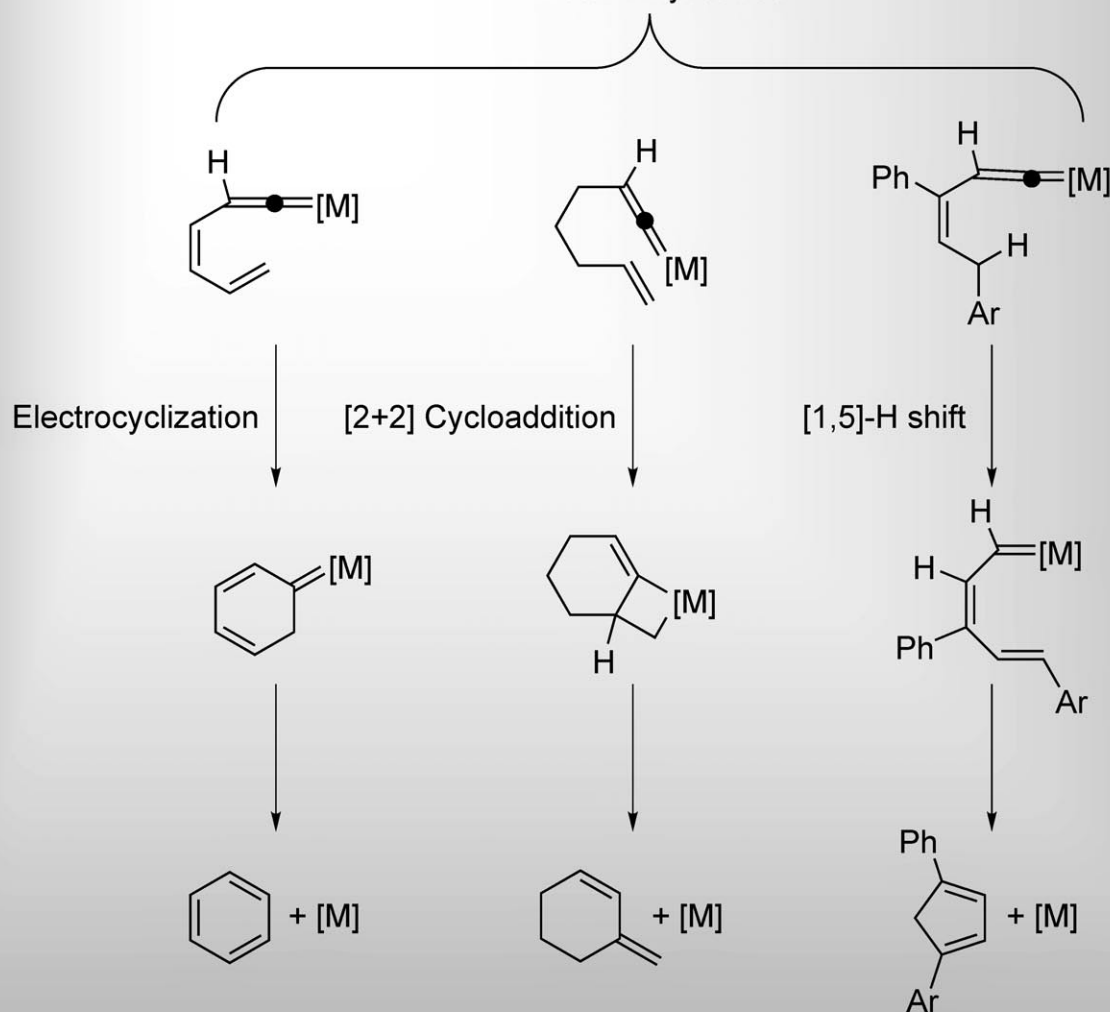
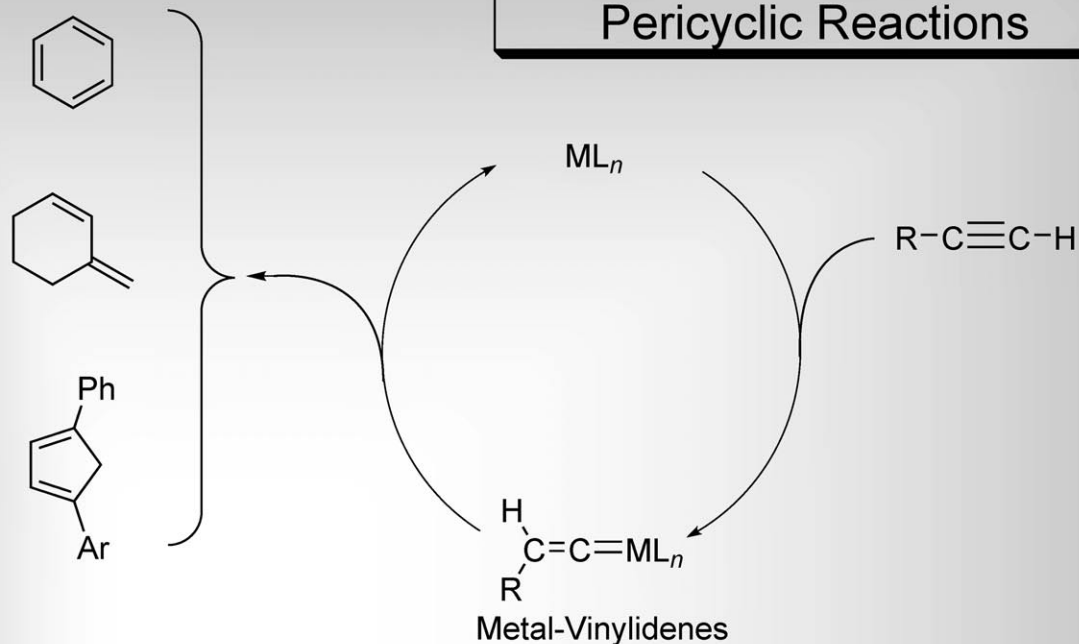


