

# Metal promoted vinylcyclopropane–cyclopentene rearrangements: Reactions ripe for mechanism-based catalyst design

Selina C. Wang, Dean J. Tantillo \*

*Department of Chemistry, University of California, Davis, 1 Shields Avenue, Davis, CA 95616, United States*

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## Abstract

This brief review describes experimental and theoretical data relevant to the mechanisms of transition metal promoted vinylcyclopropane–cyclopentene rearrangements. In particular, reactions utilizing Pd(0), Rh(I), and Ni(0) are highlighted and compared to analogous reactions not involving transition metals.

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## 1. Introduction

Organometallic chemistry has become a cornerstone of modern organic synthesis. In particular, transition metal-promoted pericyclic reactions figure prominently in many complexity-creating synthetic transformations [1–6]. The appeal of such reactions lies in the fact that by using appropriate metal promoters, reactions that are sluggish or even orbital-symmetry-forbidden [7] in the absence of the metal can be achieved efficiently. Although metal-promoted cycloadditions have found many applications in synthesis, the synthetic potential of metal-promoted sigmatropic rearrangements has been largely untapped.

One particular type of sigmatropic rearrangement that has been utilized on occasion in syntheses of complex organic molecules that contain five-membered rings is the [1,3] sigmatropic rearrangement that interconverts vinylcyclopropanes and cyclopentenones (Scheme 1) [8]. Although significant success has been achieved in this area—both with and without metal promoters and catalysts—room remains for designing improved transition metal-based catalysts with broad substrate scope and the ability to reliably con-

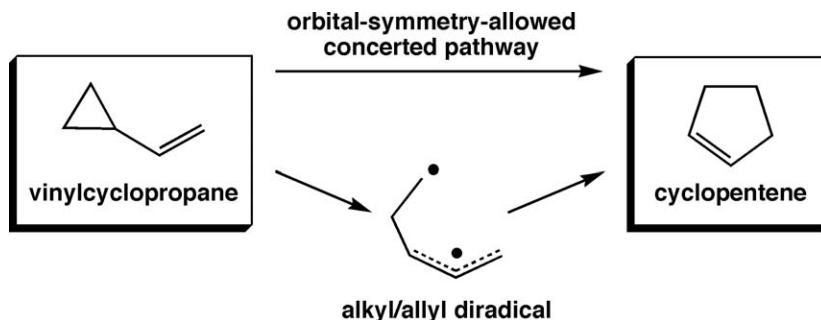
trol the regio- and stereoselectivity of such reactions. In order to design such catalysts, one must have some knowledge of the mechanistic details of the reactions, in particular the structures of the rate-, regio-, and stereoselectivity-determining transition structures. In this brief review, we discuss the available mechanistic information on metal-promoted vinylcyclopropane–cyclopentene rearrangements.

## 2. The mechanism without the metal

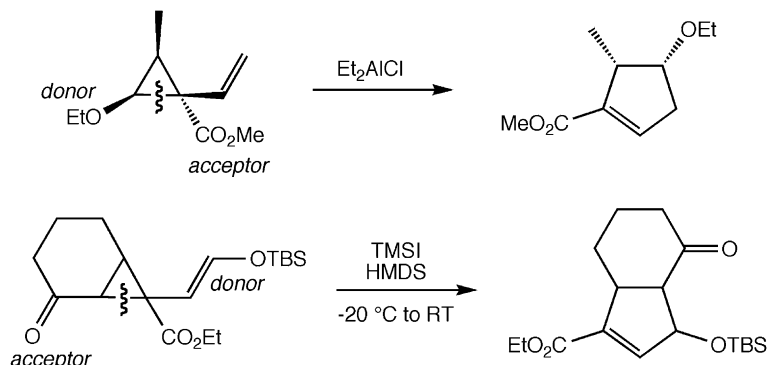
Metal-free [1,3] shifts of simple vinylcyclopropanes (i.e., without polar substituents) generally require high temperatures and tend to produce mixtures of products [9]. The mechanism of this reaction has been studied in great detail, through many elegant and challenging experiments and theoretical studies, for a variety of vinylcyclopropanes [9]. Although such reactions are orbital-symmetry-allowed as concerted antarafacial/suprafacial sigmatropic rearrangements [7], their mechanisms tend to involve homolytic cleavage of one cyclopropane C–C bond (the weakest if substituents are attached) to produce alkyl/allyl diradicals (Scheme 1). These sorts of diradicals often exist on relatively flat energy surfaces and their transformation to products is therefore often influenced by dynamic factors. The activation energy for the parent vinylcyclopropane–cyclopentene

\* Corresponding author.

