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Highly General Synthesis of [*E*]- and [Z]-3-Alkylsubstituted Allylboronates *via* One-Carbon Homologation of Stereospecific 1-Alken-1-ylboronates

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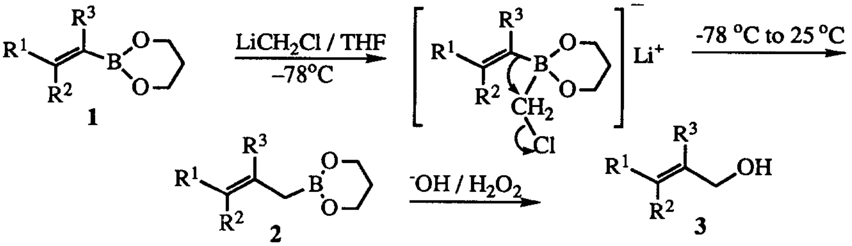
Abstract: *Stereospecific 1-alken-1-ylboronates readily react with in situ generated chloromethyllithium, producing the corresponding allylboronate in good yields and in excellent stereochemical purities These are very important synthetic intermediates and conversion of a representative derivative,* [E]*-2-(2-heptenyl)-1,3,2-dioxaborinane, 2 ($R^1 = C_4H_9$, $R^2 = R^3 = H$), into several compounds of synthetic interest is described.*

Allylboronates are very promising organoborane intermediates for the formation of carbon-carbon bonds.[1] They have been synthesized and utilized very efficiently in the synthesis of natural products by Schlosser,[2] Roush,[3] Hoffmann,[4] Wuts[5] and others. In general the allylboronates are synthesized by the reaction of an allylmetal with a haloborane[4] or a trialkoxyborane.[3] This is the best known method for the synthesis of both [*E*]- and [Z]-crotylborane, but the yields or the isomeric purities decrease considerably for straight chain and substituted straight chain olefins.[2,6]

Wuts and coworkers[7] have prepared these allylboronates by reacting stereospecific alkenyllithiums with pinacol chloromethylboronate. Drawback of this procedure are its poor yields (~ 50%) and the variable isomeric purity depending on the starting alkenyllithium. Matteson et. *al* [8] have reported the homologation of alkenylboronates utilizing (dichloromethyl)lithium, $LiCHCl_2$. More recently, Suzuki[9] and coworkers have synthesized them by the palladium catalyzed hydroboration of 1,3-dienes, but only the [*Z*]-allylboronates can be prepared in this way. However, no truly general procedure has been developed for the synthesis of both [*E*]- and [*Z*]-allylboronates. One-carbon homologation of [*E*]- and [Z]-alken-1-ylboronates should give the corresponding [*E*]- and [*Z*]- crotylboronates and [*E*]- and [*Z*]-3-alkylsubstituted allylboronates.

We have previously reported procedures for the stereospecific synthesis of both [*E*]- and [Z]-1-alken-1-ylboronates *via* haloboranes[10] and utilized them in various synthetic transformations.[11] Moreover, it is well known that the homologation reaction proceeds with retention of configuration at the migrating center.[12] Consequently, the allylboronate synthesized through such homologation of alkenylboronates should reflect the very high isomeric purity of the [*E*]- or [Z]-1-alken-1-ylboronates utilized. Encouraged by Matteson's observations and our success in homologating boronates[13] and cyclic borinates[14] using *in situ* generated chloromethyllithium, it appeared desirable to explore the possibility for applying such homologation, for the synthesis of pure [*E*]- and [*Z*]- allylboronates.

Indeed, we succeeded in developing a general synthesis of pure [*E*]- and [Z]-3-substituted allylboronates *via* one-carbon homologation of stereospecific [*E*]- and [Z]-alkenylboronates using the *in situ* generated



chloromethyllithium, $LiCH_2Cl$.

