117. A Convenient and Diastereoselective Route to Homoallyl Alcohols: Addition of (*Z*)- or (*E*)-Alkenyl-dimethoxyboranes to Aldehydes[1])

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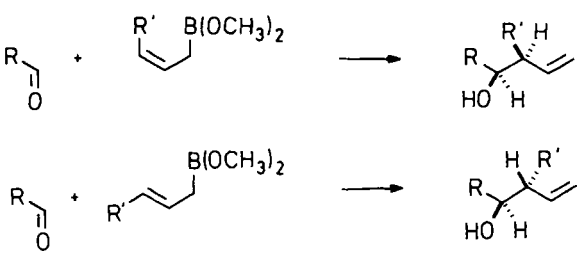
(5.IV.82)

Summary

(*Z*)-2-Butenyl-dimethoxyborane adds smoothly to propanal and benzaldehyde to afford the homoallyl alcohols (*R**, *R**)-**1** and (*R**, *R**)-**2**. In contrast (*E*)-2-butenyl-dimethoxyborane leads to adducts having the (*R**, *S**)-configuration. Dimethoxy-(*Z*)-2-pentenylborane, dimethoxy-(*Z*)-(2-methyl-2-butenyl)borane and (2*Z*,4*E*)- or (2*E*,4*Z*)hexadienyl-dimethoxyborane, treated with propanal, give (*R**, *R**)-**3**, (*R**, *R**)-**4**, (*E*),(*R**, *S**)-**5** and (*Z*),(*R**, *R**)-**5**, respectively. A transition state model implying a pericyclic electron motion is in perfect agreement with the regio- and stereoselective outcome of these borane reactions.

Alkenes are easily converted to pure (*Z*)- or (*E*)-alkenyl-dimethoxyboranes employing allyl-type organopotassium compounds as key intermediates in stereodefensive [2] or stereoselective reaction sequences [3] [4]. As anticipated [5–8], these alkenyl-dialkoxyboranes add to aldehydes in a regioselective *and* stereoselective manner. The vinylogous position with respect to the boron-bearing C-atom attacks the carbonyl group. Therefore, the formation of a new C,C-linkage is accompanied by a double-bond shift. Furthermore, one diastereoisomer is obtained almost exclusively in every case: (*Z*)-alkenylboranes produce *erythro*-adducts; (*E*)-isomers lead to *threo*-adducts.

Scheme 1



[1]) Part X of the series 'Selective Syntheses with Organometallics'; part IX: [1].

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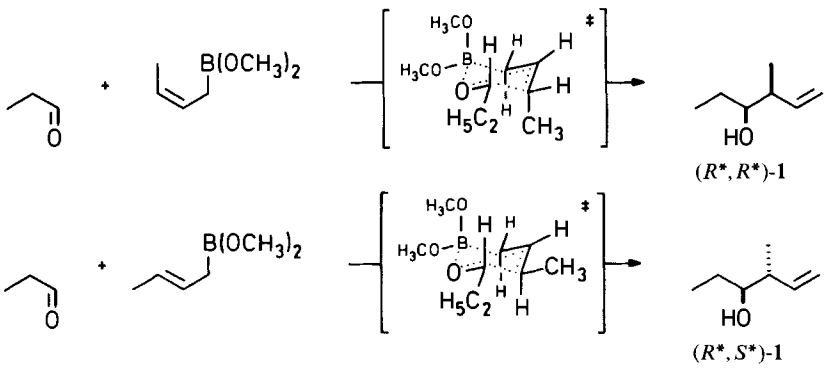
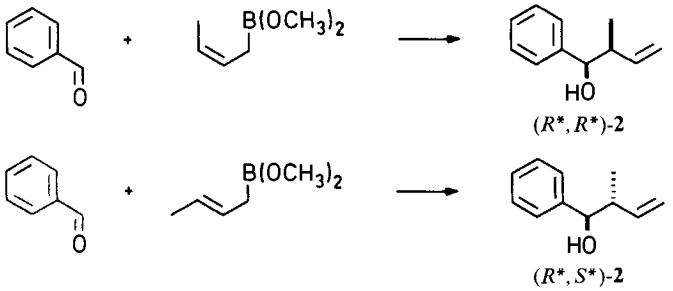
When (*Z*)-butenyl potassium [9] was treated consecutively with fluorodimethoxyborane and propanal at −75°, 62% of (*R**, *R**)-4-methyl-5-hexen-3-ol ((*R**, *R**)-**1**) was obtained after warming up to 25°. Only traces of the other stereoisomer were detected, the diastereoisomeric composition being 96:4 on average. The same reaction sequence applied to (*E*)-butenyl potassium yields essentially pure (*R**, *S**)-**1** (61%; *erythro/threo* 3:97). A sound explanation of the stereoselectivity may be based on the assumption of having a chair-like transition state mediating a cyclic transfer of electrons and the boryl group. To avoid steric repulsion by one of the methoxy substituents, the ethyl moiety of the propanal must occupy a pseudo-equatorial position.

