

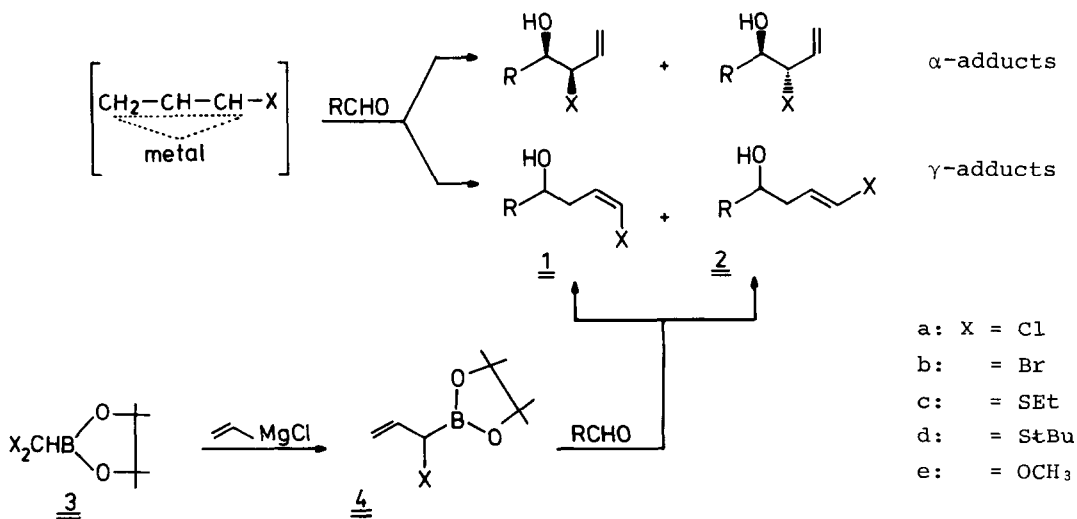
Z-SELECTIVE FORMATION OF SUBSTITUTED HOMOALLYL ALCOHOLS

Reinhard W. Hoffmann and Bernd Landmann

Fachbereich Chemie der Philipps-Universität, Hans-Meerwein-Straße  
 D-3550 Marburg an der Lahn

**Abstract:** The  $\alpha$ -substituted allylboronates 4 add to aldehydes giving with high  $Z$ -preference the homoallyl alcohols 1. The  $Z$ -vinyl bromides obtained were further converted into  $\delta$ -lactones.

The addition of monosubstituted allylmetal compounds to aldehydes may lead to four different adducts. In consequence this reaction would be useful for preparative chemistry, provided that not only the problems of  $\alpha/\gamma$ -selectivity <sup>1)</sup>, but also of stereoselectivity can be solved. Hence, even if the  $\gamma$ -adducts 1, 2 can be generated preferentially, further selectivity is desired with respect to the E or Z-configuration of the double bond. Stereohomogeneous Z-olefins 1 can be obtained from allyllithium compounds in which X is a nitrogen-<sup>2)</sup> or oxygen-functionality<sup>3)</sup>. However, compounds 1 and 2, in which X is a sulphur-, silicon- or halogen-substituent, command more interest, since these functionalities can be further elaborated maintaining the geometry of the double bond. Selective routes to either 1, X = S<sup>-</sup><sup>4)</sup>, or 2, X = StBu<sup>5)</sup> or X = Me<sub>3</sub>Si<sup>6,7)</sup> are known, while the problem of  $\alpha/\gamma$ -selectivity has not yet fully been solved. This holds also for the recently disclosed <sup>8)</sup> approach to 1 X = Cl<sup>9)</sup>.



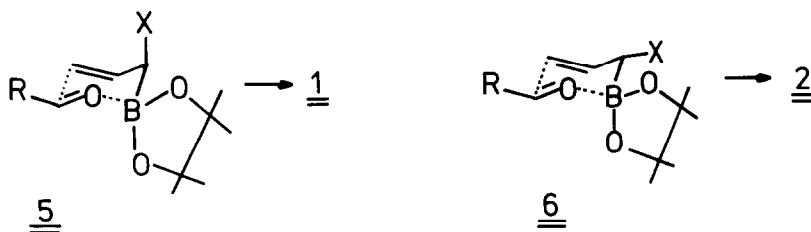
We report here a method for the selective generation of 1, X = Br, Cl, OR, with the aid of  $\alpha$ -substituted allylboronates 4. The  $\alpha$ -halo-allylboronates 4a, b were readily prepared from dichloro- and dibromomethyl-lithium <sup>10)</sup> via the dihalo-methaneboronates 3 <sup>11)</sup>. 4a was stable on storage, whereas 4b deteriorated rapidly. It sufficed however to react the crude undistilled allylboronates with the various aldehydes to give after the usual workup <sup>12)</sup> the homoallyl alcohols 1, preferentially, and 2 in good yield (cf. table). The  $\alpha$ -bromo allylboronate 4b was converted to the sulphur analogs 4c, d by boron-assisted nucleophilic substitution <sup>13)</sup> using the appropriate lithium thiolates in THF. The reaction of the sulphur substituted allylboronates 4c, d with 2-methylpropanal resulted in a somewhat diminished Z/E-selectivity, cf. table. The methoxy-derivative 4e obtained similarly gave on addition to 2-methylpropanal selectively the adduct 1e with Z-configuration of the double bond <sup>14)</sup>.

