1,4-Asymmetric induction in reactions between [2-(1-alkoxyalkyl)-propenyl](tributyl)stannanes and aldehydes promoted by tin(IV) halides

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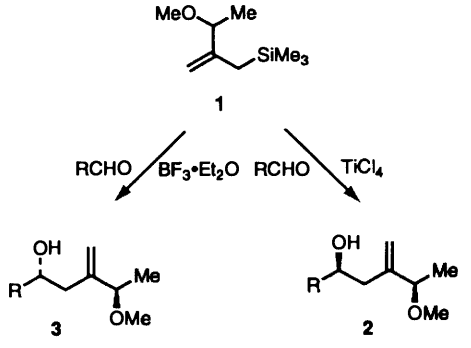
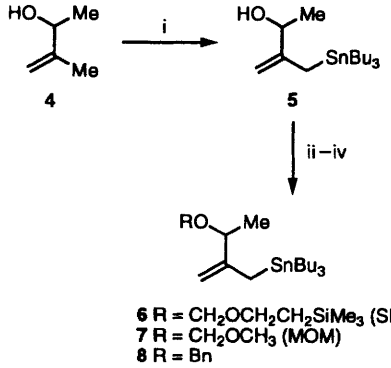
Transmetallation of [2-(1-alkoxyalkyl)propenyl](tributyl)stannanes with tin(IV) bromide or chloride generates an allyltin trihalide which reacts with aldehydes with useful 1,4-asymmetric induction.

Alk-2-enyl(tributyl)stannanes with heteroatom substituents at the 4-, 5- and 6-positions react with aldehydes with useful levels of remote asymmetric induction.[1] 1,4-Asymmetric induction has been observed in reactions of [2-(1-methoxyalkyl)propenyl](trimethyl)silane **1** with aldehydes which give either the 1,4-



syn- or 1,4-*anti*-alcohol **2** or **3** as the major product depending on the Lewis acid used.[2] We now describe reactions of [2-(1-alkoxyalkyl)propenyl](tributyl)stannanes with aldehydes which proceed with stereoselectivity in favour of 1,4-*anti*-isomers together with aspects of the chemistry of the products.

The [2-(1-hydroxyethyl)prop-2-enyl](tributyl)stannane **5** was prepared by lithiation of 3-methylidenebutan-2-ol **4** and quenching with tributyltin chloride,[3] and was alkylated to give the (2-trimethylsilylethoxy)methyl ether **6**, the methoxymethyl ether **7** and the benzyl ether **8** (Scheme 1).



Scheme 1 *Reagents:* i, 2 BuLi, Bu_3SnCl (46%); ii, SEMCl, Pr^i_2NEt (89%); iii, MOMCl, Pr^i_2NEt (76%); iv, NaH, Bu_4NI, BnBr

Reactions with aldehydes were carried out by adding a solution of the tin(IV) halide to the allylstannane at −78 °C, followed, after 5–10 min, by the aldehyde. With benzaldehyde and tin(IV) bromide, the 2-(hydroxyethyl)propenylstannane **5** gave the 1,4-*syn* and 1,4-*anti* products **9** and **10** with modest stereoselectivity, *ca.* 60:40 in favour of the *syn*-isomer **9**. The reactions with the 2-(alkoxyethyl)propenylstannanes were more stereoselective, and the stereoselectivity was reversed. For example, the (2-trimethylsilylethoxy)methoxy ether **6** gave the 1,4-*syn* and 1,4-*anti* products **11** and **12** in a ratio of 15:85.

The configurations of the products **9**† and **10** from the reaction of the hydroxystannane **5** with benzaldehyde were established by correlation with an authentic sample of the *syn*-methoxyalcohol **2**.[2] Methylation of this alcohol (NaH, MeI, 85%) gave the 1,4-*syn*-dimethyl ether **13** which was identical to the dimethyl ether obtained from the major diol **9** (NaH, MeI, 93%) and distinctly different from the dimethyl ether **14** obtained by methylation of the minor diol **10**. Treatment of the 1,4-*syn*-diol **9** with (2-trimethylsilylethoxy)methyl chloride gave the *minor* product from the reaction of benzaldehyde and the 2-(alkoxyethyl)propenylstannane **6** together with the regioisomeric ether **15**, so showing that the major product from this reaction had been the *anti*-isomer **12**. This major product **12** was converted into the minor product **11**, identical to that prepared from the 1,4-*syn*-diol **9**, by using diethyl azodicarboxylate, triphenylphosphine and *o*-nitrobenzoic acid[4] followed by saponification of the inverted *o*-nitrobenzoate. Finally, oxidation of both of the 1,4-*syn*- and *anti*-hydroxy ethers **11** and **12** gave the same ketone **16**.

