

Account

Base-Promoted, Ketene-Forming Elimination Reactions. Mechanistic Borderline between E2 and E1cb Mechanisms

Sang Yong Pyun[†] and Bong Rae Cho^{*}

[†]Department of Chemistry, Pukyong National University, Busan 608-737, Korea
Department of Chemistry, Korea University, Seoul 136-701, Korea. *E-mail: chobr@korea.ac.kr

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Elimination reactions of $\text{XC}_6\text{H}_4\text{CH}_2\text{CO}_2\text{C}_6\text{H}_5$ -2-Y-4- NO_2 have been studied under various conditions. When X was moderately electron-withdrawing, Y = H, and base-solvent was $\text{R}_2\text{NH-MeCN}$, the reaction proceeded by the E2 mechanism *via* an E1cb-like transition state. Concave downward curve was noted in the Hammett plots. When X = 4- NO_2 , Y = Cl, CF_3 , NO_2 , and the base-solvent was $\text{R}_2\text{NH/R}_2\text{NH}_2^+$ in 70 mol % MeCN(aq), the reaction proceeded by the E2 mechanism. The mechanism changed to a competing E2 and E1cb when X = 4- NO_2 and Y = H, MeO, and to the E1cb when X = 2,4-(NO_2)₂, and Y = NO_2 . From these results, a plausible pathway of the change of the mechanism from E2 to the E1cb extreme is proposed.

Key Words : Elimination reactions, Mechanistic borderline, E2 and E1cb mechanisms

Introduction

Base-promoted elimination reactions are generally divided into α -, β - and γ -eliminations based on the relative positions of atoms bearing the hydrogen and leaving group. In a β -elimination reaction, two atoms or group are removed from adjacent atoms and a new multiple bond is formed. Three principal mechanisms of β -elimination reaction in solution

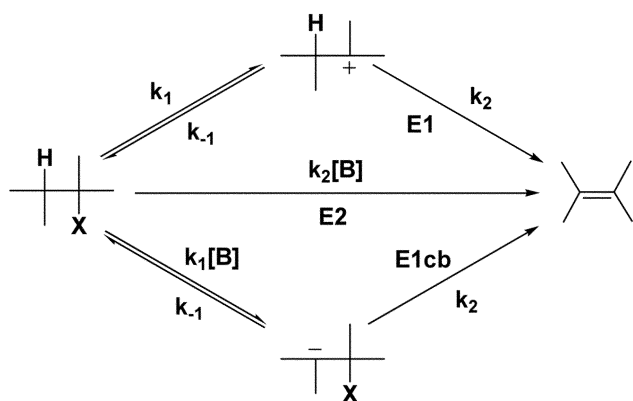


Figure 1. Mechanism of elimination reactions.

have been recognized and are termed E2, E1, and E1cb mechanisms (Figure 1).

The structure-reactivity relationships in elimination reactions have been extensively investigated for more than 50 years.¹⁻¹⁰ One of the most important achievements from this study is the development of the More-O' Ferrall-Jencks energy diagram, which has become a useful tool for the interpretation of not only elimination reactions, but also substitution reactions and the reactions of carbonyl compounds, and found its way in Advanced Organic Chemistry textbooks.^{3,11,12}

Most of the structure-reactivity relationship studies on elimination reactions have been focused on how the E2 transition state changes from E2-central toward E1-like or E1cb-like. The change of E2 transition state toward E1-like has been previously reviewed by one of us.^{4,7} However, relatively little is known about the effects of reactant structure on the E1cb-like transition state.

Perhaps the most important problem in elimination mechanism studies may be the mechanistic borderlines. It is conceivable that the change of the elimination mechanism may occur by "merging" of the transition states, *i.e.*, the concerted mechanism is enforced by the change in the lifetime of the intermediate. The mechanistic changes from

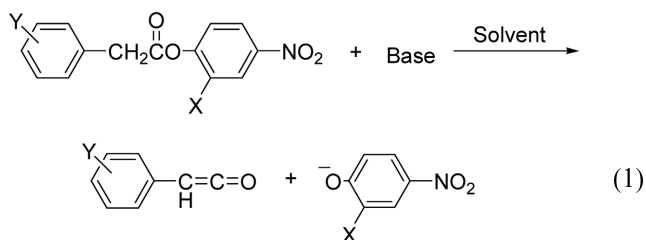
Sang Yong Pyun received his B.S. from Chungnam National University in 1982, his M.S.(1984) and Ph.D.(1990) from Korea University. After his postdoctoral training with Prof. J. M. Takacs at University of Nebraska, he joined Pukyong National University as a full time lecturer in 1993. Currently he is a full professor of organic chemistry at the same university. He has been collaborating with Prof. Cho as a principal researcher since 1985.

Bong Rae Cho was born in Sanchung, Kyungnam in 1949. He obtained his B.S. degree from Seoul National University in 1971.

His Ph.D. degree was granted by Texas Tech University, in 1980, where he studied the mechanism of imine-forming eliminations. After postdoctoral research at UCLA and SRI International, he joined the faculty of Chemistry Department of Korea University in 1982. His research interests varies from mechanistic organic chemistry to the synthesis of organic nonlinear optical materials and two-photon materials. Very recently, he has made another switch in the research area to the development of two-photon probes for application in the real time imaging of living cells by using two-photon microscopy.

E2 to E1cb for eliminations reactions of (2-arylethyl)-ammonium ions¹³ and 9-(2-chloro-2-propyl)fluorene¹⁴ have been concluded to be of this type. Alternatively, the change in mechanism may also involve two concurrent mechanisms having different transition state structures. A change in experimental condition or reactant structure may lower the energy of one of the transition states, which may in turn induce a shift in the major reaction pathway. Such examples have been reported in the E2 and E1 borderline for the methoxide-promoted eliminations from 2-chloro-2-methyl-1-phenylpropane¹⁵ and *N*-(arylsulfonyl)-*N*-alkylbenzylamines⁷ as well as for the solvolytic elimination of 9-(1-*X*-ethyl)fluorenes.⁸ If the E2 mechanism can change to E1 *via* the competing mechanism, similar route should also be possible in the E2 and E1cb borderline. However, no clear evidence for the concurrent E2 and E1cb mechanisms was reported.

