Sonochemistry of Homogeneous Ionic Reactions

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Abstract: Besides the well-known role of ultrasound in initiation and acceleration of radical reactions, this low-energy acoustic field has recently become a valuable tool for physico-chemical investigations of solvation phenomena in homogeneous ionic reactions in aqueous and aqueous-organic solutions. In this mini-review we summarize these experimental data, showing that the application of classical quantitative methods, such as reaction kinetics and correlation analysis, if combined with sonication of the reaction medium, can reveal subtle hydrophobic interactions that remain hidden in the conventional experiments. Correlation of kinetic sonication effects with substrate hydrophobicity has revealed that independent of the reaction mechanism the decrease in reaction rate with the increasing content of different hydrophobic co-solvents can be explained by the reaction ground-state stabilization, which is largely of hydrophobic origin. When ultrasound suppresses this hydrophobic stabilization of reagents, it accelerates the reaction. On the contrary, if sonication perturbs the stabilization of encounter complexes between reagents, it hinders the reaction. Many of the conclusions reviewed in this article make a contribution to the chemistry of solutions and physical organic chemistry.

Keywords: Sonochemistry, ultrasound, hydrophobic interactions, polar reactions, solvation phenomena, water-organic binary solvents.

1. INTRODUCTION

Because ultrasound (US) promotes or accelerates a wide range of chemical and physical processes [1-4], it has been used for a variety of purposes in areas as diverse as surface cleaning, food technology, medical diagnosis and therapy, chemical synthesis and sewage treatment.

There are essentially two distinct technical fields in US applications: low-power, high-frequency US (1 MHz - 10 MHz) or diagnostic US, involving non-destructive testing of materials and medical scanning, and high-power, low-frequency US (20 kHz - 100 kHz) that originated in engineering and processing to include cleaning, welding and industrial processing of materials. The latter field also includes sonochemistry, particularly organic synthesis, catalysis and fundamental studies of cavitation phenomena. Sonochemistry has proven to be an invaluable and unique tool for making nanomaterials [5], the synthesis of polymers, as well as their controlled degradation [6, 7], for green technologies [8], and, first of all, organic synthesis [9, 10].

In heterogeneous systems the mechanical effects of ultrasonic irradiation are responsible for mass transfer, surface activation of solid reagents or catalysts, the dispersion of particulate material, improved mixing, and so forth. Many homogeneous and heterogeneous reactions can be initiated or accelerated by US through the generation of free radicals that give rise to chain reactions. As this mechanism has been canonized in sonochemistry, homogeneous ionic reactions have long been confined to a marginal place in this vast domain of chemical reactivity. However, more recent applications of quantitative methods like reaction kinetics and the linear free-energy analysis, also known as correlation analysis, have lead to a better understanding of sonochemical effects also in ionic reactions, as well as in the solvation phenomena taking place in binary solvents.

2. PRINCIPAL CONCEPTS OF SONOCHEMISTRY

As US has been widely employed in chemistry and chemical technology, the background of its influence has been extensively investigated. As numerous exhaustive monographs [1-4] and reviews [9, 10, 11] have been published, (a few of which are referred to in this review), there is no need for us to expatiate on the topic. however, a short explanation of current concepts of sonochemistry seems to be useful for introducing the matter of this paper.

It is certain that sonochemical effects cannot be caused by direct impact of the acoustic field on the reacting molecules since the energy of US is too low to alter their electronic, vibrational, or rotational states [1-4]. The effect of US has been explained by the "hot spot" theory, which assumes the involvement of cavitation bubbles. Like any kind of sound, US is transmitted by waves that alternately compress and stretch the medium through which it travels. During a rarefaction phase, when a liquid is subjected to a large negative pressure, intermolecular forces are not strong enough to maintain cohesion, hence small gas-filled cavities, called cavitation bubbles, are formed. The rapid nucleation, growth and collapse of these bubbles constitute the cavitation phenomenon. According to the "hot spot" theory, each cavitation bubble acts as a localized microreactor in which high temperatures and pressures are generated, reaching several thousand degrees and hundreds atmospheres, thus effectively concentrating within "hot spots" the diffuse energy of the sound wave [1-3]. As the nearly adiabatic bubble collapse will thus enhance molecular energy by almost nine orders of magnitude, it is no wonder that US can affect chemical reactions.

The sonochemical process is usually thought to be localized either inside the cavitation bubble or in the liquid shell surrounding it, or in both simultaneously. A general model developed by Reisse *et al.* [12] considers the cavitating liquid as heterogeneous: each collapsing bubble, acting as a closed microreactor, presents a physical environment that is quite different from that of the bulk liquid phase. However, its outer boundary is diffuse rather than definite.

Sonochemistry in solution has been often rationalized in terms of this theory: solvents that are volatile enough can be vaporized into the bubble where they will undergo pyrolytic cleavage to form radicals or excited chemical species (Fig. **1**). These may induce subsequent reactions with less volatile substrates at the bubble shell or, perhaps most frequently, in the bulk medium. It is hardly possible to conceive of a neat heterolytic reaction in the gas-face of the bubble, however, such reactions can take place in the liquid shell.

It is important to mention that intense shock waves form upon the collapse of cavitation bubbles, causing various mechanical actions. These are the mainstays of the explanation of sonochemical effects on heterogeneous processes (enhanced reaction rates and yields), which often do not differ from those obtained by the use of a high-speed stirrer [13].

