

Editorial

# Metal-Free Organocatalysis

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Fostering research in fundamental organic transformations is of utmost importance for the development of science. Catalysts based on transition metals are generally costly and contaminating. There are applications where even the tiniest amount of a heavy metal is not tolerated in the end product of an organic synthesis. The pharmaceutical industry may be one of the most representative cases of this situation. Therefore, the search for environmentally benign catalysts capable of increasing the rates of carbon-carbon and carbon-heteroatom bond formation under metal-free conditions becomes a hot research topic in fundamental organic chemistry. An increase in this know-how will stimulate new practical applications of relevant findings.

This issue contains one review, three articles and two communications.

The review article by Pierre Vogel, Yu-hong Lam, Adam Simon, and Kendall N. Houk [1] discusses the applications of several organocatalysts. It is organized according to the mechanism of the reactions that they catalyze rather than by the identity of the catalyst. It focusses on four classes of fundamental organic reactions: acyl group transfers (esterification and ester hydrolysis, acid or base-catalyzed acyl transfers, use of amphoteric compounds as catalysts for acyl transfers, catalysis by nucleofugal group substitution, *N*-heterocyclic carbene-catalyzed transesterifications, enzyme-catalyzed acyl transfers, mimics of carboxypeptidase-A, direct amide bond formation from amines and carboxylic acids), nucleophilic additions to the carbonyl group (nucleophilic additions to aldehydes, ketones and imines, bifunctional catalysts for nucleophilic addition/elimination,  $\sigma$ - and  $\pi$ -nucleophiles as catalysts for nucleophilic additions to aldehydes and ketones, self-assembled encapsulation, catalysis of conjugate additions), anionic nucleophilic displacement reactions (reactions in the gas phase, pulling on the leaving group, phase transfer catalysis, asymmetric ion-pairing catalysis), and C–C bond-forming reactions involving umpolung (umpolung of aldehydes—benzoin condensation, Stetter reaction—, umpolung of enals, umpolung of Michael acceptors, the Rauhut–Currier reaction, the Morita–Baylis–Hillman reaction, nucleophilic catalysis of cycloadditions). It shows how the knowledge of the reaction mechanisms has led to the invention of homogenous molecular catalysts for the most important organic reactions. In summary, a tutorial on metal-free catalysis in only 65 pages!

The reactions of boronic acids and their derivatives under metal-free conditions constitute a new rapidly expanding field of organoboron chemistry. Yuri Bolshan et al. [2] present herein a new C–C bond-forming reaction of potassium trifluoroborates. They have discovered that in the presence of a Brønsted acid (HBF<sub>4</sub>), potassium alkenyl- and alkynyltrifluoroborates react with oxocarbenium ions generated from cyclic acetals to form ethers.

Zhen Li, Jing Chen et al. [3] have used pyrrolidine and its derivatives, pyrrolidine-3-amine in particular, to catalyze aldol and Knoevenagel condensations for the formation of C=C bonds. The reactions are carried out under solvent-free conditions, providing an environmentally friendly and high-yielding synthetic methodology for procuring a variety of  $\alpha,\beta$ -unsaturated compounds.

Yi-Wei Zhu et al. [4] have developed a novel fluorinated hydrazine-1,2-bis(carbothioate) catalysts for carbon-heteroatom bond-formation. These catalysts are used for the chloroalkoxylation of alkenes towards the synthesis of  $\beta$ -chloroethers. The new fluorinated organocatalysts can be recovered and reused several times.

Asymmetric organocatalysis for the synthesis of spirocyclic compounds is represented by two papers. The one by Rui Tan, Zhi-Ping Tong, Yan-Kai Liu et al. [5] shows how lactols and cyclic hemiaminals can be directly used in a one-pot asymmetric [2+2+2] tandem reaction for the asymmetric construction of six-membered spirocyclic oxindoles with six continuous stereogenic centers. This one-pot multicomponent reaction consists of an enamine-based stereoselective Michael addition followed by triethylamine-catalyzed Michael/Henry sequential reactions. The final six-membered carbocycles have versatile molecular complexity, and potential applications in synthetic organic chemistry and in the pharmaceutical industry. The paper by Cheng Peng, Wei Huang et al. [6] develops a Wolff rearrangement–amidation–Michael–hemiaminalization stepwise reaction towards the synthesis of spirocyclic piperidones with three stereogenic centers and multiple functional groups. The sequence takes place in good yields, with moderate diastereoselectivities and high enantioselectivities. Product stereocontrol can be achieved by adjusting the sequence of steps in this one-pot multicomponent reaction.

In conclusion, these six papers clearly show the importance of organocatalysis in the development of new transformations under environmentally benign conditions. I would like to thank all the authors of this Special Issue, as well as the reviewers and all the staff of the Catalyst Editorial Office. It has been an honor to be the Guest Editor of this Special Issue on Metal-free Organocatalysis.

**Conflicts of Interest:** The author declares no conflict of interest.

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