Intriguing Salt Effects in the Formation of Hydroxamic Acids from Aldehydes and Nitroso Compounds

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Addition of inorganic chlorides and perchlorates into the reaction mixture in water leads to a significant increase of the rate constants observed for the formation of *N*-phenyl hydroxamic acids from nitrosobenzene and formaldehyde or acetaldehyde. The rate enhancements (relative to the reaction rate constant in »pure water«) vary from the 7.4-fold increase observed on addition of 2.0 mol dm^{-3} Mg(ClO$_4$)$_2$ into the reaction mixture to the 230.0-fold increase in the case of 2.0 mol dm^{-3} of MgCl$_2$ added. Linear correlation between log k_{obs} for the formation of the *N*-phenylformohydroxamic acid from nitrosobenzene and formaldehyde and the concentration of the anion of the salt added has been observed for MgCl$_2$, CaCl$_2$, LiCl, Mg(ClO$_4$)$_2$ and NaClO$_4$, but different correlations were obtained for NaCl, HCl and HClO$_4$. The observations are discussed in terms of ion pairing between the unstable cation reaction intermediates and the anion of the salt. The results obtained suggest that stabilization of the unstable cationic reaction intermediate by the formation of an ion pair with the salt anion is of key importance for the formation of hydroxamate from aldehydes and nitrosobenzenes in more concentrated inert salt water solutions.

Key words: salt-effects, ion-pairs, hydroxamic acids, hydroxamates, kinetics.

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INTRODUCTION

Salt effects are of great importance to organic chemistry and biochemistry.[1–5] The role of the salts in mechanistic organic chemistry is well known.[2] There is a great range of phenomena connected with salts, such as, for example, the influence of salts on the reaction stereochemistry, regioselectivity and equilibria, now used in synthetic organic chemistry.[1,3] Salt bridges, on the other hand, have clearly defined roles in the organization of multimeric proteins and complexes and, among others, bear considerably on electron transport within the biological milieu of proteins and enzymes.[4] The involvement of salts in the enzyme function is well recognized.[5]

In continuing up the investigation of the reactions of nitrosobenzenes with carbonyl compounds[6,7] and with a number of important biomolecules,[6d] we have been interested in the salt effects in these reactions.[7] The reactions lead to the formation of *N*-phenylhydroxamic acids, (Scheme 1). It is worthwhile noting the chemical/biochemical, pharmaceutical and industrial significance of hydroxamic acids and that they have applications as, among
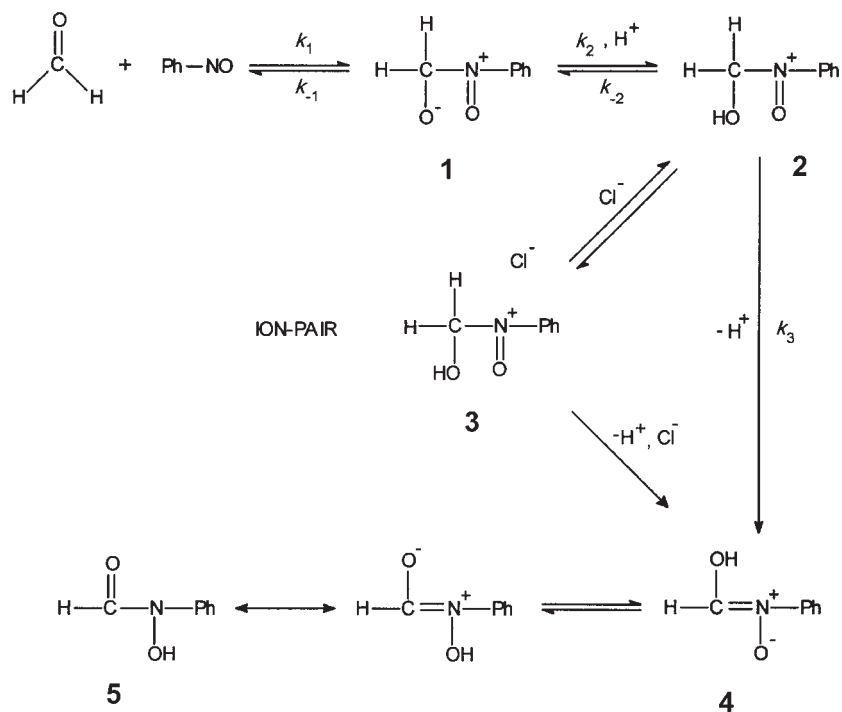
Scheme 1.

others, important siderophores and enzyme inhibitors.[8,9] Nitrosobenzenes,[10] on the other hand, are formed in biological systems either by the metabolic oxidation of aryl amines or by the reduction of aromatic nitro compounds.[11] They can interact, for example, with reduced glutathione,[10j,11] NADH,[10g,12] and can participate in some DNA damaging processes.[10g]

Recently, we have reported about the salt effects and kinetic isotope effects in the reaction of nitrosobenzene with formaldehyde in mixed solvents with a high organic cosolvent content (*e.g.* 92.6% of acetonitrile or acetone).[7] The results strongly suggest that at least in these mixed solvents and in the presence of very small quantities of chloride, the formation of hydroxamic acid in the reaction proceeds preferentially *via* the nitrosocarbinolic cation intermediate-chloride ion pair, such as (**3**) in (Scheme 1). An open question remains about the salt effects of inorganic salts, especially in water solution, including the question of whether an ion-pair mechanism, which is predominant in mixed solvents with a high content of organic cosolvent, can operate in the formation of hydroxamic acids in a more concentrated water solution of an inert salt. This issue is of importance, among others, because the nature of the salt effects observed in many reactions, including important syntheses,[13] has been little understood despite its obvious usefulness and applicability.

