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SALT AND SOLVENT EFFECTS ON ALKALINE HYDROLYSIS OF *N*-HYDROXYPHTHALIMIDE. KINETIC EVIDENCE FOR ION-PAIR FORMATION

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The effects of the concentrations of LiCl, NaCl, KCl, CsCl, Na_2CO_3 and $BaCl_2$ on the rates of reactions of hydroxide ion with ionized *N*-hydroxyphthalimide (NHP^-) at 30 °C and in H_2O–MeCN solvents containing 10, 50, 60, 66, 70, 76 and 80% (v/v) MeCN reveal the formation of ion-pair complexes between cations of the salts, which probably exist in solvent-separated loose ion-pair forms ($M^{n+} \cdots X^{k-}$) and NHP^-. An increase in MeCN content from 2 to 76% (v/v) causes an increase in the association constants (*K*) by factors of 40, 21 and 9 for LiCl, NaCl and KCl, respectively, while the respective increase in the rate constants (k'_{s1}) for the collapse of the ion-pair complexes to product is *ca* two-fold. The values of k'_{s1} remain almost unchanged whereas the values of *K* increase 7·5-fold with an increase in MeCN content from 2 to 70% (v/v) for CsCl. Ion-pair complex formation was not detected in the presence of Me_4NCl at 70% (v/v) MeCN. The observed pseudo-first-order rate constants are highly sensitive to the valence state of cations and almost insensitive to the valence state of the anions of the salts.

INTRODUCTION

The observed pseudo-first-order rate constants for alkaline hydrolysis of phthalimide,[1] maleimide,[2] methyl,[3] ethyl[4] and phenyl salicylates,[5] dimethyl phthalate[6] and methyl 4-hydroxybenzoate[7] were found to decrease with increase in the contents of organic cosolvents (up to ⩾65%, v/v) in mixed aqueous–organic solvents. These results could be attributed to the consequence of several effects such as solvation, dielectric constant and concentration effects and perhaps some other effects. Recently, we observed[8] that the pseudo-first-order rate constants for the reaction of OH^- with ionized *N*-hydroxyphthalimide (NHP^-) decreased with increase in the contents of MeOH, EtOH and MeCN up to *ca* 80%, 75% and 40% (v/v), respectively. The rate constants increased sharply with increase in MeCN content at ⩾50% (v/v) in mixed aqueous–organic solvents.[8] These results were explained in terms of ion-pair formation and a specific solvation effect. The proposed ion-pair formation in this reaction was further investigated by studying the effects of salts of cations and anions of different valence states and characteristics in a predominantly aqueous solvent.[9] It is well known that ion-pair formation becomes much more stronger in aprotic organic solvents than in water. Therefore, in order to confirm the proposed occurrence of ion-pair formation in these reactions, we carried out the present study, which included salts of different characteristics and mixed H_2O–MeCN solvents.

EXPERIMENTAL

Materials

N-Hydroxyphthalimide (NHPH), $LiOH \cdot H_2O$, NaOH, KOH, Me_4NCl, LiCl, NaCl, KCl, CsCl, Na_2CO_3, $BaCl_2$ and MeCN were of reagent grade and were obtained from Aldrich or BDH. Stock solutions of NHPH were prepared in MeCN and were always stored at low temperature whenever they were not in use. Stock solutions of organic and inorganic salts were freshly prepared in glass-distilled water.

Kinetic measurements

The reaction rates were studied spectrophotometrically by monitoring the disappearance of ionized *N*-hydroxyphthalimide (NHP^-) as a function of time at

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410 nm and 30 °C . The details of the experimental procedure and data analysis are described elsewhere.[10]

RESULTS AND DISCUSSION

Effect of $[M_kX_n]$ at different contents of MeCN

A series of kinetic runs were carried out at 0·01 M and at different concentrations of a salt (M_xX_n) in mixed H_2O–MeCN solvents. The observed data for salts such as LiCl, NaCl, KCl, CsCl, Me_4NCl, Na_2CO_3 and $BaCl_2$ at different MeCN contents in mixed aqueous solvents are shown in Figures 1–4. It is evident from these results that the observed rate constants, k_{obs}, increased sharply with increase in $[M_kX_n]$ at low $[M_kX_n]$ followed by a slow increase at high $[M_kX_n]$. A similar dependence of k_{obs} on $[M_kX_n]$ was obtained when the reactions were carried out in the alkaline aqueous solvents containing 2% (v/v) MeCN.[9] The most plausible explanation of these results may be given in terms of the ion-pair formation mechanism as shown in Scheme 1, where C_1 and C_2 represent the respective ion-pair complexes formed between anionic substrate and cations of salts and alkali which, presumably, exist in the solvent-separated loose ion-pair forms ($M^{n+}\cdots X^{k-}$ and $M^+\cdots OH^-$) in mixed aqueous acetonitrile solvents. K_A and K'_A represent the association constants for the formation of the ion-pair complexes (C_1 and C_2) and k_{s0}, k_{s2}, k_{s1} and k_{OH} are the respective rate constants for uncatalysed and hydroxide ion-catalysed conversion of C_2, C_1 and NHP^- to product.

