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Alternative Mechanistic Scheme for Salt Effects on Solvolysis Reactions of Haloalkanes and Related Compounds in Binary DMSO/H$_2$O Solvent Mixture

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In 75% (v/v) DMSO/H$_2$O solvent mixture, salt effects on the solvolysis reaction rates of haloalkanes and related compounds (RX) have been examined. In spite of the decreased water activity in the solvent mixture, the $\log(k/\mathrm{s}^{-1})$ values of typical S$_{\rm N}$1 substrates, such as 1-bromoadamantane, increase with increasing concentration of added metal perchlorates (the order: $\mathrm{Li}^+ < \mathrm{Na}^+ < \mathrm{Mg}^{2+} < \mathrm{Ba}^{2+}$), which is attributed to the direct chemical interaction between the leaving-group anion and the metal cation in the "modified" solution. Contrastingly, the $\log(k/\mathrm{s}^{-1})$ value of an S$_{\rm N}$2 substrate decreases with increasing concentration of the metal perchlorates. When nonmetallic salts containing anions ($\mathrm{Y}^- = \mathrm{Cl}^-$ or Br^-) different from RX ($\mathrm{X}^- = \mathrm{Cl}^-$, Br^-, or TsO^-) are present, solvolyses of S$_{\rm N}$2, such as 1-bromohexane, are subjected to an anion-exchange reaction. By the detailed examination of $\Delta\log(k/\mathrm{s}^{-1})/\Delta[\mathrm{Mg(ClO_4)_2}]$ for typical S$_{\rm N}$1, S$_{\rm N}$1–S$_{\rm N}$2 borderline, and S$_{\rm N}$2 substrates, we were able to demonstrate a linearity between the Mg(ClO$_4$)$_2$ effects in the solvolysis rates and the carbocation stabilities expressed by the Gibbs free energy values (ΔG°) of RX in the gas phase. The salt effects on the solvolyses of S$_{\rm N}$1 to S$_{\rm N}$2 substrates are accounted for without relying on Winstein's reaction scheme or the arbitrary function of ion pairs of two types.

Nucleophilic substitution reactions, especially, solvolysis reactions have been vastly studied and discussed.[1] The reaction rates of S$_{\rm N}$1 solvolysis of haloalkanes and related compounds are often subject to positive salt effects.[2] Bunton et al.[3] reported exponential increases in the methanolysis rates of S$_{\rm N}$1 substrates with increasing concentration of salts. Even though the cation effects appear to be large, they insisted small cation effects for Li$^+$, Na$^+$, and Et$_4$N$^+$ and attributed the difference to the anion effect: $\mathrm{ClO_4}^- > \mathrm{TsO}^- \approx \mathrm{NO_3}^- \approx \mathrm{Br}^- > \mathrm{Cl}^- \approx$ no salt. However, Allen et al.[4] have reported a superior salt effect of LiClO$_4$ over n-Bu$_4$NClO$_4$ on the solvolysis of 4-methoxybenzyl chloride in 85% (v/v) aqueous 1,4-dioxane. Many negative salt effects for unimolecular heterolysis have been reviewed by Russian investigators.[5] Hughes et al.[6] studied the kinetics of the exchange of chlorine between trityl chloride (chlorotriphenylmethane) and n-Bu$_4$NCl in a nonpolar solvent, benzene. The kinetic form and rate are practically unaffected by added n-Bu$_4$NClO$_4$. However, the kinetic form is changed, and the initial rate is reduced by added n-Bu$_4$NN$_3$, which concurrently produces a relatively inert substrate, trityl azide (azidotriphenylmethane).

Winstein and co-workers[7] proposed an ion-pair scheme for the solvolyses of aryl alkanesulfonates (basically S$_{\rm N}$1–S$_{\rm N}$2 borderline substrates) in an ionizing but only slightly dissociating solvent, especially, acetic acid ($\varepsilon_{\rm r} = 6.2$). According to Winstein's interpretation, the "normal" salt effect on the acetolysis rate is due to acceleration of the substrate ionization step leading to the contact ion pair (CIP, $\mathrm{RX} \rightleftharpoons \mathrm{R^+X^-}$) while the "special" salt effect is the result of an exchange reaction between two solvent-separated ion pairs (SSIPs), as shown in eq 1.

$$\mathrm{R^+\|X^-} + \mathrm{M^+\|ClO_4{}^-} \rightleftharpoons \mathrm{R^+\|ClO_4{}^-} + \mathrm{M^+\|X^-} \qquad (1)$$

His interpretation and related scheme is so well accepted that anyone would be apt to apply it to many solvolysis reactions of various types.[8,9] That is, salt effects on the solvolyses often rely on the formation of two types of ion pairs ($\mathrm{R^+X^-}$ and $\mathrm{R^+\|X^-}$) and the return to RX and/or the exchange between the ion pairs from RX and from an added (perchlorate) salt.

It is true that the conventional scheme is quite convenient to use, however, we are afraid that no driving force is involved for encouraging the ion pair exchange reaction (eq 1) to go forward. Loupy et al.[8b] have mentioned that the exchange of ions between SSIPs is shown on several occasions and that its mechanism is not yet known.[10–12] Dvorko et al.[13] have reviewed critically the special salt effect in unimolecular heterolysis reactions.

The solvent[14] and salt effects in organic reactions have been widely discussed.[1,15] A review by Bentley and Schleyer[1a] is excellent for medium effects on the rates and mechanisms of solvolytic reactions. The development of laser-flash photolysis supplied the necessary tool to study chemical systems on the nano-second and pico-second time scales relevant to ion-pair dynamics. Bockman and Kochi[16] mentioned unfortunately that the original goal of finding a spectroscopic distinction between CIPs and SSIPs remains unfulfilled. Based on the conventional scheme for salt effects, even though, no one can predict whether a certain solvolysis reaction is accelerated or decelerated by an added salt, presupposes that any salt effect is a superposition of positive and negative salt effects.

