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A Stereoselective Synthesis of 3,3-Disubstituted Allylborane Derivatives Using Haloboration Reaction and their Application for the Diastereospecific Synthesis of Homoallylic Alcohols Having Quaternary Carbon

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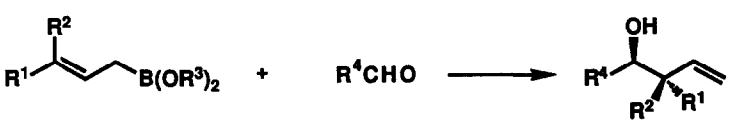
Abstract: 3,3-Disubstituted allylborane derivatives (**1c**) can be prepared stereoselectively from the haloboration adducts of 1-alkynes and they afford homoallylic alcohols having quaternary carbon (**2c**) diastereospecifically by the reaction with aldehydes.

Allylic boranes are one of the most useful reagents for a carbon-carbon bond formation under controlling the stereochemistry in acyclic systems. Especially, (E)- and (Z)-crotylborane derivatives (**1a,b**) have widely been used to prepare homoallylic alcohols, because they provide syn- or anti-products (**2a,b**) diastereospecifically by the reaction with aldehydes and stereoselective synthesis of **1a** and **1b** is well established.[1] Similarly, 3,3-disubstituted allylborane derivatives (**1c**) are expected to give the homoallylic alcohols having quaternary carbon (**2c**) (Eq. 1). However, the difficulty associated with the stereoselective synthesis of **1c** has prevented the adequate development of the reaction using **1c**.[2] We now wish to report here the stereoselective synthesis of **1c** and their application for the diastereospecific synthesis of homoallylic alcohols having quaternary carbon (**2c**) by the reaction with aldehydes.



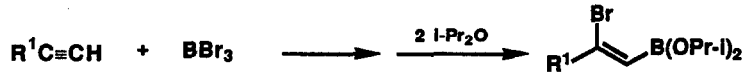
(Eq. 1)

1a; R^1 = Me, R^2 = H
1b; R^1 = H, R^2 = Me
1c; R^1 = alkyl, R^2 = alkyl

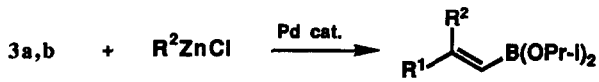
2a; R^1 = Me, R^2 = H
2b; R^1 = H, R^2 = Me
2c; R^1 = alkyl, R^2 = alkyl

Stereoselective synthesis of **1c** was carried out by the homologation reaction of 2,2-disubstituted vinylboranes prepared from haloboration adducts of 1-alkynes.[5] (E)-(2-Methyl-1-hexenyl)-diisopropoxyborane (**4a**) was prepared from 1-hexyne by the bromoboration reaction, followed by cross-coupling reaction with methylzinc chloride. Homologation reaction of **4a** was achieved by the reaction with

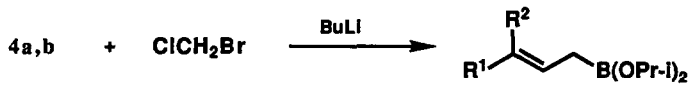
chloromethyllithium[6] to provide (E)-(3-methyl-2-heptenyl)diisopropoxyborane (**5a**) stereoselectively (E ≥ 95 %). (Z)-Isomer (**5b**) was also prepared from 1-propyne in the same manner. However the isomeric purity of **5b** was lower than that of **5a** (Z ≈ 85%)[7] (Scheme 1).



3a; R^1 = Bu, Yield; 82%, b.p. 68°C/0.07mmHg
3b; R^1 = Me, Yield; 70%, b.p. 40°C/0.07mmHg



4a; R^1 = Bu, R^2 = Me
Yield; 88%, b.p. 57-60 °C/0.07 mmHg
4b; R^1 = Me, R^2 = Bu
Yield; 60%, b.p. 57-60 °C/0.07 mmHg

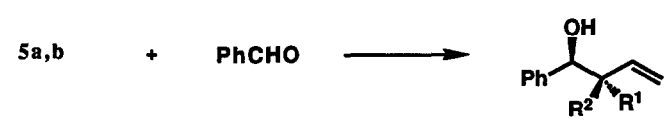


5a; R^1 = Bu, R^2 = Me
Yield; 80%, b.p. 60-64 °C/0.05 mmHg
5b; R^1 = Me, R^2 = Bu
Yield; 79%, b.p. 60-64 °C/0.05 mmHg

Scheme 1

As expected, **5a** reacted with benzaldehyde diastereospecifically and the homoallylic alcohol (**6a**) was obtained in good yield with high selectivity (97%). The isomer (**6b**) was also obtained from **5b** with moderate selectivity (88%) (Eq. 2). Other aldehydes also reacted with **5a** and **5b** in good yields and both diastereomers of homoallylic alcohols (**2c**) were given specifically as shown in Table 1.

