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Substituent-Control of Stereoselectivity in the Reaction of Allylic Tins. *Anti*-Selective Lewis Acid-Promoted Reaction toward Aldehydes

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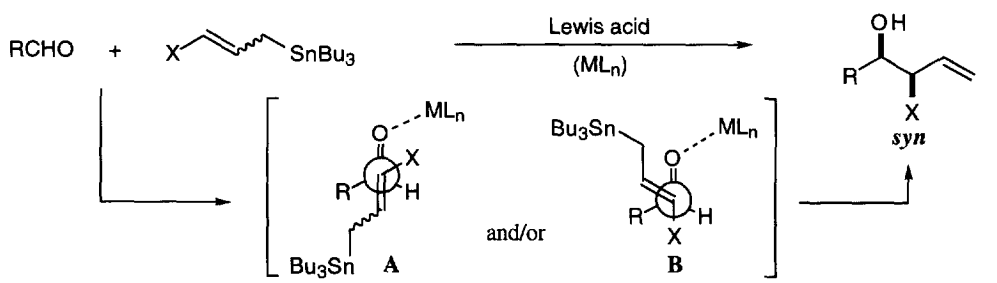
Abstract: In the reaction of *cis*-2-alkenyltins (allylic tins) toward aldehydes, unusual *anti*-homoallyl alcohols were selectively obtained when the substituent at the 2-position of the alkenyltin reagent was a bulky one such as a *tert*-butyl or trialkylsilyl group. This reaction is assumed to proceed via the inverse antiperiplanar acyclic transition state. Copyright © 1996 Published by Elsevier Science Ltd

The reactions of allylic tin reagents are now important tools for the stereoselective C–C bond formation in organic synthesis.[1] Among them, the Lewis acid-promoted reaction toward aldehydes is extremely useful as terminally substituted allyltins exhibit *syn*-diastereoselectivity regardless of their geometry, *trans* or *cis*. This selectivity is explained by considering the acyclic transition states (Scheme 1). Initially, Yamamoto proposed the antiperiplanar conformation (**A**),[2] and then Keck recently stated the contribution of the *syn*-synclinal one (**B**).[3] Keck has also pointed out that this contribution may cause decrease in the *syn*-selectivity of *cis*-allyltins. On the other hand, the *anti*-selective reactions promoted by Lewis acids are slightly known: chelation-controlled reactions between α-alkoxyaldehyde and 2-methylcrotyltin[4] or optically active allylic tins,[5] and $ZnCl_2$-promoted reaction of 3-arylallyltins in a donating solvent.[6]

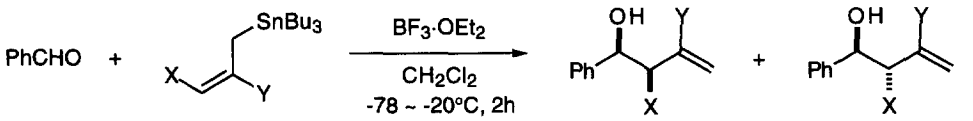


Scheme 1.

We herein make a preliminary report that *cis*-allylic tin reagents[7] having the bulky substituents at their 2-position showed unusual *anti*-selectivity in the Lewis acid-promoted reaction toward simple aldehydes. The diastereoselectivity is controlled mainly by the bulkiness of the 2-substituents of allylic tins. From the synthetic viewpoint, the *anti*-selective Lewis acid-promoted reaction is important for the development of diverse C–C bond forming reactions.

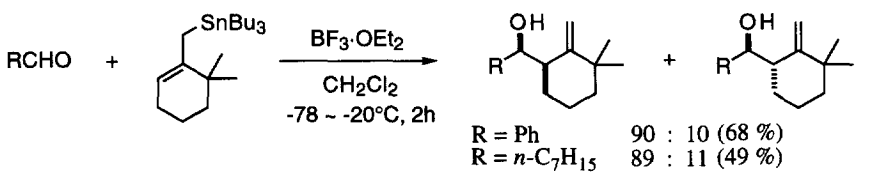
Because we can readily obtain substituted 2-pentenyltins,[8] we investigated the reaction of 2-substituted-*cis*-2-pentenyltins toward benzaldehyde (Table 1).[9] As expected from the previously reported reactions of

