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1,5-Asymmetric Induction in Reactions of δ-Alkoxyallylstannanes: Stereoselective Reactions with Chiral Aldehydes

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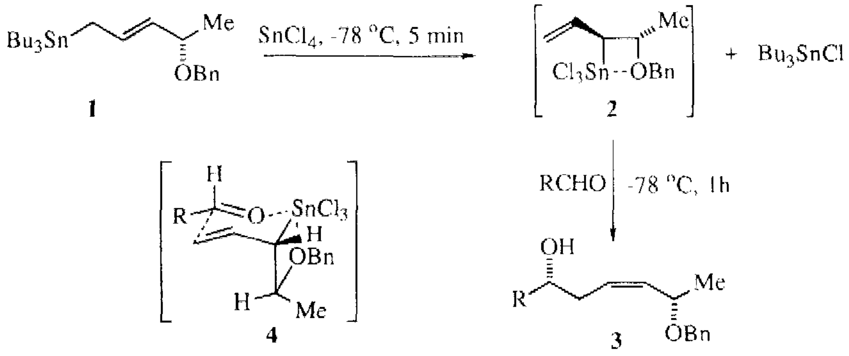
Key Words: Allylstannane; alkoxyaldehyde; stereoselectivity; remote asymmetric induction; tin(IV)chloride

Abstract: *Transmetallation of (4S,2E)-4-phenylmethoxypent-2-enyl(tributyl)stannane 1 using tin(IV)chloride generates a reagent which shows excellent 1,5-stereoselectivity in reactions with aldehydes: with chiral aldehydes, the stereochemical preference of the reagent dominates the course of the reaction.*

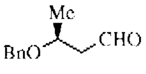
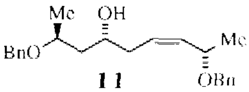
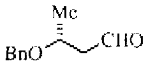
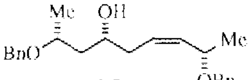
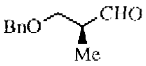
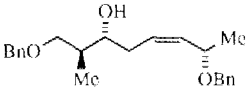
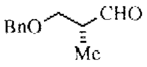
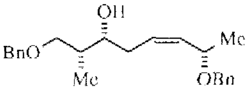
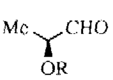
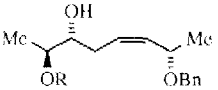
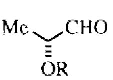
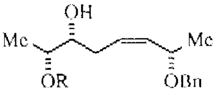
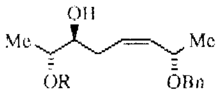
Allylstannanes are being developed into useful reagents for organic synthesis.[1] It was shown recently that addition of tin(IV)chloride to a solution of (4*S*,2*E*)-4-phenylmethoxypent-2-enyl(tributyl)stannane **1** generated an intermediate which reacts regio- and stereo-selectively with aldehydes to give the monoprotected 1,5-diols **3**.[2] The selectivity was explained by invoking transmetalation of the allyl(tributyl)stannane **1** *via* an SE' process to generate the allyltin trichloride **2**. It was suggested that this intermediate is stabilised with respect to 1,3-migration of the tin by a hypervalent Sn-O interaction,[3,4] and that subsequent reaction with the aldehyde takes place *via* the cyclic, chair-like, transition state **4**, in which the substituent α to tin is axial.[2] This known preference of α-substituted allylstannanes,[5] together with the preference of the R group of the aldehyde to adopt an equatorial position, determines which face of the aldehyde is approached by the stannane, and hence the configuration of the hydroxyl bearing stereogenic centre in the product. Participation of intermediate **2** rather than the isomeric intermediate in which the vinyl and methyl substituents are *cis*-disposed about the four membered ring, is consistent with steric effects. In the absence of heteroelement containing functional groups at the remote allylic or homoallylic positions, mixtures of regio- and stereo-isomers are obtained.[6,7]



These reactions of allylstannane **1** and aldehydes show excellent 1,5-asymmetric induction. As examples of such remote asymmetric induction are rather rare,[8] it was decided to investigate the stereoselectivities of tin(IV)chloride promoted reactions between the allylstannane **1** and chiral α- and β-alkoxyaldehydes.

The products obtained are given in the **Table**. In all cases, a cooled solution of tin(IV)chloride was added to a solution of the stannane **1** in dichloromethane at -78 °C. The mixture was stirred at this temperature for five minutes before the addition of a cooled solution of the aldehyde. After 1h at -78 °C, conventional work-up gave the products which were isolated by flash chromatography.[9]

Table: Tin(IV)chloride induced reactions between δ-alkoxyallylstannane **1** and chiral alkoxyaldehydes.

