

# SUBSTITUENT EFFECTS FOR THE $\text{BF}_3$ -MEDIATED REACTIONS OF ALLYLTRIBUTYLTIN AND ALLYLTRIETHYLLEAD WITH BENZALDEHYDE

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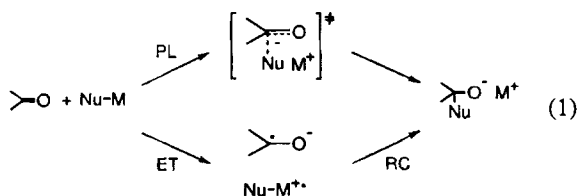
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Substituent effects were measured for the reactions of substituted benzaldehydes with allyltributyltin (1) and allyltriethyllead (2) reagents in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$  in  $\text{CH}_2\text{Cl}_2$ . The Hammett  $\rho$  values were small and positive at 25 °C and negative at -78 °C for both 1 and 2. These could be interpreted in terms of the contribution of electrophilic complexation between the aldehyde function and  $\text{BF}_3$  as a rate-limiting step. A large negative  $\rho$  value was observed for the complex-formation equilibria between substituted benzaldehydes and  $\text{BF}_3$ .

## INTRODUCTION

The substituent effect on reactivity, measured as the  $\rho$  value in the Hammett equation, is one of the most useful tools in studying the mechanism of organic reactions. In the course of our studies on the mechanism of nucleophilic additions to carbonyl compounds, the magnitude of  $\rho$  values has been used as one of the criteria in determining the reaction pathways [equation (1)]; here the polar nucleophilic process (PL) was differentiated from the rate-determining electron-transfer mechanism (ET rate determining) by the  $\rho$  value characteristic of the polar process.<sup>1</sup> In typical examples, the large  $\rho$  value (2.45 at 25 °C in 2-PrOH) observed for the reactions of substituted benzophenones with  $\text{NaBH}_4$  was consistent with the PL mechanism, while the  $\rho$  value of 0.27 (at 0 °C in  $\text{Et}_2\text{O}$ ) for the reactions



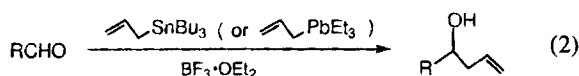
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of substituted benzophenones with MeLi was interpreted in terms of the ET mechanism.<sup>2,3</sup> However, the size of  $\rho$  depends on a variety of factors such as temperature, solvent and transition state position, and therefore an apparent  $\rho$  value should be interpreted with care.

It was reported that the reactions of Sb- and Pb-promoted Barbier-type reactions of allyl iodide with substituted benzaldehydes gave  $\rho$  values of 1.57 and 1.19, respectively at 25 °C in DMF.<sup>4</sup> These  $\rho$  values could reasonably be interpreted in terms of the PL mechanism. On the other hand, we have previously reported in a preliminary form that a much smaller  $\rho$  value (0.64) was observed for the  $\text{BF}_3$ -mediated addition of allyltributyltin to substituted benzaldehydes at 0 °C in  $\text{CH}_2\text{Cl}_2$ .<sup>5</sup> Since other evidence suggests that the PL mechanism operates for these reactions,<sup>4</sup> understanding of the reason for this difference is important in using  $\rho$  values as a mechanistic criterion to distinguish between the PL and the ET pathways. In the present paper, we report the results of more detailed studies of the substituent effects for the reactions of benzaldehydes with allyltin and allyllead reagents and present the reason for the difference in the  $\rho$  values for these reactions.