*E-mail address:* [tantillo@chem.ucdavis.edu](mailto:tantillo@chem.ucdavis.edu) (D.J. Tantillo).



Scheme 1.



Scheme 2.

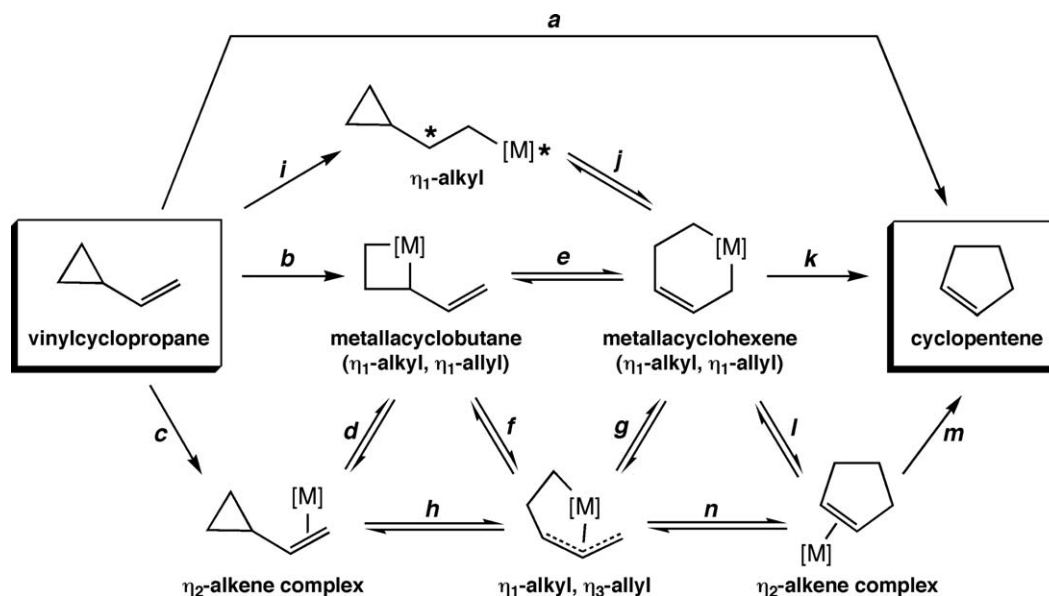
rearrangement is estimated to be  $\sim 52$  kcal/mol [9], but this barrier can be reduced by appending radical-stabilizing substituents to the cyclopropane ring. In some cases, cyclopropanes bearing both electron-donating (EDG) and electron-withdrawing (EWG) groups on one of their C–C bonds have proven useful in synthesis (examples are shown in Scheme 2) [9–12]. The various donor and acceptor substituents in such cases are set up to favor stepwise rearrangement pathways by promoting initial cleavage of one particular cyclopropane C–C bond. It should be noted, however, that such substituents can stabilize both radicals and ions and the preference for diradical versus zwitterionic intermediates in such reactions is often not clear-cut [9]. Lewis acids can also be used to accelerate these reactions by increasing the electron-withdrawing ability of the acceptor group [10], and added nucleophiles [13] or radicals [14] can also promote some vinylcyclopropane–cyclopentene rearrangements. Another strategy for accelerating vinylcyclopropane–cyclopentene rearrangements is oxidation—removal of an electron from vinylcyclopropane itself leads to a radical cation that can rearrange with a barrier of only  $\sim 20$  kcal/mol [15]. Again, flat energy surfaces are observed that contain exit channels that lead to various byproducts. Nonetheless, the significant lowering of the barrier upon oxidation hints that electron-accepting transition metal catalysts may also be capable of accelerating the rearrangement.

