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Green chemistry in APIs manufacturing:
A forthcoming revolution now mature

Faced by increasing manufacturing cost and by numerous quality problems, the fine chemicals and pharmaceutical industries are slowly, but inevitably, shifting to green chemistry synthetic methods: Biocatalysis and homogeneous catalysis first; and then to heterogeneous catalysis, well beyond typical hydrogenation reactions over Pt/C or Pd/C conventional catalysts. We have explained in detail elsewhere how, dwarfed by the typical E-factor = 0.1 value of the petrochemicals industry, the E-factor (kilogram of waste per kilogram of API manufactured) approaching 200 typical of homogeneously catalyzed API synthetic processes has marked for the last decade the industry's *process* obsolescence (1).
Yet this situation is now changing thanks to the concomitant introduction of new heterogeneous catalysts coupled to manufacturing under flow conditions. Second-generation commercial heterogeneous catalysts suitable for carbon-carbon coupling, debenzylation, hydrosilylation and many other industrially relevant reactions, including conversion of natural terpenes into fragrances, perfumes, flavours, pharmaceuticals and synthetic intermediates, are now commercially available.
Using 3-D encapsulated, rather than 2-D surface-derivatized materials, heterogeneously catalyzed processes make use of entrapped enzyme, organo- or metal catalyst to selectively mediate the desired reaction, avoiding waste generation while attaining higher conversion and yield than reaction under batch.
As we write, furthermore, we witness to the first small molecule fine chemicals and pharmaceuticals being produced continuously in flow, in what Trout has called the "ultra-lean way of manufacturing" (2). Regulatory problems have indeed been overcome, with the first harmonized regulatory guidelines accepted across various regulatory authorities.
Contrary to mainstream thinking, China and India not only give every year eminent contributes to advance the science and technology of heterogeneous catalysis for fine chemical and API manufacturing, but companies based in these huge countries where the production of APIs and fine chemicals has been largely outsourced from Europe and the US, already lead the field along with companies based in Switzerland, Germany, Sweden, the US and Austria.
This global effort, we argue in conclusion, will help to regain control on product quality, ending what Grayson, has called in this Journal (2) the «madness» of fine chemistry during two decades of economic globalization. Eventually, within the next decade, the pharmaceutical and fine chemicals industries will rely on chemical manufacturing with little or no waste generation, minimal energy and resource utilization, based on continuous manufacturing in flow reactors equipped with solid catalysts, located in industrial plants 20 or 30 times smaller than today's batch plants of similar output.
It is the task of us chemistry scholars, to make flow and nanochemistry-based catalysis a part of the course curriculum for chemists, filling the "talent shortage" lately identified by us (3) and by Jamison (4), a professor and pioneer in flow chemistry, as today's main barrier to the industry's adoption of nanochemistry and catalysis under flow as the most promising green chemistry technologies.

REFERENCES

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