Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 1405–1408

TETRAHEDRON LETTERS

Reversible stereocontrol in the Lewis acid promoted reaction of alkoxyaldehydes toward various allyltins

Yutaka Nishigaichi* and Akio Takuwa

Department of Material Science, Faculty of Science and Engineering, Shimane University, 1060 Nishikawatsu-cho, Matsue, Shimane 690-8504, Japan

Received 21 November 2002; revised 17 December 2002; accepted 19 December 2002

Abstract—In the reactions of variously substituted allyltin reagents toward achiral alkoxyaldehydes, one of the diastereomeric homoallyl alcohols was stereoselectively obtained by the help of BF_3, while $TiCl_4$ preferentially gave the other diastereomer, though (*E*)- and (*Z*)-3-monoalkylallyltin reagents were exceptional. This reversible diastereoselectivity can be explained by the coordination geometry (*anti* or *syn*) of the Lewis acids toward alkoxyaldehydes.

Reaction between aldehydes and allyltin reagents is known as a useful synthetic method to control diastereoselectivity.[1] One of the most mentioned selectivities is referred to as prochirality matching.[2] For example, the *syn*-selectivity for the Lewis acid-promoted reaction between an achiral aldehyde and 3-mono-substituted allylic tin reagents such as crotyltin[3] is the most representative. As generally accepted, the characteristic feature of this selectivity is that it is not affected seriously by the *cis*/*trans*-geometry of the reagent[4] and the coordination mode of the applied Lewis acid, chelation or non-chelation.[5] This is one reason why the methodology has been widely applied to the stereoselective organic synthesis.

In contrast to the current understanding, we will describe here that such Lewis acid promoted reactions of various allylic tin reagents toward achiral alkoxyaldehydes are often affected by the coordination mode of the Lewis acid and the selectivity can be controlled efficiently by the applied Lewis acid.

Recently, we have reported stereospecific nature of the Lewis acid promoted reaction of 3,3-disubstituted[6] and 3-deuterated[7] allyltin reagents toward aldehydes. This stereospecificity was accounted by the *syn*-synclinal transition state[5b,8] where the allyltin reagent was assumed to approach the aldehyde from the opposite direction to the coordinated Lewis acid. Thus, we were stimulated to investigate the relation between the coordination site of the Lewis acid and the stereoselectivity using simple achiral alkoxyaldehydes to control the coordination.

At first, α-benzyloxyacetaldehyde **1** as a most simple alkoxyaldehyde was employed. As a non-chelative Lewis acid, $BF_3{\cdot}Et_2O$ was used. On the other hand, for a chelation controlled reaction, $TiCl_4{\cdot}2Et_2O$ was employed, which is known to be effective to suppress the Sn–Ti transmetallation.[9] Allyltins investigated here were (*Z*)-3-deuterioallyltin (**2a**)[7,10] as unsubstituted one, (*E*)-crotyltin (**2b**), (*Z*)-pentenyltin (**2c**)[11] and (*E*)-cinnamyltin (**2d**) as 3-mono-substituted ones, and geranyltin (**2e**) and neryltin (**2f**) as 3,3-disubstituted ones. The results are collected in Table 1.

In the BF_3-promoted reactions (entries 1–6), most of variously substituted allylic tins exhibited good to high stereoselectivity (product **3**), which is parallel to the previously reported results for non-chelative aldehydes.[1,6,12] One exception was the reaction of (*Z*)-reagent **2c** (entry 3). Its low *syn*-selectivity (product **4**) was also similar to the previous result reported by Keck.[5b]

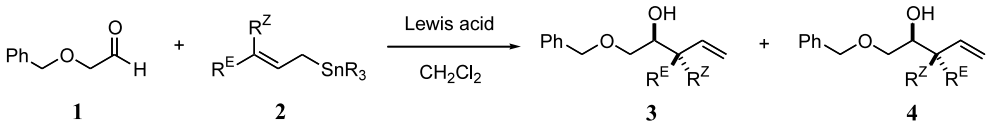
Interestingly, the $TiCl_4$-promoted reactions (entries 7–12) showed essentially opposite and good to high stereoselectivity (product **4**), except for the reaction of **2b** (entry 8) which underwent an unselective reaction. (*Z*)-Reagent **2c**, in this case (entry 9), behaved like other reagents and exhibited much higher diastereoselectivity of **4** compared with entry 3. Because the $TiCl_4$-

Keywords: allylation; chelation; diastereoselection; stereocontrol; tin and compounds.

