Tetrahedron. Vol. 27. pp. 323 to 330. Pergamon Press 1971. Printed in Great Britain

THE PARTICIPATION OF WATER IN THE NEF REACTION OF *ACI*-NITRO COMPOUNDS

S. F. Sun and J. T. Folliard

Department of Chemistry, St. John's University, Jamaica, New York, 11432

(*Received in USA* 14 *August* 1970; *Received in the UK for publication* 4 *September* 1970)

Abstract—A kinetic study of the effect of water content on the hydrolysis of three nitro aliphatic compounds in methanol, ethanol and dioxan solutions reveals the existence of two reaction pathways for the Nef reaction. The experimental results are shown to follow the rate law:

$$\frac{-d[HA]}{dt} = \left(\frac{k_a}{[H_2O]} + k_b \cdot [H_2O]\right)[H_3O^+][HA]$$

where HA represents the *aci*-nitro compound. The constants k_a and k_b are evaluated and a reaction mechanism consistent with all available experimental evidence is presented.

The preparation of aldehydes and ketones by the Nef reaction from primary and secondary nitro compounds has been extensively studied. A mechanism of the Nef reaction was proposed by several investigators.[1-3] These workers have concluded that the slow step in the reaction mechanism is most probably the attack of a water molecule on the protonated *aci*-form. While studying the effect of water content on the hydrolysis of 2-nitro propane in methanol, we observed an unexpected effect: as the water concentration increased, the rate constant decreased. This behavior is not consistent with the established mechanism.

In order to substantiate this effect and gain a more detailed understanding of the mechanism, the kinetic effects of water on the hydrolysis of three nitroalkanes, 2-nitropropane, 2-nitrobutane and 2-nitrooctane were studied in methanol, ethanol and dioxan.

RESULTS

Plots of log absorbance *vs* time at various acid concentrations established in all cases that the reaction was pseudo-first-order. Fig 1 illustrates the dependence of the first-order rate constants for the hydrolysis of 2-nitropropane at various water concentrations in methanol, on the acid concentration. The standard deviation of the slopes of the lines in Fig 1 is less than 5% for all cases. To determine the activation parameters for the reaction, determinations of the rate constants at three temperatures in several mixtures were carried out. Table 1 contains the representative experimental activation parameters for 2-nitropropane in methanol-water mixtures. From a graphical analysis of a plot of the second-order rate constant versus the reciprocal of the water concentration it was found that the experimental rate constants could be expressed by the following equation:

