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Kinetic effects of ultrasound
in aqueous acetonitrile solutions



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CONTENTS

LIST OF PUBLICATIONS.....	6
LIST OF ABBREVIATIONS.....	7
1. INTRODUCTION.....	8
2. ULTRASOUND EFFECTS ON HOMOGENEOUS REACTIONS IN SOLUTIONS	10
3. METHODS	14
3.1. Ultrasonic on-line system	14
3.2. Kinetic measurements.....	16
3.3. Chemical dosimetry	16
4. RESULTS AND DISCUSSION	18
4.1. Kinetic sonication effect in aqueous acetonitrile	18
4.1.1. Reaction rate levelling by ultrasound.....	20
4.1.2. Kinetic sonication effects in light of MD simulation	21
4.2. Impact of ultrasound in absence of the cavitation.....	26
5. CONCLUSIONS.....	29
6. SUMMARY IN ESTONIAN.....	31
7. REFERENCES.....	33
8. ACKNOWLEDGEMENTS	35
PUBLICATIONS.....	37
CURRICULUM VITAE	87

LIST OF PUBLICATIONS

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- Paper II **S. Piiskop**, G. Raidaru, S. Salmar. Ultrasonic on-line spectrophotometric system for reaction kinetic measurements. Proc. Est. Acad. Sci. Chem., 2012, 61(1), 52–57.
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- Paper I Responsible for all performed kinetic experiments and calculations. Participated in the writing of the manuscript.
- Paper II Responsible for all performed kinetic experiments and calculations. Mainly responsible for the preparation of the manuscript.
- Paper III Responsible for interpretation of MD simulation data. Participated in the writing of the manuscript.
- Paper IV Responsible for all of the performed kinetic experiments and interpretation of MD simulation data. Mainly responsible for the preparation of the manuscript.
- Paper V Responsible for all performed kinetic experiments and calculations. Participated in the writing of the manuscript.

LIST OF ABBREVIATIONS

EtOAc	–	ethyl acetate
EtOH	–	ethanol
GLC	–	gas-liquid chromatography
HPLC	–	high-pressure liquid chromatography
KI	–	potassium iodide
LFER	–	Linear Free Energy Relationship
MD	–	molecular dynamics
MeCN	–	acetonitrile
NMR	–	nuclear magnetic resonance
PTFE	–	polytetrafluoroethylene
TA	–	terephthalic acid
UV-Vis	–	ultraviolet-visible spectroscopy
X_s	–	molar ratio of co-solvent

I. INTRODUCTION

Ultrasound has been widely employed for variety of purposes in the laboratory and industrial practice, including chemical synthesis, food processing, waste treatment, biofuels production, synthesis of nanostructured materials etc. Influence of ultrasound on chemical and physical processes has been conventionally explained by formation of acoustic cavitation bubbles, and following this understanding the sonochemical effects should derive mostly from destruction of chemical species inside the cavitation bubbles, as radical reactions taking place inside or in the vicinity of the bubbles. Therefore many homogeneous reactions activated by sonication have been referred to proceed via formation of radical or radical-ion intermediates.

As this reaction mechanism has been canonized in sonochemistry, the homogeneous ionic reactions, which cannot be switched to a radical pathway, should not be susceptible to ultrasound. However, numerous examples of homogeneous reactions, including hydrolysis and solvolysis reactions, which definitely proceed by non-radical mechanism, have been accelerated by ultrasound. Many of these reactions have been kinetically investigated in binary aqueous-organic solvents.

In earlier works, the effect of sonication has been related to properties of binary solvents and has been explained by breaking down the solvation structure or by shifting the solvation equilibria. Further progress in understanding of the molecular structure of binary solvents has revealed more specific relations between the observed effects of selective solvation and hydrophobic interaction in the solutions.

Until recently, kinetic sonochemical investigations have been carried out predominantly on reactions occurring in water-ethanol binary mixtures. In this work we have extended these investigations into aqueous acetonitrile solvent system. In connection to this, it was necessary to improve the method of kinetic measurements under ultrasonic irradiation. Hence, a unique ultrasonic on-line system was developed and set up for further sonochemical studies under ultrasound.

Acetonitrile is a more polar co-solvent than ethanol, but incomparably poorer in hydrogen bond formation. Such diversities in the physical properties of co-solvents lead to substantial dissimilarities in the structure of the corresponding aqueous binary mixtures. Thus, in acetonitrile solutions specific solvation features as well as novel kinetic sonication effects could be expected. Indeed, we found different sonication effects if compared this system with the water-ethanol solvent system.

To obtain a better insight into these phenomena, we invoked also molecular dynamics (MD) simulations in both solvent systems. By contrasting these results with experimental data we were able to explain the solvation effects as well as sonication effects at the molecular level. Based on these results, the

principal conclusion of this work was that ultrasound induces changes in the solvation of reagents thus affecting the reaction rate.

In the present thesis the rate levelling effect of ultrasound in polar reactions in aqueous-organic binary solvent was described. Addition of co-solvent into the reaction mixture decreased the reaction rate, while the rate observed under ultrasound depended only marginally on the solvent composition. This phenomenon appeared to contribute much to explanation of the sonication effects.

One of the most intriguing findings of this work was that significant kinetic sonication effects were found below the cavitation threshold. This could be a principal extension of the sonochemical method, and could open new perspectives for the physicochemical investigations into variety of chemical and biochemical processes.

2. ULTRASOUND EFFECTS ON HOMOGENEOUS REACTIONS IN SOLUTIONS

Ultrasound is now an established tool for chemists and chemical technologists in the laboratory and in the industrial scale. Ultrasound technology is widely used for medical applications, drug delivery, polymer chemistry, waste treatment, food processing, nanotechnology, surface disinfection and cleaning and of course for synthetic applications [1–7].

It has long been known that ultrasound enhances chemical and physical changes in a liquid medium through the generation, growth and subsequent collapse of cavitation micro-bubbles. Sonophysical effects are caused by physical actions such as micro-jets and shock waves caused by the collapse of bubbles, micro-streaming, and possibly by violent acoustic waves. Sonochemical effects include destruction of chemical species inside the cavitation bubbles, which can be thought of as closed high temperature and high-pressure micro reactors, and radical reactions inside or in the immediate vicinity of the bubbles [4,5].

Sonochemical reactions in solutions have mainly been rationalised in terms of cavitation theory. Following this idea, a rule was formulated by Luche [6,7] that homogeneous reactions activated by sonication should proceed exclusively via radical or radical-ion intermediates, and ionic reactions which cannot be switched to a radical pathway should not be susceptible to ultrasound. However, numerous examples of homogeneous polar reactions, which definitely proceed by non-radical mechanism, have been accelerated by ultrasound. For review see Refs. [8–10].

Most of the processes in which sonication effects were quantified by ratio $k_{\text{son}}/k_{\text{non}}$, were hydrolysis and solvolysis reactions [8–17]. It is noteworthy that only very small sonication effects have been found in water. In contrast to this, moderate to large ultrasonic acceleration effects were reported in water-organic binary mixtures. For example, sonication effect 2.5 was observed for the acid-catalysed hydrolysis of alkyl esters in water-ethanol binary mixtures [14–16]. Large sonication effects up to 20 times were observed in the solvolysis reaction of 2-chloro-2-methylpropane in aqueous mixtures of ethanol [11–13], propan-2-ol [11] and 2-methyl-2-propanol [11] by Mason's group.

