# Kinetic study of BH$_3$ reduction of benzaldehydes: identification of effective reducing species

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A kinetic study was carried out for the reaction of benzaldehyde and borane (BH$_3$) in tetrahydrofuran. The effect of BH$_3$ concentration on the rate constant showed that the reaction order with respect to BH$_3$ was 1.6. Substituent effects gave a linear Hammett plot with a $\rho$ value of $-0.51$. It was concluded that the reaction proceeds through a rate-determining hydride-transfer transition state with two BH$_3$ molecules, in which one molecule of BH$_3$ acts as a reducing agent and the other serves as a catalyst. Copyright © 2011 John Wiley & Sons, Ltd.

**Keywords:** catalytic transition state; metal hydride reduction; reaction order; substituent effect

## INTRODUCTION

The reduction of aldehydes and ketones is one of the most fundamental reactions in organic chemistry. Metal hydrides are common reducing reagents for such a reaction in an organic laboratory, and the reaction mechanism has been studied extensively.[1–7] Simple metal hydrides such as borane (BH$_3$) and aluminum hydride have interesting characteristics in that they are Lewis acids and thus electrophilic at the metal center, whereas the hydrogens are nucleophilic and therefore the reactions could be either electrophilic or nucleophilic. These reductions consist of two key steps: an initial complex formation between the metal and the carbonyl oxygen and hydride transfer from the metal to the carbonyl carbon (Eqn (1)). The apparent electrophilic versus nucleophilic nature of the reaction depends on the position of the rate-determining step and the relative stability of the complex. If the $k_1$ step is rate-determining, the reaction becomes electrophilic. If, on the other hand, the initial equilibrium lies largely on the complex side, the complex becomes an effective reactant and hence the reaction becomes nucleophilic.

The mechanism of the reactions of benzophenone with four simple metal hydride reagents has been examined experimentally. The Hammett $\rho$ values were reported to be $-0.12$, $-0.76$, 1.03, and 0.47 at 25 °C for the reactions of BH$_3$/Et$_2$O, 9-borabicyclo[3.3.1] nonane/tetrahydrofuran (THF), AlH$_3$/Et$_2$O, and diisobutylalumi-nun hydride/hexane, respectively.[8] The Hammett plots show that the electronic effects on the reaction rates varied depending on the reagents; the balance of electrophilic and nucleophilic attacks by the metal atom and the hydrogen atom differs for these reagents.

Further mechanistic complexity arises from the monomer–dimer equilibrium. It has been shown that borane exists in THF as the BH$_3$–THF complex and species like B$_2$H$_6$ or B$_2$H$_6$–THF plays a negligible role in THF.[9–11] On the other hand, a computational study on the reactions of benzaldehyde (BA) and BH$_3$ in the literature showed that the hydride-transfer step from the encounter complex had a much smaller activation free energy (7.2 kcal/mol) for the dimer reaction than for the monomer reaction (16.2 kcal/mol) at MP26-311 G*.[12] The initial complex formation of BA with free BH$_3$ was exergonic ($-5.4$ kcal/mol), whereas it was

endergonic (18.7 kcal/mol) with B$_2$H$_6$. Thus, the monomer complex is more stable than the dimer complex, but the hydride-transfer transition state (TS) is more stable with the dimer in the gas phase. It is thus not *a priori* clear whether an actual reacting species is monomer or dimer for the reaction of a carbonyl compound with BH$_3$ in THF.

In the present study, we have carried out a kinetic experiment for the reaction of ring-substituted benzaldehydes (1-X) and BH$_3$ and examined the effects of the substituent and the concentration of BH$_3$ to answer two important questions: (1) whether the reaction is electrophilic or nucleophilic in nature and what is the origin of that, and (2) which is the actual reacting species, monomer or dimer, at the rate-determining TS? The results showed that the overall reaction is electrophilic, that both free BA and the BA–BH$_3$ complex exist in pre-equilibrium, and that the subsequent rate-determining hydride-transfer TS contains two molecules of BH$_3$, one acting as a reducing agent and the other as a catalyst.

