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Notes

Elimination Reactions of (*E*)-2,4-Dinitrobenzaldehyde *O*-Benzoyloximes

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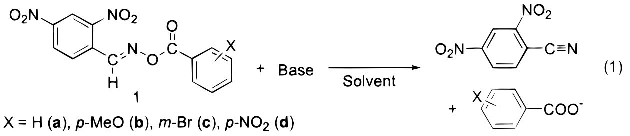
Extensive study of the structure−property relationship revealed that the nitrile-forming syn eliminations from (*E*)-benzaldehyde *O*-aryloximes proceed by the E2 mechanism via the E2-central transition state under various conditions.[1−10] Similarly, the *E* and *Z* isomers of benzaldehyde *O*-pivaloyloximes and benzaldehyde *O*-benzoyloximes reacted with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in MeCN by the same E2 mechanism, despite the 20000−36000-fold difference in rate.[11,12] The transition state for the anti-elimination reaction was slightly more product-like with smaller degrees of proton transfer and N_α−OC(O)Ar bond cleavage, less negative charge development at the β-carbon, and a greater extent of triple-bond formation than that for the corresponding syn elimination. Only a small difference in the transition-state structure was noted. The results are somewhat surprising since the latter has syn stereochemistry, a poor leaving group, and a sp^2-hybridized β-carbon atom. It is well established that the transition state for the syn elimination has more carbanion character than that for anti elimination because of the poor overlap of the developing p-orbitals.[13−16] Moreover, carboxylates are poor leaving groups, which should also increase the negative charge density at the β-carbon in the transition state.[16] Furthermore, an sp^2-hybridized β-carbon atom should stabilize the negative charge density more than an sp^3-hybridized carbon atom.[14,16] All of these factors favor an E1cb or E1cb-like transition state. However, such a transition state has never been observed in the nitrile-forming syn-elimination reactions.

Table 1. Rate Constants for Eliminations from (*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_4X$[a] Promoted by R_2NH in MeCN at 25.0 °C

R_2NH	10^2k_2,[c,d] $M^{-1}\,s^{-1}$			
	X = H	X = *p*-MeO	X = *m*-Br	X = *p*-NO_2
Bz(*i*-Pr)NH	0.789	0.360	2.33	4.36
i-Bu_2NH	2.91	1.54	7.33	13.9
i-Pr_2NH	4.78	3.02	12.8	24.2
2,6-DMP	8.22	5.28	21.5	34.1

[a] [Substrate] = 4.0×10^{-5} M. [b] [Base] = 1.8×10^{-2} M. [c] Average of three or more rate constants. [d] Estimated uncertainty, ±3%.

To determine whether a change to the E1cb mechanism could be realized by introducing a more electron-withdrawing β-aryl substituent, we studied the reactions of (*E*)-2,4-dinitrobenzaldehyde *O*-benzoyloxime with R_2NH in MeCN and *i*-Pr_2NH/*i*-$Pr_2NH_2^+$ in 70% MeCN(aq) (eq 1). This substrate is the most strongly activated one studied so far in the (*E*)-benzaldehyde *O*-benzoyloxime series.



X = H (**a**), *p*-MeO (**b**), *m*-Br (**c**), *p*-NO_2 (**d**)

Base-Solvent = R_2NH in MeCN, $R_2NH/R_2NH_2^+$ in 70 % MeCN(aq)

R_2NH = Bz(*i*-Pr)NH, *i*-Bu_2NH, *i*-Pr_2NH, 2,6-DMP

Results

The (*E*)-2,4-dinitrobenzaldehyde *O*-benzoyloximes **1a**−**d** were synthesized by the reaction of (*E*)-2,4-dinitrobenzaldehyde oxime with substituted benzoyl chlorides, as described previously.[11,12] The reaction of **1a** with *i*-Pr_2NH in MeCN produced (*E*)-2,4-dinitrobenzonitrile in 93% yield. No trace of (*E*)-2,4-dinitrobenzaldoxime could be detected by TLC.

Rates of reactions between **1a**−**d** and R_2NH in MeCN were followed by monitoring the decrease in absorption of the reactant at 280 nm, as described previously.[11,12] Excellent pseudo-first-order kinetic plots, which covered at least 3 half-lives, were obtained. Dividing the pseudo-first-order rate constants by the base concentration provided the second order-rate coefficients, k_2, presented in Table 1.