Solvent mixtures were often regarded being a continuous medium. However, measurement of kinetic effects of power ultrasound has shown nonlinear dependence on the composition of aqueous binary mixtures as illustrated by the examples shown in Figure 1. These data indicate that solvation in these media should be a complex phenomenon, where the preferential solvation of the reagent by some components of the mixture should be taken into consideration [19]. In highly structured liquids, which can form extensive networks of hydrogen bonds, solvation effects depend also on structure of the reaction medium. Therefore the extremities shown in Figure 1 were related to changes in the solvent structure and the effect of sonication was explained by breaking

down the solvation structure, or by shifting the solvation equilibria [12,13,18]. Therefore investigation into kinetic sonication effects could be particularly fertile in elucidation of the solvation phenomena in reactions taking place in water-organic solvents [7–9].

It is clear that ultrasound effects on polar reactions cannot be caused by the direct impact of the acoustic field on reacting molecules or on the transition states of reactions, since the energy of the ultrasound field is too low to alter their rotational, electronic or vibrational states [1–4]. However, pressure waves associated with the propagation of ultrasound as well as shock waves generated during cavitation bubble collapse can cause changes in the translational energy of species and this, in turn, may result in changes to the reaction rate [20, 21].

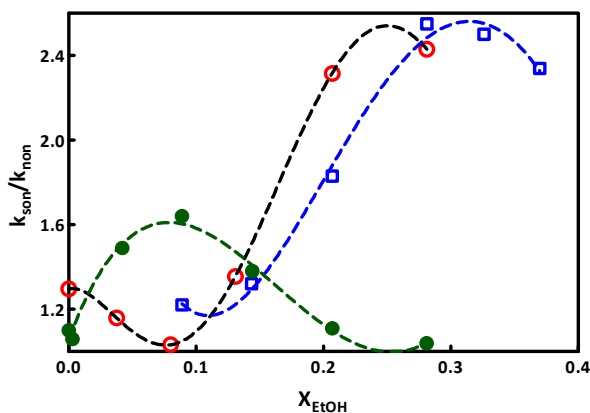


Figure 1. Rate enhancements induced by ultrasonic irradiation in water-ethanol binary mixtures. (\square) Solvolysis of 2-chloro-2-methylpropane at 20 °C [12], (\circ) acid-catalysed hydrolysis of ethyl acetate at 18 °C [14], and (\bullet) base-catalysed hydrolysis of 4-nitrophenyl acetate at 20 °C [17].

Along with progress in understanding the microscopic structure of binary solvents, sonication effects can be more specifically related to actual solvation phenomena. Spectroscopic, neutron diffraction, X-ray diffraction and mass spectrometric investigations have shed light on the structure of binary water-organic solvent mixtures [18–22]. Experimental evidence has been obtained of incomplete mixing at the microscopic level in these solvents, although their mixtures are homogeneous at the macroscopic scale. This means that water-organic binary mixtures experience microscopic phase separation at the cluster level, i.e. water-rich clusters and co-solvent-rich clusters coexist, showing microscopic phase separation in wide mixing ratios.

When passing from water to pure organic solvents the micro-heterogeneous structure of the binary solvent undergoes large and nonlinear changes [22]. For example, observations suggested that associates of ethanol molecules start to

grow and the water 3D structure breaks down in ethanol-water mixtures at $X_{\text{EtOH}} > 0.1$. In mixtures at $X_{\text{EtOH}} > 0.15$ a large number of water-ethanol bonds are formed, and water-water bonds are broken. The resulting structure is described by a cluster model of a stacked ethanol core and a thin water shell [23–25]. Ultrasound effects show a distinct maximum for hydrolysis of ethyl acetate and for the solvolysis of 2-chloro-2-methylpropane in this critical cluster region at 0.2–0.3 mol fraction of ethanol, as can be seen in Figure 1.

The interpretation of these sonication effects in water-ethanol environments can proceed from the cluster model of Japanese authors [23–25]. Presumably, the clusters could hide a substrate molecule, e.g. of an ester, in their hydrophobic interior, thus making it less reactive. Ultrasound, by disrupting the cluster structure, would allow more favourable solvation of the substrate and result in enhanced rates of reaction [9]. Indeed, kinetic sonication effects were in quantitative agreement with the hydrophobicity of the aliphatic esters studied and the decrease in reaction rates with increasing ethanol content in the solvent system was related mainly due to ground-state stabilization, which is largely of hydrophobic origin. [13,18,21]. It was highlighted that ultrasound can reveal subtle solute-solvent interactions that remain hidden in conventional kinetic studies and it has become a useful instrument for physicochemical investigations [21].

More extensive kinetic sonochemical investigations have been carried out predominantly on reactions of solvolysis and ester hydrolysis, occurring in ethanol-water binary mixtures, while aqueous 1,4-dioxane, 2-propanol and 2-methyl-2-propanol were rare exceptions [8–10]. In the present work we extend the list of exploited binary solutions to the aqueous acetonitrile (cyanomethane) solvent system by substituting frequently used ethanol for an aprotic and highly polar co-solvent, with the aim of elucidation of the sonication effect on homogeneous polar reactions in water-organic solvent mixtures.

Acetonitrile, like ethanol, is miscible with water at any ratio under ambient conditions. However, acetonitrile exceeds ethanol considerably by polarity (dielectric constants being 35.94 and 24.55, respectively) but is incomparably feeble in hydrogen bond formation [27]. Such diversities in the physical properties of co-solvents lead to substantial dissimilarities in the structure of the corresponding aqueous binary mixtures [22,29,30]. Thus, in acetonitrile solutions, specific solvation features as well as novel kinetic sonication effects could be expected if compared with the commonly used water-ethanol solvent system.

Interpretation of sonication effects on polar reactions in water-organic mixtures are gone hand in hand with the elucidation of the solvation phenomena which occur in these solutions. Conclusions drawn so far have been merely based on observed sonication effects in reaction kinetics and clarified liquid structure of binary solutions at the molecular level by different physical techniques. However, recent investigations into the cluster structure of binary water-ethanol mixtures have revealed that large additives of hydrophobic

compounds (or ‘impurities’) can considerably alter the structure and distribution of molecular clusters in the reaction mixture [26].

In this thesis molecular dynamics (MD) simulations were used to cast light on the solvation of solutes in aqueous organic mixtures to obtain better insight into the sonication effects at the molecular level.

3. METHODS

3.1. Ultrasonic on-line system

It is rather complicated to carry out the kinetic measurements under ultrasound reproducibly. For instance, kinetic sonication effects found for some ester hydrolysis reaction in aqueous organic solvent systems were considerably low [10], thus any disturbing factor (alteration of temperature from cavitation or volume of the reaction system etc.) may affect the kinetic measurements carried out under sonication. Therefore it is often difficult to make adequate comparisons between studies performed under ultrasound and without sonication even in the same reaction system. Hence for extensive sonochemical investigations of homogeneous polar reactions it was essential to guarantee stable conditions to perform kinetic measurements accurately and reproducibly.

Predominantly most of the kinetic studies of hydrolysis and solvolysis reactions, including our study of pH-independent hydrolysis of 4-nitrophenyl chloroacetate in water-alcohol mixtures (**Paper I**), have been performed with the sample withdrawal method and aliquots were analysed by a variety of methods, e.g. GLC, HPLC, spectrophotometrically etc [10]. Withdrawing aliquots is generally preferred because continuous kinetic measurements directly in ultrasonic field involve numerous complications. Mason et.al has followed conductometrically the kinetics of 2-chloro-2-methylpropane solvolysis in aqueous ethanol under sonication employing bright Pt electrodes [12]. Nevertheless, cavitation causes erosion of various materials damaging electrodes and reducing their lifetime. Metal traces from the immersed titanium sonication horn or other materials may also cause difficulties contaminating the reaction mixture [17]. A significant disadvantage of withdrawing aliquots is the permanent decrease in the volume of the reaction medium during kinetic measurements, which may affect the sonication effect. Also, withdrawing aliquots for analysis could be time-consuming that hampers kinetic measurements in the case of fast reactions. Moreover, performing experiments in inert atmosphere may be complicated in this case.

