

Remote Asymmetric Induction in Reactions between 4- and 5-Benzyloxy-pent-2-enyl(tributyl)stannanes and Chiral Imines prepared from Butyl Glyoxylate

David J. Hallett and Eric J. Thomas*

Department of Chemistry, University of Manchester, Manchester, UK M13 9PL

Transmetalation of 4- and 5-benzyloxy-pent-2-enyl(tributyl)stannanes **13** and **18** with tin(IV) chloride generates intermediate allyltin trichlorides which react with imines **9** and **ent-9**, prepared from butyl glyoxylate and either (*R*)- or (*S*)-1-phenylethylamine, with effective 1,5-asymmetric induction.

Allylstannanes are being developed into useful reagents for stereoselective synthesis.¹ Recently, 4-, 5- and 6-alkoxyalk-2-enylstannanes and analogous amino- and alkylthio-stannanes have been shown to react with tin(IV) halides to generate allyltin trihalides which react with aldehydes with effective 1,5-, 1,6- and 1,7-asymmetric induction.² We now report the results of a study of their reactions with chiral imines.

Imines react with allyl(trialkyl)stannanes in the presence of strong Lewis acids, typically BF₃·OEt₂ or TiCl₄, to give homoallylic amines³ with useful stereoselectivity in favour of the *syn* products **3**.⁴

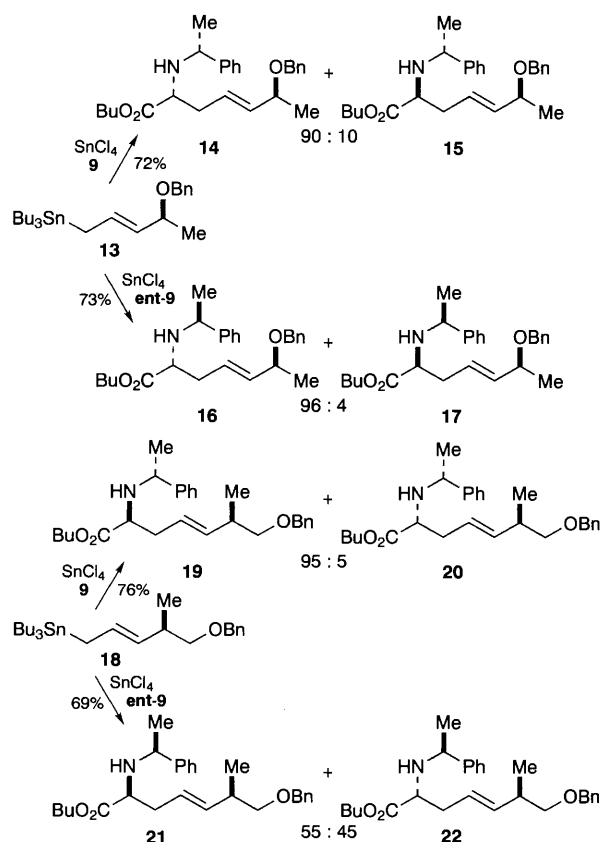
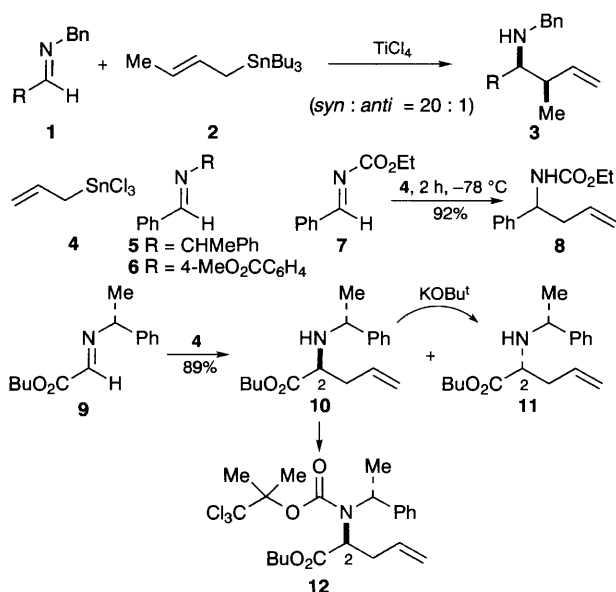
Tin(IV) halides are more effective than other Lewis acids, including BF₃·OEt₂ and TiCl₄, in promoting stereoselective reactions between 5-alkoxyallylstannanes and aldehydes. In particular, the participation of an allyltin trihalide in which the electron-deficient tin is coordinated to the oxygen-containing substituent is believed to be important for remote asymmetric induction.^{2,5} It was therefore necessary to establish conditions for reactions between allyltin trihalides and imines before the effect of remote substituents in the stannane on the stereoselectivity of the process could be investigated.

