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On the Reaction Pathway and Stereochemistry of Allylic Tin Reagents-Benzaldehyde Condensation. A Substituent Effect Study

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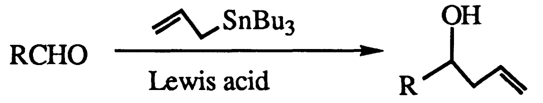
A substituent effect study on the reactivity and stereoselectivity of the Lewis acid mediated addition of allyl- and crotylstannanes to arylaldehydes indicates that the reaction proceeds via a polar antiperiplanar transition state with the exception of 2,4,6-trimethylbenzaldehyde, for which a cyclic pathway competes with the open pathway.

The Lewis acid mediated addition of allylstannanes to carbonyl compounds is well recognized as a useful synthetic reaction (Eq. 1).[1)] An open antiperiplanar transition state (TS) geometry has been assumed on the basis of erythro selectivity in the reaction of aldehyde with both *E*- and *Z*-crotyl reagents.[2)] However, bias to a synclinal (cyclic) TS was observed in a certain case and it was suggested that the allylstannane-aldehyde reaction under Lewis acid catalysis does not necessarily go through an open antiperiplanar TS.[3)]

In general, nucleophilic additions to carbonyl compounds have two possible mechanistic issues; whether the reaction proceeds via a polar or an electron-transfer pathway, and whether the TS geometry is cyclic or acyclic. Allylic lithium[4)] and magnesium reagents[5)] are likely to proceed via the ET mechanism, while allylic tin reagents are assumed to go through the polar pathway. Here we report the results of substituent effect experiments on reactivity and stereoselectivity as well as competition experiments in the reactions of allyl- and crotyltributylstannane with arylaldehydes, which allow to discuss on the two mechanistic issues. Reactions of allylic magnesium reagents were also carried out for comparison.



(1)

Reactions of substituted benzaldehydes with allyltributylstannane and allylmagnesium bromide were carried out at 0 °C and the substituent effect on the reactivity in these reactions was determined by the competition experiment as described previously.[6)] The Hammett plots of these reactions were shown in Fig. 1.[7)] The Hammett ρ value for the Grignard reaction (Fig. 1b) was very small and similar in magnitude to that observed previously for the reaction with benzophenone.[5)] This strongly suggests that the reaction mechanism for the benzaldehyde-allylmagnesium bromide system is the same with that for the benzophenone-allylmagnesium bromide case, namely the rate-determining electron transfer mechanism.[5)] In contrast, the reaction of benzaldehydes with allyltributylstannane gave a medium sized ρ value (Fig. 1a), which is consistent with the polar nucleophilic addition as usually assumed.

