

TRANSITION METAL CATALYZED CARBON-CARBON BOND CLEAVAGE OF STRAINED RING SYSTEMS

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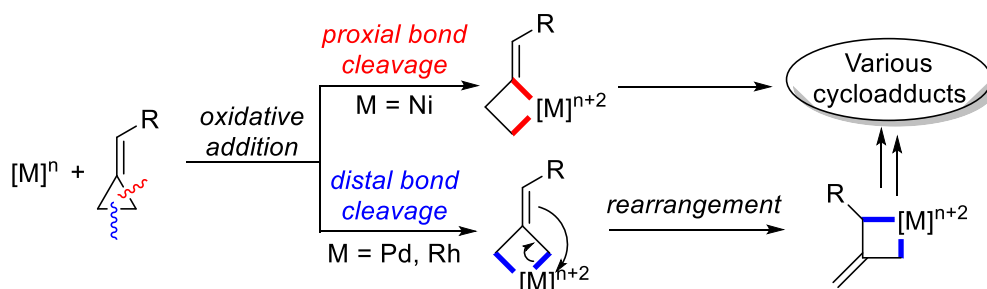
INTRODUCTION

Transition metal catalyzed C-C bond activation shows an atom-economical synthetic pathway to construct the carbon-carbon connectivity. However, the activation of C-C σ bond often encounters four major challenges¹: (1) Steric inaccessibility due to C-H bonds surrounding C-C single bonds, (2) Orbital directionality of sp^3 -hybridized orbitals of C-C single bonds, (3) higher BDE of C-C bonds and metal-hydride bond than metal-carbon bond. To overcome these problems, small ring systems that bear a high ring strain have gained a lot of interest in order to lower the kinetic barrier by utilizing “banana-shape” HOMO of cyclopropane and cyclobutene ring system, as well as to provide a thermodynamic driving force from strain relief.^{1a} Transition metal catalyzed C-C bond activation of strained ring systems can be classified into two mechanistic categories, (a) the oxidative addition and (b) the β -carbon elimination.²

OXIDATIVE ADDITION PATHWAY

One of the most widely used classes of cyclopropane-based ring system are alkylidenecyclopropanes (Scheme 1). Oxidative addition of nickel catalysts into alkylidenecyclopropanes proceed by proximal bond cleavage, whereas palladium and rhodium complex insert via distal bond cleavage to generate two different metallacyclobutane intermediate. The following cycloaddition reactions provide a

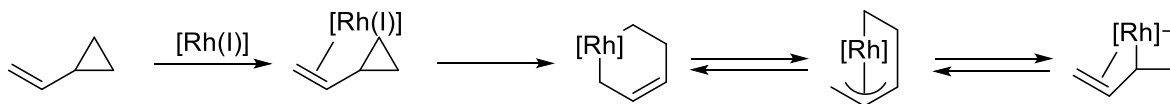
Scheme 1. Transition Metal Insertion Into Alkylidenecyclopropane



number of cyclization products. Based on the cleavage of the proximal and distal bond with nickel and palladium catalysts, respectively,

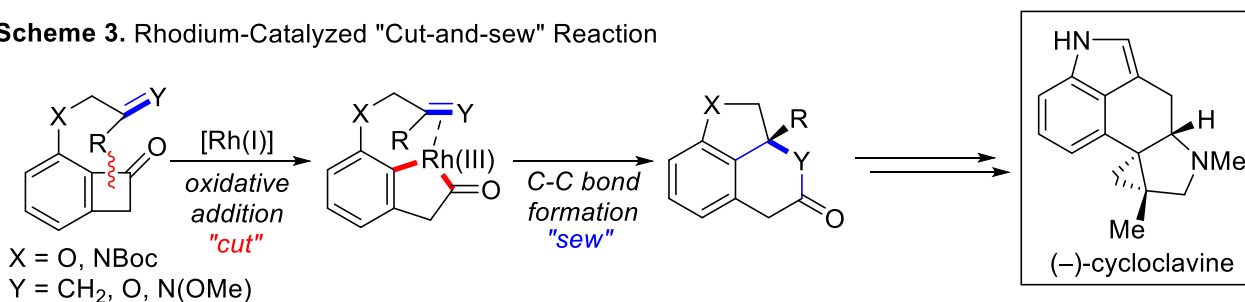
Mascareñas and coworkers reported intramolecular [3+2+2], [3+2] and [4+3] cycloadditions of alkyne- or alkene-tethered alkylidenecyclopropane substrates to provide a variety of bicyclic products in excellent yields and selectivity. Another important substrate for oxidative addition pathway is vinylcyclopropane, which provides rhodacyclic intermediate via oxidative addition of rhodium catalyst. (Scheme 2) Wender group employed the rhodacycles as a five-carbon source for Rh(I)-catalyzed [5+2] cycloaddition of vinylcyclopropane with ynones or allene equivalent to provide cycloheptenone products.

Scheme 2. Oxidative Addition of Rh(I) to Vinylcyclopropanes



Dong group utilized the insertion of Rh(I) into benzocyclobutenones in their rhodium-catalyzed insertion of tethered C=Y double bond into benzocyclobutenones to provide tricyclic products. This “cut-and-sew” reaction was applied to their recent total synthesis of (–)-cycloclavine (Scheme 3).³

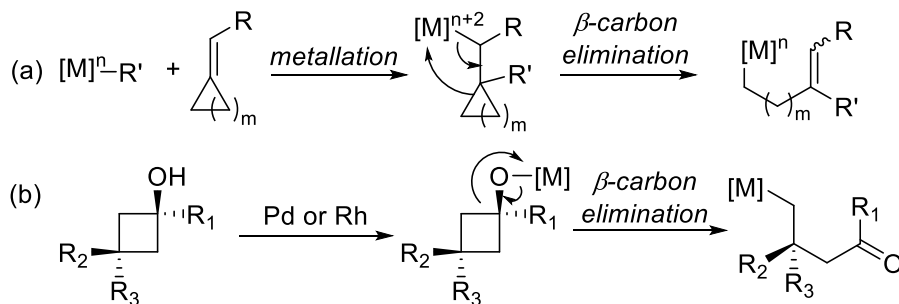
Scheme 3. Rhodium-Catalyzed "Cut-and-sew" Reaction



BETA-CARBON ELIMINATION PATHWAY

The other important mechanistic pathway of C-C bond cleavage is redox-neutral β -carbon elimination. Alkylidenecyclopropanes undergo metallation onto the exo-alkene moiety followed by β -carbon elimination, which provides a complementary pathway to oxidative addition method (Scheme 4a). Cyclobutanols undergo β -carbon elimination with palladium or rhodium catalysts (Scheme 4b).

Scheme 4. β -Carbon Elimination of Alkylidenecyclopropanes and Cyclobutanols



Cramer and coworkers reported the enantioselective synthesis of indanols and tetralones from chiral cyclobutanols via β -carbon elimination and subsequent Rhodium shift and reductive

elimination. The Rh(I)-catalyzed cyclobutanol ring opening was utilized in total synthesis of Phomactin diterpenoids reported by Sarpong and coworkers.⁴

REFERENCES

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4. Sarpong, R. et al. *J. Am. Chem. Soc.* **2018**, *140*, 9810-9813