

ASYMMETRIC SYNTHESIS AND APPLICATIONS OF CYCLOPROPENES

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INTRODUCTION

Cyclopropenes are a unique class of carbocyclic compounds with unsaturated, highly strained three-membered ring structures. High strain and unsaturation make cyclopropenes versatile synthons for a wide variety of synthetic organic transformations. Consequently, optically active derivatives are useful chiral building blocks, and a significant effort has been devoted to the development of asymmetric synthesis of cyclopropenes, as their further transformation enables access to densely functionalized cyclopropenes containing enantioenriched all-carbon quaternary stereogenic centers. This seminar will focus on recent developments toward asymmetric cyclopropene formation and their use in synthesis.

REACTIONS OF CYCLOPROPENES

The significant strain of cyclopropene makes these species great energy reservoirs and accounts for their unusually high reactivity. Due to this energy, transformations previously unknown for normal olefins are allowed. The most well represented type of reaction, which has recently attracted much attention, involves metal-catalyzed addition of various entities across the double bond of cyclopropene, which can proceed both with and without ring opening. These include carbo-, and hydrometalation, addition of nitrogen- and oxygen-based nucleophiles, hydrogenation, the Pauson-Khand reaction, [3+2] cycloadditions and ROM reactions. Another important type of transformation involves substitution reactions, which proceed with preservation of the small cycle and the strained double bond, exemplified by various types of cross-coupling reactions. Recently, Rubin reported rhodium-catalyzed hydroformylation of cyclopropenes.¹ Fox developed directed transformations of cyclopropenes via a carbozincation reaction.²

ASYMMETRIC FORMATION OF CYCLOPROPENES

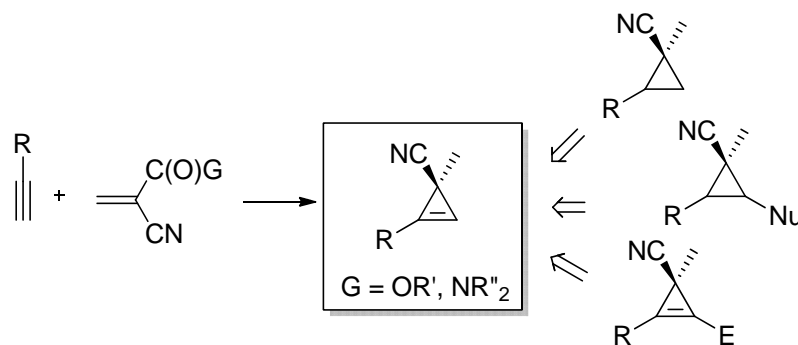
In 1992, Doyle and Muller et al. reported a seminal study on enantioselective cyclopropenation using α -diazoacetates with a catalytic amount of dirhodium(II) complexes, which provided enantiomerically enriched cyclopropenes in moderate yields.³ Corey and co-workers described a very efficient catalyst, $[\text{Rh}_2(\text{OAc})(\text{dpti})_3]$ for the cyclopropenation of terminal alkynes. The results of this study show that ethyl diazoacetate in the presence of 0.5 mol% of this catalyst leads to 2 substituted

2-cyclopropene-carboxylic acid ethyl esters with excellent ee and yields.

Moreover, the scope of this reaction was extended to provide access to products containing a quaternary stereocenter. Davies et al. reported asymmetric cyclopropenation using α -aryl- α -diazoacetates, a donor/acceptor substituted diazo compound, and

$\text{Rh}_2(\text{S-DOSP})_4$ as a catalyst.⁴ More recently, two different groups reported asymmetric cyclopropenations of alkynes with acceptor/acceptor substituted diazo reagents. Katsuki and coworkers demonstrate this with an iridium complex in good yield and high ee.⁵ Furthermore, Zhang et al. reported this transformation with Co(II) catalyst (Scheme 1) in high yield and excellent ee.⁶ These studies show that the reaction is tolerant of a variety of functional groups and exhibits a remarkably broad substrate scope. Furthermore, Zhang demonstrated that the cyclopropenes can be further functionalized. These are practical methods for the preparation of multifunctionalized cyclopropenes bearing enantioenriched all-carbon quaternary stereogenic centers that may serve as useful chiral synthons for stereoselective synthesis of wide variety pharmaceutical and other synthetic targets.

Scheme 1. Synthesis of Cyclopropenes Bearing Quaternary stereocenters and Their Further Potential Transformations



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