Chemical effects of US will only occur if the particular reaction is the sonication-sensitive step or when the active species released

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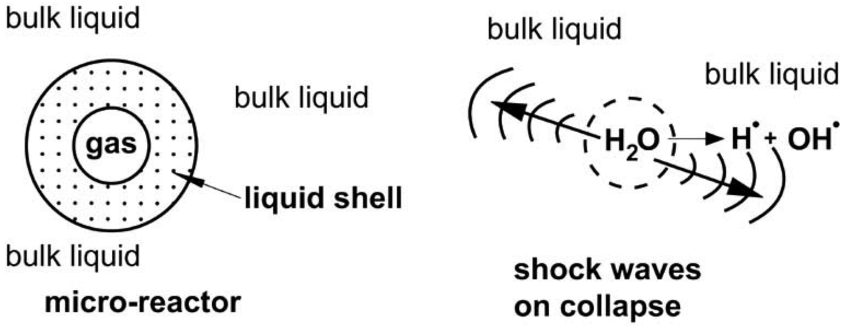

Fig. (1). Cavitation bubble as a chemical microreactor: cleavage of a water molecule to free radicals that are transferred to the bulk liquid, as well as formation of shock waves on collapse are schematically depicted.

from cavitational collapse participate as reaction intermediates. Luche *et al.* [14] have distinguished sonochemical applications resulting from "true" or "false" effects: the former are real chemical effects induced by cavitation ("true sonochemistry"), while the latter can be mainly ascribed to the mechanical impact of bubble collapse. A set of empirical rules have been established to tell them apart [4, 14]. While Rules II and III by Luche concern heterogeneous reactions, the Rule I states that homogeneous reactions activated by sonication are those proceeding via radical or radical-ion intermediates. Thus, acording to Luche [14] homogeneous ionic reactions should not be affected by sonication.

However, examples of ultrasonic acceleration of homogeneous ionic reactions, albeit not numerous, had been reported already before the formulation of the Rules. Although they provided a challenging puzzle, scarce attention was paid to them by sonochemists until recently, perhaps because these reactions profit but slightly from the use of sonication in comparison with synthetically important ones.

3. HOMOGENEOUS IONIC REACTIONS ACCELERATED BY ULTRASOUND

According to current tenets of sonochemistry (*vide supra*), an ionic reaction which cannot be switched to a radical pathway should not be susceptible to US effects. However, several examples of homogeneous polar reactions accelerated by US have been found, mostly hydrolysis and solvolysis reactions that have been kinetically investigated for sonication effects. In the first paper of this kind [15], published in 1953, the acid-catalyzed hydrolysis of ethyl acetate in aqueous solution was studied at three frequencies and various energy levels. The sonication effect was very small but in several cases it exceeded the experimental error.

Later, the acid-catalyzed hydrolysis of methyl acetate was investigated by three groups [16-18] under similar experimental conditions; the kinetics was followed by titration of the formed acid. The reaction was performed in water without sonication and under sonication at 23 kHz [16], at 27.5 kHz [17], and at 540 kHz in a water-acetone binary solvent [18]. The sonication effect was low to moderate, the rate enhancement not exceeding 60%.

Under conditions affording more pronounced sonication effects, a manifold acceleration of the acid-catalyzed hydrolysis of ethyl acetate in water was attained at 22 kHz [19]. However, later investigations found that sonication effects did not exceed 30% in a water medium containing 0.25 mol % of 2-butanol as the internal standard for GLC measurements [20, 21].

A still lesser effect by US (14-15%) was reported for the alkaline hydrolysis of 4-nitrophenyl esters of several aliphatic carboxylic acids in a water-acetonitrile mixture [22]. Kinetics were followed by spectrophotometric monitoring of 4-nitrophenol formation. Similarly, for the base-catalyzed hydrolysis of 4-nitrophenyl acetate in water accelerations in the 10-12% range were found [23].

The hydrolysis of phthalic acid esters in aqueous solution was performed under US at 200 kHz [24]. Moderate US-accelerations were found over the 4-13 pH range.

In contrast to these findings, an ultrasonic acceleration by 2 orders of magnitude was reported by Hua *et al.* [25] for the hydrolysis of 4-nitrophenyl acetate in aqueous solution over the pH range of 3 - 8 at 20 kHz. However, the reliability of their experimental procedure has been questioned and just a moderate ultrasonic acceleration was found by Ando *et al.* [26]. Later on, the comparative use of titanium and quartz immersion horns [23] allowed such a disagreement of experimental results to be rationalized. We can now conclude that the very large accelerations observed by Hua *et al.* were not merely due to direct effects of US but also involved a considerable contribution from catalytic effects probably due to metal traces from titanium horns [23].

It is remarkable that only negligible to small sonication effects have been found in water, whether pure or in mixtures with organic solvents of low ability to form hydrogen bonds. However, large sonication accelerations (up to 20 times) were observed conductometrically by Mason’s group for the solvolysis of 2-chloro-2-methylpropane (*tert*-butyl chloride) in ethanol-water [27-30], isopropanol-water [28] and *tert*-butanol-water [28] (Fig. **2a**). Surprisingly, these effects showed a nonlinear dependence on the composition of the aqueous binary mixtures. For example, at 10^{o}C under US the solvolysis rate in 20 wt% ethanol was twice that found in the absence of irradiation, whereas at 40% and 60% ethanol the rate increases were six- and 20-fold, respectively.

The solvolysis of 1-bromo-1-phenylethane in ethanol-water mixtures was studied by others [31] who also observed an ultrasonic acceleration. Kinetic investigation of sonication effects in water-organic binary mixtures, mainly water-ethanol, was recently reopened by the research group at the University of Tartu [20, 21, 23, 32-34]. Acid-catalyzed hydrolysis of alkyl esters (Fig. **2b**) in water-ethanol and in water-1,4- dioxane binary mixtures were studied [20, 21, 34]. For an example, see Table **1**. The base-catalyzed hydrolysis of 4-nitrophenyl acetate (Fig. **2c**) [23] as well as the benzoin condensation of benzaldehyde in water and in ethanol-water binary mixtures [32, 33] were also investigated for sonication effects.

As already observed in solvolysis reactions in water-alcohol mixtures, nonlinear dependences of kinetic sonication effects (k_{son}/k_{non}) on the composition of water-organic binary mixtures were found. A few examples are presented in Fig. (**3**).

Results of this extensive investigation led to a number of important conclusions about the mechanism of sonication effects for homogeneous ionic reactions as well as on the nature of solvation phenomena in aqueous-organic systems, thus crossing the frontiers of conventional sonochemistry.