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Table 2. Brönsted β Values for Nitrile-Forming Eliminations from (*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_4X^a$ Promoted by R_2NH in MeCN at 25.0 °C

X	$pK_{lg}{}^a$	β
p-MeO	21.3	0.55 ± 0.05
H	20.7	0.47 ± 0.04
m-Br	19.5	0.45 ± 0.05
p-NO_2	18.7	0.43 ± 0.04

[a] Reference 22.

Table 3. Brönsted β_{lg} Values for Nitrile-Forming Eliminations from (*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_4X^a$ Promoted by R_2NH in MeCN at 25.0 °C

R_2NH	$pK_a{}^a$	β_{lg}
Bz(*i*-Pr)NH	16.8	- 0.41 ± 0.03
i-Bu_2NH	18.2	- 0.36 ± 0.02
i-Pr_2NH	18.5	- 0.35 ± 0.02
2,6-DMP	18.9	- 0.32 ± 0.01

[a] Reference 23.

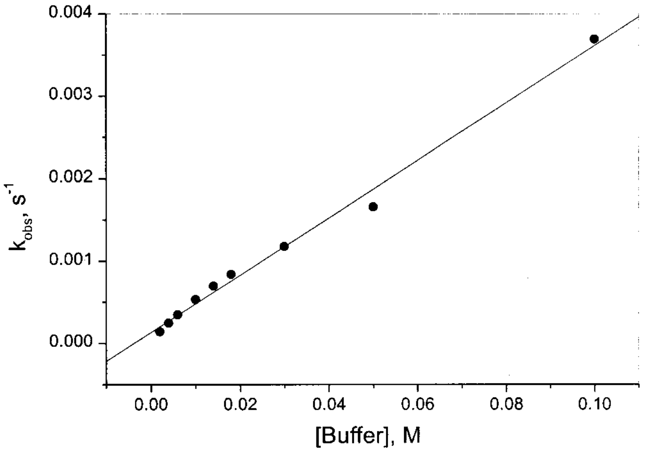

Figure 1. Plot of k_{obs} vs buffer concentration for elimination from *(E)*-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_5$ promoted by *i*-Pr_2NH/*i*-$Pr_2NH_2{}^+$ in 70% MeCN(aq) at 25.0 °C.

The k_2 values showed excellent correlation with the pK_a values of the promoting base on Brönsted plots (not shown). The β value decreases as the leaving group is made less basic (Table 2). Similarly, the k_2 values correlated satisfactorily with the leaving group pK_a values (plots not shown). The $|\beta_{lg}|$ value decreases with a stronger base (Table 3).

Elimination reactions of **1a** with *i*-Pr_2NH/*i*-$Pr_2NH_2{}^+$ buffer in 70% MeCN(aq) were also briefly studied. The k_{obs} values are summarized in Table 4. The k_{obs} values increase linearly with buffer concentration (Figure 1).

Discussion

Mechanism of Elimination from 1 Promoted by R_2NH in MeCN. Results of the kinetic investigations and product studies clearly establish that the reactions of (*E*)-2,4-dinitrobenzaldehyde *O*-benzoyloximes **1** with R_2NH in MeCN proceed via an E2 mechanism. Since the reactions produced only elimination products and exhibited second-order kinetics, all but bimolecular pathways can be ruled out. In addition, an E1cb mechanism is negated by the substantial values of β and $|\beta_{lg}|$.[15,16]

