Organocatalysis: A Complementary Catalysis Strategy Advances Organic Synthesis

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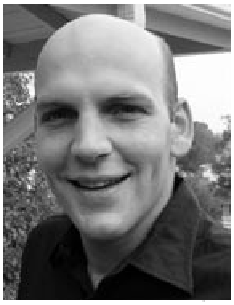

For a long time, there seemed to have been an unwritten rule that organocatalysts, in contrast to transition metal complexes or enzymes, cannot be efficient and selective catalysts. In retrospect, this judgement is surprising, considering that about half of all enzymes are metal-free and that the first reported asymmetric catalysts were purely organic molecules. Moreover, already in the 1960s and 1970s selected organocatalysts were shown to be highly enantioselective, and efficient non-asymmetric catalysts such as DMAP are also known since then. Yet only in recent years has the scientific community begun to appreciate the great potential of organocatalysis as a broadly useful methodology, advancing organic synthesis. Significantly, organocatalysis seems to complement rather than compete with metal and enzyme catalysis. For example, certain recently developed reactions such as the exceptionally important transition metal-catalyzed cross-coupling and metathesis reactions are unlikely candidates for organocatalysis. Yet other processes, for example, those using aldehydes as nucleophiles in asymmetric catalysis, seem to only work within the realm of organocatalysis. Both transition metal catalysis and organocatalysis have allowed the realization of catalytic asymmetric processes that were considered extremely challenging if not impossible before. Organocatalytic examples include highly enantioselective direct catalytic asymmetric cross-aldolizations, alkylations, and other C–C bond forming reactions, as well as oxidations and hetero-functionalizations. That organocatalysts are often compatible with the production of chiral pharmaceuticals and are easily synthesized and attached to a polymer support comes as an additional bonus. Exciting recent results reported by various groups have stimulated an explosive development of the field and even with all the appropriate caution, further exhilarating discoveries can be expected. I believe the chemical synthesis of the future to be even more inspired by Nature’s enzymes. Not only will we continue to use biocatalysts and transition metal catalysts and to optimize their properties through design and molecular evolution; we will also further apply the mechanistic principles of Nature’s metal-free catalysts to our synthetic low molecular weight analogues. Novel and improved organocatalysts as well as new and often unexpected reactions will be the result of such studies. With some certainty, significant applications in an industrial context can be envisioned within a short timeframe. Overall, the use of organocatalysts is likely to grow strongly for a while to come. The superb contributions of various laboratories from all over the world to this special issue of *Advanced Synthesis & Catalysis* are a tribute to this development.

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