## RESULTS AND DISCUSSION

Relative reactivities were determined for the addition reactions of  $\text{CH}_2=\text{CHCH}_2\text{SnBu}_3$  (**1**) and  $\text{CH}_2=\text{CHCH}_2\text{PbEt}_3$  (**2**) with substituted benzaldehydes in  $\text{CH}_2\text{Cl}_2$  in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$  by competition experiments [equation (2)], and the results are summarized in Table 1.<sup>3</sup> The substituent effects measured at 0 °C are illustrated in Figure 1. Here, the  $\log(k_x/k_H)$



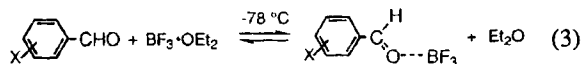
values for the *ortho*-substituted derivatives were plotted against the corresponding *para*-substituent constants and indicated by closed circles, and were not used for calculating the  $\rho$  values. Two points are noticeable in these Hammett plots: (1) the  $\rho$  values are much smaller than those of the corresponding Barbier-type reactions, especially for **2** ( $\rho=0.28$  for **2** and  $\rho=1.19^4$  for  $\text{CH}_2=\text{CHCH}_2\text{I} + \text{Pb}$  in DMF at 25 °C); and (2) *ortho*-halogen-substituted derivatives deviate upward from the correlation lines.

The *ortho*-halogen acceleration can be rationalized by the chelation between the halogen atom and Sn (or Pb); this chelation effect was described previously for the reaction of allyltributyltin,<sup>5</sup> and it will not be repeated here. In the present paper, we would like to focus on the interpretation of the small  $\rho$  values. One way to interpret the results is to assume that the reactions proceed via the rate-determining ET mechanism as in the reaction of benzaldehyde with allyllithium or allylmagnesium halide.<sup>6</sup> This possibility can be tested by measuring the relative reactivity of benzaldehyde and benzophenone with a given reagent; if the PL mechanism operates, benzaldehyde should react much faster than benzophenone for steric reasons, while the reactivity

would nearly be the same for the ET mechanism since the reduction potentials of benzaldehyde and benzophenone are similar. Similar reactivity has indeed been observed previously for reactions with allylmagnesium bromide ( $k_{\text{BP}}/k_{\text{BA}}=0.76$ ).<sup>5</sup>

In the present experiments, both **1** and **2** reacted only with benzaldehyde in the presence of benzophenone, indicating that the reactions proceed via the polar pathway. A dehalogenation probe (ketyl radical probe) experiment<sup>1</sup> was found to be negative for these reagents, consistent also with the PL mechanism. Thus, the observed small  $\rho$  values should be rationalized within the framework of the PL mechanism.

In order to elucidate the variation of the  $\rho$  values with temperature, the substituent effects were measured at -78 °C and the results are listed in Table 1. As can be seen in Figure 2, the observed  $\rho$  values are close to zero for  $\text{CH}_2=\text{CHCH}_2\text{SnBu}_3$  and even negative for  $\text{CH}_2=\text{CHCH}_2\text{PbEt}_3$  at low temperature. A negative  $\rho$  value implies that the electrophilic interaction between  $\text{BF}_3$  and benzaldehyde plays an important role in governing the reactivity. It is therefore reasonable to assume that the magnitude of the substituent effect is determined by the combination of the  $\text{BF}_3$ -benzaldehyde complex formation [equation (3)] and the nucleophilic attack of an allylmetal reagent to the  $\text{BF}_3$ -benzaldehyde complex; the former equilibrium would give a negative  $\rho$  value, while the latter step should yield a positive  $\rho$  value.



It has been demonstrated previously that benzaldehyde and  $\text{BF}_3$  formed a 1:1 complex and that the equilibrium between the complexed and uncomplexed aldehyde could be measured by NMR.<sup>7-9</sup> The magnitude

Table 1. Relative reactivities for the reactions of substituted benzaldehydes with **1** and **2**<sup>a</sup>