### 3. Means of metal manipulation

In principle, a transition metal (with its associated ligands; referred to here as [M]) can intervene in the vinyl-

cyclopropane–cyclopentene rearrangement in various ways. An overview of the various metal-containing intermediates that could arise in such processes is shown in Scheme 3. Although other mechanistic pathways are perhaps possible, an attempt was made here to include the most likely options. The complexity associated with conformational properties of intermediates and possible  $\sigma$ -complex formation is not included. Nonetheless, it is hoped that this Scheme will facilitate the discussion and comparison of mechanisms of known metal-promoted vinylcyclopropane–cyclopentene rearrangements as well as provide a reasonable framework for guiding future laboratory and theoretical experiments.

Pathway **a** represents a concerted but metal-assisted conversion of a vinylcyclopropane to a cyclopentene. Such a process can be thought of as selective complexation by [M] of the transition state structure for the concerted process in the absence of the metal (or a reasonable model thereof). Examples of such “transition state complexation” for other types of pericyclic transition state structures have been described [6,16]. Pathways **b** and **c/d** correspond to metal-promoted breaking of one C–C bond of a vinylcyclopropane via oxidative addition (with or without precomplexation) to form a vinylmetallacyclobutane. This species could then rearrange to a metallacyclohexene either directly via pathway **e** (itself a [1,3] sigmatropic rearrangement where it is [M] that shifts) or via pathway **f/g** (slippage/hapticity change through an  $\eta_1$ -alkyl/ $\eta_3$ -allyl intermediate). Alternatively, a metallacyclohexene could be formed directly without the intermediacy of a vinylmetallacyclobutane from an alkene  $\pi$ -complex and  $\eta_1$ -alkyl/ $\eta_3$ -allyl



Scheme 3.

intermediate (pathway **c/h/g**) or via an  $\eta_1$ -alkyl intermediate with a cyclopropylcarbinyl radical, cation, or anion (pathway **i/j**). The  $\eta_1$ -alkyl/ $\eta_3$ -allyl intermediate can be viewed as the diradical from Scheme 1 or the transition state structure for a concerted vinylcyclopropane-to-cyclopentene rearrangement stabilized by “metal intrusion” (note that the latter would be different than the “transition state complexation” described for pathway **a**). Reductive elimination of [M] from the metallacyclohexene (directly or with formation of an intermediate alkene  $\pi$ -complex; pathways **k** and **l/m**, respectively) would produce the cyclopentene product. It is also possible that the metallacyclohexene could be avoided entirely (pathway **n/m**). Which of these pathways will occur depends on the specific metal and ligands used.

Fig. 1 shows representative examples of reactions (some stoichiometric with respect to the metal and some catalytic) for which vinylmetallacyclobutane, metallacyclohexene, and/or  $\eta_1$ -alkyl/ $\eta_3$ -allyl intermediates arising from vinylcyclopropanes have been proposed [17–26]. At the top of this figure (in bold boxes) are shown examples of metal-promoted vinylcyclopropane–cyclopentene rearrangements. So far, successful rearrangements have been reported using Pd(0), Rh(I) and Ni(0).

### 3.1. Palladium

Some vinylcyclopropane–cyclopentene rearrangements can be catalyzed by Pd(0) [18]. Oshima and co-workers have described rearrangements of dienyl cyclopropanes catalyzed by Pd(PPh<sub>3</sub>)<sub>4</sub> (e.g., Scheme 4) [18a,18b]. Several substrates were studied and it was concluded that the diene (rather than just a single alkene [18c,18d]) as well as two electron-withdrawing groups attached to the cyclopropane (esters, ketones, and sulfones were used) are required for

successful rearrangement. Based on this observation, it was proposed that a zwitterionic intermediate might arise via nucleophilic attack of Pd, which promotes heterolytic cleavage of one bond of the cyclopropane to produce an anion stabilized by the electron-withdrawing groups and a pentadienyl cation stabilized through complexation by the Pd (Scheme 5). This intermediate is similar to the  $\eta_1$ -alkyl/ $\eta_3$ -allyl intermediate shown in Scheme 3, but with the allyl substructure replaced by a pentadienyl substructure and the alkyl ligand not necessarily attached directly to the metal. This reaction is closely related to the examples described above involving donor–acceptor cyclopropanes (e.g., Scheme 2).

