New cyclizations via catalytic ruthenium vinylidenes*

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Abstract: New carbocyclizations that proceed via catalytic metal-vinylidenes are presented. Metal-vinylidene catalytic species, which are easily accessible from terminal alkynes and catalytic amounts of transition-metal complexes, can be involved either in pericyclic reactions or in tandem processes triggered by nucleophilic attack at the electrophilic position of the vinylidene. In both cases, a wide variety of valuable cyclic compounds are easily accessible. Some recent carbocyclizations will be described.

Keywords: cyclizations; metal-vinylidenes; pericyclic reactions; nucleophilic additions; carbocycles.

INTRODUCTION

Many natural products and functionalized organic materials have carbocyclic structures. In particular, natural products containing medium-sized carbocycles continue to be important targets because of the synthetic challenges that they present and the potent biological activity that they frequently possess [1]. For this reason, the discovery of new reactions that allow the implementation of novel strategies for medium ring-sized carbocycles continues to be an important endeavor in organic synthesis [2]. Ideally, these strategies should conform to the atom-economy principle [3], occurring with high efficiency, selectivity, and in an environmentally benign fashion. In this sense, transition-metal catalysts continue to occupy a central role in modern organic reactions and have shown an increasing ability to accomplish these goals, both in improving existing processes and in the discovery of new ones. Among these systems, metal-vinylidene complexes, which are easily formed by activation of terminal alkynes with several transition metals [4], have emerged as very useful catalytic species in pericyclic reactions on the double bond of the vinylidene or through the exploration of the electrophilic nature of Cα of the metal-vinylidene with different nucleophiles [5].

A review of new and useful cyclization processes involving metal-vinylidenes is provided here.

VINYLIDENES IN PERICYCLIC REACTIONS

Metal-vinylidenes can take part in electrocyclizations, cycloadditions, or sigmatropic rearrangements to give five- or six-membered carbocycles [5d].

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Electrocyclizations involving catalytic metal-vinylidenes

Double bonds of Ru-vinylidenes of type I, obtained by the treatment of dienynes with available Ru(II)-complexes, can participate in a 6 e⁻ π electrocyclization to Ru-carbene II. β-Hydride elimination from II followed by reductive elimination liberates benzene derivatives and the Ru-catalyst is regenerated (Scheme 1).

Scheme 1 Proposed mechanism for the electrocyclization of Ru-vinylidenes.

Several examples of 6 e⁻ π electrocyclizations involving metal-vinylidenes, such as Ru [6] or W [7], have been reported (Scheme 2).

Scheme 2 Ru- and W-catalyzed cycloisomerizations of dienynes to aromatic compounds.
More complex polycyclic structures can be achieved by regioselective 1,2-alkyl shift after the electrocyclization reaction of cyclopropylidenyl and cyclobutylidenyl derivatives 5 and 6 (Scheme 3) [8].

Surprisingly, when cyclopentylidene derivative 9 was used, polycyclic benzene 10 with an unexpected methyl group was obtained [8]. This transformation probably involves an initial 6 e⁻ π electrocyclization followed by a regioselective 1,2-alkyl shift and the transfer of a methylene group (Scheme 4).

Scheme 3 Cyclization of 3,5-dien-1-ynes with 1,2-alkyl shift.

Scheme 4 Ru-catalyzed methylene transfer reaction.

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**[2+2] Cycloadditions involving catalytic metal-vinylidenes**

Double bonds of metal-vinylidenes can also be involved in [2+2] cycloaddition reactions with unsaturated compounds, either inter- or intramolecularly. For example, treatment of 1,6-enyne 11 with [Rh(cod)Cl]₂ catalyst in the presence of a 10 mol % of P(4-FC₆H₄)₃ in DMF at 85 °C for 24 h afforded the cyclohexene 12 in excellent yield (Scheme 5) [9]. The proposed mechanism involves the initial formation of a Rh-vinylidene species and this undergoes a [2+2] cycloaddition with the pendant alkene followed by ring-opening of the rhodacyclobutane.

![Proposed mechanism for [2+2] cycloadditions of Rh-vinylidenes.](image)

**Scheme 5** Proposed mechanism for [2+2] cycloadditions of Rh-vinylidenes.

**Sigmatropic rearrangements involving catalytic metal-vinylidenes**

Metal-vinylidene complexes can also participate in sigmatropic rearrangements to give carbocyclic compounds. For example, reaction of cis-vicinal vinyl-ethynylcyclopropanes 13 with catalytic amounts of group 6 transition-metal complexes affords a mixture of cycloheptatrienes 14 and 15 (Scheme 6) [10]. The formation of cycloheptatrienes can be explained in terms of a [3,3]-sigmatropic reaction of the initially formed vinylcyclopropylvinylidene 16 to give a seven-membered carbene complex 17. Formation of the two isomeric 1,3,5-cycloheptatrienes can be explained by assuming the subsequent [1,5]- and [1,3]-hydrogen shifts in complex 17 followed by reductive elimination (Scheme 6).

