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NUCLEOPHILIC CLEAVAGE OF N–O BOND IN *O*-(2, 4-DINITROPHENYL)CYCLOHEXANONE OXIME IN AQUEOUS-METHANOL

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Abstract—The order of nucleophilic reactivity towards nitrogen in *o*-(2, 4 - dinitrophenyl) cyclohexanone oxime with various nucleophiles in aqueous-methanol has been found to be: $N_2H_4 > OH^- > PhO^- >$ urea > thiourea > $SO_3^{2-} > CH_3COO^- > NO_2^- > S_2O_3^{2-} > SCN^- > Cl^- > Br^-$. A SN_2 type of reaction involving a polar transition state on the oxime N is indicated. Bronsted relationship is applicable ($\beta = 0.09$). The substrate is reducible at the dropping mercury electrode. Kinetics of the reaction has been followed both spectrophotometrically and polarographically with excellent conformity.

o-Substituted oximes have been variously studied mostly relating to complex formation,[1] Beckman rearrangement,[2] photochemical reactions[3,4] and reductions,[5,6] but no attempts seem to have been made in determining reactivity of the oxime N. In fact only limited data on nucleophilic reactivity towards nitrogen in general exist in the literature.[7-10]

In this paper nucleophilic reactivity towards the sp^2 N in *o*-(2, 4-dinitrophenyl) cyclohexanone oxime evaluated on the basis of kinetic studies are presented and discussed.

RESULTS AND DISCUSSION

Alkaline hydrolysis of *o*-(2, 4-dinitrophenyl) cyclohexanone oxime resulted in the splitting of the N–O bond. The rate followed eqn (1)

$$\text{rate} = k_0\,[\text{substrate}]. \qquad (1)$$

where k_0 is the rate constant observed for the cleavage of the N–O bond and [substrate] refers to the stoichiometric concentration of *o* - (2, 4 - dinitriphenyl) cyclohexanone oxime. The second order rate coefficient, k_2 for the cleavage followed eqn (2) and was obtained from the slope of the best straight line for the plot of k_0 vs [Nucleophile]

$$\text{rate} = k_2\,[\text{substrate}]\,[\text{nucleophile}]. \qquad (2)$$

Reactions were studied at various hydroxide ion concentration in aqueous-methanol (50 : 50 V/V) at 40 ± 0.1° and showed a linear dependence on hydroxode ion concentration. A plot of concentration vs rate was linear (Fig. 1).

There was no change in the pH of the mixture during the course of the reaction and rate constant remained unaffected by the variation in ionic strength. Reactions were carried out at various temperatures and activation parameters were evaluated from the Arrhenius plot (Fig. 2). $\Delta S^{\neq}$ was negative ($-80.5\ \text{kJ mol}^{-1}$) and the energy of activation was found to be $95.3\ \text{kJ mol}^{-1}$. A study of the reaction in various aqueous–methanol mixtures in which the percentage of water varied from 30 to 90 (Fig. 3) showed a gradual increase in rate indicating that the transition state leading to the products is stabilized by polar solvents. Further, the reaction was accelerated by cationic micelles of cetyl trimethylammonium bromide and cetyl pyridinium bromide, slightly by non-ionic micelles but there was no effect of anionic micelles.[11] This indicates that there is an accumulation of negative charge in the transition state. Isolation of 2, 4-dinitrophenoxide ion in quantitative yield support such a view.

Existence of any stable intermediate during the alkaline hydrolysis of the substrate in question can be

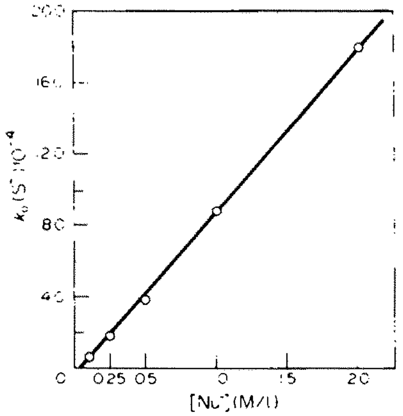


Fig. 1. Reaction of *o*-(2, 4-dinitrophenyl) cyclohexanone oxime in 50 : 50 methanol-water mixture (v/v) with various concentrations of hydroxide at 40 ± 0.1.