$$k_2 = \frac{k_a}{[H_2O]} + k_b[H_2O] \tag{1}$$

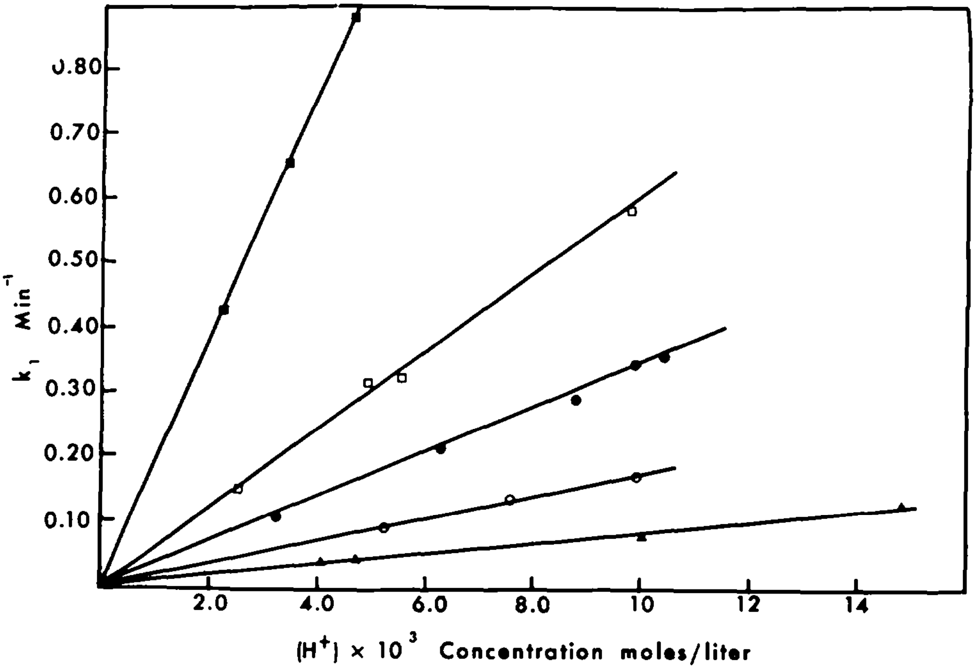


FIG 1. Dependence of the pseudo first-order rate constant for the hydrolysis of *aci*-2-nitropropane on the concentration of acid at 25° in water–methanol mixtures. The symbols for the water content in mole l^{-1} are ■ 0·379; □ 1·665; ● 2·775; ○ 5·550; ▲ 22·22

TABLE 1. KINETICS OF THE HYDROLYSIS OF *aci*-2-NITROPROPANE IN WATER–METHANOL MIXTURES

[H_2O] moles/liter	k_2 in l mole^{-1} min^{-1}			E_{act} kcal/mole	ΔH‡ (25°) kcal/mole	ΔS‡ (25°) e.u.
	15°	25°	35·1°			
1·67	33·4	59·8	97·2	9·39	8·79	−18·8
2·78	18·6	34·9	60·7	10·4	9·80	−16·5
5·55	8·08	17·3	35·1	12·9	12·3	− 9·41
11·1	4·49	10·2	17·8*	14·3	13·7	− 5·31
22·2	3·38	8·23	15·4*	16·0	15·4	−0·870

* These two points were taken at 31·5°.

where k_2 is the experimental second-order rate constant, k_2 is the initial slope of the plot and k_b is determined from a plot of k_2–k_a/[H_2O] versus [H_2O]. The results of such calculations are shown in Fig 2, where the logarithm of the second-order rate constants are plotted against the logarithm of the water concentration for the representative compound, 2-nitropropane in methanol-water mixtures at 25°. The curve was obtained by substituting into Eq 1 the appropriate values of k_a and k_b as determined above. The agreement between the calculated (using Eq 1) and experimental rate constants in most cases is within five per cent. Table 2 contains the values of k_a and k_b.

