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KINETIC PROBE TO STUDY THE STRUCTURAL BEHAVIOUR OF MIXED AQUEOUS–ORGANIC SOLVENTS. EFFECTS OF INORGANIC AND ORGANIC SALTS ON THE KINETICS AND MECHANISM OF INTRAMOLECULAR GENERAL BASE-CATALYSED METHANOLYSIS OF IONIZED PHENYL SALICYLATE

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The effects of inorganic and organic salts on the rates of methanolysis of ionized phenyl salicylate, PS^-, were studied at 30 °C in H_2O–MeOH solvents. The observed pseudo-first-order rate constants, k_{obs}, for methanolysis of PS^- represent a non-linear increase with increase in methanol contents in mixed H_2O–MeOH solvents. The observed data are explained in terms of the proposal that methanol molecules exist in monomeric, dimeric and in general polymeric forms in H_2O–MeOH solvents. The rate constants, k_{obs}, at alkanol [ROH (R = Me, $HOCH_2CH_2$)] contents of *ca* $\leqslant 55\%$ (v/v), fit the relationship $k_{obs} = k[ROH]_T/(1 + k_A[ROH]_T/(1 + K_A[ROH])$, where k and K_A represent the nucleophilic second-order rate constant for the reaction of ROH with PS^- and the association constant for the dimerization of ROH, respectively, and $[ROH]_T$ is the total concentration of ROH. The rate constants, k, appear to be independent of total concentrations of inorganic salts $[MX]_T$ (M = Li, Na, K and X = OH, Cl), but the values of K_A increase with increase in $[MX]_T$ and this increase varies in the order $Li^+ > Na^+ > K^+$. The values of both k and K_A show a decrease with increase in the total concentrations of organic salts, $[R_4MX]_T$ (R = Et, Pr^n, Bu^n and X = Br, I). The effects of $[MX]_T$ and $[R_4MX]_T$ on k_{obs} versus content of ROH (%, v/v) profiles reveal the following inferences: (i) in the water-rich region of H_2O–ROH solvents [at *ca* $< 55\%$ (v/v) ROH] the solvation shells of M^+ and X^- contain preferentially only water molecules whereas in the methanol-rich region [at *ca* $> 55\%$ (v/v) ROH] of solvents some cosolvent methanol molecules also enter into these solvation shells; (ii) the solvation shells of tetraalkylammonium ions, R_4N^+, contain some methanol molecules even in the water-rich region of the solvents; (iii) Li^+ cause a methanol structure-making effect whereas Na^+ and K^+ ions show a methanol structure-breaking effect; and (iv) organic cations such as Et_4N^+, $Pr^n_4N^+$ and $Bu^n_4N^+$ reveal a methanol structure-breaking effect through an interaction mechanism different from that operating for Na^+ and K^+. Both k and K_A show significant normal deuterium isotope effects in the reactions of MeOH and PS^- which indicates the probable occurrence of proton transfer in the rate-determining step.

INTRODUCTION

The rates of hydrolysis of several organic compounds in mixed aqueous–organic solvents have been used to study the structural behaviour of mixed aqueous solvents.[1] Shaskus and Haake[2] have discussed the importance of such studies. Irwin *et al.*[3] demonstrated the occurrence of transesterification of salicylate esters in an alkaline alcoholic medium. The rates of alkanolysis of ionized phenyl salicylate (PS^-) have been shown to be increased by *ca* 10^6-fold owing to the occurrence of intramolecular general base catalysis through an intramolecular intimate ion pair (**1**) formation.[4] The efficient transesterification of PS^- has been used to study the structural behaviours of mixed aqueous–alkanol solvents. Such studies led us to propose that alkanols exist in polymeric forms of different chain lengths in the water–alkanol mixed solvents. However, it is known

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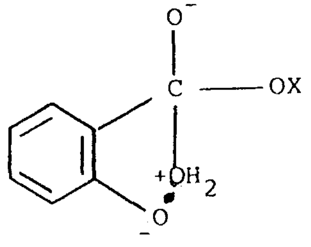


1

X = Ph ,

R

that the mixed aqueous–monohydric alkanol solvents [known as typically aqueous (TA) solvents] are characteristically different from aqueous–polyhydric alkanol solvents [known as typically non-aqueous (TNA) solvents.[1] Both TA and TNA solvents are generally attributed to contain at least two phase transition mole fractions (within its range 0–1) where the structural behaviour of the mixed solvents changes. The kinetics of the solvolytic reactions may be considered as one of the important tools for diagnosing the structural changes of mixed aqueous solvents with change in the mole fractions of organic cosolvents.[5]

Previously, we studied the methanolysis and ethanolysis of PS$^-$ in mixed aqueous solvents where the apparent association constants, K_A, of methanol at 0·01 and 0·05 M NaOH were determined.[6] The effect of temperature on K_A for propan-1-ol (Pr^{n}OH) in mixed aqueous solvents was also studied.[4] The change in temperature did not appear to change the structural behaviour of H_2O–Pr^{n}OH solvents. The rates of reactions of ethane-1,2-diol with PS$^-$ were studied in mixed aqueous solvents and the structural behaviour of this solvent system (TNA) was found to be different, especially at higher contents of organic cosolvents, from that of TA solvents.[7] Since the structures of both TA and TNA systems are markedly influenced by the presence of different cations and anions,[5,8] we decided to study the effects of alkali metal and tetraalkylammonium cations on methanolysis of PS$^-$ in H_2O–MeOH solvents. The results and their probable explanations are described in this paper.

EXPERIMENTAL

Materials. Tetraalkylammonium bromide (Et_4NBr), tetra-*n*-propylammonium bromide (Pr^n_4NBr) and tetra-*n*-butylammonium bromide (Bu^n_4NBr) were obtained from Schuchardt. Tetra-*n*-butylammonium iodide (Bu^n_4NI) was obtained from BDH. All other reagent-grade chemicals were obtained from BDH and Aldrich. Slightly yellowish Pr^n_4NBr was crystallized from chloroform and the colourless, fine, needle-like crystals of purified Pr^n_4NBr were used in the kinetic runs.

Stock solutions of all the organic salts were freshly prepared in methanol. Stock solutions of all the inorganic salts were freshly prepared in glass-distilled water. Deuterated methanol (CD_3OD) and D_2O with minimum isotopic purities of 99·0% and 99·7%, respectively, were obtained from BDH. Stock solutions of phenyl salicylate (PSH) were frequently prepared in acetonitrile and were kept below 0 °C.

Kinetic measurements. The rates of methanolysis of ionized phenyl salicylate (PS$^-$) in mixed H_2O–MeOH solvents were studied by monitoring the appearance of the product, phenolate ion, at either 280 or 290 nm spectrophotometrically.[9]

The observed first-order rate constants for pH-indepenent (i.e. [HO$^-$] range *ca* 0·005–0·050 M) hydrolyses of phenyl and methyl salicylates turned out to be $3{\cdot}60\times10^{-4}\,s^{-1}$ ($=k_{obs\,2}$) and $1{\cdot}07\times10^{-4}\,s^{-1}$ ($=k_{obs\,3}$), respectively, at 30 °C and 99% (v/v) H_2O.[10] The value of k_{obs} at 10% (v/v) MeOH (the lowest content of methanol attained in the present study) is $43.6\times10^{-4}\,s^{-1}$ (Table 1).

The values of $k_{obs\,2}$ and $k_{obs\,3}$ at 90% (v/v) H_2O should be slightly lower than the corresponding values at 99% (v/v) H_2O. These results indicate that $(k_{obs}-k_{obs\,2}-k_{obs\,3})/(k_{obs\,2}+k_{obs\,3})\geqslant 8$ and under such conditions $k_{obs\,2}+k_{obs\,3}$ may be neglected compared with the rate constant ($k_{obs\,1}$) for methanolysis of PS$^-$. It may be noted that $k_{obs\,1}$ obtained by considering $k_{obs\,2}=k_{obs\,3}=0$ is only 5% larger than that obtained without such a consideration in the methanolysis of PS$^-$ at 0·05 M NaOH and 10% (v/v) MeOH.[6] These observations revealed that the rate constants for hydrolyses of PS$^-$ and the transesterified product (ionized methyl salicylate) were significantly smaller than those for methanolysis of PS$^-$ under the present experimental conditions. All the kinetic runs were carried out for a period of more than seven half-lives of the reactions and the observed data obeyed the first-order rate law. The details of the data analysis have been described elsewhere.[10]

RESULTS

Effects of inorganic salts

The rates of methanolysis of PS$^-$ were studied at 30°C, 0·01 M MOH (with M = Li, Na and K) and with methanol contents 10–97% (v/v) in mixed H_2O–MeOH solvents containing 1% (v/v) MeCN. The reaction rates were also studied at different [MCl] ranging from 0·05 to 0·13 M in H_2O–MeOH solvents containing 0·01 M MOH. The methanol content of the mixed solvents was varied from 15 to 90% (v/v) at each [MCl]. The observed pseudo-first-order rate constants, k_{obs}, versus contents of MeOH (%, v/v) at a few [MCl] are shown graphically in Figure 1.