One of the promising compounds that may be useful to investigate this problem is the aryl esters of phenylacetic acids. It has been reported that the base-catalyzed hydrolysis of aryl *p*-nitrophenylacetates¹⁶⁻²¹ and other activated esters²¹ proceed by an E1cb elimination to afford the ketene intermediate followed by the addition of water under various conditions. It occurred to us that the ketene-forming eliminations may proceed by the E2 mechanism *via* an E1cb-like transition state if the reactions were conducted under conditions where the carbanion intermediate is destabilized. Concurrent E2 and E1cb mechanisms may also be observed if the reaction conditions are varied so that the



X = H (1), MeO (2), Cl (3), CF₃ (4), NO₂ (5)

Y = H (a), Y = *p*-MeO (b), Y = *m*-Cl (c), Y = *m*-NO₂ (d),

Y = *p*-NO₂ (e), Y = 2,4-(NO₂)₂ (f)

Base-Solvent = R₂NH-MeCN, R₂NH/R₂NH₂⁺- 70 mol % MeCN(aq)

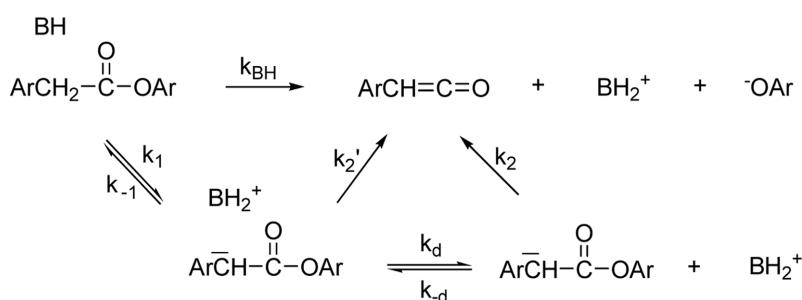
R₂NH = Bz(*i*-Pr)NH, *i*-Bu₂NH, *i*-Pr₂NH, 2,6-DMP, morpholine, tetrahydroisoquinoline, piperidine, pyrrolidine

energies of the two transition states become almost the same. Accordingly, we have investigated a series of reactions between aryl esters of substituted phenylacetic acids **1-5** and secondary amines under various conditions (eq. 1). Sterically bulky amines have been employed to avoid the complications that may be caused by the aminolysis of the substrates. This account summarizes the results of these studies aiming at exploiting the mechanistic borderline between E2 and E1cb mechanisms.

Structure-Reactivity Relationships of E1cb-like Transition State

Reaction Mechanism and Transition State Structure for Eliminations from 1a-d and 5a-e Promoted by R₂NH in MeCN. Reactions of **1a-d** and **5a-e** with R₂NH in MeCN produced benzamides and aryloxide in nearly quantitative yields. The reactions proceeded by the amine-promoted elimination to afford the ketenes followed by the addition of the R₂NH to the intermediate to afford the products. Addition-elimination mechanism (B_{AC}2) is ruled out by the negligible rates of aminolysis compared with the overall rates. Under the reaction condition reported here, the ketene-forming eliminations from **1** and **5** must proceed either via a one-step concerted mechanism or *via* carbanion intermediates (free or ion-paired) in a stepwise mechanism as depicted in Scheme 1.²² The observed general base catalysis with the Brønsted β values ranging from 0.44 to 0.84 rule out the (E1cb)_R, (E1cb)_{ip}, and internal return mechanisms because these mechanisms would exhibit either a specific base catalysis or Brønsted β values near unity.^{3,22} The possibility that the relatively large β values for eliminations from **1a-c** and **5b** are caused by the change to an E1cb mechanism is negated by the interaction coefficients, *i.e.*, $p_{xy}' < 0$, $p_{xy} > 0$, and $p_{yy}' < 0$ (*vide infra*). In addition, the values of $|\beta_{lg}| = 0.41-0.50$ rule out a mechanism in which either $k_1[(E1cb)_{irr}]$ or k_d is rate limiting, for which a small or negligible leaving group effect is expected (Table 1).^{3,22} On the other hand, the results are consistent with an E2 mechanism in which there is partial cleavage of the C_β-H and C_α-OAr bonds in the transition state.

The structure of the transition states have been assessed by the Brønsted β, Hammett ρ, and β_{lg} values. For R₂NH-promoted eliminations from **1a-e** and **5a-e**, values of β = 0.44-0.84, ρ = 2.0-3.6, and $|\beta_{lg}| = 0.41-0.50$ were determin-



Scheme 1

Table 1. Effect of Aryl Substituents upon Brønsted β and β_{lg} Values for Eliminations from $YC_6H_4CH_2CO_2C_6H_3-2-X-4-NO_2$ Promoted by R_2NH in MeCN at 25.0 °C

Y	β		β_{lg}^a
	X = H (1)	X = NO ₂ (5)	
<i>p</i> -OCH ₃	0.84 ± 0.01	0.72 ± 0.02	-0.50
H	0.82 ± 0.01	(0.77 ± 0.03) ^b	-0.43
<i>m</i> -Cl	0.81 ± 0.02	0.56 ± 0.02	-0.41
<i>m</i> -NO ₂	0.68 ± 0.01	0.52 ± 0.02	-0.41
<i>p</i> -NO ₂	—	(0.66 ± 0.07) ^b	—

^aThe base was Bz(*i*-Pr)NH. ^bCalculated with the k_2^E values for eliminations from **1a** and **1e** promoted by $R_2NH/R_2NH_2^+$ buffer in 70 mol%MeCN (aq) at 25.0 °C.