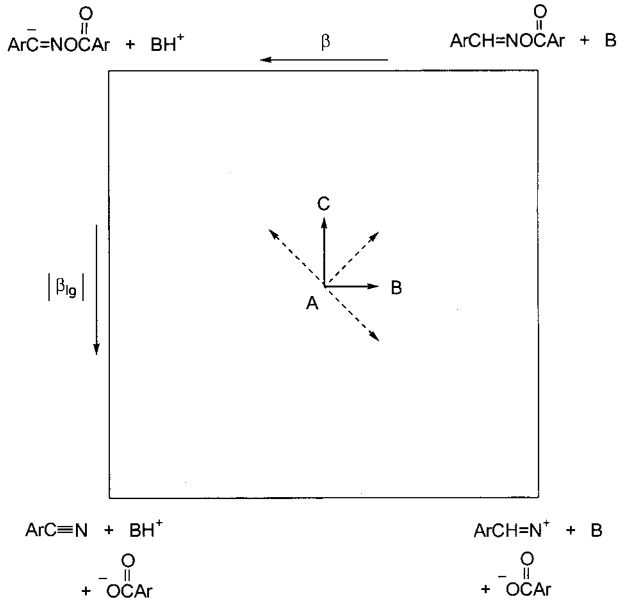

Figure 2. Reaction coordinate diagram for nitrile-forming eliminations from (*E*)-2,4-dinitrobenzaldehyde *O*-benzoyloximes. The effects of the change to a better leaving group and a stronger base are shown by the shift of the transition state from A to B and A to C, respectively.

This conclusion is supported by the interaction coefficients. Table 2 shows that the β values for **1** decrease slightly as the leaving groups are made less basic. The result can be described by a positive p_{xy} interaction coefficient, $p_{xy} = \partial\beta/\partial pK_{lg} = \partial\beta_{lg}/\partial pK_{BH}$, that describes the interaction between the base catalyst and the leaving group.[16,17] The observed increase in the $|\beta_{lg}|$ values as the catalyst is less basic is another manifestation of this effect, i.e., $p_{xy} = \partial\beta_{lg}/\partial pK_{BH} > 0$. On the More–O'Ferall–Jencks energy diagram shown in Figure 2, a change to a better leaving group will raise the energy of the top edge of the diagram. The transition state on the vertical reaction coordinate will then move slightly toward the right as depicted by a shift from A to B on the energy diagram, resulting in a decrease in β (vide supra).[18,19] Similarly, a stronger base will raise the energy of the right side of the energy diagram and shift the transition state from A to C to decrease the extent of N_α–OC(O)Ar bond cleavage. The positive p_{xy} coefficients are inconsistent with an E1cb mechanism for which $p_{xy} = 0$ is expected, but provide additional support for the concerted E2 mechanism.[16,17] All of these results are very similar to those for closely related eliminations from (*E*)- and (*Z*)-benzaldehyde *O*-benzoyloximes.[12]

It is conceivable that a change to a more protic solvent may lower the energy of the carbanion intermediate, which may in turn induce a change in the reaction mechanism from E2 to E1cb. To assess this possibility, we have investigated the elimination reactions of **1a** with *i*-Pr_2NH/*i*-$Pr_2NH_2{}^+$ buffer in 70% MeCN(aq). Figure 1 shows that the plot of k_{obs} vs buffer concentration is a straight line passing through the origin, i.e., $k_{obs} = k_2$[buffer]. If the reaction proceeds via a carbanion intermediate, the rate equation can be expressed as $k_{obs} = k_1k_2[B]/(k_{-1}[BH^+] + k_2)$ (Scheme 1).[16] This predicts that the plot of k_{obs} should change from a straight line at a low buffer concentration, i.e., $k_{obs} = k_1[B]$ when $k_{-1}[BH^+] \ll k_2$, to a plateau at a higher base concentration, i.e.,

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Table 4. Rate Constants for Elimination from (*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_5$[a] Promoted by *i*-$Pr_2NH$/*i*-$Pr_2NH_2^+$ in 70% MeCN(aq) at 25.0 °C[b]

10^2[buffer],[c] M	0.200	0.400	0.600	1.00	1.40	1.80	3.00	5.00	10.0
$10^3 k_{obs}$,[d,e] s^{-1s}	0.138	0.245	0.347	0.530	0.696	0.839	1.18	1.66	3.69

[a] [Substrate] = 4.0×10^{-5} M. [b] Ionic strength = 1.0 M ($Bu_4N^+Br^-$). [c] Buffer ratio = 1.0. [d] Average of three or more rate constants. [e] Estimated uncertainty, ±3%.

