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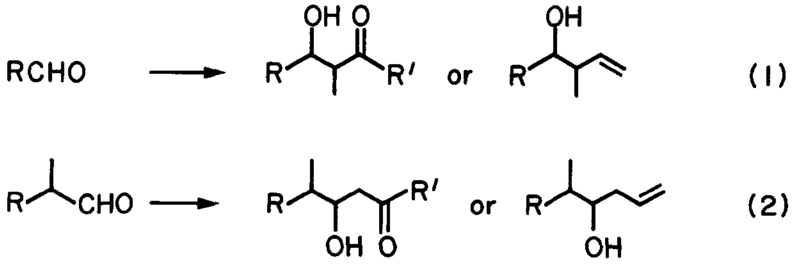
ACYCLIC STEREOSELECTION. 20. HIGH DIASTEREOFACIAL SELECTIVITY IN THE STANNIC CHLORIDE MEDIATED REACTIONS OF ALLYLSILANES WITH CHIRAL α- AND β-ALKOXY ALDEHYDES.[1]

Syun-ichi Kiyooka[2] and Clayton H. Heathcock*

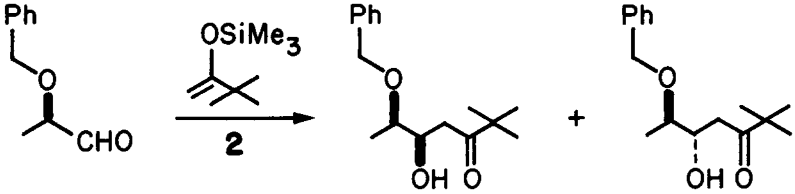
Department of Chemistry, University of California
Berkeley, California 94720

Abstract: Stannic chloride is an effective catalyst for the reaction of allylsilanes with chiral α- and β-alkoxy aldehydes. In the case of α-alkoxy aldehyde **1**, the diastereofacial preference is outstanding (>35:1). With β-alkoxy aldehydes **5** and **6**, selectivity is lower, but still quite acceptable (7-12:1).

In recent years, there has been extensive investigation of the stereochemistry of the addition of enolates and crotylorganometallic reagents to aldehydes.[3,4] As a result, rather reliable methods now exist for achieving good diastereoselectivity in additions to achiral aldehydes (eq 1). Recently, good progress has also been made in finding ways to control diastereofacial selectivity in additions to chiral aldehydes (eq 2). One way in which this problem has been addressed is by the use of chiral reagents that have such pronounced diastereofacial preferences that the modest diastereofacial preference of the chiral aldehyde is overwhelmed.[5] We have reported that the BF_3-mediated reactions of enolsilanes to chiral aldehydes proceed with exceptional diastereofacial selectivity.[6] In addition, Reetz and Jung have recently found that good 1,3-asymmetric induction is observed in the titanium tetrachloride mediated reactions of β-alkoxy aldehydes with allylsilanes and enolsilanes.[7]

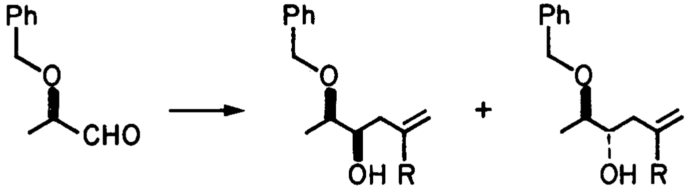


In our previous investigation of the stereochemistry of additions to chiral aldehydes,[6] we found that the BF_3 mediated addition of enolsilanes to aldehyde **1** proceed with low stereoselectivity. For example, the reaction of **1** with enolsilane **2** in methylene chloride at -78 °C gives a 1:1 mixture of β-hydroxy ketones **3** and **4**. Consequently, we surveyed a variety of different Lewis acids for their



1 **3** **4**

utility with α- and β-alkoxy aldehydes, both in reactions with enolsilanes[8] and with allylsilanes.[9] As substrates for the study, we employed aldehydes **1**, **5**, and **6** (eq 3-5). In this Letter, we report that good to excellent diastereofacial selectivity can be achieved in the reactions of α-alkoxy aldehyde **1** and β-alkoxy aldehydes **5-6** with allyltrimethylsilane (**7**) or methallyltrimethylsilane (**8**), provided stannic chloride is employed as the Lewis acid.[10]

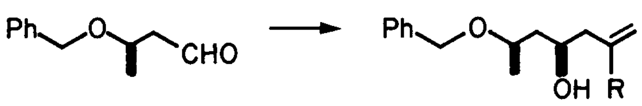


(3)

1 **9** **10**

(4)

5 **11** **12**



(5)

