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Preface

New applications of metal catalysis in natural product synthesis

Metal catalysis has dramatically altered the way we design syntheses and assemble natural products. Moreover, metal catalysis provides entry to molecular structures and functionalities that were previously inaccessible or difficult to obtain using more classical approaches. The contributors to this symposium have provided a snapshot of recently discovered methods involving metal catalysis and the application to natural product synthesis. Importantly, the scope of each of these methods has been extended by the pursuit of natural product synthesis.

For example, Diver and Mori have given us a new way to think about assembling functionalized dienes. Substituted cyclohexadienes are obtained via a ruthenium catalyzed tandem metathesis reaction between a diene and an alkyne. This protocol is used by Diver to access the cyclohexenyl subunits of pentacyclic core of scabrosin. In addition, Mori has validated the synthetic usefulness of an intramolecular ruthenium catalyzed enyne metathesis reaction, which affords an azabicyclo[4.2.1]nonene ring system possessing an appropriately placed diene particularly well-suited for the enantioselective synthesis of anatoxin A.

Hsung has shown that the ruthenium catalyzed metathesis conditions are mild enough to afford spiroketals stereoselectively via the reaction of a diene possessing a ketal tethering unit. This strategy for preparing sprioketals has been successfully applied to the synthesis of an insect pheromone and a key fragment of spirastrellolide.

The wide-ranging utility of palladium catalyzed allylic alkylation reactions has been reaffirmed by Wipf and Lovely in their efficient synthetic approaches to the alkaloid cores of naphthyridinomycin and iroidins, respectively. Martin and Davies used chiral rhodium(II) catalysis to install the requisite absolute stereochemistry in their respective targets and both showcase the power of tandem transition-metal catalyzed reactions. Martin has prepared tremulenolide A and tremulenediol A using an enantioselective rhodium(II) catalyzed cyclopropanation reaction followed by a tandem rhodium(I) catalyzed allylic alkylation and carbocyclization reaction. Davies has successfully applied a C–H activation/Cope rearrangement strategy to the first synthesis of (+)-elisabethadione.

Malacria and our group have shown that a selective reaction of one double bond of an allene gives unprecedented substructures. In Malacria's case an allenediyne provides the steroidal carbocyclic core in one-step via an intramolecular Co(I) mediated [2+2+2] cycloaddition reaction. A carbocyclization reaction of an allenyne has been accomplished in our group, leading to a carbocyclic skeleton that will be used as a framework in the projected synthesis of ovalicin.

Suffert has extended the scope of the 4-*exo-dig* cyclocarbopalladation/Stille cross coupling reaction by adding on an 8π electrocyclization reaction. This extraordinary cascade of reactions lead to carbocyclic cores present in a number of biologically important terpenes. Finally, a complement to palladium catalyzed alpha arylation of ketones has been provided by the Krische laboratory where they have shown that enones can be regioselectively alpha arylated via the conjugate addition of tributylphosphine and trapping the resulting enolate with an aryl bismuth reagent. Using this method an enantioselective synthesis of paroxetine was accomplished.

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