# Effective 1,7-Asymmetric Induction in Reactions between 6-Hydroxyallylstannanes and Aldehydes promoted by Tin(IV) Bromide

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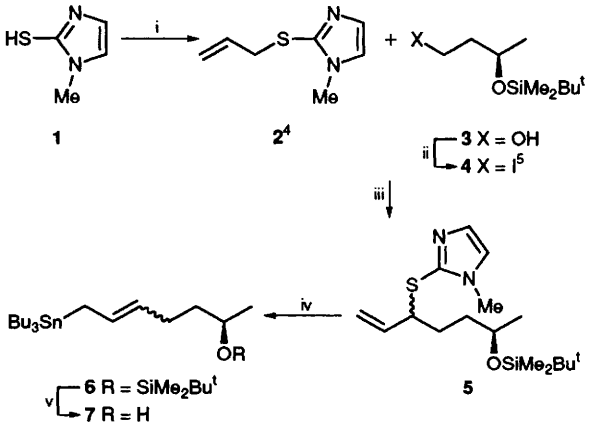
Transmetallation of tributyl[(6*R*)-6-hydroxyhept-2-enyl]stannane **7** by tin(IV) bromide generates an allyltin tribromide which reacts with aldehydes to give 1-substituted 1,7-dihydroxyoct-3-enes with effective 1,7-asymmetric induction.

Reactions of allylstannanes with aldehydes are useful for the synthesis of homoallylic alcohols.[1] It has been shown that 4- and 5-alkoxy- and -hydroxy-allylstannanes undergo transmetallation with tin(IV) halides to generate allyltin trihalides which react with aldehydes with excellent 1,5- and 1,6-stereochemical control.[2,3] We now report that 6-hydroxyallylstannanes undergo analogous reactions with aldehydes with useful 1,7-asymmetric induction, providing stereoselective access to 1,7-diols.

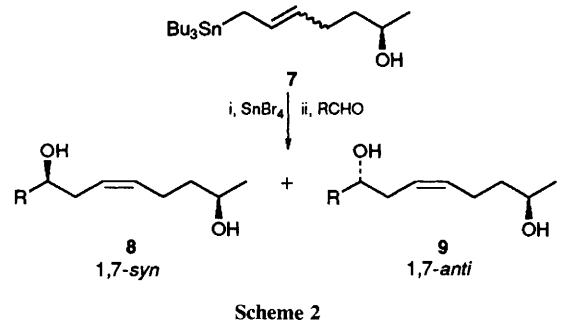
Tributyl[(6*R*]-6-hydroxyhept-2-enyl]stannane **7** was prepared from the (*R*)-alcohol **3**[3] as a mixture of (*E*)- and (*Z*)-isomers, (*E*) : (*Z*) = 2 : 1, as shown in Scheme 1. Reactions of this stannane with aldehydes were carried out by treatment of the stannane with tin(IV) bromide at −78 °C for 10 min, followed by addition of the aldehyde (Scheme 2). After 1 h, the reactions were quenched by the addition of aqueous $NaHCO_3$ and the products purified by flash chromatography. The results obtained are shown in Table 1.

In all cases mixtures of diols **8** and **9** were obtained with selectivity, typically 90 : 10, in favour of the 1,7-*syn*-diastereoisomer **8**.† The configuration of the new chiral centre in the major product **8** (R = Ph) was established by ozonolysis of its diacetate followed by a reductive work-up, which gave (−)-3-acetoxy-3-phenylpropanol **10**, $[\alpha]_D$ −72.4, corresponding to the (*S*)-enantiomer,[2] see Scheme 3. The configuration of the hydroxy group in **8** (R = Ph) was also consistent with the relative chemical shifts of the (*R*)- and (*S*)-acetylmandelates **12** prepared from the *tert*-butyldimethyl silyl ether **11**.[6] The hydroxysilyl ether **11** was also converted into the inverted *p*-nitrobenzoate **13** which was taken through to the *anti*-1,7-diol **9** (R = Ph) to confirm that the *syn*- and *anti*-1,7-diols could be distinguished by NMR spectroscopy. The geometry of the double bonds of the products was assigned on the basis of coupling constants of *ca.* 11 Hz between the vinylic protons. Similar correlations confirmed the structure of the major product **8** (R = Pr$^i$) from the reaction of the stannane with 2-methylpropanal. The structures of the other products were assigned by analogy and were consistent with their spectroscopic data.

