Sonication effects on ester hydrolysis in alcohol–water mixtures

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Abstract. Kinetics of the neutral hydrolysis of 4-nitrophenyl chloroacetate was investigated in water and in the presence of 1 mol % of ethanol, propanol, and n-butyl alcohol without sonication and under ultrasound at 25 kHz. Similarly, the kinetics of the acid-catalysed hydrolysis of n-propyl acetate in ethanol–water binary solutions was investigated without sonication and under ultrasound at 22 kHz. The results are discussed together with corresponding data for ethyl and n-butyl acetate from previous works. It was concluded that for ester hydrolyses the solvent effects in an aqueous alcohol binary mixture are limited almost entirely to the hydrophobic ground-state stabilization by the organic co-solvent.

Key words: binary solvent mixtures, ester hydrolysis, hydrophobic interactions, ultrasound.

INTRODUCTION

Ultrasonic acceleration effects on chemical processes are widely used both in laboratory and industrial practice [1, 2]. Sonication mostly affects reaction rates, yields, and in some cases the ratios of reaction products. Besides bringing about mechanical effects, cavitation induced by sonication can promote many homogeneous and heterogeneous reactions by generating radicals that give rise to chain reactions in solution.

According to current tenets of sonochemistry [1], an ionic homogeneous reaction that cannot switch to a radical pathway should not be susceptible to ultrasound effects. However, a number of homogeneous polar (heterolytic) reactions have been found that are, in fact, accelerated or even suppressed by

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ultrasound [3–10]. These effects have been explained by the influence of ultrasound on specific solute–solvent interactions of hydrophobic nature that are not manifested in conventional reaction kinetics [4–11]. Moreover, we were able to show that in these cases the sonochemical effects can be related to the destruction of hydrophobic solute–solvent interactions [8–11].

Recent spectroscopic, X-ray diffraction, and mass spectrometric investigations have shed light on the structure of alcohol–water solutions [12–14]. As to the ethanol–water solutions, these observations suggested formation of associates between ethanol molecules and breakdown of the bulk water structure at $X_E > 0.1$ (X_E is the ethanol molar ratio). In water–ethanol mixtures at $X_E > 0.15$ a large number of ethanol–water bonds are formed at the expense of water–water bonds, and this situation is described by a cluster model envisaging a stacked ethanol core surrounded by a thin water shell [12–14].

This model has allowed a straightforward interpretation of our results: as a hydrophobic reagent could be hidden inside the clusters it seems to be unavailable for reaction. If ultrasound breaks these hydrophobic clusters, this reagent becomes again available and acceleration of the reaction can be observed. Alkyl acetates were used as probes to study this possible cluster formation effect on the reaction rate. Indeed, sonication affected the acid-catalysed hydrolysis of these esters in the region $0.2 < X_E < 0.3$ and this effect matched in reverse order with the hydrophobicity of the esters. Butyl acetate should be held most effectively by clusters, and sonication was the least efficient in this case [8]. However, in previous papers [8, 9] we have evasively discussed the observed sonication effects in the region $X_E < 0.15$, as we were unable to suggest any unambiguous mechanism of the solute–solvent interaction.

In this report we have set out a broader investigation into hydrophobic effects of aliphatic alcohols as co-solvents on ester hydrolysis in water, and studied the neutral hydrolysis of 4-nitrophenyl chloroacetate in the presence of small amounts of alcohols. It is important to stress the advantages of this experiment in comparison with the measurement of ester hydrolysis by using the GLC technique (see in [8]). The spectrophotometric method was used in the former case and this enabled us to apply a very low ester concentration (10^{-5} M) and to exclude the use of an internal standard. The results obtained together with our former data cast light on the nature of sonication effects and the hydrophobic interactions in the region of small to moderate molar ratios of alcohols in water.

EXPERIMENTAL

Neutral hydrolysis of 4-nitrophenyl chloroacetate

Aqueous solutions were prepared by weighing Milli-Q$^+$ water and carefully purified alcohols. The pH of the solutions was maintained at 3.65 ± 0.05 with HCl. Calculated amounts of the ester or 4-nitrophenol as the reference compound were dissolved in analytical grade acetonitrile. Injection of 10 μL of this solution

into 100 mL of the reaction mixture, placed in the reaction cell, provided 10^{-5} M initial concentration of the reagents.

