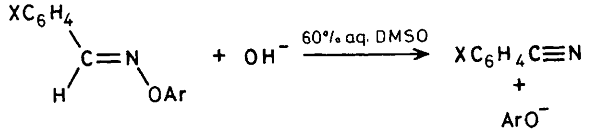
Eliminations from (*E*)-*O*-Arylbenzaldehyde Oximes Promoted by Hydroxide in 60% aq. Dimethyl Sulphoxide. Mechanism and Transition-state Characteristics of Nitrile-forming Eliminations

Bong Rae Cho,* Jong Chan Lee, Nam Soon Cho, and Kee Dong Kim
Department of Chemistry, Korea University 1-Anamdong, Seoul, Korea

Reactions of the (*E*)-*O*-arylbenzaldehyde oximes (**1**; Ar = 2,4-dinitrophenyl), (**2**; Ar = *p*-nitrophenyl), and (**3**; Ar = phenyl) with OH^- in 60% aq. DMSO have been investigated. The eliminations are quantitative, producing only benzonitriles and aryloxides. The observation of second-order kinetics, $k_2^{OD^-}/k_2^{OH^-}$ = 1.15—1.84, and β_{lg} = −0.59 is consistent with an *E*2 mechanism. The Hammett ρ and $k_2^{OD^-}/k_2^{OH^-}$ values increased with poorer leaving groups. For a given substrate the $k_2^{OD^-}/k_2^{OH^-}$ value remained (within experimental error) roughly constant, in spite of changes in the β-aryl substituents. These changes in transition state parameters can be interpreted in terms of the differing nitrile-forming transition states involved.

Recently, detailed studies of base-promoted imine-forming eliminations from *N*-haloamines and *N*-arenesulphonates have been reported.[1–10] These studies revealed that the reactions were normal E2 reactions and that the structure of the transition state ranged from E2 central to E1-like depending upon the leaving group and the reaction conditions. The effects of leaving group, base–solvent, and base strength upon the transition-state structure have also been determined. In contrast, only a few kinetic investigations of related nitrile-forming eliminations have been reported. Hauser and co-workers[11] have studied the reactions of ArCH=NCl with OH^- in aqueous EtOH. Eliminations from (*E*)-ArCH=NOTS promoted by AcO^- in EtOH have been reported by Crawford and Woo.[12] Recently, Hegarty and Tuohey[13] have probed OH^- induced eliminations from ArCH=NOR in water–dioxane (4:1). Although each of these investigations has added to the meagre store of information available on nitrile-forming eliminations, each has used different leaving group or base–solvent systems which have had little analogy with each other.

In order to provide a better insight into these nitrile-forming eliminations we investigated the reactions of a series of (*E*)-*O*-arylbenzaldehyde oximes with OH^- in 60% aqueous dimethyl sulphoxide (DMSO) (Scheme 1). The influence of aryl substituents and leaving groups was investigated in order to understand the characteristics of the transition state involved in the nitrile-forming eliminations. The results of these studies are now presented.



(*E*)-*O*-arylbenzaldehyde oxime

Ar	X
(**1**) $C_6H_3(NO_2)_2$-2,4	**a** H
(**2**) $C_6H_4NO_2$-4	**b** 4-OMe
(**3**) C_6H_5	**c** 4-Cl
	d 4-NO_2

Results

(*E*)-*O*-Arylbenzaldehyde oximes (**1**)–(**3**) were prepared by reaction of the appropriate benzaldehyde oxime with aryl halides[14] or benzaldehydes with *O*-arylhydroxylamines.[13,15,16] The physical data and spectral and analytical data of the compounds were consistent with the proposed structures.

Reaction of (**1**)–(**3**) with OH^- in 60% aq. DMSO produced quantitatively benzonitriles and aryloxides. The rate of elimination was monitored by the change in $\lambda_{max.}$ for the aryloxides (**1**) and (**2**) or for the substrate (**3**) [at 25.0 °C and c = 0.30 mol dm^{-3} (KCl)]. Excellent pseudo-first-order kinetic plots which covered at least two half lives were obtained. Pseudo-first-order rate constants were divided by the base concentration to provide second-order rate constants which remained constant for five- to ten-fold variation in base concentration. The reactions of (**1**)–(**3**) with OD^- in 60% DMSO–40% D_2O were followed by the same method. In general, the rate data for the more reactive compound (**1**) were not as easily reproduced as those for compounds (**2**) and (**3**). The $k_2^{OH^-}/k_2^{OD^-}$, $k_2^{OD^-}/k_2^{OH^-}$, and β values calculated from the relationship[17] $2.0^{\beta} = k^{OD^-}/k^{OH^-}$ are listed in Table 1.

