1,5-Asymmetric Induction in Lewis Acid-promoted Reactions of (5-Alkoxy-2,4-dimethylpent-2-enyl)tributylstannanes and Aldehydes

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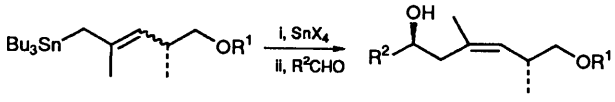
Allyltin trihalides generated *in situ* from (5-alkoxy-2,4-dimethylpent-2-enyl)tributylstannanes **8–10** and tin(IV) halides react with aldehydes with excellent 1,5-stereocontrol.

Allylstannanes are useful reagents for the stereoselective synthesis of homoallylic alcohols.[1] It has been found that allylstannanes with alkoxy substituents in remote positions are transmetallated by tin(IV) halides to generate (alkoxyallyl)tin trihalides which react with aldehydes to give (*Z*)-homoallyl alcohols with useful 1,5-, 1,6- and 1,7-asymmetric induction.[2–4] We now report that an additional alkyl substituent at C-2 of the allylstannane is compatible with this long range stereoselectivity so providing access to trisubstituted (*Z*)-3-alkylalk-3-enols of importance for natural product synthesis.

[(*R*)-2,4-Dimethyl-5-*tert*-butyldimethylsiloxypent-2-enyl]-tributylstannane **7**, a mixture of (*E*)- *and* (*Z*)-isomers, was prepared from methyl (*S*)-3-hydroxy-2-methylpropanoate **1** as outlined in Scheme 1. Treatment with anhydrous tetrabutylammonium fluoride (TBAF) gave the hydroxyallylstannane **8** which was protected as its methoxymethyl ether **9**. The optical purity of the hydroxy stannane **8**, a mixture of (*E*)- and (*Z*)-isomers, was estimated to correspond to an enantiomeric excess (e.e.) of *ca.* 50% by treatment of its (*R*)- and (*S*)-Mosher's derivatives with ethanolic hydrogen bromide.[5] This gave the 2,4-dimethylpent-4-enyl esters **11** which were studied by ^1H and ^{19}F NMR spectroscopy. The racemic 5-benzyloxypentenylstannane **10** was similarly prepared from (±)-3-benzyloxy-2-methylpropanol.

Reactions of the stannanes **8**, **9** and **10** with aldehydes were carried out in dichloromethane at −78 °C by addition of a solution of the tin(IV) halide to a solution of the stannane, stirring for *ca.* 10 min, and then adding the aldehyde. The results obtained are summarised in Table 1.

Table 1



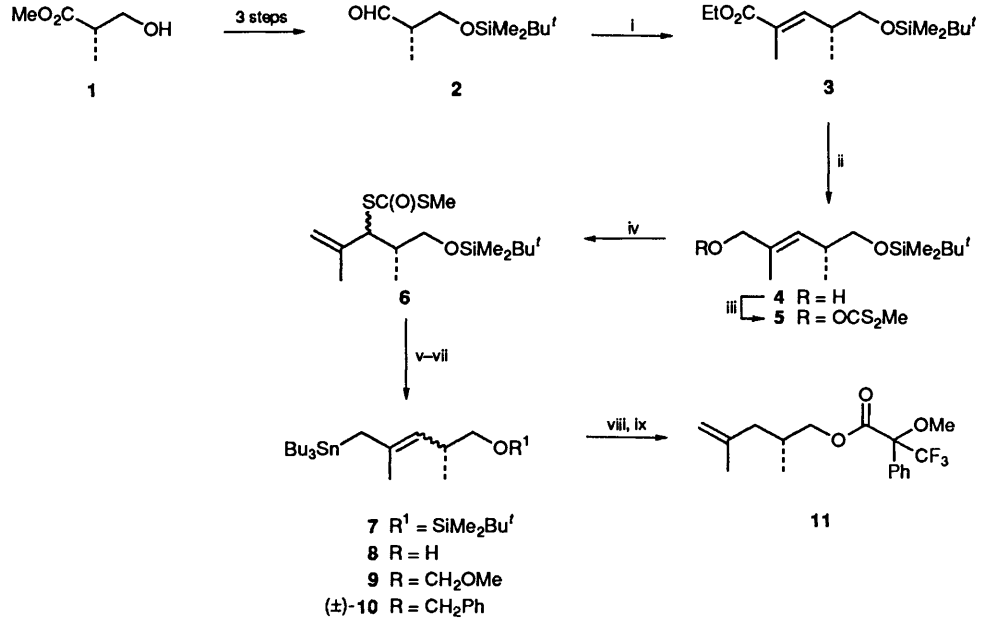
8 R^1 = H
9 R^1 = CH_2OMe
10 R^1 = CH_2Ph