Substituent	<b>1</b>		<b>2</b>	
	0 °C	-78 °C	0 °C	-78 °C
2,4,6-Me <sub>3</sub>	0.24 ± 0.04	0.09 ± 0.03	0.74 ± 0.10	0.79 ± 0.12
<i>p</i> -Me	0.89 ± 0.02	0.77 ± 0.07	0.81 ± 0.04	1.38 ± 0.20
<i>m</i> -Me	0.85 ± 0.02	1.04 ± 0.05	0.90 ± 0.06	1.19 ± 0.04
<i>o</i> -Me	0.75 ± 0.02	1.21 ± 0.04	0.91 ± 0.01	1.46 ± 0.06
<i>p</i> -Cl	1.31 ± 0.04	0.88 ± 0.01	1.04 ± 0.03	0.63 ± 0.08
<i>m</i> -Cl	2.25 ± 0.03	0.79 ± 0.02	1.16 ± 0.11	0.37 ± 0.05
<i>o</i> -Cl	3.68 ± 0.33	1.20 ± 0.07	1.48 ± 0.05	0.53 ± 0.05
<i>p</i> -F	0.79 ± 0.03	0.91 ± 0.07	0.88 ± 0.05	0.95 ± 0.12
<i>o</i> -F	3.21 ± 0.26	1.24 ± 0.13	1.43 ± 0.02	0.68 ± 0.03
<i>p</i> -CF <sub>3</sub>	2.19 ± 0.11	0.89 ± 0.04	1.41 ± 0.25	0.38 ± 0.07
<i>m</i> -CF <sub>3</sub>	1.59 ± 0.03	0.77 ± 0.07	1.14 ± 0.04	0.40 ± 0.03

<sup>a</sup> Errors are the standard deviations of multiple measurements.