Table 2. Effect of Base Strength upon the ρ_{H1} , τ , and β_{lg} Values for Eliminations from $YC_6H_4CH_2CO_2C_6H_3-2-X-4-NO_2$ Promoted by R_2NH in MeCN at 25.0 °C

base	X = H (1)		X = NO ₂ (5)		β_{lg}^a
	ρ_{H1}	τ	ρ_{H1}	τ	
Bz(<i>i</i> -Pr)NH	3.5 ± 0.1	-2.2 ± 0.1	2.0 ± 0.1	-0.44 ± 0.07	-0.43
<i>i</i> -Bu ₂ NH	3.3 ± 0.1	-1.9 ± 0.1	2.1 ± 0.1	-0.43 ± 0.10	-0.40
<i>i</i> -Pr ₂ NH	3.6 ± 0.1	-2.3 ± 0.1	2.1 ± 0.1	-0.43 ± 0.08	-0.38
2,6-DMP ^b	3.5 ± 0.1	-1.6 ± 0.1	2.1 ± 0.1	-0.48 ± 0.10	-0.37

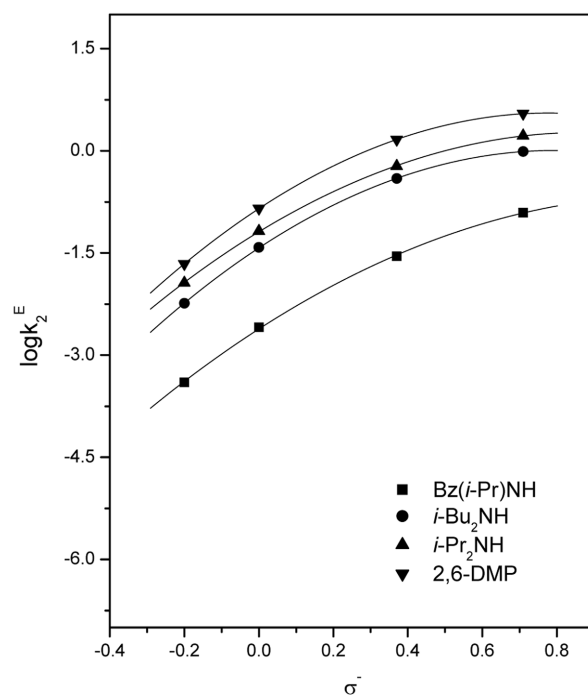
^aY=H. ^b*cis*-2,6-Dimethylpiperidine.

ed (Tables 1 and 2). This indicates moderate to extensive cleavage of the C β -H bonds, significant negative charge development at the β -carbon, and limited extents of C α -OAr bond cleavage in the transition states. Additional support for this conclusion is provided by the interaction coefficients, *i.e.*, $\rho_{xy'} < 0$, $\rho_{xy} > 0$, and $\rho_{yy'} < 0$. The combined results reveal that the ketene-forming eliminations from **1a-d** and **5a-e** proceed by the concerted E2 mechanism via an E1cb-like transition state.

Curved Hammett Plots. An interesting observation from this study was the concave downward Hammett plots in R_2NH -promoted eliminations from **1a-e** (Figure 1). The rate data could be correlated with eq. 2 using a nonlinear regression analysis program, where ρ_{H1} and τ values are the slope of the Hammett plot when Y=H and the proportionality factor by which the ρ value is influenced by the electron-withdrawing ability of the substituents, respectively.

$$\log(k/k_0) = \rho_{H1}\sigma^- + \tau(\sigma^-)^2 = (\rho_{H1} + \tau\sigma^-)\sigma^- \quad (2)$$

Causes for the curved Hammett plots have been attributed to (i) the change in mechanism, (ii) a single mechanism with a different extent of bond formation and cleavage in the transition state, and (iii) a different balance of polar and resonance effects by different substituents in the transition state.²³⁻²⁶ The origin of the downward curvature observed in this study can be attributed to the possibility (ii). Since the reactions proceed by a common E2 mechanism, possibility (i) can be ruled out. Possibility (iii) can also be negated because the downward curvature is caused by the stronger

**Figure 2.** Hammett plots for the ketene-forming eliminations from $YC_6H_4CH_2CO_2C_6H_3-2-MeO-4-NO_2$ promoted by R_2NH in MeCN at 25.0 °C.

electron withdrawing groups, not by the electron-donating groups such as *p*-MeO, which is the only *para* substituent employed in this study that may cause such an effect. On the other hand, the results can readily be interpreted in terms of a gradual decrease in the transition state carbanionic character with a stronger electron-withdrawing β -aryl substituent. Because the ketene-forming elimination is assumed to proceed *via* an E1cb-like transition state on the horizontal reaction coordinate, the transition state would be shifted toward the reactant by a stronger electron-withdrawing β -aryl substituent, to decrease the extent of negative charge development. The transition state would not be stabilized as effectively by the substituent as when there is no such effect. Hence, the rates of eliminations from such substrates would become slower than expected from the substituent effect, which in turn cause a downward curvature in the Hammett plot. Furthermore, this effect would be more pronounced for a more carbanionic transition state, to increase the curvature. Consistent with this prediction is the excellent linearity in the plot of $|\tau|$ against ρ_{H1} values noted for eliminations from **1-5** with R_2NH in MeCN (plot not shown). Therefore, the observed values of $\rho_{H1} = 3.5-2.0$ for the ketene-forming eliminations can be interpreted with a significant negative charge development at the β -carbon in the transition states, which decreases gradually as the electron-withdrawing ability of the substituent increases. It should be noted that concave upward Hammett plots were observed in elimination reactions that proceed *via* the E1-like transition state.²⁷⁻²⁹ The opposite curvatures observed for these two extremes in the spectrum of the variable E2 transition state seem to have a common origin, *i.e.*, the change in the charge