12

Stannane	Tin(IV) halide	Aldehyde	Yield (%)
9	$SnCl_4$	PhCHO	69[a,b]
9	$SnCl_4$	*p*-$MeOC_6H_4CHO$	49[a,b]
9	$SnCl_4$	Me_2CHCHO	57[a,b]
9	$SnCl_4$	MeCH=CHCHO	68[a,b]
8	$SnBr_4$	PhCHO	92[a]
8	$SnBr_4$	MeCH=CHCHO	89[a]
(±)-**10**	$SnCl_4$	PhCHO	78[c]

[a] The 1,5-*syn*-diastereoisomer could not be detected in the reaction mixture (< 1%). [b] Variable amounts (typically < 10%) of **12** (R^1 = CH_2OCH_2OMe) were isolated owing to an impurity in the stannane. [c] 1% of the 1,5-*syn*-diastereoisomer isolated in this case.

In all cases the reactions were highly stereo- and regioselective giving essentially a single product which was purified

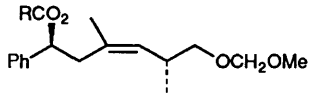


7 R^1 = $SiMe_2Bu^t$
8 R = H
9 R = CH_2OMe
(±)-**10** R = CH_2Ph

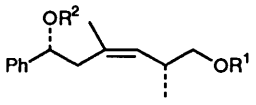
11

Scheme 1 *Reagents and conditions:* i, $Ph_3P{=}CMeCO_2Et$ (82%); ii, DIBAL-H (84%): iii, NaH, CS_2, MeI (94%); iv, 110 °C (75%); v, Bu_3SnH, azoisobutyronitrile; vi, TBAF (88% from **6**); vii, $MeOCH_2Cl$, Hunig's base (79%); viii, (*R*)- or (*S*)-Mosher's acid chloride, pyridine (40–68%); ix, HBr, EtOH (90%)

by flash chromatography. The structures of the products were initially assigned by analogy with those obtained from analogous (alkoxyallyl)stannanes.[2] The (*Z*)-stereochemistry of the products **12** (R^1 = $MeOCH_2$, $PhCH_2$; R^2 = Ph) obtained



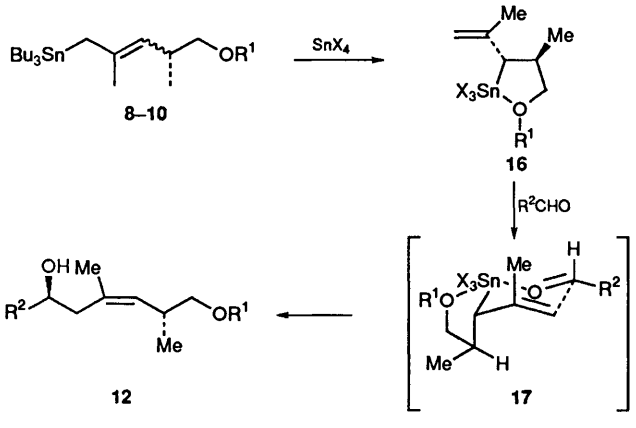
13 R = PhCH(OAc)



14 R^2 = COC_6H_4-*p*-NO_2, R^1 = CH_2OMe, Bn
15 R^2 = H, R^1 = CH_2OMe, Bn

from benzaldehyde was confirmed by NOE observations; specifically enhancements of the vinylic proton (*ca.* 9%) were observed on irradiation of the vinylic methyl group. The configuration of (1*S*,5*R*)-1-phenyl-3,5-dimethyl-6-(methoxymethoxy)hex-3-enol **12** (R^1 = $MeOCH_2$, R^2 = Ph) at C-1 was consistent with the relative shifts of the (*R*)- and (*S*)-acetylmandelates **13**.[6] The benzaldehyde products **12** (R^1 = $MeOCH_2$, $PhCH_2$; R^2 = Ph) were converted into their 1,5-*syn*-diastereoisomers **15** by inversion at C-1 using a Mitsunobu reaction to give the *p*-nitrobenzoate esters **14** followed by saponification. The 1,5-*anti*- and 1,5-*syn*-products **12** and **15** were clearly distinguishable by ^1H NMR. Apart from *ca.* 1% isolated from the reaction between benzaldehyde and the *O*-benzylstannane, the 1,5-*syn*-isomers were not detected in the products from the reactions of the allylstannanes with benzaldehyde.