## RESULTS AND DISCUSSION

It has been reported that the presence of NaBH$_4$ as a stabilizer in a commercial BH$_3$–THF solution leads to a drastic acceleration of the reduction.[5] To examine the intrinsic reactivity of BH$_3$, we prepared a fresh THF solution of BH$_3$ by the reaction of BF$_3$ and NaBH$_4$ according to the literature.[13] The concentration of the BH$_3$ solution was determined by azotometry, in which the amount of H$_2$ gas evolved by mixing BH$_3$–THF and 50% aqueous glycerol was measured. The rates of the reactions of 1-X and BH$_3$ were determined by running the reaction of 1-X (1 mM) with a large excess of BH$_3$ (35.8 mM) and by following the decay of absorbance of 1-X photometrically at 25 °C.

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## Concentration effect

The effect of BH$_3$ concentration on the reaction rate was measured to examine the reaction order in BH$_3$. In Table 1 are listed pseudo first-order rate constants for the reaction of 1-H (1.0 mM) with BH$_3$ of variable concentrations. Logarithmic plots between the pseudo first-order rate constants and the concentrations of BH$_3$ gave a linear correlation with a slope of 1.58 (Fig. 1).

In a previous kinetic study, Jockel and Schmidt reported that the reaction order of BH$_3$ for the reaction of pinacolone and BH$_3$ in THF was 1.0.[5] They also carried out AM1 calculations and estimated reaction enthalpies for the initial complex-formation and subsequent hydride-transfer steps as $-11$ and $-137$ kcal/mol, respectively. It was then concluded that the complex-formation step is rate determining because the step was much less exothermic than the second step. The proposed mechanism with the rate-determining complex formation was claimed to be consistent with the reaction order of 1.0.[5] However, it should be noted that a large exothermic step does not necessarily have a low barrier and hence the computational results were not conclusive without information on the activation energies. A kinetic deuterium isotope effect ($k_{BH3}/k_{BD3} = 1.07$) was measured for the oxazaborolidine-catalyzed reaction of acetophenone, which indicated that the hydride-transfer step is rate-determining.[14] The relatively small isotope effect lets authors suggest an early TS,[14] which was later supported by calculations.[7] A carbonyl carbon kinetic isotope effect ($k_{12}/k_{14} = 1.035 \pm 0.002$) determined for the BH$_3$ reduction of benzophenone in THF also suggested that the C–H bond-formation step is rate-determining.[8]

Kinetic analyses of the BH$_3$ reduction are not simple because of the secondary reactions of the initially formed alkoxide (ROBH$_2$). Nevertheless, the present kinetic study provides information on the reaction of BH$_3$ because the reactions were carried out with a large excess of BH$_3$ over benzaldehyde. The concentration dependence in Fig. 1 reveals that the reaction of benzaldehyde with BH$_3$ in THF is 1.6th order with respect to
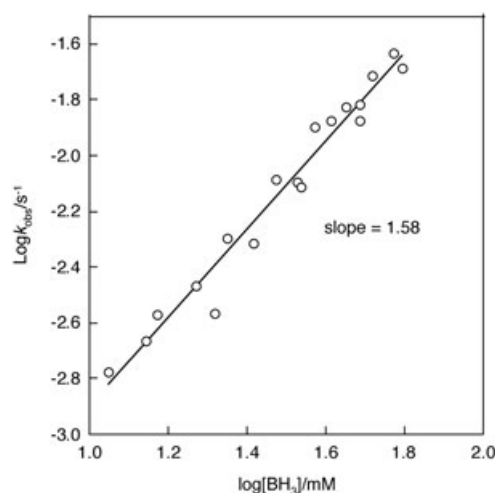


**Figure 1.** Logarithmic plots between pseudofirst-order rate constants and concentrations of BH$_3$ for the reduction of PhCHO in THF at 25 °C. [PhCHO] = 0.1 mM

BH$_3$, which differs from the reported value of 1.0 for the reaction of pinacolone with BH$_3$.[5] The origin of the discrepancy is not clear, but the difference in BH$_3$ concentration would be responsible; a high concentration range (0.1–0.6 M) was used in the previous study, whereas we used a much lower concentration range (0.011– 0.063 M) because of a larger absorbance of 1-H than pinacolone (*vide infra*).

