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A SIMPLE PROCEDURE FOR THE SYNTHESIS OF THREE-CARBON HOMOLOGATED BORONATE ESTERS AND TERMINAL ALKENES *VIA* NUCLEOPHILIC DISPLACEMENT IN α-HALOALLYLBORONATE ESTER

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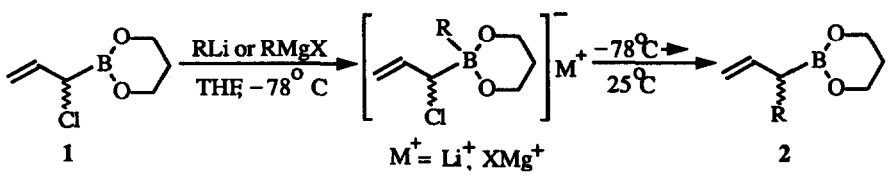
Summary: The transfer reactions of α-haloallylboronate ester **1** with representative organolithium and Grignard reagents provide α-alkyl- or α-aryl-substituted allylboronate esters, readily converted into three-carbon homologated boronate esters and terminal alkenes.

The ease of preparation and the control of stereochemistry of α-haloboronate esters augur favorably for their application in transfer reactions involving organoboranes.[1,2] In recent years, Matteson *et al* have demonstrated an elegant approach for their utility in transfer reactions with a variety of nucleophiles and extended this approach to a truly general asymmetric synthesis.[2] This development makes the chemistry of α–haloallylboronate ester even more fascinating because of the presence of both the α-halo- moiety and the enhanced reactivity of the boron-allyl system. The chemistry of the boron-allyl system has been explored in the laboratories of Hoffmann[3] and Roush.[4] For instance, Hoffmann *et al* have demonstrated the utility of α-haloallylboronate esters for the transfer of chirality in the allylboration of aldehydes[5] and further extended this approach to the synthesis of mycinolide[6] and the Prelog-Djerassi aldehyde.[7] Roush *et al* have also demonstrated the synthetic utility of the boron-allyl system for the asymmetric allylboration of aldehydes.[4] As regards the transfer reaction involving the α-halo- moiety, there are scattered reports in the literature. Matteson *et al* have illustrated the utility of such α-haloallylboronate esters for transfer reactions with *t*-butyl lithioacetate[8], lithiohexamethyldisilazane[9], and with an alkyl Grignard reagent.[10] Hoffmann has reported[3] the transfer reaction of α-haloallylboronate with nucleophiles, such as alkoxide and thioalkoxides, for the preparation of α-hetero-substituted allylboronates. However, the synthetic utility of such α-substituted allylboronates has not been studied systematically, except for the allylboration of aldehydes.

In the preceding letter we have demonstrated[17] a convenient, high yield synthesis of α-haloallylboronate ester **1** *via* the *in situ* reaction of α–haloallyllithium with a borate ester. Conceivably, the reaction of such α-haloallylboronate ester with an organyllithium or a Grignard reagent should afford the corresponding α-alkylsubstituted allylboronate ester. Having developed[17] a facile synthesis of α-haloallylboronate ester **1** we proceeded to investigate the transfer reaction with representative organolithium and Grignard reagents (eq 1).



1 **2** (1)

Gratifyingly, the reaction of **1** with an equivalent of an organyllithium or Grignard reagent in THF at –78 °C, followed by warming up to 25 °C, furnished the desired α-substituted allylboronate ester **2** in excellent yield. The results are summarised in Table 1.

Table 1. Nucleophilic Displacement of the α-Chloroboronate Ester **1** by Representative RLi or RMgX Reagents.

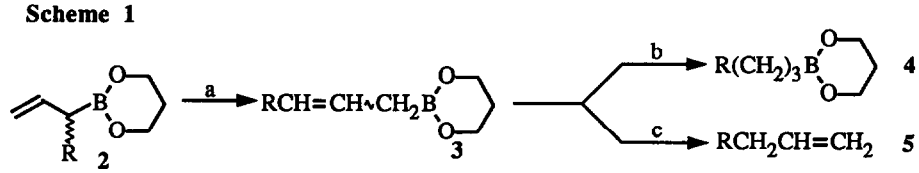
		product, $RCH(CH{=}CH_2)BO_2(CH_2)_3$, **2**			
entry	nucleophile RLi or RMgX	**2** R=	^{11}B NMR ($CDCl_3$), δ	isolated yield[a](%)	oxidation product[b] $RCH(CH{=}CH_2)OH$
1	*n*-C_4H_9Li	*n*-C_4H_9	32	78	Hex-1-en-3-ol
2	*n*-$C_6H_{13}MgCl$	*n*-C_6H_{13}-	32	80	Non-2-en-3-ol
3	*sec*-C_4H_9Li	*sec*-C_4H_9-	31	72	4-Methyl-hex-1-en-3-ol
4	ChxMgCl	Chx-	31	80	1-Cyclohexyl-prop-2-en-1-ol
5	*t*-C_4H_9MgCl	*t*-C_4H_9-	30	70	4,4-Dimethyl-pent-1-en-3-ol
6	C_6H_5Li	C_6H_5-	29	75	1-Phenyl-prop-2-en-1-ol
7	$C_6H_5CH_2MgCl$	$C_6H_5CH_2$-	30	77	1-Benzyl-prop-2-en-1-ol
8	AllylMgCl	Allyl-	31	75	1-Phenyl-hepta-3,6-dien-1-ol[c]