$$NHP^- + M^{n+}\cdots X^{k-} \xrightleftharpoons{K_A} C_1$$

$$NHP^- + M^+\cdots OH^- \xrightleftharpoons{K'_A} C_2$$

$$NHP^- + M^+\cdots OH^- \xrightarrow{k_{OH}} \text{o-Carboxybenzohydroxamic acid}$$

$$C_2 \xrightarrow{k_{s0}} \text{o-Carboxybenzohydroxamic acid}$$

$$C_2 + M^+\cdots OH^- \xrightarrow{k_{s2}} \text{o-Carboxybenzohydroxamic acid}$$

$$C_1 + M^+\cdots OH^- \xrightarrow{k_{s1}} \text{o-Carboxybenzohydroxamic acid}$$

Scheme 1

In terms of Scheme 1, the general rate law for the alkaline hydrolysis of *N*-hydroxyphthalimide in the presence of a salt may be given as

$$\text{rate} = k_{s0}[C_2] + (k_{OH}[NHP^-] + k_{s1}[C_1] + k_{s2}[C_2])[M^+\cdots OH^-] \quad (1)$$

The observed rate law ($\text{rate} = k_{obs}[Sub]_T$, where $[Sub]_T = [NHP^-] + [C_1] + [C_2]$ and $[NHPH] \approx 0$) and equation (1) can lead to the the equation

$$k_{obs} = \frac{k'_{OH} + k'_s K'_A[MOH] + k'_{s1}K_A[M_kX_n]}{1 + K'_A[MOH] + K_A[M_kX_n]} \quad (2)$$

where $k'_{OH} = k_{OH}[MOH]$, $k'_s = k_{s0} + k_{s2}[MOH]$ and $k'_{s1} = k_{s1}[MOH]$. Equation (2) may be rearranged to give

$$k_{obs} = \frac{k_0 + k'_{s1}K[M_kX_n]}{1 + K[M_kX_n]} \quad (3)$$

where $k_0 = (k'_{OH} + k'_s K'_A[MOH])/(1 + K'_A[MOH])$ and $K = K_A/(1 + K'_A[MOH])$.

In the data treatment with equation (3), the rate constant k_0 was obtained experimentally at $[M_kX_n] = 0$. The non-linear least-squares technique was used to calculate the unknown parameters, k'_{s1} and K from

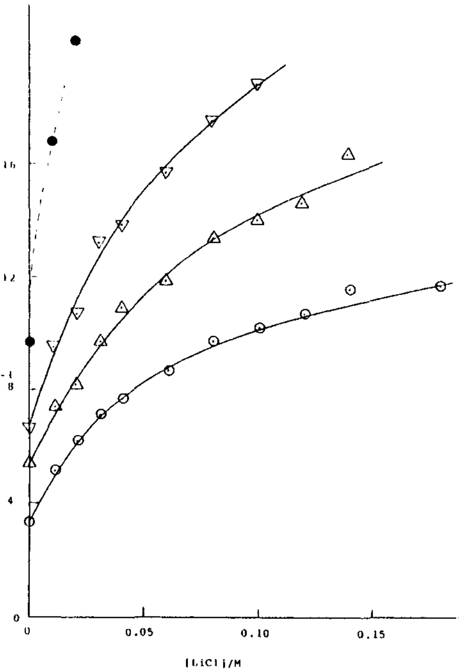


Figure 1. Dependence of observed rate constants, k_{obs}, for alkaline hydrolysis of NHP^- on total salt concentration, [LiCl], in H_2O–MeCN solvents containing (⊙) 60%, (▲), 66% (▼) 70% and (●) 76% (v/v) MeCN. The solid lines are drawn through the least-squares-calculated points using equation (3) and kinetic parameters listed in Table 1

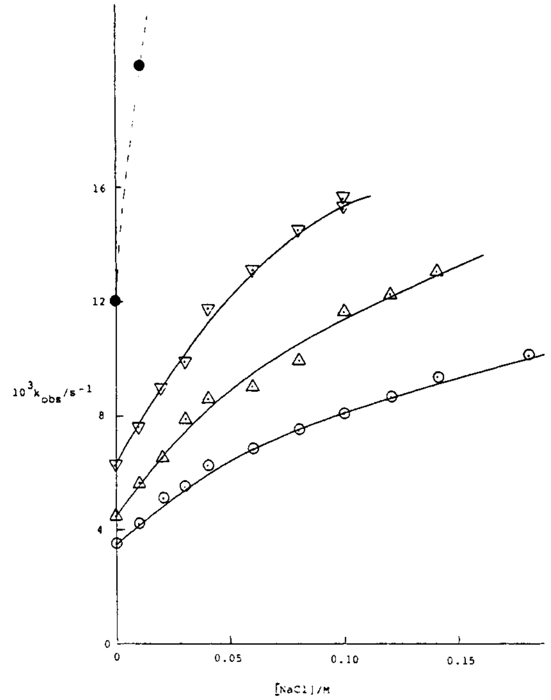


Figure 2. Observed rate constants, k_{obs}, versus total salt concentration [NaCl], for alkaline hydrolysis of NHP^- in mixed aqueous solvents (H_2O–MeCN) containing (⊙) 60%, (▲) 66%, (▼) 70% and (●) 76% (v/v) MeCN. The solid lines are drawn through the least-squares-calculated points using equation (3) and kinetic parameters listed in Table 1