Ultrasound acceleration effects may be as low as only a few per cent, as was reported for some ester hydrolysis reactions in water-organic solvents. Therefore temperature control is decisive in correct and reproducible kinetic investigations of sonication effects [10].

Considering all these aspects, it was inevitable to elaborate an on-line system, which allowed performing continuous ultrasonic kinetic measurements of homogeneous reactions very accurately and with high reproducibility, and can be used for detection of small sonication effects in different processes.

For these kinetic studies it was also important to choose an appropriate type of ultrasound source. In general, on the laboratory scale there are three types of commercial sonicators that commonly operate at lower frequencies (e.g. 20, 25, 45 kHz): ultrasonic cleaning bath, cup-horn sonicator and ultrasonic probe

system [1–4]. For sonochemists ultrasonic probe and cup-horn systems have numerous advantages compared to ultrasonic cleaning bath, mostly because of the supply of higher power into the reaction vessel. However, several problems such as difficult temperature control and well-known erosion of equipment materials caused by cavitation arise in kinetic measurements. For instance, metal particles dispersing from the sonication horn and contaminating the reaction mixture may interfere with various kinetic measurements or even catalyse the reactions under examination [17]. To consider the above-mentioned problems, we concluded that the best ultrasonic device for kinetic studies is the classic ultrasonic bath.

Due to ultrasonic heating, the temperature inside the reaction vessel is usually higher than in the ultrasonic bath. Therefore both the ultrasonic bath and reaction vessel were thermostatically controlled.

We have studied the kinetics of pH-independent hydrolysis of 4-nitrophenyl chloroacetate in alcohol-water mixtures under ultrasound by using spectrophotometric method (**Paper I**). Consequently we preferred a HPLC UV/Vis detector to follow the reaction kinetics in our ultrasonic on-line system. The HPLC UV/Vis detector has many advantages, including high sensitivity and direct electrical readout. Furthermore, an important feature of the chosen detector was small capacity of the flow cuvette. Thus only a fractional part of the total reaction solution is temporarily out of the ultrasonic field. However, it was possible to use different type of detectors in this on-line system. For example, all experiments of terephthalic acid dosimetry were carried out with the fluorescence detector (**Paper V**).

Online detection of the reaction kinetics requires continuous circulation of the reaction mixture from the ultrasonic cell through the detector. Preliminary tests with different peristaltic pumps showed that many disturbing factors and problems, such as rising pressure, leaks, and gas bubbles may appear. In addition, in the case of these pumps a large part of the total reaction mixture was outside of the ultrasonic irradiation field because it was necessary to use large diameter tubes. Also temperature control was poor. All these circumstances reduced the reproducibility of kinetic measurements.

Examination of a HPLC pump gave an excellent results. The capacity of the whole circulation system was considerably small, 0.4 mL. Thus, if there is 100 mL of reaction mixture in the sonication reactor, only 0.4% of the total amount of the reaction mixture will be temporarily out of the ultrasonic field. Notably at the maximum flow rate of the pump (5mL/min), the dead time of the system was approximately 2.5 s. Thus it is possible to register sonication effects that occur during a very short time.

In conclusion, a unique ultrasonic on-line system was developed, and successfully applied for sonochemical investigation of various homogeneous reactions. For more details about the setup see **Paper III**.

3.2. Kinetic measurements

All water-acetonitrile solvent mixtures were prepared by weighing calculated amounts of Millipore Milli-Q water and analytical grade acetonitrile (purchased from Sigma-Aldrich). 4-methoxyphenyl dichloroacetate was prepared according to a literature procedure [31]. 4-methoxyphenol, 4-nitrophenol and starting materials for the synthesis were purchased from Aldrich and were used as received without further purification.

All kinetic measurements were carried out using the on-line system developed for kinetic measurements under ultrasound. Kinetic experiments of the hydrolysis reaction of 4-methoxyphenyl dichloroacetate without sonication and under ultrasound were carried out at 25 °C and under argon atmosphere. The pH of the solutions was maintained at 3.6 with HCl.

For kinetic measurements under ultrasound, 150 mL of the water-acetonitrile solvent mixture was transferred into the reaction vessel, the ultrasound was switched on and the power of the cleaning bath was adjusted (cleaning bath adjusted at 50% of the input energy was equivalent to 1.6 ± 0.5 W/150 mL). Temperatures in both the ultrasonic bath and the reaction vessel were maintained at 25.0 ± 0.1 °C. The temperature of the reaction mixture was recorded and after equilibration of the whole system 10 μ L of 4-methoxyphenyl dichloroacetate dissolved in acetonitrile was injected into the reaction cell, providing 10^{-5} M initial concentration of the ester. The formation of 4-methoxyphenol was monitored spectrophotometrically at 290 nm. The first-order rate constants were calculated from the obtained kinetic curves by means of a differential method [32]. Measurements without sonication were performed similarly using the same protocol and equipment. Reproducibility of the rate constants was found to be within 3–8 % as indicated by at least two repeated experiments. For more details see **Paper IV** and **V**.

3.3. Chemical dosimetry

Potassium iodide (KI) and terephthalic acid (TA) dosimetry reactions were carried out at irradiation intensities corresponding to 7, 10, 20, 30, 40, and 50% of the input energy of the ultrasonic bath at the same experimental conditions as the kinetic measurements described above. Certainly, the same on-line spectrometric system was used.

KI dosimetry was performed with the solution of 0,1 M potassium iodide (KI) prepared in 10 wt% acetonitrile-water solvent mixture. To enhance the oxidation of iodide [33], few drops of carbon tetrachloride were added to 150 ml of KI solution in the reaction vessel. Sonication time was 30 min. The formation of I_3^- was monitored at 355 nm (the molar absorptivity $\epsilon = 26300$ dm³ mol⁻¹ cm⁻¹ from calibration) with UV/Vis detector. The KI dosimetry measurements were performed for each applied irradiation levels in at least two independent runs with reproducibility ± 4 %.

TA dosimetry reactions were carried out according to the standard procedure [34]. Weighed quantities of terephthalic acid (TA) 0.332 g, NaOH 0.20 g and the phosphate buffer (pH 7.4; KH_2PO_4 0.589 g and Na_2HPO_4 0.981 g) were dissolved in 1 dm³ of deionised water. 150 ml of this TA stock solution (2.0×10^{-3} M) was transferred into the reaction vessel and the ultrasound was switched on. During sonication of 30 min, fluorescence intensity of 2-hydroxyterephthalic acid (HTA) was directly recorded using the on-line system connected with the fluorescence detector (excitation and emission wavelengths of 310 nm and 425 nm, respectively). Recorded signal of the fluorescence of HTA was measured repeatedly at different ultrasonic powers with reproducibility of $\pm 5\%$.

4. RESULTS AND DISCUSSION

4.1. Kinetic sonication effect in aqueous acetonitrile

For sonochemical investigations in aqueous acetonitrile, pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate was chosen as a model reaction.