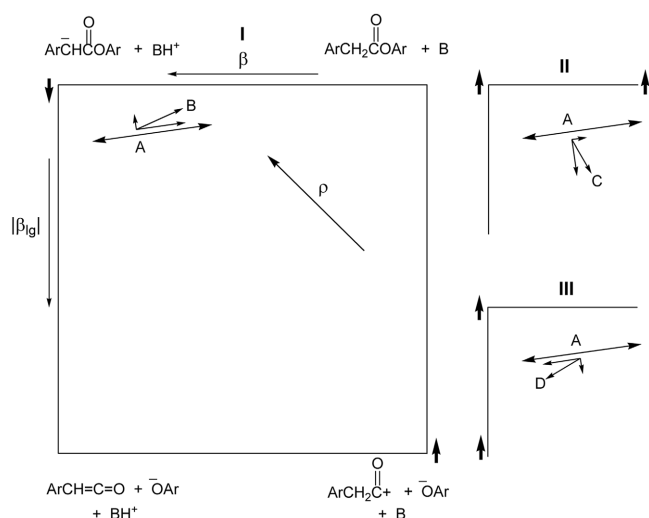


Figure 3. Reaction coordinate diagram for ketene-forming eliminations. The effects of the change to a stronger electron-withdrawing substituent, a better leaving group, and a weaker base are shown by the shift of the transition state from A to B, A to C, and A to D in I, II, and III, respectively.

character of the E2 transition state.

Structure-Reactivity Coefficients. Changes in structure reactivity parameters that reflect changes in the transition state structure can provide additional evidence for the mechanism of the elimination reactions.^{13,22,30-32} These changes can usefully be described on energy surface of More-O'Ferrall-Jencks diagram.^{22,30} An energy surface for the elimination reactions of R_2NH -promoted eliminations from **1a-d** and **5a-e** in MeCN is shown in Figure 3.

Table 3 shows that the Brønsted β values for R_2NH -promoted eliminations from **1a-d** and **5a-e** decrease as the electron withdrawing ability of the β -aryl substituent is increased. The results can be described by a negative $p_{xy'}$ interaction coefficient, $p_{xy'} \delta\beta' \delta\sigma = \delta\rho' \delta\rho K_{\text{BH}}$, that describes the interaction between the base catalyst and the β -aryl substituent.^{22,30} Negative $p_{xy'}$ coefficients are consistent with an (E1cb)_{ir} mechanism, which has been ruled out by the substantial values of the $|\beta_{lg}|$ and an E2 mechanism and a reaction coordinate with a large horizontal component corresponding to proton transfer.^{13,22,30-32}

These changes in the β values can be described on More-O'Ferrall-Jencks energy diagram (Figure 3). An electron withdrawing β -aryl substituent will lower the energy of the carbanion intermediate in the upper left corner of the energy diagram. The transition state on the horizontal reaction coordinate will then move toward the right, with less proton transfer and smaller β , as depicted by a shift from A to B in Figure 3I.³⁰

For all β -aryl substituents the Brønsted β values decrease as the leaving group is changed from 4-nitrophenoxide to 2,4-dinitrophenoxide (Table 1). This effect corresponds to a positive p_{xy} interaction coefficient, $p_{xy} = \delta\beta' \delta\rho K_{lg} = \delta\beta_{lg}' / \delta\rho K_{\text{BH}}$ that describes the interaction between the base catalyst and the leaving group.^{22,30} The observed increase in the $|\beta_{lg}|$ values as the catalyst is made less basic (Table 2) is

Table 3. Solvent Effect on the Ketene-Forming E2 Reaction of $\text{Y}\text{C}_6\text{H}_4\text{CH}_2\text{COOC}_6\text{H}_4\text{-}p\text{-NO}_2$ (**1a-e**)

solvent	MeCN	70 mol% MeCN (aq)
rel rate ^{a,b}	1	0.6
ρ_{H} ^b	3.6 ± 0.1	1.8 ± 0.1
β	0.82 ± 0.01	0.77 ± 0.03
$\beta_{lg}^{a,c}$	-0.38	-0.26

^aY = H. ^bBase-solvent = *i*-Pr₂NH in MeCN and *i*-Pr₂NH/*i*-Pr₂NH₂⁺ buffer in 70 mol% MeCN(aq), respectively. ^cBase-solvent = R₂NH in MeCN and R₂NH/R₂NH₂⁺ buffer in 70 mol% MeCN(aq), respectively.

another manifestation of this effect, *i.e.*, $p_{xy} = \delta\beta_{lg}' / \delta\rho K_{\text{BH}} > 0$.^{22,30} On the More-O'Ferrall-Jencks reaction coordinate diagram in Figure 3, a change to a better leaving group will raise the energy of the top edge of diagram. The transition state on the horizontal reaction coordinate would then move slightly toward the right as depicted by a shift from A to C on the energy diagram, resulting in a small decrease in β (Figure 2II).³⁰ Similarly, a weaker base will raise the energy of the left side of the diagram and shift the transition state from A to D to increase in the extent of C-OAr bond cleavage (Figure 2III).³⁰ The positive p_{xy} coefficients are not consistent with an E1cb mechanism for which $p_{xy} = 0$ is expected, but provide additional support for the concerted E2 mechanism.^{13,22,30-32} As shown in Table 1, there is a progressive decrease in the $|\beta_{lg}|$ values as the β -aryl substituent is changed from *p*-MeO to H to *m*-Cl to *m*-NO₂. This result can be described by a negative $p_{yy'}$ interaction coefficient, $p_{yy'} = \delta\beta_{lg}' / \delta\sigma^- = -\delta\rho' \delta\rho K_{lg}$, that describes the interaction between the leaving group and the β -aryl substituent.^{12,22} The decrease in the ρ_{H} values with a better leaving group (Table 2) provides additional evidence for this effect, *i.e.*, $p_{yy'} = -\delta\rho_{\text{H}} / \delta\rho K_{lg} < 0$.^{13,22} The negative $p_{yy'}$ coefficients observed in these reactions are consistent an E2 mechanism and a reaction coordinate that has a large component of proton transfer so that stabilization of the carbanion intermediate result in a net shift from A to B in Figure 2I, in the direction of decreased C $_{\alpha}$ -OAr bond cleavage and smaller $|\beta_{lg}|$ values.^{13,22,30-32} Moreover, a better leaving group would shift the transition state from A to C in Figure 2II to decrease the extent of negative charge development and the ρ_{H} values.³⁰