Now, we report the results of the study of salt effects caused by the inorganic salts in the reactions of nitrosobenzene with aldehydes in water solutions, especially with regard to the intriguing finding that the observed reaction rate constants for the particular reaction system can be interconnected in an unusual and unexpected fashion with the concentration of the anion of the added salt or with the pH value (as measured by a glass electrode) of the reaction medium.

EXPERIMENTAL

Salts and strong acids employed were of analytical grade (Merck), and were used without further purification. High quality double-distilled water was used to obtain solutions throughout. pH measurements were performed using a Radiometer PHM 84 pH-meter or Mettler Toledo MP230 equipped with the corresponding combined glas electrode and following the well-known standard procedures. Kinetics were performed as described elsewhere.[6a,b] Very good first-order rate constants were obtained by measuring the disappearance of the absorbance of nitrosobenzene at 320 nm. Kinetics was initiated by adding an appropriate solution of nitroso compound in methanol or acetonitrile into the water acidic salt solution using a microsyringe (Hamilton) and the organic cosolvent content was always below 0.2% (volume fraction). Usually, formaldehyde dihydrate was in 5000–6000 fold excess over nitrosobenzene, using the initial concentrations of 0.600–1.200 mol dm^{-3} of formaldehyde

dihydrate, and the rate constants quoted in Table I. are an average of 3–4 runs. In the case of the reaction of acetaldehyde, $[H_3O^+]$ was 1.0 M (HCl), and $[CH_3CHO]$ was also 1 mol dm^{-3}, throughout.

TABLE I

Rate constants for the reactions of nitrosobenzene with formaldehyde in more concentrated water salt solutions

Salt	$\dfrac{c}{\text{mol dm}^{-3}}$	pH	$\dfrac{10^3 k_{\text{obs}}}{\text{s}^{-1}}$	Salt	$\dfrac{c}{\text{mol dm}^{-3}}$	pH	$\dfrac{10^3 k_{\text{obs}}}{\text{s}^{-1}}$
NaCl	0.10	1.36	0.74	LiCl	0.50	1.21	1.42
	0.50	1.27	1.55		1.00	1.11	2.69
	1.00	1.19	3.05		2.00	0.91	7.05
	2.00	1.00	7.70		3.00	0.59	18.00
	3.00	0.83	16.95		4.00	0.35	52.93
	4.00	0.59	30.96				
MgCl$_2$	0.17	1.28	1.25	NaClO$_4$	0.50	1.35	0.62
	0.33	1.20	2.12		1.00	1.28	0.84
	0.66	0.99	4.81		2.00	1.03	1.43
	1.00	0.78	10.42		3.00	0.77	2.42
	1.33	0.53	23.56		4.00	0.60	4.14
	1.92	0.05	91.98	x	5.75	0.16	11.78
	2.00	0.04	111.53^c				
CaCl$_2$	0.17	1.32	1.10	Mg(ClO$_4$)$_2$	0.17	1.34	0.55
	0.33	1.25	1.64		0.33	1.27	0.66
	0.66	1.13	2.78		0.66	1.12	0.87
	1.00	0.98	5.35		1.00	0.90	1.20
	1.33	0.82	11.20		1.33	0.74	1.66
	2.00	0.45	50.10		2.00	0.20	3.06
HCl	0.10	1.12	1.27	HClO$_4$	0.10	1.04	0.92
	0.20	0.83	3.35		0.20	0.75	1.94
	0.30	0.69	6.17		0.30	0.60	3.17
	0.40	0.57	8.87		0.40	0.49	4.64
	0.50	0.43	14.34		0.50	0.45	6.12
	0.70	0.30	27.94		0.60	0.37	7.75
	0.80	0.26	35.97		0.70	0.30	9.66
	0.90	0.17	45.80		0.80	0.24	12.11
	1.00	0.12	57.19		0.90	0.19	14.05
					1.00	0.14	16.66

[a] At 25 °C.

[b] Concentrations of HCHO, H_3O^+ and nitrosobenzene were 6×10^{-1}, 5×10^{-2} and 1×10^{-4} mol dm^{-3}, respectively.

[c] Extrapolated value.