The selective formation of the *syn*-1,7-diols in these reactions is consistent with a reaction pathway in which the tributylallylstannane **7** is transmetallated after addition of




**Scheme 1** *Reagents*: i, $CH_2$=$CHCH_2Br$, $K_2CO_3$ (80%); ii, $I_2$, $PPh_3$, imidazole (74%); iii, Bu$^n$Li (83%); iv, $Bu_3SnH$, azoisobutyronitrile (92%); v, tetrabutylammonium fluoride (TBAF) (80%)

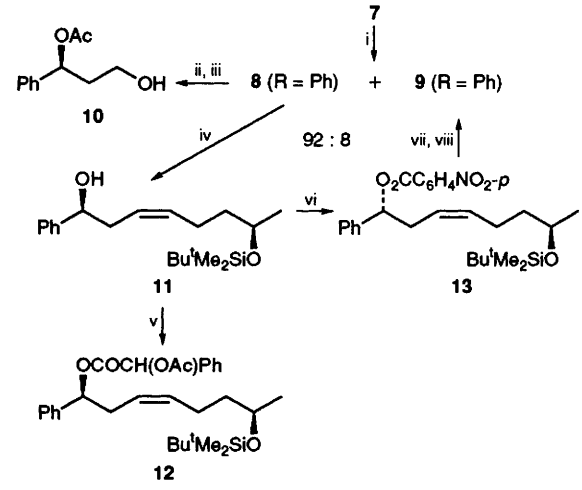



**Scheme 2**

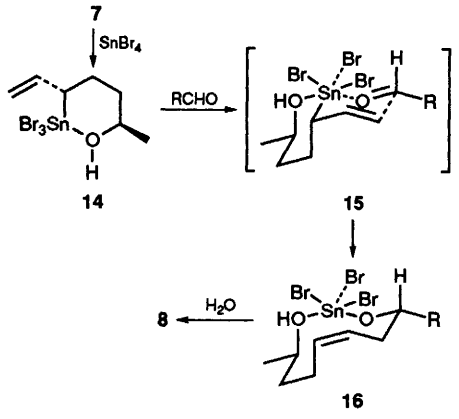
**Table 1** Yields and *syn* : *anti* ratios for Scheme 2

| RCHO | Yield (%) | *Syn* : *Anti*[a] |
|---|---|---|
| PhCHO | 72 | 92 : 8[b] |
| *p*-$ClC_6H_4CHO$ | 71 | 92 : 8[b] |
| *p*-$MeOC_6H_4CHO$ | 47 | 89 : 11[b] |
| 2-NaphthylCHO | 65 | 93 : 7[b] |
| $Me_2CHCHO$ | 63 | 89 : 11[c] |
| MeCHO | 36 | 90 : 10[c] |
| EtCHO | 61 | 91 : 9[c] |
| $Me_2CHCH_2CHO$ | 58 | 85 : 15[c] |
| $Me_3CCHO$ | 38 | 95 : 5[c] |

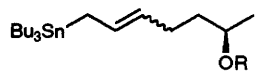
[a] 1–2% of a third component present. [b] By $^1H$ NMR spectroscopy. [c] By pulse-delayed $^{13}C$ NMR spectroscopy.



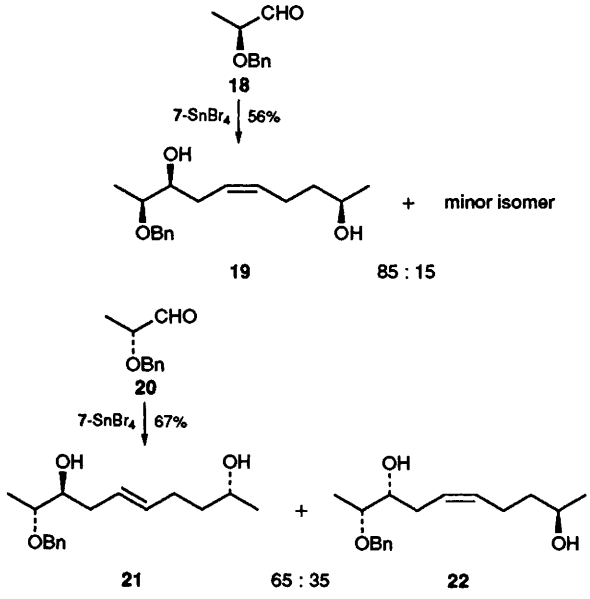

**Scheme 3** *Reagents and conditions*: i, $SnBr_4$, −78 °C, 10 min, then PhCHO, −78 °C, 1 h (72%); ii, $(MeCO)_2O$, $Et_3N$, 4-dimethylaminopyridine (96%); iii, $O_3$, $CH_2Cl_2$, then $Me_2S$ followed by $NaBH_4$; iv, $Me_2Bu^tSiCl$, imidazole [63% of **11** plus 5% of the isomeric monosilyl ether, 15% bis-silylated material, and 14% unchanged **8** (R = Ph)]; v, $PhCH(OAc)CO_2H$ [79% for (*R*)-mandelate; 83% for (*S*)-mandelate]; vi, $Ph_3P$, diethyl azodicarboxylate, *p*-$O_2NC_6H_4CO_2H$ (74%); vii, NaOH, MeOH (93%); viii, TBAF (96%)




Scheme 4




17 R = Me, $PhCH_2$ (Bn), and $MeOCH_2$




tin(IV) bromide to generate the allyltin tribromide **14** in which the hydroxy group is coordinated to the electron-deficient tin, see Scheme 4.[7] The stereoselective formation of this intermediate may be due to kinetic control, the tribromotin moiety being delivered intramolecularly to one face of the double bond of the allylstannane **7** by the hydroxy group, or to thermodynamic control, the *cis*- and *trans*-allyltin tribromides equilibrating with the *trans*-isomer **14** accumulating. The intermediate **14** then reacts with the aldehyde *via* the six-membered ring transition state **15** to give the 1,7-*syn*-product **8**. In the second step of this reaction there would appear to be a strong preference for the group α to the tin to adopt the axial position. It is this preference which results in the introduction of the *cis*-double bond, and determines which face of the aldehyde is attacked, so providing the 1,7-stereochemical control.‡