Scheme 2



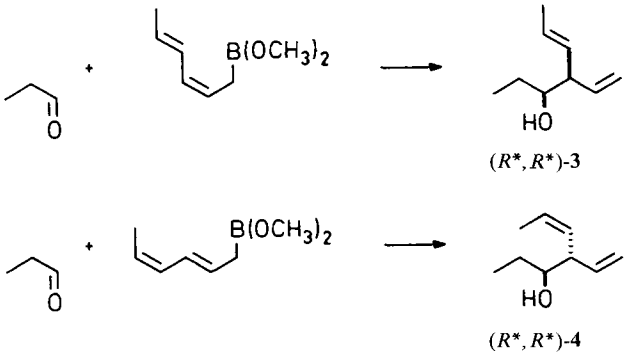
The variation of the aldehydes and boranes only slightly affects the stereoselectivity of the addition and not its regioselectivity. (*Z*)-2-Butenyldimethoxyborane combined smoothly with benzaldehyde to afford 2-methyl-1-phenyl-3-hexen-1-ol (**2**, 40%; (*R**, *R**)/(*R**, *S**) 96:4). The (*E*)-isomer of the same borane gave **2** (50%; (*R**, *R**)/(*R**, *S**) 1:99).

Scheme 3



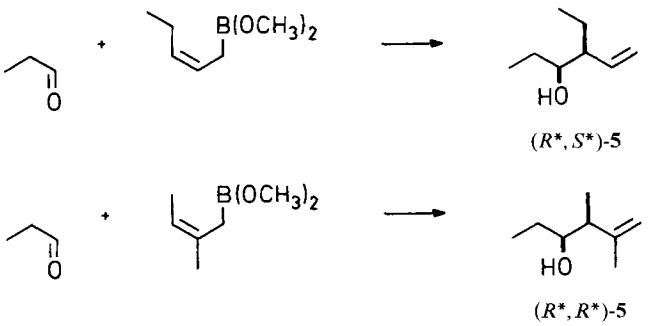
The addition of dimethoxy-(*Z*)-2-pentenylborane and dimethoxy-(*Z*)-(2-methyl-2-butenyl)borane to propanal afforded, respectively, (*R**, *R**)-4-ethyl-5-hexen-3-ol (**3**, 44%), and (*R**, *R**)-4,5-dimethyl-5-hexen-3-ol (**4**, 34%). In the latter case the diastereoisomeric homogeneity of the product was superior (98:2) to the former (90:10).

Scheme 4



Dienylboranes also exhibited regio- and stereoselective behavior. The U-shaped *exo*-hexadienylpotassium, generated from (*E*)-1,4-hexadiene, produced (2*Z*,4*E*)-hexadienyldimethoxyborane, which, by reaction with propanal, gave (*R**, *S**)-4-vinyl-5-(*E*)-hepten-3-ol [(*R**, *S**)-**5**, 36%]. The isomeric (2*E*,4*Z*)-hexadienyldimethoxyborane, derived from the W-shaped *endo*-hexadienyllithium (resulting from the lithiation of (*Z*)-1,4-hexadiene) afforded (*R**, *R**)-**5** (31%).

