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# (*E*)-α-Substituted γ-Alkoxyallylboronic Esters as New Reagents: Synthesis and Reactivity toward Aldehydes

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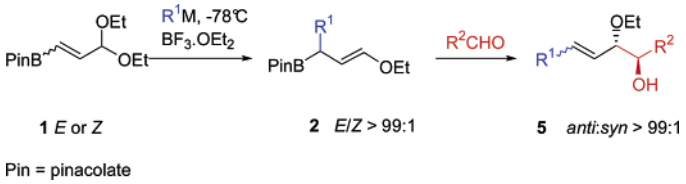


We have developed a synthesis of new allylboration reagents based on an allylic rearrangement. This approach led to the α-substituted γ-alkoxyallylboronates **2** with a high stereoselectivity in favor of the *E*-isomer, independent of the organometallic used. We have also studied the reactivity of these reagents toward aldehydes, showing that the allylboration reaction occurs with an excellent diastereoselectivity to give the *anti*-diol derivatives **5**. Moreover, the sequence can be carried out in a "one-pot" procedure avoiding the purification of allylboronates.

## Introduction

Allylboranes represent an important structural class of organoboron derivatives widely employed in organic synthesis.[1] Their addition to aldehydes, one of the most powerful methods to prepare homoallylic alcohols, proceeds via a six-membered transition state, which accounts for the excellent levels of stereocontrol mostly observed in these reactions.[2] However, the success of this approach implies a strict control of geometry of the double bond of the allyborane to secure the obtention of the corresponding vicinal diol in good diastereo- and enantiomeric purity. In the field of polyhydroxylated compounds, many reports have shown interest in using the γ-alkoxyallylboranes.[3] If (*Z*)-γ-alkoxyallylboronates were easily prepared by borylation of (*Z*)-γ-alkoxyallyl anions, due to their configurational stabilities,[4] more problems are associated to the stereoselective preparation of *E*-isomer.[5] Barrett et al. proposed an alternative and indirect method using *B*-[3-((diisopropylamino)dimethylsilyl)allyl]diisopinocampheylborane.[6] Following the allylboration reaction, the silyl residue was converted to the desired oxygen functionality. More recently, two supplementary strategies emerged for the synthesis of (*E*)-γ-alkoxyallylborane reagents. The first one is based on a catalyzed isomerization of γ-alkoxyvinylboronates,[7] while the second one exploits the homologation reaction with $LiCH_2Cl$ to convert vinylboronates into allylboronates.[8] However, to our knowledge, among all published methods, none of them described the access to acyclic α-substituted species.[9]

In the light of these observations and due to the synthetic potential of this class of reagents, we planned to develop a

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(4) (a) Wuts, P. G. M.; Bigelow, S. S. *J. Org. Chem.* **1982**, *47*, 2498. (b) Hoffmann, R. W.; Kemper, B. *Tetrahedron Lett.* **1982**, *23*, 845.

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(6) Barrett, A. G. M.; Malecha, J. W. *J. Org. Chem.* **1991**, *56*, 5243.

(7) Yamamoto, Y.; Miyairi, T.; Ohmura, T.; Miyaura, N. *J. Org. Chem.* **1999**, *64*, 296 and references cited therein.

(8) Hoffmann, R. W.; Krüger, J.; Brückner, D. *New J. Chem.* **2001**, *25*, 102.

(9) Some publications reported the synthesis of cyclic γ-alkoxyallylboronates and their utilization in total synthesis, see: (a) Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *Synthesis* **2000**, 778. (b) Gao, X.; Hall, D. G.; Deligny, M.; Favre, A.; Carreaux, F.; Carboni, B. *Chem. Eur. J.* **2006**, *12*, 3132 and references cited therein. (c) Carreaux, F.; Favre, A.; Carboni, B.; Rouaud, I.; Boustie, J. *Tetrahedron Lett.* **2006**, *47*, 4545.

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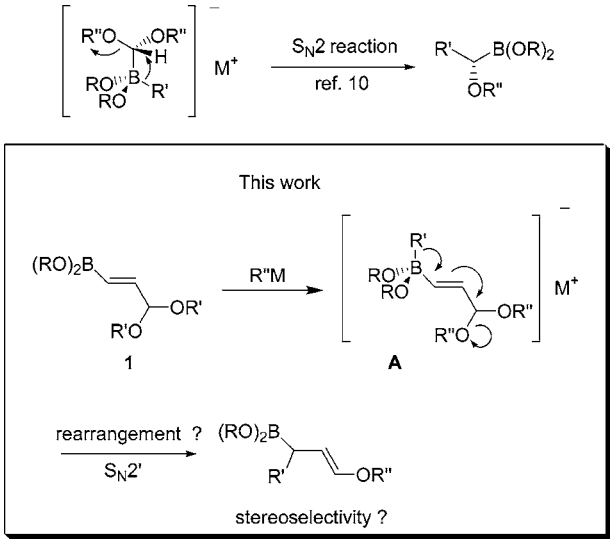
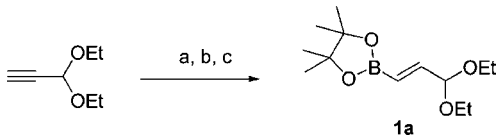