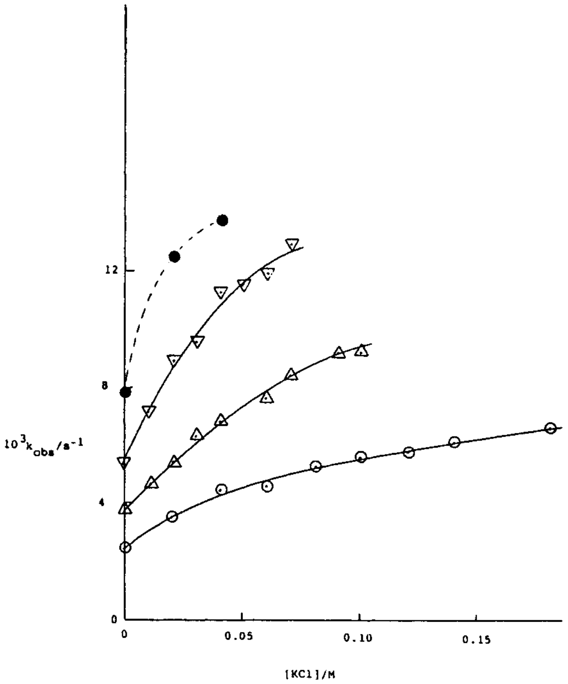


Figure 3. Dependence of observed rate constants, k_{obs}, for alkaline hydrolysis of NHP^- on total salt concentration, [KCl], in H_2O–MeCN solvents containing (⊙) 60%, (▲) 70%, (▼) 76% and (●) 80% (v/v) MeCN. The solid lines are drawn through the least-squares-calculated points using equation (3) and kinetic parameters listed in Table 1

equation (3). The results obtained for different salts at varying contents of MeCN in mixed aqueous solvents are summarized in Table 1. The fit of the observed data to equation (3) is evident from the standard deviations associated with the calculated parameters (Table 1) and from the calculated values of rate constants shown graphically in Figures 1–4. It should be noted that the reasonably good fit of the observed data to equation (3) indicates the insignificance of ion-pair formation between solvated cations (M^{k+} and M^+) and NHP^- and the reactions of C_1 and C_2 with hydrated OH^-.

When the same cation exists in both alkali and salt, such as NaCl + NaOH, KCl + KOH and LiCl + LiOH, it can be assumed that $K_A = K'_A$ because it has been demonstrated in related studies[9,11] that the nature of the anion of the salt does not affect the association constants. Under such conditions, the rate of reaction may be considered to be governed by Scheme 2, where C^- represents the counter ion (both OH^- and X^-). The observed rate law and Scheme 2 yielded the equation

$$k_{obs} = \frac{k'_{OH} + k'_{s2}K_{A2}[M^+]_T}{1 + K_{A2}[M^+]_T} \qquad (4)$$

where $[M^+]_T$ is the total concentration of cations, $k'_{OH} = k_{OH}[MOH]$ and $k'_{s2} = k_{s0} + k_{s2}[MOH]$. Equation (4) was used to calculate k'_{OH}, k'_{s2} and K_{A2} using the non-linear least-squares technique. The calculated values of these parameters are summarized in Table 2.

$$NHP^- + M^+\cdots C^- \overset{K_{A2}}{\rightleftharpoons} C_2$$

$$NHP^- + M^+\cdots OH^- \xrightarrow{k_{OH}} o\text{-Carboxybenzohydroxamic acid}$$

$$C_2 \xrightarrow{k_{s0}} o\text{-Carboxybenzohydroxamic acid}$$

$$C_2 + M^+\cdots OH^- \xrightarrow{k_{s2}} o\text{-Carboxybenzohydroxamic acid}$$

