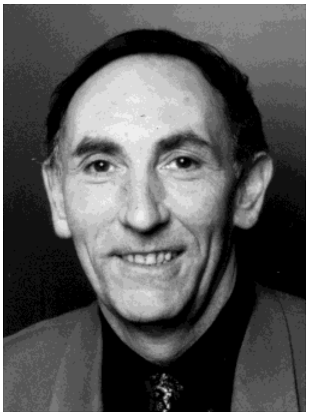
Guest Editorial



There is no doubt that catalysis will play an integral role in shaping the future of organic synthesis. Increasingly stringent environmental and safety regulations have become the driving force for the development of cleaner, more atom-efficient technologies that minimize, or preferably eliminate, the generation of waste and avoid, where possible, the use of toxic and/or hazardous reagents. These concepts are embodied in the now widely accepted terms Green Chemistry and Sustainable Development. Sustainability is the goal and Green Chemistry is the means to achieve it.

The solution is evident: the widespread substitution of classical "stoichiometric" organic syntheses by cleaner, catalytic alternatives, i.e., the integration of catalysis and organic synthesis. If the solution is so obvious why is its implementation taking so long? There are various reasons for this. First, owing to the relatively small production volumes involved, fine chemicals manufacturers were not, until fairly recently, confronted with the need to change their processes.

Second, from the time of Berzelius, who coined the terms organic chemistry and catalysis in 1807 and 1835, respectively, organic synthesis and catalysis evolved as separate disciplines. Catalysis evolved largely as a subdiscipline of physical chemistry. With the advent of the petrochemicals industry in the 1930's, catalysis was widely applied in oil refining and bulk chemicals manufacture. Organic synthesis, in contrast, evolved along a largely "stoichiometric pathway". Consequently, fine chemicals manufacture, the domain of the synthetic organic chemist, is rampant with classical organic reactions employing stoichiometric reagents, e.g., metal oxidants, metal hydride reducing agents and a variety of Brønsted and Lewis acids. The problem begins with the teaching of organic chemistry in university curricula where scant attention is generally paid to catalytic methodologies.

Third, a major obstacle to the widespread integration of catalytic methodologies in industrial organic synthesis is the longer development time that is often needed, compared to the well-tried and broadly applicable stoichiometric reagents. In the fine chemicals industry "time to market" is of the essence and, consequently, there is a marked tendency to choose the easy "stoichiometric" solution. The conclusion is clear: the development time of catalytic processes needs to be reduced. Fortunately, the solution is at hand: new advances in combinatorial synthesis of catalysts combined with high-throughput screening and experimentation are paving the way for dramatic reductions in the time needed to develop new catalytic processes. In the case of enzymes, *in vitro* evolution combined with high-throughput screening is being used to achieve major improvements in performance in a matter of weeks compared to the millions of years that natural evolution takes.

Catalysis itself has also not evolved as a single, unified discipline. The world of catalysis is divided into three camps – heterogeneous, homogeneous, and enzymatic – that do not communicate well with each other and tend to speak in "different languages". Here also there is a pressing need for integration. After all, the industrial process chemist is interested in performing a particular conversion and does not really care how it is done (as long as it is green, we could add).

The three catalysis communities can learn much from each other and more integration would certainly lead to more cross-fertilization of ideas. For example, immobilization is very important for improving the performance of enzymes and scientists involved in biocatalysis can learn from those concerned with heterogeneous catalysis. Similarly, techniques for immobilizing enzymes are often applicable to the immobilization of homogeneous metal complex catalysts, and *vice versa*. An advantage of heterogeneous catalysts is their facile recovery and recycling by simple filtration. Alternatively, facile catalyst recovery can also be achieved by using liquid-liquid biphasic systems. This overlaps with another issue in the context of green chemistry: solvents. The use of toxic and/or hazardous solvents, e.g., chlorinated hydrocarbons, is becoming prohibitive and, combined with the need for facile catalyst recovery, has stimulated re-

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search on catalysis in novel media, e.g., aqueous and fluorous biphasic systems, supercritical carbon dioxide and ionic liquids. Here again synergy can be achieved by integration of homogeneous, heterogeneous and enzymatic catalysis.

The ultimate synergy is the integration of chemo- and biocatalytic steps affording catalytic cascades, as separate unit processes or in one-pot syntheses. Enzymatic kinetic resolution combined with *in situ* racemization catalyzed by a metal complex, is an elegant example of this. Such catalytic cascade processes come close to emulating the elegant orchestration of various biocatalytic steps that occurs in the living cell. In the words of the late Russian chemist, N. N. Semenov, “By applying the ideas of biochemistry, chemical science may solve the energy crisis, make industrial production infinitely more efficient, and provide mankind with wings”. This is surely advanced synthesis and catalysis!

Leading References

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