From a completely different viewpoint, therefore, we have studied the solvolyses (hydrolyses) of haloalkanes and related

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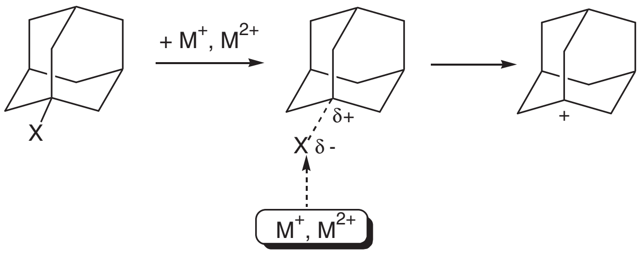


Scheme 1. The proposed mechanism for S_N1 solvolysis in the presence of $MClO_4$ and $M(ClO_4)_2$.

compounds.[17–21] Exponential increases in rate constants of typical S_N1 substrates are observed with increasing concentration of added alkali metal (M^+) and alkaline earth metal (M^{2+}) perchlorates: in most cases, the cation effects increase in the order $Na^+ < Li^+ < Mg^{2+}$, Ba^{2+} in 80% (v/v) MeOH/H_2O ($\varepsilon_r = 49$),[17] and 50% (v/v) organic solvent systems of acetone/H_2O ($\varepsilon_r = 55$),[18] 1,4-dioxane/H_2O ($\varepsilon_r = 44$),[19] sulfolane/H_2O,[20] and DMF/ or DMA/H_2O.[21] Citing our papers, Ji et al.[22] have mentioned that salt effects by $LiClO_4$ on the reaction rates can be used to distinguish between S_N1 and S_N2 processes. We have also established that the solvolysis rate constants of typical S_N1 substrates should decrease in the presence of nonmetallic salts at higher concentrations because of a decrease in water activity.[17–21] Judging from the rate increase $[\log(k_1/k_0)]$ in the presence of $1.0\,\mathrm{mol\,dm^{-3}}$ $LiClO_4$, we can indicate that a phenyl group of the substituted halomethane acts just as two methyl groups would on the carbon center.[19] A correlation has been observed between the σ^+ values in the Hammett equation[1c] and the $\Delta\log(k/\mathrm{s^{-1}})$ for substituted benzyl halides upon the addition of $1.0\,\mathrm{mol\,dm^{-3}}$ $LiClO_4$, as well as between the $\log(k_x/k_H)$ values themselves.[19]

The mechanism of the metal cation effect on a S_N1 substrate can be illustrated by Scheme 1. In an "aqueous medium," the direct chemical interaction should operate between added metal cations and the leaving-group anion. However, some difficulties may arise from the following two points: (a) The coordination ability of alkali metal and alkaline earth metal ions should be much weaker than that of transition-metal ions because of the lack of partly filled d- or f-shells. (b) In aqueous solution, strong solvation (hydration) may shade completely the chemically interacting sites not only on alkali metal or alkaline earth metal cations but also on anions, even if they have some potential for such chemical interaction in addition to the electrostatic interaction.

Nevertheless, we have postulated that a very small but direct "chemical" interaction can operate between M^+ or M^{2+} and simple anions, such as halide ions, even in aqueous or organic–aqueous solutions when water molecules are modified to "dihydrogen ether" ([R](H)–O–(H)[R])[17–21] conditions. In a review article, Fromm[23] stated that "the coordination chemistry of group 1 and 2 metal compounds with organic ligands in the widest sense has been, until relatively recently, largely unknown compared to transition-metal coordination networks." Reichardt et al.[24] described, citing our papers[17,19] that, at high salt concentrations ($c > 5\,\mathrm{mol\,dm^{-3}}$), region **C** of ion solvation, according to Frank and Wen,[25] can be abolished and only regions **A** and **B** survive, resulting an aqueous solvent called "dihydrogen ether."

Olah[26] reviewed the significance of carbocations in chemistry; in general, stable carbocations are prepared in superacidic media. Schaller and Mayr[27] made it possible to monitor photometrically the formation of the carbocation of 4,4′-dimorpholinobenzhydryl carboxylates in aqueous acetone and acetonitrile. However, we have discovered that stable carbocations can be produced from trityl halides by addition of the perchlorates salts of Li^+, Na^+, Mg^{2+} (Ca^{2+}, Sr^{2+}), and Ba^{2+} in acetonitrile;[28–30] which have been detected by UV–visible,[28] ^1H and ^{13}C NMR spectroscopy.[29,30a] For a fluoran-based black color former in acetonitrile, the color has been developed by the addition of the alkali metal (M^+) or alkaline earth metal (M^{2+}) perchlorates.[30] The extraordinary chemical reactions with alkali metal and alkaline earth metal ions in higher relative permittivity media, which possess lower solvation abilities, have been reviewed.[31] It is an easy task for us to produce the CIPs and SSIPs separately from nitrophenols in the presence of appropriate bases in acetonitrile: the addition of $MClO_4$ and $M(ClO_4)_2$ causes the formation of CIPs between the phenolate and M^+ or M^{2+} ions while Et_4NX (X = Cl or Br) produces the free phenolate ions or SSIPs.[32]

In order to confirm further our proposal in previous solvolytic studies,[17–21] we examine the influence of various types of salts, $MClO_4$, $M(ClO_4)_2$, and R_4NX (R = Et, Pr, or *n*-Bu; X = ClO_4, Cl, Br, or OTs) on the solvolysis reactions of typical S_N1 and S_N2 substrates in a 75% (v/v) DMSO/H_2O solvent mixture. The relative permittivity and basicity of DMSO are rather high, $\varepsilon_r = 46.5$[33] and Gutmann's donor number (DN) = 29.8,[34] while the acidity of the solvent is low or small, e.g., the acceptor number (AN) = 19.3.[34] Solubilities of substrates are insufficient in a 50% (v/v) DMSO/H_2O mixture, therefore, a system with a higher DMSO content is utilized. The substitution (or "anion exchange") reactions of leaving groups with added salt anions for typical S_N2 substrates are examined in the same binary solvent system. A linear relationship is observed between the stabilities of carbocations (ΔG°) and the $Mg(ClO_4)_2$ effects on the solvolysis rate constants of the various substrates (S_N1, S_N1–S_N2 borderline, and S_N2). In a previous study,[21] the relation between the $LiClO_4$ effects vs. ΔG° was examined.