Scheme 1

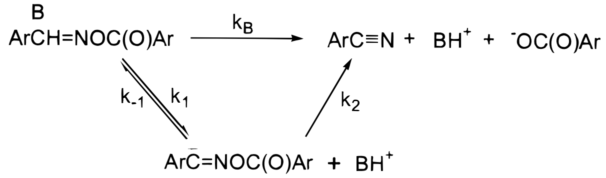

Table 5. Relative Rate, Brönsted *β*, and β_{lg} Values for Eliminations from (*E*)-$YC_6H_4CH{=}NO(O)C_6H_4X$

	Y = H[a]	Y = 2,4-$(NO_2)_2$
base−solvent	DBU−MeCN[b]	R_2NH−MeCN
pK_a	19.4	18.5[c]
relative rate[d]	1	10
β[d]	>0.5[e]	0.47 ± 0.04
β_{lg}	−0.49 ± 0.02	−0.35 ± 0.02

[a] Reference 12. [b] DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene. [c] R_2NH = *i*-Pr_2NH. [d] X = H. [e] Estimated from $k_H/k_D = 3.3$ (see text).

$k_{obs} = k_2$ when $k_{-1}[BH^+] \gg k_2$. Hence the straight line observed in Figure 1 provides strong evidence that the reaction proceeds by the E2 mechanism even under with additional favoring conditions for the E1cb mechanism.

Effect of *β*-Aryl Group on the Nitrile-Forming Transition State. Table 5 shows that the rate of elimination from **1a** is only 10-fold faster than that from the unsubstituted (*E*)-benzaldehyde *O*-benzoyloxime. Although this result may in part be attributed to the weaker basicity of *i*-Pr_2NH than DBU, the difference is surprisingly small considering the large difference in the electron-withdrawing ability of the *β*-aryl substituent.[11]

Comparison of the transition-state parameters reveals that the structure of the transition states for these two reactions are also similar. It was previously reported that the DBU-promoted elimination from (*E*)-benzaldehyde *O*-benzoyloxime proceed via a slightly E1cb-like transition state, in which the C_β−H bond cleavage has progressed to a greater extent than the N_α−OAr bond rupture.[11,12] Although a direct comparison between the k_H/k_D and β values is not possible, $\beta = 0.47$ for elimination from **1** appears to indicate a smaller extent of proton transfer than the $k_H/k_D = 3.3$ value for the former since the latter was attributed to more than half proton transfer.[11,12] In addition, the smaller $|\beta_{lg}|$ value for the former can also be explained with a lesser degree of N_α−OAr bond cleavage. These results indicate that the transition state for elimination from **1** is slightly more reactant-like with lesser extents of C_β−H and N_α−OAr bond cleavage. However, it should be noted that the difference is remarkably small considering the large difference in the *β*-aryl substituent.

The small difference in the transition-state structures may be attributed to the geometry of the reactant structure. It has been well established that the benzaldoxime esters have planar structures.[11,12,20] Hence, if the planarity is retained in the transition state, the π orbitals of the *β*-aryl groups should be nearly orthogonal to the developing negative charge at the *β*-carbon in the transition state.[20] This would predict that the electronic effect of the *β*-substituent should be transmitted to the reaction site only through an inductive effect. Furthermore, the negative charge density developed on the *β*-carbon would be less sensitive to the substituent effect because it should be more stable than that on a sp^3 hybridized carbon atom. It appears that the nitrile-forming transition states are intrinsically insensitive to the reactant structure variations because of the lack of resonance stabilization of charge density on the *β*-carbon and the increased carbanion stabilizing ability of the sp^2-hybridized *β*-carbon atom.

Experimental Section

Materials. (*E*)-2,4-Dinitrobenzaldehyde *O*-benzoyloximes **1a**−**d** were synthesized by the reaction of (*E*)-2,4-dinitrobenzaldehydeoxime with benzoyl chlorides, as described elsewhere.[11,12] The spectral and analytical data for the compounds were consistent with the proposed structures. The yield, melting point, IR (KBr, cm^{-1}), NMR ($CDCl_3$, *J* values are given in Hz), and combustion analysis data for the new compounds follow.

