Tetrahedron Symposium-in-Print - "Engineering Chemistry for the Future of Organic Synthesis"

Preface – S.V. Ley

Societal and commercial pressures are impacting more than ever on the methods and techniques by which we assemble today's functional molecules. A holistic appreciation of this complex eco-system necessitates the invention of new tools and stimulates innovative thinking. In particular, the labour intensive and unsustainable practices of the past are being replaced by a more machine-based approach. This engineering of chemistry goes beyond the design of simple, enabling mechanical contrivances to encompass a full range of artificial intelligence (AI) methods, machine learning algorithms, advanced robotics and reaction profiling techniques. Integration of these systems with data collection and evaluation are the new drivers for success. Access to wider process windows, improved mixing and mass and heat transfer methods are providing early kinetic data that aids discovery. Mechanochem, photo-redox and electrochemical devices are further adding to the repertoire of the synthetic chemist. Flow chemistry and continuous processing methods are similarly breaking new ground as delineated by many of authors in this Symposium in Print. Indeed, flow chemistry has proven to be very amenable to automation over several telescoped reaction steps leading to complex natural products and active pharmaceutical ingredients (API's) in particular. The modular nature and flexibility of these systems assists in designing reactor configurations that can accommodate in-line purification, which are increasingly being used in downstream product processing.

As more and more people acquire the skills to be able to conduct these continuous processing techniques, we are seeing innovative applications to many other areas, especially in materials synthesis, for example. Improved reactor design and in-line

analytics help to provide robust and reproducible reaction platforms. The concepts are readily adapted for compound library synthesis and screening, scale-up, self-optimisation reactions and other repetitive experimentation and may be used to discover of novel chemical reactivity. The use of the internet adds another element to allow chemists to port information to the Cloud and to control reactions from remote locations. These concepts are designed to encourage sharing of knowledge through open innovation mechanisms. Current developments using cheap low-power micro-processing chips, such as Arduino or the Raspberry Pi, facilitate communication and collective control between equipment purchased from diverse sources. These methods can also help in providing improved chemical experiment audit trails and can track and connect failing equipment autonomously. Likewise, camera monitoring and digital recording can improve safety and reaction understanding through, for example, thermal imaging or high speed video capture.

Compartmentalisation techniques, plug flow methods, droplet microfluidics are all similarly adding to the array of enabling systems to provide opportunities for screening and evaluation or design of new catalysts significantly beyond our current capabilities. Finally, it is interesting to note how well established chemistry in photo- or electro-chemistry for example, can be massively enhanced by re-engineering the equipment and the methods used. It is very timely, therefore, that this Symposium collates some of the new work in this rapidly developing in the area.

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