

# On the Mechanism of Addition of Lithium Pinacolone Enolate to Benzaldehyde: Polar or Electron Transfer?

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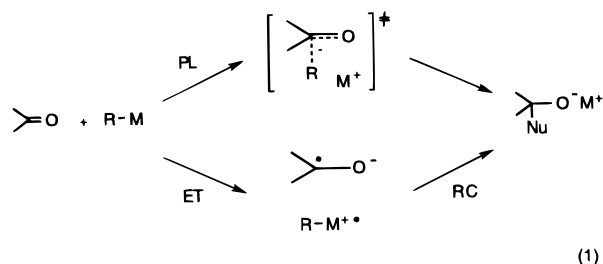
**Abstract:** The carbonyl-carbon kinetic isotope effect (KIE) and the substituent effect were measured for the reaction of lithium pinacolone enolate ( $\text{CH}_2=\text{C}(\text{OLi})\text{C}(\text{CH}_3)_3$ ) with benzaldehyde, and the results were compared with those for other lithium reagents such as MeLi, PhLi, and  $\text{CH}_2=\text{CHCH}_2\text{Li}$ . Ab initio MO calculations ( $\text{HF}/6\text{-}31+\text{G}^*$ ) were carried out to estimate the equilibrium IE on the addition to benzaldehyde. A carbonyl addition reaction, in general, proceeds by way of either a polar direct nucleophilic attack (PL) in a one-step or a two-step process going through a radical ion intermediate (eq 1). The carbonyl-carbon KIE is of primary nature for the PL or the RC rate-determining ET mechanism, while it is considered to be secondary for the ET rate-determining mechanism. The reaction of lithium pinacolone enolate with benzaldehyde gave a small positive KIE ( $^{12}\text{k}/^{13}\text{k} = 1.019$ ), which is larger than the theoretical equilibrium IE ( $^{12}\text{K}/^{13}\text{K} = 1.006$ ) determined by the MO calculations. Thus, there is a reaction-coordinate contribution to the observed KIE. This is in sharp contrast to the absence of KIE ( $^{12}\text{k}/^{14}\text{k} = 1.000$ ) measured previously for the MeLi addition. Dehalogenation and enone-isomerization probe experiments showed no evidence of a single electron transfer to occur during the course of the reaction. The primary carbonyl-carbon KIE together with the substituent effect and chemical probe experiments led to the conclusion that the reaction of lithium pinacolone enolate with benzaldehyde proceeds via the polar mechanism.

## Introduction

Lithium enolate is an important reagent in its versatile synthetic utility, especially for enantioselective reactions. Design of the reaction, which is critical to attain high selectivity, requires the knowledge of the mechanistic details. However, understanding of the mechanism of this fundamental transformation is still incomplete. The well-known tendency of the organolithium reagent to form aggregates<sup>1</sup> is a source of difficulty in understanding the mechanism, but a more fundamental question remained to be solved is the course of the reaction.

There are in general two possible reaction routes, the polar addition (PL) mechanism and the electron transfer (ET) - radical coupling (RC) sequence, eq (1), in nucleophilic addition reactions, and the mechanism is highly nucleophile dependent. Recently Arnett reported that the reaction of lithium pinacolone enolate with benzaldehyde proceeds via the polar mechanism on the basis of the comparison of the experimental activation energy with the energy required for ET determined electrochemically.<sup>1a,2</sup> The conclusion was different from that for the reaction of the same nucleophile with benzophenone drawn by Ashby, who clearly indicated the occurrence of an electron

transfer during the reaction by observing an EPR spectrum and by analyzing kinetic behavior of the spectrum.<sup>3</sup>



We have previously reported that mechanistic criteria such as kinetic isotope effect (KIE), substituent effect, and chemical probe experiments are useful in clarifying the reaction pathway of nucleophilic addition reactions of RLi, RMgX, and Wittig reagents.<sup>4–6</sup> For example, the addition reactions of MeLi, PhLi, and  $\text{CH}_2=\text{CHCH}_2\text{Li}$  with benzophenone and benzaldehyde gave in all cases a very small carbonyl-carbon KIE and a small Hammett  $\rho$  value, except for the reaction of highly hindered mesityl phenyl ketone. This suggested that most of these reactions proceed via a rate-determining ET mechanism. Mesityl phenyl ketone reacted with MeLi much slower than other