**FIGURE 1. Strategy for the synthesis of α-substituted γ-alkoxyallylboronates.**

**SCHEME 1. Synthesis of 1a**[a]



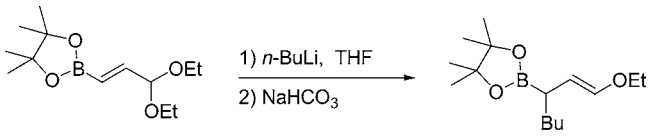

[a] Reagents and conditions: (a) $(Ipc)_2BH$ (1 equiv), THF, 0 °C, 1 h, then, rt., 1 h; (b) $CH_3CHO$ (20 equiv), 0 °C, 1 h then, rt, 48 h; (c) pinacol (1 equiv), $Et_2O$, rt, 18 h, 60%.

simple and straightforward route to stereodefined α-substituted γ-alkoxyallylboronates. In our laboratory, we previously demonstrated that boronic esters can be homologated via a 1,2-migration of an alkyl group from boron to the adjacent atom with displacement of an alkoxy group.[10] We now envisioned that the borate intermediate **A** could also rearrange itself to afford the corresponding γ-alkoxyallylboronates (Figure 1). This borate could be prepared by treatment of a vinylboronic ester **1** with an organometallic reagent. If a similar migration was already described in the case of α,β-unsaturated organoboranes containing an halogen as leaving group,[11] no example of such an S$_N$′ process was hitherto reported with acetal derivatives.[12] In this paper, we report our first results in this topic as well as a study of the reactivity of these new reagents toward aldehydes.

## Results and Discussion

**Optimization of the Enol Ether Formation.** The model substrate chosen to test this strategy was 2-[(1*E*)-3,3-diethoxyprop-1-en-1-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **1a**. It can be prepared on gram scale by hydroboration of commercially available 3,3-diethoxyprop-1-yne with diisopinocampheylborane, followed by dealkylation of the isopinocampheyl group with a large excess of acetaldehyde and transesterification by 2,3-dimethylbutane-2,3-diol (pinacol) (Scheme 1).[13,14]

**TABLE 1. Optimization of the 1,4-Addition Reaction with *n*-BuLi**[a]




| entry | *n*-BuLi[b] (equiv) | $BF_3{\cdot}OEt_2$[c] (equiv) | *T* (°C) | time (h) | conv[d] (%) (yield[e] (%)) |
|---|---|---|---|---|---|
| 1 | 1.2 | | rt | 12 | 20 (nd) |
| 2 | 1.2 | 1 | rt | 12 | 50 (nd) |
| 3 | 1.2 | 1 | −78 | 0.25 | 50 (nd) |
| 4 | 1.2 | 2 | −78 | 0.25 | 90 (nd) |
| 5 | 1.5 | 2 | −78 | 0.25 | 100 (50) |

[a] Reactions were conducted on a 1.5 mmol scale. [b] *n*-BuLi was added at −78 °C. [c] The Lewis acid was added at −78 °C, 20 min after the addition of *n*-BuLi. [d] Determined by $^1$H NMR spectroscopy. [e] Yield of isolated product after purification by column chromatography on silical gel.

We initially examined the reaction of **1a** with organolithium reagents which are known to react preferentially in S$_N$′ manner with nonboronated allylic acetals.[15] In a first attempt, **1a** was treated with *n*-BuLi in THF at −78 °C in the absence of Lewis acid (Table 1, entry 1). The resulting solution was warmed to room temperature and stirred for 12 h. After workup, the analysis of the crude mixture by $^1$H NMR indicated the formation of a single product with a 20% conversion. This product, **2a**, was identified as being the result of a 1,4-addition with concomitant cleavage of the acetal group on the basis of two signals of vinylic protons characteristic of an enol ether (δ 4.71 and 6.15). The reaction is highly stereoselective since the *E*-isomer was only detected. Taking into account of this promising result, we then examined the influence of a Lewis acid that should facilitate the displacement of the alkoxy group. As expected, the use of 1 equiv of $BF_3{\cdot}OEt_2$ enhanced the conversion of **1a** into **2a**, however, with a concomitant formation of a secondary product.[16] Fortunately, this process took place more cleanly when the temperature was maintained at −78 °C. After several attempts, full conversion was obtained using 2 equiv of Lewis acid and 1.5 equiv of *n*-BuLi at −78 °C for 25 min (Table 1, entry 5). It is important to note that, even in the presence of an excess of organolithium reagent, the product resulting from a 1,2-addition was not detected. Under these experimental conditions, the *E*-isomer was still obtained exclusively (within the limits of the $^1$H NMR measurement) and was isolated in a pure form by flash chromatography in 50% yield, due to a partial degradation on deactivated silica gel.