Scheme 2

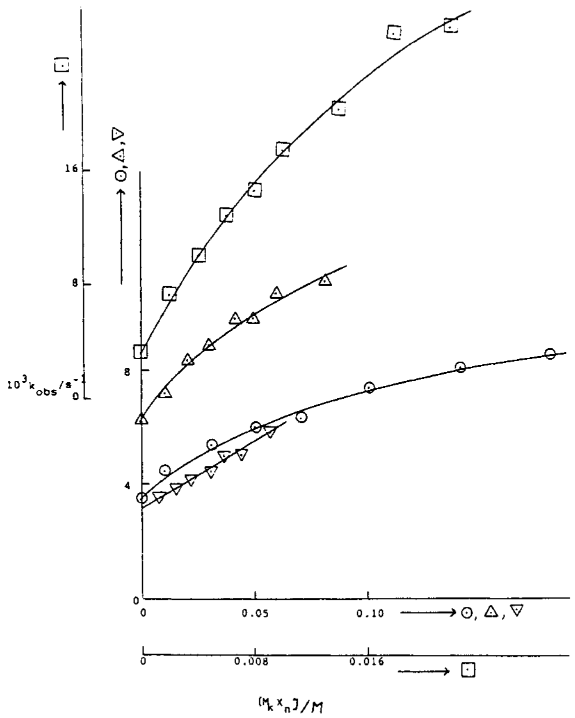


Figure 4. Dependence of observed rate constants, k_{obs}, for alkaline hydrolysis of NHP$^-$ on total salt concentration, $[M_kX_n]$, at [NaOH] = 0·01 M and H_2O–MeCN solvents containing (○) 60% and (△) 70% (v/v) MeCN for $M_kX_n = CsCl$, (□) 10% (v/v) MeCN for $M_kX_n = BaCl_2$ and (▽) 50% (v/v) MeCN for $M_kX_n = Na_2CO_3$. The solid lines are drawn through the least-squares-calculated points using equation (3) and kinetic parameters listed in the text and Table 1

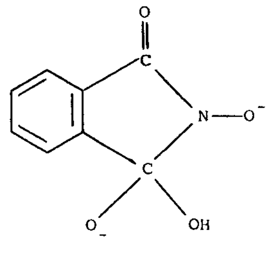
Equation (4) was derived based on the assumption that $K_A = K'_A = K_{A2}$. Since $K = K_A/(1 + K'_A[MOH])$, then $K_{A2} = K/(1 - K[MOH])$. This relationship was used to calculate K_{A2} at different MeCN contents for LiCl, NaCl and KCl. These values of K_{A2}, given in parentheses in Table 2, are comparable to the corresponding values obtained from equation (4).

The rate constant k_{OH} ($= k'_{OH}/[OH^-]$) represents the second-order rate constant for the reaction between NHP$^-$ and OH$^-$. According to simple electrostatic theory,[12] k_{OH} or k'_{OH} at a constant [OH$^-$] should decrease with decrease in the dielectric constant of the reaction medium. However, the calculated values of k'_{OH} do not appear to be influenced significantly by the increase in the MeCN contents from 2 to 76% (v/v). There could be many reasons for these results including, the following.

(i) Electrostatic theory portrays the medium effect in terms of the dielectric constant of the bulk medium. However, in mixed aqueous–organic solvent such as H_2O–MeCN, highly hydrophilic ions (M^{n+} and X^{k-}) of relatively high charge density are preferentially solvated by water molecules whereas NHP$^-$ ions with a large hydrophobic area are preferentially solvated by MeCN molecules. Hence the local dielectric constant, i.e. the dielectric constant in the neighbourhood of these ions, is expected to be different from that in the bulk solvent. The rate data obtained in the mixed solvents where local dielectric constants are effective are therefore not expected to fit to an equation derived on the basis of simple electrostatic theory.[12] (ii) As the MeCN content increases in H_2O–MeCN solvents, the relative contribution of k'_{OH} compared with $k'_{s2}K_{A2}[M^+]_T$ decreases, which in turn decreases the statistical reliability of the calculated values of k'_{OH}.

In a detailed kinetic study of the alkaline hydrolysis of *N*-hydroxyphthalimide, we have shown that the hydroxide ion attack at the carbonyl carbon of NHP$^-$ to form a transient intermediate (T) is the rate-determining step.[13] The product of alkaline hydrolysis of NHP$^-$ has been shown to be *o*-carboxybenzohydroxamic acid within a [KOH] range of 0·004–0·022 M.[13]

The rate constant k'_{s1} or k'_{s2} represents the sum of the rate constants k_{s0} and k_{s1} or k_{s2}, where k_{s0} is the first-order rate constant for the cleavage of the ion-pair complex. The rate constant, k_{s0}, may be expected to be effective only if the unimolecular cleavage of the ion-pair complex involves the occurrence of intramolecular general base catalysis through a transition state (TS).



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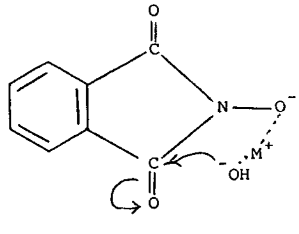

TS

Table 1. Calculated kinetic parameters, k'_{s1} and K, from equation (3)[a]