The nitration of phenols in reversed micelle systems has been reported and an enhanced oxidation ability of diluted nitric acid (<2.0 molarity) has also been demonstrated in concentrated salt (bulk) solutions.[35] Apparent contradictions between NMR and Raman evidence have been discussed and integrated successfully in terms of a distortion of the bulk water structure in the presence of high salt concentrations, such as Li^+ and Na^+ as well as Mg^{2+} and Ca^{2+}, in aqueous solution.[35]

Results and Discussion

Metal Salt Effects on a Typical S_N1 Substrate. Figure 1 shows the changes in the solvolysis rate of 1-bromoadamantane with the addition of alkali metal or alkaline earth metal perchlorates in the 75% (v/v) DMSO/H_2O solvent mixture at 50 °C. The "pseudo" first-order reaction rate constant ($k/\mathrm{s^{-1}}$) increases exponentially with increasing concentration of $LiClO_4$, $NaClO_4$, $Mg(ClO_4)_2$, or $Ba(ClO_4)_2$, i.e., linearity is observed between $\log(k/\mathrm{s^{-1}})$ and the concentration of each metal perchlorate. The effects of metallic ions enlarge in the

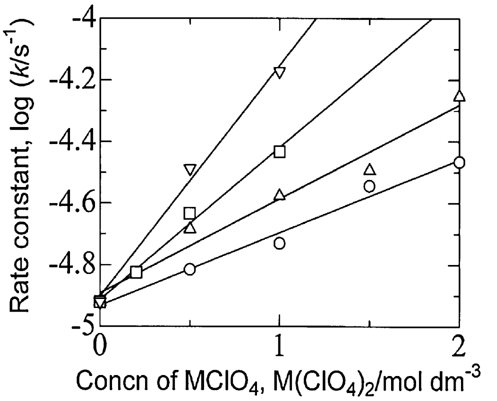


Figure 1. Changes in the solvolysis rate of 1-bromoadamantane with the addition of various salts in 75% (v/v) DMSO/H_2O at 50 °C: (△) $LiClO_4$; (○) $NaClO_4$; (□) $Mg(ClO_4)_2$; (▽) $Ba(ClO_4)_2$.

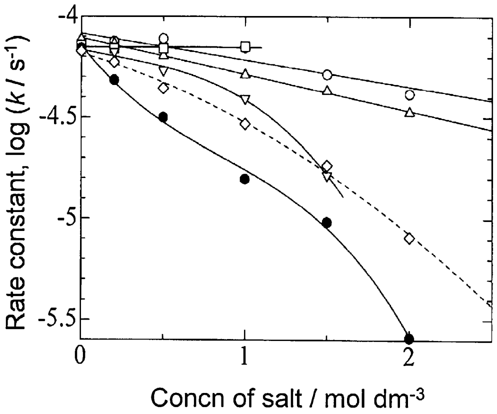


Figure 2. Changes in the solvolysis rate of 1-bromoadamantane in the presence of nonmetallic salts in 75% (v/v) DMSO/H_2O at 70 °C: (○) Et_4NBr; (△) Et_4NCl; (□) Et_4NClO_4; (▽) Et_4NOTs; (◇) Pr_4NBr; (●) n-Bu_4NBr.

Table 1. First-Order Reaction Rate Constants of the Solvolyses for a Typical S_N1 Substrate, 1-Bromoadamantane, in the Presence of Various Salts in a 75% (v/v) DMSO/H_2O Solvent Mixture

Substrate	Temp/°C	Salt[a]	k/s^{-1}	$\log(k/s^{-1})$	$\Delta\log(k/s^{-1})$[b]
1-Bromoadamantane	50	No salt	1.20×10^{-5}	−4.92	—
	50	$LiClO_4$	2.65×10^{-5}	−4.58	+0.34
	50	$NaClO_4$	1.86×10^{-5}	−4.73	+0.19
	50	$Mg(ClO_4)_2$	3.69×10^{-5}	−4.43	+0.49
	50	$Ba(ClO_4)_2$	6.73×10^{-5}	−4.17	+0.75
	70	No salt	7.40×10^{-5}	−4.13	—
	70	Et_4NClO_4	7.08×10^{-5}	−4.15	−0.02
	70	Et_4NCl	5.14×10^{-5}	−4.29	−0.16
	70	Et_4NBr	6.99×10^{-5}	−4.16	−0.03
	70	Et_4NOTs[c]	3.93×10^{-5}	−4.41	−0.28
	70	Pr_4NBr	2.49×10^{-5}	−4.53	−0.40
	70	n-Bu_4NBr	1.57×10^{-5}	−4.80	−0.67

a) The salt concentration is 1.0 mol dm^{-3}. b) $\Delta\log(k/s^{-1}) = \log(k_1/s^{-1})$[with salt] − $\log(k_0/s^{-1})$[no salt] for each substrate. c) p-Toluenesulfonate (tosylate) salt.

order $Na^+ < Li^+ < Mg^{2+} < Ba^{2+}$ (Table 1). The difference in the salt effects between Mg^{2+} and Ba^{2+} is obvious. In 50% (v/v) DMF/water[21] also, an obvious superiority of Ba^{2+} over Mg^{2+} has been observed, while the superiority between Mg^{2+} and Ba^{2+} (of up to 1.5 mol dm^{-3} salt concentration) has been neither observed in 50% (v/v) DMA/water[21] nor sulfolane/water solvent mixtures.[20]

In spite of a decrease in the activity of (solvent) water in the presence of salts, the solvolysis rate of 1-bromoadamantane increases remarkably in this solvent mixture. The observed results can be accounted for by the interaction between the leaving-group anion (Br^-) from the substrate and the added metal cations. First of all, however, the properties of the DMSO/H_2O or bulk waters are altered to get closer to that of a "nonaqueous" solvent by the added salts in order to condition the medium for favorable chemical interaction between Br^- and the metal ions. Thus, the produced 1-adamantyl cation can promptly react with H_2O, even if the activity of water is much decreased (Scheme 1).

