

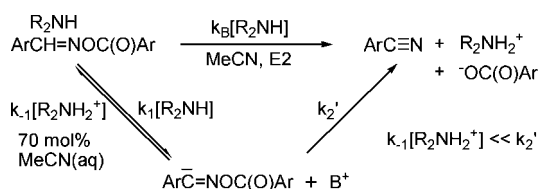
Elimination Reactions of (*E*)-2,4-Dinitrobenzaldehyde *O*-Benzoyloximes Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq). Change of Reaction Mechanism

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Elimination reactions of (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)-C₆H₄X (**1**) promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) have been studied kinetically. The reactions are second-order and exhibit Brønsted β = 0.27–0.32 and |β_{lg}| = 0.28–0.32. The result can be described by a negligible p_{xy} interaction coefficient, p_{xy} = ∂β/∂pK_{lg} = ∂β_{lg}/∂pK_{BH} ≈ 0, which describes the interaction between the base catalyst and the leaving group. The negligible p_{xy} coefficients are consistent with the (E1cb)_{irr} mechanism.

We have reported previously that elimination reactions of (*E*)- and (*Z*)-YC₆H₃CH=NOC(O)C₆H₄X promoted by R₂NH in MeCN proceed by the E2 mechanism.¹ The transition state for the *syn*-elimination from the (*E*)-isomer shifted slightly toward E1cb-like with greater extent of C_β-H bond cleavage, more negative charge development at β-carbon, and a smaller extent of triple bond formation than that of *anti*-elimination from the (*Z*)-isomer. To determine whether a change to an E1cb mechanism could be realized by introducing a more electron-withdrawing β-aryl substituent, we studied the elimination reactions of (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄X (**1a–d**) with R₂NH in MeCN.² However, only a modest change in the transition-state structure was observed. Moreover, an E2 mechanism was proposed for the reaction of **1a** with *i*-Pr₂NH/*i*-Pr₂NH₂⁺ in 70 mol % MeCN(aq), a solvent capable of stabilizing the developing negative charge density at the β-carbon, and thereby additionally favoring the E1cb mecha-

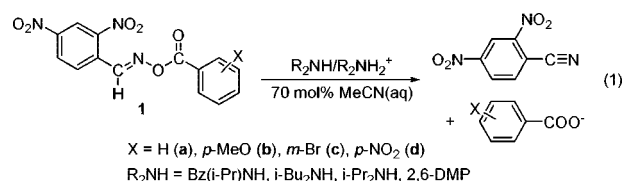
TABLE 1. Second-Order Rate Constants for Nitrile-Forming Elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄X^a Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq)^{b,c} at 25.0 °C

| R ₂ NH ^d | pK _a ^e | 10 ² k ₂ , M ⁻¹ s ⁻¹ ^{f,g} | | | |
|--------------------------------|------------------------------|---------------------------------------------------------------------------------|-------------------|------------------|-------------------------------|
| | | X = H | X = <i>p</i> -OMe | X = <i>m</i> -Cl | X = <i>p</i> -NO ₂ |
| Bz(<i>i</i> -Pr)NH | 16.8 | 1.04 | 0.820 | 2.12 | 4.24 |
| <i>i</i> -Bu ₂ NH | 18.2 | 3.20 | 1.86 | 7.40 | 12.8 |
| <i>i</i> -Pr ₂ NH | 18.5 | 2.09 | 1.38 | 4.43 | 8.50 |
| 2,6-DMP ^h | 18.9 | 4.79 | 3.12 | 10.7 | 19.8 |

^a [Substrate] = 5.0 × 10⁻⁵ M. ^b [R₂NH]/[R₂NH₂⁺] = 1.0. ^c μ = 0.1 (Bu₄N⁺Br). ^d [R₂NH] = 2.0 × 10⁻² M. ^e Reference 4. ^f Average of three or more rate constants. ^g Estimated uncertainty, ±3%. ^h *cis*-2,6-Dimethylpiperidine.

nism. However, the conclusion was based on the linear increase in k_{obs} with buffer concentration. Therefore, a detailed structure–reactivity relationship study seems necessary to provide a more convincing evidence for the proposed mechanism.

To gain a better insight into the nitrile-forming eliminations, we have now studied the reactions **1a–d** with R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) (eq 1). By comparing with the existing data for **1a–d** with R₂NH in MeCN, the effects of the base–solvent on the nitrile-forming elimination was assessed.



