PART B

Role of water as solvent in sonic reactions
IIB. 1. INTRODUCTION TO SONICATED REACTIONS IN WATER: WATER, A BLESSING MOLECULE

Two decades ago chemists began to retrieve the benefits of water as a lively substitute to the conventional organic solvents, use of water not only is the environment concern but also important in the organic reaction outcome. Solvent less or neat reactions, solid state reactions, ultrasound and microwave–promoted aqueous reactions, reactions in ionic liquids, and reactions in supercritical fluids (SCF) such as the supercritical CO₂ were also conceived as friendly alternatives. Professor Ronald Breslow was the first who resuscitated the use of water as a medium in Diels–Alder (DA) reactions; he carried out the cycloaddition of cyclopentadiene with methyl vinyl ketone in water and found that its rate to be unexpectedly enhanced by a factor of more than 700 compared with the reaction in isooctane.[1] This was a revolution in the field of synthetic organic chemistry. With its ubiquity and abundance, chemists have been undoubtedly tempted or wished to use water as a medium, but the lingering belief of its man–created enmity for organic reactions impeded any attempt. However, switching to water should be deemed not as a significant achievement but a rational and normal return to the realm of life, that is, to follow the nature lead. Therefore, one should not be stunned by the fact that water–promoted in vitro organic reactions afford better results compared with those in organic solvents, as a startling number of in vivo organic reactions occur entirely in water. Fairly noting is that organic reactions were essentially realized in water a century ago, before the emergence of the organic polar solvents. Novel mechanistic views of water–mediated organic reactions are being elicited. In fact, new terms and new reactivity coupled with some new effects that are thought to be the promoting forces for the reactions course, has cropped up. Yet it is fair to mention that the development of these reactivity and effects owes to the chemistry already founded by the organic solvent–based synthesis. A new chemistry termed as "Green chemistry" or "Sustainable chemistry" has emerged and water is unanimously viewed as a greener solvent.[2,3]


Sonicated organic reactions in water
The most important effects encountered water as solvent are hydrophobic effect, hydrophobic packing, antihydrophobic effect, pro-hydrophobic effect, dichotomous salts effect. Organic reactions in water have mostly been performed using a co-solvent to engender some solubility. Today's status, the insolubility of organic reactants in water, once considered a drawback, has turned out to be advantageously a leading factor for the success of organic reactions in pure water.
IIB. 2. SOME INTERESTING AND USEFUL AQUA MEDIATED SONIC REACTIONS

An efficient and simple catalyst–free one pot synthesis of biscoumarins by condensing 4-hydroxycoumarin with aromatic aldehydes in water under ultrasound irradiations at ambient temperature with excellent yield of the desired products in shorter reaction time is described (Scheme IIB.1).[4]

![Scheme IIB.1.](image)

A green and efficient method for the preparation of 5-aryl-4-hydroxy-2-methyl-1H-pyrrole-3-carboxylic acid esters and 6-aryl-3-methylpyridazine-4-carboxylic acid esters via three-component reaction of arylglyoxal hydrates with β-dicarbonyl compounds in the presence of ammonium acetate and hydrazine hydrate using water as solvent under ultrasonic irradiation is described. The reactions proceed rapidly and affords the corresponding pyrroles and pyridazines in good to high yields in very short reaction time (Scheme IIB.2).[5]

![Scheme IIB.2.](image)

The piperidine–catalysed reaction between piperonal and malonic acid at room temperature with pyridine as the solvent was carried out under ultrasound irradiation, and Knoevenagel reaction product is formed in yields of 91.0% after three hours.

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*Sonicated organic reactions in water*
When carried out under reflux conditions, the same reaction forms the Knoevenagel reaction product in yields of 52.0% after three hours (Scheme IIB.3).[6]

![Chemical reaction image]

**Scheme IIB.3.**

A novel approach to Aldol reaction under high-intensity ultrasound for 45 minutes is presented in the Scheme IIB.4.[7]

![Chemical reaction image]

**Scheme IIB.4.**

A short, efficient synthesis of 2-methoxy-6-alkyl-1,4-benzoquinones is available. Ultrasound assisted Wittig reaction of alkyltriphenyl phosphonium bromides with o-vanillin in basic aqueous conditions followed by reduction with Na/n-BuOH gives 2-methoxy-6-alkylphenols. Oxidation of 2-methoxy-6-alkylphenols with Fremy’s salt produced the desired compounds (Scheme IIB.5).[8]

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*Sonicated organic reactions in water*
**Scheme IIB.5.**

A green and convenient approach to the synthesis of 2-amino-4,6-diphenylnicotinonitriles via four-component reaction of malononitrile, aromatic aldehydes, acetophenone derivatives and ammonium acetate in water under ultrasound irradiation is described. The combinatorial synthesis was achieved for this methodology with applying ultrasonic irradiation in water. In comparison to conventional methods, experimental simplicity, good functional group tolerance, excellent yields, short routine, and selectivity without the need for a transition metal or base catalyst are prominent features of this sonocatalyzed reaction (Scheme IIB.6).[9]

**Scheme IIB.6.**

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*Sonicated organic reactions in water*
Syn-triazenes are known for their antitumor, antimicrobial and anti-cancer actions. A variety of 1,3,5-triaryl-1,3,5-hexahydotriazine have been synthesized using ultrasound assisted reaction of aryl amines with aqueous formaldehyde. Furthermore, a special study on the effect of different solvents revealed that, a mixture of water and ethanol is a best solvent (Scheme IIB.7).[10]

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\text{NH}_2 \quad + \quad \text{HCHO} \quad \xrightarrow{\text{ultrasound assisted reaction}} \quad \text{X}
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\text{X} = \text{H}, \text{CH}_3, \text{OCH}_3, \text{NH}_2, \text{Cl}, \text{NO}_2
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Scheme IIB.7.