### 3.2. Rhodium

Various examples of Rh(I)-promoted vinylcyclopropane–cyclopentene rearrangements have been reported (e.g., Scheme 6) for which the corresponding thermal rearrangements without Rh present generally occur at much higher temperatures [19]. In many cases, however, other reactions compete with or even predominate over Rh(I)-promoted vinylcyclopropane–cyclopentene rearrangements [19d], and the best results have been observed when additional alkene or carbonyl groups are attached to the cyclopropane.

The mechanisms of Rh(I)-promoted vinylcyclopropane–cyclopentene rearrangements have been considered in detail, especially by Brown and co-workers [19b–e]. Scheme 7 shows the mechanistic possibilities that are consistent with reported experiments, most of which were carried out on divinylcyclopropanes. Complexation of the reactant and product is generally invoked and is consistent with the fact that Rh(I) complexes of both have been isolated in certain systems [19a–c,e].  $\eta_1$ -Alkyl/ $\eta_3$ -allyl intermediates are

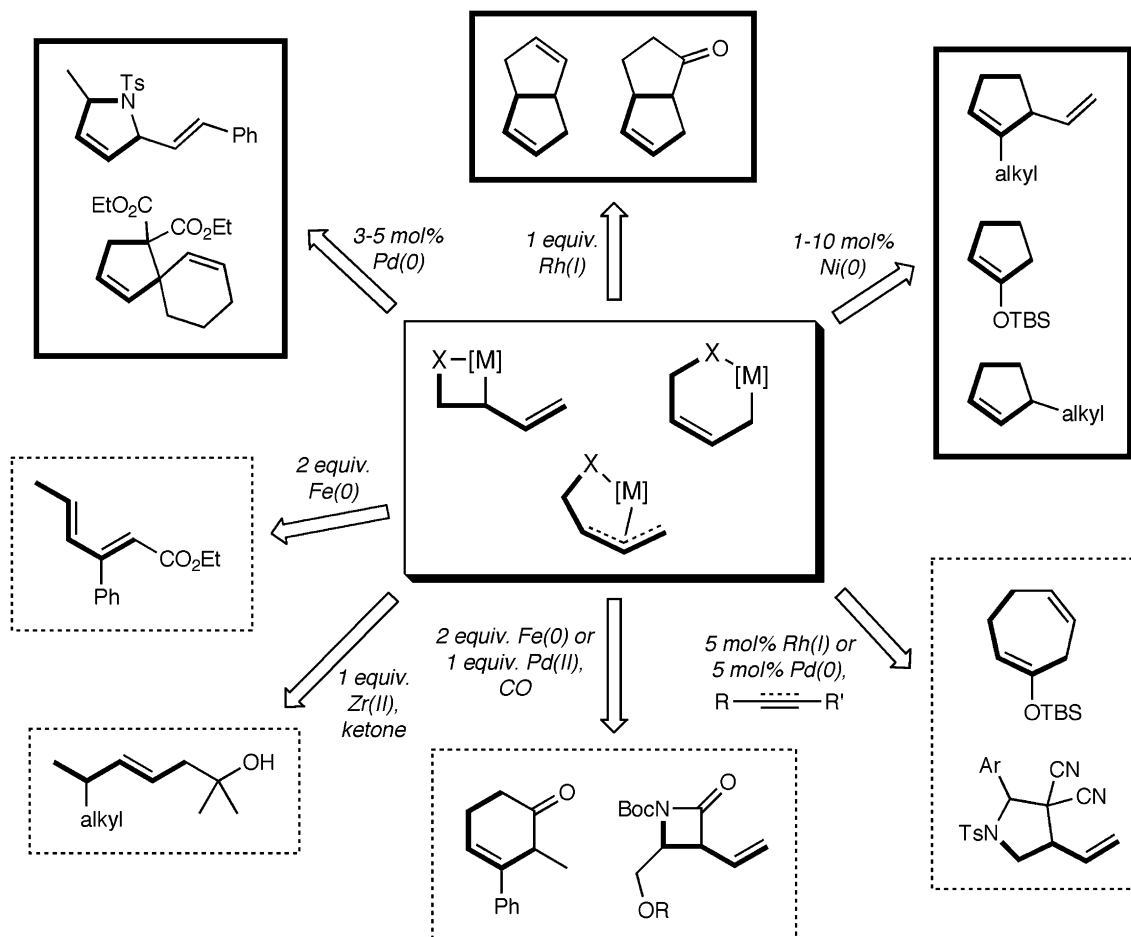
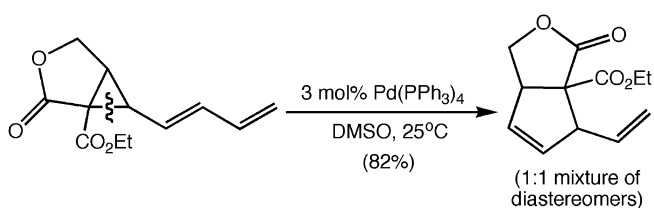
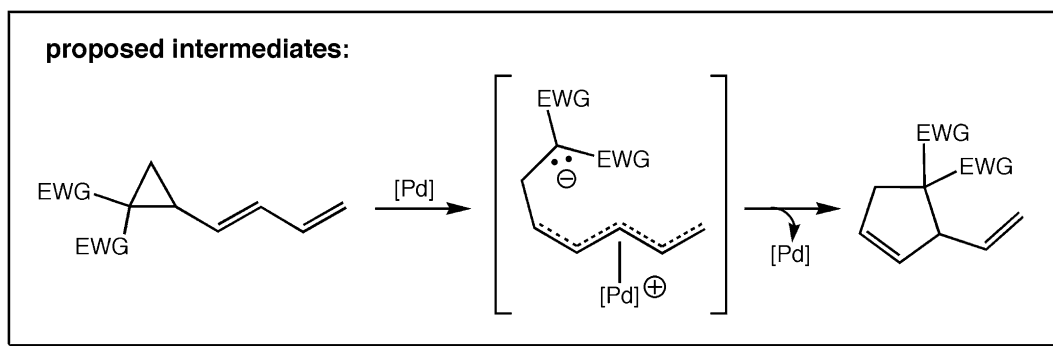