**Scope of Organometallic Reagent and Substrate**. Several other organometallics were then explored in order to assess the

(10) Carmès, L.; Carreaux, F.; Carboni, B. *J. Org. Chem.* **2000**, *65*, 5403.
(11) (a) Zweifel, G.; Horng, A. *Synthesis* **1973**, 672. (b) Midland, M. M.; Preston, S. B. *J. Org. Chem.* **1980**, *45*, 748. (c) Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2330. (d) Lombardo, M.; Morganti, S.; Trombini, C. *J. Org. Chem.* **2000**, *65*, 8767. (e) Lombardo, M.; Morganti, S.; Tozzi, M.; Trombini, C. *Eur. J. Org. Chem.* **2002**, 2823. (f) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron Lett.* **2005**, *46*, 8981.
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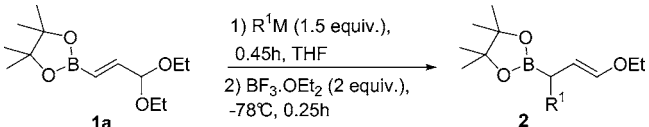
(14) For other synthesis of **1a**, see: (a) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127. (b) Kalinin, A. V.; Scherer, S.; Snieckus, V. *Angew. Chem., Int. Ed.* **2003**, *42*, 3399.
(15) (a) Mioskowski, C.; Manna, S.; Falck, J. R. *Tetrahedron Lett.* **1984**, *25*, 519. (b) Bailey, W. F.; Zartun, D. L. *J. Chem. Soc., Chem. Commun.* **1984**, 34. (c) Alexakis, A.; Mhamdi, F.; Lagasse, F.; Mangeney, P. *Tetrahedron: Asymmetry* **1996**, *7*, 3343.
(16) This compound was not definitively identified, but must be probably the result of a 1,3- boratropic shift.

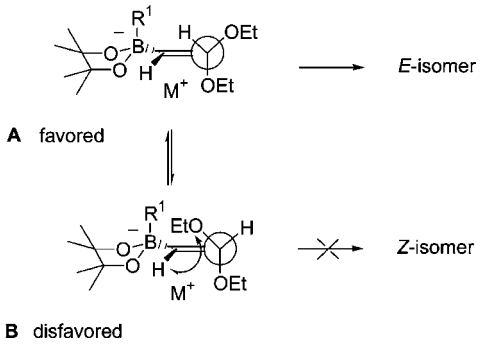
**TABLE 2. Synthesis of (*E*)-α-Substituted γ-Ethoxyallylboronates 2a−e from 1a[a]**




| entry | organometallic $R^1M$ | $T$ (°C) | conv[b] (%) | $E/Z$ ratio[b] | products (yield, %)[c] |
|---|---|---|---|---|---|
| 1 | *n*-BuLi | −78 | 100 | 100/0 | **2a** (50) |
| 2 | MeLi | −78 | 100 | 100/0 | **2b** (nd) |
| 3 | PhLi | −78 | 100 | 100/0 | **2c** (nd) |
| 4 | *s*-BuLi | −78 | 100 | 100/0 | **2d** (65) |
| 5 | *n*-BuMgCl | −78 | 63 | 100/0 | **2a** (nd) |
| 6 | *n*-BuMgCl | −60 | 100 | 100/0 | **2a** (49) |
| 7 | *i*-PrMgCl | −78 | 0 | | **2e** (nd) |
| 8 | *i*-PrMgCl | −45 | 100 | 100/0 | **2e** (54) |

[a] Reactions were conducted on a 1.5 mmol scale. [b] Determined by $^1$H NMR spectroscopy of the crude product. [c] Isolated yield after flash chromatography.

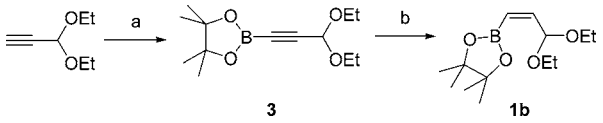
**SCHEME 2. Allylic 1,3-Strain in the $S_N2'$ Reaction**




generality of this methodology (Table 2). In every case, independent of the size of the entering alkyl group, the 1,4-addition is the exclusive pathway with a high stereoselectivity in favor of the *E*-isomer. Concerning the organolithium reagents, the allylic rearrangement took place in all cases at −78 °C with a full conversion. When the reaction was performed at the same temperature with a Grignard reagent, such as *n*-BuMgCl, the conversion was incomplete (63%) while with *i*-PrMgCl, the starting material was totally recovered without any decomposition. To observe a full conversion, it was necessary to carry out the reaction at −60 °C (*n*-BuMgCl) or −45 °C (*i*-PrMgCl), which allowed a complete complexation on the boron atom (Table 2, entries 6 and 8). Except when the substituents at the α position are methyl **2b** and phenyl **2c**, the (*E*)-α-substituted-γ-alkoxyallylboronates **2** were isolated in moderate yields by flash chromatography due to their low stability during the purification step.

In order to clarify the mechanism of this transformation, the reaction of **1a** with *n*-BuLi was followed by $^{11}$B NMR. At −78 °C, the spectrum of the reaction mixture showed that the starting alkene ($\delta$ +29.7 ppm) was completely converted into an "ate" complex ($\delta$ +8.0 ppm), which is the result of the addition of *n*-BuLi to the boron atom (Scheme 2). The addition of the Lewis acid at this same temperature caused a gradual disappearance of this signal. After treatment with a saturated solution of $NH_4Cl$ and extraction with dichloromethane, the $^{11}$B NMR of the crude mixture showed a new peak (**2a**, $\delta$ +33.4 ppm), shifted downfield from the starting material **1a**. With *n*-BuMgCl, at −78 °C, the complexation of boron was only