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substituted benzophenone derivatives and showed a sizable carbonyl-carbon KIE, and the results were ascribed to a slower RC step for this sterically hindered ketone and hence a shift of rate-determining step from ET (for benzophenone) to RC (for mesityl phenyl ketone).<sup>5</sup> In sharp contrast, the reaction of RMgX gave medium sized KIEs in most cases, and this was concluded to be due to rate-determining RC mechanism.<sup>4</sup>

Our conclusion that the reaction of MeLi, PhLi, and CH<sub>2</sub>=CHCH<sub>2</sub>Li with the aromatic carbonyl compounds proceed via an ET process was different from that by Arnett for the reaction of lithium pinacolone enolate. The discrepancy should be due to either the difference of reagents or the difference of the mechanistic criteria. In the present study, the KIE, substituent effect, and chemical probe experiments were carried out for the addition reaction of lithium pinacolone enolate with benzaldehyde. The results clearly show that the mechanism for the enolate is different to other RLi and is polar.

## Results and Discussion

Lithium pinacolone enolate was prepared from the reaction of pinacolone and lithium diisopropylamide in THF at -78 °C and allowed to react with benzaldehyde at 0 °C. Substituent effects were determined by competition experiments as previously reported,<sup>4-6</sup> and carbonyl carbon-13 and C<sub>6</sub>D<sub>5</sub> KIEs were measured as described in the Experimental Section. We used in the present study FT ion-cyclotron resonance mass spectrometry (FT-ICR MS) to determining the carbon KIE of <sup>13</sup>C-labeled compound rather than the conventional liquid scintillation counting method of radioactive <sup>14</sup>C compounds. This new method can be a powerful tool in mechanistic study by allowing us to measure KIEs of nonradioactive elements, such as <sup>18</sup>O, <sup>15</sup>N, D, etc. in addition to <sup>13</sup>C. The FT-ICR method has previously been used to determine equilibrium IEs successfully.<sup>10</sup> Two chemical probe experiments, enone isomerization and dehalogenation probes, were carried out as described previously.<sup>6c,7</sup> Ab initio MO calculations were carried out to estimate the magnitude of equilibrium IEs for the polar process by using the Gaussian 92 and 94 packages of program.<sup>8,9</sup>

**Carbon KIE.** Among the three possible mechanistic alternatives, distinction of the rate-determining ET mechanism from PL and rate-determining RC can be achieved in a rather straightforward manner by using the carbonyl-carbon KIE as a probe. A carbon KIE is larger if the labeled carbon atom is involved to a greater extent in the reaction-coordinate vibrational motion at the rate-determining transition state,<sup>11,12</sup> and thus the

**Table 1.** Kinetic and Equilibrium Isotope Effects for the Reaction of Lithium Pinacolone Enolate and Benzaldehyde

labeled position	$k/k^*$ <sup>a</sup>	$K/K^*$ <sup>b</sup>
$k_H/k_{D5}$	1.031 ± 0.004	1.094
$k_{D5}/^{13}k$	0.988 ± 0.002	
$^{12}k/^{13}k$	1.019 ± 0.004 <sup>c</sup>	1.006

<sup>a</sup> Experimental kinetic isotope effect in THF at 0 °C. <sup>b</sup> Calculated equilibrium isotope effect on the addition process at 0 °C. <sup>c</sup> Calcd from  $k_H/k_{D5}$  and  $k_{D5}/^{13}k$ .

carbonyl carbon KIE is expected to be large for the PL and the rate-determining RC mechanism because the carbonyl carbon is heavily involved in these C–C bond forming processes. On the other hand, the carbon KIE is expected to be small for the rate-determining ET mechanism since there is no contribution from the reaction-coordinate motion. Distinction between PL and rate-determining RC is more difficult, and kinetic methods like KIE are almost ineffective because the two transition states behave in a similar manner in kinetic criteria. Another way to differentiate these two mechanisms is needed which examines the possible intervention of a radical ion-pair intermediate in the ET-RC sequence, and this will be discussed later.