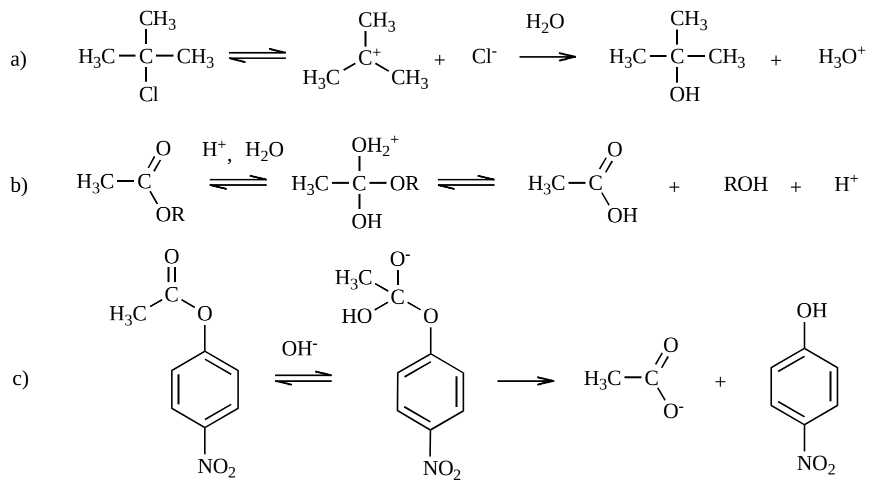

Fig. (2). **a**) Solvolysis of 2-chloro-2-methylpropane; **b**) acid-catalyzed hydrolysis of an alkyl acetate; **c**) base-catalyzed hydrolysis of 4-nitrophenyl acetate.

Table 1. Results of Kinetic Measurements for the Acid-catalysed hydrolysis of Propyl Acetate at 20 °C [34]

Molar Ratio of Ethanol, X_{EtOH}	Rate Constant $k \times 10^4$ (s^{-1})		Ultrasonic Acceleration, (k_{son}/k_{non})
	k_{non}	k_{son}	
0.042	0.89	1.42	1.59
0.055	0.97	1.41	1.44
0.089	0.99	1.20	1.21
0.144	0.75	0.74	0.99
0.207	0.66	0.93	1.41
0.281	0.64	1.11	1.75

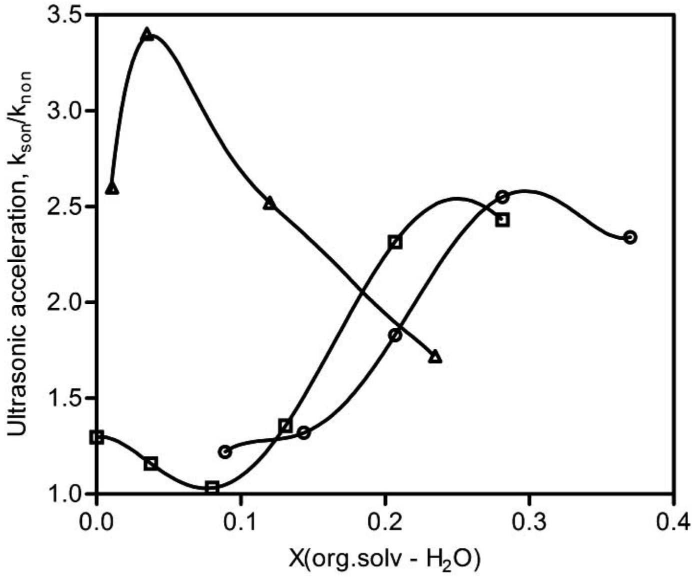

Fig. (3). Rate enhancements induced by ultrasonic irradiation in water-organic binary solvents (X is the molar ratio of the organic component in the mixture).
Δ- acid-catalyzed hydrolysis of ethyl acetate in 1,4-dioxane-water mixtures at 18°C [21]
□- acid-catalyzed hydrolysis of ethyl acetate in ethanol-water mixtures at 18°C [20]
○- solvolysis of *tert*-butyl chloride in ethanol-water mixtures at 20°C [29]

4. INFERENCES FROM THE OBSERVED SONICATION EFFECTS

4.1. Hydrophobic Interactions

A crucial step in developing a green chemical process in solution is the choice of a safe, non-toxic and cheap solvent [8]. Water is rarely considered as the solvent of choice in synthetic organic chemistry, not only because it is a poor one for nonpolar compounds but also because it is a relatively reactive compound. Despite these hurdles, organic chemists have recently become quite interested in water as a reaction medium. This interest also arises from the fact that the reactivity of some compounds and the course

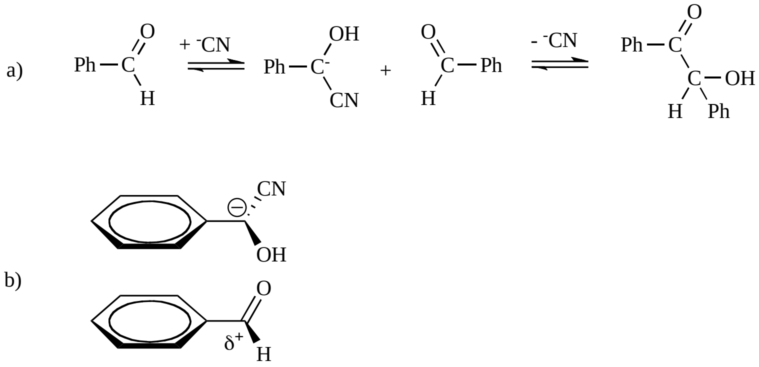

Fig. (4). Mechanism of the benzoin condensation of benzaldehyde (**a**); stacking of the benzene rings in the rate-determining step (**b**).

of some chemical reactions often benefit from the unique properties of liquid water, mainly resulting from its small molecular size, three-dimensional hydrogen-bond network and strong hydrophobic interactions to which amphiphilic species are subjected when dissolved in it [35-37]. The most recent developments like the "on-water chemistry" pioneered by Sharpless *et al.* [38] deserve serious attention (for a review see [39]).

Solvation of reactants is one of the most important factors governing the rates of polar reactions [40]. In binary solvents the dependence is complicated by the occurrence of selective solvation. This means that the composition of the solvation shell around reacting species is different from that of the bulk solvent. In solvents that can form hydrogen bonds the structure of the medium is also of great importance [41].