![1,5]-Sigmatropic rearrangements of Ru-vinylidenes A derived from cis-enynes 18 followed by electrocyclization and reductive elimination of the intermediate Ru-carbene B to give cyclopentadienes 19 have also been reported (Scheme 7) [11].

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Scheme 6 Proposed mechanism for Cr-catalyzed [3,3]-sigmatropic rearrangement of metal-vinylidenes.

Scheme 7 Proposed mechanism for the cycloisomerization of enynes through [1,5]-sigmatropic rearrangements.
NUCLEOPHILIC ADDITION TO VINYLIDENES

The electrophilic nature of the C\(_\alpha\) of metal-vinylidenes makes these species very reactive toward different types of nucleophiles to give Fisher-type carbene complexes, which can ultimately evolve to give useful functionalized carbocycles [5,12].

Addition of C-nucleophiles

A variety of C-nucleophiles have been added to metal-vinylidenes to give five- or six-membered carbocycles (Scheme 8). For example, intramolecular attack of activated methylenes 20 or silyl-enol ethers 22 to Mo-vinylidenes [13] or W-vinylidenes [14] affords cyclopentenes 22 and cyclohexenes 23, respectively.

Addition of hetero-nucleophiles to catalytic metal-vinylidenes

Addition of H\(_2\)O

An efficient, substituent-tolerant and highly regioselective anti-Markovnikov hydration of terminal alkynes to aldehydes takes place by addition of water to the electrophilic C\(_\alpha\) of Ru-vinylidenes [15]. Recently, a tandem hydration/cyclization reaction of 1,5-enynes 24 to afford cyclopentanones 25 has been described (Scheme 9) [16]. The reaction begins with the anti-Markovnikov hydration of the terminal alkyne via a Ru-vinylidene followed by the cyclization of an acylmetal species onto the conjugated alkene.
Addition of $\text{AcOH}$

Reaction of terminal alkynals 26 in the presence of catalytic amounts of $[\text{CpRu(CH}_3\text{CN)}_3]\text{PF}_6$ in acetic acid at 90 °C affords cycloalkenes 27, with the loss of one carbon, in excellent yields (Scheme 10) [17].

A series of experiments was carried out in an effort to clarify the scope and limitations of this transformation (Scheme 11):

- Alkynone 28 afforded the corresponding cyclopentene 29, indicating that an oxidative addition of the Ru to the aldehyde C–H bond is unlikely.
- Both 1,8-alkynals 26b ($n = 3$, Scheme 10) and alkynes without the aldehyde group (30) gave rise to noncyclized acetals 31 and 32, respectively, with the loss of one carbon. This suggests that the terminal carbon of the alkyne is the one lost during the reaction.
- When nonterminal alkynal 33 was used, a cycloisomerization occurred to give ketone 34.
- Interestingly, terminal 1,6- and 1,7-alkynals were able to cycloisomerize to conjugated aldehydes (all of the carbons from the starting material remained) on using only CpRu(dppm)Cl as the catalyst in iPrOH/H$_2$O as solvent.
A plausible mechanism for the Ru-catalyzed cyclization of terminal alkynals is depicted in Scheme 12. After the initial formation of Ru(II) vinylidene species III, nucleophilic addition of the acetic acid would afford the vinyl Ru species IV. A subsequent aldol-type condensation would give the acyl Ru hydride V. Reductive elimination products derived from intermediates IV (vinyl acetate) or V (aldehyde) did not afford the observed cycloalkene 27 after heating their solutions in AcOH at 90 °C in the presence of the Ru catalyst, showing that such a process is unlikely to occur. Finally, decarbonylation (in which the terminal carbon of the alkyne is lost as CO) followed by reductive elimination would afford the observed cycloalkenes 27. When CpRu(dppe)Cl was used as a catalyst, the conjugated aldehydes 35 were obtained by reductive elimination from V (decarbonylation did not take place in this case due to the bidentate nature of the dppe ligand).

Very recently, a new Ru-catalyzed tandem addition/cyclization of 1,6-diynes 36 and carboxylic acids has been reported and gives six-membered-carbocyclic systems 37 (Scheme 13) [18]. A mechanistic proposal for this transformation involves the initial formation of the Ru-vinylidene 38 with the pendant alkyne coordinated to the metal center. Addition of the carboxylic acid to the alkyne moiety would afford vinylruthenium species 39. The final protiodemetallation then furnishes the product and turns the catalyst over.

Scheme 11 Scope and limitations of the Ru-catalyzed reaction of terminal alkynals.
Scheme 12 Plausible mechanism for the decarbonylative Ru-catalyzed cyclization of terminal alkynals.

Scheme 13 Proposed mechanism for carboxylative diyne cyclization.
CONCLUSIONS

In summary, the use of catalytic-metal vinylidenes is emerging as one of the most powerful methodologies for the activation of functionalized compounds bearing terminal alkynes. Pericyclic reactions involving the metal-vinylidene double bonds or tandem reactions triggered by nucleophilic attack at the electrophilic C of the vinylidene give rise to functionalized carbocyclic compounds in a very efficient manner.

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REFERENCES