Preliminary investigations into reactions between prop-2-enyltin trichloride **4**, generated from prop-2-enyl(tributyl)stannane and SnCl₄,⁶ and simple imines were not encouraging. For example, no reaction was observed at -78 °C between the propenyltin trichloride **4** and the benzaldehyde-derived imines **5** and **6**. However, imines activated towards nucleophilic attack by electron-withdrawing substituents gave useful yields of products. The *N*-ethoxycarbonylimine **7** gave 1-(ethoxycarbonylamino)-1-phenylbut-3-ene **8**, and the imine **9**,⁸ prepared from butyl glyoxylate and (*R*)-1-phenylethylamine, reacted stereoselectively to give a mixture of the (*2S*)- and (*2R*)-diastereoisomers **10** and **11**, ratio 93:7, respectively. The

stereoselectivity of this reaction is of interest because the analogous reaction with prop-2-enyl 9-borabicyclo[3.3.1]nonane is known to proceed with the opposite stereoselectivity, **10** and **11** being obtained in a ratio of 10:90.⁸

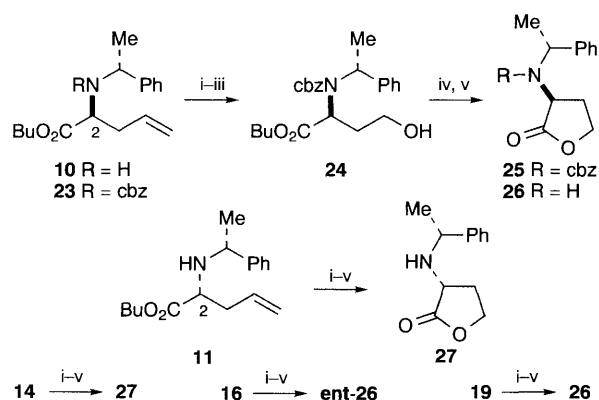
Structures were assigned to the products **10** and **11** on the basis of spectroscopic data and comparison with samples prepared using prop-2-enyl 9-borabicyclo[3.3.1]nonane.⁸ ¹H NMR spectra were useful for assigning the configuration at C(2) relative to the imine-derived chiral centre in products prepared from the imine **9**, since 2-H was invariably more shielded for the *syn* epimer, compare δ 3.1 for **11** with δ 3.35 for the *anti* epimer **10**. The stereochemistry of **10** was also confirmed by an X-ray crystal structure determination for its 1,1,1-trichloro-2-methylpropyloxy carbonyl derivative **12**. Interestingly, the *anti* epimer **10** gave a mixture containing predominantly *syn* diastereoisomer **11**, ratio **10**:**11** = 15:85, on treatment with KOBu^t and acid.