Hammett plots for the eliminations from (**1**)–(**3**) are shown in Figure 1. For the reaction of (**2**) and (**3**) the influence of aryl substituents on the rate correlated well with the σ values (Figure 1). However, the rate data for (**1**) were scattered significantly from the Hammett plot. Although the reason for this large deviation is not clear at present, the ρ value was calculated for comparison with other systems. The Hammett ρ values are listed in Table 1. On the other hand, the influence of the leaving group variation (**1a**)–(**3a**) upon the rate correlated with σ^- values. The ρ_{lg} value is 1.4 ± 0.1. The β_{lg} value (calculated from the rate data for (**1a**)–(**3a**) and the pK_{lg} values† of the aryloxides[18,19]) is −0.59 ± 0.01.

The rates of elimination from (**1a**) was measured at three temperatures spanning 20 °C. An Arrhenius plot was linear with excellent correlation. The calculated enthalpy and entropy of activation are 14.5 ± 0.1 kcal mol^{-1} and −6.4 ± 0.1 e.u. respectively.

The reaction of (*E*)-*O*-picrylbenzaldehyde oximes‡ with OH^- was also briefly examined. The reaction produced

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† The pK_{lg} values for 2,4-dinitrophenol (5.9) and *p*-nitrophenol (9.0) in 60% aq. DMSO were estimated from the pK_{lg} values in H_2O[18] and ΔpK_{lg} (H_2O–60% aq. DMSO) = 1.8 for phenol.[19]

‡ Picryl = 2,4,6-trinitrophenyl.

Table 1. Rate constants, $k_2^{OD^-}/k_2^{OH^-}$, β, and ρ values for eliminations from (*E*)-*O*-arylbenzaldehyde oxime promoted by OH^- and OD^- in 60% aq. DMSO at 25.0 °C and *c* = 0.30 mol dm^{-3} (KCl).

Compound[a,b]	$10^2\ k_2^{OH^-}$/mol^{-1} dm^3 s^{-1}	$10^2\ k_2^{OD^-}$/mol^{-1} dm^3 s^{-1}	$k_2^{OD^-}/k_2^{OH^-}$	β[d]	ρ
(1a)	517 ± 8[c]	799 ± 70	1.40 ± 0.14	0.49 ± 0.14	0.2 ± 0.45
(1b)	112 ± 12	140 ± 5	1.25 ± 0.18	0.32 ± 0.21	
(1c)	356 ± 20	415 ± 35	1.17 ± 0.17	0.23 ± 0.21	
(1d)	268 ± 8	307 ± 48	1.15 ± 0.19	0.20 ± 0.24	
(2a)	7.99 ± 0.01	13.4 ± 0.1	1.68 ± 0.02	0.75 ± 0.02	1.9 ± 0.1
(2b)	4.02 ± 0.04	5.99 ± 0.03	1.49 ± 0.02	0.58 ± 0.02	
(2c)	25.4 ± 0.1	41.6 ± 0.2	1.64 ± 0.01	0.72 ± 0.01	
(2d)	315 ± 1	509 ± 2	1.62 ± 0.01	0.70 ± 0.01	
(3a)	0.182 ± 0.004	0.334 ± 0.006	1.84 ± 0.07	0.88 ± 0.06	2.2 ± 0.1
(3b)	0.0610 ± 0.0001	0.104 ± 0.006	1.71 ± 0.10	0.77 ± 0.02	
(3c)	0.667 ± 0.004	1.17 ± 0.01	1.75 ± 0.02	0.81 ± 0.02	
(3d)	11.2 ± 0.1	19.0 ± 0.1	1.70 ± 0.02	0.77 ± 0.02	

[a] [Substrate] = 5.0 × 10^{-5}—1.0 × 10^{-4} mol dm^{-3}. [b] [Base] = 2.44 × 10^{-3}—2.44 × 10^{-1} mol dm^{-3}. [c] k_2 = 12.7 ± 0.2 at 35.0 °C and 28.3 ± 0.5 at 45.0 °C. [d] Calculated from the relationship[17] $2.0^{\beta} = k^{OD^-}/k^{OH^-}$.