**SCHEME 3. Synthesis of 1b[a]**




[a] Reagents and conditions: (a) *n*-BuLi (1 equiv.), −78 °C, isopropyl pinacol borate (1 equiv) and HCl/$Et_2O$, 60%; (b) $H_2$ (20 bar), Pd/$CaCO_3$, quinoline, dioxane, rt, 94%.

partial, whereas there was no addition with *i*-PrMgCl, probably due to a steric hindrance of the alkyl group. Addition of $BF_3$·$OEt_2$ caused the disappearance of the "ate" complex, while the uncomplexed starting material remained unchanged. These observations clearly show that the allylic rearrangement only occurred from a key borate species. Furthermore, taking into account Midland's report,[11b] we assumed that the 1,2-migration occurred in a $S_N2'$ manner, *anti* to the leaving group. The obtention of a single *E*-isomer can be therefore rationalized by the presence of an allylic 1,3-strain in transition state **B** involving one of the ethoxy groups (Scheme 2).[17] The intramolecular migration involved in this process also explained its high regio- and stereoselectivity, compared with the results described in the literature for nonboronated analogues.[15,18]

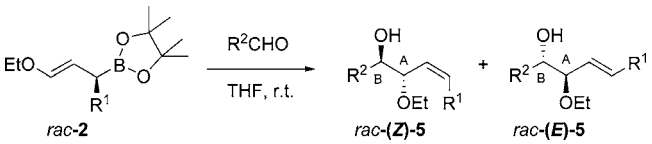
To check a possible influence of the geometry of the double bond of **1a** and to confirm our mechanistic hypothesis, we then decided to test the reaction with the *Z*-isomer. 2-[(1*Z*)-3,3-Diethoxy-1-propenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **1b** was previously prepared in the literature by hydrozirconation of the corresponding 1-alkynylboronate.[19] However, the authors reported a partial decomposition of the acetal under these experimental conditions. To obtain cleanly **1b** with a pure *Z* geometry, we developed another route based on the *cis*-hydrogenation of the 1-alkynyldioxaborolane **3** (Scheme 3).[20] Condensation at −78 °C of isopropyl pinacol borate with lithium acetylide, obtained from 3,3-diethoxyprop-1-yne, furnished, after treatment by anhydrous hydrogen chloride, **3** in 60% yield. Several hydrogenation experiments were conducted in changing the catalyst, solvent, and pressure of $H_2$.[21] The best result was obtained using the Lindlar catalyst with quinoline in 1,4-dioxane and a pressure of 20 bar of $H_2$ (94% yield, isomeric purity >99%).

Compound **1b** was treated, as previously described, with *n*-BuLi in THF to afford **2a**. The stereoselectivity exclusively in favor of the *E*-enol ether was maintained. However, the formation of the "ate" complex from **1b** with *n*-BuLi at −78 °C is slower than with **1a**, as the migration of the butyl group (complete conversion after 4h at −78 °C for the *Z*-isomer compared to 25 min for the *E*-isomer). After flash chromatography on deactivated silica gel, **2a** was obtained in 55% yield.

**Reactivity of 2 toward Aldehydes under Thermal Conditions.** Having in hand an efficient access to allylboronic esters **2**, we then turned our attention to their reactivity toward aldehydes. First, the allylboration reactions were carried out under standard thermal conditions, using 2 equiv of aldehyde

(17) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
(18) Addition of Grignard reagents to α,β-unsaturated, see: Normant, J. F.; Commerçon, A.; Bourgain, M.; Villieras, J. *Tetrahedron Lett.* **1975**, *44*, 3833 and references cited therein.
(19) Deloux, L.; Srebnik, M. *J. Org. Chem.* **1994**, *59*, 6871.
(20) For a general synthesis of 1-alkynyldiisopropoxyboranes, see: Brown, H. C.; Bhat, N. G.; Srebnik, M. *Tetrahedron Lett.* **1988**, *29*, 2631.
(21) Srebnik, M.; Bhat, N. G.; Brown, H. C. *Tetrahedron Lett.* **1988**, *29*, 2635.

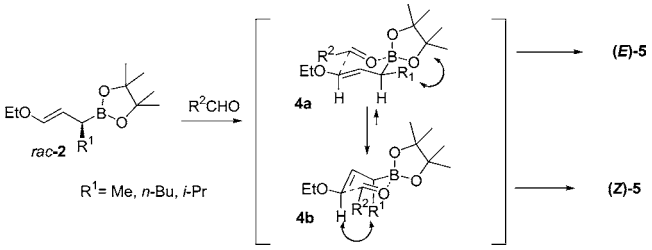
**TABLE 3. Allylboration of 2 under Standard Thermal Conditions**[a]




| entry | no. | $R^1$ | $R^2$ | time (h) | *Z*/*E* ratio[b] | products (yield,[c] %) |
|---|---|---|---|---|---|---|
| 1 | **2a** | *n*-Bu | Ph | 144 | 75/25 | **5a** (75) |
| 2 | **2b** | Me | Ph | 24 | 74/26 | **5b** (50) |
| 3 | **2c** | Ph | Ph | 72 | 5/95 | **5c** (63) |
| 4 | **2d** | *s*-Bu | Ph | 192 | nd | **5d** (nd) |
| 5 | **2e** | *i*-Pr | Ph | 192 | 75/25 | **5e** (76) |
| 6 | **2f** | *n*-Bu | $C_5H_{11}$ | 144 | 71/29 | **5f** (71) |

[a] Reactions were conducted on 1.5 mmol scale. [b] *Z*/*E* ratio was determined by $^1$H NMR spectroscopy of the crude product. [c] Isolated yield after flash chromatography.