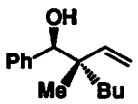
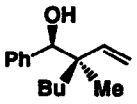
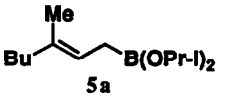
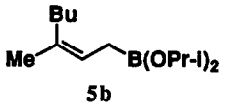
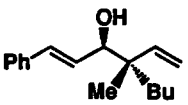
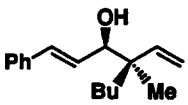
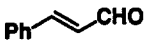
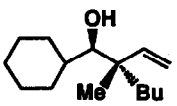
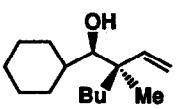
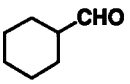
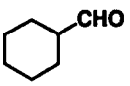
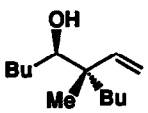
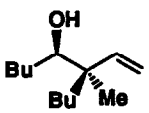
The following procedure for the synthesis of **6a** is representative. To a THF solution (10 ml) of **5a** (360 mg, 1.5 mmol) was added a THF solution (3 ml) of benzaldehyde (106 mg, 1 mmol) at - 78 °C, and the mixture was stirred at the temperature for 10 min and then at room temperature overnight. The product was extracted with ether and dried over magnesium sulfate. After concentration, **6a** (R^1 = Bu, R^2 = Me) was isolated by column chromatography (silica gel/ hexane : ether = 95 : 5) in 95 % yield with 97% of selectivity.[8]



(Eq. 2)

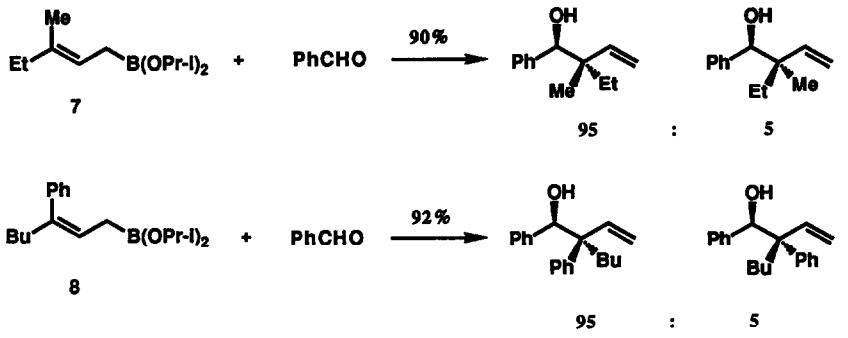
6a; R^1 = Bu, R^2 = Me
6b; R^1 = Me, R^2 = Bu

Table 1. Reaction of 3,3-Disubstituted Allylborane Derivatives with Aldehydes

Borane	Aldehyde	Product isomer ratio[a]			Yield[b]
					
 5a	PhCHO	97	:	3	95
 5b	PhCHO	12	:	88	96
					
5a		95	:	5	96
5b		10	:	90	95
					
5a		95	:	5	84
5b		11	:	89	82
					
5a	BuCHO	95	:	5	89
5b	BuCHO	11	:	89	81

a. Determined by NMR. b. Isolated yield based on aldehyde used.

As R^1 and R^2 of **5a,b** are derived from alkyl groups of 1-alkynes and organozinc compounds respectively, the present method is applicable for the synthesis of a variety of 3,3-disubstituted allylborane derivatives (**1c**). For instance, (E)-(3-methyl-2-pentenyl)diisopropoxyborane (**7**) was prepared by the homologation of (E)-(2-methyl-1-butenyl)diisopropoxyborane which was obtained by the bromoboration of 1-butyne, followed by methylation with methylzinc chloride. Phenylation of (Z)-(2-bromo-1-hexenyl)diisopropoxyborane (**3a**) with phenylzinc chloride followed by homologation reaction provided (Z)-(3-phenyl-2-heptenyl) borane derivative (**8**) stereoselectively. From both **7** and **8**, homoallylic alcohols could be obtained selectively as shown in Eq. 3. According to our method, a variety of substituents can be introduced into the syn- and anti-positions of hydroxy group of **2c**.



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2. As for the stereoselective synthesis of 3,3-disubstituted allylborane derivatives, only the synthesis of one alkyl group and one heteroatom substituted allylborane derivatives such as (3-methoxy-2-butenyl)boranes[3] and (3-trimethylsilyl-2-butenyl)boranes[4] was reported previously.
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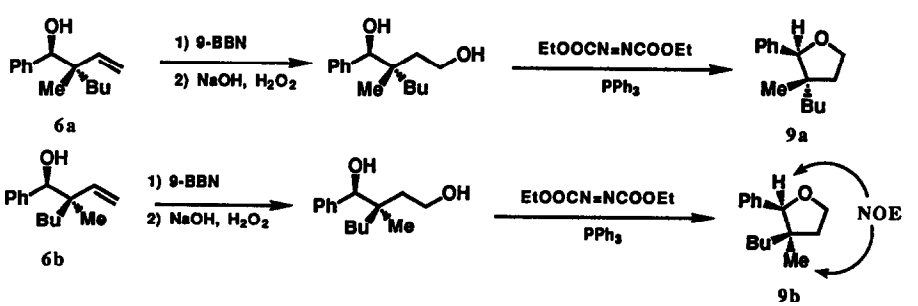
6. Sadhu, K. M.; Matteson, D. S. *Organometallics*, **1985**, *4*, 1687; Brown, H. C.; Singh, S. M.; Rangaishenvi, M. V. *J. Org. Chem.*, **1986**, *51*, 3150.
7. The relatively low isomeric purity of **5b** is due to the bromoboration step. Bromoboration reaction of 1-propyne with tribromoborane proceeds with exceptionally low stereoselectivity (Z = 88%) compared with the bromoboration reaction of other 1-alkynes.
8. From the mechanism proposed for the reaction of crotylboranes with aldehydes, the structures of **6a** and **6b** could be expected as shown in Eq. 3. It was confirmed by the conversion of **6a** and **6b** into the cyclic ether (**9a** and **9b**). As the NOE was observed between methyl group and benzylic proton only in the NMR spectrum of **9b**, the expected structures of **6a** and **6b** were shown to be correct.



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