Isotope effects were determined for C<sub>6</sub>D<sub>5</sub>CHO vs C<sub>6</sub>H<sub>5</sub>CHO and C<sub>6</sub>H<sub>5</sub><sup>13</sup>CHO vs C<sub>6</sub>D<sub>5</sub>CHO in order to avoid the interference of <sup>13</sup>C natural abundance in intensity measurement. The observed KIEs at 0 °C were listed in Table 1. In discussing the observed KIEs, it is useful to know the magnitudes of IEs on the corresponding equilibria. For this purpose, theoretical isotope effects on the addition equilibrium were computed by using ab initio MO methods. Thus, benzaldehyde and benzaldehyde–methyl lithium adduct were fully optimized at HF/6-31+G\*, and their vibrational frequencies were calculated. MeLi was used here instead of lithium pinacolone enolate for simplicity assuming that the equilibrium IEs are not much different for the MeLi addition and the lithium enolate addition. Equilibrium IEs for carbonyl-<sup>13</sup>C, aldehyde-*d*<sub>1</sub>, and phenyl-*d*<sub>5</sub> species were computed from the frequencies of isotopomers by using eq 2 and listed in Table 1. The HF frequencies were scaled down by a factor of 0.89 in the IE calculations.

$$\frac{k_1}{k_2} = \frac{\left[ \frac{\nu_{L1}^\ddagger}{\nu_{L2}^\ddagger} \right] \prod_{i=1}^{3n-6} \frac{u_{2i}^\ddagger}{u_{1i}^\ddagger} \prod_{i=1}^{3n-6} \left( \frac{1 - e^{-u_{1i}^\ddagger}}{1 - e^{-u_{2i}^\ddagger}} \right) \exp \left[ \sum_{i=1}^{3n-6} (u_{1i}^\ddagger - u_{2i}^\ddagger) / 2 \right]}{\prod_{i=1}^{3n-7} \frac{u_{2i}^\ddagger}{u_{1i}^\ddagger} \prod_{i=1}^{3n-7} \left( \frac{1 - e^{-u_{1i}^\ddagger}}{1 - e^{-u_{2i}^\ddagger}} \right) \exp \left[ \sum_{i=1}^{3n-7} (u_{1i}^\ddagger - u_{2i}^\ddagger) / 2 \right]} \quad (2)$$

The experimental carbonyl-<sup>13</sup>C KIE was small positive ( $^{12}k/^{13}k = 1.019$ ), which corresponds to 1.039 of <sup>14</sup>C KIE. This value is similar to carbonyl-<sup>14</sup>C KIEs previously observed for polar nucleophilic additions to benzophenone;  $^{12}k/^{14}k = 1.035$  (BH<sub>3</sub>/THF), 1.021 (AlH<sub>3</sub>/Et<sub>2</sub>O), LiAlH<sub>4</sub>/THF (1.017), LiAlH<sub>4</sub>/Et<sub>2</sub>O (1.024), LiBH<sub>4</sub>/Et<sub>2</sub>O (1.043), and NaBH<sub>4</sub>/2-PrOH (1.066).<sup>13</sup> The theoretical equilibrium IE at carbonyl <sup>13</sup>C for the addition to benzaldehyde was found to be small ( $^{12}k/^{13}k = 1.006$ ). The fact that the experimental carbonyl-<sup>13</sup>C KIE is larger than the corresponding equilibrium IE indicates that the carbonyl-carbon KIE is of primary nature, suggesting that the bonding to the carbon is changing at the rate-determining transition state. The IE results are consistent with the PL mechanism for the addition reaction, although the IE results by themselves do not eliminate the possibility that the reaction proceeds via fast ET followed by a slow rate-determining RC step.