**SCHEME 4. Postulated Competing Transition States in the Allylation of Aldehydes with (*E*)-α-Substituted γ-Ethoxyallylboronates 2**

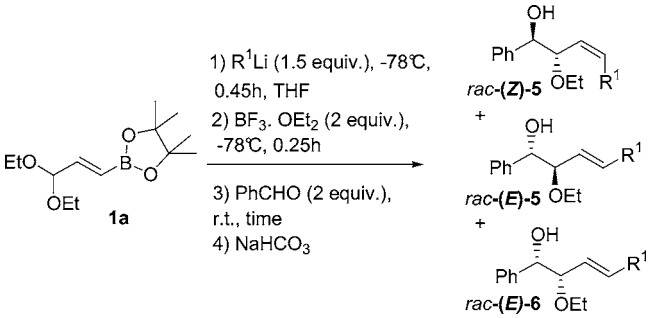



at room temperature. In a general way, the reactivity of **2** is weaker compared to the corresponding allylboronates with no substituent in the α-position (several days at room temperature).[22] It is also highly dependent upon the nature of the α-substituent ($R^1$) as shown in Table 3. The yields of **5**, after purification by flash chromatography, vary from 50 to 76%. The α-*sec*-butyl-substituted reagent **2d** did not lead to the formation of the allylboration product with benzaldehyde even after 192 h at room temperature.[23] The *anti*-diol derivatives were obtained exclusively, that is in conformity with the formation of a cyclic six-membered transition state. The relative stereochemistry of these adducts was assigned by analogy with related additions to aldehydes and on the basis of the coupling constants between the protons $H_A$ and $H_B$ ($J_{A,B}$= 4.0−4.5 Hz).[24] Concerning the geometry of the double bond, the formation of the *Z*-isomer is mostly favored as expected (isomer *Z*, *J*=11.1−11.9 Hz; isomer *E*, *J*=15.4−16.2 Hz). The ratio of *Z*/*E* did not vary significantly with the steric hindrance of the α-substituent ($R^1$) (entries 1−2 and 5) and the nature of the $R^2$ residue of the aldehyde (entries 1 and 6). It is worthy to note the inversion of selectivity when the α-substituent is a phenyl group (entry 3).

According to literature dealing with the origin of stereoselectivity in the reactions of α-substituted allylboronates with aldehydes,[25] the ratio of *Z*/*E* isomers can be explained from the two competing chair-type transition states as shown in Scheme 4. When the substituent is a nonpolar alkyl group, the preference for the *Z*-homoallylic alcohol was attributed to a disfavored interaction in transition state **4a** between the pseudoequatorial α-substituent $R^1$ and the bulky glycol component of the boronate, although there is an unfavorable allylic interaction in **4b**. It was also shown in the literature that the *Z*/*E* ratio decreased when the size of the boron substituents increased.[25b]

In our case, the formation of the *Z*-isomer is effectively predominant, but no significant modification was observed with an isopropyl group compared with a methyl substituent (Table 3, entries 2 and 5), that seems to indicate that, for these new reagents, the steric effect does not play a decisive role in the stereocontrol. The stereoselectivity obtained with **2c** ($R^1$ = Ph) on addition to benzaldehyde can be explained by the fact that the phenyl group has a preference for the equatorial position, thus stabilizing **4a** compared to **4b**.

**TABLE 4. Synthesis of Homoallylic Alcohols from 1a Using a One-Pot Process** [a]




| entry | no. | $R^1$ | time (h) | *anti*/*syn* ratio[b] | *Z*/*E* ratio of **5**[b] | products (yield,[c] %) |
|---|---|---|---|---|---|---|
| 1 | **2a** | *n*-Bu | 72 | 99/1 | 45/55 | **5a**, **6a** (66) |
| 2 | **2b** | Me | 24 | 95/5 | 37/63 | **5b**, **6b** (73) |
| 3 | **2c** | Ph | 24 | 88/12 | 3/97 | **5c**, **6c** (50) |
| 4 | **2d** | *s*-Bu | 144 | 99/1 | 29/71 | **5d**, **6d** (49) |

[a] Reactions were conducted on 1.5 mmol scale. [b] Determined by $^1$H NMR spectroscopy of the crude product. [c] Isolated yield after flash chromatography.

**"One-Pot" 1,4-Addition/Allylboration.** Due to the difficulties encountered in the purification of α-substituted γ-ethoxyallylboronates **2**, we examined the possibility of carrying out the allylic rearrangement and the allylboration in "one-pot" process. After completion of the first step, 2 equiv of benzaldehyde was added at −78 °C, before the mixture was warmed at room temperature. After workup with a saturated solution of $NaHCO_3$, homoallylic alcohols were purified by flash chromatography (Table 4). Using this experimental procedure, the allylboration reaction is clearly accelerated. The more significative example is given by the 1,4-addition of the *sec*-butyl group on the α-position of the boron atom followed by the addition to benzaldehyde (entry 4). In the two-step process without Lewis acid, the allylboration product was not detected at room temperature after 8 days. By contrast, this latter could be obtained in 49% yield after 6 days using the one-pot process. This improvement is probably due to the presence of the trifluoroborane etherate, which accelerates the allylboration reaction.[26] However, under these conditions, the diastereoselectivity was not preserved, although the formation of the *anti*-

(22) Concerning the reactivity of unsubstituted γ-methoxyallylboronates, see: Hoffmann, R. W.; Kemper, B.; Metternich, R.; Lehmeier, T. *Liebigs Ann. Chem.* **1985**, 2246.