Briefly, due to the fact that most of the kinetic sonochemical investigations have been carried out mainly in water-ethanol binary solvent systems we extended these studies into the aqueous acetonitrile solvent system and it was intriguing to compare the effects of different co-solvents in context of the kinetic sonication effects in different water-organic solvent systems.

We have previously carried out sonochemical investigations of pH-independent hydrolysis of 4-nitrophenyl chloroacetate in aqueous alcohol solvent systems in the presence of 1 mol% of different aliphatic alcohols (See **Paper I**). A main reason for selection of this model reaction was that it was possible to monitor the process spectrophotometrically and the reaction rates matched with our experimental capability. Yet, it appeared that hydrolysis of 4-nitrophenyl chloroacetate proved to be considerably slower in aqueous acetonitrile solvent mixtures. Hence, we had to choose more suitable model ester for kinetic measurements, and this compound was 4-methoxyphenyl dichloroacetate.

Experiments with the chosen model reaction were carried out under ultrasound and without sonication, and various water-acetonitrile binary mixtures containing 0.008–35 wt% of acetonitrile were used. Corresponding molar ratios of acetonitrile (X_{MeCN}) in these solutions thus varied from 0.000034 to 0.191. Further augmentation of acetonitrile content in the solvent mixture was not practicable since the nonsonic reaction rates decreased significantly and that made kinetic measurements unreliable.

The kinetic measurements were carried out under ultrasonic irradiation with application of 10% and 50% of the maximum power of the equipment. The first-order rate constants and the kinetic sonication effects ($k_{\text{son}}/k_{\text{non}}$) obtained were presented in Table 1. The dependence of the reactivity on the composition of the binary mixture was outlined in Figure 2. It appeared that addition of acetonitrile to the reaction mixture substantially slowed down the hydrolysis rate of this ester.

Unexpectedly, the rate constants for the reaction under ultrasonic irradiation revealed relatively feeble susceptibility to the increase in the solvent composition higher than $X_{\text{MeCN}}=0.10$, while the kinetic sonication effects ($k_{\text{son}}/k_{\text{non}}$) increased rapidly, reaching the maximum acceleration effect ~ 4.5 at $X_{\text{MeCN}}=0.19$. Also it was observed that the kinetic sonication effect determined at the 10% power and at the 50% power did not differ noticeably.

Table 1. Rate constants and sonication effects for pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate in water-acetonitrile binary mixtures at 25 °C.

MeCN in water		rate constant $k \times 10^4 \text{ (s}^{-1}\text{)}^a$			ultrasonic acceleration	
% w/w	X	without ultrasound	under ultrasound		$k_{\text{son}}/k_{\text{non}}$	
			10% ^b	50% ^c	10% ^b	50% ^c
0.008	0.00	27.82 ± 0.95	35.6 ± 1.20	36.9 ± 1.45	1.28	1.33
10	0.05	7.84 ± 0.29	10.01 ± 0.47	10.47 ± 0.60	1.28	1.34
15	0.07	4.55 ± 0.25	4.98 ± 0.33	5.27 ± 0.38	1.09	1.16
20	0.10	2.19 ± 0.15	2.9 ± 0.23	3.32 ± 0.22	1.32	1.51
25	0.13	1.31 ± 0.1	2.76 ± 0.20	2.63 ± 0.20	2.11	2.01
30	0.16	0.83 ± 0.06	2.09 ± 0.14	1.85 ± 0.14	2.52	2.24
35	0.19	0.47 ± 0.03	2.5 ± 0.15	2.08 ± 0.17	5.32	4.45

^a rate constants with average absolute deviation

^b ultrasound input energy 10%

^c ultrasound input energy 50%

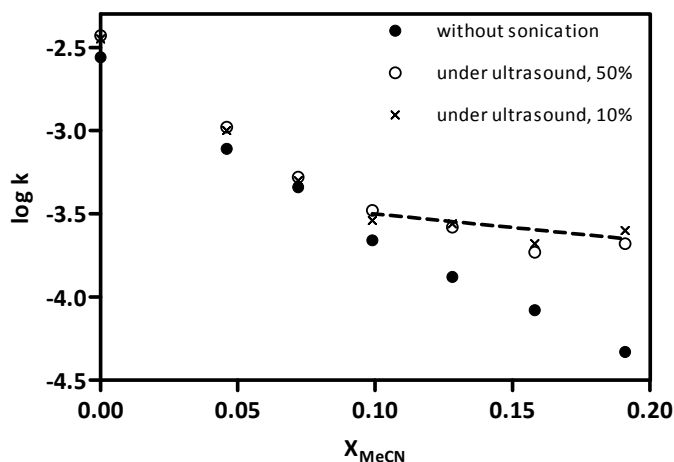


Figure 2. Rate constants for the pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate in aqueous acetonitrile solutions at 25 °C: ● – nonsonic, ○ – under ultrasound (ultrasound input energy 50%), × – under ultrasound (ultrasound input energy 10%) (25 kHz). The dashed line conjoins sonic rate constants in the region of acetonitrile mole fraction from 0.10 to 0.191.

It is remarkable that in previous works of our research group kinetic data for hydrolysis of different alkyl esters and 4-nitrophenyl acetate did not reveal so large solvent effect in water-ethanol binary mixtures, where the rate constants at $X_{\text{EtOH}} = 0.2$ were merely 2–3 times smaller when compared to these values obtained in water [14,17]. Likewise, the sonication effects found in these works were also relatively moderate.

However, large sonication effects, accelerating the reaction up to 20 times, were observed for solvolysis of 2-chloro-2-methylpropane in water-ethanol solutions [12,13]. On the other hand, the addition of ethanol decreased the rate of this reaction by several orders of magnitude, thus revealing considerable solvent effects.

In summary, it was revealed that large kinetic sonication effects could be observed if the influence of solvent is significant and small sonication effects could be observed in the case of small solvent effects.

4.1.1. Reaction rate levelling by ultrasound

Interestingly, it appeared from Figure 2 that the reaction rate was almost independent of the solvent composition if measured under sonication in the region of acetonitrile mole fraction above $X_{\text{MeCN}}=0.10$.

We have found a similar rate levelling effect of ultrasound, using earlier experimental data of our research group [14,15] by analysing the plot of the rate constants of the acid-catalysed hydrolysis of ethyl acetate vs. mole fraction of ethanol (**Paper III**, *Fig.4*). The rate constant under sonication at $X_{\text{EtOH}} = 0.25$ was around $6.5 \times 10^{-5} \text{ s}^{-1}$. Despite the large scattering of rate constants, it was obvious that the reaction rate measured under sonication was practically independent of the composition of the solution in the region $0.06 < X_{\text{E}} < 0.30$.

Further, in this thesis, the rate levelling effect of ultrasound was also observed in the pH-independent hydrolysis of 4-nitrophenyl chloroacetate, studied in water and in 1 mol% (the molar fractions equal to 0.01) solutions of ethanol, 1-propanol and 1-butanol (see **Paper I**). However, differently from these data, the observed rate of the hydrolysis decreased in the presence of aliphatic alcohols the rate constants were not different under ultrasound. It can be seen in Figure 3 that ultrasound was able to disturb interactions between ester and co-solvent molecules regardless of the alcohol structure.