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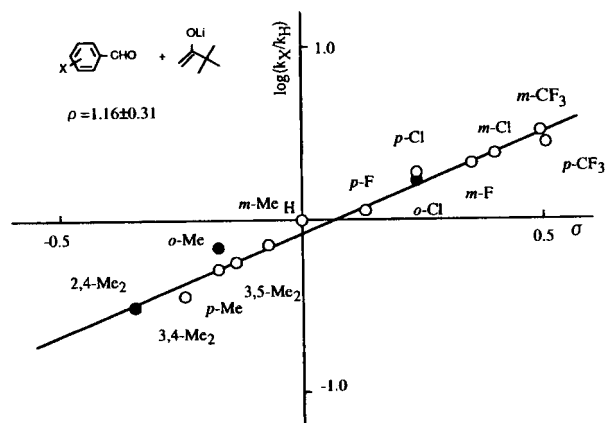
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**Figure 1.** Variations of reactivity with  $\sigma$  values for the reaction of lithium pinacolone enolate and substituted benzaldehydes in THF at 0 °C.

The magnitude of the carbonyl carbon KIE for the present reaction is clearly different from those observed for nucleophilic additions to benzophenone of other RLi reagents; all the reactions of MeLi, PhLi, and  $\text{CH}_2=\text{CHCH}_2\text{Li}$  with benzophenone as well as the reaction of PhLi with benzaldehyde gave very small carbonyl carbon KIEs, from which the rate-determining ET mechanism was concluded.

Since  $\text{D}_5$  KIE is a secondary effect, the contribution from reaction-coordinate vibration to the IE is negligible or very small if any. The magnitude of the KIE should thus be in between 1.0 and the equilibrium IE (1.094), depending on the position of the TS along the reaction coordinate. The observed  $\text{D}_5$  KIE of 1.032 is one-third of the equilibrium IE, which suggests that the TS is reached at about one-third along the reaction coordinate if the reaction proceeds via the PL mechanism.

**Substituent Effects.** Substituent effects on the reactivity of substituted benzaldehydes with lithium pinacolone enolate were measured in THF at 0 °C by competition experiment. Figure 1 shows the relationship between  $\log(k_X/k_H)$  and substituent constant  $\sigma$ . Since the  $\sigma$  constants of the ortho substituents were not available, the  $\log(k_X/k_H)$  values for the ortho derivatives were plotted against the corresponding para-substituent constants and are indicated by closed circles, and the  $\rho$  value was calculated from the meta- and para-substituted derivatives. The observed medium-sized  $\rho$  value ( $1.16 \pm 0.31$ ) indicates that the substituent electronic effect is significant in the reaction. The results are in sharp contrast to those observed for the reactions of MeLi, PhLi and  $\text{CH}_2=\text{CHCH}_2\text{Li}$ , in which much smaller  $\rho$  values were observed. Thus, the character of the rate-determining TS is different for the lithium enolate and for MeLi, PhLi, and  $\text{CH}_2=\text{CHCH}_2\text{Li}$ .

If the addition reaction proceeds via the PL mechanism, the structure of benzaldehyde should vary monotonically on going from the reactant state to the product state. The ratio of the Hammett  $\rho$  value on rate to that on equilibrium may be taken as a measure of the position of the TS along the reaction coordinate. Arnett determined the substituent effects on the heat of reaction for the addition equilibrium of the lithium enolate and para-substituted benzaldehydes in THF by the thermochemical method.<sup>1a</sup> Assuming that the entropy contribution to the equilibrium is the same for a family of substituted benzaldehydes, the reported value gives  $\rho = 2.70$  on the  $\log(k/k_0)$  scale at 0 °C, which allows us to estimate the position of the TS of the present reaction as roughly 40% ( $1.16/2.70$ ). This estimation is in fair agreement with the result based on the  $\text{D}_5$  IE.

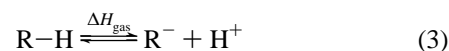
**Probe Experiments.** Although the results of KIEs and substituent effects are fully consistent with the PL mechanism,