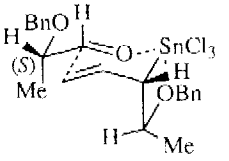
Aldehyde	% Yield	Products	Product Ratio[a]
 **5**	76	 **11**	-^{b}
 **6**	85	 **12**	-^{b}
 **7**	55	 **13**	-^{c}
 **8**	66	 **14**	-^{c}
 **9a** R = Bn **9b** R = $SiMe_2Bu^t$ **9c** R = MOM	90 72 72	 **15a** R = Bn **15b** R = $SiMe_2Bu^t$ **15c** R = MOM	-^{b} -^{b} -^{b}
 **10a** R = Bn **10b** R = $SiMe_2Bu^t$ **10c** R = MOM	89 65 68	 +  **16a** R = Bn **17a** R = Bn **16b** R = $SiMe_2Bu^t$ **17b** R = $SiMe_2Bu^t$ **16c** R = MOM **17c** R = MOM	70:30^{d} 70:30^{d} 65:35^{d}

[a] Ratio determined by ^{1}H n.m.r. of the product mixture. [b] Less than 4% of any other diastereoisomer detected. [c] Partial racemisation of aldehydes **7** and **8** gave 5-7% crossover product. [d] Ratio corresponds to **16** : **17**.

The (*R*)- and (*S*)-β-alkoxyaldehydes **5** - **8** were found to react with the intermediate from stannane **1** and tin(IV)chloride to give the products **11** - **14** containing less than 4% of any other diastereoisomer (^{1}H n.m.r.), whereas for the α-alkoxyaldehydes, the stereoselectivity was found to depend upon the configuration of the aldehyde. The (2*S*)-2-alkoxyaldehydes **9a-c** gave the alcohols **15a-c** with excellent stereoselectivity, whereas mixtures of products **16a-c** and **17a-c** were obtained from the (2*R*) 2-alkoxyaldehydes **10a-c**.

In all cases the major product had the stereochemistry expected from participation of the allyltin trichloride **2** which reacted with the aldehyde *via* the transition state **4**. Indeed for the β-alkoxyaldehydes **5** - **8**, this process dominated the course of the reaction. In contrast, the stereoselectivities of the reactions of the stannane with the α-alkoxyaldehydes **9** and **10** were found to be sensitive to the configuration of the aldehyde, with the (4*S*)-stannane **1** and a (2*S*)-2-alkoxyaldehyde **9** constituting a "matched" pair, whereas the (4*S*)-stannane **1** and a (2*R*)-2-alkoxyaldehyde **10** correspond to a "mismatched" pair.

The reactions between stannane **1** and the α-alkoxyaldehydes **9** and **10** would appear to be following the Felkin Anh model for carbonyl attack.[12] The products from the reactions between the "matched" (4*S*)-allylstannane **2** and the (2*S*)-alkoxyaldehydes **9a-c** are consistent with participation of transition state **18** in which the intermediate allyltin trichloride **2** approaches the *re* face of the aldehyde in line with the Felkin Anh model.[12] However, the analogous transition state **19** for the reaction of the (2*R*)-alkoxyaldehydes **10a-c**, also requires attack on the *re* face of the aldehyde, which is contrary to the Felkin Anh model for (2*R*)-alkoxyaldehydes, and alternative processes leading to the formation of the minor products **17a-c** are able to compete.[13,16]



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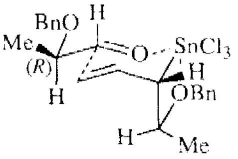

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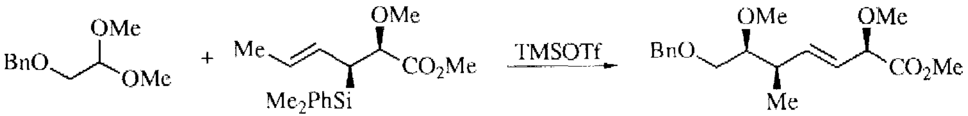
The reactions of the allyltin trichloride **2** with aldehydes can be compared with the Lewis acid induced reactions of α-substituted allylsilanes, e.g. **21**, with acetals.[17] The allylsilanes are isolable compounds, unlike the allyltin trichloride **2** which is generated in solution, and react with acetals in the presence of Lewis acids, to give (*E*)-alkenes, e.g. **22**.