RESULTS AND DISCUSSION

We have observed as follows:

– Addition of inorganic chlorides and perchlorates into the reaction mixture in water leads to a significant increase of the rate constants observed for the formation of hydroxamic acids from nitrosobenzene and formaldehyde or acetaldehyde (Figure 2), varying from the 7.7-fold increase (relative to the reaction rate constant in »pure water«) observed on addition of 2.0 mol dm^{-3} $Mg(ClO_4)_2$ into the reaction mixture to the 230.0-fold increase in the case of 2.0 mol dm^{-3} of $MgCl_2$ added. The rate increases exponentially with the addition of the salt, (Figure 2). Relative rate enhancements were one order of magnitude greater for the chlorides than for the perchlorates added. Addition of salts into the reaction mixture in water caused only a change of the rate constants observed. N-phenylformohydroxamic acid was the only product of the reaction, regardless of the medium used, as evidenced spectroscopically and by product analysis.

– Linear correlation (with the correlation coefficient of the straight lines of 0.999 or better) between log k_{obs} for the formation of N-phenylformohydroxamic acid from nitrosobenzene and formaldehyde and the concentration

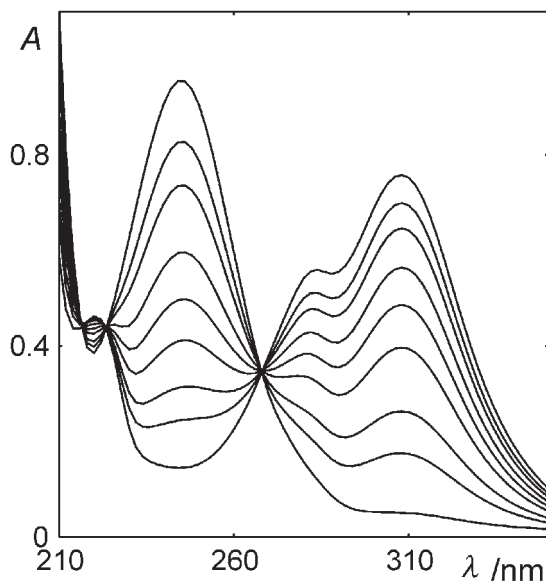Figure 1. Change in the UV spectra during the course of reaction of 0.575 mol dm^{-3} HCHO with 1×10^{-4} mol dm^{-3} nitrosobenzene at 25 °C. Concentration of H_3O^+ ($HClO_4$) and the added $CaCl_2$ were 0.050 and 0.550 mol dm^{-3}, respectively.
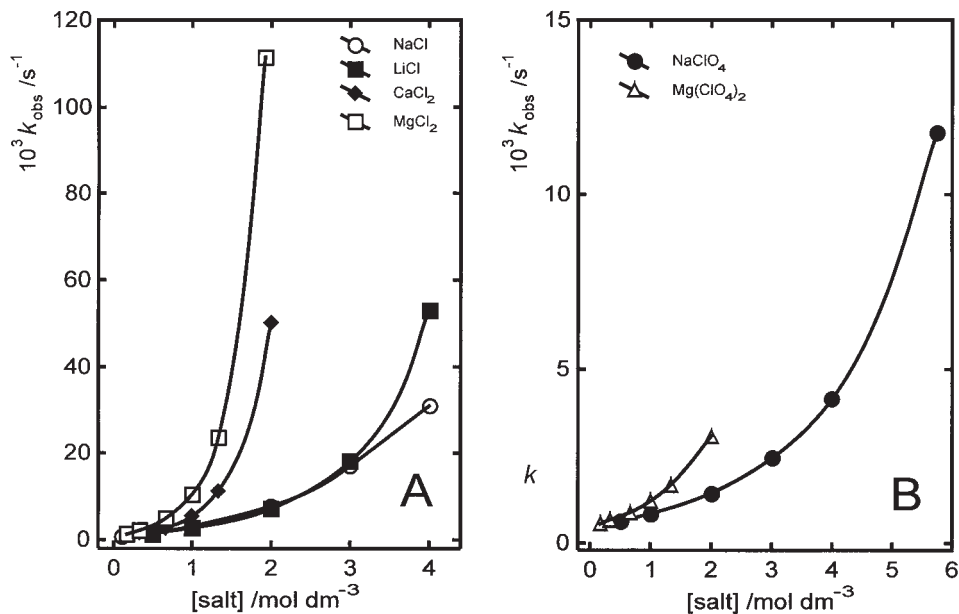
Figure 2. Plot of the k_{obs} *vs.* salt concentration for the reaction of nitrosobenzene with formaldehyde: A) NaCl, LiCl, $CaCl_2$ and $MgCl_2$; B) $NaClO_4$ and $Mg(ClO_4)_2$. Data from Table I.

of the anion[*] of the salt added into the water acidic reaction mixture has been observed (Figure 3). The slopes of the corresponding straight lines, in the concentration range 0.1–4.0 mol dm^{-3} (0.1–5.75 mol dm^{-3} in the case of $NaClO_4$) of the salt are 0.526, 0.447 and 0.438 for $MgCl_2$, $CaCl_2$ and LiCl, respectively, and 0.241 and 0.203 for $NaClO_4$ and $Mg(ClO_4)_2$, respectively. For the formation of *N*-phenylacetohydroxamic acid from nitrosobenzene and acetaldehyde, the plot of log k_{obs} *vs.* [NaCl] is also linear, with the slope of 0.348.