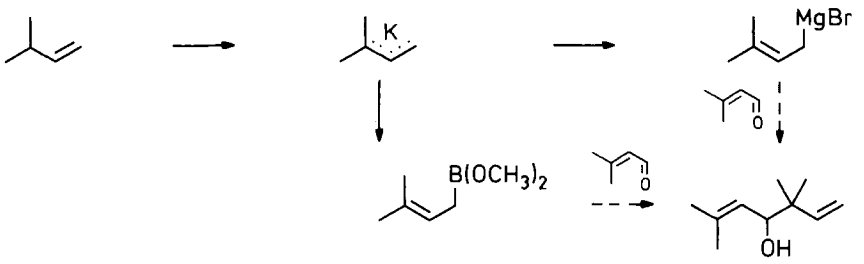
Scheme 5



The diastereoisomers **1**–**5** were identified by comparison with (*erythro*/*threo*)-mixtures obtained from the addition of the corresponding allylmagnesium compounds to propanal or benzaldehyde. Although these reactions revealed again a high A'_{Nu}-regioselectivity, they are stereochemically randomized.

In one case, both the *Grignard* and the borane route turned out to be unsatisfactory. No matter whether dimethoxy-(3-methyl-2-butenyl)borane or (3-methyl-2-butenyl)magnesium bromide were treated with 3-methyl-2-butenal, a complex reaction mixture resulted and 3,3,6-trimethyl-1,5-heptadien-4-ol (artemesia alcohol, **6**) was only formed in poor yield. If the transition state model presented *(Scheme 2)* is correct, γ,γ-disubstituted allyl-type dialkoxyboranes cannot escape from placing one substituent in the sterically hindered pseudo-axial position. Thus, a sluggish and unselective reaction was to be expected.

Scheme 6



The (*R**, *R**)- and (*R**, *S**)-configurations were assigned on the basis of their gas chromatographic properties and NMR. data. Generally, the (*R**, *R**)-component has a longer retention time [10] and its vinylidene signals appear at slightly higher field.

Financial support provided by the *Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung* is gratefully acknowledged. *Sumitomo Chemical Company*, Takaratsuka-Shi, kindly gave the permission for *K. F.*'s scientific leave. Finally, the authors thank Dr. *E. Moret*, Lausanne, for his collaboration and valuable suggestions.

Experimental Part

General remarks. See [9] [11] [12].

Condensation of alkenyl-dimethoxyboranes with aldehydes (general procedure). A solution of 45 mmol alkene, 40 mmol butyllithium and 40 mmol *t*-BuOK in 30 ml THF was kept 15 h at –50°. At –75° 20 ml of the fluorodimethoxyborane/ether (1:1)-adduct (88 mmol)[2]) and, 1 h later, 44 mmol of carefully purified aldehyde were slowly added under vigorous stirring. After keeping for another hour at –75°, the mixture was warmed up (in the course of 30 min) to 25° and was diluted with ether (100 ml), washed with brine (3×50 ml) and evaporated. The product was eluted from Kieselgel 60 (50 g) using hexane/ether 4:1 *(v/v)*. It was further purified by distillation and, if necessary, preparative gas chromatography.

Table 1. *Gas chromatographic separation of compounds* **1**–**5**: *oven temperatures*

	Analytical columns (2.3 mm inner diameter)		Capillary column (0.5 mm inner diameter)	Preparative columns (8.0 mm inner diameter)	
	2 m 15% *C-20M*	2 m 15% *SE-30*	26 m *C-20M** (22,800 plates)	3 m 20% *C-20M**	1 m 10% *C-20M**
1	140°	60°	70°	170°	–
2	210°	140°	150°	–	180°
3	150°	90°	73°	180°	–
4	130°	60°	72°	–	100°
5	160°	100°	90°	–	120°

[2]) In many cases, a strictly stoichiometric amount of fluorodimethoxyborane will suffice. The *t*-BuOLi, which is formed in the metallation step, was recognized to promote condensation and *Tischtschenko*-type dismutation reactions of enolizable aldehydes leading to erratic yields and stereoselectivity. Such complications were avoided by trapping the alcoholate with excess fluorodimethoxyborane or with added boron trifluoride. At 0° or 25°, boranes added always smoothly, although with somewhat lower stereoselectivity, to aldehydes without need of any special precaution.