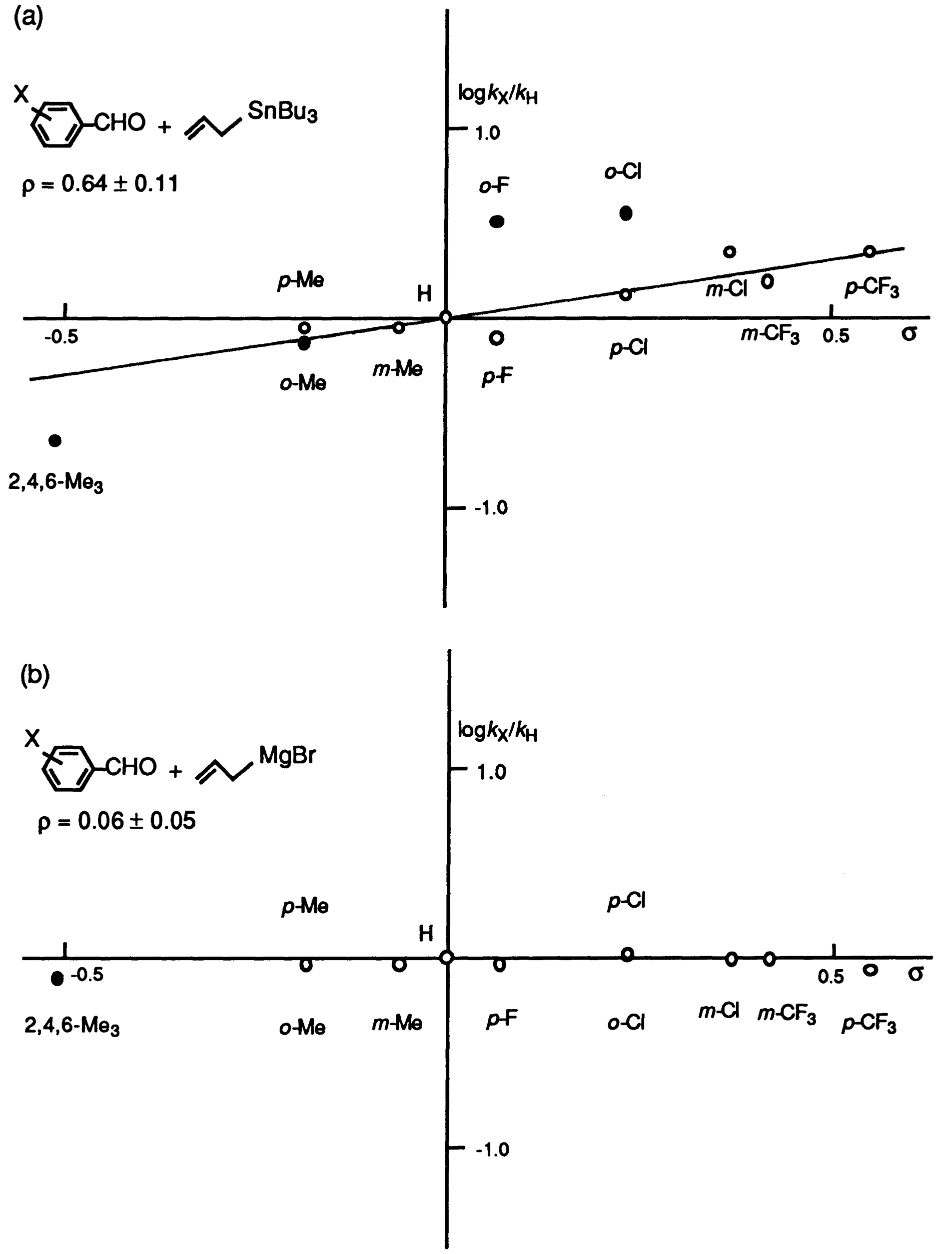


Fig. 1. Variations of reactivity with σ values for the reactions of substituted benzaldehydes with (a) allyltributylstannane in CH_2Cl_2 in the presence of $BF_3 \cdot Et_2O$ and (b) allylmagnesium bromide at 0 °C.

The relative reactivity of benzaldehyde (BA) vs. benzophenone (BP) is also informative. In the allylmagnesium bromide reaction, the reactivities of the two carbonyl compounds were similar (k_{BA}/k_{BP} = 0.76), while only benzaldehyde reacted in the presence of benzophenone in the allylstannane reaction. These relative reactivities are consistent with the rate-determining ET mechanism for the Grignard reagent and the direct nucleophilic addition for allylstannane.

It can be seen in Fig. 1a that the ortho substituted derivatives showed peculiar behavior in the allylstannane reaction. Thus, the 2,4,6-Me_3 substituents decrease the reactivity probably due to the steric hindrance of the two Me groups in the ortho positions, while *o*-Cl and *o*-F substituents accelerate the reaction, suggesting that some chelating effect is operating to stabilize the TS. Molecular model consideration indicates that such chelation is possible if the reaction proceeds via an antiperiplanar acyclic TS (Fig. 2). On the other hand, no chelating geometry is possible in a cyclic TS. It can thus be concluded that the reaction essentially proceeds through an acyclic TS.

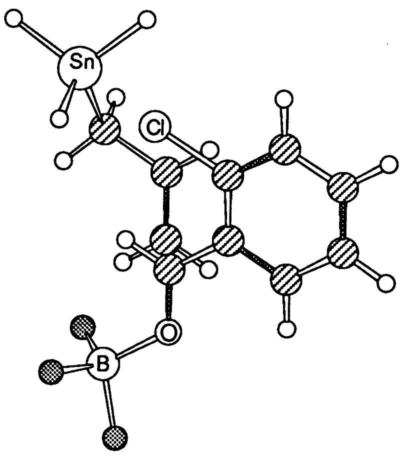


Fig. 2. The schematic antiperiplanar TS geometry of the BF_3-catalyzed reaction of allyltributylstannane with *o*-chlorobenzaldehyde. The tributyl moieties were replaced by hydrogens for clarity.