The selective formation of the 1,5-*anti*-products **12** is consistent with the reaction pathway outlined in Scheme 2.



8–10 **16** **17** **12**

Scheme 2

Transmetallation of the pentenyltributylstannane gives the intermediate allyltin trihalide **16** which then reacts with an aldehyde *via* the six-membered cyclic transition state **17** with the group α to tin in the axial position.[7] The overall stereoselectivity of the process depends on the configuration of the allyltin trihalide **16** and the stereoselectivity of its reaction with aldehydes. It is clear that the geometry of the starting allylstannane is not important since highly stereoselective reactions were obtained with *E*,*Z*-mixtures. Moreover the 2-methyl substituent does not interfere with reactions with aldehydes; indeed, if anything, the overall stereoselectivity is increased.[8,*]

This work extends the use of (alkoxyallyl)stannanes to include the stereoselective synthesis of homoallylic alcohols with trisubstituted double-bonds.

Experimental

Typical Procedure for Allylstannane–Aldehyde Reactions.—(1S,5R)6-(*Methoxymethoxy*)-3,5-*dimethyl*-1-*phenyl*-*hex*-3-*enol* **12** (R^1 = $MeOCH_2$, R^2 = Ph). A cooled solution of tin(IV) chloride in CH_2Cl_2 (1.02 mol dm^{-3}; 0.53 cm^3, 0.55 mmol) was added dropwise to a stirred solution of the stannane **9** (0.2 g, 0.45 mmol) in CH_2Cl_2 (4.6 cm^3) at −78 °C under an atmosphere of argon. After 10 min, a cooled solution of benzaldehyde (3.46 mol dm^{-3}; 0.16 cm^3, 0.55 mmol) in CH_2Cl_2 was added dropwise and the reaction mixture was stirred for 1 h. Saturated aqueous $NaHCO_3$ (2.5 cm^3) was added, and the mixture was allowed to warm to room temperature. The mixture was partitioned between CH_2Cl_2 and water and the organic phase was washed with brine (3 × 10 cm^3) and dried ($MgSO_4$). Concentration under reduced presure gave an oil. Flash chromatography on silica (hexane–diethyl ether, 3:1) gave the *title compound* as an oil (83 mg, 69%) (Found: M^+ + NH_4, 282.2087, $C_{16}H_{28}NO_3$ requires, *M* + NH_4, 282.2069); $[\alpha]_D^{22}$† −54.04 (*c* 0.9, $CHCl_3$); ν_{max}/cm^{-1} 3455, 3062, 3029, 1453, 1041, 756 and 701; δ_H(300 MHz; $CDCl_3$)‡ 0.87 (3 H, d, *J* 6.5, $CHCH_3$), 1.85 (3 H, s, $C{=}CCH_3$), 2.15 (1 H, dd, *J* 13.5 and 2.5, 2-H), 2.70 (1 H, dd, *J* 13.5 and 10.5, 2-H'), 2.82 (1 H, m, 5-H), 3.25 (1 H, t, *J* 9, 6-H), 3.37 (3 H, s, OCH_3), 3.51 (1 H, dd, *J* 9 and 4.5, 6-H'), 3.88 (1 H, d, *J* 2.5, OH), 4.60 and 4.65 (each 1 H, d, *J* 6, $OCHHO$), 4.78 (1 H, dt, *J* 10 and 2.5, 1-H), 5.14 (1 H, d, *J* 10, 4-H) and 7.25–7.40 (5 H, aromatic H); δ_C (75 MHz; $CDCl_3$) 17.3, 23.6, 32.8, 43.4, 55.4, 71.2, 96.1, 125.6, 127.1, 128.3, 132.4, 132.8 and 145.3; *m*/*z* (CI/NH_3) 282 (M^+ + NH_4, 3.5%), 264 (M^+, 4) and 247 (M^+ − OH, 100).

Further elution gave the methoxymethoxymethoxy compound **12** (R^1 = $MeOCH_2OCH_2$, R^2 = Ph) (< 8 mg, 6%).

Acknowledgement

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* A 2-methyl-3-(furan-2-yl)propenylstannane has been reported to react with aldehydes to give (*E*)-homoallylic alcohols in contrast to the stereoselectivity observed for stannanes **8–10**.[9] It is likely that this different stereoselectivity is due to the inability of the furanyl oxygen to coordinate to the tin trichloride intermediate because of bond angle strain, and not to the 2-methyl substituent.

† $[\alpha]_D$ Values are given in units of 10^{-1} deg cm^2 g^{-1}.

‡ *J* Values are given in Hz.

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