B-(γ-(Trimethylsilyl)propargyl)diisopinocampheylborane: A New, Highly Efficient Reagent for the Enantioselective Propargylboration of Aldehydes. Synthesis of Trimethylsilyl-Substituted and Parent α-Allenic Alcohols in High Optical Purity

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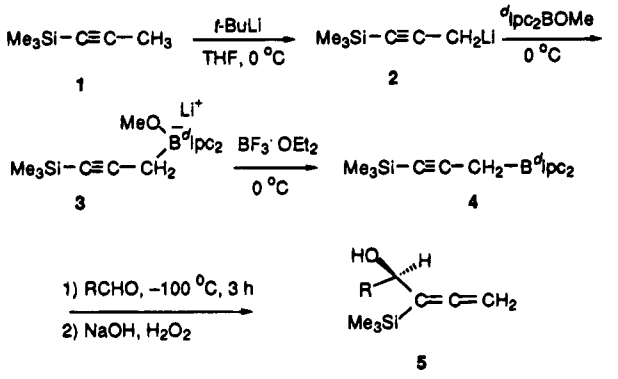
Asymmetric allylboration and related reactions mark a major development in acyclic stereocontrol in recent years.[3] In particular, the terpene-based reagents are spectacularly useful for the conversion of prochiral aldehydes into homoallylic alcohols.[4] This fact is reflected in numerous applications they have found in the stereoselective synthesis of natural products.[5] Our recent studies on the recovery and recycle of chiral auxiliaries have significantly improved the economy of these reactions.[6]

α-Allenic alcohols are highly versatile synthetic intermediates. For example, they can be stereoselectively converted into compounds such as *syn*-1,2-diols,[7] *syn*-1,2-amino alcohols,[8] 2,5-dihydrofurans,[9] vinyl epoxides,[10] vinylcyclopropanes,[11] etc., which in turn can be used to prepare a variety of useful products. Moreover, some naturally occurring compounds, such as Kumausallene,[12] contain an α-allenic alcohol moiety in their structure.

Scheme 1



dIpc = Isopinocampheyl derived from (+)-α-pinene

The preparation of homopropargylic and α-allenic alcohols poses difficulties due to the ambient nature of propargylic carbanions, which generally exist as an equilibrating mixture of allenic and propargylic organometallic derivatives.[13] However, in spite of these complications, in recent years some methods have been developed for the regiospecific construction of homopropargylic and α-allenic alcohols. We recently demonstrated the use of *B*-allenyl-9-BBN for the synthesis of homopropargylic alcohols from carbonyl compounds.[14] Previously, Wang *et al.* have shown the use of a boron-based reagent for the preparation of racemic trimethylsilyl-substituted α-allenic alcohols.[15] Yamamoto *et al.* described an asymmetric synthesis of homopropargylic alcohols based on chiral auxiliary derived from tartaric acid,[16] whereas Corey *et al.* used a chiral auxiliary derived from 1,2-diphenyl-1,2-diaminoethane for the asymmetric synthesis of homopropargylic and α-allenic alcohols.[17] Recently, 3-(trimethylsilyl)-3,4-pentadien-2-ol has been resolved using enzyme-mediated acylation (31% yield, 81% ee).[18] However, a simple, general method for the asymmetric synthesis of such trimethylsilyl-substituted α-allenic alcohols has been lacking. In our continued efforts at developing new applications for our pinanyl-based chiral auxiliaries, we describe herein the synthesis of *B*-(γ-(trimethylsilyl)propargyl)diisopinocampheylborane (**4**) as a highly enantioselective reagent for the propargylboration of prochiral aldehydes.