* Corresponding author. Fax: +81 852 326429; e-mail: nishigai@riko.shimane-u.ac.jp

0040-4039/03/$ - see front matter
PII: S0040-4039(02)02867-8

Table 1. Reactions between benzyloxyacetaldehyde and various allyltins



Allyltin reagent			[Entry] Product ratio, **3**/**4** (yield/%)	
R^E, R^Z	R		$BF_3{\cdot}Et_2O$[a]	$TiCl_4{\cdot}2Et_2O$[b]
H, D	Ph	**2a**	[1] 89/11 (quant.)	[7] 20/80 (quant.)
Me, H	Bu	**2b**	[2] 85/15 (69)	[8] 50/50 (69)
H, Et		**2c**	[3] 34/66 (72)	[9] 9/91 (67)
Ph, H		**2d**	[4] 90/10 (87)	[10] 3/97 (80)
$Me_2C{=}CHCH_2CH_2$, Me		**2e**	[5] 96/4 (90)	[11] 1/99 (83)
Me, $Me_2C{=}CHCH_2CH_2$		**2f**	[6] 95/5 (83)	[12] <1/99 (75)

[a] To a mixture of **1** (0.2 mmol) and **2** (0.3 mmol) in CH_2Cl_2 (2 mL) was added $BF_3{\cdot}Et_2O$ (0.4 mmol) at −78°C under N_2. The mixture was stirred for 2 h at the same temperature and then quenched with an aqueous $NaHCO_3$ solution. The CH_2Cl_2 extract was dried (Na_2SO_4) and concentrated, and the products were isolated by TLC.

[b] To a solution of **1** in CH_2Cl_2 (1 mL) were added Et_2O (0.4 mmol) and $TiCl_4$ (0.2 mmol) successively at −78°C under N_2. After 5 min, **2** (0.3 mmol) in CH_2Cl_2 (1 mL) was added and the mixture was stirred for 2 h at −78°C. The work-up procedure was the same as above.

promoted reaction was highly regioselective in every case and the diastereoselectivity was stereospecific as typically shown by the reactions of **2a** (entry 7), **2e** (entry 11), and **2f** (entry 12), the influence of the transmetallated allyltitanium species could be excluded.

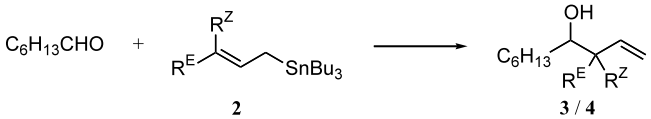
In addition, it is noteworthy that in the reactions of non-chelative heptanal with **2d** and **2e** (Scheme 1), the both Lewis acids gave preferentially the same stereoisomers in more than 90% selectivity which corresponded to the diastereomer **3**.

These results suggest that the present binary stereocontrol especially in the cases of **2a**, **2d**–**f** was achieved by the benzyloxy substituent. Because benzyloxyacetaldehyde simply coordinates BF_3 as a monodentate ligand, the complex takes *anti*-conformation[13] (Scheme 2, **A**). On the other hand, because $TiCl_4$ can take two more ligands, the alkoxyaldehyde chelates it as a bidentate ligand to form a cyclic complex, i.e. *syn*-conformation[14] (Scheme 2, **B**). Then, if an allylic tin reagent comes from the opposite direction to the coordinating Lewis acid to afford the *syn*-synclinal conformation as proposed for the reaction of an allylsilicon reagent,[8a] diastereomer **3** or **4** would be selectively obtained from the complex **A** or **B** via the transition structure **C** or **D**, respectively. In contrast to these cases, the exceptional behaviour of 3-monoalkyl-substituted allyltin reagents **2b** and **2c** can not be fully explained so far. But, as pointed out previously,[8a] the transition structures **C′** and **D′** which give the other diastereomers may be included especially in the cases of entries 3 and 8.