 – The corresponding plot of log k_{obs} *vs.* [NaCl] for the formation of *N*-phenylformohydroxamic acid is curved, but an excellent linear correlation has been found between log k_{obs} and the square root of the chloride concentration.

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[*] Note that plotting of the anion concentration instead of salt concentration corresponds to the plotting of ½[salt] in the cases of divalent salts, analogously to the usual presentation of salting-out parameters. The salting-out parameters are the slopes of the straight lines obtained by plotting log f_a *vs.* salt concentration.
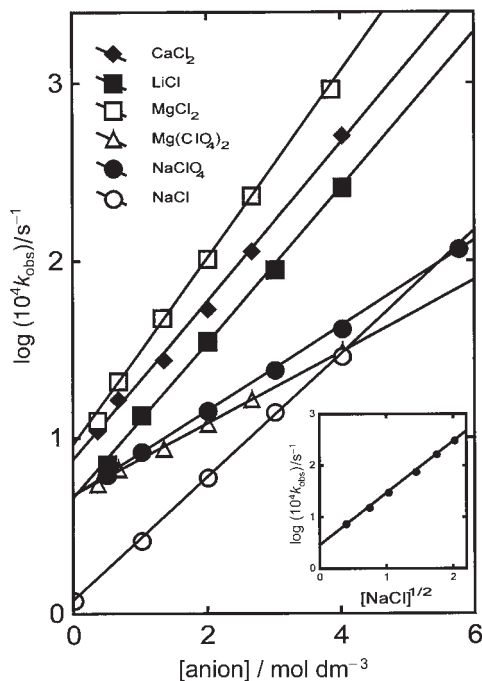
Figure 3. Plot of log k_{obs} *vs.* anion concentration for LiCl, CaCl$_2$, MgCl$_2$, NaClO$_4$ and Mg(ClO$_4$)$_2$ for the reaction of formaldehyde with nitrosobenzene. Open circles: reaction of 1 mol dm^{-3} acetaldehyde with 1×10^{-4} mol dm^{-3} nitrosobenzene in the presence of 1 mol dm^{-3} HCl. Salt: NaCl. Line for LiCl is shifted by 0.3 downward, for clarity. Inset: Plot of log k_{obs} for the reaction of formaldehyde with nitrosobenzene *vs.* the square root of the NaCl concentration. Data from Table I.

    – Linear correlation ($r = 0.99$ or better) between log k_{obs} and pH (measured with a glass electrode) has been observed for the corresponding reaction solution containing MgCl$_2$, CaCl$_2$, LiCl and NaClO$_4$ in the range 0.1–4.0 mol dm^{-3} (0.1–5.75 mol dm^{-3} in the case of NaClO$_4$), (Figure 4). The corresponding plot of log k_{obs} *vs.* pH for NaCl appears to be curved, but a straight line ($r = 0.993$) has been obtained on plotting log(k_{obs}/[NaCl]$^{1/2}$) *vs.* pH, (Figure 4, inset).

    – Log k_{obs} for the reaction of formaldehyde and nitrosobenzene correlate linearly (r better than 0.999) with pH values (measured with a glass electrode) of the reaction solution containing HClO$_4$ or HCl in the concentration range of 0.1 to 1.0 mol dm^{-3} of the strong acid and without addition of the inert salt (Figure 5a). The plot of log (k_{obs}/ [HClO$_4$]) *vs.* [HClO$_4$], is a straight line (with $r = 0.997$, Figure 5b). The analogous correlation in the case of HCl
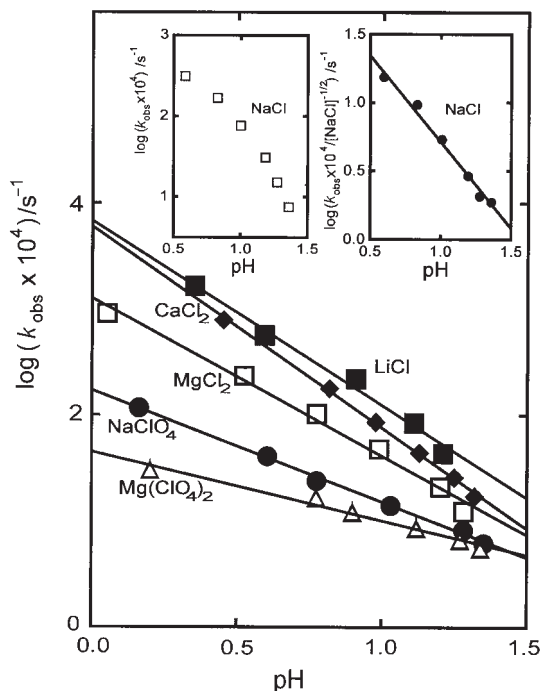
Figure 4. Plot of log k_{obs} for the reaction of formaldehyde with nitrosobenzene *vs.* pH of LiCl, CaCl$_2$, MgCl$_2$, NaClO$_4$ and Mg(ClO$_4$)$_2$ solutions. Lines for CaCl$_2$ and LiCl are shifted by 0.2 and 0.5 upward, respectively, for clarity. Insets: Plot of log k_{obs} *vs.* pH and log $(k_{obs}/[NaCl]^{1/2})$ *vs.* pH for NaCl. Data from Table I.

is nonlinear, but plotting of log(k_{obs}/[HCl]) *vs.* [HCl]$^{1/2}$ gives a straight line (r = 0.997, Figure 5c).