This reagent **4** can be readily prepared using commercially available *B*-methoxydiisopinocampheylborane[4a] (Scheme 1). Metalation of 1-(trimethylsilyl)propyne with *t*-BuLi in THF at 0 °C[15a] followed by addition of *B*-methoxydiisopinocampheylborane gives ate complex **3**. Treatment of **3** with 1.33 equiv of $BF_3{\cdot}OEt_2$[19] liberates the required propargylborane reagent **4**. Reagent **4** reacts with various aldehydes at −100 °C to give after alkaline peroxide oxidation, the corresponding trimeth-

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Table 1. Asymmetric Propargylboration of Aldehydes

entry	RCHO R =	isolated yield[a] (%)	% ee of **5**[b]	$[\alpha]_D^{25}$, $CHCl_3$	confign
1	Me	72	87	+11.9 (*c* 1.27)	*R*[d]
2	*i*-Pr	76	99	−5.3 (*c* 1.96)	*R*[e]
3	*t*-Bu	75	92	+5.4 (*c* 2.60)	*R*[e]
4	Chx	78	96	−20.4 (*c* 1.76)	*R*[f]
5	(*E*)-propenyl	68	87[c]	−87.8 (*c* 1.60)	*R*[e]
6	Ph	74	89	−139.4 (*c* 1.40)	*R*[f]

[a] All compounds exhibited satisfactory ^1H and ^{13}C spectral properties which were consistent with those reported in the literature.[15,17] [b] Determined by capillary GC analysis of the corresponding Mosher ester derivative unless otherwise mentioned. [c] Determined by ^1H NMR using the chiral shift reagent, Eu(hfc)$_3$. [d] Based on ref 12. [e] Predicted by analogy. [f] Trimethylsilyl-substituted allenic alcohols were desilylated using tetrabutylammonium fluoride to obtain the corresponding allenic alcohols, and their sign of rotation was compared with the values reported.[24]

ylsilyl-substituted α-allenic alcohols **5** in high yields and optical purities (Table 1).[20]

It can be seen from Table 1 that the reaction is quite general since high enantioselectivities are obtained with a variety of prochiral aldehydes. The enantiomeric excesses of the α-allenic alcohols were determined either by analysis of the corresponding Mosher ester derivatives on capillary GC or by ^1H NMR using chiral shift reagent. The absolute stereochemistry of **5** (R = cyclohexyl, phenyl; Chx, Ph) was established by comparing the sign of the optical rotation of the desilylated alcohols with the two reported in the literature. The absolute stereochemistries thus established for **5** (R = Chx, Ph) proved to be the same as for those compounds previously prepared by allylboration with ^{d}Ipc$_2$BAll.[4] Consequently, we felt it safe to assign the absolute configuration to the remaining four derivatives by analogy. As in the case of allyl- and crotylboration, this reaction is operationally very simple: the chiral auxiliary is readily recyclable and provides access to both enantiomers since both antipodes of α-pinene are commercially available.

We also investigated the desilylation of α-allenic alcohols **5** (R = Chx, Ph) under various conditions. Reaction of **5** (R = Chx) with commercially available 1.0 M THF solution of tetrabutylammonium fluoride (containing about 5% water) at 0 °C for 5 min gave a 7:3 ratio of desilylated allenic:alkynic products. When the desilylation was attempted at −78 °C to suppress the isomerization, the reaction did not take place at all. We came across a recent report which claimed that the desilylation of similar trimethylsilyl-substituted and triphenylsilyl-substituted α-allenic alcohols can be achieved without isomerization with KF in DMF.[21] However, in our hands the desilylation of **5** (R = Chx, Ph) under these conditions was very slow and the alkynic product was still visible. After considerable experimentation, we found the best desilylation conditions to be treatment with a 1.0 M THF solution of tetrabutylammonium fluoride (dried over 4 Å molecular sieves) at −78 °C for 4 h.[22] Under these conditions, an 87:13 ratio of allenic:alkynic product ratio was achieved from which the pure desilylated α-allenic alcohols could be isolated in 72% and 74% yield, respectively, by simple flash column chromatography on silica gel.

