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Editorial

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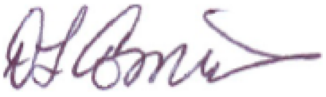
Editorial for the Special Issue on Heterocycles

Heterocycles constitute the largest group in the massive family of organic compounds. It is estimated that of the over 50 million recorded organic compounds in *Chemical Abstracts*, approximately half are heterocyclic. Heterocyclic chemistry has a long history going back to the early 1800s when the first descriptions of organic compounds appeared. Some early discoveries include the characterization of morphine (Serturner, 1816), the isolation of alloxan from uric acid (Brugnatelli, 1818), the synthesis of furfural from starch and sulfuric acid (Dobereiner, 1832), the isolation of pyrrole by dry distillation of bones (Runge, 1834), the synthesis of indigo dye (Friedlander, 1906), the one-pot synthesis of tropanone (Robinson, 1917), the isolation of chlorophyle (Treibs, 1936), and the role of purines and pyrimidines in the genetic code (Chargaff, 1951).

Since the 1950s, heterocyclic chemistry has exploded with a corresponding impact in all areas of organic, bioorganic, and medicinal chemistry.[1] Heterocycles are found in the majority of pharmaceuticals, agrochemicals, dyestuffs, and natural products. In organic synthesis, heterocycles are used as protecting groups, reagents, solvents, chiral auxiliaries, ligands, synthetic intermediates, organic materials, and polymers. There has been a proliferation of new syntheses of heterocycles in the literature driven in part by the recent emphasis on small molecule drug discovery.[2] Innovative methodologies continue to appear using C−H activation,[3] photoredox chemistry,[3] solid-phase techniques,[4] solvent-free reactions,[5] and cross-coupling strategies,[6] among others. The rapid growth of heterocyclic chemistry is seen in the estimate that approximately 85% of all publications in organic chemistry involve heterocycles in some way.[7] For this reason, *The Journal of Organic Chemistry* is highlighting this growing and energetic field with a special issue. There is a strong international flavor contained in the 50 contributions covering a broad range of modern heterocyclic chemistry that will be of interest to most organic chemists.

This special issue contains a Perspective, three *JOC*Synopses, and 46 original research articles. In their Perspective, Reiser and co-workers summarize recent progress in the development of new methods for heterocycle synthesis, particularly using catalytic methodologies. Vaquero's JOCSynopsis describes recent progress in the assembly of azonia aromatic heterocycles by using ring-closing metathesis (RCM) reactions and annulation reactions based on C−H bond activation. Joullié's JOCSynopsis highlights recent progress in production of complex heterocycles through a combination of fermentation and chemical synthesis. Scheidt's JOCSynopsis discusses recent methods for generating quinone methides and their applications in heterocycles synthesis. From these contributions, we can see how new methodologies greatly influence heterocycle synthesis. Indeed, about two-thirds of the original articles in this special issue deal with new synthetic methods, including use of asymmetric organo- and metal-catalyzed reactions to assemble saturated heterocycles and catalytic coupling reactions, direct C−H bond functionalization reactions, and cycloaddition reactions to synthesize aromatic heterocycles. Obviously, new methodologies can prompt the discovery of novel routes for assembling complex heterocyclic natural products, which are found in nine articles covering the total synthesis of naturally occurring alkaloids, or their core structures, and peptides. The new methodologies allow one to further explore the chemical space of heterocycles and investigate their bioactivities and material properties. This trend is seen in eight papers in the Special Issue in which the properties of heterocycles as materials and pharmaceutical agents are described. Their special properties include serving as new fluorophores and agents for nuclear waste treatment and a variety of biological activities such as inhibition of autophagy and HIV-1 integrase, opioid receptor antagonists, promotors of self-renewal of human hematopoietic stem cells, and molecules with antimitotic activity.

This special issue on heterocycles is a joint effort between *The Journal of Organic Chemistry* and the International Society for Heterocyclic Chemistry (ISHC). For more information, see the ISHC Web site (http://www.ishc-web.org). Several members of the JOC Advisory Board and JOC Associate Editors have been members and officers of the Society. Three current JOC Associate Editors are past ISHC presidents (Al Padwa, Dawei Ma, and Dan Comins). In addition, the majority of the authors in this special issue are members of the ISHC as indicated by a notation in the Author Information. The current president of the ISHC is Oliver Reiser, who is an author of the Perspective entitled "The Modern Face of Synthetic Heterocyclic Chemistry". It is an interesting and educational read you should all enjoy.



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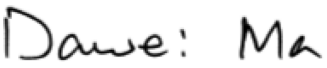

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AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

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