The substituent effects on diastereoselectivity in the reaction of arylaldehydes with crotyltributylstannane (*E* : *Z* = 45:55 by ^{119}Sn-NMR) in CH_2Cl_2 and with crotylmagnesium bromide in ether were determined at 0 °C for selected substituents and the results are listed in Table 1.8) In the Grignard reaction, the diastereoselectivity is low as reported in the literature9a) and no substituent effect was observed on the selectivity. The lack of substituent effect is consistent with a cyclic TS,5) because the product diastereoselectivity should be essentially controlled by the geometry of the crotyl reagent and independent of the substituent on benzaldehyde in a cyclic TS. In the crotylstannane reaction, on the other hand, a higher erythro selectivity was observed for the parent and the *p*-substituted derivatives.10) However, noticeable decrease in the erythro selectivity was detected for the *o*-Cl and the 2,4,6-Me_3 substituted derivatives.

The decrease in erythro selectivity for *o*-Cl coincides with the enhanced reactivity of this compound. The attractive interaction between *o*-Cl and Sn not only accelerates the reaction but fixes the position of the Sn moiety in an acyclic TS as shown in Fig. 2, through which the *Z*-crotylstannane will give the erythro product while the *E*-crotylstannane will afford the threo isomer. In the case of 2,4,6-trimethylbenzaldehyde, the two *o*-methyl groups exert steric repulsion in the acyclic antiperiplanar TS especially for *E*-crotylstannane and therefore a cyclic TS becomes favorable. As a result, more threo product is formed for this compound.

In summary, the present substituent effect study revealed that the $BF_3 \cdot Et_2O$ mediated addition of allylic tin reagents to benzaldehyde proceeds via a polar mechanism and that the stereoselectivity and the reaction

Table 1. Erythro : threo selectivity of the reactions of substituted benzaldehydes with crotylstannane and crotylmagnesium bromidea)

Reagent	Substituent					
	p-Me	*o*-Me	2,4,6-Me_3	H	*p*-Cl	*o*-Cl
$CH_3CH{=}CHCH_2Sn(n\text{-}Bu)_3$	78:22	67:33	40:60	80:20	78:22	57:43
$CH_3CH{=}CHCH_2MgBr$	56:44	52:48	60:40	52:48	52:48	53:47

a) All reactions were carried out as described in Ref. 8. Figures are the averages of at least two runs and the reproducibility is better than 2%.

pathways (cyclic or acyclic) can be easily changed by interactions between the reagent and the substrate.

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6) The reaction of allylstannane was carried out by adding allylstannane (33 mg, 0.1 mmol) to a CH_2Cl_2 solution of a mixture of two differently substituted benzaldehydes (0.2 mmol in total) and $BF_3 \cdot Et_2O$ (14 mg, 0.1 mmol) at 0.0±0.1 °C. The solution was allowed to react for 15 min. The reactions of allylmagnesium bromide were carried out in diethyl ether. Material balance of these reactions was confirmed excellent (99.8%). For details of the competition experiment procedures, see Ref. 4a.

7) Since the σ constants of the ortho substituents are not available, the $\log(k_X/k_H)$ values for the ortho derivatives were plotted against corresponding σ_p and are indicated by closed circles. Other substituents gave reasonably good straight lines in these reactions, from which the ρ values were calculated.

8) The reaction of crotylstannane was carried out as follows: in a flame dried test tube was placed a substituted benzaldehyde (0.5 mmol, ca. 0.05 g) and CH_2Cl_2 (2 mL). To the test tube $BF_3 \cdot Et_2O$ (0.5 mmol, 0.07 g) was added and the solution was stirred for 10 min at 0.0 °C. To this mixture crotyltributylstannane (0.5 mmol, 0.17 g) was added and the solution was allowed to react for 15 min. After appropriate workup, the product was purified by PTLC and analyzed by ^1H-NMR (Bruker-AM360).9) The reaction of crotylmagnesium bromide was performed in a similar manner and the product was analyzed by capillary GLC (CBP20, 25 m).

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10) The selectivity was somewhat lower than the reported value at -78 °C2a) probably because of the influence of temperature and other minor reaction conditions.

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