[a] Purification by distillation is avoided to prevent possible isomerization due to boratropic rearrangement. [b] Oxidation was performed *via* inverse addition of allylic boronate ester to the preformed peroxyanion using H_2O_2-NaOH and the product alcohols were purified by fractional distillation and preparative GC. [c] Product characterized by allylboration with PhCHO.

We decided to explore the thermally induced boratropic rearrangement with the α-substituted allylboronate esters **2**. Such permanent allylic rearrangement of α-substituted allylboranes into the thermodynamically more stable isomers **3** with the boron atom on the less substituted carbon atom has been studied only for the α-substituted allyldialkyl(or diaryl)boranes, [11] but is relatively unexplored with the α-substituted allylborinate or boronate esters. We decided to forego all preconceived ideas and test such thermally induced boratropic rearrangements with boronate esters **2**. Gratifyingly, the reaction of **2** in refluxing toluene over a period of 24 h (36 h for R=*t*-Bu) places the boron atom on the less substituted primary carbon atom to provide allylboronate esters **3** (Scheme 1). The results are summarised in Table 2. The assigned structures **3** were ascertained by the spectral and GC analyses of the oxidation products(allylic alcohols). As anticipated, the allylicboronate esters **3** were a mixture of stereoisomers, with the E isomer predominating.

We thought it was worthwhile to explore the catalytic hydrogenation[12] and protonolysis of the allylboronate esters **3**. Such catalytic *cis*-hydrogenation has been reported in the literature for alkynylboronate esters[12] and allyldialkylboranes, [13] but are relatively unexplored with allylboronates. The catalytic hydrogenation[12] of the allyl boronate **3** over 5% Pd-C in THF at 25 °C and 1 atmospheric pressure using the Brown/Brown automatic gasimeter[14] proceeds smoothly to provide the boronate **4** (Scheme 1). The results are summarized in Table 3.

Scheme 1



Conditions: a.Δ ,toluene, 24-36h ; b.H_2, Pd-C, THF ; c. H^+, AcOH or THF-$MeSO_3H$

Consequently, by following the above reaction sequence we have achieved the three-carbon homologation of representative 2-alkyl- and 2-aryl-1,3,2-dioxaborinanes. To the best of our knowledge this is the first report in the literature of a simple three-carbon homologation of boronate esters and nicely supplements to the already established procedures for the sequential one-carbon homologation of organoboranes.[2,15]

Table 2. Thermally Induced Boratropic Rearrangement[a] of the Allylboronate Esters **2**

		Isomerization Product, $RCH{=}CH{\sim}CH_2BO_2(CH_2)_3$, **3**				
entry	boronate ester, **2**, R=	isomerized boronate **3** R=	^{11}BNMR ($CDCl_3$), δ	bp, °C (torr)	isolated yield(%)	oxidation product[c] $RCH{=}CHCH_2OH$
1	*n*-C_4H_9-	*n*-C_4H_9-	32	112-14 (17)	88	Hept-2-en-1-ol[d]
2	*n*-C_6H_{13}-	*n*-C_6H_{13}-	32	80-82 (0.1)	90	Non-2-en-1-ol
3	*sec*-C_4H_9-	*sec*-C_4H_9-	31	89-92 (10)	92	4-Methyl-hex-2-en-1-ol
4	Chx-	Chx-	31	75-78 (0.1)	90	3-Cyclohexyl-prop-2-en-1-ol
5	*t*-C_4H_9-	*t*-C_4H_9-[b]	30	84-85 (10)	84	4,4-Dimethyl-pent-2-en-1-ol
6	C_6H_5-	C_6H_5-	29	110-13 (20)	91	3-Phenyl-prop-2-en-1-ol[d]
7	$C_6H_5CH_2$-	$C_6H_5CH_2$-	31	103-05 (8)	90	4-Phenyl-but-2-en-1-ol

[a] Performed in refluxing toluene for 24h. [b] Required 36h for the completion of isomerization. [c] Oxidation was performed via inverse addition of allylic boronate ester to the preformed peroxyanion, and the product alcohols were purified by fractional distillation and preparative GC. [d] GC analyses reveals an E:Z mixture of 9:1.