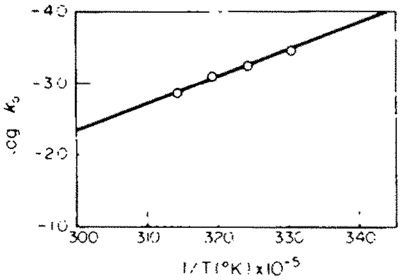


Fig. 2. Arrhenius plot for the reaction of *o*-(2, 4-dinitrophenyl) cyclohexanone oxime with hydroxide ion in 50 : 50 methanol-water mixture (v/v).

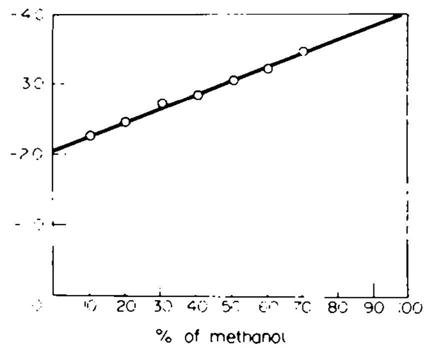
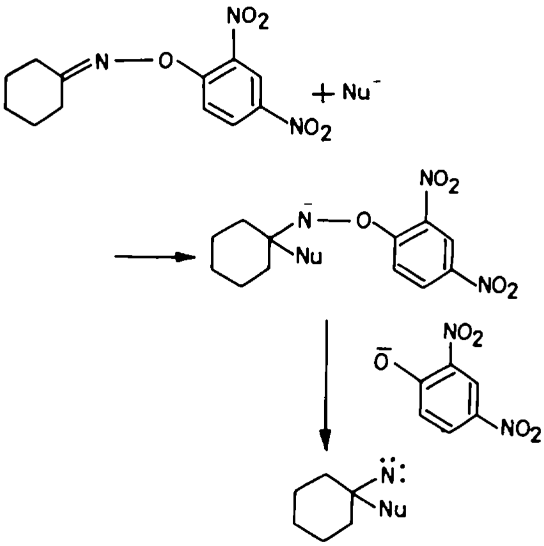


Fig. 3. Reaction of *o*-(2, 4-dinitrophenyl) cyclohexanone oxime with hydroxide ion in different methanol-water mixtures (v/v) at 40 ± 0.1°.



ruled out on the basis of a clear isosbestic point[12] at 322 nm. A possibility that the nucleophilic attack occurs at the oxime carbon, followed by the expulsion of the anion to give nitrene was considered.

But isolation of cyclohexanone oxime in good yield in addition to the 2, 4-dinitrophenoxide ion and absence of any other organic species as revealed by TLC clearly shows that the site of attack is the oxime N

On the basis of the above, a SN_2 type of reaction involving a polar transition state on the oxime N is indicated.

Reactions were studied with a range of nucleophiles, pK_a varying from −7.74 to 15.74. The results are summarised in Table 1. Bronsted plot (Fig. 4) is linear (with

Table 1. Kinetic data for the nucleophilic cleavage of the N-O bond: in *o*-(2, 4-dinitrophenyl) cyclohexanone oxime; in 50–50 methanol-water (V/V) at 40 ± 0.1°, [Nu] = 1.0 m