   – The linear correlation between pH values, as measured with a glass electrode, and the concentration of the particular salt has been found (Figure 6) for the series of inert salt solutions, including NaClO$_4$, LiCl, NaCl, CaCl$_2$, MgCl$_2$ and Mg(ClO$_4$)$_2$, in the concentration range of 0.1–4.0 mol dm^{-3} (0.1–5.75 mol dm^{-3} for NaClO$_4$, each containing 0.05 mol dm^{-3} of HClO$_4$,). The obtained straight lines diverge one from the other. The only intersection appears to be for 2.67 mol dm^{-3} NaClO$_4$ and NaCl, having pH = 0.873.

   The empirical rate law for the formation of *N*-phenylhydroxamic acids from aldehydes and nitrosobenzenes is

$$k_{obs} = k \; [HCHO][H^+][Ph\text{-}NO] \tag{1}$$

$$Ph = phenyl$$
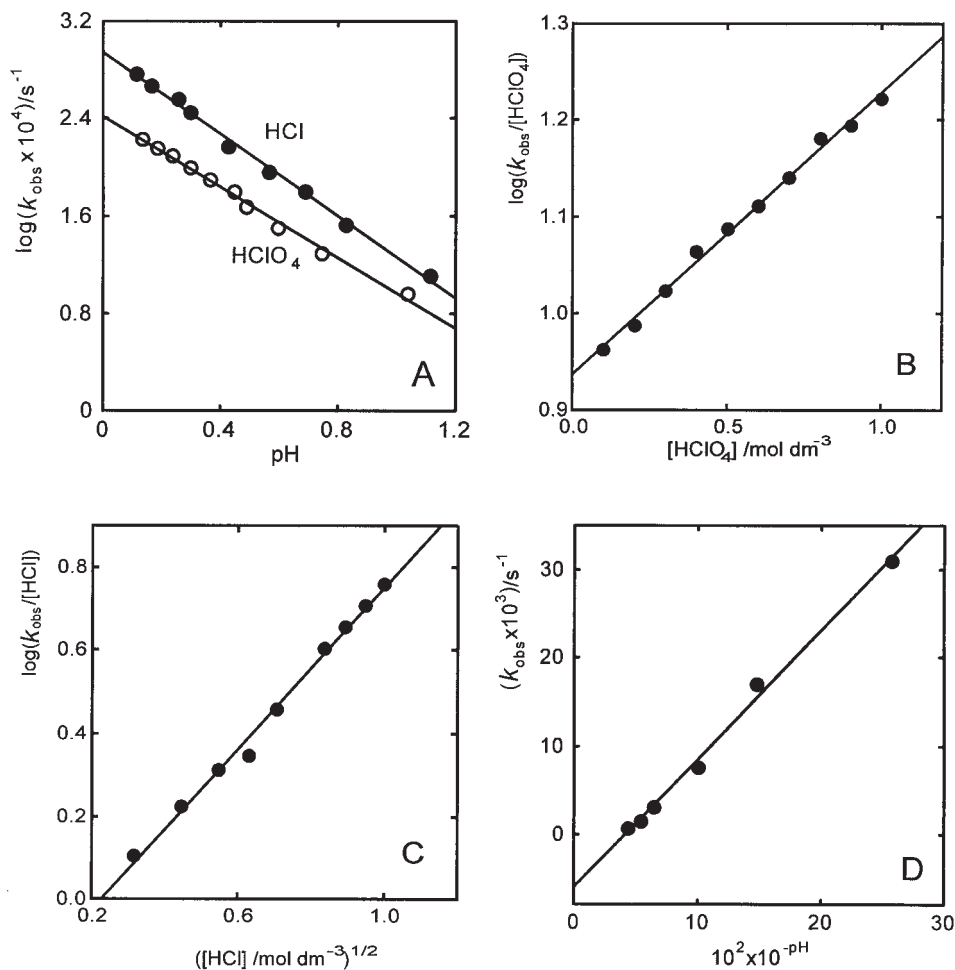
Figure 5. Plots of: log k_{obs} vs. pH for HCl and HClO$_4$ added in the reaction solution, without salt added, (A); log $(k_{obs} / [HClO_4])$ vs. concentration of HClO$_4$ (B); log $(k_{obs} / [HCl])$ vs. the square root of the HCl concentration (C); k_{obs} vs. 10^{-pH} for NaCl salt solutions, (D); k_{obs} obtained for the reaction of formaldehyde with nitrosobenzene. Data from Table I.