The rates of reactions of ethane-1,2-diol with PS$^-$ were studied at 30°C with ethane-1,2-diol contents ranging from 10 to 97% (v/v) in $H_2O-HOCH_2CH_2OH$ solvents containing 1% (v/v) MeCN and 0.01 M LiOH. The results are shown in Figure 2.

The deuterium isotope effects on rates of methanolysis of PS$^-$ were studied by carrying out a series of kinetic runs at 30°C, 0·01 M NaOH and CD_3OD contents in the range 10–97% (v/v) in D_2O-CD_3OD solvents containing 1% (v/v) MeCN. The minimum isotopic purity in each kinetic run was *ca* 98%. The results are summarized in Table 1.

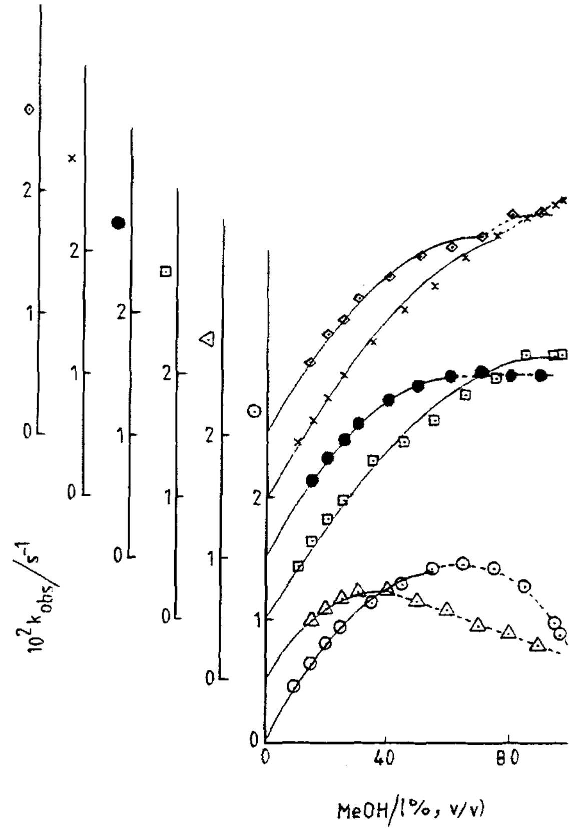


Figure 1. Plots showing the dependence of observed rate constants, k_{obs}, for methanolysis of PS$^-$ on the contents of methanol in reaction mixtures containing mixed aqueous solvent, 1% MeCN, 2×10^{-4} M PS^{-1} and (○) 0·01 M LiOH, (△) 0·01 M LiOH + 0·13 M LiCl, (⊡) 0·01 M NaOH, (●) 0·01 M NaOH + 0·13 M NaCl, (X) 0·01 M KOH and (◇) 0·01 M KOH + 0·13 M KCl. The reaction mixture containing 0·01 M KOH, 0·13 M KCl, 1% MeCN and 90% MeOH became a saturated solution, i.e. $[K^+]_T < 0·14$ M

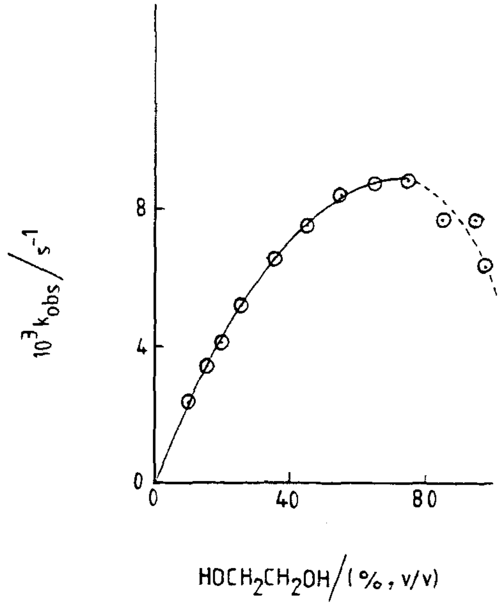


Figure 2. Observed rate constants, k_{obs}, versus content of ethane-1,2-diol for the reaction of PS$^-$ with ethane-1,2-diol in mixed aqueous solvents containing 1% MeCN, 2×10^{-4} M PS$^-$ and 0·01 M LiOH

Effects of organic salts

The effects of different organic salts such as Et_4NBr, Pr^n_4NBr, Bu^n_4NBr and Bu^n_4NI on the rate of methanolysis of PS$^-$ were studied at 30°C in mixed H_2O–MeOH solvents containing 0·01 M NaOH and 1% (v/v) MeCN. The methanol contents in the mixed aqueous solvents were varied from 15 to 97% (v/v) at 0·01 and 0·3 M Et_4NBr and Pr^n_4NBr and from 15 to 90% (v/v) at 0·07–0·24 M Et_4NBr and Pr^n_4NBr. Similarly, the methanol contents were varied from 15 to 97% (v/v) at $\leqslant 0·07$ M Bu^n_4NBr and Bu^n_4NI, from 15 to 90% (v/v) at 0·12–0·24 M Bu^n_4NBr, from 25 to 90% (v/v) at 0·12–0·18 M Bu^n_4NI and from 40 to 90% (v/v) at 0·24 M Bu^n_4NI. The observed pseudo-first-order rate constants, k_{obs}, for methanolysis of PS$^-$ are shown graphically in Figure 3 at a few typical concentrations of Et_4NBr, Pr^n_4NBr and Bu''_4NBr. We could not carry out kinetic runs at 0·12–0·18 M Bu^n_4NI and 0·24 M Bu^n_4NI in mixed aqueous solvents containing $\leqslant 20$ and $\leqslant 35$% (v/v) MeOH, respectively, because the reaction mixtures became turbid before the addition of required amount of PSH. This shows that the solubility of Bu^n_4NI is less than 0·12 and 0·24 M in H_2O–MeOH solvents with MeOH contents of 20 and 30% (v/v), respectively.

Table 1. Deuterium isotope effect on the rate constants, k_{obs}, for methanolysis of ionized phenyl salicylate[a]

CH_3OH[b] or CD_3OD[c] (%, v/v)	$10^3 k_{obs}^{CH_3OH}$ (s^{-1})	$10^3 k_{calcd}^{CH_3OH}$ (s^{-1})	$10^3 k_{obs}^{CD_3OD}$ (s^{-1})	$10^3 k_{calcd}^{CD_3OD}$ (s^{-1})	$k_{obs}^{CH_3OH}/k_{obs}^{CD_3OD}$
10	4·36 ± 0·05[d]	4·59[e]	2·26 ± 0·04[d]	2·56[e]	1·93
15	6·45 ± 0·03	6·51	3·25 ± 0·04	3·70	1·99
20	8·20 ± 0·04	8·24	4·36 ± 0·05	4·76	1·88
25	9·93 ± 0·08	9·79	5·44 ± 0·04	5·74	1·83
35	13·0 ± 0·1	12·5	6·89 ± 0·10	6·67	1·89
45	14·5 ± 0·1	14·7	8·16 ± 0·07	7·53	1·78
55	16·2 ± 0·1	16·6	9·34 ± 0·11	9·11	1·73
65	18·3 ± 0·2	18·3	10·7 ± 0·1	10·5	1·73
75	19·7 ± 0·1	19·7	11·8 ± 0·2	11·8	1·67
85	21·7 ± 0·2	21·0	12·7 ± 0·2	12·9	1·71
95	21·6 ± 0·3	22·1	13·7 ± 0·2	13·9	1·58
97	21·7 ± 0·3	—	13·8 ± 0·3	—	1·57

[a] $[PS^-]_0 = 2 \times 10^{-4}$ mol dm^{-3}, MeCN = 1% (v/v), temperature = 30 °C and [NaOH] = 0·01 mol dm^{-3}.
[b] Cosolvent is H_2O.
[c] Cosolvent is D_2O.
[d] Error limits are standard deviations.
[e] Calculated from equation (6) using the values of k and K_A as listed in Table 2.