6 **13** **14**

Results are summarized in Table I. Aldehyde **1** shows outstanding selectivity, giving compounds **9** and **10** in ratios of >35:1[11] in excellent chemical yield. With BF_3, the yield is lower and there is almost no stereoselectivity. Indeed, the modest stereoselection that is observed is in the opposite sense. The $TiCl_4$ mediated reaction of **1** with allylsilane gives chlorine-containing products in which the benzyl group has been lost. In the case of aldehyde **5** the $SnCl_4$ mediated reaction again gives an excellent chemical yield; diastereofacial selectivity is on the order of 10:1, with compound **11** being the major product.[11] With this aldehyde, BF_3 gives none of the normal addition product. The problem in this case seems to be β-elimination of the alkoxy group. β-Alkoxy aldehyde **6** shows a diastereofacial preference of 9:1 with silane **7** and 7:1 with silane **8**; the predominant isomer is alcohol **12**.[11] In this case also, we found $SnCl_4$ to be a superior catalyst to BF_3 or $TiCl_4$. With neither of the latter Lewis acids did we observe any of the normal addition product. In our hands, $TiCl_4$ gave only chlorine-containing, debenzylated products, in contrast to the report of Reetz and Jung.[8]

The diastereofacial preferences exhibited by aldehydes **1**, **5** and **6** in eq 3-5 are in accord with the hypothesis of chelation-control[12] in reaction of the allylsilane with the hexacoordinated tin intermediates **15-17**. It is not surprising that diastereoselectivity is highest in the more rigid five-membered chelate **15** than in the more flexible six-membered analog **16**, or that diastereo-

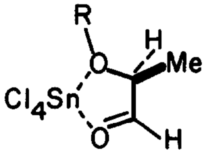
TABLE I

Diastereomer Ratios in the Reactions of Allylsilanes with Chiral Aldehydes (eq 3-5)

Entry	Aldehyde	Allylsilane	Lewis Acid	Yield (%)[a]	Diastereomer Ratio[b]
1	**1**	**7**	$SnCl_4$	94	35:1
2	**1**	**7**	$TiCl_4$	0[c]	---
3	**1**	**7**	$BF_3 \cdot Et_2O$	50	1:1.5
4	**1**	**8**	$SnCl_4$	81	45:1
5	**1**	**8**	$BF_3 \cdot Et_2O$	40	1:2.6
6	**5**	**7**	$SnCl_4$	92	12:1
7	**5**	**7**	$BF_3 \cdot Et_2O$	0[c]	---
8	**5**	**8**	$SnCl_4$	83	10:1
9	**6**	**7**	$SnCl_4$	97	9:1
10	**6**	**7**	$TiCl_4$	0[c]	---
11	**6**	**7**	$BF_3 \cdot Et_2O$	0[c]	---
12	**6**	**8**	$SnCl_4$	86	7:1

a. Isolated by silica gel chromatography; diastereomers were not separated. b. Ratios were determined by 250 MHz ^1H NMR and 62.9 MHz ^{13}C NMR. c. These reactions gave none of the normal product; see text.

selectivity is further diminished in addition to chelate **17**, in which the chiral center is one position farther from the carbonyl group.



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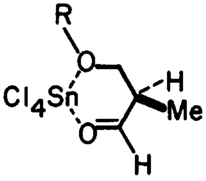

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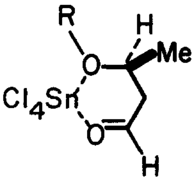

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1. For part 19, see C.H. Heathcock and S.H. Montgomery, *Tetrahedron Lett.*, in press.

2. Current address: Faculty of Science, Kochi University, Kochi 780 Japan.

3. For reviews of aldol stereoselection, see: (a) C.H. Heathcock, *Science*, **214**, 395 (1981); (b) D.A. Evans, J.V. Nelson and T.R. Taber in "Topics in Stereochemistry, Vol. 13," E.L. Eliel and S.H. Wilen, Eds., Wiley-Interscience, New York, 1982; (c) C.H. Heathcock in "Comprehensive Carbanion Chemistry, Vol. II," T. Durst and E. Buncel, Eds., Elsevier, 1983; (d) C.H. Heathcock in "Asymmetric Organic Reactions, Vol. 3," J.D. Morrison, Ed., Academic Press, New York, 1984.

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9. A. Hosomi and M. Sakurai, *Tetrahedron Lett.*, 1295 (1976).

10. Results with enolsilanes, which show more complex behavior, will be reported later in a full paper; C.H. Heathcock, L.A. Flippin and K.T. Hug.

11. In each case, the products were identified by catalytic hydrogenolysis, with concomittant saturation of the double bond (H_2-Pd/C) to give a diol, which was identified by comparison with an authentic specimen prepared by a stereochemically secure route. Details will be given in the full paper.

12. For previous examples of chelation control in additions to alkoxy aldehydes, see: (a) D.J. Cram and K.R. Kopecky, *J. Am. Chem. Soc.*, **81**, 2748 (1959); (b) M.L. Wolfrom and S. Hanessian, *J. Org. Chem.*, **27**, 1800 (1962); (c) T. Nakati and Y. Kishi, *Tetrahedron Lett.*, 2745 (1978); (d) E.L. Eliel, J.K. Koskimies and B. Lohri, *J. Am. Chem. Soc.*, **100**, 1615 (1978); (e) W.C. Still and J.H. McDonald, *Tetrahedron Lett.*, **21**, 1031 (1980); (f) R. Bernardi, *ibid.*, **22**, 4021 (1981); (g) ref 8.

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