Solvent Effect. For eliminations from **1a** promoted by *i*-Pr₂NH, the rate decreases slightly as the base-solvent system is changed from *i*-Pr₂NH-MeCN to *i*-Pr₂NH/*i*-Pr₂NH₂⁺-70 mol % MeCN-30% H₂O, apparently because of the decreased basicity of the promoting base in more protic solvent.^{24,33} On the other hand, the extent of C $_{\beta}$ -H bond cleavage decreases slightly and the degrees of negative charge development at the β -carbon and the C $_{\alpha}$ -OAr bond cleavage decrease considerably as revealed by the small to significant decrease in the Brønsted β , ρ , and $|\beta_{lg}|$ values in R₂NH/R₂NH₂⁺-70 mol % MeCN(aq) as the base-solvent system (Table 3). The changes in the transition state structures with the base-solvent system variation may be attributed to a solvent effect. Due to the electronegativity difference, the

Table 4. Brønsted β Values for Elimination from 4-NO₂C₆H₄CH₂CO₂C₆H₃-2-X-4-NO₂ Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C^{a,b}

X	H (1e)	OCH ₃ (2e)	Cl (3e)	CF ₃ (4e)	NO ₂ (5e)
pK _{lg} ^c	20.7	20.6	18.1	17.0	16.0
β	0.47 ± 0.01 ^d	0.44 ± 0.08 ^d	0.25 ± 0.01	0.21 ± 0.04	0.14 ± 0.01

^a[R₂NH]/[R₂NH₂⁺] = 1.0. ^bm = 0.10 M (Bu₄N⁺Br⁻). ^cReference 30. ^dk₂^E values calculated from the k_{obs} by using eq. 3 have been used.

negative charge developed at the β -carbon in the ketene-forming transition state may be delocalized more on the carbonyl oxygen than on the β -carbon. Moreover, this effect would be amplified in the buffer solution because the former can be better stabilized by forming a stronger hydrogen bond with R₂NH₂⁺. This would predict that less negative charge would remain at the β -carbon to decrease both ρ_{H} and $|\beta_{\text{lg}}|$ values, as observed (Table 3).³⁴

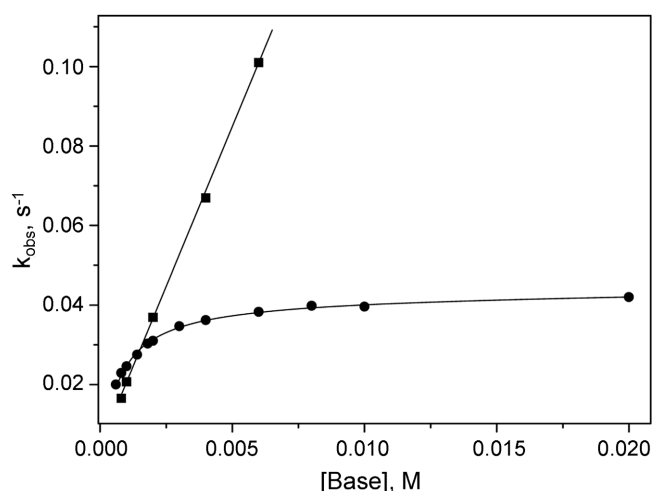
Change of the Mechanism

Mechanism of Elimination from 3e-5e and 1f. Figure 4 shows the plots of k_{obs} vs base concentration for eliminations from 4-NO₂C₆H₄CH₂CO₂C₆H₃-2-X-4-NO₂ (X = Cl, 3e) and 2,4-(NO₂)₂C₆H₃CH₂CO₂C₆H₄-4-NO₂ (1f) promoted by Bz(*i*-Pr)NH/Bz(*i*-Pr)NH₂⁺ in 70 mol % MeCN(aq). When X = Cl (3e), CF₃ (4e), NO₂ (5e), the plots are linear, indicating that the eliminations are second order, first order to the substrate

Table 5. Values of β_{lg} for Elimination from 4-NO₂C₆H₄CH₂CO₂-C₆H₃-2-Y-4-NO₂ Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN (aq) at 25.0 °C^{a,b}

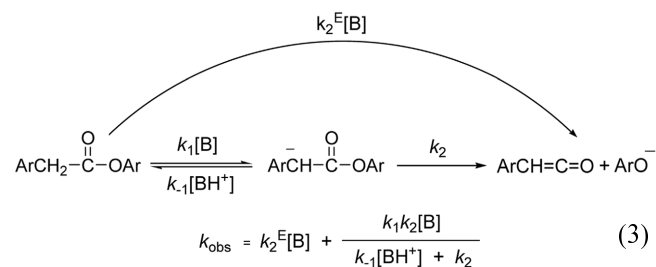
R ₂ NH	Bz(<i>i</i> -Pr)NH	<i>i</i> -Bu ₂ NH	2,6-DMP ^c
β_{lg}	-0.21 ± 0.01	-0.15 ± 0.04	-0.10 ± 0.01

^a[R₂NH]/[R₂NH₂⁺] = 1.0. ^b μ = 0.10 M (Bu₄N⁺Br⁻). ^c*cis*-2,6-Dimethylpiperidine.

