Organometallics in heterocyclic chemistry

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Organometallic chemistry continues to be a fruitful source of new methods for organic synthesis. This issue will summarize a number of recent applications of organometallics for the selective synthesis of heterocycles. Experts in their respective fields have written these reviews and they give a critical analysis of the scope of the specific synthetic methods and its potential for future development.

Selective methods for metalation of heterocycles have broad application in synthesis. The tutorial by Schlosser and Mongin gives an overview of the guiding principles for elaboration of pyridines by means of organolithium intermediates. This is followed by a review by Stanetty and co-workers on the halogen dance reaction, which involves a cascade of reactions, in which the initial organometallic species is transferred to another by a halogen exchange before reacting with an appropriate electrophile. This cascade sequence can be applied to numerous heterocyclic systems, leading to useful substitution patterns.

Metal catalyzed cross-coupling reactions are now standard reactions for the synthesis of heterocycles, but still very innovative variations continue to be discovered. Most spectacular has been the development of C–H functionalization approaches, combined with the cross coupling chemistry. Gevorgyan gives an overview of palladium catalyzed functionalization of nitrogen heterocycles, while three reviews describe various aspects of C–H functionalization approaches. Seregin and Gevorgyan focus on the direct functionalization of heteroaromatic compounds. Fairlamb expands the discussion to include palladium catalyzed cross-coupling and direct arylation processes for the regioselective functionalization of a range of heterocyclic compounds. Campeau and Fagnou describe the applications of an alternative to electron deficient azine organometallics in metal-catalyzed cross-coupling reactions. In addition, Campos reports on direct sp^3 C–H bond activations in N-heterocycles.

Many strategies have been developed that use metal-mediated convergent reactions for the rapid construction of highly functionalized heterocycles. Heller and Hapke describe the scope of the metal-catalyzed [2 + 2 + 2] cycloaddition for the synthesis of pyridine derivatives. A further development is the use of multi-component reactions for the synthesis of heterocycles by transition-metal catalysis, which is covered by D'Souza and Müller. Davies and Hedley describe the rules that govern the intermolecular reactions of electron-rich heterocycles with copper and rhodium carbenoids and illustrates how these transformations can applied to the synthesis of various mono- and bicyclic heterocycles.

Certain classes of heterocycles have generated considerable interest because of their special properties and this has spurred the invention of new methods for their synthesis. Senanayake and co-workers describe how organometallic methods can be used for the synthesis of azaindoles, while Nishiyama focuses on the synthesis and use of bisoxazolinyl-phenyl pincers.

Transition-metal catalyzed addition of nitrogen nucleophiles to alkanes is now recognized as a very useful approach for the synthesis of saturated nitrogen heterocycles. Minatti and Muñiz describe the palladium-catalyzed amination of alkenes, while Chemler and Fuller describe a complimentary method using copper catalysis.

In conclusion, the broad variety of organometallic reactions and heterocyclic systems described in this Themed Issue underscores the central role organometallic chemistry plays in the modern approaches for the synthesis of heterocycles. The field is still wide-open for innovation and will continue to advance as even more versatile transformations are developed.

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