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## STEREOSELECTIVE ALLYL- AND CROTYLBORATION OF ALPHA- HYDROXYKETONES VIA NEIGHBORING GROUP CONTROL

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Abstract: Allylboronates and crotylboronates react with alpha-hydroxyketones to yield tertiary homoallylic alcohols in a highly stereocontrolled manner. The reaction presumably proceeds via a rigid bicyclic transition state. The alpha-hydroxy substituent exerts a remarkable and predictable effect on the diastereoselectivity of the reaction. Homoallylic alcohols are formed with diastereoselectivities approaching 100%.

The development of new methods for acyclic diastereo- and enantiomeric control of chiral centers is of major importance in synthetic organic chemistry<sup>1</sup>. The stereoselective allylation of prostereogenic carbonyl compounds is one of the most useful stereoselective reactions in that several stereogenic centers can be generated in a single step<sup>2</sup>. However, the allylation of ketones is difficult<sup>3</sup>; for example, the addition of (E)- and (Z)-pentenylboronates to ketones requires high pressure and 4-5 days<sup>4</sup>.

It is known that alpha-alkoxy substituents accelerate the reaction rate in aldol condensations<sup>5</sup> and organometallic addition reactions<sup>6</sup>. It is also known that the hydroxy group can diastereoselectively direct an incoming reagent by coordinating with it, e.g. intramolecular Tishchenko<sup>7</sup> and Sakurai<sup>8</sup> allylsilylation reactions. We wish to report that allyboronate <u>1</u>, (E)crotylboronate <u>2</u>, and (Z)-crotylboronate<sup>9</sup> <u>3</u> react with alpha-hydroxyketones <u>4</u> to yield tertiary homoallylic alcohols <u>5</u> stereoselectively. The essential functions of the OH group are: (1) activation of the carbonyl group and (2) stereocontrol at carbons 1 and 2 (structure <u>5</u>). The configuration at the allylic position (carbon 3 in <u>5</u>) is determined by the borane reagents (<u>2</u> or <u>3</u>). Our results suggest that the reaction proceeds through a rigid bicyclic transition state <u>7</u> (Scheme 1). Bulky R<sub>2</sub> groups favor the transition state <u>7</u>a over <u>7</u>b and lead to syn/anti ratios approaching 100%.



Scheme-1. Proposed Transition States of the Allyl- and Crotylboration of Hydroxyketones.



As illustrated in Table I, treatment of alpha-hydroxyketone  $\underline{4}a$  with triethylamine (1.0 equivalent, -78 °C for 5 minutes) followed by the addition of an allyl- or crotylboronate at -78 °C, and then warming to room temperature, produced tertiary homoallylic alcohols in good yields and with excellent stereoselectivities.

Table	I.	Reaction	of	Acetol	( <u>4</u> a)	with	Boronates.
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a) Isolated yields. b) The structures were determined by NMR analyses and confirmed by elemental analyses and the syn/anti ratios were determined by NMR analyses. c) Maximum ratio which could be obtained = 98/2 based on the purity of the starting material 2. d) Maximum ratio which could be obtained = 95/5 based on the purity of the starting material 3.

A plausible mechanism for the triethylamine initiated allyl and crotylboration involves a ligand exchange<sup>10</sup> to form a mixed boronate which then reacts via transition state  $\underline{7}a$  involving

coordination between the boron atom and the carbonyl group. The outstanding stereoselectivity of the allyl- and crotylboration of hindered alpha-hydroxyketone  $\underline{4}b$  (benzoin), Table II, supports this postulation.

Preliminary solvent investigations revealed that the reactions are faster in methylene dichloride than in THF which is consistent with recent observations<sup>11</sup>. Preliminary studies also revealed that the isopropyl boronates react faster than pinacol boronates; no differences in stereoselectivity were observed at room temperature. However, under refluxing conditions, the stereoselectivity decreased for reactions run in THF.

The stereochemistry of each of the products was determined by NMR analysis<sup>7,12</sup>. The structure of the product of the reaction of 2 and benzoin was confirmed by X-ray crystallographic analysis.

	∕O <u>i</u> Pr ∕OiPr	+ Ph-	Ph Et <sub>3</sub> N OH CH <sub>2</sub> Cl <sub>2</sub>	HO BE RZC		
Compound	R <sub>E</sub>	R <sub>Z</sub>	Rxn Time (hr)	% Yield <sup>a</sup>	1,2-Syn <sup>b</sup>	2,3-Syn or Anti
<u>l</u>	Н	Н	12 (-10 °C - reflux)	94	100	
2 E/Z=98:2	CH3	н	24 (-10 °C - reflux)	83	100	98(syn) <sup>c</sup>
<u>3</u> Z/E=95:5	н	СНЗ	32 (-10 °C - reflux)	80	100	95(anti) <sup>d</sup>

Table II. Reaction of Benzoin (4b) with Boronates.

a) Isolated yields. b) The structures were determined by NMR analyses and confirmed by elemental analyses and the syn/anti ratios were determined by NMR analyses. c) Maximum ratio which could be obtained = 98/2 based on the purity of the starting material 2. d) Maximum ratio which could be obtained = 95/5 based on the purity of the starting material 3.

In summary, alpha-hydroxy substituents exert a remarkable effect on the diastereoselectivity of the allylboration and crotylboration reactions. The rigid bicyclic transition state produces diastereoselectivities approaching 100%.

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