Pressure waves associated with the propagation of US as well as shock waves generated during bubble collapse can affect the medium. Evidently, sonication can cause changes in the translational energy of species, thus breaking down solvent structure or shifting solvation equilibria, or possibly doing both. Preliminary qualitative explanations of the sonochemical effects were based on these ideas of perturbation of the molecular organization of the reacting system [30, 42].

Recent spectroscopic, X-ray diffraction, and mass-spectrometric investigations have shed light on the structure of alcohol-water binary mixtures [43-45]. As regards ethanol-water solutions, these studies suggested that ethanol molecules associated and the bulk water structure broke down at $X_E>0.1$ (where X_E is the ethanol molar fraction). 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 [43, 44]. These findings led to a better understanding of sonochemical effects and to the conclusion that sonochemical accelerations could be correlated with the perturbation of hydrophobic solute-solvent interactions [23, 32, 33]. For aqueous solutions, these interactions have been much investigated recently [35-39, 46]. The formation of encounter complexes between reactants and hydrophobic cosolvents appears to be particularly important. The more hydrophobic are reagents and cosolvents (e.g. alcohols), the more will reagents be included in the encounter complexes and thus rendered less reactive.

Hydrophobic reagents can be so hidden in the clusters as to become inaccessible for the reaction. When US is able to break interactions within the hydrophobic interior of the cluster, it accelerates the reaction. In a recent work [21] ethyl, *n*-propyl, and *n*-butyl acetates were used as probes of reagent inclusion in the clusters. Indeed, the sonication effect for acid-catalyzed hydrolysis in the region $0.2<X_E<0.3$ stood in reverse correlation with the hydrophobicity of esters. As butyl acetate should have been the most effectively held by clusters, sonication was least efficient in its case. It was concluded that the accelerating effect of US is related to the perturbation of solute-solvent interactions [21].

4.2. Ultrasonic Retardation of Reactions

A logical inference from the results of kinetic sonication experiments with esters was that US should decrease, rather than increase, the rate of reactions that are promoted by hydrophobic interactions, e.g. the Diels-Alder reaction, the benzoin condensation, etc. [36-37, 47, 48]. Although an ultrasonic retardation for chemical reactions has been predicted [42], this effect had never been reported in the sonochemical literature. However, it cannot be excluded that some researchers may have encountered the phenomenon and discarded the result as due to error.

The benzoin condensation of benzaldehyde was chosen as a model, because its mechanism is well established (Fig. **4**) [49] and the reaction has been investigated in detail for hydrophobic effects [47, 48, 50]. It has been shown that it is promoted by hydrophobic packing of reactants in the transition state. In the rate-determining step of the reaction two benzene rings become stacked (Fig. **4b**), a hydrophobic interaction that is favored in aqueous media. In ethanolic solutions the stacking effect should be greatly reduced; as a matter of fact the reaction is much slower than it is in water [50].

As expected, the reaction was found to be slowed down by US [32, 33]; the effect was most pronounced in pure water (about 20%) and decreased gradually with increasing ethanol content. The observed, statistically significant decrease of the rate of benzoin condensation means that the reaction was either wholly quenched in 20% of the total volume of water solution or was hindered to a lesser extent in a larger part of the solution. This was strong evidence that a nonradical homogeneous sonochemical process occurred in the bulk solution, i.e. outside of cavitational bubbles as was predicted previously [42] and recurringly debated [21, 32]. The mode of action of US in such systems has been discussed in detail recently [21].

Breafly summarizing this issue, it has to be stressed that according to the current understanding of the matter less than 0.1% of the reaction solution is under cavitation at any instant [21, 32, 33]. This means that homogeneous ionic reactions occur in the bulk solution and an insignificant part of conversions takes place inside the cavitational bubbles (degradation processes) or at the bubble surface (radical reactions with adsorbed hydrophobic compounds). Moreover, expected products of such minor processes have not been observed in detectable amounts when sonication experiments with alkyl esters and benzaldehyde were carried out [21, 32]. Sonochemical degradation of 4-nitrophenol during kinetic measurements of the hydrolysis of 4-nitrophenyl acetate and its impact on the results have been discussed extensively [23].

Apart from fundamental conclusions above, kinetic investigations of sonochemical effects in water-alcohol binary mixtures led

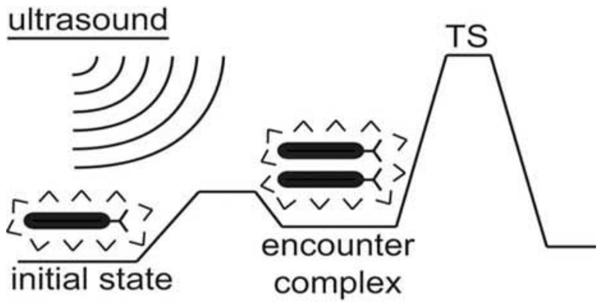

Fig. (5). Schematic representation of the energetic profile of a bimolecular reaction (TS = transition state). If US destabilizes the solvation of the reagents, it accelerates the reaction, while if it breaks down the encounter complex it will slow down the reaction.

to an important generalization which can be called the Fourth Rule of sonochemistry (a sequel to the Rules by Luche [4, 14]): if it breaks down the stabilization of the encounter complexes between the reagents, sonication decreases the reaction rate; on the contrary, if it perturbs solvent stabilization of the initial state of the reagents, it accelerates the reaction [32, 33] (Fig. **5**).

4.3. Quantitative Considerations

It has been concluded that in aqueous-organic binary solvents sonochemical effects for ionic reactions may be correlated with the breakdown of hydrophobic solute-solvent interactions [21, 23]. However, this was a merely qualitative deduction from observed sonication effects in reaction kinetics. To obtain a quantitative proof, sonication effects were further related to the Hansch-Leo hydrophobicity parameter logP [33, 51], where P is the partition coefficient of the substrate between 1-octanol and water [52, 53], by subjecting the data to linear free energy analysis [54, 55].