M_kX_n	MOH[b]	MeCN (%, v/v)	$10^4k_0^0$ (s^{-1})	$10^3k'_{s1}$ (s^{-1})	K ($l\ mol^{-1}$)	[M_kX_n] range (M)	No· of runs
LiCl	LiOH	60	32·9 ± 0·3[d]	14·5 ± 0·4[d]	16·5 ± 1·1[d]	0·01–0·18	11
		66	53·3 ± 0·3	22·4 ± 1·5	11·0 ± 1·4	0·01–0·14	10
		70	66·0 ± 0·3	27·2 ± 1·7	13·9 ± 1·6	0·01–0·10	8
		76	95·8 ± 0·2	31·2[e]	49·1[e]	0·01–0·02	3
NaCl	NaOH	60	34·3 ± 0·4	15·4 ± 0·8	6·6 ± 0·6	0·01–0·18	11
		66	44·3 ± 0·2	21·5 ± 2·6	6·9 ± 1·3	0·01–0·14	10
		70	61·5 ± 0·5	27·0 ± 2·4	8·1 ± 1·1	0·01–0·10	9
		76	80·0 ± 0·3	30·1[e]	21·3[e]	0·01–0·02	3
KCl	KOH	60	25·2 ± 0·2	9·1 ± 0·6	8·4 ± 1·1	0·02–0·18	9
		70	36·6 ± 0·4	16·1 ± 1·3	8·3 ± 1·0	0·01–0·10	10
		76	54·1 ± 0·3	19·8 ± 2·1	14·8 ± 2·7	0·01–0·07	8
		80	77·3 ± 0·3	15·9[3]	67·8[e]	0·02–0·04	3
CsCl	NaOH	60	34·3 ± 0·4	11·5 ± 0·9	9·2 ± 1·4	0·01–0·18	8
		70	61·5 ± 0·5	15·6 ± 1·3	14·2 ± 2·0		7
$BaCl_2$	NaOH	10	31[f]	55·9 ± 7·0	36·7 ± 7·1	0·002–0·022	9

[a] $[NHPH]_0 = 12 \times 10^{-4}$ M, temperature = 30 °C and $\lambda = 410$ nm.
[b] [MOH] = 0·01 M.
[c] Obtained at 0·01 M MOH in the absence of M_kX_n.
[d] Error limits are standard deviations.
[e] Calculated from two data points using the linearized form of equation (3), $(k_{obs} - k_0)^{-1} = (k'_{s1} - k_0)^{-1} + \{(k'_{s1} - k_0)K[M_kX_n]_T\}^{-1}$.
[f] Obtained from the interpolation of the plot of k_{obs} versus % (v/v) MeCN.

Table 2. Calculated kinetic parameters, k'_{OH}, k'_{s2} and K_{A2} from equation (4)[a]

M_kX_n	MOH[b]	MeCN (%, v/v)	$10^4k'_{OH}$ (s^{-1})	$10^3k'_{s2}$ (s^{-1})	K_{A2} l mol^{-1})	R[b]	Y[c]
LiCl	LiOH	60	14·2 ± 3·8[d]	14·7 ± 0·4[d]	18·0 ± 2·4[d] (19·8)[e]	0·88	13·41
		66	35·4 ± 6·6	22·9 ± 1·9	11·3 ± 3·0 (12·4)	1·36	8·94
		70	35·9 ± 7·8	27·7 ± 2·1	15·1 ± 3·6 (16·1)	1·66	11·30
		76	–	–	–	1·90	39·9
NaCl	NaOH	60	26·9 ± 1·9	15·7 ± 1·0	6·8 ± 1·1 (7·1)	0·97	6·60
		66	33·3 ± 5·9	22·2 ± 3·9	6·9 ± 2·9 (8·8)	1·35	6·90
		70	41·8 ± 4·2	28·2 ± 2·8	8·4 ± 2·0 (8·8)	1·70	8·10
		76	–	–	–	1·89	21·30
KCl	KOH	60	20·2 ± 2·0	9·2 ± 0·7	8·5 ± 2·1 (9·2)	0·88	5·25
		70	25·2 ± 2·6	16·1 ± 1·5	9·2 ± 2·1 (9·1)	1·59	5·19
		76	28·1 ± 8·1	19·7 ± 2·3	17·9 ± 6·5 (17·4)	1·92	9·25
		80	–	–	–	1·54	42·38
CsCl	NaOH	60	–	–	–	0·90	4·84
		70	–	–	–	1·22	7·47
$BaCl_2$	NaOH	–	–		–	0·94	1·75

[a] $[NHPH]_0 = 12 \times 10^{-4}$ M, [MOH] = 0·01 M and $\lambda = 410$ nm·
[b] $R = k'_{s1}/k'_{s1,2\%(v/v)MeCN}$, where the rate constants $[k'_{s1,2\%(v/v)MeCN}]$ at 2% (v/v) MeCN were obtained from Ref. 9.
[c] $Y = K/K_{2\%(v/v)MeCN}$, where the association constants $[k_{2\%(v/v)MeCN}]$ at 2% (v/v) MeCN were obtained from Ref. 9.
[d] Error limits are standard deviations.
[e] $K_{A2} = K/(1 - K[MOH])$.