Catalytic Metal-Vinylidenes in Pericyclic Reactions



Pericyclic Reactions Involving Catalytic Metal–Vinylidene Complexes

Jesús A. Varela* and Carlos Saá^[a]

Dedicated to the memory of Marcial Moreno Mañas

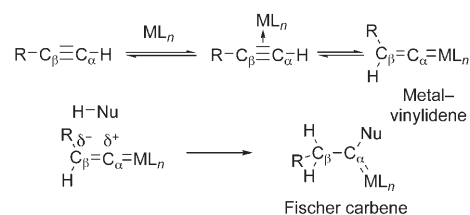
Abstract: The formation of complex polycyclic systems from terminal alkynes based on the concept of pericyclic reactions of catalytic metal–vinylidenes is presented. Metal–vinylidenes, easily formed from terminal alkynes with catalytic amounts of several metal complexes, can be used in electrocyclizations, cycloadditions or sigmatropic rearrangements to afford valuable compounds.

Keywords: cycloaddition • electrocyclization • metal–vinylidenes • pericyclic reactions • sigmatropic rearrangement

Introduction

Modern chemistry requires the continuous discovery of new synthetic methods allowing transformation of substrates into high valuable chemicals required by society. These transformations should occur with high efficiency, selectivity, and in an environmentally benign fashion. Transition-metal catalysts continue to occupy a central role in modern organic reactions with an increasing ability to fulfill these goals, both in improving existing processes or in discovering new ones. Among these, the chemistry of catalytic metal–vinylidenes has emerged as one of the leading methods for the selective transformations of terminal alkynes matching the atom economy principle.^[1] After the first formation and stabilization of vinylidenes at a transition-metal center reported in 1966,^[2] examination of the organometallic literature revealed that terminal alkynes can be converted into η^2 -vinylidene–metal complexes by many middle and late transition-metal reagents,^[3] and many examples of catalytic applica-

tions of metal–vinylidene complexes have been reported.^[4] Most of these reactions deal with the attack of different nucleophiles to the electrophilic C_α position of the metal–vinylidene to afford Fischer-type metal carbenes (Scheme 1). The subsequent evolution of these carbenes lead to a high variety of compounds (aldehydes, dihydropyrans, furans, β,γ -unsaturated ketones, etc.).^[5]



Scheme 1. Metal–vinylidene generation and nucleophilic addition to afford Fischer carbenes.

This article emphasizes the concept of using metal–vinylidenes in pericyclic reactions, that is, electrocyclizations, cycloadditions and sigmatropic rearrangements.