**Table 2.** Z-E Isomerization during the Reaction of Z-Enone with Lithium Pinacolone Enolate in THF at 0 °C

reagent	time, min	recovered Z:E
enolate	1	99.6:0.4
	60	98.7:1.3
	120	97.9:2.1
blank	60	99.8:0.2

it is important to consult with other experimental criteria to distinguish the PL mechanism from the RC mechanism in which the radical coupling process following a fast ET step is rate determining. One way to determine whether the reaction proceeds via the PL or RC mechanism is to detect the presence of radical ion pair intermediate during the reaction. Two chemical probe experiments, dehalogenation<sup>7</sup> and enone isomerization,<sup>14</sup> have been shown to be useful in detecting the intermediate for the additions of Grignard and Wittig reagents.<sup>6,7</sup> These are probes that measure whether a reagent has enough ability to transfer an electron to halobenzophenone and enone, respectively, and therefore, if these two probes were positive, then there would be a good possibility that the reaction proceeds via the ET-RC sequence. The basis idea of these probes were discussed previously in detail.<sup>6c</sup> In the dehalogenation probe experiment, *o*-iodobenzophenone was mixed with lithium pinacolone enolate in THF at 0 °C, and after appropriate reaction time the reaction mixture was analyzed by GC. The reaction gave no dehalogenated product and only the starting *o*-iodobenzophenone was recovered, and thus the dehalogenation probe was negative for the lithium enolate. In the enone isomerization, (*Z*)-2,2,6,6-tetramethylhept-4-ene-3-one was mixed with lithium pinacolone enolate in THF at 0 °C, and the reaction mixture was analyzed by GC. As listed in Table 2, slight enone isomerization was detected only for a prolonged reaction time, and thus the enone-isomerization probe was negative for the lithium enolate. In summary, these two probe experiments suggest that ET is not involved during the reaction of lithium pinacolone enolate with benzaldehyde.

**Mechanistic Consideration.** On the basis of the present experiment, we could conclude that the reaction of lithium pinacolone enolate with benzaldehyde proceeds via the polar mechanism. In Table 3 were summarized the results of mechanistic study on the addition reactions of several organolithium reagents with benzaldehyde and benzophenone. There can be seen a clear mechanistic gap between the lithium enolate and the other lithium reagents. It is worthy to note that the mechanistic difference correlates with the stability of the reagents measured by the intrinsic acidity of the conjugate acids of R anions in the gas phase. The intrinsic acidity of R-H can be estimated from the gas phase heat of formation (eq 3) from the data compiled in the literature:<sup>15</sup> 416.8 kcal/mol (R = Me), 400.8 (Ph), 390.7 ( $\text{CH}_2=\text{CHCH}_2$ ), and 368.0 ( $(\text{CH}_3)_3\text{CC}(\text{=O})\text{CH}_2$ ). The enolate reagent whose conjugate acid is the most



acidic reacts with benzaldehyde via the polar mechanism whereas the reagents whose conjugate acids are less acidic go through the ET process. It is thus implied that the rate of the ET step depends more on the reactivity of a nucleophile than the rate of the PL step as schematically shown in Figure 2 and that the crossing point is in between allyllithium and lithium pinacolone enolate for the reaction with benzaldehyde.

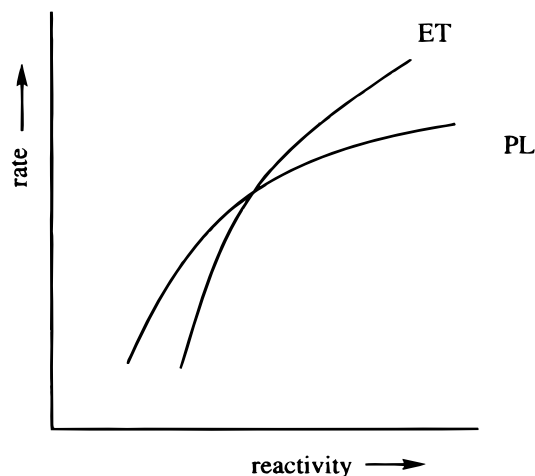
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**Table 3.** Mechanism of the Reactions of Organolithium Reagents with Aromatic Carbonyl Compounds<sup>a</sup>

Li reagent	substrate	carbonyl-carbon KIE <sup>b</sup>	Hammett $\rho$ value	dehalogen <sup>c</sup>	enone isomeriz <sup>c</sup>	rate determ <sup>c</sup> step
MeLi	benzophenone	1.000 $\pm$ 0.002	0.23 $\pm$ 0.09	(yes) <sup>c</sup>	no	ET
PhLi	benzophenone	1.003 $\pm$ 0.001	0.19 $\pm$ 0.08			ET
PhLi	benzaldehyde	0.998 $\pm$ 0.003	0.13 $\pm$ 0.07			ET
AllylLi	benzophenone	0.994 $\pm$ 0.003	0.21 $\pm$ 0.09			ET
Li enolate	benzaldehyde	1.039 $\pm$ 0.009 <sup>d</sup>	1.16 $\pm$ 0.31	no	no	PL