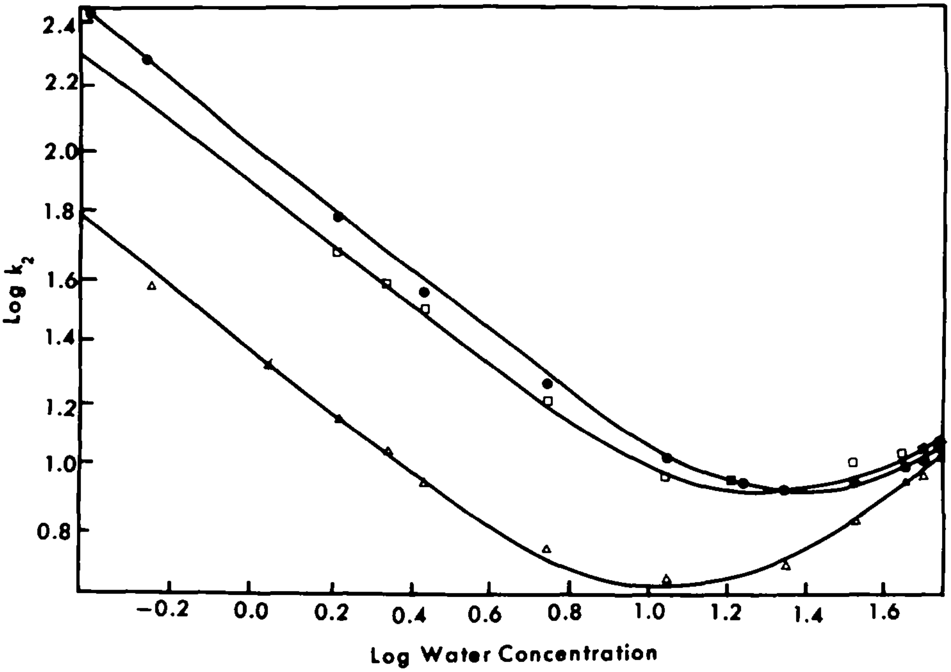


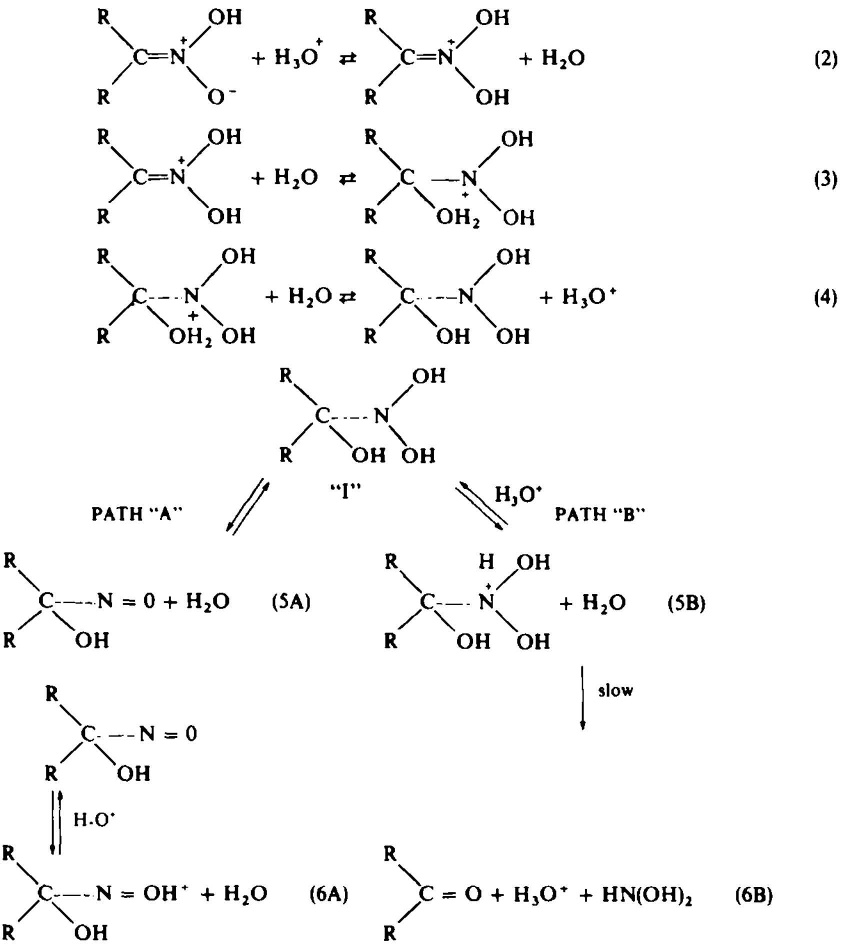
Fig 2. A comparison of the calculated second-order rate constants at 25° for the hydrolysis of *aci*-2-nitropropane in: ● methanol-, △ ethanol-, and ☐ dioxane–water mixtures with the experimental values. The curve represents the calculated rate constants and the points are the experimental values.

Table 2. Calculated values of the rate constants for paths "a" and "b" of the Nef reaction at 25°

	Methanol		Ethanol		Dioxan	
Compound	k_a min^{-1}	k_b l^{2}mole^{2}min^{-1}	k_a min^{-1}	k_b l^{2}mole^{2}min^{-1}	k_a min^{-1}	k_b l^{2}mole^{2}min^{-1}
2-Nitropropane	101·1	0·169	22·5	0·186	79·6	0·200
2-Nitrobutane	105·5	0·222	19·4	0·236	79·6	0·270
2-Nitrooctane	15·8	0·0512	2·40	0·0550		