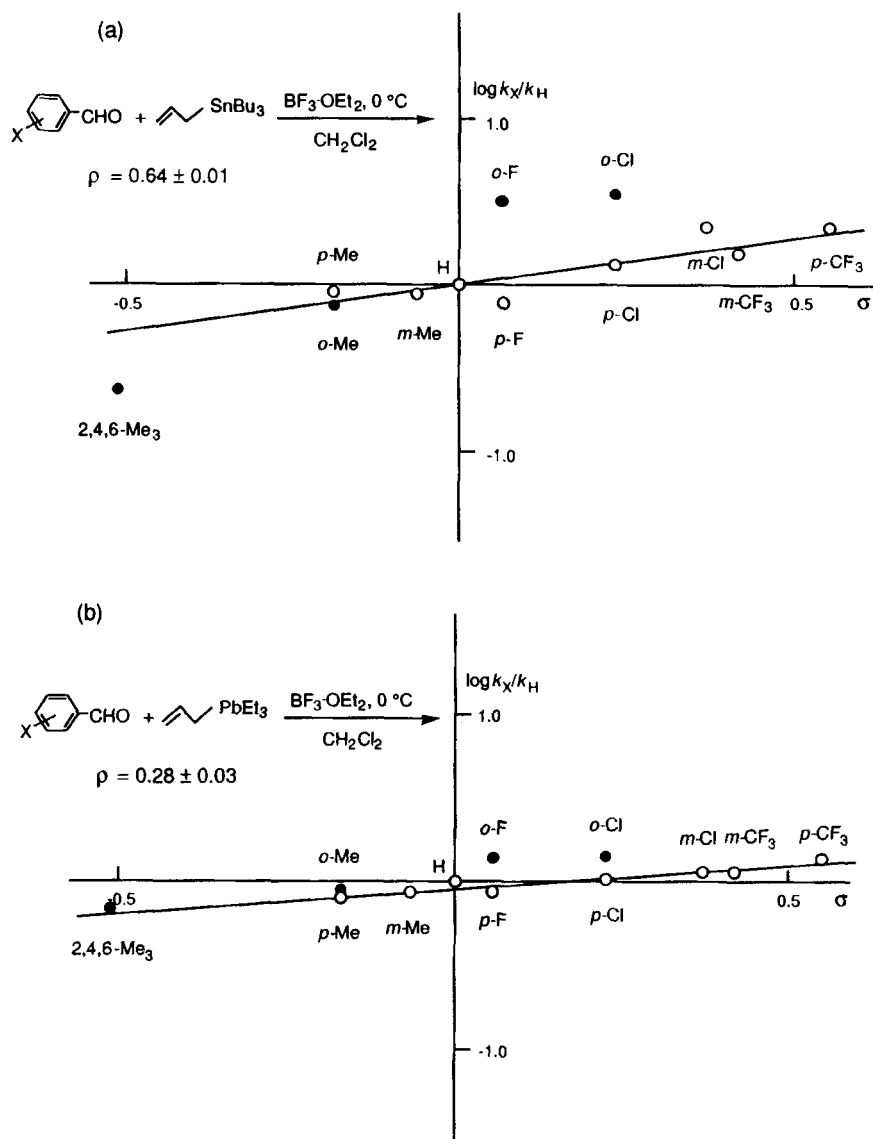


Figure 1. Hammett  $\rho$  plots for the reactions of substituted benzaldehydes with (a) 1 and (b) 2 in the presence of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  at  $0^\circ\text{C}$  in  $\text{CH}_2\text{Cl}_2$

of the substituent effect on the complex formation was then determined at  $-78^\circ\text{C}$  by NMR. The signal of the formyl proton of the benzaldehyde- $\text{BF}_3$  complex lies  $0.35$  ppm higher field relative to free benzaldehyde, in agreement with previous reports.<sup>9-11</sup> The equilibrium constant was calculated from the relative intensity of these signals. The chemical shifts<sup>10</sup> and the equilibrium constants determined for substituted benzaldehydes are listed in Table 2, and show that the position of the

equilibrium depends very much on the substituent. The plot of  $\log K$  vs the Hammett  $\sigma$  values is shown in Figure 3; here the standard  $\sigma$  constants, rather than  $\sigma^+$ , were used since the uncertainties involved in the equilibrium constants did not allow a clear distinction between them. The  $\rho$  value was calculated to be  $-3.5$ , small enough to account for the negative  $\rho$  value ( $-0.92$ ) observed for the reaction of 2 at  $-78^\circ\text{C}$ .