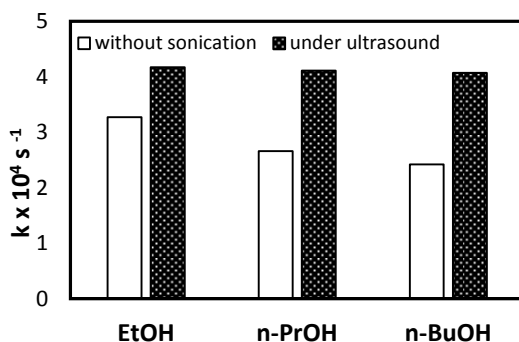


Figure 3. Diagrammatic representation of the rate constants for the hydrolysis of 4-nitrophenyl chloroacetate without sonication and under ultrasound. The alcohols were present as co-solvents in 1 mol% amount. The initial concentration of the ester was 10^{-5} M .

Since in earlier works in the field, the results of ultrasonic kinetic investigations on polar homogeneous reactions were interpreted on the basis of sonication effects, ($k_{\text{son}}/k_{\text{non}}$) (see Figure 1), the reaction rates measured under ultrasound did not receive so much attention. However, already in 1997, Tuulmets [18] analysed experimental kinetic data of Mason's group [12,13] for the solvolysis of 2-chloro-2-methylpropane in aqueous ethanol and pointed out that the reaction rate measured under sonication depended only marginally on the solvent composition, and extrapolation of sonication data to pure water resulted in an almost negligible sonication effect (See **Paper IV**, *Fig.6*). This phenomenon was interpreted as a consequence of the shift of the solvation equilibria under the influence of sonication.

It can be concluded that in aqueous-organic binary solvents, independently of the solvent composition, the ultrasonic irradiation changes solvation of reagents and results in their identical solvation states. Macroscopically, this is manifested by the reaction rate levelling effect. Obviously, the level to which the rates of a reaction are approaching is determined by the applied acoustic power and other experimental conditions. However, the phenomenon of rate levelling by ultrasound contributes significantly to understanding of the sonication effects on polar reactions in aqueous organic binary solutions.

4.1.2. Kinetic sonication effects in light of MD simulation

To obtain better insight into the kinetic sonication effects discussed in the previous sections, we invoked molecular dynamics (MD) simulations, and this analysis was technically implemented by Dr A. Kuznetsov. Details of the method of MD simulation were described in **Paper III** and **IV**.

The MD simulations provided valuable molecular level information about structure of water-acetonitrile and water-ethanol solutions of ethyl acetate, which was selected as a model ester to facilitate interpretation of simulation outputs. The selection of the model ester was guided by two points. Firstly, Rispens et al have used MD simulation to study the effect of hydrophobic co-solutes (2-methyl-2-propanol and ethanol) on the hydrolysis of 4-methoxyphenyl dichloroacetate in water, and hinted that the presence of phenyl ring complicated interpretation of the obtained results. Secondly, it was taken into consideration that our research group has previously studied the ultrasound effect on the acidic hydrolysis of ethyl acetate in aqueous ethanol, and contrasting these experimental data with the results of MD simulations could help to explain the kinetic sonication effects at the molecular level. Evidently, the conclusions made for ethyl acetate should apply to other esters at least on the qualitative level.

A set of co-solvent-water mixtures containing 500 molecules in corresponding simulation boxes and involving 1 molecule of ethyl acetate in each were examined. Thus, the concentration of the ester in these cubes was about 0.056 M. Two different solvent systems, in composition regions in which the smallest and the greatest ultrasound effects were observed, were chosen for the

simulation for both co-solvent-water mixtures. The greatest sonication effect, $k_{\text{son}}/k_{\text{non}}$, was measured for the pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate in water-acetonitrile mixture at $X_{\text{MeCN}} = 0.20$, while at region of $X_{\text{MeCN}} = 0.06$ marginal sonication effect was observed (Figure 2). In the case of the acid catalysed hydrolysis of ethyl acetate corresponding regions of ethanol molar fractions were $X_{\text{EtOH}} = 0.25$ and $X_{\text{EtOH}} = 0.08$ (see **Paper III**, Fig. 4).

The most important conclusion from these calculations was as follows: the ester molecule was preferentially solvated by co-solvent in all studied co-solvent-water binary mixtures. Although this solvation of the solute molecule builds up a specific solvent cluster, which is different from the clusters in the bulk solution, this conclusion does not contradict the cluster model for binary water-organic solvents (see Chapter 2). This was evident from the radial distribution functions, which showed remarkable selectivity of solvation. However, a closer look at these results revealed somewhat different solvation patterns in acetonitrile and ethanol aqueous solutions.

In Figure 4 intermolecular atom-atom pair correlation functions (radial distribution functions) $g(r)$ are shown for the interaction between the carbonyl carbon of ethyl acetate and the methyl carbon of acetonitrile and for the interaction between the carbonyl carbon of ethyl acetate and the oxygen atom of water. Panel A in Figure 4 displays $g(r)$ functions for the solution containing 6 mol% of acetonitrile, while in Panel B the same functions for 20 mol% of acetonitrile are represented. The abundance of acetonitrile relative to water in the first solvation shell grows fast with the increase in the molar ratio of the co-solvent in the bulk solution. In parallel to the displacement of water by acetonitrile in the first solvation shell, the formation of a distinct second solvation shell takes place.

As estimated from the areas of peaks integrated to $r = 6.3 \text{ \AA}$, the ratio of acetonitrile to water in the first solvation shell, in terms of radial distribution functions, was 1.7 at 6 mol% of acetonitrile in the solution and 2.33 when the content was 20 mol%. It can be seen from Figure 4A that in the 6 mol% solution of acetonitrile the second solvation shell extends to $r \approx 9 \text{ \AA}$ with no striking excess of acetonitrile to water. However, the second solvation shell at 20 mol% of acetonitrile stretches at least to $r \approx 10 \text{ \AA}$ holding the ratio as great as 1.24.

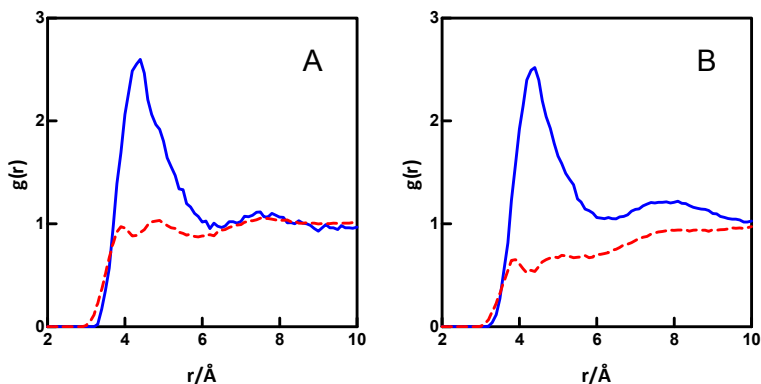


Figure 4. Intermolecular atom-atom pair correlation functions $g(r)$ for the interaction between the carbonyl carbon of the ethyl acetate and the methyl carbon of acetonitrile (solid line) and for the interaction between the carbonyl carbon of the ethyl acetate and the oxygen atom of water (dashed line) in water-acetonitrile binary mixtures at 300 K. A: 6 mol% of acetonitrile, B: 20 mol% of acetonitrile in the solution.

In Figure 5 the results of MD simulation of the ester solution in water-ethanol mixture with $X_{\text{EtOH}} = 0.08$ (8 mol%) (Panel A) and 0.25 (25 mol%) (Panel B) were presented for comparison. Figure 5 displays intermolecular atom-atom pair correlation functions $g(r)$ for interaction between the carbonyl carbon of the ester and the β -carbon of ethanol and for interaction between the carbonyl carbon of the ester and the oxygen atom of water. The solvation shell of the ester is broader than that in acetonitrile solutions, extending to $r \approx 7 \text{ \AA}$, but is somewhat poorer in the co-solvent: the ratios of the $g(r)$ functions were 1.32 and 2.1, respectively. The second solvation layer was hardly discernible in this case.