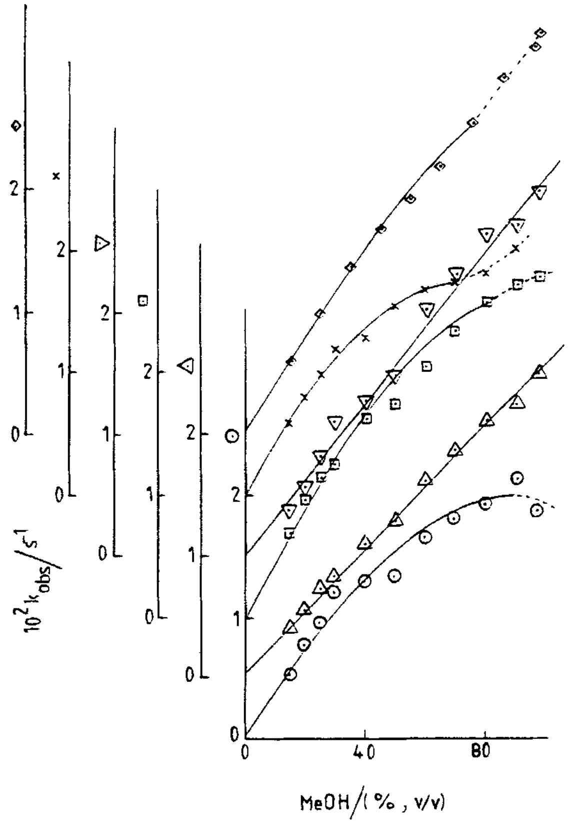


Figure 3. Plots showing the dependence of observed rate constants, k_{obs}, on the content of methanol in reaction mixtures containing mixed solvent, method–water, 1% MeCN, 2×10^{-4} M PS^- and 0·01 M NaOH at different [Et_4NBr] [(⊙) 0·01 M; (△) 0·30 M], [Pr_4^nNBr] [(□) 0·01 M; (▽) 0·30 M] and [Bu_4^nNBr] [(X) 0·005 M; (◇) 0·070 M]

DISCUSSION

The observed pseudo-first-order rate constant, k_{obs}, for methanolysis of PS^- [obtained in H_2O–MeOH solvent containing 97% (v/v) MeOH, 1% (v/v) MeCN and 0·01 M NaOH] is nearly 40 times larger than the rate constant, k_0, for hydrolysis of PS^- [obtained in H_2O–MeOH solvent containing 97% (v/v) H_2O, 1% (v/v) MeCN and 0·01 M NaOH). The apparent molar concentrations of H_2O and MeOH in solvents containing 97% (v/v) H_2O and MeOH are 53·9 and 23·9 M, respectively. The corrections for the concentration effect would make the reactivity of MeOH larger than that of H_2O toward PS^- by a factor of more than 40.

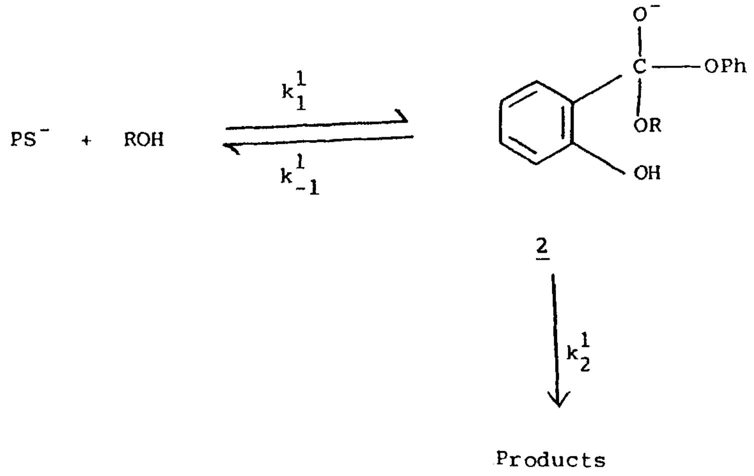
The rate of hydrolysis of PS^- has been shown to involve intramolecular general base catalysis in which an ionized *o*-OH group is acting as an intramolecular general base catalyst.[9,11,12] The presence of such an internal catalysis is shown to increase the rate of hydrolysis of PS^- by nearly 10^6-fold.[13] The more than 40 times larger value of k_{obs} than k_0 reveals the presence of intramolecular general base catalysis in the methanolysis of PS^-. We have concluded elsewhere[6] that methanolysis of PS^- at 0·01 M NaOH represents the region on the pH–rate profile where the rate is independent of $[\mathrm{HO}^-]$. Under such experimental conditions, the hydrolysis and alkanolysis of phenyl salicylate have been shown to involve intramolecular general base catalysis rather than kinetically indistinguishable intramolecular general acid catalysis.[4]

A stepwide mechanism as shown in Scheme 1 involves the formation of the reactive intermediate **2** by concerted intramolecular general base (IGB)-catalysed nucleophilic attack of ROH at carbonyl carbon of PS^-. A similar mechanism has been proposed in the hydrolyses of salicylate esters.[12] The observed first-order rate constants (k_{obs}) for pH-independent hydrolyses of salicylate esters[10] at 30°C turned out to be $3\cdot 60\times 10^{-4}\ \mathrm{s}^{-1}$ for phenyl salicylate, $1\cdot 07\times 10^{-4}\ \mathrm{s}^{-1}$ for methyl salicylate, $1\cdot 20\times 10^{-4}\ \mathrm{s}^{-1}$ for ethyl salicylate, $1\cdot 24\times 10^{-4}\ \mathrm{s}^{-1}$ for 2-ethoxyethyl salicylate, $1\cdot 23\times 10^{-4}\ \mathrm{s}^{-1}$ for 2-hydroxyethyl salicylate and $1\cdot 07\times 10^{-4}$ for *N*, *N*-bis(2-hydroxyethyl)aminoethyl salicylate. Similarly, the values of k_{obs} for ethanolysis of methyl[3] and phenyl[6] salicylates are $10\cdot 0\times 10^{-4}\ \mathrm{s}^{-1}$ (at 37°C and 80% ethanol) and $12.6\times 10^{-4}\ \mathrm{s}^{-1}$ (at 30°C and 96% ethanol), respectively. These and other reported observations[12] indicate that the rate constants for hydrolyses and alkanolyses of alkyl and aryl salicylates are not highly sensitive to the $\mathrm{p}K_\mathrm{a}$ of the leaving groups. These results, coupled with significant $\mathrm{D_2O}$ solvent isotope effects observed in the hydrolyses of phenyl and methyl salicylates[14] and methanolysis of PS^- (Table 1), show that the k_2^1 step (Scheme 1) cannot be rate limiting. It is therefore obvious that the k_1^1 step should be the rate limiting. If the k_1^1 step is rate limiting, then in terms of kinetic consequence $k_2^1 \gg k_{-1}^1$. It can be easily concluded in the following that the requirement for $k_2^1 \gg k_{-1}^1$ is not true for most of the alkyl and aryl salicylates.