The results of reactions of the stannanes **6–8** and benzaldehyde, acrolein and 2-methylpropanal, promoted by both tin(IV) bromide and tin(IV) chloride are summarised in Table 1. To a first approximation, the stereoselectivities of the reactions of the 2-(alkoxyalkyl)stannanes are independent of the nature of the alkoxy group, the aldehyde, and whether tin(IV) bromide or chloride is used. In all cases the 1,4-*anti* product is preferred, stereoselectivity *ca.* 85:15. Similar results were obtained with the 3-alkoxy-4-methyl-2-(tributylstannylmethyl)pent-1-enes **18** and **19**, prepared by stannylation of 2,4-dimethylpent-1-en-3-ol **17**,[5] which on transmetallation with tin(IV) bromide reacted with benzaldehyde to give the 1,4-*anti* products **20** and **21**, stereoselectivities *ca.* 85:15 (Scheme 2).

The stereoselectivity of these reactions of the 2-(alkoxyalkyl)-stannanes **6–8**, **18** and **19** with aldehydes is consistent with transmetallation with the tin(IV) halide to generate an allyltin trihalide **22** in which the electron-deficient tin atom is co-ordinated to the oxygen substituent. Reaction with the aldehyde on the less hindered face of the allyltin trihalide *via* the six-membered, chair-like, cyclic transition state **23** would then lead to the observed 1,4-*anti*-stereoselectivity. Why the reversed

† The structure of the *syn*-1,4-diol **9** has been confirmed by X-ray diffraction. Details will be published in a full paper.

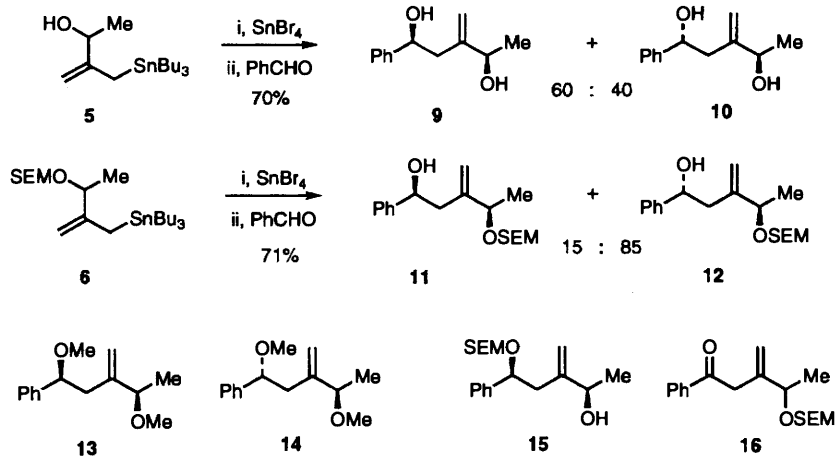
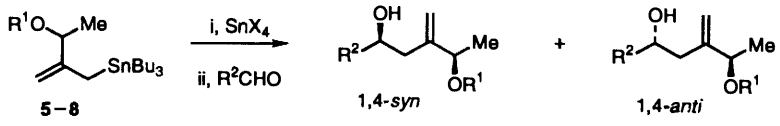
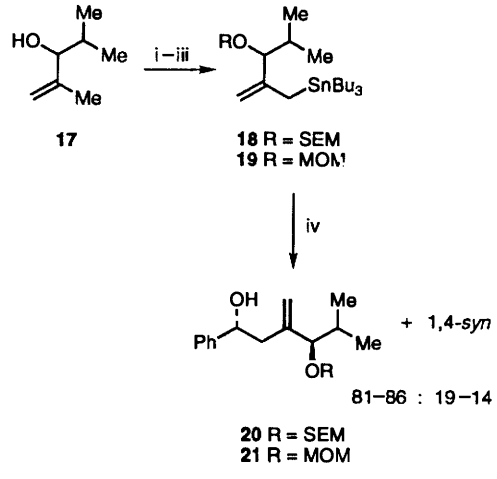


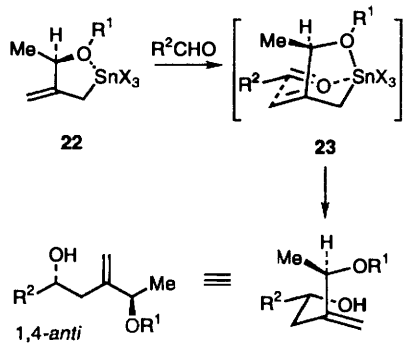
Table 1



Stannane R^1	Lewis acid SnX_4	Aldehyde R^2	Yield[a] (%)	1,4-*syn*:1,4-*anti*[b]
H	$SnBr_4$	Ph	70	60:40[c]
H	$SnCl_4$	Ph	55	67:33[c]
SEM	$SnBr_4$	Ph	71	15:85
SEM	$SnCl_4$	Ph	79	17:83
MOM	$SnBr_4$	Ph	70	14:86
MOM	$SnCl_4$	Ph	82	20:80
Bn	$SnBr_4$	Ph	62	15:85
SEM	$SnBr_4$	$H_2C{=}CH$	77	23:77
SEM	$SnBr_4$	Me_2CH	75	13:87

[a] Isolated yield. [b] By ^1H NMR of product mixture. [c] By GLC.