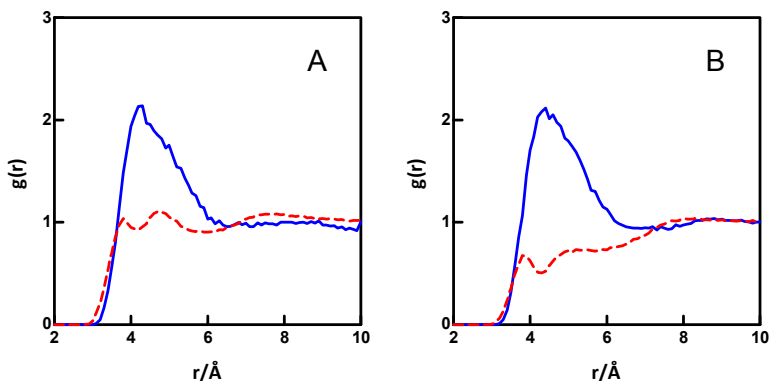


Figure 5. Intermolecular atom-atom pair correlation functions $g(r)$ for the interaction between the carbonyl carbon of the ester and the β -carbon of ethanol (solid line) and for the interaction between the carbonyl carbon of the ester and the oxygen atom of water (dashed line) in the water-ethanol binary mixtures at 300 K. A: 8 mol% of ethanol, B: 25 mol% of ethanol in the solution.

Addition of ethanol to the aqueous solution of ethyl acetate consistently decreased the rate of hydrolysis of the ester (**Paper III, Fig. 4**). It can be seen in Figure 6 that the rate constant depended almost linearly on the ethanol-to-water ratio in terms of radial distribution functions for the first solvation shell. This finding highlighted the paramount importance of the preferential solvation of substrates. Attendance of water is inevitable for the reaction to occur. An increase in the ethanol content in the solvation shell resulted in decreased water activity in the microenvironment and, accordingly, in a decreased reaction rate.

Similarly, the above-described mode of solvation of the ester in water-acetonitrile solutions can be taken as the main reason of the dramatic drop in the reaction rate with an increase in acetonitrile content in the solution (see Chapter 4.1, Figure 2). Although acetonitrile exceeds ethanol by polarity, it cannot replace water either as an electrophilic or as a basic catalyst, both being essential for the hydrolysis reaction, while ethanol is able to do that to some extent. Moreover, the presence of the two sequential solvation shells enriched in the co-solvent limited the access of water to the reaction centre.

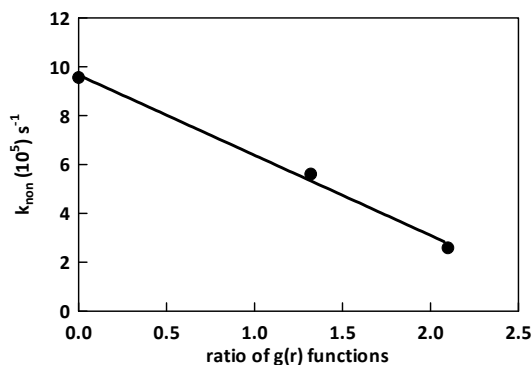


Figure 6. Rate constants of the acidic hydrolysis of ethyl acetate plotted vs. ethanol/water ratio in terms of $g(r)$ functions for the first solvation shell of the ester.

We have analysed the MD simulations data performed in the system corresponding to 25 mol% of ethanol at 280 and 330 K. The $g(r)$ functions presented in Figure 7 convincingly show that by rising of temperature, ethanol molecules were to a great extent replaced by water in the first solvation shell. With the temperature increase from 280 K to 330 K the $g(r)$ ratio for ethanol/water decreased from 2.17 to 1.66. This is in full accordance with the principle of thermo-solvatochromism [35] which predicts depletion in the solvation shell of the organic solvent at high temperature.

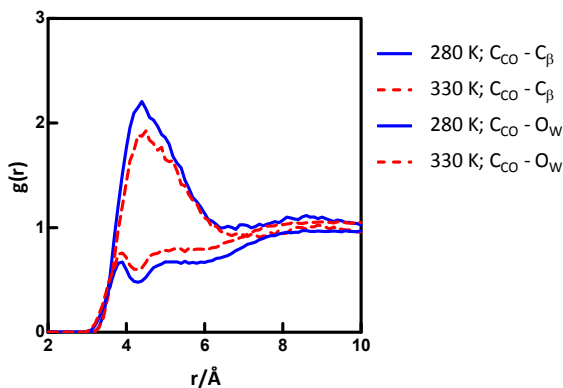


Figure 7. Intermolecular atom-atom pair correlation functions $g(r)$ for $C_{CO} - C_{\beta}$ interaction between the carbonyl carbon of the ester and the β -carbon of ethanol and for $C_{CO} - O_W$ interaction between the carbonyl carbon of the ester and the oxygen atom of water at 280 K (solid line) and 330 K (dashed line). Composition of the solvent $X_E = 0.25$ simulated.

As follows from the MD analysis, rise of temperature is accompanied by a noticeable exchange of alcohol molecules to water in the first solvation shell, and therefore the reaction rate should also increase. The same principle can be used to explain the sonication effect on ester hydrolysis rate in ethanol-water mixtures: ultrasound causes noticeable exchange of ethanol for water molecules in the first solvation shell, and therefore an increase in the reaction rate can be observed.

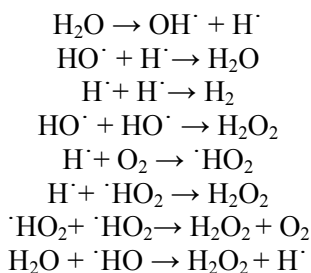
It is relevant to mention that all kinds of external forces, including those arising from cavitation, can change the kinetic energy of species in the solution. Ultrasound can act via the pressure waves of sound as well as via the shock waves generated by the bubble collapse. In each case, species or aggregates of molecules obtain enhanced kinetic energy. In the case of acetonitrile aqueous system, more facile destruction of the diffuse second solvation shell of the ester molecule occurred in the region of $0.08 < X_{MeCN} < 0.20$ and rearrangement of the remaining solvent layer by sound waves may explain the sonication effect in ester hydrolysis reactions as well the rate levelling taking place in acetonitrile-water mixtures.

Clearly, the power ultrasound does not completely break down the solvent shells or clusters of molecules, as was previously believed [8–10]. In contrast to this, ultrasound merely evokes shifts in the solvation equilibria of species that is, however enough to control rate of ionic reactions. As this control takes place through control of weak interactions between reacting species in water solutions, this phenomenon may have rather complex impact on living organisms, much more complex than the destructive effects caused by cavitation phenomena.

4.2. Impact of ultrasound in absence of the cavitation

In the Chapter 4.1 sonication effects for the pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate in acetonitrile-water binary mixtures were presented for two different input energies (Table 1). These results revealed that the kinetic sonication effects determined at two distinct powers of ultrasound did not differ noticeably. To cast light upon reasons of such result, a more detailed examination of the impact of sonication intensity on reaction rates was carried out and kinetic sonication effects were determined for the model reaction in solvent mixtures containing 10 wt% and 25 wt% of acetonitrile at irradiation intensities corresponding to 7, 10, 20, 30, 40, and 50% of the maximal input energy.