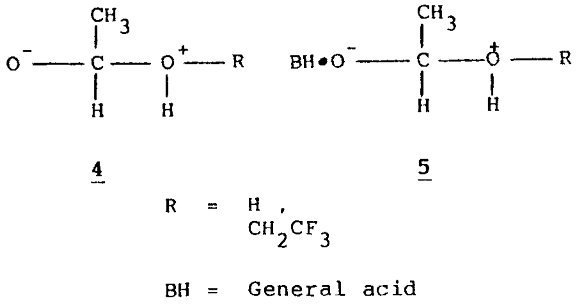
According to the principle of microscopic reversibility, the k_{-1}^1 step should involve intramolecular general acid (IGA) catalysis because the k_1^1 step involves IGB. The occurrence of IGA in the k_{-1}^1 step is expected to increase greatly the apparent leaving ability of the leaving group in the k_{-1}^1 step. The rate constants for neutral hydrolysis of *p*-nitrophenyl acetate[15] and phthalamic acid[16] are $5.5\times 10^{-7}\ \mathrm{s}^{-1}$ (at 25°C) and $20\cdot 0\times 10^{-4}\ \mathrm{s}^{-1}$ (at 48°C), respectively. Nearly a 10^3 times larger value of the rate constant for hydrolysis of phthalamic acid (with leaving group of $\mathrm{p}K_\mathrm{a}$ 34[17]) compared with that of *p*-nitrophenyl acetate (with leaving group of $\mathrm{p}K_\mathrm{a}$ 7·14[18]) may be attributed to the occurrence and non-occurrence of IGA in these respective reactions. The occurrence of IGA in the k_2^1 step is less probable, as discussed elsewhere.[13]

An alternative and preferred mechanism for alkanolysis of PS^- is shown in Scheme 2. A similar mechanism has been proposed and supported for the hydrolysis of PS^-.[13] The highly reactive intermediate **3** is considered to be an intramolecular intimate ion pair which does not involve any solvent molecule between positively and negatively charged centres of the charged atoms or groups. Although the internal proton transfer in the k_2^2 step is extremely fast, the expulsion of the leaving group in the k_{-1}^2 step is assumed to be even faster than this. The estimated values of the rate constants for the expulsion of $\mathrm{H_2O}$ and $\mathrm{F_3CCH_2OH}$ from **4** are 10^{20} and $10^{23}\ \mathrm{s}^{-1}$, respectively.[19] It may be noted that the stability of a hydrogen-bonded dipolar intermediate (**5**) is nearly 10^6 times larger than that of **4**. This could be attributed to the existence of intermolecular hydrogen bonding between **4** and general acid (BH).[19] The conversion of the intramolecular intimate ion pair (**3**) to a oxymonoanionic tetrahedral intermediate (**2**), involving intramolecular proton transfer, is considered to be the rate-determining step.

Deuterated methanol ($\mathrm{CD_3OD}$) appeared to be *ca*



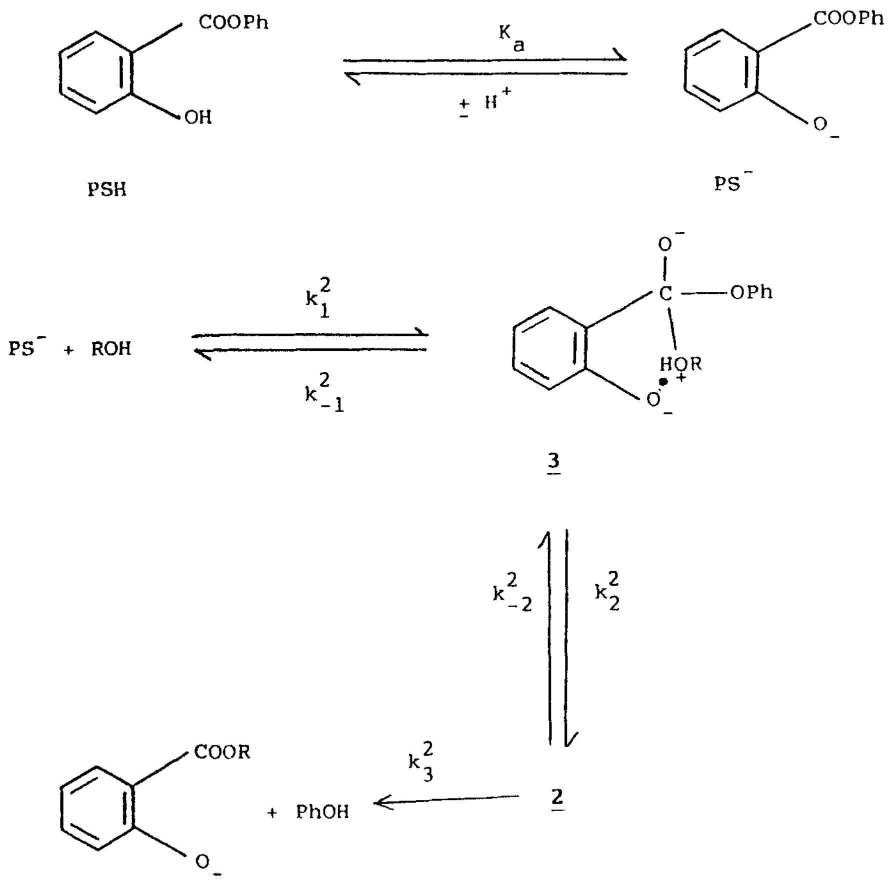
Scheme 1



1·6–2·0 times less reactive than methanol toward PS⁻ under similar experimental conditions. This is consistent with the proposal that reaction involves proton transfer as the rate-determining step. It may be noted that the deuterium solvent isotope effect for hydrolysis of PS⁻ turned out to be 1·6,[10] which is comparable to $k_{obs}^{CH_3OH}/k_{obs}^{CD_3OD}$ = 1·57 at 97% (v/v) CD_3OD (Table 1).

If the reactions between MeOH and PS⁻ follow a simple second-order rate law in mixed H_2O–MeOH solvents, then the plots of k_{obs} versus content of MeOH (%, v/v) should be linear with nearly zero intercepts. However, such plots (Figures 1–3) show distinct deviations from linearity at low [R_4NX] (with R = Et, Pr^n and Bu^n and X = Br) and different [MX] (with M = Li, Na, K and X = OH, Cl). Similar observations were previously obtained in the reactions of PS⁻ with ethanol,[6] propan-1-ol[7] and ethane-1,2-diol.[7] The non-linear plots of k_{obs} versus contents of alkanols (%, v/v) have been attributed to the change in the structural behaviour of alkanols with the change in the contents of alkanols in the mixed water–alkanol solvents.

The observed pseudo-first-order rate constants, k_{obs}, for the reactions of MeOH, EtOH and H_2O are 225×10^{-4} s^{-1} [in mixed solvent MeOH–MeCN–H_2O (96·0:3·2:0·8)], $12·6 \times 10^{-4}$ s^{-1} [in mixed solvent EtOH–MeCN–H_2O (96·0:3·2:0·8)] and $5·0 \times 10^{-4}$ s^{-1} [in mixed solvent H_2O–MeCN (96:4)], respectively.[6] The second-order rate constants, k_2 (= k_{obs}/[ROH] with R = Me, Et, H), turned out to be 95×10^{-5} dm^3 mol^{-1} s^{-1} for MEOH, $7·7 \times 10^{-5}$ dm^3



Scheme 2

$mol^{-1}\,s^{-1}$ for EtOH and $0{\cdot}94 \times 10^{-5}\,dm^3\,mol^{-1}s^{-1}$ for H_2O. It is generally believed that H_2O is a stronger base than MeOH and other alkanols,[8] and hence a slight difference in nucleophilicity of MeOH and H_2O cannot be ascribed to the larger reactivity of MeOH than of H_2O toward PS^-. The dielectric constants, ε, of MeOH, EtOH, MeCN and H_2O at 25°C are 32·7,[1] 24·6,[1] 37·0[20] and 78·3,[1] respectively, and according to the electrostatic theory, a bimolecular reaction involving an ionic and a neutral reactant should proceed faster in a medium of low dielectric constant.[21] It is therefore apparent that these observations cannot be explained easily only in terms of polarity of the reaction medium.