The Arrhenius plots of the solvolysis reaction (55–70 °C) of 1-bromoadamanane in the 75% (v/v) DMSO/H_2O mixture gave activation energies (E_a) of 91.6, 89.7, and 99.4 kJ mol^{-1} for 0.0, 0.5, and 1.0 mol dm^{-3} $Mg(ClO_4)_2$, respectively. No remarkable difference is observed by the addition of increasing concentrations of the metal perchlorate. We have discussed such results in terms that no alternation is involved in the fundamental scheme of solvolysis in the absence and presence of metal perchlorates.[20]

Effects of Nonmetallic Salts on the Typical S_N1 Substrate. The influences of nonmetallic salts on the S_N1 solvolysis rate were examined in the 75% (v/v) DMSO–H_2O solvent mixture. Figure 2 shows the change in the solvolysis rate of 1-bromoadamantane with increasing concentration of $Et_4N^+X^-$ ($X^- = ClO_4^-, Cl^-, Br^-$, and TsO^-) at 70 °C. All the tetraethylammonium salts cause the deceleration of the solvolysis rate; the tosylate anion, which is the most bulky among the four anions studied in the series, causes the most remarkable decrease in the $\Delta\log(k/s^{-1})$ value of −0.28, i.e., its solvolysis rate decreases to be a half at 1.0 mol dm^{-3} of the ammonium salt, compared with that in the absence of the salt [$\log(k_0/s^{-1}) = -4.13$] at 70 °C. Tetraethylammonium salts cause the deceleration of the order of $ClO_4^- < Br^- < Cl^- < TsO^-$ for the anions. Similar and distinct effects ($ClO_4^- < Br^- < Cl^- < TsO^-$) of Et_4N^+ salts on 1-chloroadamantane have been observed in 50% (v/v) DMA/water[21] or sulfolane/water.[20] We may mention that, in 50% (v/v) DMF/H_2O, the order of $ClO_4^- < Br^- < Cl^-$ has been observed for 1-chloroadamantane at 70 °C as well as for 1-bromoadamantane at 45 °C.[21] Leffek[36] has reported that the perchlorate catalysis in the methanolysis of chlorotriphenylmethane is suppressed by the addition of *n*-Bu_4NCl (10^{-5} mol dm^{-3} levels).

The deceleration effect must be brought by a decrease in the activity of water (with increasing salt concentrations) in the $DMSO/H_2O$ solvent mixture. The solvolysis of a typical S_N1 substrate should be initiated by the attack of water molecules toward the substrate molecules in order to produce the carbocations. The solvation manners of the anions may result in the difference of "effective" water activities. The distortion of the water structure in the presence of tetraalkylammonium and metal salts has been discussed based on ^1H NMR and Raman spectral data in previous papers.[19–21,35]

As shown in Figure 2, a more remarkable deceleration in the solvolysis rate is caused by other tetraalkylammonium bromides, the deceleration effect as $Et_4N^+ < Pr_4N^+ < n\text{-}Bu_4N^+$: the changes in the logarithm factors [$\Delta\log(k/s^{-1})$] are −0.03, −0.40, and −0.67 with the 1.0 mol dm^{-3} salts at 70 °C, respectively. At any rate, however, the nonmetallic salt effect on the typical S_N1 substrate in the $DMSO/H_2O$ solvent mixture is found to be much smaller than that in aqueous DMA[21] or sulfolane[20] solvent mixtures.

Metal Perchlorates on an S_N2 Substrate. The changes in the solvolysis rates, $\log(k/s^{-1})$, were examined for 1-bromohexane with 0.0–1.5 mol dm^{-3} $LiClO_4$ in 75% (v/v) DMSO–H_2O at 80 °C (Figure 3). In contrast to the typical S_N1 substrates, the solvolysis rate of the S_N2 substrate is not accelerated but decelerated by the addition of the metal perchlorates. The $\log(k_0/s^{-1})$ value (−4.02) of 1-bromohexane without salt decreases linearly with increasing $LiClO_4$ concentration, e.g., $\Delta\log(k/s^{-1}) = -0.16$ at 1.0 mol dm^{-3} $LiClO_4$ (Table 2). The deceleration effect of Na^+ is very close to that of Li^+, however, those of alkaline earth metal ions (Mg^{2+} and Ba^{2+}) are much more remarkable than those of the alkali metal ions.

In the S_N2 solvolysis (hydrolysis) system, an activated complex ($H_2O\cdots C^{\delta+}H_2R\cdots X^{\delta-}$) or an associate ($RX\cdot H_2O$) may briefly exist in the solution. At any case, the metal cations have no way to give more of the activated species. The deceleration in the solvolysis in the presence of metal perchlorates can be attributed to the decrease in the activity of water, which attacks the substrate in order to initiate the solvolysis reaction.

S_N2 Solvolyses Accompanied by Anion-Exchange Reactions. Figure 4 shows the changes in the solvolysis rates of 1-chloro-, 1-bromo, and 1-tosylhexane in the presence of 0.0–0.5 and 1.0 mol dm^{-3} $Me_4N^+Cl^-$, $Et_4N^+Br^-$, and $Et_4N^+TsO^-$ in

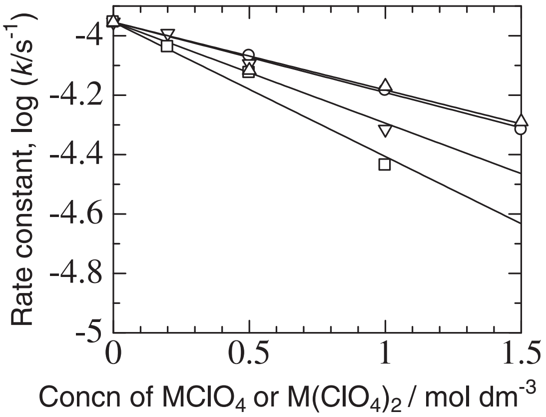


Figure 3. Changes in the solvolysis rate of 1-bromohexane with the addition of various metal perchlorates in 75% (v/v) $DMSO/H_2O$ at 80 °C: (○) $LiClO_4$; (△) $NaClO_4$; (□) $Mg(ClO_4)_2$; (▽) $Ba(ClO_4)_2$.