The influence of complex formation on the relative

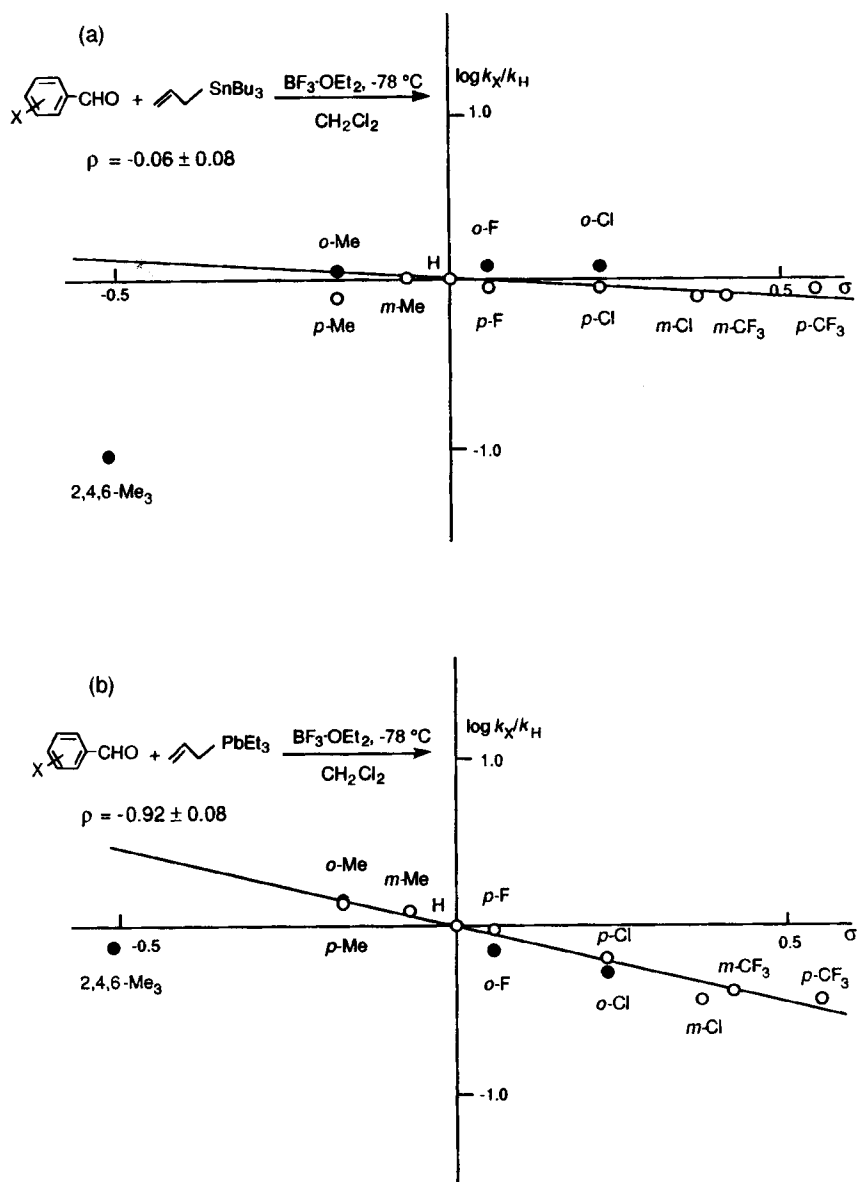


Figure 2. Hammett  $\rho\sigma$  plots for the reactions of substituted benzaldehydes with (a) **1** and (b) **2** in the presence of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  at  $-78^\circ\text{C}$  in  $\text{CH}_2\text{Cl}_2$

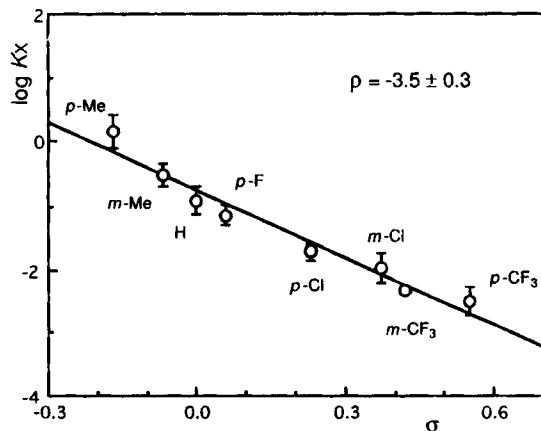
reactivity is larger for a more reactive reagent (**2** compared with **1**) for which the nucleophilic addition step is faster. The fact that the  $\rho$  values are positive at  $0^\circ\text{C}$  but negative at  $-78^\circ\text{C}$  indicates that the complexation equilibrium becomes more important at lower temperature. The reason for this is not clear, but it may imply that the rate of the nucleophilic addition step is less temperature dependent and thus becomes relatively less

important in governing the reactivity at lower temperature. In any event, the present results clearly indicate the importance of the equilibrium of the aldehyde- $\text{BF}_3$  complex formation as a rate-limiting process. The kinetically important step could change with change in the reagent in addition to the reaction temperature, hence the interpretation of the observed  $\rho$  value should be made carefully.

Table 2. Chemical shifts of the formyl protons of free benzaldehyde and the benzaldehyde-BF<sub>3</sub> complex and the equilibrium constants<sup>a</sup>

Substituent (X)	Chemical shift, $\delta$		Equilibrium constant ( $K_X$ )
	Free aldehyde	BF <sub>3</sub> complex	
<i>p</i> -Me	9.98	9.55	1.30 $\pm$ 0.70
<i>m</i> -Me	10.01	9.62, 9.60	0.27 $\pm$ 0.10
H	10.05	9.68	0.11 $\pm$ 0.05
<i>p</i> -F	10.00	9.65	0.064 $\pm$ 0.023
<i>p</i> -Cl	10.02	9.67	0.017 $\pm$ 0.005
<i>m</i> -Cl	10.01	9.72, 9.69	0.010 $\pm$ 0.005
<i>m</i> -CF <sub>3</sub>	10.10	9.99, 9.97	0.0042 $\pm$ 0.0003
<i>p</i> -CF <sub>3</sub>	10.13	9.87	0.0028 $\pm$ 0.0013

<sup>a</sup>At -78 °C in CDCl<sub>3</sub>-CDCl<sub>2</sub> (3:1). Errors are the standard deviations of duplicate measurements.