In parallel, at the same irradiation levels responses of the potassium iodide (KI) and the terephthalic acid (TA) dosimeters were registered. These dosimeters monitor radicals generated in the process of formation and/or collapsing of cavitation bubbles. Under these conditions water decomposes into H and OH radicals, which may undergo a series of reactions as shown in Scheme 1 [5].



Scheme 1. Sonochemical generation and recombination of radical species in water [5].

The TA dosimeter is specific for HO[·] radicals, which react with terephthalate anions and form highly fluorescent 2-hydroxyterephthalic acid (HTA). This highly sensitive dosimeter is most often used for determining the cavitation threshold [36]. The KI dosimeter is susceptible to H₂O₂[·], HO₂[·], and other species listed in Scheme 1, and formation of I₃⁻ as the end product can be monitored with UV/Vis detector [36].

Application of these both dosimeters in our on-line system revealed that the results of both tests were linear to the sonication intensities expressed in per cents of the input energy of the equipment (**Paper V**, *Fig. 1*). More importantly, the dosimeters started to indicate formation of radicals at sonication intensity that was higher than 10% of the input energy, pointing to the fact that no cavitation occurred in the solutions irradiated at 10% or at lower input energies

(Figure 8). Therefore it was rather interesting to compare the results of dosimetry with kinetic sonication effects represented in Figure 8.

Usually kinetic data obtained for reactions in solutions do not permit to discern the true acoustic-field effects from those caused by shock waves produced by cavitation and other cavitation phenomena [8–10]. However, as seen in Figure 8, clear kinetic sonication effect emerged at very low irradiation intensities, and was half as great as the maximum value at 10% of sonication power, where cavitation was not detectable. This means that significant kinetic sonication effect can be observed below the cavitation threshold. In other word, the results provided experimental evidence for possibility of kinetic sonication effects in the absence of cavitation.

There is no consensus among investigators in establishing the threshold of cavitation, and estimations made by different authors cover a vast region of intensities e.g. relatively great thresholds in water from 0.4 to 4 W/cm² have been suggested [37]. In this work the calorimetrically estimated energy of the ultrasound at 50% input energy was 1.6 W/150 mL in water. If recalculated for the dimensions of the reaction cell, this energy was equivalent to intensity around 0.2 W/cm². However, attempts to use the calorimetric measurements at 10% of input power were not successful, as experimental uncertainties were too large.

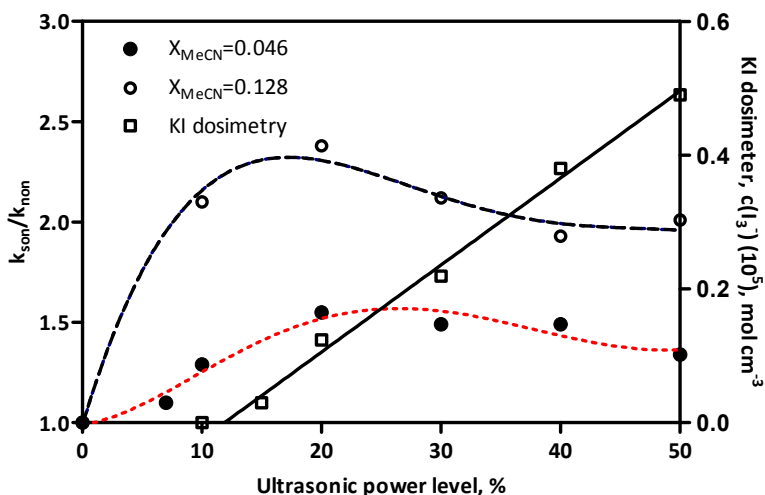


Figure 8. The kinetic sonication effects for the pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate in acetonitrile-water binary mixtures containing 10 wt% (●) and 25 wt% (○) of acetonitrile and the responses of KI (□) dosimeter in acetonitrile-water binary mixtures containing 10 wt% acetonitrile versus the sonication intensities expressed in per cents of the input energy of the equipment.

As can be seen in Figure 8, the kinetic sonication effects in both investigated solutions, after passing the maximum at the 20% power, decrease with an increase in the supplied acoustic power. Generally, for any sonochemical process, there is an optimum power for the maximum effect [38]. An effect, where the efficiency of sonication power suddenly decreases above a certain level, is known as the decoupling [38]. A classical example provided in Ref. [38] is the KI dosimeter [39]. The initial iodine yield in the sonochemical oxidation of iodide anion to iodine first increases in a linear mode above the cavitation threshold but then reaches a plateau before decoupling sets in and the yield drops dramatically, despite the increased irradiation power.

As an example of ionic reactions in solutions, Fogler and Barnes have reported about sharp maxima in the yield of acid-catalysed hydrolysis of methyl acetate at varied sonication power and temperature [40]. Similarly, Lorimer et al have found optimum power levels for the solvolysis reaction of 2-chloro-2-methylpropane in water-ethanol binary mixtures [13].

What concerns our results presented in Figure 8, the dosimetric measurements exclude any decoupling in the region of applied power. It is obvious, that with increasing cavitation in the solution the kinetic sonication effect upon the hydrolysis reaction gradually decreases. Consequently, a disturbing action of cavitation on the ultrasonic acceleration of the reaction can be inferred in this case. This conclusion has definitely a general importance for understanding the impact of ultrasound on non-radical reactions taking place in solutions, the biochemical processes included.

The mechanism of the interaction between cavitation and the acoustic field is still obscure and needs elucidation at the molecular level. The explanation presented by Fogler and Barnes [40] in terms of the Rayleigh collapse time for the cavitating bubbles can hardly be applied to ionic reactions proceeding in the bulk solution as the mode of the ultrasound has been discussed in earlier works [14,18].

It has been suggested recently that ultrasound may become a useful tool to reveal and investigate subtle interactions in solutions [8–10]. Now we can stress more definitely that the ultrasound of very low intensity is capable to control reactions by affecting weak interactions in solutions. More specifically, disposal of sonication effects in the absence of cavitation opens new perspectives for investigation of biochemical reactions with assistance of ultrasound at no risk of damaging the enzymes by cavitation.

5. CONCLUSIONS

In the present work kinetics of the pH-independent hydrolysis of 4-methoxyphenyl dichloroacetate was investigated with and without ultrasonic irradiation in water-acetonitrile binary mixtures with molar ratios of acetonitrile from 0.008 to 35 wt% and the kinetic sonication effects ($k_{\text{son}}/k_{\text{non}}$) were calculated. All experiments were carried out with a unique on-line system designed for this study.

Our results revealed that addition of acetonitrile to the reaction medium substantially decreased the rate of hydrolysis of the ester, while rate constants determined under ultrasound showed little susceptibility to changes in solvent composition. Evidently, the size of kinetic sonication effects is related to the size of solvent effects.

In parallel, MD simulations of the structure of the water-ethanol and water-acetonitrile solutions were performed with ethyl acetate as the model ester to cast light on solvent effects in aqueous-organic solutions. Ethyl acetate was preferentially solvated by co-solvent in all of these cases, however, the different solvation patterns in acetonitrile and ethanol aqueous solutions were found.

MD simulations of ethyl acetate solution in aqueous ethanol medium were performed at 280 K and 330 K. With increasing temperature, a significant proportion of alcohol molecules were replaced by water molecules in the first solvation shell. This result confirmed the principle of thermo-solvatochromism, which predicts depletion of the solvation shell of the organic solvent with rising temperature. The addition of ethanol to the aqueous solution of ethyl acetate decreased the rate of hydrolysis of the ester. It was found that the decrease of the reaction rate was almost linearly related to the increase in the ethanol content in the first solvation shell of the ester.