Nu	$10^3 \underline{k}_0$ (s^{-1})	$10^3 \underline{k}_2$ (l. $mole^{-1}$ s^{-1})	pK_a	D^a
N_2H_4	1.22	1.22	5.54	-
OH^-	0.87	0.87	15.74	-48.1
PhO^-	0.76	0.78	10.00	-
*CO_3^{2-}	0.34	0.68	10.25	-
Urea	0.66	0.66	13.82	-
Thiourea	0.60	0.60	14.96	-
*SO_3^{2-}	0.18	0.36	7.26	-
CH_3COO^-	0.34	0.34	4.72	-
NO_2^-	0.24	0.24	3.45	-33.8
$S_2O_3^{2-}$	0.15	0.15	1.86	-
SCN^-	0.11	0.11	-0.74	-
Cl^-	0.05	0.05	-4.74	-16.0
*Br^-	0.015	0.03	-7.74	-10.5

*[Nu] = 0.5 M

$\underline{k}_0$ = Observed pseudo first order rate constant with the added Nu.

$\underline{k}_2 = \underline{k}_0/[Nu]$

pK_a values used are those in water at 25°

[a]D values reported by Marks & Drago[17,18] applicable for reactions involving acid-base interaction.

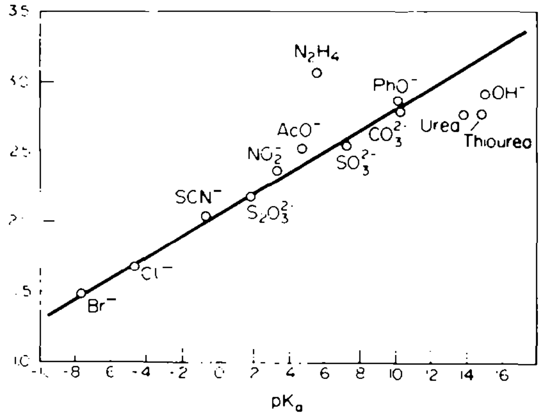


Fig. 4. Bronsted plot for the reaction of *o*-(2, 4-dinitrophenyl) cyclohexanone oxime with various nucleophiles in 50 : 50 methanol–water mixture (v/v) at 40 ± 0.0.

a few exception) suggesting that basicity is one of the factors affecting nucleophilic reactivity. However, the value of β is rather low (0.09). Most of the points fall close to the straight line with the exception of hydrazine which comes above the line indicative of some α-effect.[13] The magnitude of α-effect estimated on the basis of deviation from the Bronsted plot is of the order of 3.5 which is rather high for a β value of 0.09 as per findings of Dixon and Brucie[14] who envisage a direct relationship between β value and α-effect. Biggi and Pietra[15] however, argue that a high Bronsted β value may not be a sufficient condition for the presence of a clear α-effect and are of the opinion that a particular structure in the transition state is needed. In the present case the hard nature of hydrazine seems to play an important part in making the transition state more favourable. Slight deviation in the case of urea and thiourea in the opposite direction may be due to their relatively soft nature.

Reaction under study is basically an acid-base interaction and a correlation with the *D* values of Marks and Drago[16–18] may be expected. Figure 5 shows a correlation between log k_2/k_{H_2O} vs available D values of some anions studied. D values are related to the enthaly of the reaction in the form:

$$-\Delta H = [(D_A - D_B)^2 + O_A O_B]^{1/2}.$$

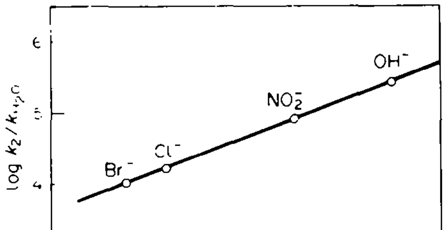


Fig. 5. Plot of D vs log k_2/k_{H_2O} for the reaction of *o*-(2, 4-dinitrophenyl) cyclohexanone oxime with various nucleophiles in 50 : 50 methanol–water (v/v) mixture at 40 ± 0.1°.

The parameters D are empirically obtained but are related to the diagonal elements of the MO secular determinant; O parameters are similarly obtained and are related to the off-diagonal elements. The suberscripts A and B refer to acid and base respectively.