Fig. 1. Products formed from reactions of vinylcyclopropanes (or vinylaziridines) proposed to involve one or more alkyl/allyl intermediates (generic structures in central box;  $X = CR_2, NR$ ). For intermediates and products, bonds originating from the vinylcyclopropane reactant are highlighted in bold. Metal promoters used in each reaction are shown for each. Products of vinylcyclopropane–cyclopentene rearrangements are enclosed in bold boxes.

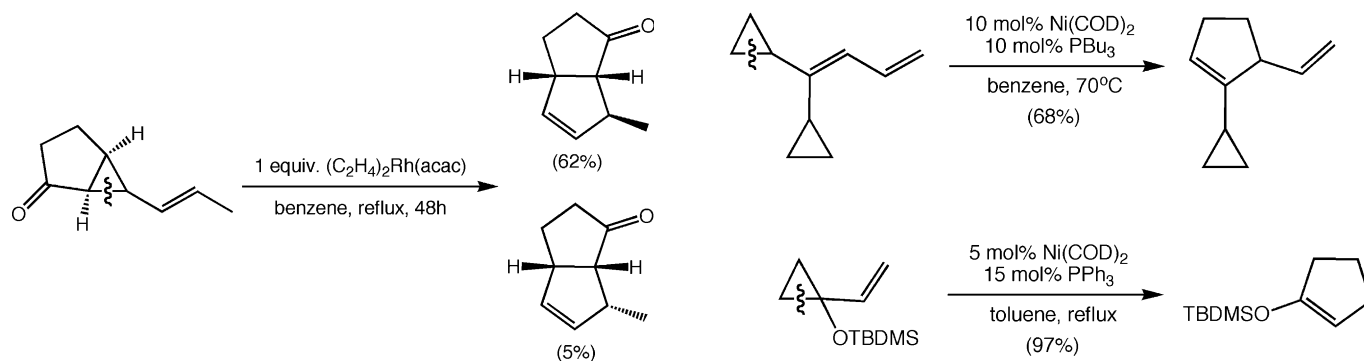


Scheme 4.

