

Eliminations from (*E*)-2,4-Dinitrobenzaldehyde *O*-Aryloximes Promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq). Effects of Leaving Group and Base-Solvent on the Nitrile-Forming Transition-State

Bong Rae Cho and Sang Yong Pyun^{†,*}

Department of Chemistry, Korea University, Seoul 136-713, Korea

[†]Department of Chemistry, Pukyong National University, Pusan 608-737, Korea. *E-mail: sypyun@pknu.ac.kr

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Elimination reactions of (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₃-2-X-4-NO₂ (**1a-e**) promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) have been studied kinetically. The reactions are second-order and exhibit Brønsted β = 0.80-0.84 and |β_{lg}| = 0.39-0.42, respectively. For all leaving groups and bases employed in this study, the β and |β_{lg}| values remained almost the same. The results can be described by a negligible *p*_{xy} interaction coefficient, *p*_{xy} = ∂β/p*K*_{lg} = ∂β_{lg}/p*K*_{BH} ≈ 0, which describes the interaction between the base catalyst and the leaving group. The negligible *p*_{xy} interaction coefficient is consistent with the (E1cb)_{irr} mechanism. Change of the base-solvent system from R₃N/MeCN to R₃N/R₃NH⁺-70 mol % MeCN(aq) changed the reaction mechanism from E2 to (E1cb)_{irr}. Noteworthy was the relative insensitivity of the transition state structure to the reaction mechanism change.

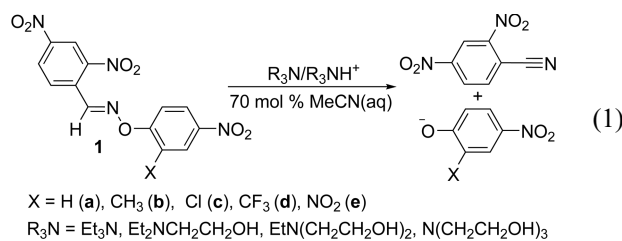
Key Words : Elimination, E1cb-like and (E1cb)_{irr}, Leaving group and base-solvent effect

Introduction

One of the most important problems in the elimination reactions is the borderline mechanism.¹⁻⁸ Some years ago, Jencks has clearly elucidated how the E2 mechanism changes to an E1cb in alkene-forming eliminations.³ More recently, we have reported imine-forming eliminations which proceeded *via* a competing E2 and E1 mechanisms.⁶ During the last two decades, we have conducted extensive research for nitrile-forming elimination from (*E*)-*O*-arylbenzaloximes to investigate the borderline mechanism between E2 and E1cb.⁹⁻¹⁶ Except for a few cases,^{15,16} however, all reactions proceeded by the E2 mechanism despite the fact that the reactants have *syn* stereochemistry, poor leaving, and an sp² hybridized β-carbon atom, all of which favor E1cb or E1cb-like transition state.

Earlier, we reported that elimination reactions of (*E*)-*O*-*p*-nitrophenyl-2,4-dinitrobenzaloxime with E₃N/Et₃NH⁺ in MeCN-H₂O proceeded by an E2 mechanism.¹⁷ The rate decreased as the mol % of MeCN increased up to 70% and then increased upon further increase in the MeCN content. However, the effect of the solvent on the transition state structure was not elucidated in detail. More recently, we investigated the elimination reactions of (*E*)-2,4-dinitrobenzaldehyde *O*-aryloximes promoted by R₃N in MeCN.¹⁸ The reactions proceeded by an E2 mechanism. When the β-aryl group was changed from Ph to 2,4-dinitrophenyl, the structure of the transition state changed from E2-central to highly E1cb-like. It occurred to us that the change in the elimination mechanism from E2 to E1cb might be realized, if the reaction is conducted in a more protic solvent which can stabilize the carbanion developed in the transition state.

In order to explore such possibility, we have now conducted a kinetic study on the elimination reactions of (*E*)-2,4-dinitrobenzaldehyde *O*-aryloxime with R₃N/R₃NH⁺-70 mol % MeCN(aq) (eq. 1). By comparing with the existing data for (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₃-2-X-4-NO₂ (**2**) with R₂NH/R₂NH₂⁺-70 mol % MeCN(aq) and **1a-e** with R₃N/MeCN, the effects of leaving group and base-solvent variations on the nitrile-forming elimination was assessed.