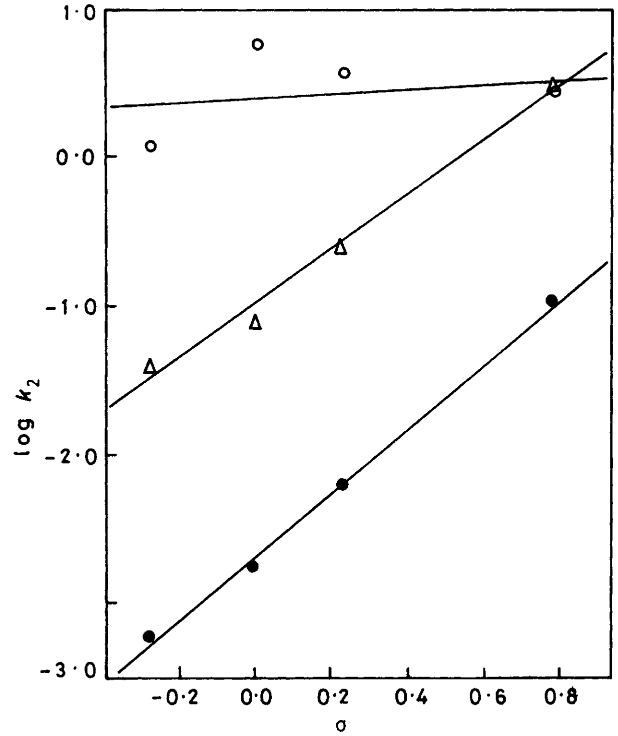


Figure 1. Hammett plots for eliminations from (*E*)-*O*-arylbenzaldehyde oximes promoted by OH^- in 60% aq. DMSO at 25.0 °C and *c* = 0.30 (KCl). Ar = 2,4-dinitrophenyl (○), 4-nitrophenyl (△), and phenyl (●), in descending order.

benzaldehyde oxime and picrate apparently by an S_NAr mechanism; the reaction was not pursued further.

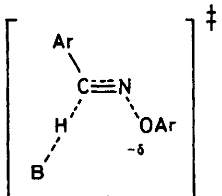
Discussion

Transition State for Elimination from (**1**) *Promoted by* OH^- *in* 60% *aq. DMSO.*—The results of product and kinetic studies clearly establish that the reactions of (**1**)–(**3**) proceed *via* an E2 mechanism. Since these reactions produced benzonitriles and aryloxides as the sole products and exhibited second-order kinetics, all but bimolecular pathways can be ruled out. In addition, an Elcb mechanism is negated by the substantial values of β and β_{lg}.[20]

For eliminations from (**1a**–**d**) a Hammett ρ value of 0.2 is obtained with poor correlation (Figure 1). Although the reason for this scatter is not clear at present, the value is much less than the ρ_{lg} value of 1.4 calculated for eliminations from (**1a**)–(**3a**). It appears that little negative charge is developed on the β-carbon and that most of the charge density is localized on the leaving group in the transition state. In addition, the rate data correlate with σ and σ^- values of the aryl substituents on the β-aryl group and the leaving group, respectively. These results reveal that the negative charge developed on the β-carbon in the transition state cannot be stabilized by through resonance with the substituents on the β-aryl group, whereas that on the leaving group can.

The secondary isotope effect $k_2^{OD^-}/k_2^{OH^-}$ can be used to assess the degree of proton transfer in the transition state. Using the relationship[17] $k_2^{OD^-}/k_2^{OH^-} = 2.0^{\beta}$ and the $k_2^{OD^-}/k_2^{OH^-}$ value of 1.40 ± 0.14 for (**1a**), the value of β = 0.49 ± 0.14 is calculated. This indicates a significant extent of proton transfer in the transition state. The degree of N_α–OAr bond cleavage in the transition state was measured by the β_{lg} value. For eliminations from (**1**)–(**3**) the β_{lg} value is −0.59 ± 0.01, indicating significant cleavage of the bond to the leaving group.

These combined results reveal that the structure of the transition state for nitrile-forming elimination from (**1**) involves significant cleavage of the C_β–H and N_α–OAr bonds, little carbanionic character on the β-carbon, appreciable charge density on the leaving group, and well developed triple bond character [see (**4**)].



(**4**)

The characteristics of this transition state can be rationalized by considering the geometry of (**4**), electronic effects, and solvent effects. In species (**4**) the developing negative charge on the β-carbon cannot be stabilized by resonance with the β-aryl group because the C_β–H bond is orthogonal to the π-orbital of the β-aryl group. On the other hand, the negative charge would be much better stabilized if it were located on the leaving group oxygen atom, owing to its electronegativity. Resonance with the