(*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_5$ (1a): yield 70%; mp 172−174 °C; IR 1759 (C=O), 1589 (C=N); NMR δ 9.22 (s, 1H), 9.02 (d, 1H, *J* = 2.4), 8.57 (dd, 1H, *J* = 8.7, 2.3), 8.48 (d, 1H, *J* = 8.4), 8.15 (d, 2H, *J* = 8.4), 7.66 (t, 1H, *J* = 7.3), 7.53 (t, 2H, *J* = 7.8). Anal. Calcd for $C_{14}H_9N_3O_6$: C, 53.34; H, 2.88; N, 13.33. Found: C, 53.20; H, 2.56; N,13.70.

(*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_4$-*p*-$OCH_3$ (1a): yield 56%; mp 158 °C; IR 1748 (C=O), 1600 (C=N); NMR δ 9.21 (s, 1H), 9.03 (d, 1H, *J* = 2.4), 8.57 (dd, 1H, *J* = 8.7, 2.3), 8.50 (d, 1H, *J* = 8.4), 8.12 (d, 2H, *J* = 8.6), 7.01 (d, 2H, *J* = 8.6), 3.91 (s, 3H). Anal. Calcd for $C_{15}H_{11}N_3O_7$: C, 52.18; H, 3.21; N, 12.17. Found: C, 52.23; H, 3.18; N,12.17.

(*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_4$-*m*-Br (1c): yield 56%; mp 178 °C; IR 1756 (C=O), 1582 (C=N); NMR δ 9.25 (s, 1H), 9.05 (d, 1H, *J* = 2.1), 8.59 (dd, 1H, *J* = 8.7, 2.3), 8.47 (d, 1H, *J* = 8.7), 8.30 (s, 1H), 8.10 (d, 1H, *J* = 7.8), 7.80 (d, 1H, *J* = 7.2), 7.42 (t, 1H, *J* = 7.7). Anal. Calcd for $C_{14}H_8BrN_3O_6$: C, 42.66; H, 2.05; N, 10.66. Found: C, 42.86; H, 2.13; N, 10.70.

(*E*)-2,4-$(NO_2)_2C_6H_3CH{=}NOC(O)C_6H_4$-*p*-$NO_2$ (1d): yield 62%; mp 172−174 °C; IR 1763 (C=O), 1589 (C=N); NMR δ 9.27 (s, 1H), 9.06 (d, 1H, *J* = 2.4), 8.61 (dd, 1H, *J* = 8.4, 2.3), 8.46 (d, 1H, *J* = 8.4), 8.39 (d, 2H, *J* = 8.9), 8.35 (d, 2H, *J* = 8.9). Anal. Calcd for $C_{14}H_8N_4O_8$: C, 46.68; H, 2.24; N, 15.55. Found: C, 46.80; H, 2.12; N, 15.29.

Buffer solutions were prepared by dissolving equivalent amounts of *i*-Pr_2NH and *i*-$Pr_2NH_2^+$ in 70% MeCN(aq). In all cases, the ionic strength was maintained at 0.10 M with $Bu_4N^+Br^-$.

Product Studies. The products of the reaction between **1a** and *i*-Pr_2NH in MeCN were identified using a more concentrated solution. A solution of **1a** was allowed to react with 10 equiv of *i*-Pr_2NH in 15 mL of MeCN for 3 h at room temperature. The solvent was evaporated, and the product was taken up in CH_2Cl_2. The solution was washed thoroughly with water, dried over $MgSO_4$, and evaporated. The product was 2,4-dinitrobenzonitrile with mp 105 °C (lit.[21] mp 104−5 °C); yield 0.36 g (93%).

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Kinetic Studies. Reactions of **1a**−**d** with R_2NH in MeCN and **1a** with of *i*-Pr_2NH and *i*-$Pr_2NH_2^+$ buffer in 70% MeCN(aq) were followed by monitoring the decrease in absorption at280 nm with reaction time by a UV−vis spectrophotometer, as described before.[11,12] For all reactions, the UV absorption of the reactants decreased and that of the products increased with time. Except for the reactions of **1a**, clean isosbestic points were observed at 245−250 nm.

Control Experiments. The stabilities of **1a**−**d** were determined by measuring the melting point and periodical scanning of their solutions in MeCN with the UV spectrophotometer.[11,12] No change in melting point or UV spectrum was detected for at least 1 month at −10 °C.

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