Table: Addition of  $\alpha$ -substituted Allylboronates to Aldehydes

Allylboronate	Aldehyde	Homoallylalcohols <u>1</u> , <u>2</u>		
		% yield	Z : E	determined by
<u>4a</u> , X = Cl <sup>22)</sup>	R = CH <sub>3</sub> -	63 (a)	93 : 7	<sup>13</sup> C-nmr
	CH <sub>3</sub> CH <sub>2</sub> -	86 (a)	94 : 6	"
	(CH <sub>3</sub> ) <sub>2</sub> CH-	83 (a)	96 : 4	"
	C <sub>6</sub> H <sub>5</sub> -	82 (a)	95 : 5	GC
<u>4b</u> , X = Br	R = CH <sub>3</sub> -	78 (b)	93 : 7	<sup>13</sup> C-nmr
	CH <sub>3</sub> CH <sub>2</sub> -	82 (b)	94 : 6	GC
	(CH <sub>3</sub> ) <sub>2</sub> CH-	83 (b)	96 : 4	<sup>13</sup> C-nmr
	C <sub>6</sub> H <sub>5</sub> -	<u>11</u> : 80 (b)	97 : 3	GC
	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> -	<u>7</u> : 69 (b)	92 : 8	<sup>13</sup> C-nmr
	CH <sub>3</sub> CH <sub>2</sub> -CH=CH-CH <sub>2</sub> -	<u>9</u> : 84 (c)	92 : 8	<sup>13</sup> C-nmr
<u>4c</u> , X = SC <sub>2</sub> H <sub>5</sub>	R = (CH <sub>3</sub> ) <sub>2</sub> CH-	85 (a)	85 : 15	<sup>13</sup> C-nmr
<u>4d</u> , X = SC(CH <sub>3</sub> ) <sub>3</sub>	R = (CH <sub>3</sub> ) <sub>2</sub> CH-	63 (a)	80 : 20	<sup>13</sup> C-nmr
<u>4e</u> , X = OCH <sub>3</sub>	R = (CH <sub>3</sub> ) <sub>2</sub> CH-	55 (a)	>95 : <5	<sup>13</sup> C-nmr

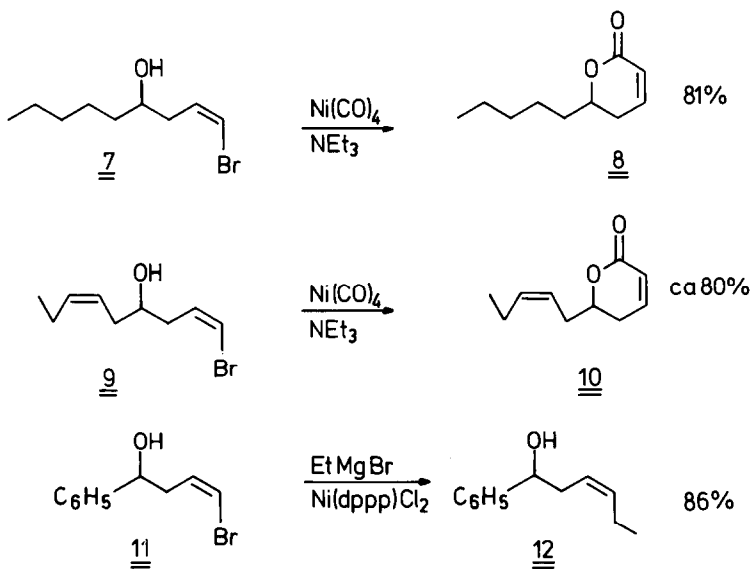
a) based on 4, b) based on 3, c) based on Aldehyde

A previous study of  $\alpha$ -methyl-allylboronates, 4, X = CH<sub>3</sub>, documented that the observed Z-preference is a consequence of the steric bulk of the ester component at boron <sup>15)</sup>. The data obtained in this study reveal that the Z-preference depends in addition on the nature of the  $\alpha$ -substituent X in the allylboronate 4: The preference for an axial disposition of X in the transition state 5 versus an equatorial arrangement in 6 decreases in the sequence X = OCH<sub>3</sub> > Cl, Br > SR  $\approx$  SiMe<sub>3</sub> <sup>16)</sup> > CH<sub>3</sub> <sup>15)</sup>.



This could be related to the anomeric effect <sup>17)</sup>, e.g. the tendency of  $\underline{4}$  to attain a transition state conformation  $\underline{5}$ , in which the dipoles of the C-X and B-O-bonds lead to the smallest net-dipole <sup>18)</sup>. Hence, a preparative useful Z-selectivity can be realized starting from allylboronates  $\underline{4}$  which carry both a polar substituent X and bulky ester residues on boron <sup>15)</sup>.

The bromo compounds  $\underline{1b}$  obtained are valuable starting materials for stereo-specific elaboration of the carbon skeleton. This is exemplified by the conversion <sup>19)</sup> of  $\underline{7}$  and  $\underline{9}$  into the  $\delta$ -lactones, massoia-lactone  $\underline{8}$  and tubero-lactone  $\underline{10}$ .



Moreover, the reaction of  $\underline{11}$  with ethylmagnesium bromide under catalysis by  $\text{Ni(dppp)Cl}_2$  <sup>20)</sup> led to the homoallyl alcohol  $\underline{12}$ . Compound  $\underline{12}$  can be considered as a model for various fragrant substances possessing the Z-pentenyl side chain <sup>21)</sup>. As discussed above,  $\underline{12}$  could probably not be obtained with similar Z-selectivity starting from  $\underline{4}$ , X = Et.

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