Table 2. *^{1}H-NMR. spectra of compounds* **1–5** (360 MHz, $CDCl_3$)

	R″	H^{cis}	H^{trans}	H(−C−OH)	H(−C−R′)	H(−O−)	R	R′
(*R*,R**)-**1**	5.79 *d*×*d*×*d* (17.2, 10.8, 7.2)	5.06 *d*[a]) (17.5)	5.05 *d*[a]) (10.5)	3.38 *d*×*d*×*d* (8.7, 5.0, 3.9)	2.27 *hex* (6.6)	1.93[b])	1.54 *d*×*qa*×*d* (14.0, 7.5, 3.9) 1.38 *d*×*d*×*qa* (14.0, 8.7, 7.4) 0.96 *t* (7.4)	1.02 *d* (6.8)
(*R*,S**)-**1**	5.77 *m*[c])	5.11 *d*[a]) (17.0)	5.12 *d*[a]) (10.4)	3.33 *d*×*d*×*d* (10.2, 6.3, 4.2)	2.23 *hex* (7.0)	1.67[b])	1.57 *d*×*qa*×*d* (14.0, 7.5, 4.0) 1.41 *d*×*qi* (140, 7.4) 0.97 *t* (7.4)	1.03 *d* (6.6)
(*R*,R**)-**2**	5.64 *m*[c])	4.92 *m*[c])	4.92 *m*[c])	4.47 *d* (6.1)	2.47 *hex* (6.5)	3.03[b])	7.2 *m*	0.90 *d* (6.8)
(*R*,S**)-**2**	5.79 *d*×*d*×*d* (18.0, 10.2, 8.2)	5.16 *d* (18.0)	5.15 *d* (10.0)	4.32 *d* (7.8)	2.46 *hex*	2.21[b])	7.3 *m*	0.86 *d* (7.0)
(*R*,R**)-**3**	5.57 *d*×*d*×*d*	5.07 *d*×*d*[a])	5.12 *d*×*d*	3.40 *d*×*d*×*d*	2.01 *m*[c])[d])	1.70[b])	1.6 *m*	1.3 *m*
(*R*,S**)-**3**	5.64 *d*×*d*×*d* (17.5, 10.2, 9.0)	5.09 *d*×*d*[a]) (17.5, 2.1)	5.18 *d*×*d* (10.3, 2.1)	3.39 *m*[c])	1.93 *t*×*t* (8.5, 4.8)	1.78[b])	1.6 *m*; 1.4 *m*; 0.96 *t* (7.3)	1.3 *m* 0.89 *t* (7.4)
(*R*,R**)-**4**	1.74 *d*×*d* (1.5, 1.0)	4.84 *d*×*qa* (2.0, 1.5)	4.77 *d*×*qa* (2.0, 1.0)	3.49 *d*×*t* (8.0, 5.0)	2.19 *qi*[a]) (6.5)	1.82[b])	1.5 *m*; 0.97 *t* (7.3)	1.05 *d* (7.5)
(*R*,S**)-**4**	1.72 *d*×*d* (1.3, 0.8)	4.89 *d*×*qa* (2.3, 1.4)	4.83 *d*×*qa* (2.3, 0.8)	3.39 *d*×*t* (8.2, 3.0)	2.20 *d*×*qa* (8.4, 7.0)	1.85[b])	1.67 *d*×*d*×*qa* (14.0, 7.4, 3.0) 1.35 *d*×*qi* (14.0, 7.3) 0.99 *t* (7.5)	1.00 *d* (7.3)
(*R*,S**)-**5**[e])	5.78 *m*[c])	5.1 *m*	5.1 *m*	3.40 *d*×*d*×*d* (8.5, 6.4, 3.8)	2.72 *qi* (7.2)	1.86[b])	1.6 *m* 1.36 *hex* (7.4) 0.93 *t* (7.3)	5.53 *d*×*d* (15.5, 6.2) 5.41 *d*×*d*×*qa* (15.5, 8.2, 1.5) 1.71 *d*×*d* (6.4, 1.3)
(*R*,R**)-**5**[e])	5.76 *m*[c])	5.15 *m*[c])	5.15 *m*[c])	3.39 *d*×*d*×*d* (8.5, 7.5, 3.3)	3.10 *qi* (8.3)	1.78[b])	1.6 *m* 1.33 *d*×*qi* (15.6, 7.1) 0.96 *t* (7.3)	5.60 *d*×*qa*×*d* (11.0, 6.8, 1.0) 5.33 *d*×*d*×*qa* (11.0, 10.0, 1.8) 1.65 *d*×*d* (7.0, 1.6)