Table 2. First-Order Reaction Rate Constants of the Solvolyses for Typical S_N2 Substrates in the Presence of Various Salts in a 75% (v/v) $DMSO/H_2O$ Solvent Mixture

Substrate	Temp/°C	Salt[a)]	k/s^{-1}	$\log(k/s^{-1})$	$\Delta\log(k/s^{-1})$[b)]
1-Chlorohexane	80	No salt	1.73×10^{-6}	−5.76	—
	80	Me_4NCl[c)]	1.43×10^{-6}	−5.85	−0.09
	80	Et_4NBr[d)]	3.88×10^{-5}	−4.41	+1.35
	80	Et_4NOTs[e)]	1.59×10^{-6}	−5.80	−0.04
1-Bromohexane	80	No salt	9.53×10^{-5}	−4.02	—
	80	$LiClO_4$	6.55×10^{-5}	−4.18	−0.16
	80	$NaClO_4$	6.76×10^{-5}	−4.17	−0.15
	80	$Mg(ClO_4)_2$	3.66×10^{-5}	−4.44	−0.42
	80	$Ba(ClO_4)_2$	4.84×10^{-5}	−4.32	−0.30
	80	Me_4NCl[d)]	3.36×10^{-6}	−5.47	−1.45
	80	Et_4NBr	7.40×10^{-5}	−4.13	−0.11
	80	Et_4NOTs[e)]	1.15×10^{-4}	−3.94	+0.08
1-Tosylhexane	80	No salt	3.69×10^{-4}	−3.43	—
	80	Me_4NCl[d)]	1.87×10^{-6}	−5.73	−2.30
	80	Et_4NBr[d)]	6.37×10^{-5}	−4.20	−0.77
	80	Et_4NOTs[e)]	3.49×10^{-4}	−3.46	−0.03

a) The salt concentration is 1.0 mol dm^{-3}. b) $\Delta\log(k/s^{-1}) = \log(k_1/s^{-1})$[with salt] − $\log(k_0/s^{-1})$[no salt] for each substrate. c) The salt concentration is 0.05 mol dm^{-3}. d) Only the linear part in the ln[S] vs. *t* plot was evaluated because an exchange reaction took place between the leaving group and the added salt anion. e) *p*-Toluenesulfonate (tosylate) salt.

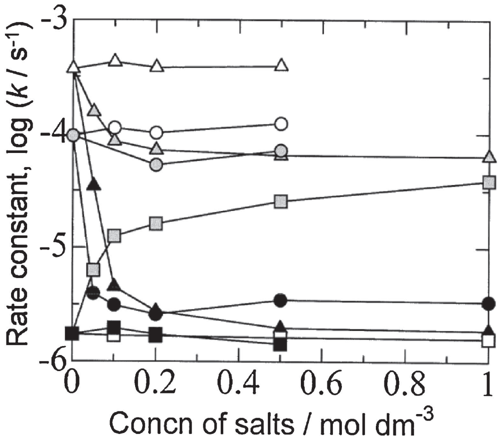


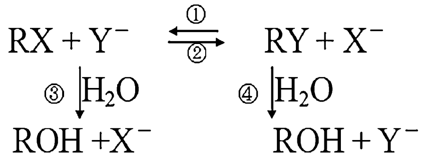
Figure 4. Changes in the solvolysis rates of 1-tosylhexane (triangle), 1-bromohexane (circle), and 1-chlorohexane (square) after addition of various salts in 75% (v/v) DMSO/H_2O at 80 °C: (black symbols) Me_4NCl; (gray symbols) Et_4NBr; (white symbols) Et_4NOTs.

75% (v/v) DMSO/H_2O at 80 °C. It should be mentioned that large differences between the effects of $Me_4N^+Cl^-$ and $Et_4N^+Cl^-$ could not be found in the present study. The solvolysis rate constants of 1-bromohexane remarkably decelerate with increasing concentration of Me_4NCl and approach that of the chloro-substrate (the intrinsic value) at 0.2 mol dm^{-3} Me_4NCl. However, Et_4NBr and Et_4NOTs cause no or just minor deceleration in the 1-bromohexane solvolysis. Additionally, Et_4NClO_4 of 0.1 and 0.2 mol dm^{-3} neither causes any change in the 1-bromohexane solvolysis.

To the contrary, the solvolysis rate of 1-chlorohexane is remarkably accelerated with increasing concentration of Et_4NBr. At 1.0 mol dm^{-3} Et_4NBr, the rate constant approaches that of 1-bromohexane (the intrinsic value). The salts of Cl^- and TsO^- cause almost no effect upon the solvolysis rate of the chloro-substrate.

The addition of 0.5 mol dm^{-3} Me_4NCl or Et_4NBr to 1-tosylhexane causes remarkable deceleration in the solvolysis rate toward that of (as if) 1-chloro- or 1-bromohexane, respectively. However, the addition of Et_4NOTs causes no significant change in the solvolysis rate of 1-tosylhexane as well as of the halo-substrates. This result may verify that the tosylate ion in the added salt has just a weak ability to substitute (or exchange) the anions from the substrates (i.e., 1-chloro- and 1-bromohexane). However, the chloride and bromide ions can substitute anions easily from all the substrates. The order of nucleophilicity for halide ions in aprotic solvents, such as acetone, is regarded to be $Cl^- > Br^- > I^-$, in contrast to $Cl^- < Br^- < I^-$ in aqueous solution.[37]

In the present solvent system, the nucleophilicity of Cl^- seems to be superior to that of Br^-, judging from the steep decreasing profile of the rate constant of 1-bromohexane with increasing Cl^- concentration, compared with the gradual increasing profile for 1-chlorohexane with increasing Br^- concentration, as shown in Figure 4. Therefore, the nucleophilicity can be ordered as $ClO_4^- < TsO^- < Br^- \lesssim Cl^-$.



Scheme 2. Anion-exchange and solvolysis (hydrolysis) reactions in the presence of foreign anions for S_N2 substrates.

The obvious acceleration and deceleration effects on the addition of foreign (different) anions for the S_N2 substrates are caused by anion-exchange reactions, which take place prior or parallel to the solvolysis (Scheme 2). In Scheme 2, the anion-exchange reaction is expressed by (1) and (2) while the solvolysis (hydrolysis) reactions by (3) and (4). The anion-exchange scheme has been demonstrated to be valid not only for the typical S_N2 substrates in sulfolane/H_2O,[20] DMF/ and DMA/H_2O[21] systems but also for S_N1–S_N2 borderline substrates, such as halomethylene(benzene) (benzyl halides), in the DMA/H_2O system.[21] Winstein et al.[7d] also have reported the anion-exchange reaction between 1-anisyl-2-propyltoluenesulfonate (in IUPAC, 1-anisylethyltoluenesulfonate) and added Br^- ions in acetic acid. In benzene, as reported by Hughes et al.,[6] an anion exchange can be observed for trityl chloride by means of a radioactivity technique.