The abundance of acetonitrile relative to water in the solvation shell grew fast with the increase in the co-solvent content in the bulk solution. In parallel to this, the formation of a second acetonitrile-rich solvation shell was observed. This mode of ester solvation caused dramatic drop in the reaction rate with the increase in the acetonitrile content in the reaction mixture, as enhanced co-solvent content in the solvation shell decreased water activity in the microenvironment and lowered reaction rate.

The principal conclusion from the MD simulation study was that ultrasound enhanced the kinetic energy of molecules and through this effect shifted solvation equilibrium and affected reaction rate. At the same time it appeared that ultrasound did not completely break down the solvent shells or clusters in the solution, as was believed previously. In contrast to this, application of high energy was not required to affect reaction rates.

The rate levelling effect, observed in aqueous-organic binary solvents under ultrasound radiation, was independent of the solvent composition, pointing to almost identical solvation state of the reagents that could explain this rate levelling phenomenon.

Finally, significant kinetic sonication effects were found at the intensity of irradiation that was not capable to induce cavitation in the solution. This result provided direct experimental evidence that the observed kinetic effects of ultrasound could occur without cavitation. This finding could lead to a principal extension of the sonochemical method and could open new perspectives for the physicochemical investigations into variety chemical and biochemical processes.

6. SUMMARY IN ESTONIAN

Kineetilised ultraheliefektid vesi-atsetonitriil solventsegudes

Tänapäeval leiab ultraheli laialdast rakendust nii laborites kui tööstuses tänu ainulaadsele kavitatsioonifenomenile, mis kiirendab ja soodustab mitmeid keemilisi ja füüsikalisi protsesse. Peale mehhaaniliste efektide võib ultraheli initsieerida mitmeid homogeenseid ja heterogeenseid reaktsioone, genereerides selleks vabu radikaale. Vastavalt kehtivatele sonokeemia tõekspidamistele, ei tohiks homogeenne polaarne (iooniline) reaktsioon, mis pole võimeline ümberlülituma radikaalsele rajale, olla tundlik ultraheli suhtes. Siiski on teada mitmeid näiteid ultraheli toimel kiirenenud homogeensetest polaarsest reaktsioonidest (enamasti hüdrolüüsi ja solvolüüsi reaktsioonid). Ultraheliefekte on peamiselt täheldatud vesi-orgaaniliste segasolventide kasutamisel reaktsioonikeskkonnana. Intuitiivselt arvati, et heliefektid on seotud ultraheli solvendi-struktuuri lõhkuva toimega, mistõttu muutub solvatatsioon soodsamaks ja reaktsiooni kiirus kasvab. See arvamus leidis kinnitust ka antud töös, kuid juba molekulaarsel tasandil.

Viimaste kümnendite jooksul on üritatud järk-järgult kirjeldada vesi-orgaanika, iseäranis vesi-alkohol süsteemide vägagi komplitseeritud struktuure. Teatavasti teeb vesi-orgaaniliste solventide struktureeritus läbi suured muutused üleminekul veest puhtasse alkoholi. Eksperimentaalselt on tõestatud mikrokoopiline faasieraldus, kus laias segukoostise vahemikus eksisteerivad koos veerikkad ja etanoolirikkad klastrid. Sellisest klastrimudelist lähtudes tehti varasemalt oletus, et nt estri hüdrolüüsil vesi-etanool segus võib ester olla peidetud etanooli klastri hüdrofoobsesse sisemusse, mistõttu reaktsiooni kiirus väheneb. Ultraheli, lõhkudes klastri, vabastab substraadi ja reaktsioon kiireneb.

Enamjaolt on kineetilised ultraheliuuringud läbi viidud vesi-etanool segudes. Käesolevas töös oli vaatluse all ultraheli mõju estri neutraalse hüdrolüüsi reaktsioonile vesi-atsetonitriil segudes. Kuna atsetonitriil on polaarsem kui etanool, kuid samas ei moodusta vesiniksidemeid, siis atsetonitriili segudes võib eeldada teistsuguseid solvendiefekte. Ultraheliuuringute teostamiseks arendati antud töös välja originaalne on-line reaktsioonikineetika mõõtmise süsteem.

Leiti, et ilma ultrahelita vähenes hüdrolüüsi kiirus ühtlaselt atsetonitriili kontsentratsiooni kasvades, samas kui ultraheliga kiiritades muutus reaktsiooni kiirus üllatuslikult vähe. Seega ultraheliefekt, k_{son}/k_{non} (ultraheliga ja ilma ultrahelita mõõdetud kiiruskonstantide suhe), suureneb solvendiefekti kasvades.

Leiti, et reaktsiooni kiiruse väike muutumine ultraheli toimel, nn tasandusefekt on üldine nähtus, kuna see esineb erinevate reaktsioonide korral ja erinevates vee ja orgaanilise solvendi segudes. Võib väita, et ultraheli toob esile reaktsiooni keskkonnas selliseid muutusi, mistõttu ultraheli all on substraadi solvatatsioon enamvähem samasugune erinevate kaassolvendi koostiste juures ja seega reaktsiooni kiirused ei muutu.

Solvatatiooni paremaks mõistmiseks vesi-orgaanilistes solventsegudes teostati molekulaardünaamika (MD) arvutisimulatsioonid etüülatsetaadile, kui mudelestrile, vesi-etanool ja vesi-atsetonitriil keskkondades. Selgus, et estri molekul on eelissolvateeritud kaassolvendi molekulide poolt kõikides uuritud segudes, kusjuures esineb erinev solvatatsioon vastavalt etanooli ja atsetonitriili korral.

Etüülatsetaadi happekatalüütilise hüdrolyüsi kiirus langeb etanooli hulga suurenemisega solventsegus. Leiti, et kiiruse vähenemine on lineaarselt seotud etanooli sisalduse kasvuga estri esimeses solvaatkihis.

Atsetonitriili korral tekkis lisaks esimesele solvaatkihile estri ümber teinegi atsetonitriilirikas solvendikiht. Kaassolvendi sisalduse suurenemine solvaatkattes põhjustab vee aktiivsuse langemist selles mikrokeskkonnas ja seega reaktsiooni kiirus kahaneb.

Etüülatsetaadi lahusele vesi-etanooli segus teostati MD simulatsioonid lisaks kahel erineval temperatuuril, 280 K ja 330 K. Temperatuuri tõustes asendus etanool esimeses solvaatkattes suures ulatuses veega. Tegemist on termosolvatokromismi nähtusega, mil temperatuuri tõustes reagendi solvaatkate vaesub orgaanilise solvendi poolest.

Kõige eelneva põhjal järeldati, et ultraheli põhjustab lahuses olevate osakeste kineetilise energia suurenemise, mis toob esile muutused substraadi solvatatsioonis ning seega mõjutab reaktsiooni kiirust. Samas ilmnes, et ultraheli ei pea ilmtingimata täielikult lõhkuma solvendi klastreid lahuses, nagu varem oletati. Vastupidi, reaktsiooni kiiruse muutmiseks ei ole vaja rakendada ekstreemseid energiasid.

Lisaks leiti märkimisväärsed kineetilised ultraheli efektid heli intensiivsustel, mis ei ole võimelised tekitama kavitatsiooni. Esmakordselt tõestati eksperimentaalselt, et kineetilised ultraheliefektid võivad esineda ilma kavitatsiooni nähtuseta. See laiendab põhimõtteliselt sonokeemilise meetodi rakendusi, võimaldades füsikokeemilisi uuringuid erinevates keemilistes ja biokeemilistes protsessides.

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