

ASYMMETRIC ALLYLATION OF PROCHIRAL ALDEHYDES
WITH A NEW ENANTIOSELECTIVE ALLYLATING AGENT PREPARED
FROM STANNOUS TRIFLATE, A CHIRAL DIAMINE, AND ALLYLDIALKYLALUMINUM

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A new enantioselective allylating agent, prepared by treatment of a mixture of stannous trifluoromethanesulfonate and a chiral diamine with allyldialkylaluminum, reacts with prochiral aldehydes to give secondary homoallyl alcohols in good optical yield.

In a series of our studies on the asymmetric synthesis effected by the chelate complexes between tin(II) metal center of key reactive intermediates and a chiral diamine derived from (S)-proline, we have already demonstrated highly enantioselective cross-aldol reactions,¹⁾ asymmetric acylation of prochiral glycerol,²⁾ and asymmetric reductions of a variety of prochiral carbonyl compounds.³⁾

Now we wish to report a novel and convenient procedure for an asymmetric allylation starting directly from prochiral aldehyde and simple allyldialkylaluminum with a high degree of enantioselectivity.

Homoallyl alcohols are synthetically valuable intermediates that have been used for characteristic units of numerous macrolides and ionophore antibiotics.⁴⁾ Recently, chiral allylboranes⁵⁾ have been successfully used for enantioselective allylation of aldehydes, however, in this reaction, chirality has been induced by chiral auxiliaries covalently bonded to the allylating agent.

Our previous investigations³⁾ on the asymmetric reduction with a chiral reducing agent prepared from stannous chloride, a chiral diamine, and diisobutylaluminum hydride suggested that the employment of allyldialkylaluminum instead of diisobutylaluminum hydride would provide a reagent to achieve asymmetric allylation of aldehydes. Allyldiethylaluminum is known to be readily prepared from diethylaluminum chloride on treatment with allylmagnesium chloride.⁶⁾

Based on these considerations, asymmetric allylation was examined according to the following procedure. A mixture of stannous chloride and (S)-1-methyl-2-(piperidinomethyl)pyrrolidine as a chiral diamine was treated with allyldiethylaluminum in dichloromethane at -78 °C, and then benzaldehyde was added. Usual work-up of this reaction mixture afforded the allylation product, 1-phenyl-3-buten-1-ol, in 76% yield (Table 1, Entry 2). However, asymmetric induction could not be observed. So we screened the effect of Sn(II) compounds, and it was found

that stannous trifluoromethanesulfonate (stannous triflate) was most effective for asymmetric induction. Next, we examined the effect of the alkyl substituents of allyldialkylaluminum and it was found that optical yield increased from 61% ee to 82% ee by using allyldiisobutylaluminum⁷⁾ (Table 1, Entries 6,7).

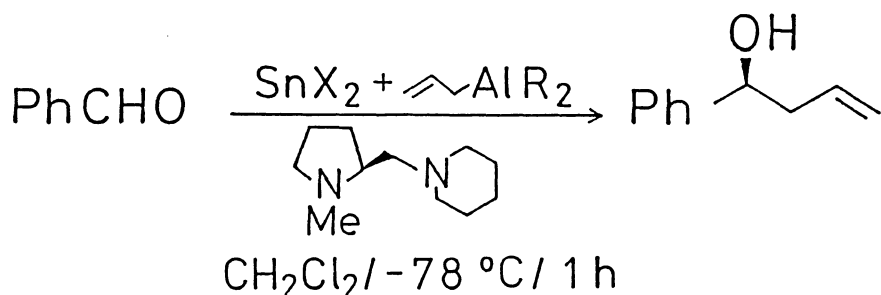


Table 1. The Effect of Tin(II) Compounds and Allylaluminum^{a)}

	SnX ₂	R	Yield/% ^{b)}	[α] _D /°(C ₆ H ₆)	Optical yield/% ee ^{c)}
1	—	Et	62	0	0
2	SnCl ₂	Et	76	0	0
3	SnF ₂	Et	71	-4.8 (c 0.55)	10
4	Sn(OAc) ₂	Et	82	0	0
5	Sn(OTf) ₂	Et	83	-25.1 (c 1.95)	52
6	Sn(OTf) ₂	Et	75	-29.8 (c 1.80)	61
7	Sn(OTf) ₂	<i>i</i> -Bu	91	-39.9 (c 2.48)	82

a) Molar ratio of aldehyde : Sn(OTf)₂ : allylAlR₂ : diamine
= 0.7 : 1.0 : 1.0 : 1.0

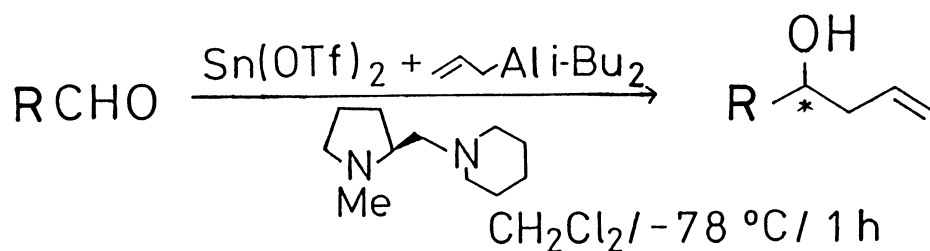
(Entries 6, 7 ; = 0.7 : 1.3 : 1.0 : 1.3)