Table 1. $BF_3{\cdot}OEt_2$-Promoted Reaction of *cis*-2-Alkenyltins toward Benzaldehyde



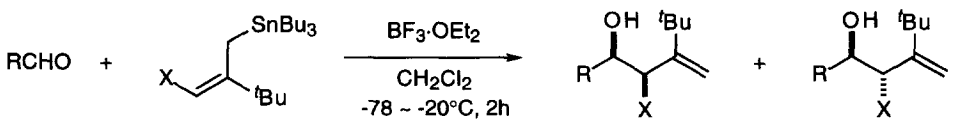
Entry	Tin reagent			Product ratio		Yield
	X	Y		*syn*	*anti*	%
1	Et	H		78	22	59
2	Et	Me		91	9	80
3	Et	^{i}Pr		84	16	92
4	Et	^{t}Bu	**1**	13	87	72
5	Et	$CH_2{}^t$Bu		91	9	83
6	Et	$SiMe_3$	**2**	33	67	79
7	Et	$SiEt_3$	**3**	30	70	61
8[a]	OMe	H		91	9	86
9	OMe	^{t}Bu	**4**	5	95	77

[a] Data are quoted from ref. 10.



Scheme 2.

Table 2. Reaction of 2-*tert*-Butyl-*cis*-2-alkenyltins toward Various Aldehydes

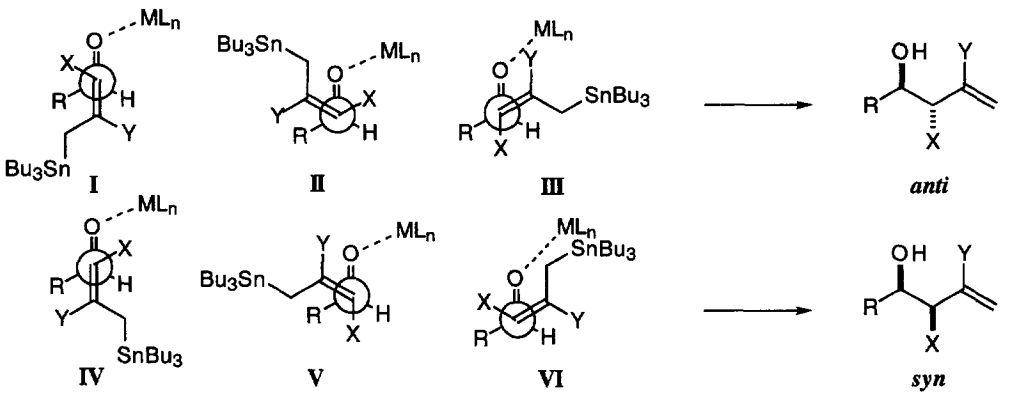


Entry	Aldehyde	Tin	Product ratio		Yield
	R	reagent	*syn*	*anti*	%
1	n-C_7H_{15}	**1**	43	57	54
2	c-C_6H_{11}	**1**	84	16	45
3	n-C_7H_{15}	**4**	10	90	59
4	c-C_6H_{11}	**4**	4	96	61
5	PhCH=CH	**4**	50	50	63

various 2-alkenyltins,[1] unsubstituted *cis*-2-pentenyltin selectively afforded the corresponding *syn*-homoallyl alcohol in the $BF_3{\cdot}OEt_2$-promoted reaction (entry 1). It was also confirmed that 2-methyl- and 2-isopropyl-*cis*-2-pentenyltins exhibited *syn*-selectivity (entries 2 and 3). In sharp contrast, however, when *cis*-2-pentenyltin had a bulky *tert*-butyl group at its 2-position (**1**), it showed high *anti*-selectivity (entry 4). As far as we know, this is the first example of the *anti*-selective reaction with a simple aldehyde promoted by $BF_3{\cdot}OEt_2$. Similarly, when the substituent (Y) was trimethylsilyl (**2**) or triethylsilyl (**3**), the diastereoselectivity remained *anti*-predominant though at somewhat decreased levels (entries 6 and 7). Furthermore, the *anti*-selectivity was also good for the reagent (**4**) with a methoxyl group as the terminal substituent (X); the selectivity increased up to 95 % (entry 9). It was previously reported that when Y was H the selectivity was highly *syn*-predominant (entry 8).[10] These results would indicate that the *anti*-selectivity was apparently caused by the bulkiness of the 2-substituent. It is noteworthy that neopentyl group, a considerably bulky substituent, did not exhibit the *anti*-selectivity but rather high *syn*-selectivity (entry 5). Tertiary substituents seem to be essential for the *anti*-selectivity. We also investigated the effect of the double bond geometry and found that the *trans*-allylic tin reagent formally corresponding to **1** showed *syn*-selectivity (Scheme 2). *Cis*-geometry is also essential for the *anti*-selectivity.