Kinetic data obtained for the N–O bond cleavage in *o*-(2, 4-dinitrophenyl) cyclohexanone oxime with the nucleophiles studied were compared with those reported for some electrophilic C[19–21] and N[7,8] centers. It was observed that the N centre in question is not comparable with any of the above centres although it was somewhat similar to the nitroso N in alkyl nitrites[9] as far as the electrophilic site is concerned.

An examination of the rate constants with various nucleophiles suggests that the order of reactivity towards the electron-deficient N in the oxime derivative studied is: $N_2H_4 > OH^- > PhO^- > \text{urea} > \text{thiourea} > SO_3^{2-} > CH_3COO^- > NO_2^- < S_2O_3^{2-} > SCN^- > Cl^- > Br^-$.
This order can be explained in terms of a moderately hard N centre.

EXPERIMENTAL

Cyclohexanone oxime was prepared as per Vogel's procedure[22] which was then converted to the *o*-(2, 4-dinitrophenyl) derivative,[23] m.p. 102° (lit.[24] m.p. 102°). Spectral data of the compound are: UV and VIS (50% methanol 40°) λ_{max} (log ϵ) 305 (4.17), IR (KCl) ν_{max} 2860 (arom.ring), 1600 (c=N), 1560 (aryl NO_2), 980 (N–O) cm^{-1}.

Kinetics studies. Kinetic studies were carried out in 50–50 MeOH–water (V/V) at 40 ± 0.1° under pseudo first order condition. The progress of the reaction was followed at 400 nm in a Carl Zeiss Zena recording spectrophotometer using a thermostatted quartz cuvette. A typical kinetic run is described below:

Soln of the substrate (10^{-3}M) prepared in the said solvent was mixed with an appropriate volume of the nucleophile soln dissolved in the same solvent after proper thermal equilibration at the temp of the reaction. A portion of the thoroughly mixed mixture was then transferred to the thermostatted cell and the formation of the product was directly followed at 400 nm. The reaction was followed for at least 3 half-lives and the infinite reading was recorded after about 10 half-lives. The rate constants were calculated either from the integrated first order rate expression or from the slope of the first order plot. Reactions were carried out in the presence of 0.0001 M NaOH to ensure that the main product was estimated as the 2,4-dinitrophenoxide ion rather than as the free phenol. As mentioned earlier, the pH of the medium remained unchanged throughout. The background rate using 0.0001 M NaOH (and also the equimolar methoxide ion) was extremely small of the order of 0.29×10^{-8} lit. mol^{-1} s^{-1}.

To follow the kinetics polarographically the reaction was started by mixing the substrate solution with the appropriate amount of the nucleophile soln in a stoppered vessel at the desired temp. Aliquots of the mixture (1 ml) was pipetted at various timed intervals and transferred to a buffer soln (1 ml KCl, 1 M; 8.0 ml of a buffer of pH 10.65) at 0° to arrest the reaction when the polarograms were recorded. Reaction was followed measuring the wave height at 0.60 V corresponding to the half-wave potential of the substrate. The reaction was followed for at least 3 half-lives and the infinite reading was recorded after about 10 half-lives, id value was almost zero indicating completion of the N–O bond cleavage.

All polarograms were recorded in a Cambridge pen recording polarograph (capillary characteristic 3 mg$^{2/3}$ sec$^{1/6}$ at 0.0 V in 1.0 M KCl). All potentials were applied against a saturated calomel electrode.

For the dropping electrode triply distilled mercury was used. All the polarograms were recorded with 1.0 ml of depolariser, 1.0 ml of KCl and 8.0 ml of the appropriate buffer solution†. In all

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†Polarograms were recorded in Britton–Robinson buffer[25] with pH range 2–12. pH of the buffers were measured by an expanded scale pH Meter standardised by Potassium hydrogen phthalate (pH = 4.001) and borate buffer (pH = 9.18).

the solns purified N_2 was passed for 10 min to remove the dissolved O_2. All reagents used were of Analar grade. Solvents were distilled prior to use.

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