20 **21** **22**

For these reactions of the allylsilanes **21**, the stereogenic centre bearing the silyl substituent controls the configurations of the newly formed, remote, stereogenic centres in the product. However, the stereoselectivity of the allylsilane reactions is explained in terms of an open chain, antarafacial SE' process,[17] unlike the cyclic, suprafacial process suggested here for the allyltin trichloride - aldehyde reactions.

It would appear that the effective 1,5-asymmetric induction observed in reactions between aldehydes and the intermediate formed on transmetallation of the stannane **1** by tin(IV)chloride is also found in reactions of α- and β-alkoxyaldehydes. The reactions are highly stereoselective with less than 4% of any other diastereoisomer being formed, except in the cases of "mismatched" α alkoxyaldehydes, although even in these cases the major product, typically accounting for 70% of the product mixture, is that expected on the basis of reagent control.

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4. The ^{1}H n.m.r. spectrum of a solution containing **2** shows the presence of a terminal double-bond, although the exact nature and binding of the ligands on tin have yet to be established; **2** δ_H(-55 °C, $CDCl_3$) 3.7 (2 H, m, 2-H and 3-H), 4.33 and 4.42 (each 1 H, d, *J* 11.5Hz, CHHPh), 5.02 (2 H, m, $=CH_2$), and 5.62 (1 H, dt, *J* 17, 8.5Hz, =CH-).

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8. Uemura, M.; Minami, T.; Hayashi, Y., *Tetrahedron Lett.*, **1988**, *29*, 6271.

9. The configurations of the products were established by comparison of the ^{1}H n.m.r. spectra of their diastereoisomeric acetoxymandelates,[2,10] and were confirmed by correlation with known compounds.[11]

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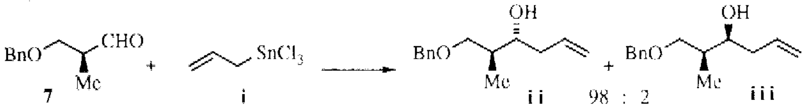
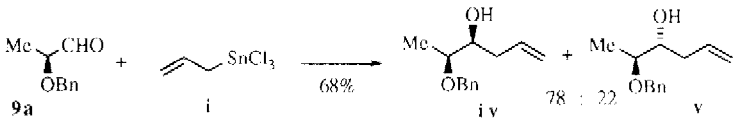
13. The preference for the α-alkoxyaldehydes **9** and **10** to react with the allyltin trichloride **2** *via* Felkin Anh transition states contrasts with chelation control found in the reactions of allyltin trichloride **i** with chiral α- and β-alkoxyaldehydes. The reaction between **i** and the 3-phenylmethoxypropanal **7** is known to give the *anti*-alcohol **ii**, the product of chelation control, with excellent stereoselectivity.[14] In our hands, the 2-phenylmethoxypropanal **9a** also reacted with the allyltin trichloride **i** to give more of the chelation controlled product iv.[9,15]

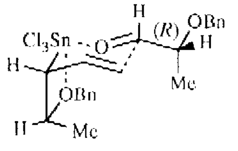




14. Keck, G. E.; Abbott, D. E., *Tetrahedron Lett.*, **1984**, *25*, 1883.

15. Keck, G. E.; Boden, E. P., *Tetrahedron Lett.*, **1984**, *25*, 265; Keck, G. E.; Andrus, M. B.; Romer, D. R., *J. Org. Chem.*, **1991**, *56*, 417.

16. The formation of the minor products **17a-c** from the reactions of the (2*R*)-alkoxyaldehydes **10** may involve equilibration of the allyltin trichloride **2** with its *cis*-diastereoisomer which reacts with the (2*R*)-alkoxyaldehyde *via* the Felkin Anh transition state **vi**. Alternatively, the allyltin trichloride **2** may be reacting with the (2*R*)-alkoxyaldehydes *via* a transition state, e.g. **vii**, in which the alkoxyalkyl group of the aldehyde is axial.



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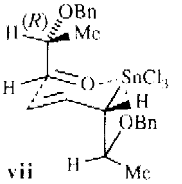

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17. Panek, J. S.; Yang, M., *J. Org. Chem.*, **1991**, *56*, 5755; Panek, J. S.; Yang, M., *J. Am. Chem. Soc.*, **1991**, *113*, 6594.

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