Results

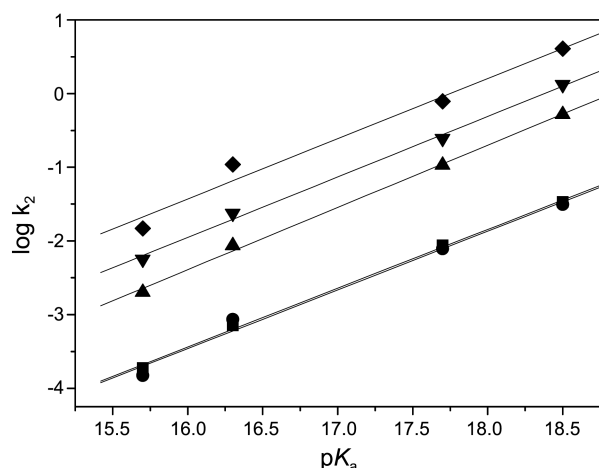
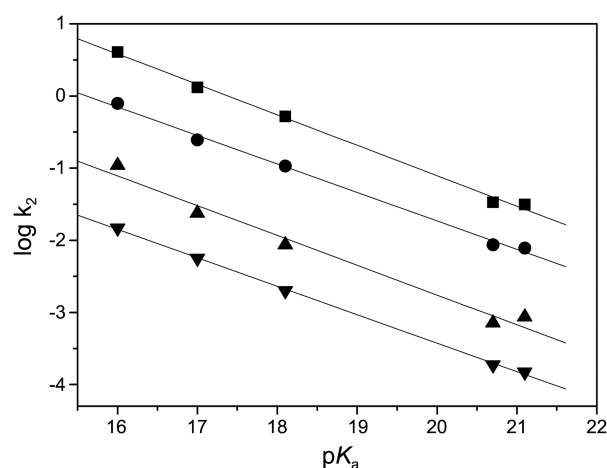
(*E*)-2,4-Dinitrobenzaldehyde *O*-aryloximes **1a-e** were available from previous studies.¹⁸ The reaction of **1a** with Et₃N/Et₃NH⁺ in 70 mol % MeCN(aq) produced 2,4-dinitrobenzonitrile in 96% yield. No trace of (*E*)-2,4-dinitrobenzaloxime could be detected by TLC. For all reactions, the yields of aryloxides determined by the comparing the absorbance of the infinity samples from the kinetic studies with those of the authentic aryloxides were in the range of 96-98%.

The rates of elimination reaction were followed by monitoring the increase in the absorption at the λ_{max} for the aryloxides in the range of 400-434 nm as described previously.⁹ Excellent pseudo-first order kinetics plots, which

Table 1. Rate constants for nitrile-forming elimination from (*E*)-2,4-(NO₂)₂C₆H₃-CH=NOC₆H₃-2-X-4-NO₂^a promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq)^{b,c} at 25.0 °C

R ₃ N ^d	pK _a ^e	10 ³ k ₂ , M ⁻¹ s ⁻¹ ^{f,g} When X is				
		CH ₃ (1b)	H (1a)	Cl (1c)	CF ₃ (1d)	NO ₂ (1e)
N(CH ₂ CH ₂ OH) ₃	15.7	0.149	0.188	2.01	5.63	14.7
EtN(CH ₂ CH ₂ OH) ₂	16.3	0.713	0.862	8.65	23.7	109
Et ₂ N(CH ₂ CH ₂ OH)	17.7	8.66	7.80	107	246	787
Et ₃ N	18.5	31.3	33.7	521	1320	4070

^a[Substrate] = 5.0 × 10⁻⁵ M. ^b[R₃N]/[R₃NH⁺] = 1. ^cμ = 0.1 (Bu₄N⁺Br⁻). ^d[R₃N] = 2.0 × 10⁻³–0.25 M. ^epK_a in MeCN taken from reference 19. ^fAverage of three or more rate constants. ^gEstimated uncertainty, ± 3%.

**Figure 1.** Brønsted plots for the elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₃-2-X-4-NO₂ promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) at 25.0 °C. [X = H (**1a**, ■), CH₃ (**1b**, ●), Cl (**1c**, ▲), CF₃ (**1d**, ▼), NO₂ (**1e**, ◆)].**Figure 2.** Plots log k₂ versus pK_{lg} values of the leaving group for the elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₃-2-X-4-NO₂ promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) at 25.0 °C. [R₃N = N(CH₂CH₂OH)₃ (■), EtN(CH₂CH₂OH)₂ (●), Et₂N(CH₂CH₂OH) (▲), Et₃N (▼)].

covered at least three half-lives were obtained. For reactions of **1a-e** with R₃N/R₃NH⁺ in 70 mol % MeCN(aq), the plots of *k*_{obs} versus base concentration were straight lines passing through the origin, indicating that the reactions are second-order, first order to the substrate and first order to the base (Figure S1-9). The second-order rate constants (*k*₂) were obtained either from the slopes of straight lines or by dividing the *k*_{obs} by base concentration. Values of *k*₂ for eliminations from **1a-e** are summarized in Table 1.