The stereochemistry of reactions between the allyltin trichloride generated from (*4S*)-4-benzyloxy-pent-2-enyl(tributyl)stannane **13** and the imine **9** and its enantiomer, **ent-9**, was found to be controlled by the stannane. Addition of the (*R*)-imine **9** to the allyltin trichloride formed by transmetalation of the (*4S*)-stannane **13** with SnCl₄ gave the (*2R,6S,4E*)-heptenoate **14** containing less than 10% of a minor product believed to be its (*2S*)-diastereoisomer **15**. The (*S*)-imine **ent-9** similarly

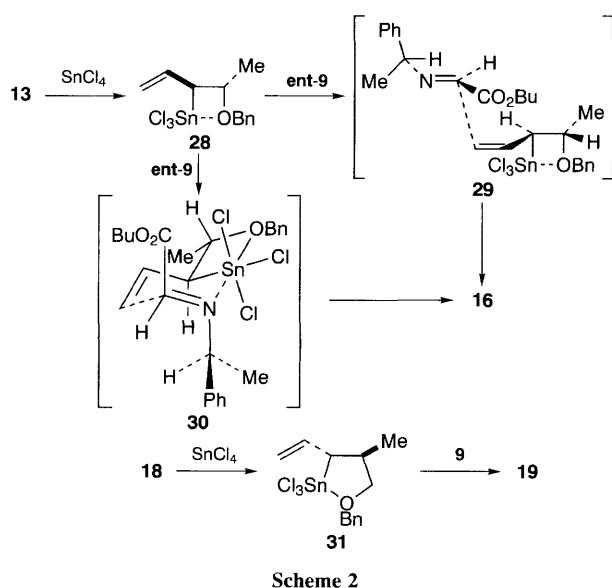


gave the (2*R*,6*S*,4*E*)-heptenoate **16** containing only ca. 4% of the (2*S*) epimer **17**. However, the analogous reactions of the (4*R*)-5-benzyloxypent-2-enylstannane **18** showed a matching and a mismatching with the two enantiomeric imines. The (4*R*)-stannane **18** is matched with the (*R*)-imine **9** since the (2*S*,6*R*,4*E*)-heptenoate **19** was obtained with excellent stereoselectivity together with only 5% of a minor product believed to be the (2*R*)-epimer **20**. In contrast, the (*S*)-imine **ent-9** gave rise to the formation of two products identified as the (2*S*,6*R*,4*E*)-heptenoate **21** together with its (2*R*)-diastereoisomer **22** in a ratio of 55 : 45.

The structures of these products were established on the basis of spectroscopic data and by conversion into the butyrolactones **26** and **27**, authentic samples of which were prepared from the 2-aminopent-4-enoates **10** and **11**, see Scheme 1. The butyl (2*S*)-2-[(*R*)-1-phenylethylamino]pent-4-enoate **10** was converted into its cbz-derivative **23** (cbz = carbobenzyloxy) which, on ozonolysis with a reductive work-up followed by further reduction with sodium borohydride, gave the alcohol **24**. Lactonisation and deprotection gave the (2*S*)-2-[(*R*)-1-phenylethylamino]butyrolactone **26**. The butyl (2*R*)-2-[(*R*)-1-phenylethylamino]pent-4-enoate **11** was similarly converted into the



Scheme 1 Reagents and conditions: i, cbz-Cl, K_2CO_3 , 75–95% ii, ozone, then dimethyl sulfide; iii, sodium borohydride, 77–86% over the two steps; iii, conc. aq. HCl in MeOH; v, ammonium formate, 10% Pd/C, 72–85% over the two steps



Scheme 2

(2*R*)-2-[(*R*)-1-phenylethylamino]butyrolactone **27**. Similar protection, ozonolysis, cyclisation and deprotection of the heptenoates **14**, **16** and **19** gave the butyrolactone **27**, the enantiomer of butyrolactone **26** and butyrolactone **26**, respectively, so establishing the configurations of these heptenoates at C(2). The configurations so obtained were also consistent with the relative chemical shifts of the C(2) protons in their 1H NMR spectra as discussed above. The (*E*)-geometries of the double bonds in the heptenoates **14–17** and **19–22** were assigned on the basis of their 4,5-coupling constants which were typically 16 Hz. The configurations of the products **21** and **22**, from the mismatched reaction between stannane **18** and the imine **ent-9**, at C(2) were assigned on the basis of their 2-H chemical shifts.