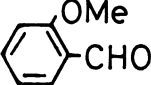
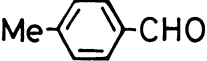
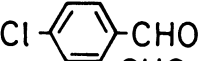
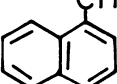
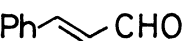
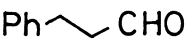
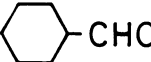
b) Isolated yields. All the products have (S)-configuration.


c) Optically pure (S)-1-phenyl-3-buten-1-ol gives [α]_D¹⁸-48.7° (c 6.92, C₆H₆).⁸⁾

It is noted that (i) efficient coordination of bidentate chiral diamine to the tin(II) metal center having vacant d orbitals and (ii) strong affinity of aluminum atom toward the oxygen atom of stannous triflate are thought to play an important role in the enantioselection of the present carbon-carbon bond forming reaction.

The reaction was conducted with various aldehydes under the optimum conditions and the results are summarized in Table 2. Higher enantioselectivities could be accomplished in the case of aromatic aldehydes. Also in the case of α,β-unsaturated aldehyde, the corresponding homoallyl alcohol was obtained in good optical yield.

Table 2. Asymmetric Allylation of Prochiral Aldehydes^{a)}

RCHO	Yield/% ^{b)}	$[\alpha]_D$	Optical yield/% ee	Abs. config.
PhCHO	91	$[\alpha]_D^{21} -39.9^\circ$ (c 2.48, C ₆ H ₆)	84 ^{c)} , 82 ^{d)}	S ^{d)}
	93	$[\alpha]_D^{23} -65.8^\circ$ (c 3.56, C ₆ H ₆)	80 ^{c)}	
	85	$[\alpha]_D^{25} -37.3^\circ$ (c 2.00, C ₆ H ₆)	82 ^{c)}	
	92	$[\alpha]_D^{23} -28.4^\circ$ (c 3.03, C ₆ H ₆)	84 ^{e)}	
	80	$[\alpha]_D^{24} -77.5^\circ$ (c 2.93, C ₆ H ₆)	80 ^{c)}	
	84	$[\alpha]_D^{19} +9.29^\circ$ (c 1.41, Et ₂ O)	64 ^{e)}	S ^{f)}
	86	$[\alpha]_D^{23} +11.1^\circ$ (c 3.14, CHCl ₃)	53 ^{c)}	R ^{g)}
	78	$[\alpha]_D^{25} -1.78^\circ$ (c 0.79, CH ₂ Cl ₂)	56 ^{c)}	

a) Molar ratio of aldehyde : Sn(OTf)₂ : -Al i-Bu₂ : diamine = 0.7 : 1.3 : 1.0 : 1.3

b) Isolated yields. All samples gave satisfactory ¹H NMR and IR spectra.

c) Determined by ¹⁹F NMR measurement of its MTPA ester.⁹⁾

d) Optically pure (S)-1-phenyl-3-buten-1-ol gives $[\alpha]_D^{18} -48.7^\circ$ (c 6.92, C₆H₆).⁸⁾

e) Determined by ¹⁹F NMR measurement of its MTPA ester in the presence of Eu(fod)₃.

f) Optically active (S)-1-phenyl-1,5-hexadien-3-ol gives $[\alpha]_D^{20} +3.60^\circ$ (c 10.08, Et₂O).¹⁰⁾

g) Optically active (R)-1-phenyl-5-hexen-3-ol gives $[\alpha]_D^{20} +16.9^\circ$ (c 1, CHCl₃).¹¹⁾

A typical procedure is described for the allylation of benzaldehyde using (S)-1-methyl-2-(piperidinomethyl)pyrrolidine as a chiral ligand; to a suspension

of anhydrous stannous triflate (224 mg, 0.54 mmol) and (S)-1-methyl-2-(piperidino-methyl)pyrrolidine (97.9 mg, 0.54 mmol) in 4 ml of dichloromethane was added dropwise allyldiisobutylaluminum (76 mg, 0.42 mmol) in 2.1 ml of dichloromethane at -78°C under argon atmosphere. After the yellow solution was stirred for 30 min, benzaldehyde (29.5 mg, 0.28 mmol) in 2 ml of dichloromethane was added dropwise at -78°C . The resulting mixture was stirred for 1 h at the same temperature, then quenched with sat. NH_4Cl aq. and 1 mol dm^{-3} HCl. The organic materials were extracted with dichloromethane and dried over anhydrous Na_2SO_4 . 1-Phenyl-3-buten-1-ol (37.2 mg, 91%) was isolated by thin layer chromatography on silica gel.

The present method well controlled by the use of the bidentate chiral diamine as a ligand is found to be applicable to the asymmetric allylation of various aldehydes by the operationally simple procedure. Further studies directed towards clarification of mechanism as well as application to other carbon-carbon bond formations using various alkylating reagents are now in progress.

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