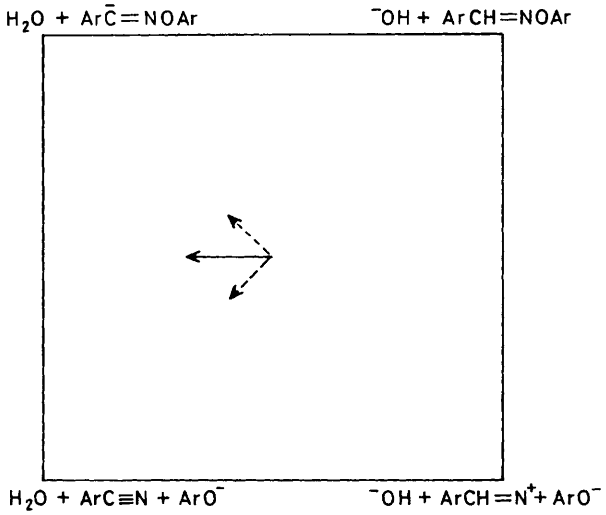


Figure 2. More O'Ferrall–Jencks reaction co-ordinate diagram for elimination reactions of (*E*)-*O*-arylbenzaldehyde oximes promoted by OH^- in 60% aq. DMSO. Energy contours are omitted. The effect of change to a poorer leaving group upon the transition-state position is shown by a solid line.

π orbital of the aryloxide and solvation effects are also stabilizing features. Therefore, the charge density on the β-carbon must be transferred between carbon and nitrogen to form a partial triple bond and to shift the negative charge onto the aryloxide in order to achieve maximum stabilization.

Effects of Leaving Group and Aryl Substituent upon the Transition State for Eliminations from **(1)**–**(3)** *Promoted by* OH^- *in* 60% *aq. DMSO.*—For eliminations from **(1)**–**(3)** the $k_2^{OD^-}/k_2^{OH^-}$ and ρ values increase as the leaving group becomes poorer, indicating a decrease in the extent of C_β–H bond cleavage and development of negative charge on the β-carbon in the transition state. For a given leaving group, however, the $k_2^{OD^-}/k_2^{OH^-}$ values are relatively invariant with changes in the aryl substituent (Table 1).

The variation in the transition-state structure with leaving group may readily be rationalized using the reaction co-ordinate diagram.[21,22] As previously mentioned, the transition state of elimination from **(2)** appears to be symmetrical to a similar extent with the C_β–H and N_α–OAr bond cleavage and thus can be located near the centre of the reaction co-ordinate diagram (Figure 2). Change to a poorer leaving group would increase the energy of the lower edge of the diagram, shifting the transition state toward the product and the E1cb intermediate. If similar effects are assumed for parallel and perpendicular motion, the effect of changing to a poorer leaving group would be to shift the transition state toward the left, as indicated in the reaction co-ordinate diagram. This corresponds to more C_β–H bond cleavage and increased carbanionic character in the transition state, as was observed.

The negligible effect of the β-aryl substituents upon the $k_2^{OD^-}/k_2^{OH^-}$ values for **(1)**–**(3)** may, in part, be attributed to solvation effects and/or relatively small variations in electronic effects due to the β-aryl substituents. Since the partial negative charge developed on the β-carbon in the transition state can be stabilized by solvation in 60% aq. DMSO, the influence of the β-aryl substituent upon the transition state structure is expected to be reduced.* Moreover, the change in the β-aryl substituents in **(1)**–**(3)** is much smaller than the leaving group variation in terms of electronic effects. Therefore, it seems reasonable to expect that the variation in the transition-state structures with the β-aryl substituents would be much less than with the leaving group variation.

Thus it appears that the reactions of **(1)** with OH^- in 60% aq. DMSO proceed *via* an E2-central type of transition state, in which most of the negative charge is delocalized on the leaving group. The position of the transition state is shifted toward the left edge in the reaction co-ordinate diagram as the leaving group becomes poorer. Noteworthy is the relative insensitivity of the transition-state structure to variation in the β-aryl substituents.

Experimental

N.m.r. spectra were recorded using EM-360 or Bruker AM-200 spectrometers. Chemical shifts are reported to the nearest 0.1 p.p.m. using $SiMe_4$ as an internal standard. I.r. spectra were recorded with a Perkin-Elmer Model 710B spectrophotometer. U.v. spectra were recorded using a Cary 17-D spectrophotometer with cuvette holders maintained at a constant temperature using a thermostat. Elemental analyses were performed by the Korea Advanced Institute of Science and Technology, Seoul, Korea.

Materials.—(*E*)-*O*-Arylbenzaldehyde oximes were prepared by the reactions of substituted benzaldehydes with the appropriate *O*-arylhydroxylamines[13,15,16] or (*E*)-benzaldehyde oximes with aryl halides.[14] The physical, spectral, and analytical data for these compounds were consistent with the proposed structures. The melting points, i.r., n.m.r., and analytical data for the new compounds are summarized in Table 2.