The kinetics of the neutral hydrolysis of 4-nitrophenyl chloroacetate was followed spectrophotometrically with a Perkin-Elmer Lambda 2S spectrometer. All hydrolysis reactions were performed without sonication and under ultrasound. Aliquots of 1 mL were withdrawn from the reacting mixtures at appropriate time intervals and the formation of 4-nitrophenol was monitored spectrophotometrically at 317 nm.

Sonication was performed under argon atmosphere with an Elma TI-H-5 MF2 cleaning bath at 25 kHz. The reaction cell, equipped with a mechanical stirrer and a digital thermometer, was reproducibly immersed in the bath thermostatted at $20.0 \pm 0.1\,°C$. The ultrasonic power of the cleaning bath was adjusted at 50% of the electrical output energy to $8.1 \pm 0.7\,W/100\,mL$ in water according to the calorimetric measurements carried out in the reaction cell.

The sonolytic degradation of 4-nitrophenol was monitored identically under the same conditions as the hydrolysis of 4-nitrophenyl chloroacetate.

Acid-catalysed hydrolysis of *n*-propyl acetate

The acid-catalysed hydrolysis of *n*-propyl acetate was performed in ethanol–water mixtures in the presence of 1 M HCl. The decrease in the ester concentration was followed by GLC. Ultrasound was generated by a UZDN-2T probe disrupter operating at 22 kHz. Its energy output, estimated calorimetrically, was 55 W/80 mL in water. An immersed sonication horn was used. The reaction temperature was $20.0 \pm 0.3\,°C$. All runs were carried out at least in duplicates. The standard deviations of mean values of the calculated rate constants did not exceed 10%. For other experimental details see our previous paper [8].

RESULTS AND DISCUSSION

The hydrolysis of 4-nitrophenyl chloroacetate was carried out at pH = 3.65 in water and in the presence of 1 mol % of ethanol, *n*-propyl alcohol, and *n*-butyl alcohol. Experiments were made without sonication and under ultrasound. Results of the kinetic measurements are presented in Table 1.

Table 1. Results of kinetic measurements for the neutral hydrolysis of 4-nitrophenyl chloroacetate in water at 20 °C

Co-solvent, 1 mol %	Rate constant $k \times 10^4$ (s^{-1})		Ultrasonic acceleration (k_{son}/k)
	Nonsonic	Sonic	
–	2.89	3.10	1.07
EtOH	3.27	4.17	1.28
n-PrOH	2.66	4.11	1.55
n-BuOH	2.42	4.07	1.69

Degradation of nitrophenol under sonication can lead to defacement of ester hydrolysis kinetics and this issue has been discussed in detail in our previous paper [9]. Therefore the rate of sonolytic degradation of 4-nitrophenol was separately studied under the same conditions as used for the hydrolysis of 4-nitrophenol chloroacetate. The first-order rate constant of this process was found to be $k_I = 7.5 \times 10^{-5}$ s^{-1}. This value is more than 50 times smaller than that for the ester hydrolysis (data in Table 1). Thus, the degradation of 4-nitrophenol can be ignored in the kinetics of ester hydrolysis.

Formation of encounter complexes between ester and alcohol, rendering the ester uncreative, was shown by Buurma et al. [15]. Indeed, it is seen in Table 1 that the rate of hydrolysis decreased in parallel with the increase in the hydrophobicity of the co-solvent. However, the sonication effect, characterized by (k_{son}/k), increased almost linearly with the number of carbon atoms in the alcohol molecule (Fig. 1), resp. with the hydrophobicity of the co-solvent.

Such unexpected at first glance dependence of sonication effects can be related to the weak solvation of esters in this region. While greater hydrophobicity leads to a stronger ground-state stabilization and hence to a greater decrease in the reactivity, ultrasound breaks down the hydrophobic interactions almost entirely, thus giving rise to larger sonication effects for more hydrophobic esters.