In Fig. (**6**) the linear free energy (LFE) relationships show how kinetic sonication effects for ester hydrolyses are related to the hydrophobic interactions of reagents with the solvent system. The plot in Fig. (**6a**) represents the relationship at X_E = 0.28 in the region of ethanol clusters, providing a convincing quantitative proof of conclusions made intuitively (*vide supra*). Plotting of sonication effects at X_E = 0.04 against hydrophobicity parameters (Fig. **6b**) also reveals a linear relationship.

The LFE test indicates that the mechanism of the sonication effect is the same for 4-nitrophenyl acetate and the alkyl acetates independent of the hydrolysis reaction mechanism (base-catalyzed *vs* acid-catalyzed reactions). In light of the sonication effects one can admit now that independent of the reaction mechanism the esters interact similarly with the solvent system. One can thus conclude that the regular decrease in the rate of ester hydrolysis with increasing alcohol content of aqueous binary solvents is mainly caused by the initial-state hydrophobic stabilization by the solvent system. This reaffirmed conclusions made by other groups for water-rich solvent mixtures [36, 37, 46, 56].

In the region X_E<0.15 (e.g., Fig. **6b**) the order of sonication effects is the reverse of that found for the region of clusters, which could be attributed to the weak solvation of esters in this range. While a greater hydrophobicity leads to stronger ground-state stabilization, hence to a decrease in reactivity, US breaks down the hydrophobic interactions almost entirely, thus causing paradoxally larger sonication effects fore more hydrophobic esters.

Recent experimental data [34] on the neutral hydrolysis of 4-nitrophenyl chloroacetate corroborated this conclusion. While the hydrolysis rate observed in the presence of 1 mol% of aliphatic alcohols decreased with increasing hydrophobicity of the co-solvent, under US the reaction rates hardly changed (Fig. **7**), thus showing a dependence of observed sonication effects similar to that in Fig. (**6b**). In other words, the applied acoustic power appeared to destroy the ester-cosolvent encounter complexes regardless of the hydrophobicity of the partners.

Kinetic sonication effects on the solvolysis of *tert*-butyl chloride in the ethanol-water binary mixtures [30, 31] were recently revisited and discussed in the light of the above conclusions [33, 51]. Ethanol in the solvent system effectively stabilizes the ground-state of *tert*-butyl chloride, leading to a dramatic decrease of the reaction rate. Sonication effects are large and increase with increasing ethanol content in the binary solvent. However, reaction rates observed under US depend only slightly on ethanol content. This indicates that in this case hydrophobic ground-state solvation is the prevalent factor. Unexpectedly (given current tenets of physical organic chemistry) other medium-related effects like polarity, electrophilicity, etc. turned out to be of lesser importance.

4.4. A Domino Effect in Understanding of Solvation Phenomena

The progress in understanding of solvation phenomena in ethanol-water binary mixtures attained through the LFE-analysis of sonication data (Section 4.3) allowed to expand the analysis to different reactions in various water-organic solvents [57].

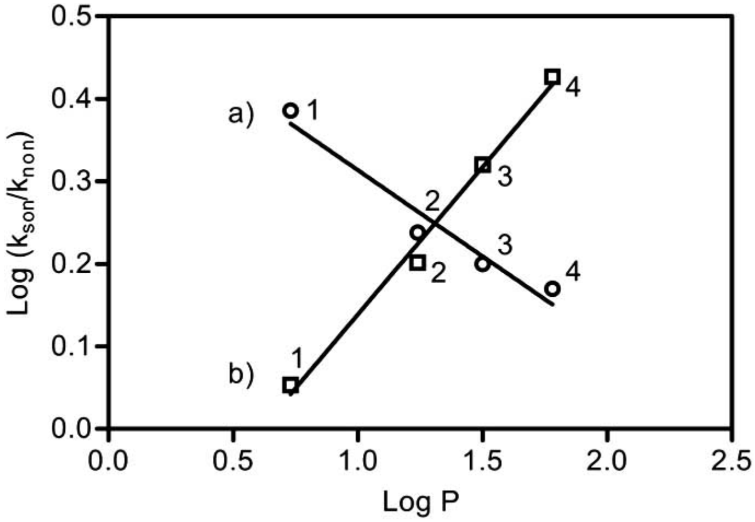

Fig. (6). Linear free energy relationships between sonication effects for ester hydrolyses and the hydrophobicity parameter (logP) for the substrates. **a** - X_E = 0.28, **b** - X_E = 0.04; 1, 2, 4: acid-catalyzed hydrolysis of ethyl, *n*-propyl and *n*-butyl acetate respectively; 3: base-catalyzed hydrolysis of 4-nitrophenyl acetate. Data from Refrs. [21], [23], and [34], normalized for sonication intensities.

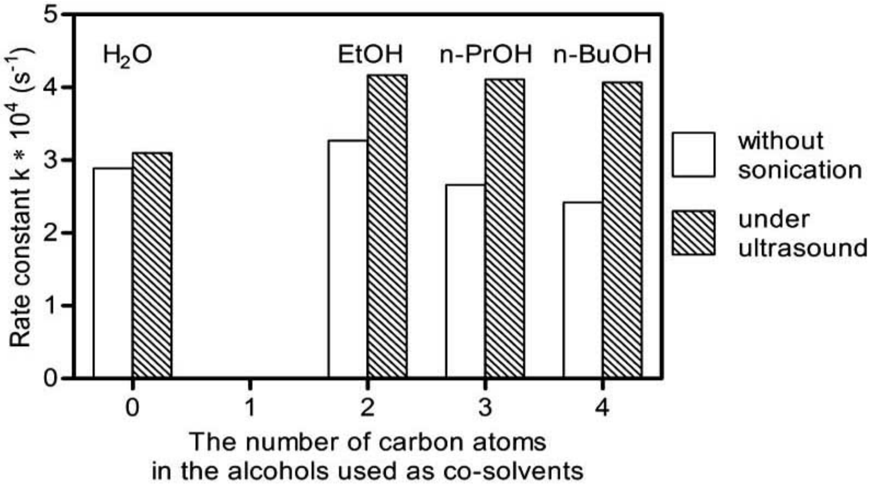

Fig. (7). Diagrammatic representation of rate constants for the hydrolysis of 4-nitrophenyl chloroacetate without sonication and under US (Ref. [34]). The alcohols are present as co-solvents in 1 mol % amount.