Protonolysis of the allylborane intermediates has been proven to proceed with permanent allylic rearrangement.[11] Very recently we have demonstrated[16] such a protonolysis study with allylboronate esters derived *via* one-carbon homologation of alkenylboronate esters. We extended this procedure of protonolysis to isomerized allylboronate esters **3**. Protonolysis of **3** in refluxing acetic acid or a refluxing THF solution of methanesulfonic acid proceeds with boratropic rearrangement to provide a terminal alkene **5**, achieving the synthesis of a three-carbon homologated alkene (Scheme 1). The results are summarized in Table 4.

Table 3. Catalytic Hydrogenation[a] of the Allylboronate Ester **3** in THF at 25 °C

		Hydrogenation Product, $R(CH_2)_3BO_2(CH_2)_3$, **4**			
entry	isomerized boronate, **3** R=	**4** R=	^{11}BNMR ($CDCl_3$), δ	isolated yield(%)	oxidation product[b] $RCH{=}CHCH_2OH$
1	*n*-C_4H_9-	*n*-C_4H_9-	32	84	Heptan-1-ol
2	*n*-C_6H_{13}-	*n*-C_6H_{13}-	32	86	Nonan-1-ol
3	*sec*-C_4H_9-	*sec*-C_4H_9-	31	83	4-Methyl-hexan-1-ol
4	Chx-	Chx-	31	88	3-Cyclohexyl-propan-1-ol
5	*t*-C_4H_9-	*t*-C_4H_9-	30	82	4,4-Dimethyl-pentan-1-ol
6	C_6H_5-	C_6H_5-	29	90	3-Phenyl-propan-1-ol
7	$C_6H_5CH_2$-	$C_6H_5CH_2$-	31	88	4-Phenyl-butan-1-ol

[a] Carried out in a Brown/Brown automatic gasimeter using 5% Pd-C catalyst over a period of 6-8h at 25 °C. [b] Oxidized using alkaline H_2O_2 at 25 °C; the oxidation product alcohol was purified by distillation and preparative GC.

In conclusion, the present methodology[18] offers a highly convenient and direct approach to the preparation of α-alkyl- and α-aryl-substituted allylboronate esters and their conversion to the three-carbon homologated

Table 4. Protonolysis[a] of the Allylboronate Ester 3

entry	boronate ester 3, R=	protonolysis product 5	isolated yield[b](%)	bp, °C (torr)	^{1}HNMR ($CDCl_3$), δ	IR(neat) cm^{-1}
1	*n*-C_4H_9-	1-Heptene	70	90-91(752)	4.8-5.1(m, 2H) 5.5-6.1(m, 1H)	1641, 907
2	*n*-C_6H_{13}-	1-Nonene	72	140-42(750)	4.8-5.1(m, 2H) 5.5-6.1(m, 1H)	1641, 907
3	*sec*-C_4H_9-	4-Methyl-1-hexene	71	79-80(752)	4.8-5.1(m, 2H) 5.6-6.2(m, 1H)	1641, 907
4	Chx-	3-Cyclohexyl-1-propene	80	80-81(60)	4.9-5.2(m, 2H) 5.6-6.2(m, 1H)	1638, 910
5	*t*-C_4H_9-	4,4-Dimethyl-1-pentene	74	90-91(752)	4.9-5.1(m, 2H) 5.1-6.4(m, 1H)	1638, 910
6	C_6H_5-	3-Phenyl-1-propene	81	80-82(60)	5.0-5.2(m, 2H) 5.7-6.3(m, 1H)	1635, 910
7	$C_6H_5CH_2$-	4-Phenyl-1-butene	84	78-79(15)	4.9-5.2(m, 2H) 5.7-6.1(m, 1H)	1637, 908

[a] Performed on a 10 mmol scale in refluxing acetic acid. [b]. Purified by distillation.

boronate esters and terminal alkenes. We are extending the present methodology for the transfer reaction of boronate and borinate esters and hope to extend this procedure both for an effective asymmetric synthesis and for the facile synthesis of medium-and large-ring boracyclanes.

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