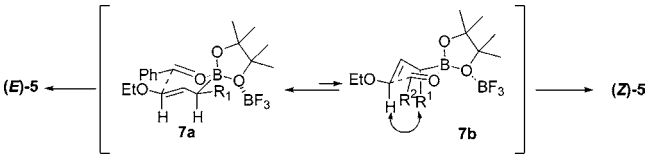
(23) It is necessary to warm the mixture at reflux to observe the formation of the allylboration product in $^1$H NMR. Unfortunately, many decomposition products are also produced.

(24) The corresponding *syn* derivatives (**6a**−**d**) obtained in presence of Lewis acid, showed coupling constants of 7.8 to 8.1 Hz for these two protons.

(25) (a) Hoffmann, R. W.; Landmann, B. *Chem. Ber.* **1986**, *119*, 1039. (b) Hoffmann, R. W.; Wolff, J. J. *Chem. Ber.* **1991**, *124*, 563.

(26) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732.

**SCHEME 5. Postulated Competing Transition States for the Formation of Homoallylic Alcohols 5 in Presence of Lewis Acid**




products **5** is still favored. The *anti*/*syn* ratio varied from 88:12 to 99:1, while, without an activation by $BF_3{\cdot}OEt_2$, the *anti*-diastereoisomer was only observed. These results seem to indicate that the chairtype cyclic transition state, usually proposed in the allylboration reaction, is probably in competition with another open transition state responsible of the formation of the *syn*-product (*E*)-**6**.[27] Concerning the *anti*-products **5**, it is interesting to note the inversion of selectivity in favor of the *E*-isomer compared to the allylboration reaction carried out in the absence of Lewis acid.

These last observations can be explained by the enhancement of the electrophicity of the boron atom due to the presence of $BF_3{\cdot}OEt_2$ (Scheme 5). Indeed, the Lewis acid can coordinate the boronate oxygen, which led to the reduction of the length of the B−O (aldehyde) bond and, on the opposite side, to an increase of the length of the B−C bond. The interaction between the $R^1$ substituent and the pinacol group then becomes less important that the 1,3-strain, thus destabilizing the **7b** transition state and favoring the formation of the *E*-isomer. In absence of Lewis acid, the importance of interactions are reversed (see Scheme 4). This explanation was already postulated in the literature with other α-substituted allylboronates, and the stereoselectivity obtained with these new allylboronates is in agreement with this suggestion.[11f,28]

## Conclusions

In summary, we have reported that the addition of organometallics to vinylboronates **1** (*E* or *Z*) possessing an acetal group in the γ-position occurred exclusively in an $S_N2'$ manner, with a complete stereoselectivity in favor of the *E*-isomer. The reaction seems to be independent of the nature of the metal and the size of the entering group. This access to the (*E*)-α-substituted γ-alkoxyallylboronates, a new class of allylic reagent, allow the introduction of a great diversity of substituents. In a preliminary study, the reactivity of these reagents toward aldehydes was examined. Under standard thermal conditions, the *anti*-diol is obtained exclusively with a preference for the *Z*-isomer of the enol ether. A loss of diastereoselectivity and an inversion of stereoselectivity was observed when the allylboration was carried out in the presence of a Lewis acid. This "one-pot" procedure avoids the tedious purification of the intermediaries allylboronates. The preparation of enantioenriched γ-alkoxyallylboronates, as well as the exploration of other aspects of the reactivity of these bifunctional reagents, are currently under investigation in our laboratory.

## Experimental Section

**General Methods.** For details, see the Supporting Information.

**Synthesis of 2-[(1*E*)-3,3-Diethoxy-1-propenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1a).** A 100 mL round-bottom flask equipped with a septum inlet was charged with borane/dimethyl sulfide complex (10 M, 2.1 mL, 21 mmol) and tetrahydrofuran (THF) (7 mL) under an argon atmosphere. (*S*)-(−)-α-Pinene (6.67 mL, 42 mmol) was then added dropwise at 0 °C. The mixture stirred for 10 min followed by 2 h at room temperature. The resulting white diisopinocampheylborane suspension was cooled to 0 °C, and propiolaldehyde diethyl acetal (3 mL, 21 mmol) was added slowly. The resulting mixture was stirred at 0 °C for 1 h, at room temperature for additional 2h, and cooled back to 0 °C again prior to the quick addition of freshly distilled acetaldehyde (29 mL). The solution was stirred for 48 h at room temperature. After evaporation of solvent and excess acetaldehyde, the residue was dissolved in $Et_2O$ (16 mL) at room temperature, and dry pinacol (2,50 g, 21 mmol) was added. After the mixture was stirred overnight, the solvent was evaporated under reduced pressure. The crude product was purified by flash column chromatography (deactivated silica gel, heptane/ethyl acetate 9/1) to give the pure product **1** as a colorless oil (3.22 g, 60%): $^1$H NMR (200 MHz, $CDCl_3$) δ 1.23 (t, $J$ = 7.1 Hz, 6H), 1.28 (s, 12H), 3.31−3.65 (m, 4H), 4.92 (dd, $J$ = 1.2, 4.6 Hz, 1H), 5.78 (dd, $J$ = 1.2, 18.2 Hz, 1H), 6.51 (dd, $J$ = 4.6, 18.2 Hz, 1H); $^{13}$C NMR (50 MHz, $CDCl_3$) δ 15.0, 24.9, 61.4, 83.6, 102.0, 121.6, 148.8; $^{11}$B NMR (96 MHz, $CDCl_3/BF_3{\cdot}OEt_2$) δ +29.7 ppm; HRMS (EI) calcd. for $C_{13}H_{25}O_4B$ *m*/*z* 256.1840, found 256.1840.