The proposed mechanism of the reaction ($1{\rightarrow}2{\rightarrow}4{\rightarrow}5$ in Scheme 1), based on the kinetic evidence with regard to the order of the reaction, the acid catalysis, the dependence of the observed rate constants on the Hammett σ parameters, solvent isotope effects and substrate kinetic isotope effects are discussed elsewhere.[6a,b,7] The linear relationship (Figure 3) between log k_{obs} for the formation of the N-phenylhydroxamic acid **4** and salt concentration
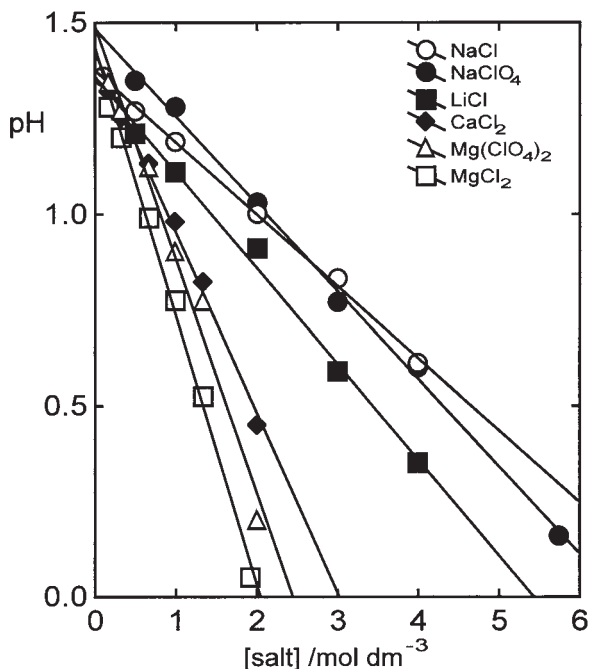
Figure 6. Plot of the pH of reaction solutions for the reaction of formaldehyde with nitrosobenzene *vs.* concentration of the salt added. Data from Table I.

could account, at least in part, for the salting-out phenomena.[14a,c] It is well known that inert salts can increase the activity coefficient of the uncharged organic substrate, and log f_a (f_a = activity coefficient of the uncharged substrate) correlates linearly with the salt concentration. The kinetics was performed under the pseudo-first order conditions, with aldehyde reactant constant (or more precisely, with the equilibrium concentration of the carbonyl compound constant) and a great excess of aldehyde dihydrate over nitrosobenzene. Hence, the change in the activity coefficient is of importance only for the aldehyde reactant, taking also into account that the activity coefficient of the aldehyde dihydrate could undergo changes owing to the salting-out phenomena. Another factor that could influence the reaction rate due to the added inert salt is the change in the hydration of the carbonyl reactant, since only unhydrated aldehyde reacts with nitrosobenzene. Addition of NaCl in the case of the reaction of nitrosobenzene with formaldehyde reveals a quite different dependence of the observed rate constants on the concentration of the added salt and should be considered separately.

The linear relationship of (Figure 3), however, cannot account only for the salting-out and dehydration phenomena connected with the addition of

inorganic salts into the reaction mixture. Firstly, the observed log k_{obs} does not correlate linearly with the salt concentration in the concentration range below 0.1 mol dm^{-3} of the salt added. Secondly, the slopes of the straight lines for MgCl$_2$, CaCl$_2$ and LiCl appear to be much greater than the greatest salting-out parameters observed, which never exceed *ca.* 0.290 in magnitude.[14c,15a]

In contrast, the corresponding figures for the perchlorates are much smaller than for the chlorides, and two different groups of lines can be seen, *i.e.* those for chlorides and those for perchlorates. The corresponding values of 0.241 and 0.203 for NaClO$_4$ and Mg(ClO$_4$)$_2$, respectively, are unusually high as compared with the ordinarily observed salting-out parameters for perchlorates,[14c,15] but can still get along with the salting-out behaviour.

Possible effects of the change in the dehydration of aldehyde due to the change of the activity coefficients of aldehyde (and aldehyde dihydrate), on the other hand, do not seem to be easily predictable. The change of the activity of water following the increase of salt concentration is not of great significance for the case in point; this change is, for example, about 21%, 15% and 17% for 4 mol dm^{-3} LiCl, 2 mol dm^{-3} CaCl$_2$ and 2 mol dm^{-3} MgCl$_2$, respectively.[15b,c] On the other hand, the rate acceleration on addition of MgCl$_2$, is significantly greater than that for the addition of LiCl, while it is very similar for LiCl and CaCl$_2$. In, addition the values of log a_w (a_w = water activity) of these salt solutions depend nonlinearly on the salt concentration.[15b,c]