It goes without saying that anion-exchange reactions cannot go forward practically when the nucleophlicities of foreign anions are much weaker than that of the substrate leaving groups, even though the concentrations of the foreign anions are very abundant. The anion-exchange reactions observed in the present study have demonstrated this tendency. Considering the very weak nucleophilicity of ClO_4^-, we are compelled to decide that such an ion-pair exchange, expressed by eq 1, should not go forward spontaneously in our solvent systems.

Relationship between $Mg(ClO_4)_2$ Effects and the Stabilities of Carbocations. Abboud and co-workers[38] have developed a method to determine the stability of carbocations in the gas phase by dissociative proton attachment (DPA) using Fourier-transform ion-cyclotron resonance (FTICR) spectroscopy. Carbocations are ranked according to their stabilities relative to the 1-adamantyl cation, based on eq 2,

$$\text{1-Ad-Cl(g)} + \text{R}^+\text{(g)} \rightarrow \text{1-Ad}^+\text{(g)} + \text{R-Cl(g)}, \Delta G^\circ \qquad (2)$$

The Gibbs free energy values (ΔG°) in the gas phase have been found to give excellent correlations with the $\log(k/\text{s}^{-1})$ values of RX in solution, where RX are not only bridgehead-type (such as 1-chloroadamantane) but also bi- and tricyclic secondary-type chloroalkanes, such as 2-chloronorbornane and 2-chloroadamantane.[21]

Figure 5 shows the relationship between the standard Gibbs energy values for eq 2 and the $Mg(ClO_4)_2$ influence on the solvolysis rate constants of various bromo-substrates in 75% (v/v) DMSO–H_2O. Bromoalkanes give a good linearity or correlation between ΔG° and $\Delta\log(k/\text{s}^{-1})/\Delta[Mg(ClO_4)_2]$; bromoalkanes examined in the present study are 1- and 2-butyl, cyclopentyl, 1-hexyl, cyclohexyl, *exo*-2-norbornyl, 1- and 2-adamantyl. *t*-Butyl chloride (2-chloro-2-methylpropane) and not the bromo-derivative was examined in this study. The previous paper in DMA/H_2O with $LiClO_4$ has indicated that bromoalkanes give a straight line below (the difference of ca. 0.1) the line of the corresponding chloro-substrates. Benzyl bromides [(bromomethylene)benzenes] give another correlation group below the group of bromoalkanes (cf. also Table 3).

In previous papers,[17–19] we have reported a linearity between the $LiClO_4$ effects and the Grunwald–Winstein *m* values[39] for S_N1 to S_N2 substrates in MeOH/water,[17] acetone/water,[18] and 1,4-dioxane/water[19] solvent mixtures. The salt effects have been expressed by the changes in solvolysis rates, $\log(k_l/k_o)$, on the addition of 1.0 mol dm^{-3} $LiClO_4$. The *m* value is the reaction's sensitivity to the solvent ionizing power Y ($m = 1$ or 1.2 for 1-AdCl),[40] and may vary not only with experimental conditions but also with the definition. Recently, Park and Kevill[41] examined the *m* values of dichlorobenzoyl chlorides.

The previous[21] and present papers, however, have demonstrated the good correlations between the $LiClO_4$ or $Mg(ClO_4)_2$ effects and the carbocation stabilities expressed by the Gibbs free energy values (ΔG°) of RX in the gas phase, where RX are not only typical S_N1 haloalkanes but also non-, mono-, bi-, and tricycle secondary-type (such as 2-hexyl, cyclopentyl, 2-norbornyl, and 2-adamantyl) and, finally, typical S_N2 haloalkanes.

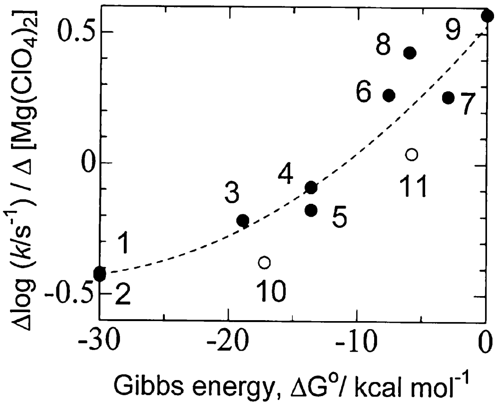


Figure 5. The relation between the salt effects of $Mg(ClO_4)_2$ in 75% (v/v) DMSO/H_2O and the stabilities of carbocations. The stability of the 1-adamantyl cation is taken as the standard value ($\Delta G^\circ = 0$): Open and solid symbols represent aliphatic and benzyl compounds, respectively. (1) hexyl-1-ylium; (2) butan-1-ylium; (3) butan-2-ylium; (4) cyclohexylium; (5) cyclopentylium; (6) adamantan-2-ylium; (7) norbornan-2-ylium; (8) 2-methylpropan-2-ylium (chloride); (9) adamantan-1-ylium; (10) 4-nitrobenzylium; (11) benzylium.

We do not think that it does matter whether primary alkyl cations are energy minima or not. The stability or instability of R^+ (in gas phase) is the most important factor. In the case of hexan-1-ylium, for instance, the stability of R^+ is very low, therefore, the leaving group, $Br^{\delta-}$, of 1-bromohexane has no chance to be assisted by the added Mg^{2+} to leave from the substrate body. The activity of water (the reactant) is much decreased by the presence of salts, e.g., $Mg(ClO_4)_2$, in the aqueous organic solvent. The hydrolysis of any substrate should be decelerated in lower water activities with the addition of salts (of higher concentrations) unless the effective assistant is available of chemical interaction between $X^{\delta-}$ and the metal ions (M^+ or M^{2+}).