The mixed aqueous solvents containing methanol as cosolvent are characterized as 'typically aqueous' (TA) solvents. At very high mole fractions of water, the added cosolvent methanol molecules merely fill the voids of the three-dimensional structural network of water molecules, thereby promoting the intermolecular hydrogen bonding between water molecules. This process thus exerts a water 'structure-forming' action. As the cosolvent methanol is added, its mole fraction reaches a particular value, x_2^*, where the added methanol molecules become larger than those required to fill the voids of the three-dimensional hydrogen-bonded network of water molecules. At this particular mole fraction x_2^*, the water structure begins to collapse and methanol molecules begin to associate themselves to form dimer, $(MeOH)_2$, trimer, $(MeOH)_3$, and probably polymers of even higher monomeric units. The water structure-breaking effect of added cosolvent methanol is expected to increase with increasing mole fraction of methanol until it becomes a maximum at a particular mole fraction, x_2^{**}. The two mole fractions, x_2^* and x_2^{**}, depend on both the cosolvent and temperature. At 25 °C, the approximate values of x_2^* and x_2^{**} are 0·09 and 0·20 for ethanol, 0·06 and 0·18 for 2 propan-2-ol and 0·04 and 0·10 for *tert*-butyl alcohol, respectively.[5] These results reveal that the values of x_2^{**} for H_2O–MeOH solvent may be assumed to be *ca* >0·20, i.e. >40% (v/v) MeOH. The presence of cationic and anionic solutes is expected to change the values of x_2^* and x_2^{**} because of the preferential involvement of a particular solvent component of mixed solvent in the solvation shells of the ions. For example, the alkali metal halide salts are preferentially solvated by water molecules of TA solvents.

It is apparent that, in H_2O–MeOH solvents, the methanol molecules exist in monomeric, (MeOH), dimeric, $(MeOH)_2$, and in general *n*-meric, $(MeOH)_n$, forms. Therefore, the total concentration of methanol, $[MeOH]_T$, may be given as

$$[MeOH]_T = [(MeOH)] + [(MeOH)_2] + \cdots + [(MeOH)_n] \quad (1)$$

For mathematical simplicity,[22,23] we assume that

$$K_1 \approx K_2 \approx K_3 \approx K_n = K_A,$$

where K_1, K_2, K_3 and K_n represent first, second, third and *n*th association constants, respectively. By introducing the association constant (K_A), equation (2) may be derived from equation (1).

$$[MeOH]_T = [(MeOH)]\{1 + K_A[(MeOH)] + K_A^2[(MeOH)]^2 + \cdots + K_A^{n-1}[(MeOH)]^{n-1}\} \quad (2)$$

Equation (2) will reduce to equation (3) provided that $K_A[(MeOH)] < 1$ if $y = 1 + x + x^2 + x^3 + \cdots + x^n$ and $x < 1$, then mathematically $y = (1 - x)^{-1}$.

$$[MeOH]_T = \frac{[(MeOH)]}{1 - K_A[(MeOH)]} \quad (3)$$

The rearrangement of equation (3) gives equation (4).

$$[(MeOH)] = \frac{[MeOH]_T}{1 + K_A[MeOH]_T} \quad (4)$$

The alkanolysis of PS^- involves intramolecular general base catalysis (Scheme 2) and such catalysis would be effective only if the nucleophile carries a mobile proton at the attacking site. It is therefore evident that the methanolysis of PS^- involves PS^- and monomeric methanol molecules as the reactants. The hydroxylic proton and lone pair of electrons of the reactant molecule MeOH should presumably be free from hydrogen bonding with water molecules in the solvation shell of MeOH. The rate constants (k_{obs}) for the reactions of PS^- with methanol, ethanol, propan-1-ol and propan-2-ol are 225×10^{-4}, $12{\cdot}6 \times 10^{-4}$, $5{\cdot}36 \times 10^{-4}$ and $0{\cdot}717 \times 10^{-4}\,s^{-1}$, respectively[6]. These results show that the alkanolysis of PS^- is highly sensitive to the steric requirements of the alkanols. The steric requirements and the probable decrease in the nucleophilicity of the nucleophilic site, due to intermolecular hydrogen bonding, of dimeric or polymeric methanol led us to assume that these polymeric methanol (or alkanol) molecules do not act as reactants.

The rate of methanolysis of PS^-, r, may be given as

$$r = k[PS^-]_T[(MeOH)] \quad (5)$$

where k is the nucleophilic second-order rate constant. The observed rate law, $r = k_{obs}[PS^-]_T$, and equations (4) and (5) can yield the equation.

$$k_{obs} = \frac{k[MeOH]_T}{1 + K_A[MeOH]_T} \quad (6)$$

In comparing the observed rate law with equation (5), we have assumed that the rate constant, k_0, for water-catalysed cleavage of PS^- is negligible compared with that for methanolysis of PS^- under the experimental conditions imposed.

Effects of inorganic salts

The observed pseudo-first-order rate constants, k_{obs}, were found to fit equation (6) with reasonable statistical reliability in H_2O–MeOH solvents with methanol contents of *ca* $\leqslant$50% (v/v) and in the presence of different concentrations of inorganic salts. However, in the presence of some inorganic salts, such as NaCl and KCl, the observed data appeared to obey equation (6) until the methanol content became *ca* $\leqslant$80% (v/v) in H_2O–MeOH solvents. However, the presence of Li^+ ions revealed the effects on the k_{obs} versus % (v/v) MeOH profiles distinctly different from those of Na^+ and K^+ ions at methanol contents above *ca* 40–50% (v/v) (Figure 1). The non-linear least-squares technique was used to calculate k and K_A from equation (6) and the results are summarized in Table 2. The fitting of the observed data to equation (6) is evident from some typical plots in Figure 1 and standard deviations associated with the calculated parameters k and K_A (Table 2).

The deuterium isotope effects for the second-order rate constant (k^{CH_3OH}/k^{CD_3OD}) and association constant ($K_A^{CH_3OH}/K_A^{CD_3OD}$) turned out to be 1·9 and 1·6, respectively. The significant kinetic deuterium isotope effect (1·9) reveals the significance of proton transfer in the transition state which is consistent with the mechanism shown in Scheme 2. However, the value of

Table 2. Values of k and K_A calculated from equation (6)[a]

Alkali	Salt	$[Salt]_T$ (M)	10^3k ($dm^3\ mol^{-1}\ s^{-1}$)	10^3K_A ($dm^3\ mol^{-1}$)	ROH range (%, v/v)	No. of runs
LiOH[b]			2·30 ± 0·09[c]	87·6 ± 7·8[c]	10–55	7
	LiCl[b]	0·05	2·40 ± 0·25	144 ± 30	15–40	5
		0·09	2·61 ± 0·41	199 ± 55	15–40	5
		0·13	2·66 ± 0·54	252 ± 81	15–40	5
			1·53 ± 0·05	79·5 ± 6·5	10–55[d]	7
NaOH[e]			2·16 ± 0·10	58·1 ± 7·0	10–55	7
			2·10 ± 0·07	52·6 ± 0·04	10–95	12
			1·12 ± 0·05	33·0 ± 4·7	10–95[f]	12
	NaCl[e]	0·05	2·19 ± 0·12	64·5 ± 8·3	15–70	8
		0·09	2·27 ± 0·11	71·3 ± 7·5	15–70	8
		0·13	2·48 ± 0·15	98·9 ± 11·6	15–70	8
KOH[g]			2·01 ± 0·04	42·7 ± 3·1	10–55	7
	KCl[g]	0·05	2·24 ± 0·05	61·3 ± 3·5	15–70	8
		0·09	2·27 ± 0·09	72·7 ± 6·1	15–70	8
		0·13	2·40 ± 0·10	86·5 ± 7·2	15–70	8
NaOH[e]	Et_4NBr	0·01	2·29 ± 0·49	79·3 ± 41·6	15–50	6
		0·07	2·30 ± 0·08	47·2 ± 5·2	15–50	6
		0·12	1·96 ± 0·11	29·6 ± 7·8	15–50	6
		0·18	1·65 ± 0·09	17·5 ± 6·3	15–50	6
		0·24	1·64 ± 0·09	4·42 ± 5·75	15–50	6
			1·47 ± 0·02[h]		15–90	10
			1·58 ± 0·02[h]		15–50	6
		0·30	1·19 ± 0·06	7·10 ± 4·80	15–60	7
			1·06 ± 0·01[h]		15–97	11
			1·10 ± 0·02[h]		15–60	7
	Pr^n_4NBr	0·01	2·44 ± 0·18	54·9 ± 12·4	15–50	6
		0·07	2·12 ± 0·12	25·4 ± 7·4	15–50	6
		0·12	1·70 ± 0·06	5·47 ± 3·64	15–50	6
			1·56 ± 0·01[h]		15–90	10
			1·61 ± 0·02[h]		15–50	6
		0·18	1·58 ± 0·08	−1·8 ± 5·1	15–50	6
			1·57 ± 0·02[h]		15–90	10
			1·61 ± 0·02[h]		15–50	6
		0·24	1·48 ± 0·05	−5·5 ± 3·1	15–50	6
			1·59 ± 0·02[h]		15–90	10
			1·57 ± 0·02[h]		15–50	6
		0·30	1·37 ± 0·24	9·3 ± 19·4	15–50	6
			1·28 ± 0·02[h]		15–97	11
			1·26 ± 0·05[h]		15–50	6