Another contribution to the unexpected increase of the observed rate constants on addition of inert salts that might be considered is the possible involvement of the hydronium ion catalyzed addition of nitrosobenzene to the aldehyde in the process where the catalytic activation of carbonyl group by hydronium ion would occur. In the dilute water acidic solution, the reaction is catalyzed by the trapping[16] of the highly unstable dipolar addition intermediate (**1** in Scheme 1) by the proton transfer from a catalyst, leading to the more stable nitrosocarbinolic cation intermediate (**2**), as discussed elsewhere.[6a] The proton transfer from the hydronium ion to an oxyanion is known to be diffusion controlled,[17] and, as a consequence, the rate of the reaction should be proportional to the concentration of the solvated proton, which indeed has been observed.[6a,b,7] The possible catalytic activation of the carbonyl group by the hydronium ion, followed by the nucleophilic attack of the nitroso group on the carbonyl group, would present the second and concurrent pathway to the nitrosocarbinolic cation intermediate (**2**), similarly as proposed for the reaction of the substituted benzaldehydes with nitrogen nucleophiles[18] at low pH values. Addition of the salts could lead to an increase of the hydronium ion activity and in a more concentrated solution log k_{obs} would no longer depend on the H$^+$ concentration. To test this hypothe-

sis, we have determined the dependence of the log k_{obs} *vs.* pH for the solutions of $HClO_4$ and HCl in the concentration range 0.1–1.0 mol dm^{-3} (see Figure 5a), without salt added. The dependencies are fairly linear, but the slopes of the straight lines for $HClO_4$ and HCl are 1.45 and 1.66, respectively, far beyond from unity, the value that would be expected for the hydronium ion catalyzed reaction. These figures, however, could be a result of the superimposition of salt effects and of the catalytic effect of the hydronium ion. However, the contribution of the salt effects to the slopes cannot correspond only to the salting-out or the dehydration effects because the departures of the observed slopes from unity are much too large to account for only these effects of the strong acid. The activity of water decreases by less than 5% on addition of 1 mol dm^{-3} of $HClO_4$ or HCl.[15] It is usually considered that the salting-out parameters for the strong acids, such as $HClO_4$ or HCl, are small or close to zero.[15] In addition, $\log(k_{obs}/[HClO_4])$ *vs.* $[HClO_4]$ gave a straight line with the slope of 0.291 (Figure 5b). The analogous correlation for HCl is nonlinear, but $\log(k_{obs}/[HCl])$ correlates linearly with $[HCl]^{1/2}$, which possibly suggests some rather specific ionic effects.

The linear correlation between $\log(k_{obs}/[HClO_4])$ and $[HClO_4]$ could be consistent with the catalysis by trapping of the dipolar intermediate (**1**) by the proton as well as with the experimentally obtained rate law (1), where the rate of the reaction should be proportional to the proton concentration, if salting-out parameter for $HClO_4$ of 0.291 were supposed. In contrast, as discussed above, the expected salting-out parameter for $HClO_4$ should probably be much smaller, or close to zero. It should be noted also that the rate enhancement for 1 mol dm^{-3} HCl is 3.4-fold greater than that of 1 mol dm^{-3} $HClO_4$ (see Table I), which suggests that the possible pH-dependent reaction is a minor part of the whole process, since the differences in the hydronium ion activities between the two series of strong acid solutions (as expressed by the pH values, Table I) are much smaller than this rate ratio.

Therefore, it seems reasonable to conclude that some rather specific salt effects, especially with regard to the role of the anion of the particular salt, should be of crucial importance for the observed behaviour of the reaction system. We believe that these effects should be considered to be a consequence of some ion-pairing between the nitrosocarbinolic cation intermediate (**2**) and the anion of the salt, similarly to what was observed for the reaction in mixed solvents.[7] However, the ionic environment of the nitrosocarbinolic cation intermediate as well as of the corresponding ion pair in a more concentrated salt solution in water should be rather different than in mixed solvents containing very small quantities of the salt. Moreover, it should be expected that the ion pairs formed between the nitrosocarbinolic cation intermediate and the anion are not entirely the same in character on going

from the mixed solvents to the water salt solution. Differences should be expected, at least with regard to the mode of solvation, including separation of the charged species of the ion pair by the solvent molecule(s). Most likely, these factors could be responsible for the two main differences in the behaviour of the reaction system in the two media, *viz*.: i) much less enhancement of the rate of the reaction on addition of inorganic salts into the water reaction mixture than it was observed in mixed solvents, and ii) absence of the change of the primary kinetic isotope effect (PKIE) on addition of inorganic salts into the water reaction solution, in contrast to the dramatic decrease of the PKIE observed for the reaction in mixed solvents, where the KIE-s drop from *ca.* 8 to *ca.* 4 on addition, for example, of 0.001 mol dm^{-3} of the salt.

The role of the anions appears to be of principal importance again, similar to the situation in mixed solvents.[7] Cations[*] on the other hand, depending on their size and charge distribution, could influence the degree of the ion pairing of the added salt, where the existence of some fraction of »free« (or »unpaired«) ions should be expected. Although small, the concentrations of »free« anions are high enough to form the ion pair with the cation intermediate of the reaction,[**] thus leading to the phenomena observed. The ion pairing of the nitrosocarbinolic cation intermediate with a small, symetrical chloride ion having a high charge density should be easier than with a bulky perchlorate ion with dispersed charge. This might explain, at least in part, the differences in the observed rate enhancements between chlorides and perchlorates.

