

Enantioselective allylation of *N*-(trimethylsilyl)benzaldehyde imine using polymer-supported chiral allylboron reagents[†]

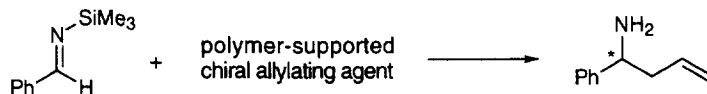
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Abstract: Polymer-supported chiral *N*-sulfonylamino alcohols **3** and **4** obtained from copolymerization of enantiomerically pure amino alcohols **1c** and **2c** derived from (1*R*)-(+)-camphor with styrene and divinylbenzene were treated with triallylborane, trimethylallylborane, and tri(3,3-dimethylallyl)borane, respectively, to give polymeric allylating agents. *N*-(Trimethylsilyl)benzaldehyde imine was allowed to react with the polymeric chiral reagents to afford the corresponding primary homoallylamines in high yield and good enantioselectivities. © 1997 Elsevier Science Ltd

The stereoselective synthesis of optically active homoallylamines remains a topic of considerable interest, since these compounds are useful starting materials for biologically active compounds. Enantioselective allylation of imines is a direct method for providing optically active homoallylamines. Although some diastereoselective allylations of imines have been studied,^{1–6} there are only a few reports concerning enantioselectivity. We have previously reported enantioselective allylation of various imines with chirally modified allylboron reagents.^{7,8} In the course of our studies of *N*-sulfonylamino alcohols as chiral auxiliaries in the allylation reaction, we reported that 3-toluenesulfonylamino-2-hydroxybornanes **1b** and **2b** are efficient chiral ligands for allylborane in the enantioselective allylation of *N*-trimethylsilylimines.⁸ On the other hand, use of polymer-supported reagents and catalysts in asymmetric synthesis offers several advantages such as simplification of reaction procedures, easy separation of supported species and products, and application to automation systems, etc.⁹ However, to our knowledge, no report has appeared where polymer-supported enantiopure ligands are utilized in enantioselective allylations of imines. The results obtained through the use of the *N*-sulfonylamino alcohols as chiral ligands encouraged us to prepare chiral polymers **3** and **4** possessing similar *N*-sulfonylamino alcohol moieties as pendant groups. We report the enantioselective allylation of *N*-trimethylsilylimine using polymer-supported chiral allylboron reagent derived from **3** and **4**.



Both chiral monomers **1c** and **2c** were readily synthesized by the sulfonylation of (+)-*endo*-2-hydroxy-*endo*-3-aminobornane **1a**¹⁰ or (–)-*exo*-2-hydroxy-*exo*-3-aminobornane **2a**¹¹ with 4-vinylbenzenesulfonyl-chloride in THF at room temperature for 1 h. These enantiopure amino alcohols were prepared from (1*R*)-(+)-camphor by reported methods.^{10,11} Copolymerization of **1c** and **2c** with styrene and divinylbenzene (DVB) under the conditions of suspension polymerization in aqueous media¹² afforded the crosslinked polymers **3** and **4**, respectively (moral

[†] This paper is dedicated to Professor Dieter Seebach on the occasion of his 60th birthday.

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ratio; **1c**, **2c**:styrene:DVB=1:8:1). These chiral polymers were then treated with triallylborane to afford polymeric allylating agents, which were used for the enantioselective allylation of *N*-trimethylsilylimine. In the case of the reactions using insoluble polymer-supported species, the use of a flask equipped with a glass frit and a stopcock permitted rapid filtration and washing of the polymer under a nitrogen atmosphere, which facilitates the reaction processes. By using this flask, excess triallylborane can be easily and completely removed. The resulting polymeric chiral allylating agent derived from **3** was then allowed to react with *N*-(trimethylsilyl)benzaldehyde imine at -78°C for 6 h to afford (*S*)-1-phenyl-3-butenamine in quantitative yield with 89% ee as shown in Table 1 (run 1). This enantioselectivity is the same as that obtained from the allylating agent derived from low molecular weight counterpart, **1b** (run 3).⁸ In each case, enantioselectivities were estimated either by HPLC using a chiral stationary phase or via specific rotation values. The enantioselective allylation with another polymeric chiral allylating agent derived from *endo* isomer **4** also gave the same homoallylamine with reversed stereoselectivity. The use of toluene and hexane as solvent resulted in lower both chemical yields and enantioselectivities to the same reaction (run 8, 9). Methallylboron and 3,3-dimethylallylboron derivatives were also readily prepared by the same method used for the preparation of allylboron reagent. The reaction with *N*-trimethylsilylimine with these reagents also took place smoothly to give the corresponding enantioenriched primary amines in high yield. Smooth reaction still occurs when the reaction temperature was lowered to -100°C . Somewhat higher enantioselectivities were obtained at this temperature. Interestingly, under the same reaction conditions, enantioselectivities obtained from polymer-supported reagents in heterogeneous systems are superior to those from the corresponding low molecular weight reagent in solution (run 4 and 6; 5 and 7; 12 and 14). Microenvironment formed in crosslinked polymer resulted in enhanced stereoselectivities in this allylation reactions, though the detailed mechanism and role of such polymeric effect is now under investigation.