Product Study. (*E*)-2,4-Dinitrobenzaldehyde *O*-benzoyl oximes **1a–d** were available from a previous study.² The reactions of **1a** with *i*-Bu₂NH/*i*-Bu₂NH₂⁺ in 70 mol % MeCN(aq) produced 2,4-dinitrobenzoxime and benzoate. The isolated yield of 2,4-dinitrobenzoxime from a large-scale reaction was 94%. No trace of (*E*)-2,4-dinitrobenzaldehyde oxime could be detected by TLC, negating the possibility of the hydrolysis reaction.

Kinetic Study. The rates of elimination reaction were followed by monitoring the decrease in the absorption at the λ_{max} for the substrates in the range of 258–280 nm as described.^{1,3} In all cases, the ionic strength was maintained to be 0.1 M with Bu₄N⁺Br⁻. Excellent pseudo-first-order kinetics plots, which covered at least 3 half-lives, were obtained. Plots of k_{obs} for the reactions of **1a** and **1d** with *i*-Bu₂NH/*i*-Bu₂NH₂⁺ and *i*-Pr₂NH/*i*-Pr₂NH₂⁺ in 70 mol % MeCN(aq) against 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.² Moreover, the k₂ values calculated from the slopes of the plots were in excellent agreement (within ±3%) with the k₂ calculated by using a single data point. Hence, the rate constants for the base-promoted eliminations from **1a–d** were determined at a single base concentration. The k₂ values were obtained by dividing the k_{obs} by the base concentration. Values of k₂ for eliminations from **1a–d** are summarized in Table 1. Except for the rate data

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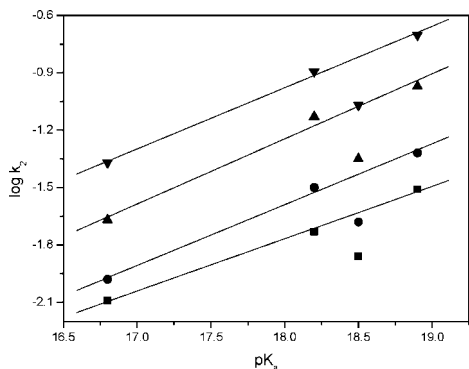


FIGURE 1. Brønsted plots for the elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄X promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C [X = H (**1a**, ●), *p*-OMe (**1b**, ■), *m*-Cl (**1c**, ▲), *p*-NO₂ (**1d**, ▼)].

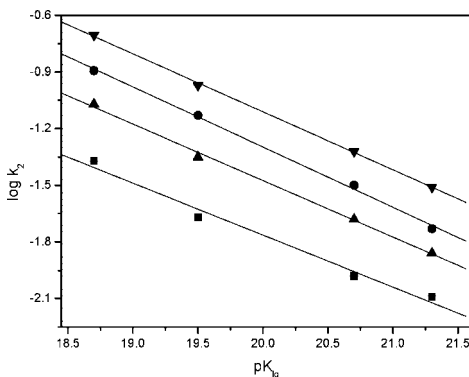


FIGURE 2. Plots of log k_2 versus pK_{lg} values of the leaving group for the elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄X (**1a–d**) promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C [R₂NH = Bz(*i*-Pr)NH(■), *i*-Bu₂NH(●), *i*-Pr₂NH(▲), 2,6-DMP(▼)].

TABLE 2. Brønsted β Values for Elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄X (**1a–d**)^a Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C

| | X = <i>p</i> -OMe | X = H | X = <i>m</i> -Cl | X = <i>p</i> -NO ₂ |
|-------------|-------------------|-------------|------------------|-------------------------------|
| pK_{lg}^a | 21.3 | 20.7 | 19.5 | 18.7 |
| β | 0.27 ± 0.01 | 0.32 ± 0.02 | 0.34 ± 0.04 | 0.32 ± 0.02 |

^a Reference 4.

determined with *i*-Pr₂NH, the rate increased with the base strength of the promoting base and the leaving group ability. The slower rate of eliminations from **1a–d** with *i*-Pr₂NH than with *i*-Bu₂NH as the base can be attributed to the greater steric requirement of the former.

The plots of k_2 values for **1a–d** against the pK_a values of the base are depicted in Figure 1. The plots are linear with excellent correlations, if the data for *i*-Pr₂NH is excluded. Therefore, the β values were calculated from the straight lines without the data for *i*-Pr₂NH. Similarly, the elimination rates determined with different leaving groups correlated reasonably well with the leaving group pK_{lg} values (Figure 2). The β and $|\beta_{lg}|$ values are in the range of 0.27–0.32 and 0.28–0.32, respectively. The β and $|\beta_{lg}|$ values remained nearly the same within experimental error for all leaving groups and bases employed in this study (Tables 2 and 3).