We next investigated the scope and limitation of the present unusually stereocontrolled reaction. The results for the reaction of some other aldehydes with **1** and **4** are collected in Table 2. While the aromatic aldehyde exhibited high *anti*-selectivity, aliphatic aldehydes such as octanal and cyclohexanecarbaldehyde markedly decreased or reversed the selectivity in the reaction with **1** (entries 1 and 2). The reagent **4** showed much wider applicability (entries 3 and 4), but cinnamaldehyde disappointingly gave a 1:1 mixture of the stereoisomers (entry 5). These results imply that the selectivity is controlled not only by the steric factor of the substituent Y but also by the electronic factor.

It is apparent that this unusual stereoselectivity can not be explained by the previously reported transition states.[2,3] Bearing in mind the effect of tertiary substituents, the present *anti*-selectivity for the major product can most reasonably be accounted for by the inverse antiperiplanar transition state **I** (Scheme 3); conformation **I** can most effectively avoid the steric congestion of Y among the *anti*-affording transition states **I–III**. A similar inverse antiperiplanar transition state that has been proposed by Heathcock in the reaction of silyl enol ethers[11] supports our finding. When the substituent Y is relatively small, transition states **IV–VI** to give *syn*-product are preferred as previously reported.[12]



Scheme 3.

Knowing such a substituent effect is helpful for designing stereocontrolled reactions. Furthermore, it would be possible to extend this methodology of stereocontrol to other synthetically useful functional groups as the bulky 2-substituent (Y) and the terminal substituent (X). Improvement of the stereoselectivity and further application of the methodology are now under study.

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7. In this report, the prefix *cis* refers to the geometry between the stannylmethyl group and the substituent X at the 3-position of allylic tins.
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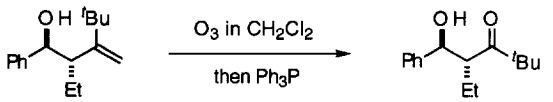
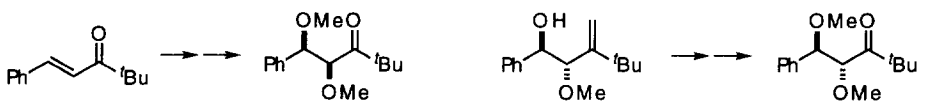
9. The stereochemistry of the products was determined by the following ways, (a), (b) and (c).
   (a) The ^{13}C NMR spectrum of the aldol compound derived as below from the product of entry 4 in Table 1 was compared to that cited in the reference, indicating the *anti*-stereochemistry of the major product. Heathcock, C. H.; Lampe, J. *J. Org. Chem.*, **1983**, *48*, 4330-4337.

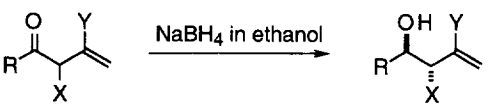


   (b) Comparison of the *syn*-isomer of dimethoxyketone prepared from the *trans*-enone (protection, OsO_4 oxidation, methylation and deprotection) and the one derived from the product of entry 9 in Table 1 (methylation and ozonolysis) showed that they had different stereochemistry.



syn-form — Major product of entry 9 in Table 1 — *anti*-form

   (c) From refs. 9 (a) and (b), the following reaction was confirmed to give the *anti*-isomers, which were spectroscopically compared to the products in Tables 1 and 2 and Scheme 2.



Anti-selective by the Cram's rule

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11. Heathcock, C. H.; Hug, K. T.; Flippin, L. A. *Tetrahedron Lett.*, **1984**, *25*, 5973-5976.
12. Of the three conformations **IV–VI**, we can not tell which one is the most applicable,[3] because the preference may be determined by the combination of steric and electronic factors of X, Y and R. Therefore, the reason for the present marked change in the stereoselectivity is not wholly clear yet.

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