Dimethyl sulphoxide (DMSO) was distilled under reduced pressure from calcium hydride. The stock KOH solution in 60% aq. DMSO was prepared by adding clean pieces of potassium to 0.4 vol of distilled water in a volumetric flask and then filling to the mark with DMSO at 25.0 °C under nitrogen. An appropriate amount of KCl was then added to the solution to maintain the ionic strength at 0.30 mol dm^{-3}. The solution was diluted with 0.30 mol dm^{-3} KCl in 60% aq. DMSO when necessary.

Kinetic Studies on the Eliminations from the (E)-O-*Arylbenzaldehyde Oximes* **(1)**–**(3)**.—Kinetics were monitored on Cary 17 D or Pye Unicam SP 500 spectrophotometers. Reactions were carried out in the presence of a large excess of base at ionic strength 0.30 mol dm^{-3}, maintained with KCl. The cuvettes were temperature-equilibrated in the cell compartment of the spectrophotometer for at least 20 min prior to a kinetic run. The cuvette was removed and the solution of **(1)**–**(3)** in DMSO (6 mm^3) was injected with a microsyringe. The cuvette was quickly shaken and returned to the cuvette compartment. The increase in $\lambda_{max.}$ for 2,4-dinitrophenoxide (410 nm) or *p*-nitrophenoxide (405 nm) with time was monitored. For reactions of **(3)** with OH^-, the decrease in absorption of the substrate at 270 nm was monitored. Plots of $-\ln(A_\infty - A_t/A_\infty - A_0)$ *versus* time were linear over at least 2 half lives of the reaction. The slope shared a pseudo-first-order rate constant. Second-order rate constants were obtained by dividing the pseudo-first-order rate constant by the base concentration.

Product Studies on the Eliminations from the (E)-O-*Arylbenzaldehyde Oximes* **(1)**–**(3)**.—The products of OH^--

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* Consistent with this view is the observation of a systematic increase in the β value with electron-withdrawing β-aryl substituents for the reaction of **(1)** with Et_3N in MeCN, where the developing negative charge density on the β-carbon in the transition state cannot be stabilized by solvation.[23]

Table 2. Melting points i.r., n.m.r., and analytical data for (*E*)-*O*-arylbenzaldehyde oximes.

Compound	M.p. (°C)	I.r. (C=N)/cm^{-1}	N.m.r. (benzal C–H/δ)	Elemental analysis					
				Calc.			Found		
				C	H	N	C	H	N
(1c)	196—198	1 600	8.6	48.5	2.51	13.1	48.4	2.40	13.0
(2c)	122—125	1 610	8.4	56.4	3.28	10.1	56.2	3.16	10.1
(3b)	30—32	1 610	8.2	74.0	5.77	6.16	74.1	5.83	6.07
(3c)	58—59	1 610	8.3	67.4	4.35	6.05	67.4	4.35	6.04

promoted eliminations from **(1)**–**(3)** were identified by u.v. and t.l.c. experiments. When the reaction mixture was scanned periodically with a u.v. spectrophotometer, the reactant peak decreased as the aryl oxide peak increased. A clear isosbestic point was noted in between the two peaks. The yield of the aryloxide, determined by comparing the u.v. absorbances of the infinity samples with those of aryloxides, was in the range 80–90%. T.l.c. of the reaction product mixture showed the presence of benzonitrile and aryloxide; no other product could be detected.

Control Experiment.—(*E*)-*O*-Arylbenzaldehyde oximes **(1)**–**(3)** were stable for several months without decomposition. However, solutions of **(1)** in DMSO decomposed after 3 weeks at room temperature.

The rate of H/D exchange between D_2O and DMSO catalysed by OD^- in 60% DMSO–40% D_2O was determined by comparing the n.m.r. peaks of H_2O and DMSO taken periodically for a solution of $0.1OD^-$ (1 mol dm^{-3}) in 60% DMSO–40% D_2O. The H_2O peak at δ 2.40 increased with time. After 67 h the amount of H_2O formed in the exchange reaction was calculated to be 9.0%. Assuming a maximum $k_2^{OD^-}/k_2^{OH^-}$ value of 2 for an E2 reaction[21] this corresponds to a decrease in $k_2^{OD^-}$ of 18%. The $k_2^{OD^-}$ value for **(3b)** was also determined periodically. The rate decreased by approximately 5, 20, and 27% after 27, 67, and 100 h respectively. Therefore, the 60% DMSO–D_2O solution was used within 27 h of preparation.

Acknowledgements

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