Chemistry in Water to the Rescue

If synthetic organic chemistry is to survive, the transition from its dependence on petroleum products, and organic solvents in particular to nature’s reaction medium, water, must happen quickly.

By Prof. Dr. Bruce Lipshutz

Do you know anyone... anyone, who would claim that we have an infinite supply of oil on planet Earth? Probably not. So, how is it that the development of modern organic chemistry has been essentially tied to the availability of petroleum and the downstream products? For over 200 years, society’s dependence on these products has been growing. From the pharmaceuticals that keep us alive to the herbicides and pesticides that enable food production that feeds a growing population, they are produced primarily in petroleum-based organic solvents, which must be disposed of properly when they are spent. What exactly does this mean? To the extent that a very healthy percentage of this organic, and therefore carbon, waste is burned, the result is CO2. Yes, CO2, and a lot of it! So, is chemistry a big contributor to climate change? Well, yes! It’s not that hard to change this. In fact, if “change” is based solely on science, then we are already there, in harmony with biology, which is water-based. And the payoff is substantial, replete with bonuses reflecting much more than minimizing pollution and ensuring that planetary resources are available to future generations. Put another way, going green is a win-win on all levels.

SEARCHING FOR THE APPROPRIATE REACTION VESSEL

The secret to doing organic chemistry in water is no secret at all; rather, it has been hidden in plain sight, perhaps for billions of years. Nature itself provides the answer: Life could not exist without enzymes, these particular biomolecules are “brain dead”; they don’t have brains; no recognition of what’s coming in to react and what products are being formed.

The bad news is that a nanoreactor must be identified that is suitable for organic synthesis; it must be capable of accommodating many different types of chemistry, such as that routinely used by the fine chemical industry (especially pharmaceutical and agrochemical companies). This has been the “valley of death” that has remained unfilled for centuries. It is the difference between recognizing the need and creating the technologies that make organic synthesis “in water” possible. Let’s understand that it’s the nanoreactors that are “in water”; the actual chemistry involving water-insoluble reactants and catalysts takes place within the inner cores, which serve as the “solvent” for various reactions.

Nature, with its membranes, vesicles and micelles, has likely relied on these concepts over the millennia for its chemistry in water, a large scale, “chemistry in water” can also be observed when oil companies clean up marine spills. It’s obvious: the know-how is already there, at least conceptually. So why has organic synthesis been so slow to adopt?

The challenge lies in finding the appropriate “reaction vessels” for water-insoluble biomolecules. Throughout evolution, nature’s reaction “flasks” for water-insoluble biomolecules have been, and still are, a variety of membranes, vesicles, and micellar arrays, in water. Could it be that simple?

Yes and no. The good news is that, in principle, organic synthesis should be possible in these reactors; the reactants would be accommodated, as well as the catalysts that speed up these reactions. Making all sorts of products would then be feasible because, unlike enzymes, these particular biomolecules are “brain dead”; they have no brains; no recognition of what’s coming in to react and what products are being formed.

As one of the pioneers of green chemistry, Prof. Bruce Lipshutz (77) was awarded the President’s Green Chemistry Challenge Award by the US Environmental Protection Agency (EPA) in the “Academics’” category in 2011. Lipshutz began teaching at the University of California, Santa Barbara, in 1979 and has been on the faculty since. The focus of his research group is organic synthesis using catalysis. He is particularly interested in micellar catalysis, which makes it possible to carry out organic reactions in water instead of in organic solvents. For this purpose he develops customised surfactants. Evonik’s Health Care Business Line offers the “Chemistry in Water” technology developed by Prof. Lipshutz for the production of pharmaceutical intermediates and active ingredients on an industrial scale.

The leading “designer” surfactant to date is TPGS-750-M, which contains the MPEG-750-containing hydrophilic group. It is divided into three parts: The hydrophilic section facing outward in water contains the building block methoxy polyethylene glycol 750 (MPEG 750). The inner, or lipophilic portion consists of the commodity chemical vitamin E. The two building blocks are connected by a succinic acid linker. Each portion of this designer surfactant is innocuous, and, due to the vitamin E present, even by itself, healthy!

ENVIRONMENTAL AND ECONOMIC BENEFITS

This micelle-forming amphiphile, TPGS-750-M, can be used to affect many different reaction types, especially those of particular interest to pharmaceutical and agrochemical companies. Key reactions, including those catalysed by palladium, amide, peptide bond formations, and Nucleophilic Aromatic Substitution reaction (SNAr) processes that have traditionally been run in organic solvents can be accommodated.

In addition to the environmental and associated economic benefits to be realized, the higher concentrations of substrates and catalyst localized within the inner micellar cores not only lead to faster reactions, but also provide opportunities to use precious metal catalysts at ppm loadings.

Since most targets are water-insoluble solids, they precipitate from the aqueous medium and need only be filtered for isolation purposes. How’s that for a “waste-less”? And what about the filtrate, the aqueous medium that often contains the catalyst? It’s recycled. Boom!

Do we really have a choice? If we already have the know-how to do much more with less? Perhaps the bigger question is, do we have the resolve in the chemical industry to make these changes? Let’s hope so. Sustainability is not just a buzzword; it has tremendous implications. Indeed, it is our future.

wever, a kit of trial and error has led to a much better understanding of surfactant design, leading to micellar catalysis which, today is becoming rich with a growing toolbox of technologies that enable just about any reaction to be run in water.

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