Continued

Table 2. (*continued*)

Alkali	Salt	$[\text{Salt}]_T$ (M)	10^3k ($dm^3\ mol^{-1}\ s^{-1}$)	10^3K_A ($dm^3\ mol^{-1}$)	ROH range (%, v/v)	No. of runs
	Bu_4^nNBr	0·005	2·35 ± 0·14	54·6 ± 9·9	15–50	6
		0·010	2·09 ± 0·18	35·5 ± 11·7	15–55	7
		0·030	1·98 ± 0·20	30·2 ± 12·2	15–55	5
		0·050	1·86 ± 0·03	18·5 ± 1·9	15–55	5
		0·070	1·78 ± 0·10	17·6 ± 6·1	15–55	5
			1·39 ± 0·02[h]		15–97	10
			1·49 ± 0·04[h]		15–55	5
		0·120	1·41 ± 0·07	0·9 ± 5·2	15–50	6
			1·28 ± 0·03[h]		15–90	10
			1·40 ± 0·02[h]		15–50	6
		0·180	1·28 ± 0·06	1·4 ± 4·5	15–50	6
			1·24 ± 0·01[h]		15–90	10
			1·27 ± 0·01[h]		15–50	6
		0·240	1·10 ± 0·03	−16·6 ± 2	15–50	6
			1·34 ± 0·02[h]		15–90	10
			1·30 ± 0·03[h]		15–50	6
	Bu_4^nNI	0·005	2·13 ± 0·21	55·4 ± 16·7	15–50	6
		0·010	2·48 ± 0·15	44·1 ± 9·0	15–55	7
		0·070	1·67 ± 0·06	7·0 ± 3·9	15–55	7
			1·41 ± 0·03[h]		15–97	12
			1·56 ± 0·02[h]		15–55	7
		0·120	1·50 ± 0·09	12·1 ± 6·0	25–60	5
			1·28 ± 0·02[h]		25–90	8
			1·31 ± 0·03[h]		25–60	5
		0·180	1·43 ± 0·09	7·0 ± 4·0	25–90	8
			1·28 ± 0·02[h]		25–90	8
			1·31 ± 0·05[h]		25–60	5
		0·240	1·18 ± 0·02	[i]	40–90	6

[a] $[PS^-]_0 = 2 \times 10^{-4}$ M, MeCN = 1% (v/v), temperature = 30 °C.
[b] [LiOH] = 0·01 M.
[c] Error limits are standard deviations.
[d] Organic cosolvent is $HOCH_2CH_2OH$.
[e] [NaOH] = 0·01 M.
[f] Mixed solvent is D_2O–CD_3OD.
[g] [KOH] = 0·01 M.
[h] Calculated from equation (7) as described in the text.
[i] The observed data could not be fitted to equation (6).

$K_A^{CH_3OH}/K_A^{CD_3OD}$ of 1·6 is surprising for the reason that O—D···O bonding of the dimer $(CD_3OD)_2$ is presumably stronger than the O—H···O bonding of $(CH_3OH)_2$.

The following information from Table 2 may be considered to be noteworthy. (i) The presence of the same amount of Li^+, Na^+ and K^+ causes an increase in the magnitudes of K_A in the order $Li^+ > Na^+ \geqslant K^-$. (ii) An increase in the concentrations of inorganic cations (Li^+, Na^+ and K^+) increases the values of K_A. Such an increase is greater for Li^+ than for Na^+ or K^+. (iii) The nature and the concentrations of inorganic salts do not appear to have detectable effects on the values of the rate constants, k.

The effects of the concentrations and nature of inorganic cations on K_A may be explained in terms of a proposal that the solvation shells of these cations are preferentially occupied by only water molecules in the water-rich region [i.e. H_2O contents of *ca* ⩾45% (v/v)]. Because of the high ionic surface charge density of Li^+, these ions form firm and tight solvation shells in which solvent molecules are highly structured. This characteristic makes Li^+ ions 'water structure-forming' agents.[24] Larger cations, such as K^+, with low ionic surface charge density, form flexible solvation shells in which solvent molecules are loosely bound and thus become less structured compared with the solvent molecules in the absence of such ions. Such behaviour makes these ions 'water structure-breaking' agents.[24] When the inorganic cations and anions are added to the H_2O–MeOH solvents [with MeOH contents ⩽55% (v/v)], some of the water molecules which are responsible for the depolymerization of the polymeric methanol structure are trapped by the solvation shells of these ions. Hence the presence of these ions causes an increase in the degree of association of methanol molecules. This shows that the values of K_A should increase with increase in the concentration of inorganic salt. The plots in Figure 4 confirm such conclusion. It may be concluded that, although the solvation shells of the ions of the inorganic salts do not seem to involve the methanol molecules in H_2O–MeOH solvents with H_2O contents of *ca* $\geqslant 45\%$ (v/v), the secondary effects of Na^+ and K^+ are methanol structure-breaking and that of Li^+ is methanol structure-forming.

When the content of methanol becomes larger than *ca* 50% (v/v), the rate constants, k_{obs}, do not appear to obey equation (6). They show a slow increase and decrease with increase in methanol contents for KCl and LiCl, respectively, at 0·13 M alkali metal salt concentration (Figure 1). However, the rate constants, k_{obs}, become independent of methanol content at $\geqslant 60\%$ (v/v) MeOH at 0·13 M NaCl (Figure 1). Such distinct changes in the k_{obs} versus % (v/v) methanol profiles occur at higher methanol contents in the presence of 0·01 M alkali metal salts (Figure 1). Deviations of the observed data from equation (6) have been found in the reactions of PS^- with ethanol,[6] 2-ethoxyethanol[7] and propan-1-ol[4] in the presence of Na^+ and K^+ ions. These observations may be explained by proposing that in the alkanol-rich region of water–alkanol solvents, some of the alkanol molecules also enter into the solvation shells of the alkali metal cations and anions. This occurs owing to a decrease in the concentration of water with increase in the concentration of cosolvent alkanol. However, the solvation shells of alkali metal cations and anions are expected to contain a larger number of water molecules than cosolvent alkanol molecules. Hence, under such conditions, the alkali metal salts begin to affect directly the structural network of cosolvent alkanol molecules. Potassium and perhaps sodium ions seem to be 'methanol structure-breaking' cations whereas lithium ions are 'methanol structure-forming' cations.

At a fixed content of methanol, the increase in the

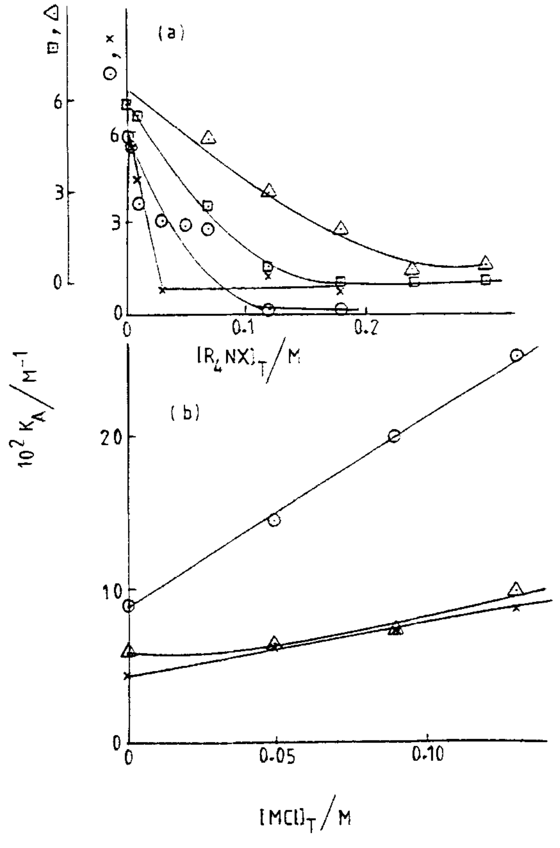


Figure 4. (a) Plots of K_A versus $[R_4NX]_T$ for (△) R = Et and X = Br, (□) R = Pr^n and X = Br, (⊙) R = Bu^n and X = Br and (X) R = Bu^n and X = I. (b) Plots of K_A versus $[MCl]_T$ for M = (⊙) Li, (△) Na and (X) K