The log *k*₂ values for eliminations from **1a-e** showed good correlation with the pK_a values of the promoting bases on the Brønsted plot (Figure 1). Similarly, the elimination rates determined with different leaving groups correlated reasonably well with the leaving group pK_{lg} values (Figure 2).

The β and |β_{lg}| values are in the range of 0.80–0.84 and 0.39–0.42, respectively. The β and |β_{lg}| values remained almost the same within experimental error for all leaving

Table 2. Brønsted β values for elimination from (*E*)-2,4-(NO₂)₂-C₆H₃CH=NOC₆H₃-2-X-4-NO₂ promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) at 25.0 °C

	X = CH ₃	X = H	X = Cl	X = CF ₃	X = NO ₂
pK _{lg} ^a	21.1 ^b	20.7	18.1	17.0	16.0
	0.80 ± 0.07	0.80 ± 0.03	0.84 ± 0.03	0.82 ± 0.04	0.82 ± 0.08

^aReference 19. ^bDetermined from the slope of the plot of vs pK_a.

groups and bases employed in this study (Tables 2 and 3).

Discussion

Mechanism of Eliminations from 1. The mechanism of elimination for **1a-e** promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) has been elucidated by the results of kinetic investigations and product studies. Because the reactions

Table 3. Brønsted β_{lg} values for elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₃-2-X-4-NO₂ promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) at 25.0 °C

R ₃ N	N(CH ₂ CH ₂ OH) ₃	EtN(CH ₂ CH ₂ OH) ₂	Et ₂ N(CH ₂ CH ₂ OH)	Et ₃ N
pK _a ^a	15.7	16.3	17.7	18.5
β _{lg}	-0.39 ± 0.01	-0.41 ± 0.03	-0.39 ± 0.01	-0.42 ± 0.01

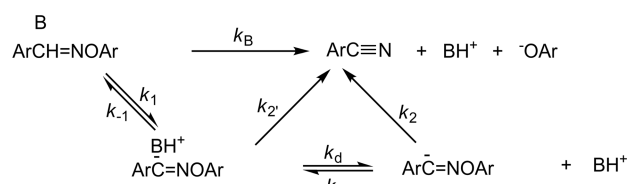
^aReference 19.

produced only elimination products and exhibited second-order kinetics, all but bimolecular elimination pathways can be negated. The (E1cb)_{ip} and internal return mechanisms were ruled out by the observed general base catalysis with the Brønsted β values ranging from 0.80 to 0.84 because these mechanisms would exhibit either a specific base catalysis or Brønsted β values near unity.^{1,20,21} Hence, the most likely mechanism for this bimolecular process is either E2 or E1cb. If the reaction proceeds *via* a carbanion intermediate, the rate equation can be expressed as $k_{\text{obs}} = k_1 k_2' [\text{B}] / (k_{-1} [\text{BH}^+] + k_2')$ (Scheme 1).^{1,20,21} The (E1cb)_R mechanism requires that the first step must be reversible, *i.e.*, $k_{-1} [\text{BH}^+] \gg k_2'$, and the rate expression can be simplified to $k_{\text{obs}} = k_1 k_2' [\text{B}] / k_{-1} [\text{BH}^+]$. This would predict that the k_{obs} should remain constant regardless of the buffer concentration because $[\text{B}] / [\text{BH}^+] = 1.0$ is maintained throughout the reaction. Hence, the (E1cb)_R mechanism is ruled out by the linear dependence of the k_{obs} values on the base concentration. On the other hand, if the reactions proceed by the (E1cb)_{int} mechanism, *i.e.*, $k_{-1} [\text{BH}^+] \ll k_2'$, the rate equation should become $k_{\text{obs}} = k_1 k_2' [\text{B}]$, which is kinetically indistinguishable from the E2 mechanism.^{1,20,21}

The distinction between the two mechanisms has been made by the interaction coefficients. The β and $|\beta_{\text{lg}}|$ values remained almost the same within experimental error regardless of the ability of the leaving groups and the base strength variation (Table 2 and 3). The results can be described by a negligible p_{xy} interaction coefficient, $p_{xy} = \partial \beta / \partial pK_{\text{lg}} = \partial \beta_{\text{lg}} / \partial pK_{\text{BH}} \approx 0$, which describes the interaction between the base catalyst and the leaving group. The negligible p_{xy} interaction coefficient is consistent with the (E1cb)_{int} mechanism.^{1,20,21}