**Figure 4.** Plots of k_{obs} vs base concentration for eliminations from 4-NO₂C₆H₄CH₂CO₂C₆H₃-2-Cl-4-NO₂ (3e, ■) and 2,4-(NO₂)₂C₆H₃CH₂CO₂C₆H₄-4-NO₂ (1f, ●) promoted by Bz(*i*-Pr)NH/Bz(*i*-Pr)NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C, [Bz(*i*-Pr)NH]/[Bz(*i*-Pr)NH₂⁺] = 1.0, m = 0.10 M (Bu₄N⁺Br⁻).

and first order to the base. In addition, $\beta = 0.14$ -0.25 and $|\beta_{\text{lg}}| = 0.21$ -0.10 were determined (Tables 4 and 5). The results are consistent with an E2 mechanism.

In contrast, the plot for 2,4-(NO₂)₂C₆H₃CH₂CO₂C₆H₄-4-NO₂ (1f) showed saturation curve, reaching at a plateau at [base] > 0.01 M (Figure 4). The result can most reasonably be explained with an E1cb mechanism, *i.e.*, k_{obs} = k₁k₂[B]/(k₋₁[BH⁺] + k₂).²² The rate data showed excellent correlation with eq. 3 when fitted without the first term. This predicts that the plot of k_{obs} should change from a straight line at a low base concentration, *i.e.*, k_{obs} = k₁[B] when k₋₁[BH⁺] << k₂, to a plateau at a higher base concentration, *i.e.*, k_{obs} = k₁k₂/k₋₁ when k₋₁[BH⁺] >> k₂. The excellent agreement between the experimental data and the theoretically fitted curve provides a strong evidence for this mechanism (Figure 4). Moreover, the calculated k₁ and k₋₁/k₂ values are consistent with the trends observed for 1e and 2e (*vide infra*). Finally, the NMR spectrum of the recovered reactant for the reaction of 2,4-(NO₂)₂C₆H₃CH₂CO₂C₆H₄-4-NO₂ (1f) with *i*-Bu₂NH/*i*-Bu₂NH₂⁺ in 70 mol % D₂O in MeCN indicated complete absence of the benzylic C-H bond at δ 4.43, providing additional support for this mechanism.



Mechanism of Elimination from 1e and 2e. The plots of the k_{obs} values for eliminations from 4-NO₂C₆H₄CH₂CO₂-C₆H₄-4-NO₂ (1e) against base concentration are curves at low buffer concentration and become straight lines at [base] > 0.01 M (Figure 5). Similar result was observed for 2e. This result cannot be explained with the change in the rate-limiting step because the rate should have reached at a plateau at a higher base concentration in such a case (*vide supra*). In contrast, the rate data can readily be explained if one assumes that the reactions proceed by the concurrent E2 and E1cb mechanisms, *i.e.*, k_{obs} = k₂^E + k₁k₂[B]/(k₋₁[BH⁺] + k₂) (eq. 3). As shown in Figure 5, the rate data for the reactions of 1e with R₂NH/R₂NH₂⁺ show excellent correlation with eq. 3. Note that the shapes of the dissected lines are typical for the E2 and E1cb mechanisms. In addition, the k_{obs} values for the reactions of 1e with Bz(*i*-Bu)NH/Bz

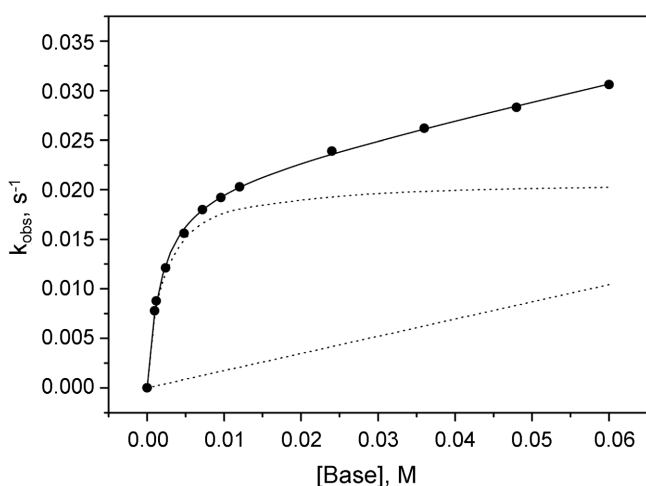


Figure 5. Plot of k_{obs} vs buffer concentration for eliminations from 4-NO₂C₆H₄CH₂CO₂C₆H₄-4-NO₂ (**1e**) promoted by Bz(*i*-Pr)NH/Bz(*i*-Pr)NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C, [Bz(*i*-Pr)NH]/[Bz(*i*-Pr)NH₂⁺] = 1.0, $m = 0.10$ M (Bu₄N⁺Br⁻). The closed circles are the experimental data and the solid line shows the computer fitted curve by using eq. 3 (see text). The curve is dissected into the E2 and E1cb reaction components (dashed lines).

(*i*-Bu)NH₂⁺ increases gradually with the change in the buffer ratio from 0.5 to 1.0 to 2.0, as expected from eq. 3 (Table 6).