Next, to clarify the scope of the reaction, various alkoxyaldehydes such as β-benzyloxy one **5**, γ-benzyloxy one **6**, and aromatic one **7**, were employed to the reactions with 3-mono-substituted cinnamyltin **2d** and 3,3-disubstituted neryltin **2f** (Table 2). BF_3-mediated reactions with **2d**[12] gave the *syn*-isomers **3** in good selectivity (entries 1, 3, and 5) as for the reaction of **1**. The corresponding $TiCl_4$-mediated reactions depended on aldehydes: aldehydes **5** (entry 2) and **7** (entry 6), which formed six-membered chelates, showed good *anti*-selectivity to give **4**, while aldehyde **6** (entry 4) which lead to a seven-membered chelate gave preferentially the *syn*-product **3**.

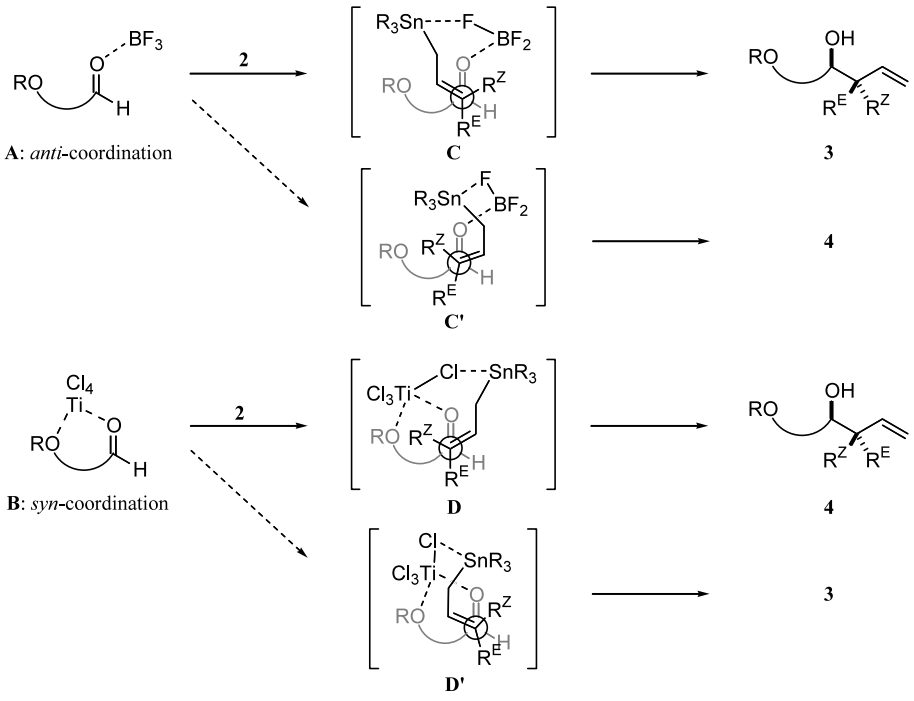
On the other hand, in the reactions with **2f**, all aldehydes **5**–**7** exhibited the binary stereoselectivity (entries 7–12). It is interesting that seven-membered chelate of **6** also preferred the product **4** in this case (entry 10). Here again, BF_3-mediated reactions followed the previously reported diastereoselectivity for the non-chelative aldehydes.[6]

In conclusion, the binary diastereoselectivity in the reaction between alkoxyaldehydes and allyltin reagents **2a** and **2d**–**f** could be controlled by the applied Lewis acid, of which coordination mode is critical for the selectivity. While there are some limitations such as BF_3-mediated reaction of **2c** and $TiCl_4$-mediated reactions of **2b** and of **2d** with **6** of which reasons are still ambiguous, this methodology is synthetically useful due to the flexible stereocontrol.