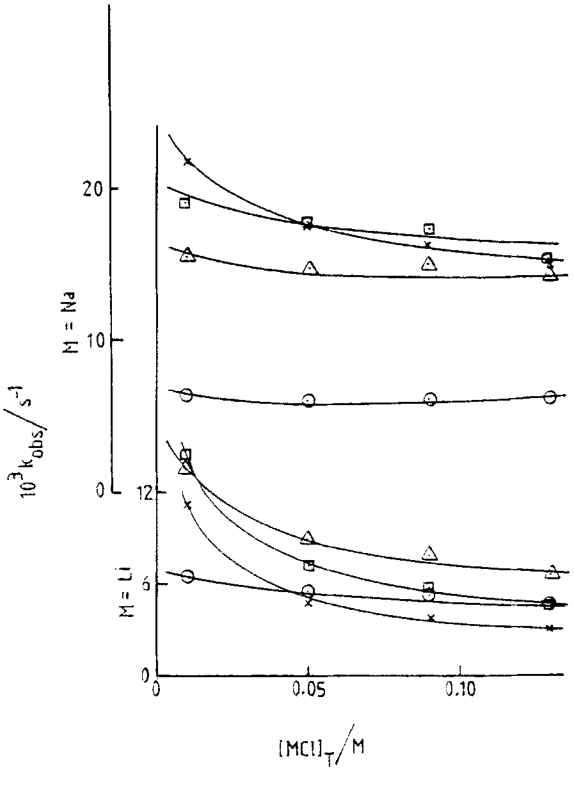


Figure 5. Plots showing the dependence of k_{obs} (for methanolysis of PS^-) on $[MCl]_T$ with M = Li or Na, in mixed methanol–water solvents containing 0·01 M LiOH or 0·01 M NaOH at contents of methanol of (⊙) 15%, (△) 50%, (□) 70% and (X) 90%

concentration of alkali metal salts would decrease the concentration of free water molecules because of the preferential incorporation of water molecules in the solvation shells of alkali metal cations and anions. The free water molecules presumably solvate the monomeric and polymeric methanol molecules. Hence the decrease in the concentration of free water molecules would cause a decrease in [(MeOH)] and consequently a decrease in the rate of methanolysis of PS^-. Such an effect is evident from the plots in Figures 5 and 6. These plots indicate that the decrease in k_{obs} with increase in [MCl] (with M = Li, Na and K) is more pronounced for MX = LiCl than for MX = NaCl or KCl. This is conceivable for the reason that because of the 'methanol structure-breaking' characteristics of K^+ and Na^+ ions, these ions increase [(MeOH)] with increase in [KCl] or [NaCl]. Hence the presence of different concentrations of KCl or NaCl in H_2O–MeOH solvents has two opposing effects on the change in [(MeOH)] and hence the effects of changes in [KCl] or [NaCl] on k_{obs} are not significantly large. Lithium ions, on the other hand, are 'methanol structure-forming' agents and hence an increase in [LiCl] causes a decrease in [(MeOH)]. For this reason, the rate constants, k_{obs}, show a relatively large decrease with increase in [LiCl].

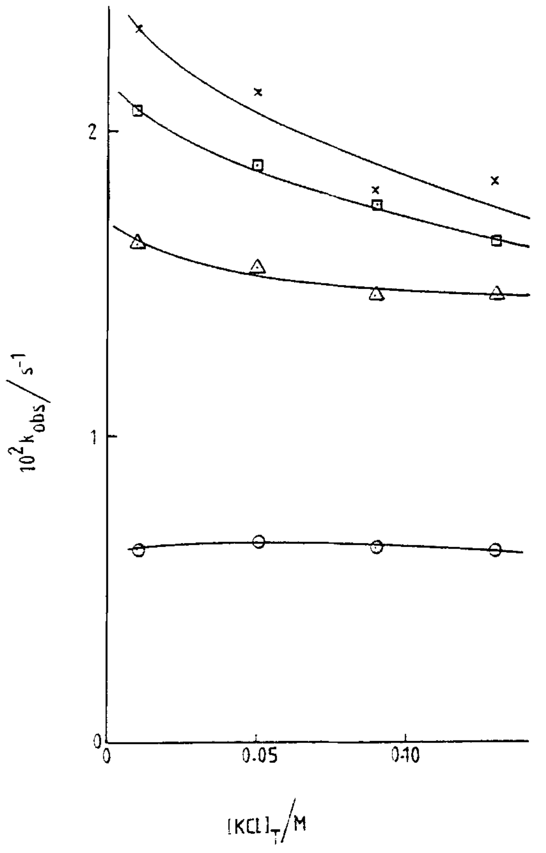


Figure 6. Observed rate constants, k_{obs}, versus $[KCl]_T$ for methanolysis of PS^- in mixed methanol–water solvents containing 0·01 M KOH at contents of methanol of (⊙) 15%, (△) 50%, (⊡) 70% and (X) 90%

Effects of organic salts

The observed rate constants, k_{obs}, obtained for the reactions of MeOH with PS^- in H_2O–MeOH solvents containing different concentrations of tetraalkylammonium salts, R_4NX, and with methanol contents of $\leqslant 55\%$ (v/v) were treated with equation (6). The calculated values of k and K_A are summarized in Table 2. These results reveal the following interesting features. (i) The magnitudes of K_A decrease with increase in $[R_4NX]$ for R = Et, Pr^n and Bu^n with X = Br and for R = Bu^n with X = I (Figure 4). (ii) The decreasing effects of $[R_4NX]$ on K_A increase in the order R = $Bu^n > Pr^n >$ Et. (iii) The nucleophilic second-order rate constants, k, decrease with increase in $[R_4NX]$ and this effect varies in the order R = $Bu^n > Pr^n >$ Et. These observations may be explained as follows.

Tetraalkylammonium ions, R^+, and monomeric methanol molecules are considered to be amphipathic molecules. When the tetraalkylammonium salts are added to H_2O–MeOH solvent, the hydrophobic parts of both R^+ and methanol interact with each other. Such a hydrophobic–hydrophobic interaction is energetically favourable in terms of overall entropy gain by the system, which results in the release of some water molecules[25] from the hydration shells of the interacting hydrophobic sites of R_4N^+ and MeOH. These liberated water molecules depolymerize the polymeric methanol molecules and hence cause a decrease in the values of K_A. The energetically favourable hydrophobic interaction between MeOH and R_4N^+ is expected to increase in the order for R = $Bu^n > Pr^n >$ Et, and this is reflected in the inference (ii) mentioned above. It may be worth mentioning that the direct hydrophobic interaction between R_4N^+ and monomeric methanol would cause a decrease in [(MeOH)]. However, at the same time, it increases the apparent number of free water molecules, which in turn causes an increase in [(MeOH)]. Hence the partial effect of the presence of R_4N^+ on rate of methanolysis of PS^- is expected to be due to the net change (either decrease or increase) in [(MeOH)] brought about by these opposing effects of the hydrophobic interaction.