The observation that log k_{obs} correlates linearly with the pH values of the salt reaction solutions containing 0.05 mol dm^{-3} of strong acid and various amounts of the salt added (Figure 4) does not necessarily suggest that the hydronium ion catalyzed nucleophilic addition of the nitroso compound to the carbonyl group is part of the whole process of formation of the hydroxamic acid product. The above considerations relating to the case of the reaction in 0.1–1.0 mol dm^{-3} of HCl or HClO$_4$ reveal that catalysis of this kind, if any, probably constitutes only a minor part of the whole process. The meaningfulness of the pH measurement in more concentrated salt solu-

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[*] Some cation effect specificity for the halides could perhaps suggest electrophilic assistance by the cation due to a possible week coordination between the carbonyl group and the cation. However, this effect, if it exists, should be only of minor importance; thus, for example, the observed ratio of the rate constants for the reaction of formaldehyde with nitrosobenzene in 2 M MgCl$_2$ and 2 M MgClO$_4$ solutions is 36.5.

[**] Simeon and Tomišić[19] have demonstrated that the formation constants for the pairing of Co^{2+} and Li$^+$ with NO$_3^-$ in water strongly depend on the concentration of the particular salt; the formation constants increase with an increase of salt concentration.

tions was demonstrated many years ago.[20] Finally, one could only infer that the factors governing the change of the pH measured are to some extent similar or perhaps interconnected with those governing the rate enhancement observed in the reaction system.

The influence of the added NaCl on the rate constants observed for the formation of *N*-phenylformohydroxamic acid from nitrosobenzene and formaldehyde is illustrated by the insets in Figure 3 and Figure 4. In contrast to the salt effects discussed above, here log k_{obs} does not correlate linearly either with the NaCl concentration or with the pH measured but does correlate linearly with the square root of the NaCl concentration, and log $k_{obs}/[NaCl]^{1/2}$ correlates linearly with pH measured. In addition, log $k_{obs}/[HCl]$ for the reaction of nitrosobenzene with formaldehyde without the added salt (Figure 5C) correlates linearly with $[HCl]^{1/2}$.

The correlations were obtained from the experiments covering the concentration range up to 4 mol dm^{-3} NaCl (1 mol dm^{-3} of HCl in case of the reaction in the acid without salt added) and the square root the chloride concentration is involved in all the correlations. Hence, it could be easily demonstrated that the correlations obtained cannot be rationalized in terms of any usually encountered quantitative or even semiquantitative treatment of the salt effect on the reaction rates.[2,14b] The treatments are necessarily related to the dilute ionic solution, and the square root of ionic concentration is not always involved. At present, we could only note that our treatment of the data obtained experimentally is somewhat reminiscent of what we have called »Kepler's approach«.[21] The correlation of Figure 5D presents a similar case and is the only such obtained correlation. It should be regarded only as another unusual and unresolved correlation pertinent to the salt effects, since the values of the pH measured are not equal to the true pH of the system but rather reflect the influence of the salt added on the pH measurement.

CONCLUSIONS

In more concentrated inert salt water solution, the formation of hydroxamic acids from formaldehyde and acetaldehyde with nitrosobenzenes involves a reaction path in which ion pairs consisting of the unstable cationic reaction intermediate and the salt anion are of prevalent importance for the reaction. Factors such as salting-out and dehydration effects could also contribute to the rate enhancements observed. The rate enhancement arising from the ion pair formation on addition of salts should be principally considered as a consequence of stabilization of the highly unstable ionic reaction intermediates in the reaction system. The correlations obtained in the case

of the formation of *N*-phenylformohydroxamic acid in NaCl solutions are unusual and intriguing. Still, the correlations reveal some obvious regularities and could perhaps be useful for possible further advancement of semiquantitative or quantitative treatment of salt effects in more concentrated salt solutions.

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SAŽETAK

**Neobični solni efekti u reakciji nastajanja hidroksamskih
kiselina iz aldehida i nitrozo-spojeva**

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Brzina nastajanja *N*-fenilhidroksamskih kiselina u reakciji supstituiranih nitrozobenzena s formaldehidom ili acetaldehidom u vodi znatno se povećava dodatkom anorganskih klorida i perklorata. Povećanje konstante brzine nastajanja hidroksamata dodatkom soli, u odnosu na odgovarajuće konstante u vodi, iznosi od 7,4 za $Mg(ClO_4)_2$ (2 mol dm^{-3}) do 230,0 za $MgCl_2$ (2 mol dm^{-3}). Dobivene su linearne ovisnosti između log k_{obs} za nastajanje hidroksamske kiseline i koncentracije aniona dodane soli za $MgCl_2$, $CaCl_2$, $LiCl$, $Mg(ClO_4)_2$ i $NaClO_4$, dok su za NaCl, HCl i $HClO_4$ nađene drugačije, također pravilne ovisnosti. O dobivenim rezultatima raspravlja se polazeći od postavke da je nastanak ionskih parova između nestabilnog nitrozokarbinolnog kationskog međuprodukta i aniona dodane soli od ključne važnosti za pojavu opaženih solnih efekata i funkcionalnih povezanosti tih efekata s reakcijskim parametrima u reakcijama nastajanja hidroksamskih kiselina. U vodenim otopinama anorganskih klorida i perklorata, reakcija nastajanja hidroksamata iz aldehida i nitrozobenzena odvija se pretežno preko spomenutih ionskih parova, što je i glavni uzrok povećanja brzine procesa.