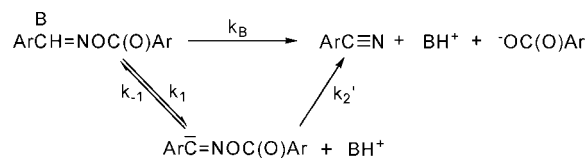
Mechanism of Elimination. The mechanism of elimination for **1a–d** promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) have been elucidated by the results of kinetic investigations and product studies. Because the reactions produced only elimination

TABLE 3. Brønsted β_{lg} Values for elimination from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₄X Promoted by R₂NH/R₂NH₂⁺ in 70 mol % MeCN(aq) at 25.0 °C

| R ₂ NH | Bz (<i>i</i> -Pr)NH | <i>i</i> -Bu ₂ NH | <i>i</i> -Pr ₂ NH | 2,6-DMP ^b |
|-------------------|----------------------|------------------------------|------------------------------|----------------------|
| pK_a^a | 16.8 | 18.2 | 18.5 | 18.9 |
| β_{lg} | -0.28 ± 0.02 | -0.32 ± 0.01 | -0.30 ± 0.01 | -0.31 ± 0.01 |

^a Reference 5. ^b *cis*-2,6-Dimethylpiperidine.

SCHEME 1



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 0.28 to 0.32 because these mechanisms would exhibit either a specific base catalysis or Brønsted β values near unity.^{6,7} 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 $k_{obs} = k_1 k_2' [B] / (k_{-1} [BH^+] + k_2')$ (Scheme 1).⁶ The (E1cb)_R mechanism requires that the first step must be reversible, i.e., $k_{-1} [BH^+] \gg k_2'$, and the rate expression can be simplified to $k_{obs} = k_1 k_2' [B] / (k_{-1} [BH^+])$. This would predict that the k_{obs} should remain constant regardless of the buffer concentration because $[B] / [BH^+] = 1.0$ is maintained throughout the reaction. Therefore, the (E1cb)_R mechanism is ruled out by the linear dependence of the k_{obs} values on the base concentration. On the other hand, the $\beta = 0.28–0.32$ and $|\beta_{lg}| = 0.28–0.32$ are consistent with an E2 mechanism with limited cleavage of the C β –H and N α –OC(O)Ar bonds in the transition state, and a mechanism in which k_1 is the rate limiting [(E1cb)_{irr}], for which a small or negligible leaving group effect is expected.⁷

The distinction between the two mechanisms has been made by the interaction coefficients. Table 2 shows that the β values for **1a** remain almost the same within experimental error regardless of the base strength. The result can be described by a negligible p_{xy} interaction coefficient, $p_{xy} = \partial\beta / \partial pK_{lg} \approx 0$, which describes the interaction between the base catalyst and the leaving group.^{6,8–11} The similar $|\beta_{lg}|$ values for all bases is another manifestation of this effect, $p_{xy} = \partial\beta_{lg} / \partial pK_{BH} \approx 0$ (Table 3). On the More–O'Ferrall–Jencks energy diagram shown in Figure 3, a change to a better leaving group will raise the energy of the top edge of the diagram. The transition state on the horizontal coordinate will remain at nearly the same position because there is no diagonal character. This would predict negligible change in β .⁸ Similarly, a change to a stronger base will raise the energy of the right side of the diagram. The

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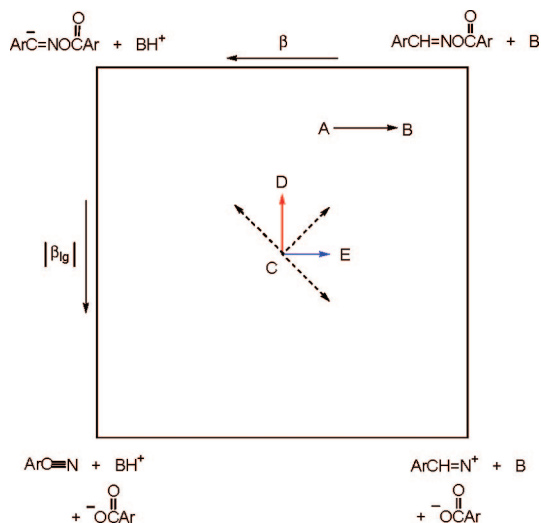


FIGURE 3. Reaction coordinate diagram for nitrile-forming eliminations from (*E*)-2,4-dinitrobenzaldehyde *O*-benzoyloximes. (Top) The effect of the change to a stronger base on the horizontal reaction coordinate is shown by the shift of the transition state from A to B. The effect of the change to a better leaving group is omitted because there will be little shift. (Center) The effects of the change to a stronger base and a better leaving group on the diagonal reaction coordinate are shown by the shifts from C to D and C to E, respectively. These effects can be described by $p_{xy} > 0$.

