Enhancement of *threo*-Selectivity in the Reaction of But-2-enyl-lithium with Aldehydes *via* Allylic Boronate Complexes

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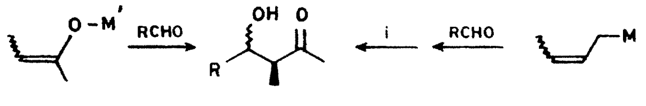
Summary The *threo*-selectivity of the reaction of but-2-enyl-lithium with aldehydes in the presence of certain trialkylboranes is enhanced, the corresponding allylic boronate complexes are presumably involved as intermediates.

RECENTLY, attention has been focused on the diastereoselective synthesis of β-hydroxylcarbonyl-compounds which may be of use in the synthesis of macrolide antibiotics [1] The stereoselective cross-aldol condensation is a very useful direct method for this purpose The indirect method, whereby allylic organometallic compounds are treated with aldehydes followed by a Wacker-type oxidation, has recently been introduced by us[2] and others[3] (Scheme 1). Notably, a completely *erythro*-selective and regioselective cross-aldol condensation is achieved *via* the (*Z*)-alken-2-yltin route.[2] Unfortunately, however, *threo*-selectivity is quite low or even negligible when but-2-enyl-lithium or -magnesium derivatives are used. We report that the *threo*-selectivity in the reaction of but-2-enyl-lithium (**1**) with aldehydes is remarkably enhanced *via* allylic boronate complexes (Scheme 2). The results are summarized in the Table.



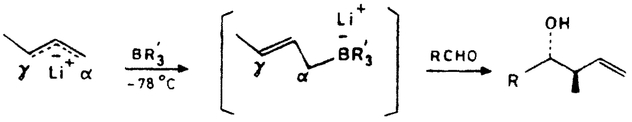
SCHEME 1. M' = Al, B, Li, Mg, Si, Sn, Zn, Zr. M = Al, B, Li, Mg, Si, Sn. i, Wacker oxidation.

TABLE. Enhancement of *threo*-selectivity in the reaction of (**1**) with aldehydes in the presence of trialkylboranes.[a]

Reaction	Aldehyde	Additive	Solvent	Product ratio/%[b] *threo* [(**3**)]	Product ratio/%[b] *erythro*	Total yield/%[c]
1	PhCHO	None	Ether	50	50	52[d]
2	PhCHO[e]	None	Ether	50	50	(92)
3	PhCHO	Et_3Al	Ether	56	44	93
4	PhCHO	Et_3B	Ether	82	18	90
5	PhCHO[e]	Et_3B	Ether	50	50	95
6	PhCHO	Et_3B	Tetrahydrofuran	83	17	91
7	PhCHO	Et_3B	Ether–HMPA[f]	83	17	83
8	PhCHO	$Bu^n{}_3B$	Ether	83	17	89
9	PhCHO	$Bu^s{}_3B$	Ether	61	39	85
10	PhCHO	1-Bu^n-3,6-Me_2-boraepan	Ether	80	20	85
11	MeCHO	Et_3B	Ether	85	15	(78)
12	Me_2CHCHO	Et_3B	Ether	68	32	(82)

[a] All reactions were carried out on a 1 mmol scale. An equivalent amount of the Lewis acids (boranes or alane) was added to a solution of (**1**) at −70 °C under N_2 and then the aldehydes were added. After 1 h, the reaction was quenched with methanol at −70 °C. The products were identified by comparison with authentic materials. 'None' indicates the normal reaction without the additives. [b] Determined by ^1H n.m.r. spectra for reactions 1—10 and by g.l.c. (CW 6000, 2m) for reactions 11 and 12. [c] G.l.c. yield (isolated yield). [d] The straight-chain product arising from the coupling at the α position of (**1**) was also detected. [e] But-2-enyl magnesium chloride was used instead of but-2-enyl-lithium. [f] HMPA = hexamethylphosphoric triamide.

As apparent, the condensation with benzaldehyde in the presence of triethylborane, tri-n-butylborane, or 1-n-butyl-3,6-dimethylboraepan produces predominantly the *threo*-derivative (reactions 4, 6—8, and 10). Interestingly, the very sterically hindered tri-s-butylborane is not so effective, presumably because of the formation of a weak complex with (**1**) (reaction 9). The lack of effectiveness of Et_3Al may also be ascribed to a weak complex, since the longer C–Al bond and its more ionic nature[4] should facilitate the dissociation of the complex into (**1**) or exert an influence on the rigidity of the cyclic transition-state.[5] The importance of the metal ions is indicated by the reaction of but-2-enyl magnesium chloride (reactions 2 and 5).



(1) (2) (3)

SCHEME 2.

The reaction presumably proceeds *via* the allylic boronate complexes (**2**).[6] Migration of the R' group is not detected and BR'_3 is recovered after completion of the reaction. The coupling always occurs at the γ-position. Thus, the behaviour of (**2**) resembles that of the but-2-enyl magnesium derivative except for its high *threo*-selectivity.† Perhaps the most remarkable feature of the present procedure for the stereochemical control is its simplicity; merely the addition of BR'_3 before addition of the aldehydes produces the *threo*-selectivity. Furthermore, the present development suggests that trialkylboranes may be useful for the stereochemical control of certain carbanions.

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† The *threo*-selectivity of trivalent but-2-enyl boranes, such as 9-but-2-enyl-9-borabicyclo[3·3·1]nonene, towards aldehydes is *ca.* 60%.

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