The reaction between the hydroxyallylstannane **7** and benzaldehyde when promoted by tin(IV) chloride was regioselective but gave a mixture of the *syn*- and *anti*-products **8** and **9** in the ratio of 75 : 25. The reactions of *O*-alkylated allylstannanes **17** (R = Me, Bn, $MeOCH_2$) after transmetallation with tin(IV) bromide or tin(IV) chloride with benzaldehyde gave mixtures of products. It would appear that the 1,7-asymmetric induction is only effective after transmetallation with tin(IV) bromide for the free hydroxyallylstannane **7**. For comparison, 1,5-induction is tolerant of a wide range of *O*-substituent, and was observed after transmetallation with either tin(IV) bromide or chloride.[2] 1,6-Induction, although requiring tin(IV) bromide as promoter, was observed for both 5-methoxy- and 5-hydroxy-allylstannanes.[3]

Finally, the reactions of the hydroxyallylstannane **7** and the chiral 2-alkoxyaldehydes **18** and **20** were studied. It was found that the (*S*)-2-alkoxyaldehyde **18** reacted with the usual reagent-controlled stereoselectivity to give the 1,7-*syn*-diol **19** together with a minor product which may have been the *anti*-diastereoisomer but which was not fully characterised.† However, the (*R*)-alkoxyaldehyde **20** gave the *anti*-(*E*)-diol **21** together with the *anti*-(*Z*)-diol **22**, ratio 65 : 35 (67%). The selective formation of a product with a *trans*-double bond has not been observed before in tin(IV) halide-promoted reactions of alkoxy- or hydroxy-allylstannanes with aldehydes.§ Moreover this major product has the expected configuration at the newly formed chiral centre.¶

The 1,7-asymmetric induction observed in these tin halide-promoted reactions of the hydroxyallylstannane **7** with aldehydes is of interest because such remote asymmetric induction is rarely observed.[13] This work also extends the application of allylstannanes in stereoselective synthesis.

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## Footnotes

† The *syn*- and *anti*-prefixes refer to the relationship between the 1,7-substituents as indicated in formulae **8** and **9**.

‡ In transition state **15** the tin is octahedral. Reactions of 1-substituted allylstannanes with aldehydes which proceed *via* a transition state in which the tin is five-coordinated also give *cis*-alkenes perhaps because of anomeric and/or steric effects.[8]

§ Preliminary results indicate that 5-acyloxyallylstannanes also react to give products with an (*E*)-double bond.[9]

¶ It may be that chelation control exercised by the aldehyde is operating in the case of the (*R*)-aldehyde **20**. Previously reagent control was observed for tin(IV)halide-induced reactions of alkoxyallylstannanes and alkoxyaldehydes.[2,3]

## References

1 W. R. Roush, in *Comprehensive Organic Synthesis*, ed. C. H. Heathcock, Pergamon, 1991, vol. 2, p. 1.
2 A. H. McNeill and E. J. Thomas, *Tetrahedron Lett.*, 1990, **31**, 6239; A. H. McNeill and E. J. Thomas, *Tetrahedron Lett.*, 1992, **33**, 1369; J. S. Carey and E. J. Thomas, *Synlett*, 1992, 585; J. S. Carey, T. S. Coulter and E. J. Thomas, *Tetrahedron Lett.*, 1993, **34**, 3933.
3 J. S. Carey and E. J. Thomas, *Tetrahedron Lett.*, 1993, **34**, 3935.
4 P. Hassanaly, H. J. M. Dou, J. Metzger, G. Assef and J. Kister, *Synthesis*, 1977, 253.
5 I. Paterson and I. Boddy, *Tetrahedron Lett.*, 1988, **29**, 5301.
6 B. M. Trost, J. L. Belletire, S. Godleski, P. G. McDougal, J. M. Balkovec, J. J. Baldwin, M. E. Christy, G. S. Ponticello, S. L. Varga and J. P. Springer, *J. Org. Chem.*, 1986, **51**, 2370.
7 E. Vedejs, S. M. Duncan and A. R. Haight, *J. Org. Chem.*, 1993, **58**, 3046.
8 A. J. Pratt and E. J. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1521; V. J. Jephcote, A. J. Pratt and E. J. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1529.
9 T. S. Coulter and E. J. Thomas, unpublished observations.
10 For other examples of 1,7-induction see: G. A. Molander and K. L. Bobbitt, *J. Am. Chem. Soc.*, 1993, **115**, 7517; Y. Tamai, S. Koike, A. Ogura and S. Miyano, *J. Chem. Soc., Chem. Commun.*, 1991, 799; S. E. Denmark and L. K. Marble, *J. Org. Chem.*, 1990, **55**, 1984.