However, a significant contribution of k_{s0} compared with k_{s1} or k_{s2} may be ruled out for the following qualitative reasons. (i) It is evident from Tables 1 and 2 that $k'_{s1} \approx k'_{s2}$ under identical conditions and Schemes 1 and 2 indicate that $k_{s1} = k_{s2}$. This implies that $k'_{s1} = k'_{s2}$ ($= k_{s0} + k_{s2}[\mathrm{MOH}]$), which in turn necessitates that $k_{s0} \ll k_{s2}[\mathrm{MOH}]$. (ii) If, on the other hand, it is assumed that $k_{s0} \gg k_{s2}[\mathrm{MOH}]$, then $k'_{s1} = k_{s0}$. The efficiency of an intramolecular reaction over an intermolecular counterpart is generally expressed in terms of effective molarity, which is the ratio of the first-order rate constant for intramolecular reaction to the second-order rate constant for analogous intermolecular reaction. The second-order rate constants (k_{OH}) for OH^--catalysed cleavage of *N*-substituted phthalimides including NHPH and NHP^- in 95% (v/v) water lie on the same Taft plot[13] and the value of k_{OH} for NHP^- is $0{\cdot}9\ \mathrm{l\ mol^{-1}\ s^{-1}}$. A change in MeCN content from 2 to 80% (V/v) is expected to decrease k_{OH} ($= 0{\cdot}9\ \mathrm{l\ mol^{-1}\ s^{-1}}$) by *ca* 75-fold. [The rate of alkaline hydrolysis of NHP^- in mixed aqueous–organic solvents containing different contents of MeOH and EtOH did not reveal the occurrence of ion-pair complexes. The observed rate constants were reduced by *ca* 75- and 4-fold due to the increase in the respective contents of MeOH and EtOH from 5 to 80% and 5 to 70% (v/v).[8] The reported dielectric constants are 37·0 (25 °C),[14] 37·5 (20 °C)[15] for MeCN, 30·7 (35 °C),[14] 32·6 (25 °C)[16] for MeOH and 22·8 (35 °C),[14] 24·3 (25 °C)[16] for EtOH. It must be noted that a 75-fold decrease in k_{OH} is based on the change in the solvent polarity only. However, the change in k_{OH} due to a change in the mixed aqueous organic solvents is caused by several factors including solvent polarity and preferential solvation effects on the reactant and transition states.[8] Hence the 75-fold decrease in k_{OH} must be considered as the upper limit.] Thus the expected value of k_{OH} is $\geqslant 0{\cdot}01\ \mathrm{l\ mol^{-1}\ s^{-1}}$ at $\leqslant 80\%$ (v/v) MeCN. The effective molarity for the intramolecular general base catalysis (TS) is equal to k_{s1}/k_{OH}, which is $\leqslant 3$ M. An intramolecular reaction with effective molarity of such a low value is considered to be unimportant compared with the intermolcular counterpart.

The effects of [CsCl] and [$\mathrm{BaCl_2}$] were studied at a constant [NaOH] of 0·01 M. The observed rate constants at different salt concentrations were found to fit to equation (3). The calculated values of k'_{s1} and K are given in Table 1. The fit of the observed data to equation (3) was good, as is evident from the plots in Figure 4, where solid lines are drawn through the least-squares-generated points.

The effect of [$\mathrm{Na_2CO_3}$] in the range of 0·007–0·057 M on k_{obs} was studied at 0·01 M NaOH and 50% (v/v) MeCN. The observed rate constants (k_{obs}), as shown graphically in Figure 4, revealed a linear relationship with [$\mathrm{Na_2CO_3}$]. This result could be explained if it is assumed that $1 \gg K[\mathrm{Na_2CO_3}]$. Under such conditions, equation (3) reduced to

$$k_{\mathrm{obs}} = k_0 + k'_{s1}K[\mathrm{Na_2CO_3}] \tag{5}$$

with $[\mathrm{M}_k\mathrm{X}_n]$ changed to [$\mathrm{Na_2CO_3}$]. The linear least-squares-calculated values of k_0 and $k'_{s1}K$ are $(31{\cdot}4 \pm 0{\cdot}8) \times 10^{-4}\ \mathrm{s^{-1}}$ and $(45{\cdot}8 \pm 2{\cdot}5) \times 10^{-3}\ \mathrm{l\ mol^{-1}\ s^{-1}}$, respectively. The use of the apparent concentration of $\mathrm{Na^+}$ ions gave the value $k'_{s1}K = (22{\cdot}9 \pm 1{\cdot}3) \times 10^{-3}\ \mathrm{l\ mol^{-1}\ s^{-1}}$. If we consider $k'_{s1} = 15 \times 10^{-3}\ \mathrm{s^{-1}}$ [the value of $k'_{s1} = 15{\cdot}4 \times 10^{-3}\ \mathrm{s^{-1}}$ was obtained at 60% (v/v) MeCN in the presence of NaCl, Table 1], then the value of K turns out to be $1{\cdot}5\ \mathrm{l\ mol^{-1}}$ (based on the apparent [$\mathrm{Na^+}$] which is twice the stoichiometric concentration of $\mathrm{Na_2CO_3}$), which is nearly 4 and 1·4 times smaller than K at 60% and 2% (v/v) MeCN, respectively.