DISCUSSION

The fact that Eq 1 describes the observed behavior of the nitro compounds in the solvent systems studied suggests that there are at least two paths by which these compounds may hydrolyze. Furthermore, the relative amount of reaction by these paths depends on the water concentration. The variation in activation parameters with water concentration can also be explained by this conclusion. A mechanism consistent with these observations can be represented by the following steps.*

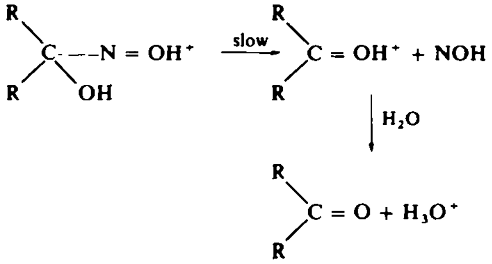


---

[*] In the following mechanism the solvated proton is represented in all cases by H_3O^+. The source for this assumption comes from the work of Salomaa[4] and Braude and Stern[5] who studied the change in acidity function, H_0, of hydrochloric acid in methanol, ethanol and dioxan caused by the addition of water. They evaluated the equilibrium constant for the reaction:

$$SH^+ + H_2O \rightleftharpoons S + H_3O^+$$

at 99 to 100% organic solvent and found that the equilibrium lies mainly to the right. Therefore, considering the low acid concentrations used in this study, the assumption that most of the protons are solvated by water seems reasonable.



(7A)

(8A)

$2\,HN(OH)_2 \rightarrow 3H_2O + N_2O$ (7B)

$2NOH \rightarrow N_2O + H_2O$ (9A)

After solving for the concentrations of the various intermediates, we obtain the rate equation,

$$\frac{-d[HA]}{dt} = \left(\frac{k_a}{[H_2O]} + k_b[H_2O]\right)[HA]\cdot[H_3O^+] \qquad (10)$$

Actually both paths have been proposed earlier. Van Tamelen and Thiede[1] first proposed path B and later Hawthorne[2] advanced path A. Since these investigators chose reaction (3) as the slow step in the mechanism, it was impossible for them to distinguish between the two paths. Our data show that reaction (3) is not the slow step in the mechanism and that the effect of water can be used to distinguish between the two paths.

Hawthorne's evidence* eliminates the possibility that reaction (3) could be a fast step since it would predict a different reaction sequence from what he observed. Our results demonstrate that reaction (3) cannot be the slow step since the effect of changing water concentration cannot be explained on that basis.† the impasse can be resolved by assuming that reaction (3) is an equilibrium controlled step with the equilibrium existing mainly to the left. This assumption permits reaction (3) to affect the overall kinetics, which in Hawthorne's case would result in the oberved reaction sequence. It also allows reactions (6A) and (5B) to affect the kinetics resulting in the observed effect of changing the water content.

The postulated equilibrium in reactions (5A) and (5B) is the departing point for paths A and B. The possibility that such an equilibrium might exist has been suggested by Hawthorne to reconcile the difference between his and Van Tamelen's approach to the decomposition of intermediate“I”.

The inverse effect of water suggests the presence of an equilibrium in which water is produced prior to the slow step. Reaction (6A) is postulated as such a step. This hypothesis is reasonable since it also produces a nitroso compound which is thought to be an intermediate in the Nef reaction.[7] In fact, Hawthorne has shown that the hydrolysis

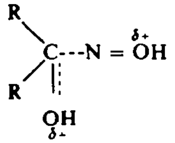
---

* Hawthorne's conclusions are based on the results of Brown *et al.*[6]

† An attempt was made to correlate the first-order rate constants using the Hammett acidity functions of hydrochloric acid in methanol, ethanol and dioxan as determined by Braude and Stern, and Salomaa. No correlation was found.