<sup>a</sup> In THF at 0 °C. Data for MeLi, PhLi, and AllylLi were taken from ref 5. <sup>b</sup> <sup>12</sup>k/<sup>14</sup>k. <sup>c</sup> Complex mixture due to radical reactions. <sup>d</sup> Corrected to <sup>12</sup>k/<sup>14</sup>k.



**Figure 2.** Schematic picture of the dependence of the rates of the PL and ET processes on the nucleophile reactivity.

The EPR study by Ashby indicated that the ET can occur between lithium pinacolone enolate and benzophenone in THF. Since the reduction potential of benzaldehyde is similar to that of benzophenone, one might expect that ET is also involved during the reaction of the enolate with benzaldehyde. However, the rate of ET to benzophenone was reported to be very slow, taking about 20 h at 25 °C for the EPR active species to be the maximum concentration.<sup>3</sup> In contrast, the reaction of the enolate with benzaldehyde is completed in 20 s. Thus, the polar addition process is much faster than the potential ET process for the reaction of the enolate with benzaldehyde.

We have studied the reaction of the enolate with benzophenone by the same criteria as for benzaldehyde. However, it was unsuccessful because the reaction with benzophenone did not go to completion due apparently to the occurrence of the backward reaction under the reaction conditions. In order to check whether the backward reaction indeed occurred for the reaction with benzophenone, the isolated addition product of benzophenone (2,2-dimethyl-5-hydroxy-5-phenyl-3-pentanone) was mixed with *n*-BuLi to generate lithium alkoxide. On standing for several minutes the solution generated benzophenone indicating the presence of the backward reaction, which deteriorates the competition experiment. Apparently methods other than the competition experiment is needed to investigate the reaction of the lithium enolate with benzophenone.

## Experimental Section

**Materials.** THF was dried over sodium/benzophenone and distilled immediately before use. All substituted benzaldehydes were commercially available and purified either by distillation or recrystallization. Benzaldehyde-*carbonyl*-<sup>13</sup>C was synthesized by the pyridinium dichromate oxidation of benzyl alcohol-<sup>7,13</sup>C, which was prepared by carbonylation of phenylmagnesium bromide with <sup>13</sup>CO<sub>2</sub> gas (99%, Aldrich) and the borane reduction of the resultant benzoic acid-<sup>7,13</sup>C. Benzaldehyde-*d*<sub>5</sub> was prepared according to the same sequence of reactions starting with bromobenzene-*d*<sub>5</sub>.

**Reactions.** All reactions were carried out at 0 °C under dry nitrogen using the Schlenk tube technique.<sup>16</sup> A lithium pinacolone enolate

solution was prepared by mixing an equimolar amount of sodium diisopropylamide and pinacolone in THF at -78 °C. The reactions of the enolate with substituted benzaldehydes gave the corresponding carbonyl adducts as the only product. The products were isolated by TLC and characterized by <sup>1</sup>H NMR (JEOL JNM-EX 400, CDCl<sub>3</sub>). Material balance of the reaction was confirmed for the parent benzaldehyde to be excellent (99.9  $\pm$  0.9%).

**Relative Reactivity Measurement.** A pair of benzaldehydes (normally the parent and a substituted one, 0.5 mmol each) and 1-methylnaphthalene (ca 0.1 mmol, internal standard) were placed in a dry, serum-capped test tube and dissolved in 3.0 mL of dry THF. The solution was divided to two parts; thus, each test tube contained two kinds of benzaldehydes, 0.25 mmol each. To one test tube out of the two was added 1.0 mL of a lithium pinacolone enolate solution (0.33 M in THF, 0.33 mmol) at 0 °C by means of hypodermic syringe. The solution was then allowed to react for 20 s. The reaction mixture was treated with aqueous NH<sub>4</sub>Cl, extracted with ether, dried over MgSO<sub>4</sub>, and subjected to HPLC analysis (P-18, CH<sub>3</sub>CN:H<sub>2</sub>O = 7:3, detected at 250 nm). The relative intensity of each reactant to that of the internal standard was compared to the corresponding relative intensity from the solution to which the lithium enolate solution was not added. The fractions of reaction (*f*) were calculated for both reactants, and the reactivity ratio was computed according to the following equation