**General Procedure for the Synthesis of Allylboranes (2). Preparation of 2-{1-[(*E*)-2-Ethoxyvinyl]pentyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2a).** To a solution of **1a** (256.2 mg, 1 mmol) in THF (4 mL) was added a solution of *n*-BuLi (0.94 mL, 1.5 mmol, 1.6 M in hexane) at −78 °C. The mixture was stirred for 45 min at this temperature before the slow addition of boron trifluoride etherate (253 μL, 2 mmol). The mixture was then stirred for an additional 25 min at the same temperature. The reaction was quenched by addition of a saturated aqueous solution of sodium hydrogen carbonate (2 mL) and extracted with dichloromethane (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), and then dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue that was purified by flash chromatography (deactivated silica gel, heptane/ethyl acetate 9:1) to afford pure allylborane **2a** (134 mg, 50%) as a colorless oil: $^1$H NMR (200 MHz, $CDCl_3$) δ 0.72−0.88 (m, 6H), 1.15−1.60 (m, 19H), 3.64 (q, $J$ = 7.0 Hz, 2H), 4.71 (dd, $J$ = 9.1, 12.6 Hz, 1H), 6.15 (d, $J$ = 12.6 Hz, 1H); $^{13}$C NMR (50 MHz, $CDCl_3$) δ 14.4, 15.1, 23.0, 25.1, 31.5, 32.0, 64.9, 83.4, 105.5, 145.8; $^{11}$B NMR (96 MHz, $CDCl_3/BF_3{\cdot}OEt_2$) δ +33.4 ppm; HRMS (EI) calcd for $C_{15}H_{29}O_3B$ *m*/*z* 268.2210, found 268.2207.

**Synthesis of 2-(3,3-Diethoxy-1-propynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3).** To a stirred solution of propiolaldehyde diethyl acetal (4.6 mL, 32 mmol) in $Et_2O$ (20 mL) was slowly added *n*-butyllithium (20 mL, 32 mmol, 1.6 M in hexane) at −78 °C under an argon atmosphere. Another 100 mL round-bottom flask was charged with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.53 mL, 32 mmol) in $Et_2O$ (40 mL), and the solution was cooled to −78 °C. The lithium acetylide from the first flask was slowly added to the second one by a double-ended needle. The reaction was maintained at −78 °C for 2 h after which time anhydrous HCl in $Et_2O$ (9.06 mL, 34 mmol) was added. The reaction was then allowed to warm to room temperature. After filtration to remove the precipitate LiCl and evaporation of the volatiles under reduced pressure, the oily slightly pale yellow liquid was distilled to led the pure product **3** as a colorless oil (4.88 g, 60%): bp 118−120 °C/1 mmHg; $^1$H NMR (200 MHz, $CDCl_3$) δ 1.22 (t, $J$ = 7.1 Hz, 6H), 1.27 (s, 12H), 3.64 (dq, $J$ = 7.1, 9.5 Hz, 2H), 3.73 (dq, $J$ = 7.1, 9.5 Hz, 2H), 5.29 (s, 1H); $^{13}$C NMR (50 MHz, $CDCl_3$) δ 15.0, 24.5, 24.6, 61.1, 83.0, 84.5, 91.1, 96.4; HRMS (EI) calcd for $C_{13}H_{23}O_4B$ *m*/*z* 254.1689, found 254.1691.

(27) The hypothesis of a partial isomerization of (*E*)-**5** to give **(*E*)-6** due to the presence of $BF_3{\cdot}OEt_2$ via a benzylic carbocation seems to be unprobable because no corresponding epimerisation was detected with (*Z*)-**5**.

(28) No attempts were conducted to examine this process in the presence of other Lewis acids or in modifying the quantity of Lewis acid.