The effects of [$\mathrm{Me_4NCl}$] on the rates of alkaline hydrolysis of NHPH were studied at 60% and 70% (v/v) MeCN and constant [NaOH] = 0·01 M. The observed rate constants (k_{obs}) at different [$\mathrm{Me_4NCl}$] are summarised in Table 3. The observed rate constants are almost independent of [$\mathrm{Me_4NCl}$] at 70% (v/v) MeCN, whereas there is a nearly 25% increase in k_{obs} with increase in [$\mathrm{Me_4NCl}$] from 0·01 to 0·18 M at 60% (v/v) MeCN. These results merely indicate the absence of ion-pair complex formation, i.e. $K \approx 0$.

The values of $k'_{s1}/k'_{s1,2\%\,(v/v)\mathrm{MeCN}}$ [$k'_{s1,2\%\,(v/v)\mathrm{MeCN}}$ represents the value of k'_{s1} at 2% (v/v) MeCN] changed from *ca* 0·9 to 2·0 with change in MeCN content from 60% to 76% (v/v) for LiCl, NaCl and KCl. Similarly, the values of $K/K_{2\%\,(v/v)\mathrm{MeCN}}$ [$K_{2\%\,(v/v)\mathrm{MeCN}}$ represents the apparent association constant at 2% (v/v) MeCN] increased from 1 to 40 for LiCl, 21 for NaCl and 42 for KCl with increase in MeCN content from 2 to 76% (v/v) for LiCl and NaCl and from 2 to 80%

Table 3. Observed pseudo-first-order rate constants for the cleavage of NHP^- in the presence of $\mathrm{Me_4NCl}$[a]

	$10^4 k_{\mathrm{obs}}$ ($\mathrm{s^{-1}}$)	
[$\mathrm{Me_4NCl}$] (M)	60% (v/v) MeCN	70% (v/v) MeCN
0·1	37·9 ± 0·4[b]	69·2 ± 0·4[b]
0·02	–	65·5 ± 0·5
0·03	41·4 ± 0·4	64·5 ± 0·7
0·04	–	64·7 ± 0·6
0·05	41·2 ± 0·3	67·8 ± 0·7
0·06	–	61·7 ± 0·4
0·07	41·5 ± 0·4	–
0·08	–	67·4 ± 0·7
0·10	43·3 ± 0·4	–
0·14	49·1 ± 0·5	–
0·18	48·0 ± 0·4	–

[a] $[\mathrm{NHPH}]_0 = 12 \times 10^{-4}$ M, [NaOH] = 0·01 M, temperature = 30 °C and $\lambda = 410$ nm.

[b] Error limits are standard deviations.

(v/v) for KCl. The nearly two-fold kinetic effects of these salts indicate the differential stabilization of the transition state and ground state of the reacting system in the rate-determining step. It has been concluded elsewhere[9] that the rate-determining step in the alkaline hydrolysis of NHPH involves hydroxide ion attack on the carbonyl carbon of ionized NHPH. The rate constant, k'_{s1}, represents the pseudo-first-order rate constant for hydroxide ion attack on the carbonyl carbon of the ion-pair complex formed between cations of the salts which presumably exist in solvent-separated loose ion-pair forms and anionic substrate (NHP^-). As the MeCN content increased in the mixed H_2O–MeCN solvents, the magnitudes of the association constants (K) also increased, which in turn increased the electrophilicity of the carbonyl carbon of complex C_1 (Scheme 1). This effect is, partially offset however, by the decrease in the nucleophilicity of the hydroxide ion due to the increase in the magnitudes of the association constants of solvent-separated loose ion-pair formation between OH^- and M^+. These two opposing effects could be responsible for the observed *ca* two-fold kinetic effect due to the increase in MeCN content from 2 to 76% (v/v) in H_2O–MeCN solvents.

The value of K ($= 1{\cdot}5\ l\ mol^{-1}$) obtained in the presence of Na_2CO_3 at 50% (v/v) MeCN does not appear to be significantly different from K obtained in the presence of NaCl under similar conditions. This shows that the magnitude of K is not dependent on the valence of anions of the salts. The value of k'_{s1} remained essentially unchanged whereas the value of K increased *ca* two-fold with change in MeCN content from 2 to 10% (v/v) in the presence of $BaCl_2$ (Table 2). Both k'_{s1} and K are many times larger than the corresponding values obtained in the presence of univalent cationic salts with identical solvent systems. The high sensitivity of both k'_{s1} and K to the valence state of cations strengthens the proposed ion-pair formation mechanism.

The absence or extremely weak ion-pair formation in the presence of Me_4NCl is probably a consequence of the positive charge on nitrogen in Me_4N^+ being considerably shielded from NHP^- and solvent molecules by the methyl substituents.