TABLE 4. Effect of the Base-Solvent on the Nitrile-Forming Eliminations from (*E*)-2,4-(NO₂)₂C₆H₃CH=NOC(O)C₆H₅

| base-solvent | R ₂ NH-MeCN ^a | R ₂ NH/R ₂ NH ₂ ⁺ -70 mol % MeCN(aq) |
|---------------------------------|-------------------------------------|----------------------------------------------------------------------------------|
| rel rate (k_2) ^b | 1.0 | 0.6 |
| β | 0.47 ± 0.04 | 0.32 ± 0.02 |
| β_{lg} ^c | -0.41 ± 0.01 | -0.28 ± 0.02 |
| p_{xy} | 0.040 ± 0.005 | ~0 |

^a Reference 2. ^b R₂NH = *i*-Bu₂NH. ^c R₂NH = Bz(*i*-Pr)NH.

transition state on the horizontal coordinate will then move toward the right as depicted by a shift from A to B, resulting in little change in $|\beta_{lg}|$.⁸ The negligible p_{xy} coefficients are inconsistent with the E2 mechanism for which $p_{xy} > 0$ is expected (Figure 3) but provide a strong evidence for the (E1cb)_{irr} mechanism.^{6,8-11}

Effect of Base-Solvent. Table 4 shows that the rate of elimination from **1a** decreases slightly as the base-solvent is changed from *i*-Bu₂NH-MeCN to *i*-Bu₂NH/*i*-Bu₂NH₂⁺ in 70 mol % MeCN(aq), presumably due to the decreased basicity in more protic solvent.¹² The extent of C_β-H and N_α-OC(O)Ar bond cleavage decreased remarkably as revealed by the large decrease in the Brønsted β and $|\beta_{lg}|$ values by the same variation of the base-solvent system (Table 4).

The change in the transition-state structure with the base-solvent variation can be attributed to a solvent effect. If the partial

negative charge developed at the β -carbon in the transition state is better stabilized by solvation in more protic 70 mol % MeCN(aq), the transition state should be less sensitive to the base strength. This would predict a smaller β value, as observed. Moreover, 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-OC(O)Ar bond. If a smaller amount of negative charge is transferred from the β -carbon, the extent of N_α-OC(O)Ar bond cleavage should be smaller too. The most interesting result from this study is the change of the reaction mechanism from E2 to (E1cb)_{irr} by the base-solvent variation as revealed by the interaction coefficients ($p_{xy} > 0 \rightarrow p_{xy} \sim 0$) (Table 4). It appears that the change in the elimination reaction mechanism has been realized by the combined effects of strongly electron-withdrawing β -aryl substituents, intrinsically carbanion stabilizing sp²-hybridized β -carbon, *syn*-stereochemistry and enhanced anion-solvating ability of more protic solvent.

Experimental Section

Materials. (*E*)-2,4-Dinitrobenzaldehyde *O*-benzoyloximes **1a-d** were available from previous investigations.² Reagent-grade acetonitrile and secondary amine were fractionally distilled from CaH₂. Buffer solutions were prepared by dissolving equivalent amounts of R₂NH and R₂NH₂⁺ in 70 mol % MeCN(aq). In all cases, the ionic strength was maintained to be 0.1 with Bu₄N⁺Br⁻.

Kinetic Studies. All of the reactions were followed using a UV-vis spectrophotometer with thermostated cuvette holders. Reactions were monitored by the decrease in the absorption of the substrate at 258–280 nm under pseudo-first-order condition employing at least 400-fold excess of the base. The pseudo-first-order rate constants were divided by the base concentration to afford the second-order rate constants, k_2 .

Product Studies. The product from the reaction of **1a** with *i*-Bu₂NH/*i*-Bu₂NH₂⁺ in 70 mol % MeCN(aq) was identified by using more concentrated solution as described previously.² A solution of 0.5 g (1.59 mmol) of **1a** and an excess amount of base in the appropriate base (15 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 the benzoate were completely removed. The product was 2,4-dinitrobenzotrile with mp 103 °C (lit.¹³ mp 104–105 °C). The yield of 2,4-dinitrobenzotrile was 0.29 g (94%).

Control Experiments. The stabilities of **1a-d** were determined as reported.^{1,2} The solutions of **1** in MeCN were stable for at least 5 weeks when stored in the refrigerator.

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