As suggested in Scheme 2, the charges on the transient intermediate **3** and consequently on the transition state are assumed to be more localized than that on ground state PS^-. The decrease in the apparent polarity of the interacting molecules of comparable hydrophobic surface areas increases the hydrophobic interaction. Hence the ground-state PS^- molecule is expected to interact hydrophobically with R_4N^+ more strongly than the transition state and consequently it should slow the rate of methanolysis. These conclusions reveal that the rate-retarding effects of R_4N^+ would vary in the order $R = Bu^n > Pr^n > Et$. The calculated values of k (Table 2) confirm these conclusions. The greater stabilization of the ground state than the transition state due to hydrophobic interaction has been concluded to be the source of the twofold decrease in the rate of the intramolecular carboxyl-catalysed hydrolysis of 2-carboxy-*N*-methyl-*N*-phenylethanesulphonamide in the presence of 0·8 mol per 55·5 mol of H_2O.[26]

It is evident from Table 2 that the values of K_A are not statistically different from zero at *ca* $\geqslant 0{\cdot}24$ M Et_4NBr, $\geqslant 0{\cdot}12$ M Pr^n_4NBr and Bu^n_4NBr and $\geqslant 0{\cdot}07$ M Bu^n_4NI. This implies that, under these conditions, $K_A[MeOH]_T \ll 1$ and hence equation (6) is reduced to

$$k_{obs} = k[MeOH]_T \qquad (7)$$

The observed data were also treated with equation (7) and the calculated values of k are summarized in Table 2.

Above a methanol content of *ca* 55% (v/v), the observed data as shown in Figure 3 at a few $[R_4NX]$ do not seem to obey equation (6). These observations may be explained as follows. As explained earlier, the hydrophobic interaction between R_4N^+ and MeOH is energetically favourable owing to entropy gain through the release of solvent water molecules from the interacting hydrophobic hydration shells. The ratio of the concentrations of these liberated water molecules to those of added water molecules increases with decrease in the water content in H_2O–MeOH solvents at a constant $[R_4NX]$. Hence the effect of these liberated water molecules on the methanol structure is expected to be smaller in water-rich regions [i.e. methanol contents of *ca* $\leqslant$55% (v/v) of H_2O–MeOH solvents. It appears that above a methanol content of *ca* 55% (v/v), the hydrophobic interaction causes the release of water molecules whose concentration becomes sufficiently large to show a more effective depolymerizing effect on methanol structure and consequently the rate constants, k_{obs}, begin to deviate positively from the plot based on equation (6).

An increase in $[R_4NX]$ decreases both k and K_A (Table 2) and equation (6) shows that, at a fixed $[MeOH]_T$, the observed rate constants, k_{obs} should decrease and increase owing to decreases in k and K_A, respectively. Hence the increase in $[R_4NX]$ should reflect both increasing and decreasing effects on k_{obs}. The plots in Figures 7 and 8 presumably represent the opposing effects of $[R_4NX]$ on k_{obs}.

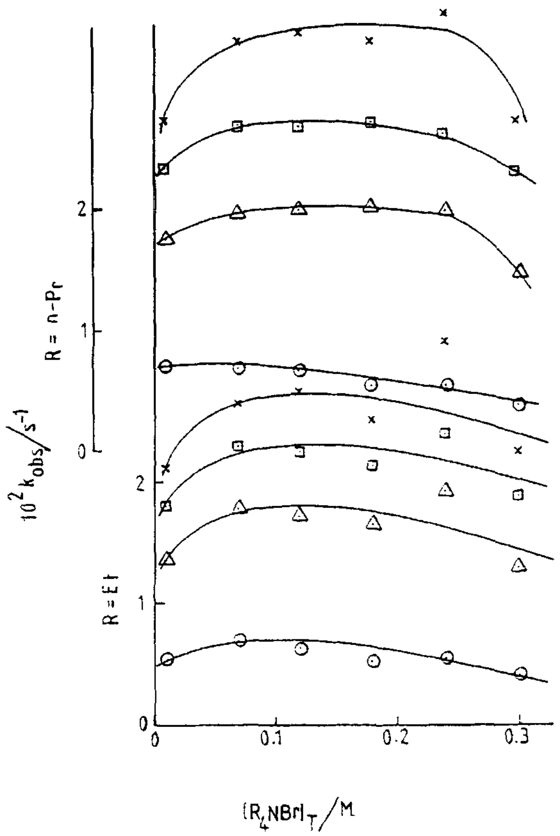


Figure 7. Plots showing the dependence of k_{obs} on $[R_4NBr]_T$ with $R = Et$ or Pr^n, in mixed methanol–water solvents containing 0·01 M NaOH at contents of methanol of (⊙) 15%, (△) 50%, (⊡) 70% and (X) 90%

Aqueous mixtures of ethane-1,2-diol represent the so-called 'typically non-aqueous' (TNA) solvents. Although TA and TNA solvents generally show some characteristically different solution properties,[5] the plot of k_{obs} versus contents of ethane-1,2-diol at 0·01 M LiOH (Figure 2) has a shape similar to those obtained for H_2O–MeOH and H_2O–C_2H_5OH[23] (TA solvents) under similar experimental conditions (Figure 1). However, such plots obtained at high contents of organic cosolvents in the presence of 0·01 M NaOH and 0·01 M KOH for H_2O–$HOCH_2CH_2OH$[7] are distinctly different from the corresponding plots obtained for H_2O–C_2H_5OH,[23] H_2O–$C_2H_5OCH_2CH_2OH$[7] and H_2O–MeOH under similar experimental conditions. The observed rate constants, k_{obs}, obeyed equation (6) at ethane-1,2-diol contents of $\leqslant$55% (v/v). The calculated values of k and K_A are shown in Table 2. The values of k and K_A are comparable with the corresponding values of $1{\cdot}52 \times 10^{-3}$ dm^3 mol^{-1} s^{-1} and $88{\cdot}4 \times 10^{-3}$ dm^3 mol^{-1} at 0·01 M NaOH and

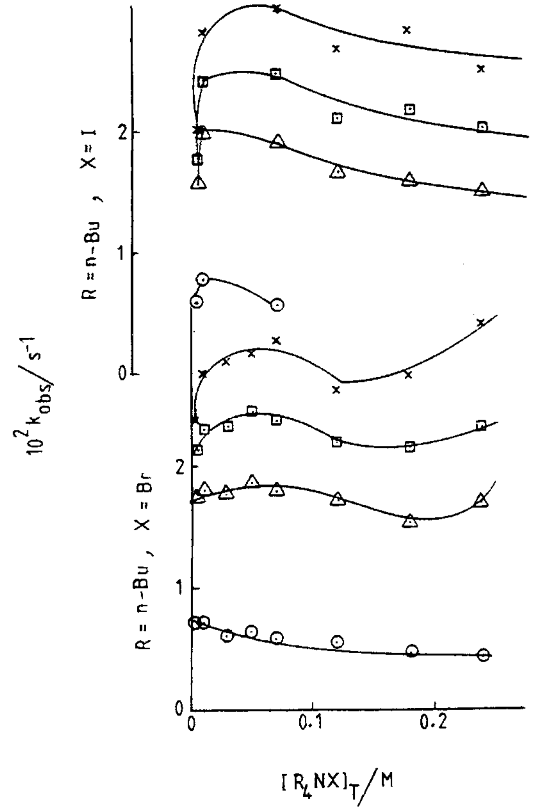


Figure 8. Plots showing the dependence of k_{obs} on $[R_4NX]_T$ with R = Bu^n and X = Br or I, in mixed methanol–water solvents containing 0·01 M NaOH at contents of methanol of (⊙) 15%, (△) 50%, (⊡) 70% and (X) 90%

$1{\cdot}53\times10^{-3}$ dm^3 mol^{-1} s^{-1} and $84{\cdot}9\times10^{-3}$ dm^3 mol^{-1} at 0·01 M KOH.[7] However, the change from 0·01 M KOH to 0·01 M LiOH has caused an increase of nearly 2-fold in K_A for MeOH in H_2O–MeOH solvents (Table 2). Similarly, the change from 0·01 M NaOH to 0·01 M LiOH appeared to increase K_A by *ca* 1·5- and 1·3-fold for H_2O–MeOH (Table 2) and H_2O–C_2H_5OH[7,23] solvents, respectively. Thus, although the shapes of the plots of k_{obs} versus contents of organic cosolvents appear to be same in water-rich regions [i.e. at H_2O contents of ⩾50% (v/v)] in both TA (H_2O–MeOH and H_2O–C_2H_5OH) and TNA (H_2O–$HOCH_2CH_2OH$) solvents, the values of K_A appear to be changed and unchanged for ROH in TA and $HOCH_2CH_2OH$ in TNA solvents, respectively, with change from O·01 M LiOH to 0·01 M NaOH or KOH.

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