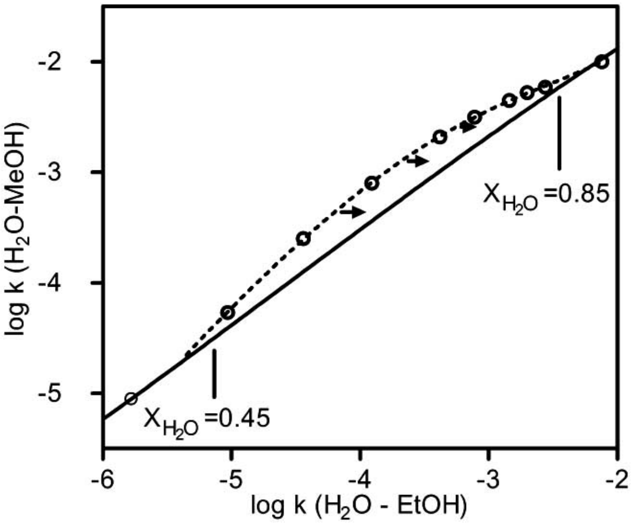

Fig. (8). Plot of log k for the solvolysis of tert-butyl chloride in water–methanol and water–ethanol binary mixtures [58]. Molar fractions of water are shown on the graph. The straight line was plotted to guide the eye and represent ideal solvation of the reagents. Arrows represent kinetic sonication effects in water–ethanol solution at the same temperature from Ref. [29].

Rate constants of reactions in aqueous organic binary solvents were correlated with those for the solvolysis of *tert*-butyl chloride in the same solvents. Correlations found were good to excellent for binary solvents ranging from water-rich systems up to mixtures with prevailing organic co-solvent, molar content of co-solvents exceeding 50 % and in several cases reaching 85 %. Numeral values of the correlation parameters reflect the susceptibility of reaction rates to changes in the solvent composition relative to solvolysis of *tert*-butyl chloride in the same binary solvent.

The most impressive conclusion from the results is the fact that good correlations have been found for such definitely different reactions as ester hydrolyses, various reactions with ionic and non-ionic reactants, a Menshutkin reaction and S_N2 replacement included. It is remarkable that all these reactions provide linear relationship with kinetic data for *tert*-butyl chloride solvolysis, an S_N1 reaction, in a wide range of the co-solvent content.

As a paramount conclusion it can be inferred that independent of substrate and reaction mechanism the nature of this phenomenon is caused by hydrophobic interactions of reagents with the reaction medium.

4.5. The Solvent Structure and Sonication Effects

Rate of the solvolysis of tert-butyl chloride in a binary solvent is nonlinear but monotonous in respect of the solvent composition and therefore does not reflect known features of the solvent structure, e.g. those in aqueous alcohols [58]. However, log k values of tert-butyl chloride solvolysis in water-methanol and water-ethanol solutions plotted against each other (Fig. **8**) [57] show a distinct deviation of points in the region of X_{H_2O} between 0.45 and 0.85. This is just the region of cluster formation in aqueous ethanol found by physical investigations [43, 45]. In aqueous methanol the cluster formation is much weaker and can be observed only at $X_{H_2O} < 0.6$ [45]. As known [21] the clusters are able to seize the reagent molecules rendering them less reactive.

It is instructive to superpose kinetic sonication effects from the work by Mason's group [29] on the graph. In Fig. (**8**), arrows represent kinetic sonication effects in water-ethanol solution at the same temperature. Evidently ultrasound breaks down the hydrophobic solvent clusters and thus brings the solvation patterns of reagents closer to each other in the solvent systems. It is not clear whether more intensive sonication would further shift the points in Fig. (**8**); similarly, sonication investigations in aqueous methanol are missing. Nevertheless, available experimental data reflect well the impact of the hydrophobicity driven solvent structure in aqueous binary solvents.

5. CONCLUSIONS AND OUTLOOK

Examples of ultrasonic acceleration of homogeneous ionic reactions have not been numerous, and until recently have attracted but scarce interest from practical sonochemists. However, the application of quantitative methods (determinations of reaction kinetics, correlation analysis, etc.) to the study of these reactions in aqueous and aqueous-organic solutions opened new perspectives for a better understanding of sonochemical processes and for broader investigations of solvation phenomena and reaction mechanisms. US has become a useful tool for physico-chemical studies, as it can reveal subtle hydrophobic interactions that remain hidden in conventional kinetic analysis. Quantitative correlation of kinetic US effects to substrate hydrophobicity has shed more light on the solvation of reagents in water-alcohol binary solutions.

An analysis of sonication data showed that independent of the reaction mechanism the decrease in reaction rate with increasing content of a hydrophobic co-solvent is mainly due to a ground-state stabilization which is largely of hydrophobic origin.

When US suppresses this hydrophobic stabilization of reagents, it accelerates the reaction; on the contrary, if sonication perturbs the stabilization of encounter complexes between reagents, it hinders the reaction.

The first experimental evidence for reaction retardation by US was found, successively providing strong evidence for ionic sonochemical processes in the bulk solution. A detailed knowledge of ultrasonic acceleration/retardation of reactions can be useful in designing processes in aqueous systems as green media and for controlling highly complex chemical processes, e.g. in the modification of proteins or in other methods of biotechnology.

The ability of US to influence reactions by affecting weak interactions between solutes also indicates that the impact of US on living organisms may involve more than simple physical and chemical destructive effects due to cavitation phenomena.

Many of these conclusions reach out beyond conventional sonochemistry and make a novel contribution to solution chemistry and physical organic chemistry.

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REFERENCES

[1] Suslick, K.S. *Ultrasound, its Chemical, Physical and Biological Effects*, VCH Publishers: New York, **1990**.

[2] Mason, T.J.; Peters, D. *Practical Sonochemistry. Power Ultrasound: Uses and Applications*, Ellis Horwood: Chichester, **2002**.

