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1,5-Asymmetric Induction in Reactions between 4- and 5-Alkoxypent-2-enyl(tributyl)stannanes and Achiral 1-Alkoxycarbonylimines

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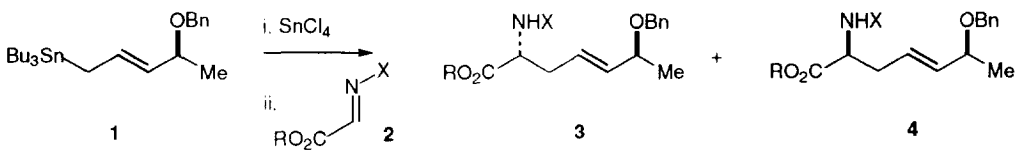
Abstract: Tin(IV) chloride promoted reactions of 4- and 5-alkoxypent-2-enyl(tributyl)stannanes **1**, **11** and **15** and 1-alkoxycarbonylimines **2** proceed with excellent 1,5-asymmetric induction.

Transmetallation of 4-, 5- and 6-alkoxyalk-2-enylstannanes with tin(IV) halides, generates allyltin trihalides which react with aldehydes with useful levels of 1,5-, 1,6- and 1,7-asymmetric induction.[1] Recently, chiral imines prepared from butyl glyoxylate and (*R*)- and (*S*)-1-phenylethylamine were also found to react with 4- and 5-benzyloxypent-2-enyl(tributyl)stannanes with effective remote stereocontrol determined by the allylstannane and not by the imine.[2] We now report reactions between 4- and 5-alkoxyallylstannanes and achiral imines derived from glyoxylates which provide stereoselective access to α-amino-acid derivatives.

The 2-nitrosulfenylimine **2a**[3] was added to a solution of (*S*)-4-benzyloxypent-2-enyltributylstannane **1**[4] which had been transmetallated by treatment with tin(IV) chloride at -78 °C. After work-up, two products were isolated, separated by HPLC, and identified as the 1,5-*anti*- and 1,5-*syn*-amino-acid derivatives **3a** and **4a**, ratio **3a** : **4a** = 89 : 11. Similar results were obtained using the benzhydrylimine **2b**, the dimethylbenzylimine **2c**, and the *O*-benzyloxime **2d**, see **Table 1**.



1 2 3 4

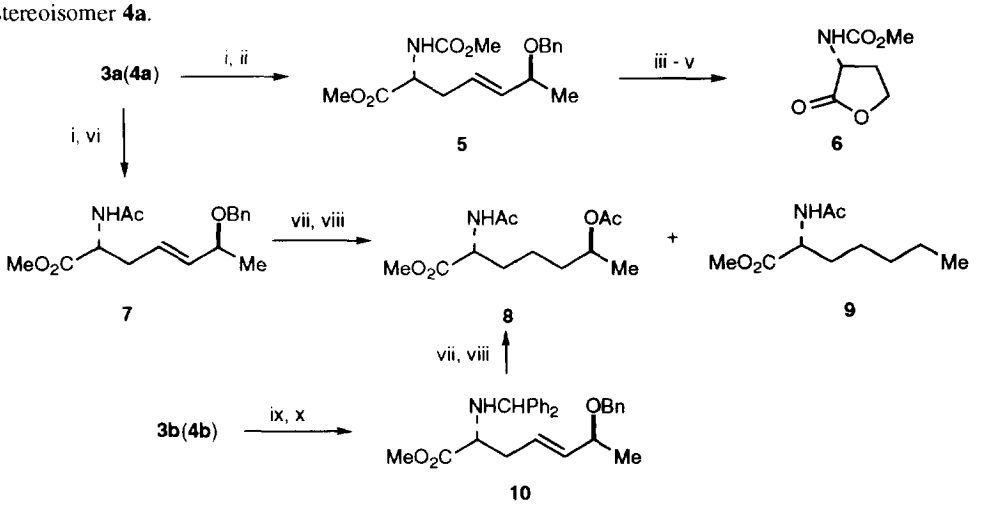
Table 1: Reactions of Stannane 1 with Imines 2

Imine	X	R	Yield (%)	1,5-*anti* (**3**) : 1,5-*syn* (**4**)
2a	SAr[a]	Me	87	89 : 11
2b	$CHPh_2$	Bu	79	90 : 10
2c	CMe_2Ph	Bu	75	90 : 10
2d	OBn	Me	67	90 : 10