The same results can be presented in a different way, as shown in Fig. 2. It can be seen that ultrasound of the applied acoustic power appears to destroy the ester–co-solvent encounter complexes regardless of the hydrophobicity of these compounds.
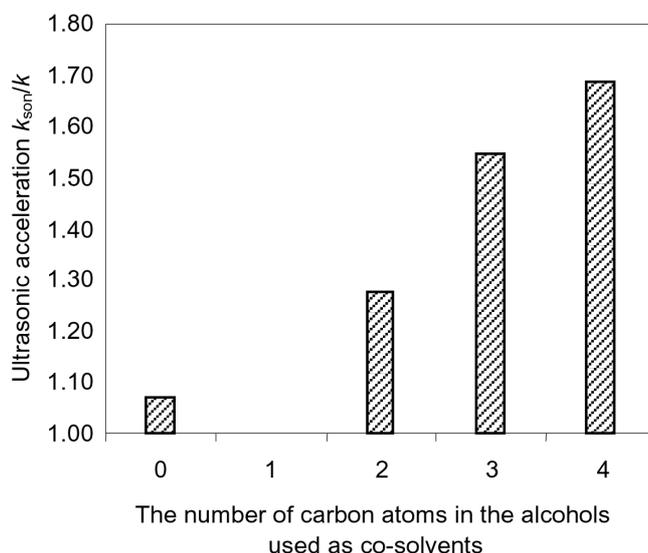
Fig. 1. Sonication effect for the hydrolysis of 4-nitrophenyl chloroacetate vs the number of carbon atoms in the alcohols used as co-solvents.
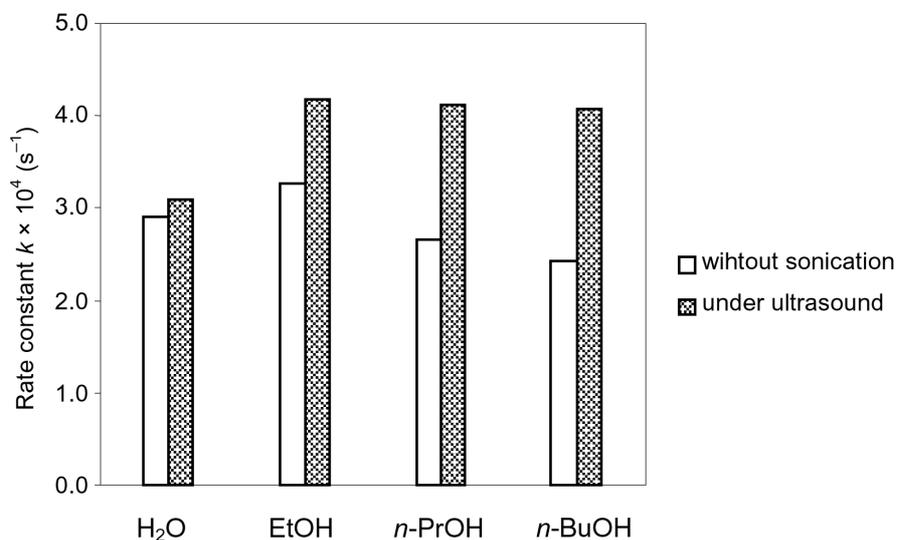
Fig. 2. Diagrammatic representation of the rate constants for the hydrolysis of 4-nitrophenyl chloroacetate without sonication and under ultrasound. The alcohols are co-solvents in 1 mol% amount.

These results encouraged us to revisit the sonication effects obtained for the acid-catalysed hydrolysis of aliphatic esters in the region $X_E < 0.15$ [8], and certain inconsistency of these data forced us to recapitulate kinetic measurements with n-propyl acetate in ethanol–water binary solutions. Rate constants for the acid-catalysed hydrolysis of this ester under ultrasound and without sonication, measured in this study, are presented in Table 2. Unfortunately kinetic measurements were not feasible in pure water because of low solubility of the ester.

The plots of sonication effects (k_{son}/k) vs solvent composition are presented in Fig. 3. The curves show minima with almost no sonication effect for ethyl and propyl acetates while the more hydrophobic ester, n-butyl acetate, may show a minimum at a higher ethanol content. We tend to attribute this phenomenon to the preferential solvation of esters in the solution.