The calculated rate constants for the E2 and E1cb pathways provide additional support for this mechanism. (i) The k_2^{E} , k_1 , and k_{-1}/k_2 values for the reactions of **1e** with Bz(*i*-Bu)NH/Bz(*i*-Bu)NH₂⁺ are very similar regardless of the buffer ratio, indicating that the same mechanism is operating under these conditions (Tables 6 and 7). (ii) The k_2^{E} values for **1e** and **2e** nicely fit in the trend observed for **3e-5e**, *i.e.*, the k_2^{E} of **1e-5e** increase gradually with a stronger base and a better leaving group (Table 6). The only exception to this trend is the larger k_2^{E} of **1e** than **2e**, which may be attributed to the leaving group steric effect. Because the *p*-nitrophenoxide in **1e** is the only leaving group without *ortho* substituent, it should be sterically less hindered than other substrates in the series, to increase the rate.³⁵ (iii) The observed increase in the k_1 with a stronger base and a more acidic benzylic C-H bond (**1f**), as well as a small decrease in

Table 6. Rate Constants for Ketene-Forming Eliminations from 4-NO₂C₆H₄CH₂CO₂C₆H₃-2-X-4-NO₂^a Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) 25.0 °C^{b,c}

R ₂ NH ^d	pK _a ^e	$k_2^{\text{E}}, \text{M}^{-1}\text{s}^{-1}$ f _g when X is				
		H (1e)	OMe (2e)	Cl (3e)	CF ₃ (4e)	NO ₂ (5e)
Bz(<i>i</i> -Pr)NH	16.8	0.170 ^f	0.130	15.5	27.1	43.6
<i>i</i> -Bu ₂ NH	18.2	0.530	0.390	34.8	60.4	70.1
<i>i</i> -Pr ₂ NH	18.6			30.9	45.0	61.0
2,6-DMP ^j	18.9	1.77	1.15	52.1	70.9	85.8

^a[Substrate] = 4.0 × 10⁻⁵ M. ^b[R₂NH]/[R₂NH₂⁺] = 1.0 except otherwise noted. ^c $\mu = 0.10$ M (Bu₄N⁺Br⁻). ^d[R₂NH] = 9.6 × 10⁻⁴ to 6.0 × 10⁻² M. ^eReference 38. ^fAverage of three or more rate constants. ^gEstimated uncertainty, ± 5%. ^hCalculated from the k_{obs} by using eq. 3. ⁱ $k_2^{\text{E}} = 0.160$ and 0.230 M⁻¹s⁻¹ when [R₂NH]/[R₂NH₂⁺] = 0.5 and 2.0, respectively. ^j*cis*-2,6-Dimethylpiperidine.

Table 7. The k_1 and k_{-1}/k_2 Values for Elimination from 2-Y-4-NO₂C₆H₃CH₂CO₂C₆H₃-2-X-4-NO₂^a Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) 25.0 °C^{b,c}

R ₂ NH ^d	$k_1, \text{M}^{-1}\text{s}^{-1}$ ^e			$k_{-1}/k_2, \text{M}^{-1}$ ^e		
	1e	2e	1f	1e	2e	1f
Bz(<i>i</i> -Pr)NH	11.7 ^f	8.10	52.3	560 ^g	677	1187
<i>i</i> -Bu ₂ NH	20.2	16.3	68.8	225	327	289
2,6-DMP ^h	31.1	22.8	92.0	56.0	73.5	133

^a[Substrate] = 4.0 × 10⁻⁵ M. ^b[R₂NH]/[R₂NH₂⁺] = 1.0 except otherwise noted. ^c $\mu = 0.10$ M (Bu₄N⁺Br⁻). ^d[R₂NH] = 9.6 × 10⁻⁴ to 6.0 × 10⁻² M. ^eCalculated from the k_{obs} by using eq. 2. ^f $k_1 = 11.7$ and 10.9 M⁻¹s⁻¹ when [R₂NH]/[R₂NH₂⁺] = 0.5 and 2.0, respectively. ^g $k_{-1}/k_2 = 551$ and 536 M⁻¹ when [R₂NH]/[R₂NH₂⁺] = 0.5 and 2.0, respectively. ^h*cis*-2,6-Dimethylpiperidine.

the k_1 with the leaving group steric effect (**2e**) is consistent with what would be expected for the deprotonation step (Table 7). (iv) The increase of the k_{-1}/k_2 values in the order **1e** < **2e** < **1f** is also consistent (Table 7). If the k_1 of **2e** is smaller than **1e**, the k_{-1} of **2e** should be larger than **1e**. On the other hand, the values of k_2 for **1e** and **2e** are expected to be similar because a fraction of the difference in the leaving group pK_{lg} values ($\Delta pK_{\text{lg}} = 0.1$) will be reflected in the k_2 . Also, the *o*-nitro group is expected to stabilize the carbanion intermediate to increase k_{-1} and decrease k_2 of **1f**, and this effect should be much larger for k_{-1} than k_2 because the second step involves higher energy barrier. A combination of these factors would be to increase the k_{-1}/k_2 values in the order **1e** < **2e** < **1f**, as observed. (v) The increase in the k_{-1}/k_2 ratio with a weaker base can also be explained similarly (Table 7). The k_{-1} should increase with the acidity of R₂NH₂⁺, although little change is expected for k_2 by the base strength variation. This predicts an increase in the k_{-1}/k_2 ratio with a weaker base.

The NMR spectrum of the recovered reactant from the reaction of **1e** with *i*-Bu₂NH/*i*-Bu₂NH₂⁺ in 70 mol % MeCN-30% D₂O at -10 °C indicated that approximately 30% of the benzylic C-H bond underwent H-D exchange. All of these results provide strong evidences that eliminations from **1e** and **2e** promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) proceed by the concurrent E2 and E1cb mechanism.^{3,22} Similar result was reported for (4-Y-C₆H₄)₂CHCO₂C₆H₃-4-NO₂ by the change of Y from H to Cl.^{36,37}

Mapping of the E2 Transition State. For elimination from 4-NO₂C₆H₃CH₂CO₂C₆H₃-2,4-(NO₂)₂ (**5e**), values of $\beta = 0.14$ and $|\beta_{\text{g}}| = 0.21-0.10$ were determined. This indicates a small degree of proton transfer and limited extent of the C_α-OAr bond rupture in the transition state. The combined results reveal that the ketene-forming eliminations from **5e** proceed by the E2 mechanism via a reactant-like transition state with limited extents of proton transfer and C_α-OAr bond cleavage. Therefore, the transition state for **5e** can be located near the right corner of the More-O'Ferrall-Jencks diagram (Figure 6).