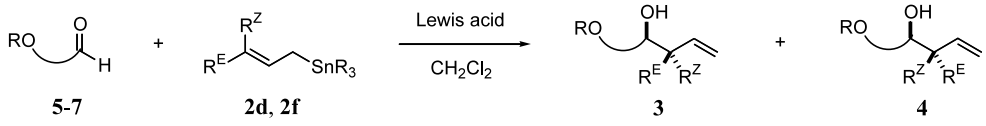
3 / **4** = 99/1 ($BF_3{\cdot}Et_2O$), 99/1 ($TiCl_4{\cdot}2Et_2O$) from **2d**
91/9 ($BF_3{\cdot}Et_2O$), 92/8 ($TiCl_4{\cdot}2Et_2O$) from **2e**

Scheme 1. Reactions of heptanal.



Scheme 2. Plausible reaction pathways.

Table 2. Reactions between various alkoxyaldehydes and allyltins **2d** and **2f**



Alkoxyaldehyde	Lewis acid	[Entry] Product ratio, **3**/**4** (yield/%)	
		with **2d**	with **2f**
3-Benzyloxypropanal (**5**)	$BF_3{\cdot}Et_2O$	[1] 96/4 (55)	[7] 90/10 (55)
	$TiCl_4{\cdot}2Et_2O$	[2] 4/96 (quant.)	[8] 7/93 (52)
4-Benzyloxybutanal (**6**)	$BF_3{\cdot}Et_2O$	[3] >99/1 (80)	[9] 85/15 (80)
	$TiCl_4{\cdot}2Et_2O$	[4] 75/25 (69)	[10] 30/70 (82)
o-Anisaldehyde (**7**)	$BF_3{\cdot}Et_2O$	[5] 79/21 (98)	[11] 68/32 (92)
	$TiCl_4{\cdot}2Et_2O$	[6] 29/71 (85)	[12] 17/83 (83)

Acknowledgements

This work was partly supported by a Grant-in-Aid for Scientific Research (No. 12640519) from the Japanese Ministry of Education, Culture, Sports, Science and Technology.

References

1. (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207; (b) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395.
2. Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31.
3. Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.
4. For exceptional cases, see: (a) Mikami, K.; Kawamoto, K.; Loh, T.-P.; Nakai, T. *J. Chem. Soc., Chem. Commun.* **1990**, 1161; (b) Marshall J. A.; Wang, X. *J. Org. Chem.* **1992**, *57*, 1242.
5. (a) Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 1879; Keck, G. E.; Abbott, D. E. *Tetrahedron Lett.* **1984**, *25*, 1883; Keck, G. E.; Abbott, D. E.; Wiley, M. R. *Tetrahedron Lett.* **1987**, *28*, 139; (b) Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889.
6. Nishigaichi, Y.; Takuwa, A. *Tetrahedron Lett.* **1999**, *40*, 109.
7. Nishigaichi, Y.; Takuwa, A. *Tetrahedron Lett.* **2002**, *43*, 3045.
8. (a) Bottoni, A.; Costa, A. L.; Tommaso, D. D.; Rossi, I.; Tagliavini, E. *J. Am. Chem. Soc.* **1997**, *119*, 12131; (b) Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970; Denmark, S. E.; Weber, E. J.; Wilson, T. M.; Willson, E. M. *Tetrahedron* **1989**, *45*, 1053.

9. Nishigaichi, Y.; Yoshikawa, M.; Takigawa, Y.; Takuwa, A. *Chem. Lett*. **1996**, 961.
10. Orain, D.; Guillemin, J.-C. *J. Org. Chem*. **1999**, *64*, 3563.
11. Nishigaichi, Y.; Ishida, N.; Takuwa, A. *Bull. Chem. Soc. Jpn*. **1994**, *67*, 274.
12. Nishigaichi, Y.; Takuwa, A. *Chem. Lett*. **1994**, 1429.
13. Corey, E. J.; Lee, T. W. *Chem. Commun*. **2001**, 1321 and references cited therein.
14. Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC Press: Boca Raton, 1996 and references cited therein.