A typical experimental procedure is described for the enantioselective synthesis of homoallylamine by nucleophilic addition of polymer-supported chiral allylboron reagent: To a suspension of chiral polymer **3** (4 mmol) in THF (25 ml) including triethylamine (0.05ml) was added a THF solution of triallylborane (5 mmol) dropwise at 0°C , and the mixture was stirred at room temperature for 2 h and then heated at reflux for 12 h to complete the formation of the polymer-supported chiral allylboron reagent. After cooling, excess of triallylborane was removed by filtration through fritted glass attached to the flask. The polymeric reagent was washed carefully with 25 ml of dry THF. Then THF solution of *N*-(trimethylsilyl)benzaldehyde imine (3.5 mmol) was added dropwise to the THF suspension of the polymeric reagent. The reaction mixture was stirred for 6 h at -78°C and quenched with 2 M HCl aqueous solution. After removal of the chiral polymer by filtration and usual workup for the filtrate, crude product was chromatographed on silica gel to afford the homoallylamine.

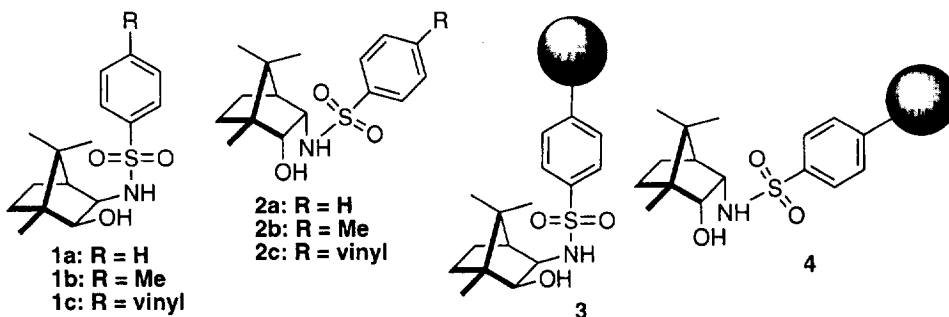
In summary, the crosslinked polymers **3** and **4** are excellent chiral ligands for the enantioselective allylation of *N*-trimethylsilylimine. The present method provides either enantiomer of primary homoallylamine by appropriate choice of 3-sulfonylamino-2-hydroxybornanes which are readily prepared from (1*R*)-(+)-camphor.

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Table 1. Enantioselective allylation of *N*-(trimethylsilyl)benzaldehyde imine using polymer-supported chiral allylboron reagents

Run	Chiral ligand	R of R ₃ B	Solvent	Reaction temp. °C	Homoallylamines formed		
					Yield, % ^{a)}	ee, % ^{b)}	Config.
1	3	allyl	ether	-78	99	89	<i>S</i>
2	3	allyl	THF	-78	87	73	<i>S</i>
3	1b	allyl	ether	-78	90	89	<i>S</i>
4	4	allyl	ether	-78	94	81	<i>R</i>
5	4	allyl	THF	-78	89	73	<i>R</i>
6	2b	allyl	ether	-78	93	72	<i>R</i>
7	2b	allyl	THF	-78	92	64	<i>R</i>
8	2b	allyl	toluene	-78	73	53	<i>R</i>
9	2b	allyl	hexane	-78	67	35	<i>R</i>
10	4	allyl	THF	-100	92	78	<i>R</i>
11	3	methallyl	ether	-78	93	90	<i>S</i>
12	4	methallyl	THF	-78	94	79	<i>R</i>
13	2b	methallyl	ether	-78	89	80	<i>R</i>
14	2b	methallyl	THF	-78	89	72	<i>R</i>
15	4	methallyl	THF	-100	92	83	<i>R</i>
16	3	3,3-dimethylallyl	ether	-78	91	84	<i>S</i>
17	4	3,3-dimethylallyl	THF	-78	93	69	<i>R</i>
18	2b	3,3-dimethylallyl	ether	-78	91	68	<i>R</i>
19	4	3,3-dimethylallyl	THF	-100	95	75	<i>R</i>

^{a)} Isolated yield. ^{b)} Enantiomeric excesses were determined by HPLC using a chiral stationary phase {Daicel Chiralcel OD-H, hexane-isopropyl alcohol-diethylamine (90 : 10 : 0.1)}.

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