Conclusion

In 75% (v/v) DMSO/H_2O solvent mixtures, salt effects on the solvolysis reaction rates of haloalkanes and related compounds (RX) have been examined. No exceptional behavior, compared with our previous results, was observed in the "pseudo" first-order rate constants (k/s^{-1}) of typical S_N1 and S_N2 substrates in the presence of metal perchlorates or nonmetallic salts. The change in water activity as well as the direct chemical interaction between the solutes should control the reaction. The salt effects on the solvolyses of S_N1 to S_N2 substrates were elucidated without relying on Winstein's scheme, that is, the ion-pair return and/or the exchange between the solvent-separated ion pair (SSIPs) from a substrate and the ion pair from an added metal perchlorate salt. Now, one could predict rather definitely whether solvolysis (hydrolysis) reaction rates of haloalkanes and related compounds are accelerated or decelerated by the addition of a certain salt.

Experimental

Materials. Dimethyl sulfoxide (DMSO) as solvent, purchased from Wako, was used as received. The substrates from TCI were used without further purification: 1-bromo-

Table 3. Stabilities of Carbocations in the Gas Phase and the $Mg(ClO_4)_2$ Effects on the Solvolysis Rate Constants of Various Bromo-Substrates in a 75% (v/v) DMSO–H_2O Solvent Mixture

Cations	Standard Gibbs energy[a)] ΔG°/kcal mol^{-1}	$Mg(ClO_4)_2$ effect[b)] $\Delta\log(k/s^{-1})/\Delta[Mg(ClO_4)_2]$
Hexan-1-ylium (**1**)	−30 (an arbitrary value)[c)]	−0.43 (80 °C)
Butan-1-ylium (**2**)	−30 (an arbitrary value)[c)]	−0.42 (80 °C)
Butan-2-ylium (**3**)	−18.9	−0.22 (80 °C)
Cyclohexylium (**4**)	Data not found	−0.09 (80 °C)
Cyclopentylium (**5**)	−13.6	−0.18 (70 °C)
Adamantan-2-ylium (**6**)	−7.6	+0.27 (60 °C)
Norbornan-2-ylium (**7**)	−3.0	+0.26 (60 °C)
2-Methylpropan-2-ylium (**8**)	−6.0	+0.43[d)] (30 °C)
Adamantan-1-ylium (**9**)	0.00 (by definition)	+0.57 (60 °C)
4-Nitrobenzylium (**10**)	−17.2	−0.38 (60 °C)
Benzylium (**11**)	−5.8	+0.04 (45 °C)

a) Standard Gibbs energy change for a reaction, 1-AdCl(g) + R^+(g) → 1-Ad^+(g) + RCl(g); cf. ref. 38. b) The $Mg(ClO_4)_2$ effect ($\Delta\log(k/s^{-1})/\Delta[Mg(ClO_4)_2]$) for each substrate was evaluated over a range of 0.0–1.0 mol dm^{-3} $Mg(ClO_4)_2$. c) cf. methylium: −77.4 kcal mol^{-1}. d) The chloro- and not the bromo-substrate.

adamantane (>97%), 2-bromoadamantane (>97%), 2-chloro-2-methylpropane (*t*-butyl chloride, >98%), 1-chloro- (>95%), 1-bromo- (>98%), and 1-tosylhexane (>98%), 1- and 2-bromobutane (99% and >98%), bromocyclopentane (>98%), bromocyclohexane (>95%), (bromomethylene)benzene (benzyl bromide, >98%). Aldrich chemicals such as 1-(bromomethylene)-4-methylbenzene (4-methylbenzyl bromide, 97%) and *exo*-2-bromonorbornane (98%) were used as received. Water was purified by means of a MilliQ system (Millipore Corp.).

The salts $LiClO_4$, $NaClO_4$, Et_4NBr, Et_4NOTs, and Pr_4NBr from Aldrich as well as $LiClO_4$, Me_4NCl, and Et_4NCl from Wako were used as received. Tetraethylammonium perchlorate (Et_4NClO_4) was prepared by adding an equivalent amount of $HClO_4$ to Et_4NBr in water. The precipitate was filtered, washed with cold water several times and were recrystallized from water, followed by drying at 70 °C in vacuo. Tetrabutylammonium bromide was prepared as follows: tributylamine and bromobutane in acetonitrile solvent were refluxed for 36 h, followed by evaporation of the solvent to dryness; the *n*-Bu_4NBr precipitate was twice recrystallized from ethyl acetate and dried at 70 °C in vacuo.

Kinetics. The solvolysis rates were determined by titration with 0.0025 mol dm^{-3} of a standard aqueous sodium hydroxide solution using phenolphthalein as indicator. The initial concentrations of the substrates were all kept at 0.010 mol dm^{-3} in the reaction vessels. All the substrates were dissolved in acetonitrile (Aldrich, anhydrous 99.8%) at first. In principle, 0–90% consumption of a substrate was followed for evaluating the rate constant, except for some cases; in S_N2 substrates containing Et_4NX salts, only the linear parts in the ln[S] vs. *t* curve were utilized. Details for the other reagents and the procedure for the kinetic experiments have been described previously.[17–21]

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References

1 a) T. W. Bentley, P. v. R. Schleyer, *Adv. Phys. Org. Chem.* **1977**, *14*, 1. b) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, NY, **1953**; 2nd ed., **1969**. c) L. P. Hammett, *Physical Organic Chemistry: Reaction Rates, Equilibria, and Mechanisms*, 2nd ed., McGraw-Hill, New York, **1970**. d) M. B. Smith, J. March, *Marche's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 6th ed., Wiley, Hoboken, NJ, **2007**, Chap. 10.