**Synthesis of 2-[(1*Z*)-3,3-Diethoxy-1-propenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1b).** A 30 mL stainless steel glass-coated autoclave was charged with a solution of **3** (3.81 g, 15 mmol) in 1,4-dioxane (12 mL), Lindlar catalyst (156 mg, 0.15 mmol), and quinoline (13 $\mu$L, 0.11 mmol). The autoclave was purged three times with argon, followed by three times with hydrogen, and the final pressure was adjusted to 20 bar. The mixture was then stirred at room temperature for 2 h and filtered through Celite. The solvent was removed, and the product **1b** was isolated by Kügelrohr distillation as a colorless oil (3.6 g, 94%): bp 128−130 °C/1 mmHg; $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 1.05 (t, $J$ = 7.0 Hz, 6H), 1.15 (s, 12H), 3.32−3.68 (m, 4H), 5.35 (d, $J$ = 7.6 Hz, 1H), 5.47 (d, $J$ = 13.9 Hz, 1H), 6.17 (dd, $J$ = 7.6, 13.9 Hz, 1H); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$ 15.7, 25.2, 62.0, 83.8, 100.2, 121.2, 148.9; HRMS (EI) calcd for $C_{13}H_{25}O_4B$ $m/z$ 256.1840, found 256.1841.

**General Procedure for the Allylboration Reactions under Thermal Conditions. Preparation of (1*S**,2*R**)-2-Ethoxy-1-phenyloct-3-en-1-ol ((*Z*)-5a, (*E*)-5a).** A solution of **2a** (268.2 mg, 1 mmol) and benzaldehyde (212.3 mg, 2 mmol) in 10 mL of THF was stirred at room temperature under an argon atmosphere. The reaction was monitored by TLC until complete consumption of **2a**. After addition of a saturated solution of $NH_4Cl$, the aqueous layer was extracted twice with $CH_2Cl_2$. Combined organic layers were washed with saturated NaCl, dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by column chromatography (heptane/ethyl acetate, 9/1) to yield **5a** (186 mg, 75% as an inseparable 75:25 mixture of *Z* and *E* isomers) as a colorless oil: $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 0.81−0.92 (m, 3H), 1.10−1.26 (m, 7H), 1.62−2.05 (m, 2H), 2.72 (br s, 0.75H), 2.86 (br s, 0.25H), 3.42 (dq, $J$ = 7.1, 9.3 Hz, 1H), 3.63 (dq, $J$ = 7.0, 9.3 Hz, 1H), 3.85 (dd, $J$ = 4.5, 7.8 Hz, 0.25H), 4.28 (ddd, $J$ = 1.0, 4.3, 9.6 Hz, 0.75H), 4.84 (d, $J$ = 4.5 Hz, 0.25H), 4.87 (d, $J$ = 4.3 Hz, 0.75 Hz), 5.33 (ddt, $J$ = 1.5, 9.6, 11.1 Hz, 1H), 5.65 (dt, $J$ = 7.3, 11.1 Hz, 1H), 7.30−7.38 (m, 5H) (the signals corresponding of the double bond of the *E*-isomer, (*E*)-**5a**, are hidden by those of the *Z* isomer, (*Z*)-**5a**); $^{13}$C NMR (50 MHz, $CDCl_3$) $\delta$ 13.8, 13.9, 15.1, 15.3, 22.0, 22.2, 27.4, 31.1, 31.5, 31.9, 63.8, 75.6, 75.7, 84.5, 88.6, 125.3, 125.6, 126.8, 127.1, 127.3, 127.7, 127.8, 136.2, 136.8, 140.2, 140.5; HRMS (EI) calcd for $C_9H_{17}O$ $m/z$ ($M^+ - C_7H_7O$), 141.1279, found 141.1281. Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.34; H, 9.74. Found: C, 77.51; H, 9.78.

**General Procedure for the Tandem Reaction. Preparation of (1*S**,2*R**)-2-Ethoxy-1-phenyloct-3-en-1-ol ((*Z*)-5a, (*E*)-5a) and (1*S**,2*S**)-2-Ethoxy-1-phenyloct-3*E*-en-1-ol ((*E*)-6a).** To a solution of **1a** (256 mg, 1 mmol) in THF (4 mL) was added a solution of *n*-BuLi (0.94 mL, 1.5 mmol, 1.6 M in hexane) at −78 °C under an argon atmosphere. The mixture was stirred for 45 min at this temperature before the slow addition of boron trifluoride etherate (253 $\mu$L, 2 mmol). The mixture was then stirred for an additional 25 min at the same temperature. Benzaldehyde (200 $\mu$L, 2 mmol) was then added, and the mixture was warmed at room temperature. The reaction was monitored by TLC and allowed to stir until complete consumption of **2a**. The reaction was quenched by addition of a saturated aqueous solution of sodium hydrogen carbonate (2 mL) and extracted with dichloromethane (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), and then dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue that was purified by flash chromatography (heptane/ethyl acetate 9:1) to give a mixture of compounds **5a** and **6a** (164 mg, 66% as an inseparable 44.5:54.5:1 mixture of (*Z*)-**5a**, (*E*)-**5a**, and (*E*)-**6a**) as a colorless oil. The NMR and analytical data of (*Z*)-**5a** and (*E*)-**5a** have been previously described. (*E*)-**6a:** $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 4.53 (d, $J$ = 7.8 Hz, 0.01H). The other peaks were hidden by those of **5a**.

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**Supporting Information Available:** Experimental details, synthetic procedures, and characterization data for all newly synthesized compounds and $^1$H/$^{13}$C NMR spectra of selected compounds **1a**,**b**, **2a**,**d**,**e**, **3**, **5a**, **6a**, **5c**, **6c**, and **5e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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