[3] Mason, T.J.; Lorimer, J. *Applied Sonochemistry: Uses of Power Ultrasound in Chemistry and Processing*, Wiley-VCH: Weinheim, **2002**.

[4] Luche, J.L. *Synthetic Organic Sonochemistry*, Plenum Press: New York, **1988**.

[5] Gedanken, A. Doping nanoparticles into polymers and ceramics using ultrasound radiation. *Ultrason. Sonochem*., **2007**, *14*, 418-430.

[6] Price, G.J. In: *Advances in Sonochemistry*; Mason, T.J. Ed.; JAI Press: London, **1990**; Vol. *1*, pp. 231-285.

[7] Cravotto, G.; Cintas, P. Molecular self-assembly and patterning induced by sound waves. The case of gelation. *Chem. Soc. Rev.*, **2009**, *38*, 2684-2697.

[8] Mason, T.J.; Cintas, P. In: *Handbook of Green Chemistry & Technology*; Clark, J.H.; Macquarrie, D.J. Eds.; Blackwell: Oxford, **2002**;.pp. 327-396.

[9] Barge, A.; Tagliapietra, S.; Tei, L.; Cintas, P.; Cravotto, G. Pd-catalyzed reactions promoted by ultrasound and/or microwave irradiation. *Curr. Org. Chem.*, **2008**, *12*, 1588-1612.

[10] Cravotto, G.; Cintas, P. Power ultrasound in organic synthesis: moving cavitational chemistry from academia to innovative and large-scale applications. *Chem. Soc. Rev.*, **2006**, *35*, 180-196.

[11] Mason, T.J. Ultrasound in synthetic organic chemistry. *Chem. Soc. Rev.*, **1997**, *26*, 443-451.

[12] Reisse, J.; Caulier, T; Dekerckheer, C.; Kegelaers, Y.; Segebarth, N.; Bartik, K. In: *Sonochemistry and Sonoluminescence*; Crum, L.A. Ed.; Kluwer Acad. Publ.: Dordrecht, **1999**; pp. 205-224.

[13] Kegelaers, Y.; Eulaerts, O.; Reisse, J.; Segebarth, N. On the quantitative measure of a sonochemical effect in heterogeneous sonochemistry. *Eur. J. Org. Chem.*, **2001**, *19*, 3683-3688.

[14] Luche, J.L.; Einhorn, C.; Einhorn, J.; Sinisterra-Gago, J.V. Organic sonochemistry: a new interpretation and its consequences. *Tetrahedron Lett.*, **1990**, *31*, 4125-4128.

[15] Thompson, D.; Vilbrand, F.C.; Gray, W.C. The effect of insonation on the specific reaction rate constant in the acid hydrolysis of ethyl acetate. *J. Acoust. Soc. Am.*, **1953**, *25*, 485-490.

[16] Chen, N.; Kalback, W.M. Effect of ultrasound on chemical reaction rate. *Ind. Eng. Chem. Fundam.*, **1967**, *6*, 175-178.

[17] Fogler, S.; Barnes, D. Shift in the optimal power input of an ultrasonic reaction. *Ind. Eng. Chem. Fundam.*, **1968**, *7*, 222-226.

[18] Couppis, E.C.; Klinzing, G.E. Effect of cavitation on reacting systems. *AIChE J.*, **1974**, *20*, 485-491.

[19] Tuulmets, A.; Raik, P. Ultrasonic acceleration of ester hydrolyses. *Ultrason. Sonochem.*, **1999**, *6*, 85-87.

[20] Tuulmets, A.; Salmar, S. Effect of ultrasound on ester hydrolysis in aqueous ethanol. *Ultrason. Sonochem.*, **2001**, *8*, 209-212.

[21] Tuulmets, A.; Salmar, S.; Hagu, H. Effect of ultrasound on ester hydrolysis in binary solvents. *J. Phys. Chem. B*, **2003**, *107*, 12891-12896.

[22] Kristol, D.S.; Klotz, H.; Parker, R.C. The effect of ultrasound on the alkaline hydrolysis of nitrophenyl esters. *Tetrahedron Lett.*, **1981**, *22*, 907-908.

[23] Salmar, S.; Cravotto, G.; Tuulmets, A.; Hagu, H. Effect of ultrasound on the base-catalyzed hydrolysis of 4-nitrophenyl acetate in aqueous ethanol. *J. Phys. Chem. B*, **2006**, *110*, 5817-5821.

[24] Yim, B.; Nagata, Y.; Maeda, Y. Sonolytic degradation of phthalic acid esters in aqueous solutions. acceleration of hydrolysis by sonochemical action. *J. Phys. Chem. A*, **2002**, *106*, 104-107.

[25] Hua, I.; Höchemer, R.H.; Hoffmann, M.R. Sonolytic hydrolysis of p-nitrophenyl acetate: the role of supercritical water. *J. Phys. Chem.*, **1995**, *99*, 2335-2342.

[26] Ando, T.; Fujita, M.; Kimura, T. *Abstracts 6th Meeting Eur. Soc. Sonochemistry, 10-14 May 1998*, Rostock-Warnemünde, Germany, **1998**; p. 46.

[27] Lorimer, J.P.; Mason, T.J. Effect of ultrasonic irradiation on the solvolysis of 2-chloro-2-methylpropane in aqueous ethanol mixtures. *J. Chem. Soc. Chem. Commun.*, **1980**, *23*, 1135-1136.

[28] Mason, T.J.; Lorimer, J.P.; Mistry, B.P. The effect of ultrasound on the solvolysis of 2-chloro-2-methylpropane in aqueous alcoholic media. *Tetrahedron Lett.*, **1982**, *23*, 5363-5364.

[29] Mason, T.J.; Lorimer, J.P.; Mistry, B.P. The effect of ultrasound on the solvolysis of 2-chloro-2-methylpropane in aqueous ethanol. *Tetrahedron*, **1985**, *41*, 5201-5204.

[30] Lorimer, J.P.; Mason, T.J.; Mistry, B.P. Effect of ultrasound on the solvolysis of 2-chloro-2-methylpropane in aqueous alcoholic solvents. *Ultrasonics*, **1987**, *25*, 23-28.