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

**Carbon-13 KIE Measurement.** The isotope effects were determined for C<sub>6</sub>D<sub>5</sub>CHO vs C<sub>6</sub>H<sub>5</sub>CHO and C<sub>6</sub>H<sub>5</sub><sup>13</sup>CHO vs C<sub>6</sub>D<sub>5</sub>CHO in order to avoid the interference of <sup>13</sup>C natural abundance in intensity measurement. Isotopically labeled and unlabeled benzaldehyde (2.0 mmol each) and 1-methylnaphthalene (0.14 mmol) were dissolved dry THF (7.6 mL), and the solution was divided into eight parts. To each solution was added at 0 °C a preset amount of lithium pinacolone enolate (0.33 M in THF) in such a manner that the fraction of reaction varies from 20% to 80%. After 20 s, the reaction solution was hydrolyzed with NH<sub>4</sub>Cl, and the organic layer was subjected to HPLC in order to determine the fraction of reaction. The organic layer was then transferred to a sample inlet tube, and the volatile materials were removed under reduced pressure. The isotopic ratio of the remaining recovered benzaldehyde was analyzed as follows.

The relative abundance of carbon-13 and -12 was measured on an Extrel FTMS 2001 Fourier transform mass spectrometer equipped with a 3.0 T superconducting magnet. To reduce experimental errors, all operating parameters to affect the relative peak heights were kept constant as far as possible. All experiments were conducted with the EI mode, pulse width of 3 ms, electron energy of 20 eV, and filament current of 2  $\mu$ A. Delay time for excitation was 20  $\mu$ s. The trapping voltage of the analyzing cell was set at 2 V. The pressure of a neutral sample was carefully controlled at  $1.3 \pm 0.1 \times 10^{-7}$  Torr using a variable leak valve (Anelva, High Vacuum Leak Valve 951), because the pressure of the neutral, the number of ions in the analyzing cell, was the most important factor for determining the relative peak heights. The pressures were measured by means of a Bayard-Alpert type ionization gauge (Anelva, MIG-430). The temperature of the sample inlet system was 25 °C, and the ICR chamber was kept at  $50 \pm 1$  °C. The data points of 64 K were used in the acquisition. The mass range for excite and detect events was from 90 to 130. The number of time-domain transients summed prior to the Fourier transform was about

1000, and a three term Blackman-Harris apodization and one zero fill were applied to the time-domain data. The transient was finally transformed into a mass spectrum. The relative abundance of carbon-13 or carbon-12 to the deuterated benzaldehyde was calculated using total peak heights of  $[M - 1]^+$ ,  $M^+$ , and  $[M + 1]^+$ . Under these conditions, the relative abundance values were reproduced to about  $\pm 0.2\%$  on repeated runs. The ICR chamber was baked out at 200 °C for an overnight in order to avoid contamination before a different sample was introduced into the analyzing cell.

**Probe Experiments.** Enone-isomerization and dehalogenation probe experiments were done in a similar manner as reported previously.<sup>6c,7</sup> Z-2,2,6,6-Tetramethylhepta-4-ene-3-one (0.5 mmol) and 1-methylnaphthalene (0.25 mmol) were dissolved in dry THF (1.5 mL), and the solution was divided into three parts. To each of the divided solution

was added lithium pinacolone enolate (0.33 M, 0.5 mL) at 0 °C. The solution was allowed to react for a preset time (1 min, 1 h, and 2 h), and the degree of isomerization was analyzed by GLC (PEG 2m, 180 °C). Dehalogenation experiment was carried out similarly using *o*-iodobenzophenone as a probe substrate instead of enone. After a preset reaction time (1 min, 10 min, and 1 h), no dehalogenated product was detected, and the starting material was recovered.

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