This conclusion is supported by the interaction coefficients. Table 4 shows that the β values of the k_2^{E} process for **1e-5e** decrease, as the leaving groups are made less basic.

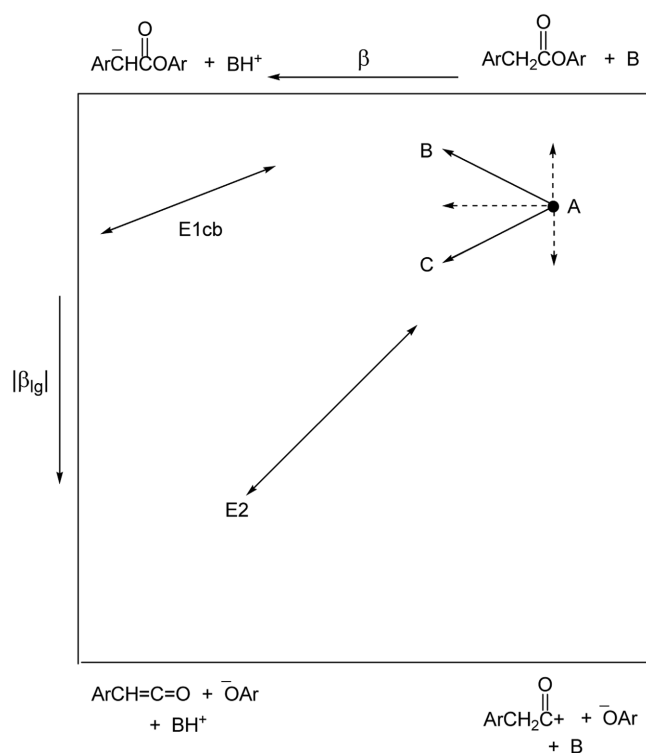


Figure 6. Reaction coordinate diagram for the ketene-forming elimination. The effect of the change to a poorer leaving group and a weaker base are shown by the shift of the transition state from A to B and A to C, respectively.

This effect corresponds to a positive p_{xy} interaction coefficient, $p_{xy} = \partial\beta/\partial pK_{\text{lg}}$, that describes the interaction between the base catalyst and the leaving group.^{16,21b} The observed increase in the $|\beta_{\text{lg}}|$ values as the catalyst is made less basic (Table 5) is another manifestation of this effect, *i.e.*, $p_{xy} = \partial\beta_{\text{lg}}/\partial pK_{\text{BH}} > 0$. On the More-O'Ferrall-Jencks diagram in Figure 6, a change to a poorer leaving group will raise the energy of the bottom edge of diagram shifting the transition state toward the product and the E1cb intermediate. The transition state on the horizontal reaction coordinate will then move toward the left, with more proton transfer and a larger β , as depicted by a shift from A to B on the energy diagram (Figure 6).^{13,22,30} Similarly, a weaker base will raise the energy of the left side of the diagram and shift the transition state from A to C to increase in the extent of C α -OAr bond cleavage (Figure 6).^{13,22,30} The positive p_{xy} coefficients are not consistent with an E1cb mechanisms for which $p_{xy} = 0$ is expected, but provide additional support for the concerted E2 mechanism.^{13,22,30}

Change of the Mechanism. The kinetic results described above clearly indicate that the elimination mechanism changes from E2 to a competing E2 and E1cb to E1cb as the reactant structure is changed from **3e-5e** to **1e-2e** to **1f**. The most reasonable explanation for this result is as follows. As discussed above, the position of the E2 transition state for the reactions from **5e** could be located at A in Figure 5. As the leaving group is made poorer (**3e**, **4e**), the reactant-like E2 transition state gradually changes to the E1cb-like, as

indicated by a shift from A to B (*vide supra*). When the leaving group ability is further decreased to Y = H & OMe (**1e**, **2e**), the E2 transition state is destabilized and the E1cb mechanism emerges simultaneously. It is interesting to note that the E2 transition states for eliminations from **1e** and **2e** are more E1cb-like than **3e-5e** (*vide supra*). Finally, when the carbanion intermediate is stabilized by the strongly electron withdrawing β -aryl group (**1f**), so that the E2 reaction can no longer compete, the E1cb mechanism becomes the predominant reaction pathway.

Conclusion

As stated in the introduction, the change of the mechanism from E2 to E1cb could occur by the merging of the transition state, if it is difficult for the energy maximum of the E2 mechanism and an energy well of the E1cb mechanism to coexist for a single compound at almost the same position on the energy diagram.^{13,14,22,30} However, if the positions of the transition states are significantly different, they should be able to coexist, as observed in the E2 and E1 borderline.^{7,8,15} The change in elimination mechanism observed in the present study is concluded to be of this type. Because the E2 transition state is located near the center of the horizontal reaction coordinate, which is far from the position of the E1cb transition state, there seems to be no reason for why the two transition states cannot coexist. Furthermore, the mechanism changes systematically from the concurrent E2 and E1cb mechanisms to E2 as the E2 transition state is stabilized by the better leaving group, and to the E1cb extreme when the strongly electron-withdrawing β -aryl group stabilizes the latter transition state. To our knowledge, this is the first example that shows a gradual change in the elimination reaction mechanism from E2 to E1cb via a competing E2 and E1cb mechanism wrought by the systematic variation of the reactant structure.

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