

Green chemistry, green solvents, and free radical reactions in aqueous media

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Since its birth over a decade ago, the field of green chemistry has seen rapid expansion, with numerous innovative scientific breakthroughs associated with the production and utilization of chemical products.¹ The concept and ideal of green chemistry now goes beyond chemistry and touches subjects ranging from energy to societal sustainability. The key notion of green chemistry is “efficiency”, including material efficiency, energy efficiency, man-power efficiency, and property efficiency (*e.g.*, desired function *vs.* toxicity). Any “wastes” aside from these efficiencies are to be addressed through innovative green chemistry means. “Atom-economy”² and minimization of auxiliary chemicals, such as protecting groups and solvents, form the pillar of material efficiency in chemical productions. By far, the largest amount of “auxiliary wastes” in most chemical productions are associated with solvent usage. In a classical chemical process, solvents are used extensively for dissolving reactants, extracting and washing products, separating mixtures, cleaning reaction apparatus, and dispersing products for practical applications. While the invention of various exotic organic solvents has resulted in some remarkable advances in chemistry, the legacy of such solvents has led to various environmental and health concerns. Consequently, as part of green chemistry efforts, a variety of cleaner solvents have been evaluated as replacements.³ However, an ideal and universal green solvent for all situations does not exist. Among the most widely explored greener solvents are ionic liquids,⁴ supercritical CO₂,⁵ and water.⁶ These solvents complement each other nicely both in properties and applications. *Importantly, the study of green solvents goes far beyond just solvent replacement.* The use of green solvents has led science to uncharted territories. For example, the study of ionic liquids made large-scale supported synthesis possible for the first time⁷ and the utilization of supercritical CO₂ has led

to breakthroughs in microelectronics and nanotechnologies.⁸ Although water is the most abundant, natural and non-toxic solvent on earth, it has been traditionally considered as a nuisance in most chemical productions. However, since Breslow’s⁹ report on the acceleration of Diels–Alder reactions in aqueous media, the re-examination of this solvent for chemical applications has exploded. The commercialization of aqueous-based hydroformylation and hydrogenation processes allow product separation and catalyst recycling readily.¹⁰ The development of aqueous organometallic reactions simplifies protection–deprotection of functional groups and allows the direct use of biomass-based feedstocks for synthetic purposes.¹¹ The innovative “on-water” concept,¹² water-tolerant Lewis acids,¹³ and aqueous organocatalyses¹⁴ led to new understandings of fundamental chemical reactivities.

Free-radicals represent a large class of chemical species such as atoms, molecules and reaction intermediates that possess unpaired electrons. Such chemical species can both be long lived and short lived. They played important roles in biological processes and regulations of the atmosphere.¹⁵ Chemically, most free radicals are highly reactive and form a fundamental class of chemical reactions.¹⁶ Such reactions generally follow a pattern of the three stages of initiation, propagation and termination. The termination only occurs when two radicals, both at very low concentrations, meet and annul each other. Sometimes, this makes the reaction disastrous (such as in ozone depletion or explosions). However, with proper design and control, radical reactions can also be very “economical”, for example in tandem reactions and atom-transfer synthesis.

Because most molecule-based radicals and reaction intermediates do not have charges, consequently radicals generally react *via* orbital–orbital interactions, which is analogous to the pericyclic reactions.¹⁷ As a first approximation,

the principles, phenomena and theories governing pericyclic reactions could be applicable to many free-radical reactions. The similarity between pericyclic reactions and radical reaction suggest that free-radical reactions can not only occur in water but may be even advantageously accelerated by water. In addition, the very strong O–H bond of water and the high energy required for homolytic cleavage of this bond suggests that water will be better than most organic solvents in preventing side-reactions. There are a variety of ways to initiate a radical reactions. Some classical radical initiators are less desirable and new ones have been developed.

The tutorial review by Tuck and co-workers¹⁸ in this issue on forming C–H bonds in aqueous media summarized recent developments on the subject of using radical chemistry to generate terminal products with the formation of C–H bonds. The review include several key sections: (i) a brief background on the subject; (ii) the fundamental ways to carbon-centered free radicals in aqueous media and selection criteria; (iii) the discussions of the advantages and the usages of three major classes (azo-based initiators, peroxides and boranes) radical initiators for aqueous free-radical reactions; (iv) the effect of substrate solubility and hydrogen-atom-transfer reactions in aqueous media; (v) discussions on various greener free-radical hydrogen donors for forming the final C–H bond as well as the concept of “on water” and “in water” related to radical reactions; and finally, (vi) several applications of the hydro-atom-transfer reactions in aqueous media including natural product syntheses, probing DNA structure, and deuterium isotopic labeling.

Green chemistry is about scientific innovations in creating new knowledge based on sustainability and resource efficiency, as well as to tackle wastes and hazards associated with the generation and utilization of chemical products. The arsenals created by green chemists

are ever increasing. The development of free radical reactions to form C–H bond in aqueous media is one more tool in the green chemistry toolbox.

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