Table 2. Results of kinetic measurements for the acid-catalysed hydrolysis of propyl acetate at 20 °C

Content of ethanol, wt % (X_{EtOH})	Rate constant $k \times 10^4$ (s^{-1})		Ultrasonic acceleration (k_{son}/k)
	Nonsonic	Sonic	
10 (0.042)	0.89 ± 0.03	1.42 ± 0.04	1.59
13 (0.055)	0.97 ± 0.07	1.41 ± 0.1	1.44
20 (0.089)	0.99 ± 0.06	1.20 ± 0.06	1.21
30 (0.144)	0.75 ± 0.02	0.74 ± 0.07	0.99
40 (0.207)	0.66 ± 0.04	0.93 ± 0.08	1.41
50 (0.281)	0.64 ± 0.06	1.11 ± 0.07	1.75
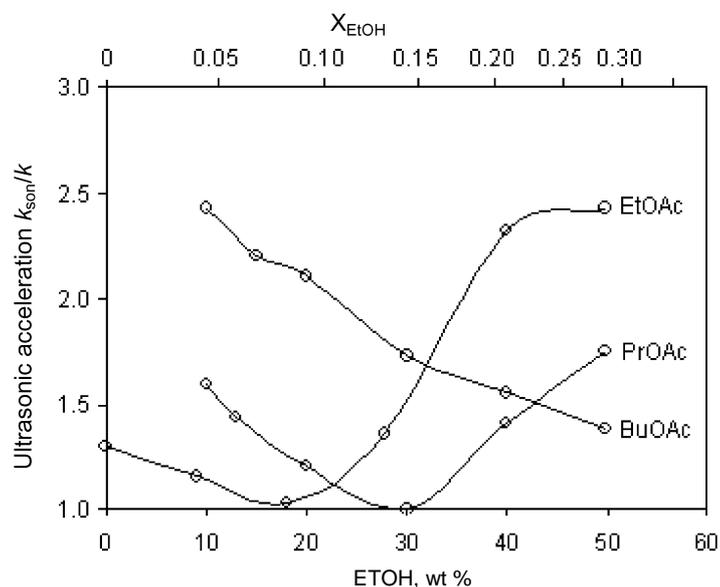
Fig. 3. Rate enhancements (k_{son}/k) for aliphatic esters induced by ultrasonic irradiation at various ethanol content.

Ultrasound seems to be responsible for the perturbation of the ground-state stabilization of the reactants [10, 11]. Therefore the sonication effect should reflect the solvation mode of ester molecules. In the region of clusters ($X_E > 0.15$) the sonication effects are large for ethyl and propyl acetates, indicating a considerable interaction of esters with the solvent system. On the other hand, moderate or negligible effects at $X_E < 0.15$ manifest relatively weak solvation, thus not dramatically affecting the reactivity when changing under sonication. The minima point at solvent compositions that provide solvation situations for ester molecules with the same reactivity as whether present or destroyed by ultrasound. Propyl acetate, more hydrophobic in comparison with ethyl acetate, apparently requires more alcohol molecules in an equilibrium solvation to show the minimum in sonication effects. As to *n*-butyl acetate, this highly hydrophobic compound seems to interact with the solvent system to such a power that at a higher content of the alcohol and under our experimental conditions ultrasound is not able to break down entirely the solvation equilibrium of the ester.

While in the cluster region ($X_E > 0.2$) the sonication effect correlates with the reverse order of the hydrophobicity of the esters in accordance with the supposed strength of the inclusion clusters, at a lower ethanol content in the solution ($X_E < 0.1$) the sonication effect increases with an increase in the hydrophobicity of esters similarly to what was observed for the alcoholic co-solvents.

As a more general conclusion concerning ester hydrolysis, it can be inferred from the results above that in an aqueous alcohol binary mixture the solvent effects are limited almost entirely to the hydrophobic ground-state stabilization by the organic co-solvent.

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Ultraheliefektid estri hüdrolüüsile alkoholi-veesegudes

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On uuritud 4-nitrofenüülkloroatsetaadi neutraalse hüdrolüüsi kineetikat vees ja 1 mol % etanooli, propanooli ning *n*-butüülalkoholi juuresolekul ultrahelita ja ultraheliga kiiritades sagedusel 25 kHz. Samuti on uuritud propüülatsetaadi happekatalüütilise hüdrolüüsi kineetikat etanooli-veesegudes ultrahelita ja ultraheliga kiiritades sagedusel 22 kHz. Tulemusi on analüüsitud koos vastavate andmetega etüül- ja *n*-butüülatsetaadi jaoks varasematest töödest. On järeldatud, et estri hüdrolüüsi solvendiefektid alkoholi-vee binaarsetes segudes on peaaegu täielikult määratud reaktsiooni lähteoleku hüdrofoobse stabiliseerimisega orgaanilise kaassolvendi poolt.