

Noncovalent Organocatalysis

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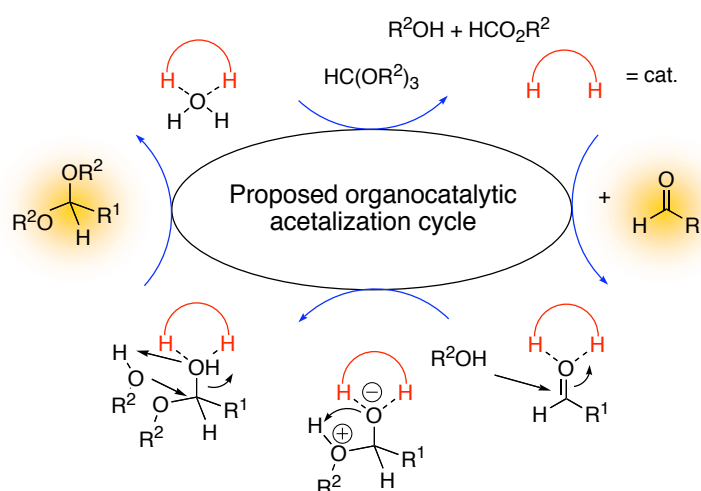
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Organocatalysis combines the concepts of molecular recognition and supramolecular chemistry with enzyme-like catalytic concepts; this branch of research may therefore be coined with the notion of “the hunt for the smallest enzyme.”¹

Noting that about half of all enzymes do *not* carry a metal center it is obvious that this approach has long been underappreciated. Although organocatalysis as such is a

new field, it is already possible to catalyze many types of organic reactions with small, well-designed organic molecules. This circumvents the use of often toxic metals, and the preparation of the catalysts is much easier as it relies on the well-developed synthetic arsenal for tailor-making organic structures. While many approaches rely on covalent attachment of the catalyst (e.g., proline catalysis), we focus entirely on non-covalently bound catalysts;² the talk will emphasize the notion of noncovalent bonding that is in line with Pauling’s paradigms of enzyme activity. In our group we have developed hydrogen-bonding thiourea-based catalysts that are effective in catalyzing Diels-Alder reactions,² acid-free acetalizations,³ epoxide openings,⁴ and other reactions. Many other groups have not picked up this catalytic principle and apply it to a manifold of fascinating reactions.

Phase-transfer catalysis (PTC) is a special case of organocatalysis that has been around for several decades; PTC has enormous industrial applications. Our aim was to develop completely novel PTC reactions, for instance, metal-free PTC *radical* reactions for the direct halogenation of unactivated hydrocarbons.⁵ This shows the power of the organocatalytic approach as some of these reactions are not even feasible (e.g., iodination) with their organometallic counterparts.



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