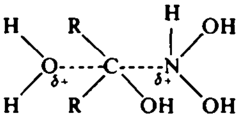
of alpha-chloro-nitroso-cyclo compounds produces a quantitative yield of the corresponding ketone presumably through an alpha-hydroxy-nitroso-intermediate. He concluded, by considering the reaction sequence, that the slow step in the mechanism was the decomposition of the protonated nitroso compound.[2] Therefore, by direct analogy it is proposed that reaction (7A) is the slow step in path A of the Nef reaction.

The proposed transition states for the two paths are:



"II"

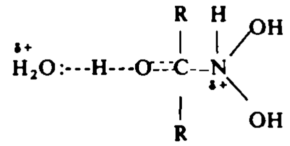
Path A



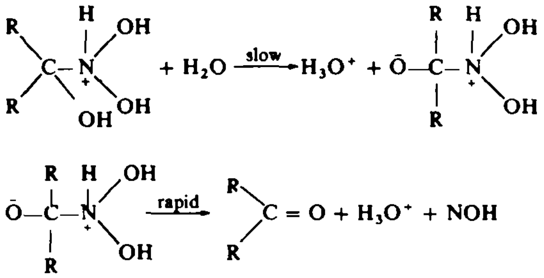
"III"

Path B

The transition state III may be expressed in a slightly different way:



Then the following mechanistic steps may be considered as alternates for (6B):



However, for the interpretation of kinetic data, transition state III is preferred.

The transition state III has a lower charge density than the reactant state. The reaction (6B) in which transition state III occurs is an ion-molecule reaction. The rate of an ion-molecule reaction is expected to be larger in a medium of lower dielectric constant.[8] This seems to be confirmed by the data in Table 2: k_b increases from methanol to dioxane.

For transition state II, the results of Table 2 show that the differences in k_a do not follow the change in solvent polarity. The results probably reflect a better solvation bonding with dioxane than ethanol in the transition state. But most likely the medium effects on k_a may come about from other factors. Since $k_a = k_{7A}K_{6A}K_5K_4K_3K_2$, it appears that those equilibrium constants involving charge transfers (K_{6A},K_4,K_3,K_2) would be affected greatly by the polarity of the medium.*

---

* We thank the referee for pointing this out to us.

The reaction sequence can be understood in terms of bulk effect. The bulkier alkyl groups in nitrooctane sterically retard the reaction.

Since transition state II results from an intramolecular reaction, it should have lower energy requirements than transition state III which results from an intermolecular reaction. This is reflected in the increase of activation energy in going from 1·6 M to 22 M water. The increase in activation entropy seems puzzling at first glance. It is expected that the incorporation of more molecules in the transition state for path B would make $\Delta S\ddagger$ more negative for path B than for path A, yet the data show the reverse. There are two possible interpretations for the negative increase of the entropy of activation from transition state III to transition state II: (1) It may be due to the internal freedom of water in transition state III, or (2) it may be due to a more concentrated charge density in transition state II than transition state III.[9] The data in Table 3 seem to support either interpretation.

Indeed, the effect of water on the rate of reaction has been shown in many cases. When present in a small amount, water may catalyze the reaction as in the alcoholysis of benzhydryl chloride[10] while it may inhibit a reaction as in the nitrosostyrene condensation in acetic acid.[11] It is to be pointed out that, in an extreme, changing a solvent from all organic solvent to 50% water could in itself exert a profound influence on the rate. The activities of the reactant, the water and the solvated proton may all be affected. It is quite possible that the phenomena we observed are not unique in the Nef reaction. However, if water participates in a reaction in the same way as we observed, it is possible that the reaction proceeds through two pathways.

