

PREFACE TO VOLUME 76

The impact of transition-metal catalysis in synthetic organic chemistry can hardly be overstated. Three of the last ten Nobel Prizes in Chemistry have been awarded for the discovery and development of transition-metal-catalyzed reactions that fundamentally changed the practice of organic synthesis (2001: oxidation/reduction (Knowles, Noyori and Sharpless); 2005: olefin metathesis (Chauvin, Grubbs, Schrock); 2010: cross coupling (Heck, Negishi, Suzuki)). In fact, 14 of the 56 chapters published in *Organic Reactions* Volumes 50–75 are dedicated to the myriad manifestations of this family of increasingly important chemical transformations. It is thus no surprise that each of the three newest family members contained in this volume describe transition-metal-catalyzed reactions.

The first chapter by Timothy J. Donohoe, Carole J. R. Bataille, and Paolo Innocenti describes a versatile modification of the osmium-catalyzed dihydroxylation of alkenes. The ability to introduce vicinal hydroxy groups with high predictability and selectivity is a powerful and enabling transform in organic synthesis (see Noe, Letavic, Snow, and McCombie in Volume 66). Whereas the directing effect of hydrogen-bonding groups on epoxidation has been known for over 50 years, the corresponding control of dihydroxylation has only recently been harnessed in a synthetically practical fashion. Pioneering studies from the Donohoe laboratories have demonstrated that hydrogen-bonding functional groups (alcohols, secondary amides, and carbamates) serve as powerful directing moieties for the introduction of vicinal diols on proximal (allylic and homoallylic) double bonds. This mode of diastereoselective oxidation has allowed the synthesis of densely functionalized building blocks as well as enabling the late-stage introduction of key functional groups on advanced intermediates in complex molecule synthesis.

The second chapter by Damien Prim, Sylvain Marque, Anne Gaucher, and Jean-Marc Campagne covers the transition-metal-catalyzed α -arylation of enolates. The formation of carbon-carbon bonds facilitated by the α -hydrogen acidity of carbonyl compounds is among the most commonly employed reactions in organic synthesis. Classic chemical transformations and their modern variants (alkylation, aldol, Claisen, and Michael reactions) are reliable workhorse processes. However, because of the inability to employ aromatic electrophiles, the formation of C-aryl bonds is notably absent from this list. Once only the purview of stoichiometric transformations involving arylbismuth and aryllead reagents, the introduction of palladium, nickel, or copper catalysis in combination with standard enolate chemistry now enables the use of common aryl electrophiles (halides and triflates) to engage in direct bond formation. The scope of this transformation is broad and allows arylation of enolates derived from ketones, aldehydes, esters, amides, nitriles, and active methylene compounds. An important variant also incorporates the use of enoxysilane derivatives of ketones and esters. As is so often the case in transition-metal-catalyzed reactions, the choice

of ligands and conditions is critical. Prim, Marque, Gaucher, and Campagne provide expert guidance for selection of these variables and show that with chiral phosphine ligands, even enantioselective C-aryl bond formation can be achieved. The usefulness of this process has been demonstrated by its application as a strategy level transform in total synthesis endeavors.

The third chapter by Sandro Cacchi, Giancarlo Fabrizi, and Antonella Goggiamani reviews the application of transition metal catalysis for the synthesis of one of the most important classes of heterocyclic compounds, namely indoles. The indole subunit is ubiquitous in alkaloid natural products as well as many signaling molecules, bioactive pharmaceutical agents, and fragrances. Because of its prevalence, many general methods for the preparation of indoles have been developed dating back to the Fischer indole synthesis reported in 1883. Indole syntheses comprise no fewer than 10 name reactions involving different precursors and bond constructions. Once again, the advent of palladium catalysis has enabled the multifaceted construction of substituted indoles from three basic building blocks: aromatic halides or anilines, alkynes, and amines. Cacchi, Fabrizi, and Goggiamani thoroughly detail the versatility of this family of reactions and illustrate the manifold strategies that can be used to create any of the four bonds comprising the pyrrole subunit of the indole moiety. Moreover, strategies that allow the simultaneous introduction of substituents on C(2) or C(3) of the pyrrole ring are described.

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