The 1.6th reaction order for BH$_3$ requires that more than 1 molecule of BH$_3$ are involved at the rate-determining TS. A likely interpretation is illustrated in Scheme 1, in which the initial complex formation is first order in BH$_3$, and the second BH$_3$ molecule attacks the complex to form a sterically favorable six-membered TS. A similar six-membered TS has been proposed for the oxazaborolidine-catalyzed BH$_3$ reduction of ketones.[7] In the TS in Scheme 1, one BH$_3$ molecule acts as a reducing agent and the other serves as a catalyst and facilitates the reaction. If the initial complexation equilibrium lies on the left-hand side, the overall reaction order of BH$_3$ would be 2. If, on the other hand, the equilibrium lies completely on the right-hand side with the formation of a stable complex, the complex becomes an effective reactant and hence the reaction order of BH$_3$ would be 1.0. Thus, the apparent reaction order of BH$_3$ can be a value somewhere between 1.0 and 2.0 depending on the position of the equilibrium. The present results can be rationalized by assuming that a mixture of free aldehyde and the BH$_3$ complex existing in equilibrium serves as an effective reactant state. It is likely that in the previous study on the BH$_3$ reduction of pinacolone, the high concentrations of BH$_3$ made the complex the effective reactant giving the reaction order of BH$_3$ of 1.0.[5]
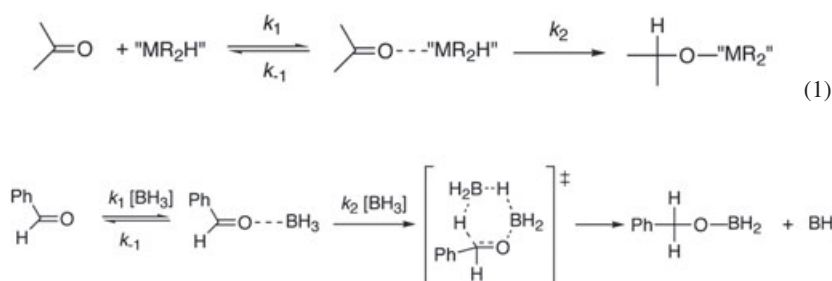
## Substituent effect

The pseudo first-order rate constants for the reactions of 1-X and BH$_3$ are listed in Table 2. The Hammett plot of the reaction is shown in Fig. 2. The observed small negative ρ value is similar to those observed for the reductions of benzophenones with boron hydride reagents and indicates that the reduction with BH$_3$–THF is electrophilic in nature.

The position of the initial equilibrium should influence the sign and the size of the Hammett ρ value for the reaction of 1-X. Because of the amphoteric nature of BH$_3$, the reactions

**Table 1.** Pseudo first-order rate constants for BH$_3$ reduction of 1-H with various BH$_3$ concentrations in THF at 25 °C[a]

| [BH$_3$]/mM | $10^3\, k_{obs}$/s$^{-1}$ |
|---|---|
| 11.25 | 1.65 ± 0.39 |
| 14.00 | 2.16 ± 0.42 |
| 15.00 | 2.63 ± 0.43 |
| 18.75 | 3.37 ± 0.70 |
| 20.85 | 2.69 ± 0.17 |
| 22.50 | 5.01 ± 0.17 |
| 26.25 | 4.80 ± 0.27 |
| 30.00 | 8.10 ± 0.63 |
| 33.75 | 7.93 ± 0.36 |
| 34.75 | 7.51 ± 0.50 |
| 37.50 | 12.5 ± 0.4 |
| 41.25 | 13.1 ± 0.4 |
| 45.00 | 14.8 ± 0.2 |
| 48.75 | 15.1 ± 0.8 |
| 48.85 | 13.2 ± 0.6 |
| 52.50 | 19.3 ± 0.6 |
| 60.00 | 23.1 ± 0.8 |
| 62.55 | 20.5 ± 0.8 |

[a][1-H] = 1.0 mM.

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(1)



**Scheme 1.** Plausible mechanism of the reaction of benzaldehyde with excess $BH_3$ in THF

**Table 2.** Pseudofirst-order rate constants for $BH_3$ reduction of 1-X in THF at 25 °C[a]

| X | $10^2\, k_{obs}/s^{-1}$ |
|---|---|
| *p*-MeO | $1.67 \pm 0.02$ |
| *p*-Me | $1.46 \pm 0.05$ |
| *m*-Me | $1.18 \pm 0.09$ |
| H | $1.11 \pm 0.03$ |
| *p*-F | $1.11 \pm 0.06$ |
| *p*-Cl | $0.896 \pm 0.074$ |
| *m*-Cl | $0.760 \pm 0.022$ |
| *m*-CF$_3$ | $0.643 \pm 0.022$ |
| *p*-CF$_3$ | $0.637 \pm 0.042$ |

[a]Concentration of 1-X is 1 mM and that of $BH_3$ is 35.8 mM. See Experimental section for details.