generally proposed for these mechanisms although direct interconversion of such species with reactant and product  $\pi$ -complexes as well as interconversion with metallacyclobutane and metallacyclohexene species has also been proposed [19b–e]. A tetrameric complex of the  $\eta_1/\eta_3$  species shown below (left) has also been characterized crystallographically (in the crystal structure each Rh also interacts with the alkene of another monomer) [19c–e], and such

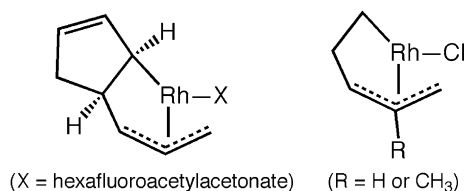


Scheme 5.



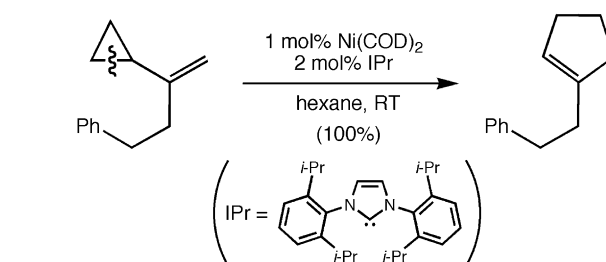
Scheme 6.

complexes have been shown to rearrange to  $\pi$ -complexes of the corresponding vinylcyclopropanes and cyclopentenes [17,19e]. In addition, the  $\eta_1/\eta_3$  species shown below (right) have been synthesized from vinylcyclopropanes, isolated, and characterized by NMR, but these species apparently do not rearrange to cyclopentenes and instead can be induced to regenerate vinylcyclopropanes by addition of phosphites or phosphines [19h]. Recently, quantum chemical calculations on a related (5+2) cycloaddition reaction of vinylcyclopropanes (see Fig. 1) with alkynes in the presence of  $[\text{Rh}(\text{CO})_2\text{Cl}]_2$  have indicated that  $\eta_1$ -alkyl/ $\eta_3$ -allyl intermediates can form from vinylcyclopropanes in the presence of Rh(I) without the intermediacy of metallacyclobutanes [21].



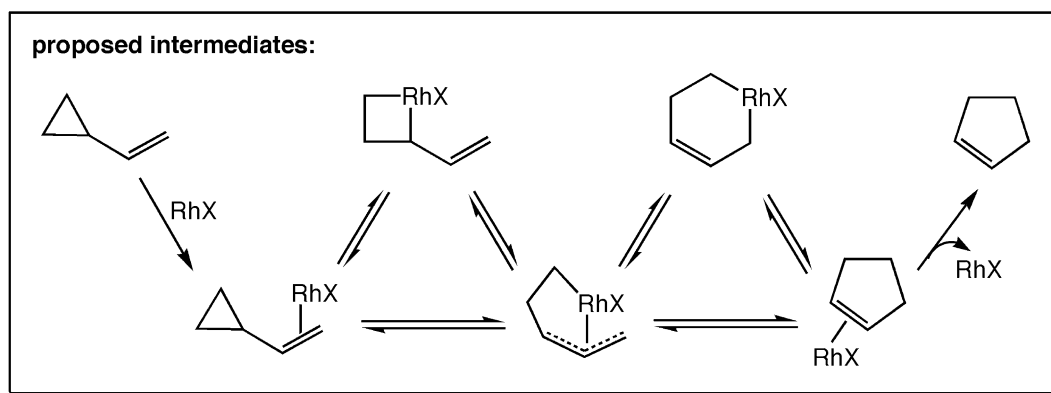
### 3.3. Nickel

Ni(0) catalyzed vinylcyclopropane–cyclopentene rearrangements have also been reported (e.g., Scheme 8) [20]. Early studies showed that Ni(0)-phosphine complexes can