A number of representative [*E*]- and [Z]-1-alken-1-ylboronates, both mono and disubstituted, were prepared using our recently developed procedures.[10] These boronates were homologated using the *in situ* generated chloromethyllithium.[13,14] A typical homologation procedure involved the dropwise addition of *n*-BuLi to a mixture of the alkenylboronate and chloroiodomethane in THF at –78 °C and allowing the reaction mixture to warm to room temperature over a period of 14 h. The homologation reaction was monitored by ^{11}B NMR (the chemical shift value changes from δ +27 for alkenylboronates to δ +30 for allylboronate).

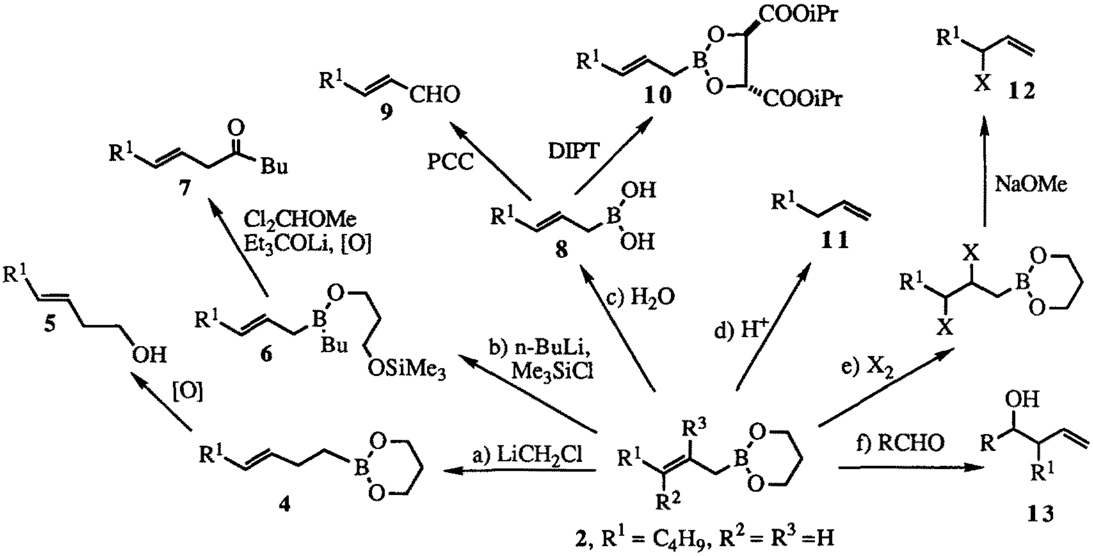
In the course of this study it was established that allylboronates undergo clean oxidation by alkaline hydrogen peroxide to give the isomerically pure allyl alcohols in excellent yields. Consequently, the allylboronate products were oxidized to the corresponding allyl alcohols and were characterized by their IR, ^1H NMR and ^{13}C NMR and the isomeric purities were determined by capillary GC (Supelcowax, 15m / SPB-5, 40m). In each case the [*E*] and [Z] isomers were prepared and were shown to possess very high isomeric purity (95-99%). The results are summarized in Table 1. The product can be isolated by stripping off THF, adding pentane to precipitate the LiCl formed, filtering the mixture under nitrogen followed by the removal of pentane and distillation of the residue under reduced pressure, to afford very good yields of the allylboronate product.

Table 1. One-Carbon Homologation of 1-Alken-1-ylboronates to the Corresponding [*E*]- and [*Z*]-3-Alkylsustituted Allylboronates and their Oxidation to Allylic Alcohols.