[a]) Additional fine-coupling, [b]) br. *s*, [c]) symmetrical, [d]) presumably *d*×*d*×*d* (~ 16. 9. 7), possibly *t*×*d*×*d* (9.5, 6.1, 3.9), [e]) the internal double-bond in the (*R*,R**)- and (*R*,S**)-diastereoisomer has respectively, the (*Z*)- and (*E*)-configuration; the allylic methyl groups of the (*Z*)-(*R*,R**)-, (*Z*)-(*R*,S**)-, (*E*)-(*R*,R**)- and (*E*)-(*R*,S**)-stereoisomer show up at 1.65, 1.64, 1.73 and 1.71 ppm.

Table 3. *Combustion analyses of compounds* **1–5**

	Empirical formula	Mol-wt.	Calc. % C	H	Found % C	H
1	$C_7H_{14}O$	114.2	73.63	12.36	73.43	12.20[a])
					73.94	12.41[b])
2	$C_{11}H_{14}O$	162.2	81.44	8.70	81.26	8.92[b])
					80.89	8.97[c])
3	$C_8H_{16}O$	128.2	74.94	12.58	75.13	12.49[c])
4	$C_8H_{16}O$	128.2	74.94	12.58	74.72	12.83[a])
					74.75	12.71[c])
5	$C_9H_{16}O$	140.2	77.09	11.50	77.05	11.55[c])

[a]) (*R**,*R**)-Stereoisomer. [b]) (*R**,*S**)-Stereoisomer. [c]) Mixture of stereoisomers.

Complete metallation of (*Z*)- and (*E*)-1,4-hexadiene was achieved respectively with *sec*-butyllithium and, butyllithium in the presence of potassium *tert*-butoxide at $-40°$ during 30 min.

Condensations of alkenylmagnesium bromides with aldehydes (general procedure). Anhydrous magnesium bromide was obtained by treating a vigorously stirred suspension of magnesium turnings in pentane/ether 1:1 *(v/v)*. The white powder was filtered off under N_2 and washed with pentane/ether. At $-75°$, 45 mmol (8.3 g) of this magnesium bromide were added to the solution of the allyl-type potassium compound, prepared as described above. After 60 min, still at $-75°$, the almost colorless mixture was treated with 45 mmol aldehyde, warmed up to r.t. and worked up.

The ((*R**,*R**)/(*R**,*S**))-ratio of the products **1–5** was 44:50, 50:50, 38:62, 64:36 and 15:85, respectively. (*R**,*R**)-**5** and (*R**,*S**)-**5** consisted each of (*Z*)- and (*E*)-isomers in the ratio of 1:1 and 3:7, respectively.

The data for efficient gas chromatographic analysis or purification of compounds **1–5** are listed in *Table 1*. Hexanol (for **1**), heptanol (**3** and **4**) and octanol (**2** and **5**) served as internal standards when the yields were determined precisely.

Tables 2 and *3* summarize respectively the NMR. microanalytical data of compounds **1–5**. Correct IR. spectra and MS. were also obtained.

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