[a]Ar = 2-$NO_2C_6H_4$-

Dedicated to the memory of Professor Hidemasa Takaya, deceased on 5 October 1995

The products obtained from the reaction between the 2-nitrosulfenylimine **2a** and the stannane **1** were shown to correspond to the *trans*-double-bond containing amino-acid derivatives **3a** and **4a** by ^{1}H NMR. Their configurations at C(2) were established by correlation with the lactone **6**, which was also prepared from homoserine. Treatment of the mixture of products **3a** and **4a** with methanolic hydrogen chloride, followed by acylation using methyl chloroformate, gave an N-methoxycarbonyl derivative shown to be **5**, containing *ca.* 10% of its 1,5-*syn*-diastereoisomer. Ozonolysis of this mixture with a reductive work-up, followed by reduction using sodium borohydride and lactonisation gave the dextrorotatory homoserine lactone which is known to correspond to the (*R*)-enantiomer **6**.[5,6] This established the configuration of the major adduct at C(2) as (*R*), so establishing its structure as the 1,5-*anti*-isomer **3a**. The minor product was identified as the 1,5-*syn*-diastereoisomer **4a**.

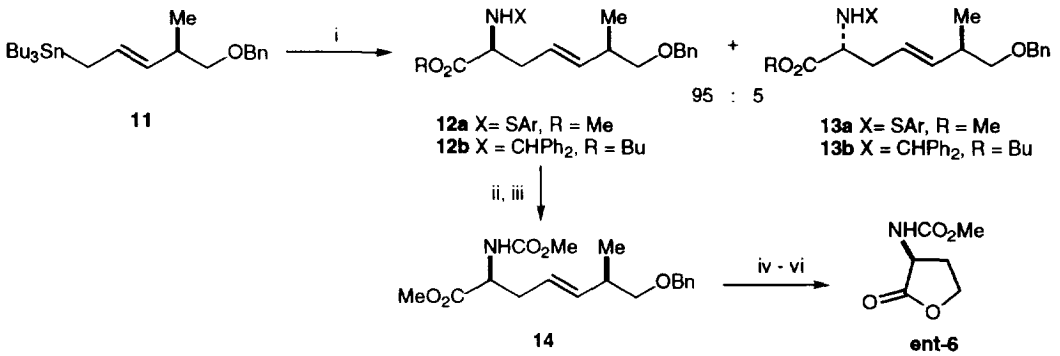


Scheme 1 ***Reagents:*** i, HCl, MeOH; ii, $ClCO_2Me$ (87% of **5** from **3a**); iii, O_3, Me_2S; iv, $NaBH_4$; v, H^+, $CHCl_3$ (73% of **6** from **5**); vi, Ac_2O, Et_3N, 4-dimethylaminopyridine (82% of **7** from **3a**); vii, HCO_2H, 10%Pd/C; viii, Ac_2O, Et_3N, 4-dimethylaminopyridine (**8**, 79%; **9**, 5%; from **7**); ix, MeOH, K_2CO_3; x, CH_2N_2 (91% of **10** from **3b**).

The products obtained from the reaction between the benzhydrylimine **2b** and the stannane **1** could not be separated. Their ratio was estimated as 90 : 10, by ^{1}H NMR of the mixture, which also established the *trans*-alkene geometry of the major component. The structure of the major component was established as **3b** by conversion of the mixture into the *anti*-heptanoate **8**, see **Scheme 1**, which was also prepared, together with a small amount of the over-reduction product **9**, from the adducts **3a** and **4a**. In both cases the major heptanoate corresponded to the 2,6-*anti*-diastereoisomer **8** so showing that the major products from the reactions between the stannane **1** and the imines **2a** and **2b** had the same configurations at C(2) and C(6) corresponding to **3a** and **3b**, respectively.[7] Structures were similarly assigned to the products **3c,d** and **4c,d** obtained from the dimethylbenzylimine **2c** and the O-benzyl oxime **2d**, with the geometry of the double-bond of the major products being established by ^{1}H NMR.

The stereoselectivity of reactions between the 2-nitrosulfenyl- and benzhydrylimines **2a** and **2b** and the allyltin trichloride generated from 5-benzyloxy-4-methylpent-2-enylstannane **11**[9] were investigated. In both cases the reactions were usefully stereoselective in favour of the 1,5-*syn*-diastereoisomers **12a** and **12b**. The structures of these products were supported by spectroscopic data, in particular ^{1}H NMR confirmed the geometry of the double-bond of the major isomer in each case. The configuration at C(2) of the major product

from the nitrosulfenylimine **2a** was established as (*S*) by conversion into the N-methoxycarbonyl derivative **ent-6** of (*S*)-homoserine lactone,[5,6] by exchange of N-substituent, ozonolysis with a reductive work-up, further reduction, and lactonisation. The structure of the major product from the reaction of the allyltin trichloride generated from the allylstannane **11** and the benzhydryl imine **2b**, was assigned by analogy.