[31] Broekaert, L.; Reisse, J. *Abstracts 4th Meeting Eur. Soc. Sonochemistry, 18-22 Sept. 1994*, Blankenberge, Belgium, **1994**; p. 49.

[32] Hagu, H.; Salmar, S.; Tuulmets, A. Impact of ultrasound on hydrophobic interactions in solutions: Ultrasonic retardation of benzoin condensation. *Ultrason. Sonochem.*, **2007**, *14*, 445-449.

[33] Tuulmets, A.; Hagu, H.; Salmar, S.; Cravotto, G.; Järv, J. Ultrasonic evidence of hydrophobic interactions. effect of ultrasound on benzoin condensation and some other reactions in aqueous ethanol. *J. Phys. Chem. B*, **2007**, *111*, 3133-3138.

[34] Piiskop, S.; Hagu, H.; Järv, J.; Salmar, S.; Tuulmets, A. Sonication effects on ester hydrolysis in alcohol-water mixtures. *Proc. Estonian. Acad. Sci. Chem.*, **2007**, *56*, 199-206.

[35] Breslow, R. In: *Organic Reactions in Water*, Lindsröm, U.M.; Ed.; Blackwell Publishers: Oxford, **2007**; pp. 1-28.

[36] Blokzijl, W.; Engberts, J.B.F.N. Hydrophobic effects: opinion and fact. *Angew. Chem. Int. Ed. Engl.*, **1993**, *32*, 1545-1579.

[37] Otto, S.; Engberts, J.B.F.N. Hydrophobic interactions and chemical reactivity. *Org. Biomol. Chem.*, **2003**, *1*, 2809-2820.

[38] Narayan, S.; Muldoon, J.; Finn, M.G.; Fokin, V.V.; Kolb, H.C.; Sharpless, K.B. "On water": Unique reactivity of organic compounds in aqueous suspension. *Angew. Chem. Int. Ed. Engl.*, **2005**, *44*, 3275-3279.

[39] Chanda, A.; Fokin, V.V. Organic synthesis "on water". *Chem. Rev.*, **2009**, *109*, 725-748.

[40] Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed. VCH: Weinheim, **2003**

[41] Franks, F.; Ives, D.J.G. Structural properties of alcohol-water mixtures. *Quart. Rev.*, **1966**, *20*, 1-44.

[42] Tuulmets, A. Ultrasound and polar homogeneous reactions. *Ultrason. Sonochem.*, **1997**, *4*, 189-193.

[43] Nishi, N.; Takahashi, S.; Matsumoto, M; Tanaka, A.; Muraya, K.; Takamuku, T.; Yamaguchi, T. Hydrogen-bonded cluster formation and hydrophobic solute association in aqueous solutions of ethanol. *J. Phys. Chem.*, **1995,** *99*, 462-468.

[44] Egashira, K.; Nishi, N. Low-frequency raman spectroscopy of ethanol-water binary solution: evidence for self-association of solute and solvent molecules. *J. Phys. Chem. B*, **1998**, *102*, 4054-4057.

[45] Wakisaka, A.; Komatsu, S.; Usui, Y. Solute-solvent and solvent-solvent interactions evaluated through clusters isolated from solutions: preferential solvation in water-alcohol mixtures. *J. Mol. Liq.*, **2001**, *90*, 175-184.

[46] Rispens, T.; Caballeiro-Lago, C.; Engberts, J.B.F.N. Kinetics of hydrolysis of 4-methoxyphenyl-2,2-dichloroethanoate in binary water-cosolvent mixtures; the role of solvent activity and solute-solute interactions. *Org. Biomol. Chem.*, **2005**, *3*, 597-602.

[47] Breslow, R.; Groves, K.; Mayer, M.U. The hydrophobic effect as a mechanistic tool. *Pure Appl. Chem.*, **1998**, *70*, 1933-1938.

[48] Breslow, R. The hydrophobic effect in reaction mechanism studies and in catalysis by artificial enzymes. *J. Phys. Org. Chem.*, **2006**, *19*, 813-822.

[49] March, J. *Advanced Organic Chemistry*, Wiley: New York, **1992**.

[50] Kool, E.T.; Breslow, R. Dichotomous salt effects in the hydrophobic acceleration of the benzoin condensation. *J. Am. Chem. Soc.*, **1988**, *110*, 1596-1597.

[51] Tuulmets, A.; Järv, J.; Salmar, S.; Cravotto, G. Ultrasonic detection of hydrophobic interactions: a quantitative approach. *J. Phys. Org. Chem.*, **2008**, *21*, 1002-1006.

[52] Hansch, C. Quantitative approach to biochemical structure-activity relationships. *Acc. Chem. Res.*, **1969**, *2*, 232-239.

[53] Hansch, C.; Leo, A.; Hoekman, D. *Exploring QSAR: Hydrophobic, Electronic and Steric Constants*, ACS: Washington DC, **1995**.

[54] Shorter, J. *Correlation Analysis in Organic Chemistry*, Clarendon Press: Oxford, **1973**.

[55] Williams, A. *Free Energy Relationships in Organic and Bio-Organic Chemistry*, RSC: Cambridge, **2003**.

[56] Blokzijl, W.; Engberts, J.B.F.N.; Jagen, J.; Blandamer, M.J. Description of solvent dependence of rate constants in terms of pairwise group Gibbs function interaction parameters. Medium effects for hydrolysis of p-methoxyphenyl dichloroacetate in aqueous solutions containing urea and alkyl-substituted ureas. *J. Phys. Chem.*, **1987**, *91*, 6022-6027.

[57] Tuulmets, A.; Järv, J.; Tenno, T.; Salmar, S. Significance of hydrophobic interactions in water-organic binary solvents. *J. Mol. Liq.*, **2009**, *148*, 94-98.

[58] Fainberg, A.H.; Winstein S. Correlation of solvolysis rates. III. t-Butyl chloride in a wide range of solvent mixtures *J. Am. Chem. Soc.*, **1956**, *78*, 2770-2777.

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