Figure 3. Hammett  $\rho\sigma$  plot for the equilibrium in equation (3)

## EXPERIMENTAL

**Materials.** Substituted benzaldehydes were obtained commercially and purified by distillation. Dichloromethane was distilled from CaH<sub>2</sub>. Allyltributyltin<sup>11</sup> and allyltriethyl-lead<sup>12</sup> were prepared according to the literature, and distilled before use.

**Reactions.** The reactions of allyltin and allyllead were carried out by adding **1** or **2** (0.1 mmol) to a CH<sub>2</sub>Cl<sub>2</sub> solution of a mixture of benzaldehydes (0.1 mmol) and BF<sub>3</sub>·OEt<sub>2</sub> (0.1 mmol) at 0 or -78 °C. The reactions gave the expected addition product exclusively. Material balance of these reactions was

confirmed excellent (102.6  $\pm$  1.6% for **1** and 98.7  $\pm$  1.0% for **2**). All products were isolated and characterized by comparing their <sup>1</sup>H NMR spectra (Bruker AM360, CDCl<sub>3</sub>) with those reported previously.<sup>4</sup>

**Relative reactivity.** The relative reactivities of substituted benzaldehydes with **1** and **2** were determined as reported previously.<sup>3</sup> A pair of substituted benzaldehydes (normally the parent and a substituted compound, 0.2 mmol each) and naphthalene (internal standard, 0.2 mmol) were placed in a flame-dried, serum-capped test-tube and dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (2 ml). Half of the solution was transferred by means of a syringe into a test-tube, to which was then added BF<sub>3</sub>·OEt<sub>2</sub> (0.2 mmol). To this solution was added **1** or **2** (0.1 mmol) and the mixture was allowed to react at 0 °C for 15 min (for **1**) or 10 s (for **2**) or at -78 °C for 30 min (for **1**) or 10 s (for **2**). The solution was hydrolysed, extracted with diethyl ether, dried over MgSO<sub>4</sub> and subjected to GC analysis (2 m glass column packed with 3% PEG HT). The relative intensity of each reactant to that of the internal standard was compared with the corresponding relative intensity from the solution that was not mixed with **1** or **2**. The fraction of reaction was calculated for both reactants and the reactivity ratio was computed according to equation (4).

$$k_A/k_B = \log(1 - f_A)/\log(1 - f_B) \quad (4)$$

**Equilibrium constant.** In a flame-dried NMR tube were placed 0.1 mmol of substituted benzaldehyde and 0.75 ml of solvent (CDCl<sub>3</sub>:CD<sub>2</sub>Cl<sub>2</sub> = 3:1), and the spectrum was recorded at -78 °C. To this solution was then added BF<sub>3</sub>·OEt<sub>2</sub> in 0.25 ml of the solvent, and the spectrum was measured again. The amount of BF<sub>3</sub>·OEt<sub>2</sub> added was 1.0 mmol for *o*-, *m*- and *p*-Cl derivatives and

0.5 mmol for all other derivatives. By comparing the spectra for the solutions with and without  $\text{BF}_3 \cdot \text{OEt}_2$ , the chemical shifts of the benzaldehyde- $\text{BF}_3$  complex were identified, and the relative intensities of the formyl protons were used to calculate the equilibrium constant.

*Ketyl radical probe experiment.* In a flame-dried test-tube were placed *o*-bromobenzophenone (0.2 mmol), a small amount of dibenzyl ether (internal standard) and  $\text{CH}_2\text{Cl}_2$  (1 ml). To half of the solution was added  $\text{BF}_3 \cdot \text{OEt}_2$  (0.1 mmol) at 0 °C, and the solution was stirred for 10 min. To this solution was then added **1** or **2** (0.1 mmol) and the mixture allowed to react for 30 min (for **1**) or 10 s (for **2**). After the usual work-up, the organic layer was analysed by GC (2 m PEG-HT column), which showed that the reaction gave only the normal adduct in addition to the recovered reactant.

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