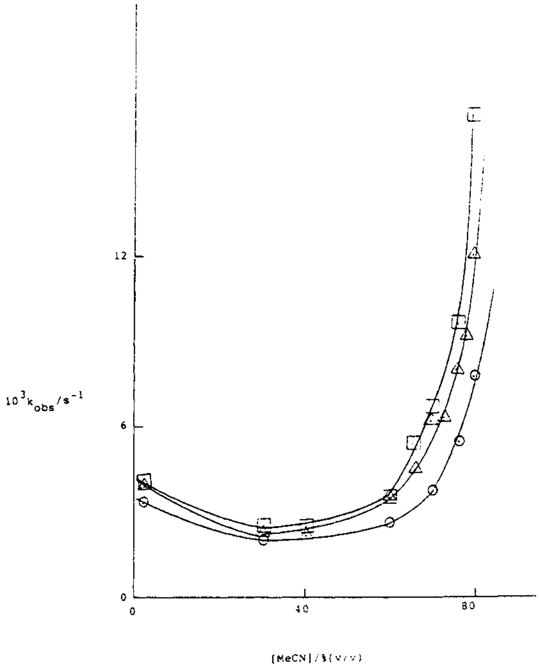

Figure 5. Dependence of observed rate constants, k_{obs}, for alkaline hydrolysis of NHP^- on content of MeCN cosolvent for reaction mixtures containing (◻) 0·01 M LiOH, (⊙) 0·01 M KOH and (△) 0·01 M NaOH. The data at 0·01 M NaOH were obtained from Ref. 8 for comparison purposes

Effect of [MeCN] at a constant [MOH] and $[M_kX_n] = 0$

The effects of mixed H_2O–MeCN solvents were studied at 30 °C and 0·01 M MOH (M = Li and K). The observed pseudo-first-order rate constants, k_{obs}, versus % (v/v) MeCN are shown in Figure 5. The values of k_{obs} were found to decrease with increase in MeCN content up to *ca* 40% (v/v). These results may be explained in terms of electrostatic theory, which predicts that k_{obs} should decrease with decrease in the dielectric constant of the reaction medium. The rate constants, k_{obs}, do not show significant variation with change from LiOH to NaOH or KOH at a constant MeCN content and [MOH] within the MeCN content range from 2 to *ca* 40% (V/V).

The rate constants, k_{obs}, increased sharply with increase in MeCN content at $\geqslant 60\%$ (v/v) MeCN (Figure 5). Similar observations have been reported in a number of related reactions.[6,17,18] Above MeCN contents of $\geqslant 60\%$ (v/v), the effects of [MOH] on k_{obs} at a constant [MeCN] vary in the order LiOH > NaOH > KOH. Although several reasons have been given to explain such observations,[17] we consider ion-pair formation and a specific solvation effect as the two most important explanations.[8]

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REFERENCES

1. M. N. Khan, M. B. U. Sumaila and A. M. Mohammad, *J. Chem. Res. (S)* 233 (1991); (*M*) 2301 (1991).
2. M. N. Khan, *J. Pharm. Sci.* **73**, 1967 (1984).
3. M. N. Khan and T. O. Olagbemiro, *J. Org. Chem.* **47**, 3695 (1982).
4. M. N. Khan and S. K. Gambo, *Int. J. Chem. Kinet.* **17**, 419 (1985).
5. W. J. Irwin, Q. N. Masuda and A. Li Wan, *Int. J. Pharm.* **21**, 35 (1984); M. N. Khan, *Int. J. Chem. Kinet.* **19**, 757 (1987).
6. M. N. Khan, *Indian J. Chem.* **25A**, 831 (1986).
7. M. N. Khan, I. L. Fatope, K. I. Isaac and M. O. Zubair, *J. Chem. Soc., Perkin Trans. 2* 655 (1986).
8. M. N. Khan, M. T. Abdullahi and Y. Mohammad, *J. Chem. Res. (S)* 52 (1990); (*M*) 473 (1990).
9. M. N. Khan, *Int. J. Chem. Kinet.* **23**, 837 (991).
10. M. N. Khan, *J. Org. Chem.* **48**, 2046 (1983); *J. Chem. Soc., Perkin Trans. 2* 1977 (1985).
11. A. K. Ray and M. N. Das, *J. Chem. Soc. A* 464 (1970).
12. A. A. Frost and R. G. Pearson, *Kinetics and Mechanism*, 2nd ed., p. 147. Wiley, New York (1962).
13. M. N. Khan, *Int. J. Chem. Kinet.* **23**, 567 (1991).
14. S. V. Anantakrishnan, *J. Sci. Ind. Res.* **30**, 319 (1971).
15. J. B. F. N. Engberts, in *Water. A Comparative Treatise*, edited by F. Franks, Vol. 6, p. 139 (1979).
16. F. Franks and D. J. G. Ives, *Q. Rev. Chem. Soc.* **20**, 1 (1966).
17. M. D. Hawkins, *J. Chem. Soc., Perkin Trans. 2* 642 (1976), and references cited therein.
18. J. Benko and V. Holba, *Collect. Czech. Chem. Commun.* **43**, 193 (1978).