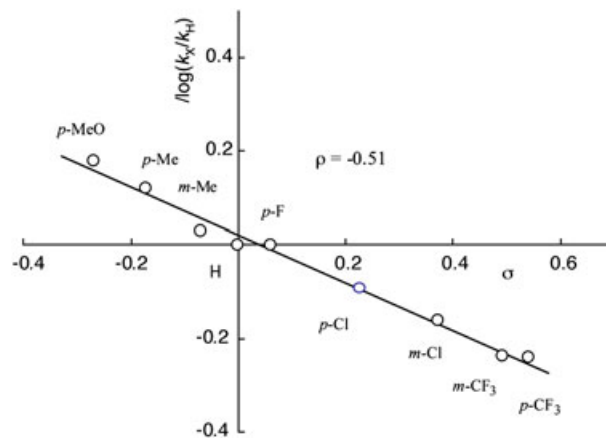**Figure 2.** Hammett correlation of the $BH_3$ reduction of $XC_6H_4CHO$ in THF at 25 °C

of 1-X may give either a positive or negative $\rho$ value. The initial complex formation is an electrophilic reaction of $BH_3$, and thus a $\rho$ value on this equilibrium should be negative. Indeed, it was reported that the Hammett $\rho$ value for the complex-formation equilibrium between 1-X and $BF_3$ in $CH_2Cl_2$ was largely negative ($-3.5$ at $-78$ °C).[15] Although $BF_3$ is a much stronger acid and therefore forms a much stronger complex with aldehyde than $BH_3$, the result clearly indicated that the complex formation is a strongly electrophilic process. The subsequent hydride-transfer step is a nucleophilic process and should give a positive $\rho$ value. A previous computational study on the reaction of benzaldehyde and $BH_3$ has shown that the Hammett $\rho$ value for the initial complex formation is $-1.71$ at MP26-311 G*, whereas the subsequent hydride-transfer step gives a positive $\rho$ value of 0.66.[12] Although a comparison between the gas-phase calculations and solution experiments is not straightforward, the calculated $\rho$ values are larger for the first step in their absolute magnitude than the second step, meaning that the reaction is electrophilic in the overall reactivity ($\rho = -1.71 + 0.66 = -1.05$). A positive $\rho$ value would be detected only when the complex serves as an effective reactant. The observed small $\rho$ value of $-0.51$ is consistent with the mechanism in Scheme 1, in which free benzaldehyde and the $BH_3$ complex coexist in equilibrium.

In conclusion, the present kinetic study revealed that the reaction of benzaldehyde and $BH_3$ in THF proceeds through a rate-determining hydride-transfer TS with two $BH_3$ molecules, in which one molecule of $BH_3$ acts as a reducing agent and the other serves as a catalyst.

## EXPERIMENTAL SECTION

### Materials

Tetrahydrofuran was dried over benzophenone ketyl and distilled before use. The $BH_3$–THF solution was prepared from $NaBH_4$ and $BF_3 \cdot O(Et)_2$ in diglyme according to the literature.[13] The concentration of $BH_3$ in THF was determined by measuring the $H_2$ evolved by adding a known amount of the $BH_3$–THF solution to $H_2O$–glycerol (1:1). Substituted benzaldehydes were commercially available and were purified by distillation.

### Kinetics

Dry THF solutions of aldehyde (2.0 mM) and $BH_3$ at preset concentrations were prepared in a constant temperature bath at $25 \pm 0.1$ °C. The reaction was carried out by mixing equal amounts (1.5 mL) of these two solutions in a UV cell at $25 \pm 0.5$ °C. Rate constants were determined under pseudofirst-order conditions by following the decay of the absorbance of aldehydes photometrically. Experimental errors listed in Tables 1 and 2 are standard deviations from at least five determinations.

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