Preface

The impact of organometallics on the synthesis of medicinal agents during the last decade cannot be overstated. Although metals or organometallic species have been used for sometime in the pharmaceutical industry, the advances in the variety of reactions and the tremendous selectivity that is often achieved has expanded the toolbox of reagents available to the medicinal and process chemist. These reagents have helped to streamline the synthetic approaches developed for medicinal agents as can be seen by the increasingly sophisticated strategies used to synthesize complex drug products. In the areas of asymmetric synthesis, pharmaceuticals can be prepared using methodology only dreamed of a few decades ago.

This volume will highlight some of the more active areas where organometallics are playing an important role in process chemistry. With the chelation effects of many chiral ligands, organolithium reagents have become key intermediates in asymmetric synthesis. Similarly, because of the great propensity of titanium to chelate and bind to heteroatoms, organotitanium reagents are extremely useful and versatile in carrying out a number of selective organic transformations. Although the asymmetric hydrogenation of α-amidoacrylates to prepare amino acids has been known for sometime, the discovery and application of new ligands and reaction classes have expanded the number of substrates that can be converted to chiral products with Rh and Ru-mediated reactions. The cyclopropyl group is a common moiety found in pharmaceutical agents. Metal-mediated methods for preparing this ring are reviewed herein. Non-reductive means to prepare the enantiomers of oxy-systems remained elusive until the reports of chiral salen ligands and osmium-mediated reactions over the past two decades. Organopalladium reactions are now so commonly used in the synthesis of complex molecules that one can forget that palladium was once used only in hydrogenation reactions. The use of metals does come with a price when preparing pharmaceuticals for human consumption. Because of the potential toxicities of the metals, only low ppm levels can remain in the active pharmaceutical ingredient. Some of the methods that have been utilized in process chemistry to remove residual metals are presented. Organometallics will certainly continue to be used extensively in the pharmaceutical industry as newer methods and applications are discovered.

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