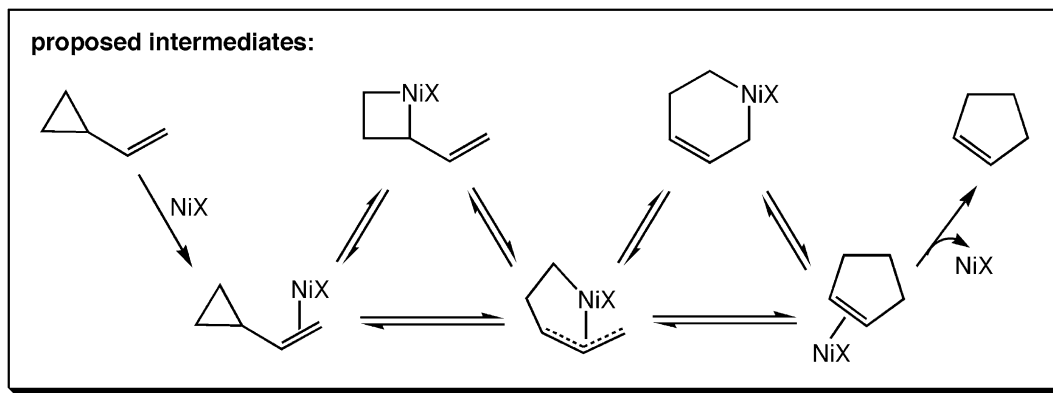


Scheme 8.

catalyze ( $\sim 10$  mol% of catalyst was used) the rearrangement of vinylcyclopropanes with extended  $\pi$ -systems (e.g., diene or styrene groups rather than simple alkenes; e.g., Scheme 8, top) [20a]. Although a variety of simple alkenylcyclopropanes were also examined, of these only 1,1-dicyclopropylethylene was observed to rearrange to a cyclopentene. Some isomerization of the products to conjugated dienes was also observed under the reaction conditions used. Siloxy-substituted vinylcyclopropanes have also been shown to rearrange in the presence of 5–10 mol%  $\text{Ni}(\text{COD})_2$  with 2–3 equivalents of added  $\text{PPh}_3$  (e.g., Scheme 8, center) [20b]. Recently, several new catalysts were described by Louie and co-workers that allow a variety of unactivated vinylcyclopropanes to rearrange to cyclopentenes at low temperatures, with comparatively low catalyst loadings (generally 1–2 mol%), and in high yields (e.g., Scheme 8, bottom) [20c]. These catalysts all involve *N*-heterocyclic carbene ligands instead of phosphines.



Scheme 7.



Scheme 9.

Mechanistic schemes similar to those proposed for Rh(I) have been proposed for the Ni(0)-catalyzed reactions [20] (Scheme 9). Again, precomplexation is generally invoked, and this is especially likely for the dienylcyclopropane substrates. As for Rh(I),  $\eta_1$ -alkyl/ $\eta_3$ -allyl intermediates are consistently proposed in Ni(0) mechanisms, while interconversion with metallacyclobutane and metallacyclohexene species is sometimes also proposed [20b]. Preliminary quantum chemical calculations on reactions catalyzed by Ni(0)-*N*-heterocyclic carbene complexes suggest that  $\eta_1$ -alkyl/ $\eta_3$ -allyl, metallacyclobutane, and metallacyclohexene intermediates may all play a role [27].

#### 4. Future prospects

Although some mechanistic information on metal-promoted vinylcyclopropane–cyclopentene rearrangements is available, many questions remain. In order to rationally design a catalyst for such a reaction, one must have access to detailed mechanistic information for these reactions. For example, if one wants to make the reaction faster, knowledge of which step is rate-determining and what its transition structure looks like will undoubtedly be helpful. If one wants to engineer in stereoselectivity, then knowledge of the transition structures for the stereoselectivity determining steps is essential. Our own future studies are aimed at obtaining such information—through quantum chemical computations coupled to experiments—and utilizing this information to design new catalysts with improved substrate scope, reduced tendencies to form byproducts, and the ability to exert effective stereocontrol.

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