no.	R^1	R^2	R^3	Oxidation Product **3**	% Yield[a]	% Isomeric Purity[a]
1	CH_3	H	H	[*E*]-But-2-en-1-ol	70	98
2	H	CH_3	H	[Z]-But-2-en-1-ol	70	96
3	*n*-C_4H_9	H	H	[*E*]-Hex-2-en-1-ol	85	≥99
4	H	*n*-C_4H_9	H	[Z]-Hex-2-en-1-ol	80	95
5	*t*-C_4H_9	H	H	[*E*]-4-Dimethylpent-2-en-1-ol	88	≥99
6	H	*t*-C_4H9	H	[Z]-4-Dimethylpent-2-en-1-ol	87	≥98
7	*c*-C_5H_9	H	H	[*E*]-3-Cyclopentylprop-2-en-1-ol	86	99
8	H	*c*-C_5H_9	H	[Z]-3-Cyclopentylprop-2-en-1-ol	84	≥99
9	Ph	H	H	[*E*]-Cinnamyl alcohol	75	≥99
10	H	Ph	H	[Z]-Cinnamyl alcohol	70	≥99
11	*n*-C_4H_9	H	*n*-C_4H_9	[*E*]-2-Butylhept-2-en-1-ol	80	96
12	H	*n*-C_4H_9	*n*-C_4H_9	[Z]-2-Butylhept-2-en-1-ol	75	97
13	*i*-C_3H_7	H	*n*-C_4H_9	[*E*]-2-Butyl-4-methylpent-2-en-1-ol	80	98
14	H	*i*-C_3H_7	*n*-C_4H_9	[Z]-2-Butyl-4-methylpent-2-en-1-ol	85	98

[a] Based on the % yield and % isomeric purity of the oxidation products **3**.

Allylboronates have been mainly used for the allylboration of aldehydes.[2-5] Consequently, it appeared desirable to explore the chemistry of a representative 3-alkyl allylboronate. A number of typical reactions of these allylboronates were explored with [*E*]-2-(2-heptenyl)-1,3,2-dioxaborinane, (**2**, $R^1 = C_4H_9$, $R^2 = R^3 = H$) (Scheme I).



2, $R^1 = C_4H_9$, $R^2 = R^3 = H$

Scheme I

As can been seen from the structure of the allylboronate, the reactions can follow two pathways 1) without allylic rearrangement and 2) with allylic rearrangement.

Reactions which occur without allylic rearrangement are as follows. a) One-carbon homologation of the allylboronate (**2**, $R^1 = C_4H_9$, $R^2 = R^3 = H$) affords the homoallylic boronate **4** with complete retention of geometry, oxidation of which gives homoallylic alcohol **5**. b) Reaction of a representative alkyllithium, such as *n*-BuLi with the allylboronate, followed by the reaction with chlorotrimethylsilane gives the borinate **6**. Reaction of this borinate with α,α-dichloromethyl methyl ether, (DCME)[15] in presence of lithium triethylcarboxide followed by oxidation gives the β,γ-unsaturated ketone, 7-dodecen-5-one **7**. c) Hydrolysis of allylboronate gives allylboronic acid **8** in about 65% yield. The unhydrolyzed boronate ester can be recovered and recycled. In the course of this study it was observed that the ethylene glycol ester hydrolyzes quantitatively to afford the allylboronic acid. PCC oxidation[16] of the allylboronic acid gives the 2-heptenal **9** in good yields. Furthermore, the allylboronic acid can be esterified[17] with a chiral auxiliary such as diisopropyl tartrate to give the allylboronate **10**, which on reaction with aldehydes should afford optically active homoallylic alcohols. In the above reactions both [*E*] and [*Z*] isomers can be synthesized using the appropriate 3-substituted allylboronate.

Reactions which occur with allylic rearrangement are as follows. d) Protonolysis[1b] of the allylboronate (2, $R^1 = C_4H_9$, $R^2 = R^3 = H$) in refluxing acetic acid or a THF solution of methanesulfonic acid gives 1-heptene **11** in excellent yield. e) Halogenation of the allylboronate (**2**, $R^1 = C_4H_9$, $R^2 = R^3 = H$) followed by reaction with NaOMe/MeOH affords the corresponding allyl halide **12**(X=Br/Cl). f) Allylboration of aldehydes, presently the most widely used reaction of allylboronate, gives homoallylic alcohols **13** with allylic rearrangement.

Conclusion

One-carbon homologation of alken-1-ylboronates is an excellent method for the preparation of [E]- and [Z]-3-alkylsubstituted allylboronates (crotyl or "higher" crotyl boronates) in good yields and excellent isomeric purities, difficult to achieve by other means. Their versatility in organic synthesis for many reactions other than allylboration greatly extends the synthetic importance of these derivatives.

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