2 C. A. Bunton, S. K. Huang, *J. Am. Chem. Soc.* **1972**, *94*, 3536.

3 C. A. Bunton, T. W. Del Pesco, A. M. Dunlop, K.-U. Yang, *J. Org. Chem.* **1971**, *36*, 887.

4 A. D. Allen, T. T. Tidwell, O. S. Tee, *J. Am. Chem. Soc.* **1993**, *115*, 10091.

5 G. F. Dvorko, E. A. Ponomareva, *Russ. J. Org. Chem.* **1998**, *34*, 487.

6 E. D. Hughes, C. K. Ingold, S. F. Mok, S. Patai, Y. Pocker, *J. Chem. Soc.* **1957**, 1220.

7 a) S. Winstein, E. Clippinger, A. H. Fainberg, G. C. Robinson, *J. Am. Chem. Soc.* **1954**, *76*, 2597. b) A. H. Fainberg, S. Winstein, *J. Am. Chem. Soc.* **1956**, *78*, 2767. c) S. Winstein, P. E. Klinedinst, Jr., G. C. Robinson, *J. Am. Chem. Soc.* **1961**, *83*, 885. d) S. Winstein, P. E. Klinedinst, Jr., E. Clippinger, *J. Am. Chem. Soc.* **1961**, *83*, 4986.

8 a) A. Loupy, B. Tchoubar, *Salt Effects in Organic and Organometallic Chemistry*, VCH, Weinheim, **1992**. b) A. Loupy, B. Tchoubar, D. Astruc, *Chem. Rev.* **1992**, *92*, 1141.

9 G. F. Dvorko, E. A. Ponomareva, M. E. Ponomarev, *J. Phys. Org. Chem.* **2004**, *17*, 825.

10 J. D. Simon, K. S. Peters, *Acc. Chem. Res.* **1984**, *17*, 277.

11 J. L. Goodman, K. S. Peters, *J. Am. Chem. Soc.* **1986**, *108*, 1700.

12 a) C. Devadoss, R. W. Fessenden, *J. Phys. Chem.* **1990**, *94*, 4540. b) C. Devadoss, R. W. Fessenden, *J. Phys. Chem.* **1991**, *95*, 7253.

13 G. F. Dvorko, E. A. Ponomareva, N. E. Ponomarev, *Russ. J. Gen. Chem.* **2006**, *76*, 1368.

14 C. Reichardt, T. Welton, *Solvents and Solvent Effects in Organic Chemistry*, 4th ed., Wiley-VCH, Weinheim, **2011**. doi:10.1002/9783527632220.

15 J. E. Gordon, *The Organic Chemistry of Electrolyte Solutions*, Wiley, New York, **1975**; *Ions and Ion Pairs in Organic Reactions: Role of Ions and Ion Pairs in Chemical Reactions*, ed. by M. Szwarc, Wiley-Interscience, New York, **1972**, Vol. 1 and **1974**, Vol. 2.

16 T. M. Bockman, J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* **1994**, 1901.

17 L. C. Manege, T. Ueda, M. Hojo, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 589.

18 L. C. Manege, T. Ueda, M. Hojo, M. Fujio, *J. Chem. Soc., Perkin Trans. 2* **1998**, 1961.

19 M. Hojo, T. Ueda, S. Inoue, Y. Kawahara, *J. Chem. Soc., Perkin Trans. 2* **2000**, 1735.

20 M. Hojo, T. Ueda, E. Ueno, T. Hamasaki, D. Fujimura, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 751.

21 M. Hojo, T. Ueda, E. Ueno, T. Hamasaki, T. Nakano, *Bull. Chem. Soc. Jpn.* **2010**, *83*, 401.

22 P. Ji, J. H. Atherton, M. I. Page, *Faraday Discuss.* **2010**, *145*, 15.

23 K. M. Fromm, *Coord. Chem. Rev.* **2008**, *252*, 856.

24 C. Reichardt, D. Che, G. Heckenkemper, G. Schäfer, *Eur. J. Org. Chem.* **2001**, 2343.

25 H. S. Frank, W.-Y. Wen, *Discuss. Faraday Soc.* **1957**, *24*, 133.

26 G. A. Olah, *J. Org. Chem.* **2001**, *66*, 5943.

27 H. F. Schaller, H. Mayr, *Angew. Chem.* **2008**, *120*, 4022; H. F. Schaller, H. Mayr, *Angew. Chem., Int. Ed.* **2008**, *47*, 3958.

28 M. Hojo, H. Hasegawa, H. Tsurui, K. Kawamura, S.-i. Minami, A. Mizobe, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1619.

29 M. Hojo, T. Ueda, M. Yamasaki, *J. Org. Chem.* **1999**, *64*, 4939.

30 a) M. Hojo, T. Ueda, M. Yamasaki, A. Inoue, S. Tokita, M. Yanagita, *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1569. b) M. Hojo, T. Ueda, A. Inoue, S. Tokita, *J. Mol. Liq.* **2009**, *148*, 109.

31 M. Hojo, *Pure Appl. Chem.* **2008**, *80*, 1539.

32 M. Hojo, H. Hasegawa, A. Mizobe, Y. Ohkawa, Y. Miimi, *J. Phys. Chem.* **1995**, *99*, 16609.

33 J. A. Riddick, W. B. Bunger, T. K. Sakano, *Organic Solvents: Physical Properties and Methods of Purification*, 4th ed., Wiley, New York, **1986**.

34 V. Gutmann, *The Donor–Acceptor Approach to Molecular Interactions*, Plenum, New York, **1978**.

35 M. Hojo, R. Kato, A. Narutaki, T. Maeda, Y. Uji-yie, *J. Mol. Liq.* **2011**, *163*, 161.

36 K. T. Leffek, *Can. J. Chem.* **1970**, *48*, 1.

37 S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, J. S. Gall, *Tetrahedron Lett.* **1960**, *1*, 24.

38 a) J.-L. M. Abboud, I. Alkorta, J. Z. Davalos, P. Müller, E. Quintanilla, J.-C. Rossier, *J. Org. Chem.* **2003**, *68*, 3786. b) J.-L. M. Abboud, I. Alkorta, J. Z. Davalos, P. Müller, E. Quintanilla, *Adv. Phys. Org. Chem.* **2002**, *37*, 57.

39 E. Grunwald, S. Winstein, *J. Am. Chem. Soc.* **1948**, *70*, 846.

40 a) T. W. Bentley, G. E. Carter, *J. Am. Chem. Soc.* **1982**, *104*, 5741. b) D. J. Raber, R. C. Bingham, J. M. Harris, J. L. Fry, P. v. R. Schleyer, *J. Am. Chem. Soc.* **1970**, *92*, 5977.

41 K.-H. Park, D. N. Kevill, *J. Phys. Org. Chem.* **2012**, *25*, 2.