The change in the β and $|\beta_{\text{lg}}|$ values can be described by the More-O'Farrell-Jencks diagram (Figure 3). On the More-O'Farrell-Jencks diagram shown in Figure 3, a change to a better leaving group will raise the energy of the top edge of the diagram. According to the Hammond postulate, the transition state on the horizontal coordinate will shift from A to B because there is no diagonal character. This would predict negligible change in β .² Similarly, a stronger base raises the energy of the right side of the diagram. The transition state on the horizontal coordinate will then move toward the right as depicted by a shift from A to C, resulting in little change in $|\beta_{\text{lg}}|$.² The negligible interaction coefficients are inconsistent with the E2 mechanism for which $p_{xy} > 0$ is expected but provide a strong evidence for the (E1cb)_{int} mechanism.^{1,20,21}

Effect of the Leaving Group on the Nitrile-Forming Transition State. Earlier it was reported that the elimination reactions of (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)Ar (**2**) with



Scheme 1

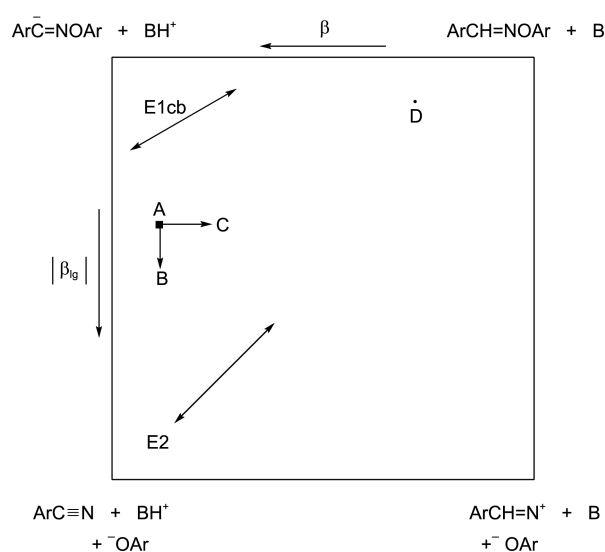
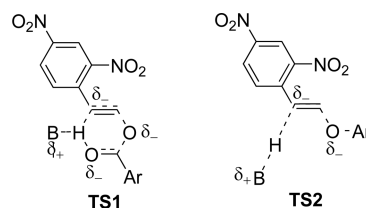


Figure 3. Reaction coordinate diagram for nitrile-forming eliminations. The transition states for eliminations from **1a** and **2** are indicated as A and D, respectively. According to the Hammond postulate, the effect of the change to a better leaving group on A is depicted by the shift from A to B, while the effects a stronger base on A are shown by the shifts from A to C, respectively.

$\text{R}_2\text{NH}/\text{R}_2\text{NH}_2^+$ proceeded *via* a cyclic transition state.¹⁵ Comparison of the transition state parameters for eliminations from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄-4-NO₂ (**2**) and (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₄-4-NO₂ (**1a**) reveals that there is a large difference in the transition state structures, despite the same leaving group pK_{a} values (Table 4). The rate of elimination increased only slightly, but the β value increased from 0.32 to 0.80, and $|\beta_{\text{lg}}|$ value increased from 0.30 to 0.42, respectively, by the change in the leaving group from 4-nitrobenzoate to 4-nitrophenoxide. This result indicates the transition state for **1a** is more sensitive to the base and leaving group variations. This outcome can be attributed to the structures of the leaving groups. In the nitrile-forming transition state from **2**, the negative charge developed at the β -carbon can be delocalized by the two oxygen atoms of the benzoate leaving group and stabilized by the intramolecular hydrogen bond as depicted in TS1. In contrast, such a delocalization is not possible in TS2. Therefore, Et₃N-promoted elimination from **1a** should be more sensitive to change the leaving group and base strength variations, as observed.



Effect of Base-Solvent. It is well established that R₃N-promoted elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₄-4-NO₂ in MeCN proceeds by an E2 mechanism.¹⁸ When the base-solvent system was changed to Et₃N/Et₃NH⁺-70 mol %

Table 4. Transition state parameters for eliminations from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOY promoted by base in 70 mol % MeCN(aq)

	Y = 4-nitrobenzoyl (2) ^a	Y = 4-nitrophenyl (1a)
Base	R ₂ NH ^b /R ₂ NH ₂ ⁺	R ₃ N ^c /R ₃ NH ⁺
pK _a (YOH)	20.7 ^{d,e}	20.7 ^{d,e}
rel. rate	0.6	1
β	0.32 ± 0.02	0.80 ± 0.03
β _{lg}	0.30 ± 0.01	0.42 ± 0.01

^aReference 15. ^bR₂NH = *i*-Pr₂NH. ^cR₃N = Et₃N. ^dpK_a of the conjugated acid of leaving group in MeCN. ^eReference 19.

