**8**) (Eq. 4). As expected, the $TiCl_4$-catalyzed reaction of vinylgermane (**8a**) gave the desired 1,2-germyl migration product (**9a**) with high *trans*-selectivity. Unfortunately, the yield of **9a** was not good due to facial protiodegermylation of **8a**. The direct cyclization leading to **10a** also was observed as a minor reaction path. Vinylgermane (**8b**), whose methylene tether is shorter than that of **8a** by one carbon, underwent the 1,2-germyl-migrative cyclization to give 3-germyltetrahydrofuran (**9b**) with high *trans*-selectivity but in a lower yield.



(4)

8, *Z*:*E* = 99:<1
8a: n = 1
8b: n = 0

9, *trans*:*cis* = 99:<1 **10**
47 h, 40% (**9a**:**10a** = 94:6)
120 h, 26% (**9b** only)

In conclusion, we have demonstrated that an internal hydroxy group smoothly adds to vinylgermanes in the presence of an acid catalyst. This cyclization is a novel type of germanium-directed reaction and valuable for the synthesis of germyl-substituted THFs. The reaction mechanism would involve the formation of a β-germylcarbenium ion intermediate. We have also developed a new 1,2-germyl-migrative reaction with high diastereoselectivity.

ACKNOWLEDGEMENT

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