TABLE 3. ACTIVATION PARAMETERS FOR THE TWO PATHS OF THE HYDROLYSIS OF *aci*-2-NITROPROPANE IN WATER–METHANOL MIXTURES

Rate constant	15°	25°	35°	E_{act} k cal/mole	$\Delta H^\ddagger$ (25°) k cal/mole	$\Delta S^\ddagger$ (25°) e.u.
k_a	48·8	101·1	177·9	11·4	10·8	--11·1
k_b	0·0506	0·169	0·570	21·4	20·8	9·62

EXPERIMENTAL

Materials. Practical grade 2-nitropropane (Matheson Coleman and Bell) was distilled on a Podbielniak column of 30 theoretical plates at a reflux ratio of 75 : 1. The first 25% of the distillate was discarded and the second 25% of the distillate was collected at 119·5°. High purity 2-nitrobutane and 2-nitrooctane (K and K Labs), MeOH (Baker and Adamson, "Reagent Grade Special Anhydrous" less than 0·005% water and acetone free) and EtOH ("Reagent Grade, Absolute") were used without further purification. Dioxan (Matheson Coleman and Bell, "Spectro-quality") was distilled from activated alumina.

Kinetic procedure. A Cary Model 14 Spectrophotometer, equipped with a constant temp cell holder was used for all kinetic measurements.

The UV absorption spectrum of *aci*-2-nitropropane exhibits a maximum at 220 mμ with an extinction coefficient of $1 \cdot 12 \times 10^4$ litermoles cm^{-1}. Since the nitro-form does not absorb appreciably in this region, this furnishes a convenient method for insuring complete conversion into the *aci*-form and for following its subsequent decomposition. The other nitro compounds exhibit similar behavior.

Several stock solns of the *aci*-nitro compounds were made by dissolving enough of the nitroparaffin to give a 0·1M soln in an accurately known excess of NaOH aq. The solns were then diluted to volume with the solvent of choice. A 100 ml aliquot of a soln of accurately known acid concentration (10^{-3} to 10^{-1}M HCl) in the solvent mixture of interest was kept at constant temp and 0·100 ml of the stock soln of 0·1M *aci*-nitro compound was added with a micro-buret. accurate to 0·0005 ml, while the soln was vigorously stirred. This was taken as zero time. The reaction mixture was added to a 1 cm glass-stoppered quartz cell and the change in absorbance was recorded as soon as possible, usually within 30 sec.

The reference soln used was identical with the reaction mixture except it did not contain the nitro compound. The temp within the cell was maintained at the desired level to within ±0·05°.

The concentration of water refers to the content of water in the final reaction mixture. The solutions containing the low concentration of water were analyzed by the Karl Fischer method, since, at these low ranges, introduction of water from the atmosphere or the added reagent might not be negligible.

Product analysis. The reaction products of the hydrolysis of *aci*-2-nitropropane were analyzed by gas chromatography using a 20% Carbowax on Anachrom column and a flame ionization detector. Acetone was identified by correlating its retention time with that of a standard acetone-MeOH soln. Quantitative analysis of the acetone in the part per million range was difficult to make since an impurity in the solvent MeOH (probably propionaldehyde) gave a peak which interfered with the acetone peak. To overcome the difficulty, a calibration curve was constructed using solns to which accurately known amounts of acetone were added. The product solns that were analyzed showed that the conversion to acetone was about 95%.

REFERENCES

[1] E. Van Tamelen and R. Thiede, *J. Am. Chem. Soc.* **74**, 2615 (1952)

[2] M. F. Hawthorne, *Ibid.* **79**, 2510, 2515 (1957)

[3] N. Kornblum and R. A. Brown, *Ibid.* **87**, 1742 (1965)

[4] P. Salomaa, *Acta Chem. Scand.* **11**, 125 (1957)

[5] E. A. Braude and E. S. Stern, *J. Chem. Soc.* 1967 (1948)

[6] H. C. Brown, J. H. Brewster and H. Sheckter, *J. Am. Chem. Soc.* **76**, 467 (1954)

[7] W. E. Noland, *Chem. Revs* **55**, 137 (1955)

[8] A. A. Frost and R. G. Pearson, *Kinetics and Mechanism*, (2nd Edition) p. 149. Wiley, New York,(1961)

[9] L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.* **1**, 1 (1963)

[10] N. T. Farinacci and L. P. Hammett, *J. Am. Chem. Soc.* **59**, 2542 (1937)

[11] C. E. Bell and T. I. Crowell, *J. Org. Chem.* **24**, 1159 (1959)