Scheme 2 *Reagents:* i, 2 BuLi, Bu_3SnCl (40%); ii, SEMCl, Pr^i_2NEt (70%); iii, MOMCl, Pr^i_2NEt (65%); iv, $SnBr_4$, PhCHO (**20**, 69%, 1,4-*anti*:1,4-*syn* = 86:14; **21**, 60%, 1,4-*anti*:1,4-*syn* = 81:19)

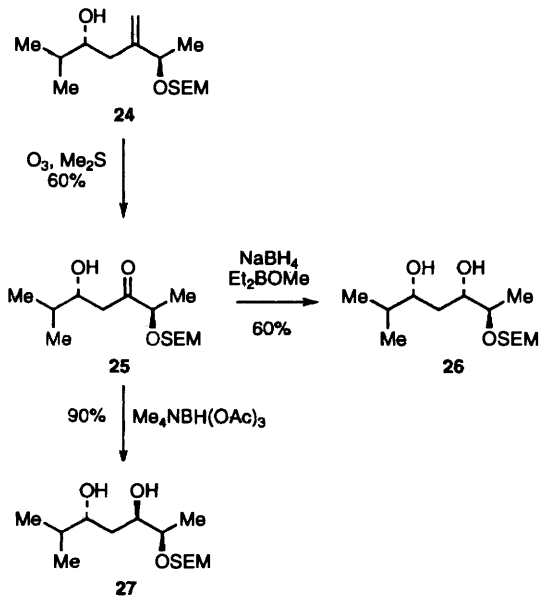
stereoselectivity is observed for the 2-(hydroalkyl)stannane **5** is not clear, perhaps a boat transition state is involved.

Finally, the *anti*-product **24** prepared using the 2-(alkoxyethyl)stannane **6** and 2-methylpropanal was ozonolysed to give the ketone **25** which was reduced stereoselectively to give either the 1,3-*syn*-diol **26** ($NaBH_4$, Et_2BOMe)[6] or the 1,3-*anti*-diol **27** $[Me_4NBH(OAc)_3]$[7] to demonstrate the use of this chemistry for the stereoselective synthesis of 1,3,4-triol derivatives.

Experimental

(1*RS*,4*RS*)-3-Methylidene-1-phenyl-4-(2-trimethylsilylethoxymethoxy)pentan-1-ol 12

A cooled solution of tin(IV) chloride (312 mg, 1.2 mmol) in dichloromethane (1.2 cm^3) was added dropwise to a stirred solution of 2-[1-(2-trimethylsilylethoxymethoxy)ethyl]prop-2-enyl(tributyl)stannane **6** (505 mg, 1 mmol) in dichloromethane (10 cm^3) at −78 °C under argon. After 5 min, a cooled solution of benzaldehyde (106 mg, 1 mmol) in dichloromethane (0.3 cm^3)



was added to it and the mixture stirred for 1 h at −78 °C. Saturated aqueous $NaHCO_3$ (10 cm^3) was added, and the mixture allowed to warm to room temperature, before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue eluting with light petroleum–ethyl acetate, gave the *title compound* **12** (254 mg, 79%) containing *ca.* 17% (^{1}H NMR) of its epimer **11** (Found: $M^+ + H$, 323.2051. $C_{18}H_{31}O_3Si$ requires *M*, 323.2043); ν_{max}/cm^{-1} (liq. film) 3443, 1647, 1494, 1453, 1375, 1249, 1105, 1024, 919, 861, 836, 756 and 700; δ_H 0.06 [9 H, s, $Si(CH_3)_3$], 0.97 [2 H, m, $CH_2Si(CH_3)_3$], 1.36 (3 H, d, *J* 6.6, 5-H_3), 2.47 (1 H, dd, *J* 15, 3, 2-H), 2.64 (1 H, dd, *J* 15, 4, 2-H′), 3.00 (1 H, br s, OH), 3.7 [2 H, m, $OCH_2CH_2Si(CH_3)_3$], 4.27 (1 H, q, *J* 6.6, 4-H), 4.66 (2 H, m, OCH_2O), 4.94 (1 H, dd, *J* 7, 4, 1-H), 5.19 and 5.04 (each 1 H, m, vinylic H) and 7.40 (5 H, m, ArH); *m*/*z* (CI) 323 ($M^+ + 1$, 2%) and 247 (40).

Acknowledgements

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