Table 5. Effect of the base-solvent on the nitrile-forming eliminations from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₄-4-NO₂

Base-solvent	R ₃ N-MeCN ^a	R ₃ N/R ₃ NH ⁺ -70 mol % MeCN(aq)
rel. rate ^b	1	0.5
β	0.86 ± 0.1	0.80 ± 0.03
β _{lg}	0.46 ± 0.04	0.42 ± 0.01

^aReference 18. ^bR₃N = Et₃N.

MeCN(aq), the elimination mechanism changed to (E1cb)_{irr} as discussed above. However, there is only modest change in the transition state structures, despite the mechanism change. The rate of elimination decreased by half with the base-solvent variation from Et₃N-MeCN to Et₃N/Et₃NH⁺-70 mol % MeCN(aq), indicating a decreased basicity in the aqueous medium.²² The extent of the C_β-H bond cleavage and N_α-OAr bond rupture decreased by the same variation of the base-solvent as revealed by the decrease in the β and |β_{lg}| values. This result can readily be attributed to a solvent effect. If the partial negative charge developed at the β-carbon is stabilized by solvation in more protic 70 mol % MeCN(aq), the transition state should be less sensitive to the base strength variation. This would predict a smaller β value, as observed. In addition, the negative charge should be transferred from the β-carbon toward the α-nitrogen to form partial triple bond and to break the N_α-OAr bond. If a smaller amount of negative charge is transferred from the β-carbon, the extent of N_α-OAr bond cleavage should be smaller too. Noteworthy is the small change in the transition state structure accompanied by the reaction mechanism change.

In conclusion, we have studied elimination reactions from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC₆H₃-2-X-4-NO₂ promoted by R₃N/R₃NH⁺-70 mol % MeCN(aq). The elimination reaction mechanism changed from E2 to (E1cb)_{irr} by the change in the base-solvent from R₃N-MeCN to R₃N/R₃NH⁺-70 mol % MeCN(aq). Noteworthy is the small change in the transition state structure accompanied by the reaction mechanism change.

Experimental Section

Materials. (*E*)-2,4-Dinitrobenzaldehyde *O*-aryloximes **1** were available from previous investigations.¹⁸ Reagent grade

acetonitrile and tertiary amine were fractionally distilled from CaH₂. The buffer solutions of R₃N-R₃NH⁺ in 70 mol % MeCN(aq) were prepared by dissolving an equivalent amount of R₃N and R₃NH⁺Cl⁻ in 70 mol % MeCN(aq). In all cases, the ionic strength was maintained to 0.1 M with Bu₄N⁺Br⁻.

Kinetic Studies. Reactions of **1** with R₃N/R₃NH⁺ in 70 mol % MeCN(aq) were followed by monitoring the increase in the absorbance of the aryloxides at 400-434 nm with a UV-vis spectrophotometer as described.⁹

Product Studies. The product from the reaction of **1a** with Et₃N/Et₃NH⁺ in 70 mol % MeCN(aq) was identified by using more concentrated solution as described previously.¹⁸ A solution of 0.50 g (1.51 mmol) of **1a** and an excess amount of base a in the appropriate base (10 mL) was stirred for 7 h at room temperature. The solvent was removed in vacuo and the residue was extracted with CH₂Cl₂ and washed thoroughly with water until all of the amine, ammonium salt, and aryloxide were completely removed. The product was 2,4-dinitrobenzoxonitrile with mp 104-106 °C (lit.²³ mp 104-105 °C). The yield of 2,4-dinitrobenzoxonitrile was 96%. For all reactions, the yields of aryloxides as determined by comparing the absorbance of the infinity absorbance of the samples from the kinetic studies with those for the authentic aryloxides were in the range of 96-98%.

Control Experiments. The stabilities of **1** were determined as reported earlier.^{14,24} The solutions of **1** in MeCN were stable for at least two days when stored in the refrigerator.

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Support Information Available. Observed rate constants for elimination from **1a-e** promoted by R₃N/R₃NH⁺ in 70 mol % MeCN(aq) and plots of *k*_{obs} vs base concentration are available on request from the correspondence author (9 pages). e-mail: sypyun@pknu.ac.kr.

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