Scheme 2 ***Reagents:*** i, $SnCl_4$, **2** (**12a/13a**, 74%; **12b/13b**, 78%); ii, HCl, MeOH; iii, $ClCO_2Me$ (77% of **14** from **12a/13a**); iv, O_3, Me_2S; v, $NaBH_4$; vi, H^+, $CHCl_3$ (62% of **ent-6** from **14**).

Finally, the stereoselectivity of reactions between the 4,5-bis-alkoxypent-2-enyltributylstannane **15**[10] and the achiral imines **2a** and **2b**, and the chiral imines **2e** and **2f** were examined. In all cases, the reactions were stereoselective in favour of the 1,5-*anti*-diastereoisomer **16**, with marginally better stereoselectivity when this 1,5-*anti*-selectivity was matched with the intrinsic facial preference of the (*R*)-imine **2f**.[2] As before, the structures of the products were established by spectroscopic methods, ^1H NMR confirming the *trans*-geometry of the double-bonds in the major products. The configuration at C(2) of the major product from the reaction with the 2-nitrosulfenylimine **2a** was established by conversion into the lactone **19**, which was shown to correspond to the (*S*)-enantiomer by comparison with an authentic sample.[11,12]

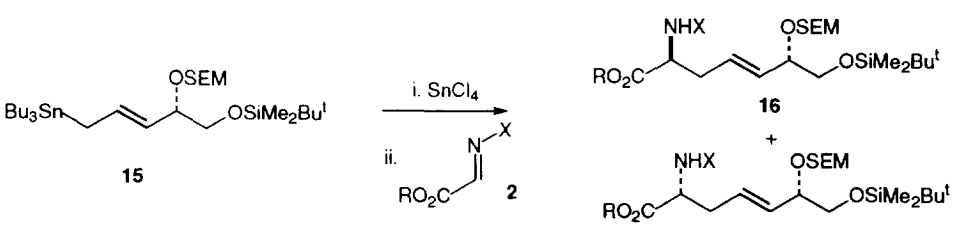
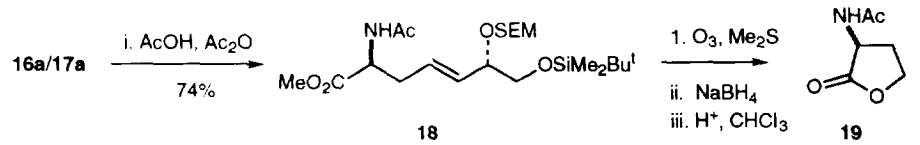


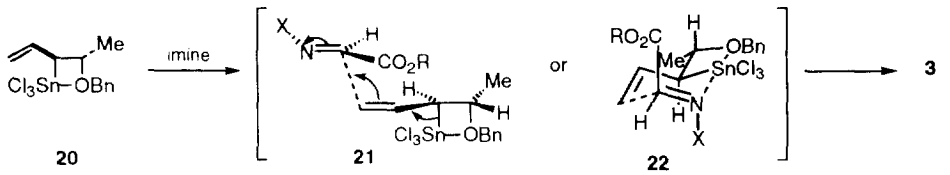
Table 2: Reactions of Stannane 15 with Imines 2

Imine	X	R	Yield (%)	1,5-*anti* (**16**) : 1,5-*syn* (**17**)
2a	SAr[a]	Me	81	96 : 4
2b	$CHPh_2$	Me	71	-[b]
2e	(*S*)-CHMePh	Bu	68	96 : 4
2f	(*R*)-CHMePh	Bu	72	99 : 1

[a]Ar = 2-$NO_2C_6H_4$-. [b]None of the *syn*-isomer **17b** was detected.



The stereoselectivities of the reactions between the intermediates generated from the allylstannanes **1**, **11**, and **15** and tin(IV) chloride, and the achiral imines **2a**-**2d** parallel those observed for the corresponding reactions with the chiral imines **2e** and **2f**, and should be useful for the stereoselective synthesis of α-amino-hydroxyacids and their derivatives.[2] The mechanisms of these reactions have not been investigated but are believed to involve stereoselective transmetallation of the allylstannanes to form allyltin trichlorides which then react with the imines.[1,2] Whether these latter reactions involve open-chain or cyclic transition states is not clear at present.[2] For example, transmetallation of the 4-benzyloxyallylstannane **1** is believed to provide the allyltin trichloride **20** which could be reacting with the imines *via* the open-chain transition state **21** or the cyclic transition state **22** to generate the preferred 1,5-*anti*-products **3**.



Further experiments are underway to underpin the participation of allyltin trichlorides, and to elucidate mechanistic aspects of their reactions with imines.

Ackowledgements

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