In conclusion, this method represents a simple and highly enantioselective approach for the preparation of both trimethylsilyl-substituted and the parent unsubstituted α-allenic alcohols. These results further substantiate the superior chiral directing properties of α-pinene based chiral auxiliaries in asymmetric synthesis.[23] We are currently investigating the extension of this methodology for the synthesis of other variously substituted α-allenic alcohols.

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(20) **General Procedure for Propargylboration: Preparation of (*R*)-(+)-3-(Trimethylsilyl)-3,4-pentadien-2-ol (5, R = Me).** To a stirred solution of 1-(trimethylsilyl)propyne (4.0 mL, 27 mmol) in THF (30 mL) was added *tert*-butyllithium in pentane (1.7 M, 27 mmol) dropwise at 0 °C, and the reaction mixture was stirred for 1 h. (−)-*B*-Methoxydiisopinocampheylborane[4a] in ether (1 M, 25 mmol, derived from (+)-α-pinene) was added at 0 °C. After the mixture was stirred for 10 min, boron trifluoride etherate (4.4 mL) was added dropwise to liberate **4**. The reaction mixture was then cooled to −100 °C and a solution of acetaldehyde (1.4 mL, 25 mmol) in ether (25 mL), maintained at −78 °C, was slowly added along the side of the flask to the reaction mixture. The reaction mixture was stirred at −100 °C for 3 h and then brought to rt (1 h). It was then oxidized by treatment with 3 N NaOH (15 mL) and 30% H_2O_2 (10 mL). The completion of oxidation was ensured by refluxing the reaction mixture for 1 h. The organic layer was separated, washed with water (20 mL), and brine (20 mL) and dried over anhyd $MgSO_4$. The residue, after removal of the solvent, was carefully fractionated to furnish (*R*)-(+)-3-(trimethylsilyl)-3,4-pentadien-2-ol (**5**, R = CH_3) in 72% yield (2.8 g): bp 94 °C/55 mm. Analytically pure material was obtained by flash column chromatography (hexane−ethyl acetate, 99:1) on silica gel: $[\alpha]_D^{25}$ = +11.9 (*c* 1.27, $CHCl_3$). GC Analysis of its Mosher ester on a capillary Supelcowax column (15m × 0.25 cm) established the alcohol to be of 87% ee: ^1H NMR ($CDCl_3$, 300 MHz) δ 0.18 (s, 9 H), 1.35 (d, 3 H), 1.75 (br s, 1 H), 4.34 (m, 1 H), 4.55 (d, 2 H).

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(22) **Representative Procedure for Desilylation: Synthesis of (*R*)-(−)-1-phenyl-2,3-butadien-1-ol.** To a stirred solution of **5** (R = Ph) (0. 54 g, 2.5 mmol) at −78 °C was added commercially available tetrabutylammonium fluoride (5.0 mL, 5.0 mmol, 1 M solution in THF, dried over 4 Å molecular sieves for 48 h) and stirring continued for 4 h. A saturated brine solution (10 mL) was added to the reaction mixture at the same temperature, and the reaction was allowed to come to rt. The organic layer was separated, and the aqueous phase was extracted with ether. The combined organic extracts were dried over anhyd $MgSO_4$. Flash column chromatography of the product mixture (hexane: ethyl acetate, 98:2) furnished the pure alcohol (*R*)-(−)-1-phenyl-2,3-butadien-1-ol (0.27g, 74%): $[\alpha]_D^{25}$ +97.02 (*c* 1.17, CCl_4) (lit.[16] $[\alpha]_D^{25}$ +45.6 (*c* 1.2, CCl_4), for 47% ee); ^1H NMR δ 2.6 (br s, 1 H), 4.9−5.0 (m, 2 H), 5.2−5.3 (d, 1 H), 5.4−5.5 (m, 1 H), 7.3−7.5 (m, 5 H); ^{13}C NMR δ 72. 01, 77.06, 95.26, 126.13, 127.88, 128.56, 142.87, 207.12.

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