The stereoselectivities of the $SnCl_4$ promoted reactions between the imines **9** and **ent-9** and the chiral allylstannanes **13** and **18** are believed to be due to the superimposition of the intrinsic facial selectivity of the imine and the 1,5-stereoselectivity of the stannane. Scheme 2 depicts an open-chain transition state **29** for the matched reaction of the allyltin trichloride **28**, derived from the (4*S*)-4-benzyloxystannane **13**, and the (*S*)-imine **ent-9**, which is consistent with the 1,5-*anti* stereoselectivity observed with this stannane, the formation of the (*E*)-double bond and the facial preference of the imine. This transition state is reminiscent of those proposed for Lewis acid catalysed reactions between aldehydes and allylstannanes which also give rise to (*E*)-alkenols.⁹ Alternatively, the six-membered, chair-like cyclic transition state **30** may be involved,¹⁰ in which the bulky group on the imine nitrogen may be responsible for destabilising the alternative transition state in which the group α to tin is axial, *cf.* reactions of the allyltin trichloride **28** with aldehydes. Analogous transition states involving the allyltin trichloride **31** are consistent with the 1,5-*syn* preference observed for the reactions of the (4*R*)-5-benzyloxypentylstannane **18**. Present work is concerned with reactions of the chiral stannanes with achiral imines.

We thank Glaxo Group Research, the EPSRC and the DTI for a studentship (to D. J. H.) under the LINK Asymmetric Synthesis Programme, and Dr R. A. E. Carr of Glaxo for help, support and guidance.

Received, 5th December 1994; Com. 4/07432G

References

- W. R. Roush, in *Comprehensive Organic Synthesis*, ed. C. H. Heathcock, Pergamon, Oxford, 1991, vol. 2, p. 1.
- A. H. McNeill and E. J. Thomas, *Tetrahedron Lett.*, 1990, **31**, 6239; 1992, **33**, 1369; J. S. Carey and E. J. Thomas, *Synlett.*, 1992, 585; *Tetrahedron Lett.*, 1993, **34**, 3935; *J. Chem. Soc., Chem. Commun.*, 1994, 283; S. J. Stanway and E. J. Thomas, *J. Chem. Soc., Chem. Commun.*, 1994, 285; *Synlett.*, in the press; A. H. McNeill and E. J. Thomas, *Synthesis*, 1994, 322.
- M. A. Ciufolini and G. O. Spencer, *J. Org. Chem.*, 1989, **54**, 4739; Y. Yamamoto and M. Schmid, *J. Chem. Soc., Chem. Commun.*, 1989, 1310; R. Yamaguchi, M. Moriyasu, M. Yoshioka and M. Kawanisi, *J. Org. Chem.*, 1985, **50**, 287.
- G. E. Keck and E. J. Enholm, *J. Org. Chem.*, 1985, **50**, 146.
- J. S. Carey, T. S. Coulter and E. J. Thomas, *Tetrahedron Lett.*, 1993, **34**, 3933.
- S. E. Denmark, T. Wilson and T. M. Willson, *J. Am. Chem. Soc.*, 1988, **110**, 984.
- J.-B. Kim, A. B. Padias and H. K. Hall, Jr., *Macromolecules*, 1990, **23**, 21.
- Y. Yamamoto, S. Nishii, K. Maruyama, T. Komatsu and W. Ito, *J. Am. Chem. Soc.*, 1986, **108**, 7778.
- Y. Yamamoto, H. Yatagai, Y. Ishihara, N. Maeda and K. Maruyama, *Tetrahedron*, 1984, **40**, 2239.
- Y. Yamamoto, T. Komatsu and K. Maruyama, *J. Org. Chem.*, 1985, **50**, 3115.