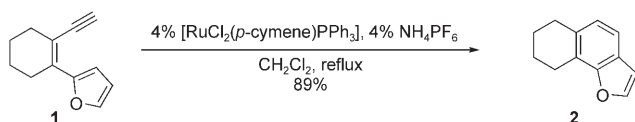
Discussion

Electrocyclizations involving catalytic metal–vinylidenes: The first example of $6e^- \pi$ electrocyclization involving Ru–vinylidenes was reported by Merlic and Pauly; they described the aromatization of dienylalkynes in the presence of an Ru catalyst.^[6] Thus, treatment of dienylalkyne **1** with a 5% of $[RuCl_2(p\text{-cymene})PPh_3]$ in CH_2Cl_2 , afforded the benzofuran **2** in excellent yield (Scheme 2).

Similarly, several other dienylalkynes underwent the electrocyclization, either by using $[RuCl_2(p\text{-cymene})PPh_3]$ or $[RuCl_2(C_6H_6)PPh_3]$ as catalysts (Table 1).

The proposed mechanism (Scheme 3) starts with the formation of Ru–vinylidene **I** followed by the formation of the Ru–carbene **II**, either by a nonpolar $6e^- \pi$ electrocyclization of the Ru–vinylidene (path A) or by a polarized transition

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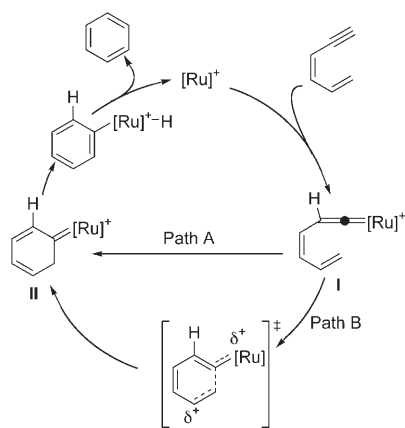


Scheme 2. Ru-catalyzed cycloisomerization of dienylnalkyne **1** to benzofuran **2**.

Table 1. Ru-catalyzed cycloisomerization of dienylnalkynes to benzenes.

Entry	Substrate	Product	Conditions ^[a]	Yield [%]
1			A	74
2			B	18
3			A	86
4			B	57
5			A	12
6			A	23

[a] Conditions: refluxing CH_2Cl_2 or $\text{C}_2\text{H}_2\text{Cl}_2$; A) 5–15% NH_4PF_6 , ~5% $[\text{RuCl}_2(p\text{-cymene})\text{PPh}_3]$; B) 6% NH_4PF_6 , ~5% $[\text{RuCl}_2(\text{C}_6\text{H}_6)\text{PPh}_3]$.

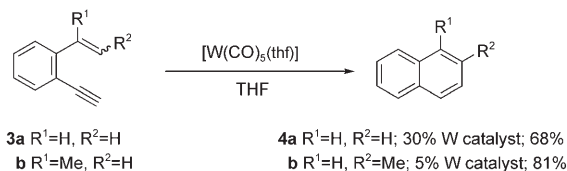


Scheme 3. Proposed mechanism for the electrocyclicization of Ru-vinylidenes.

state formed when the terminal olefin adds to the α -carbon atom of the vinylidene **I** (path B). β -Hydride elimination

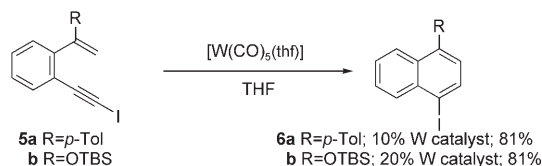
and reductive elimination generate the benzene derivative regenerating the Ru catalyst.

Iwasawa and co-workers have reported a method for the preparation of polyaromatic compounds by a tungsten-catalyzed $6e^- \pi$ electrocyclicization of vinylidenes generated from aromatic enynes through an analogous mechanism to the previously described (Scheme 4).^[7]



Scheme 4. Tungsten-catalyzed cycloisomerization of aromatic enynes **3** to naphthalene derivatives **4**.

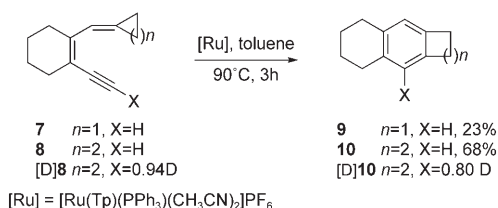
By this methodology is also possible to prepare iodoaromatic compounds starting from iodoalkyne derivatives. Thus, *o*-(iodoethynyl)styrenes **5**, in the presence of different amounts of $\text{W}(\text{CO})_5$ in THF, generate iodinated tungsten-vinylidenes, which after $6e^- \pi$ electrocyclicization give rise to iodo-substituted naphthalene derivatives **6** (Scheme 5).^[8]



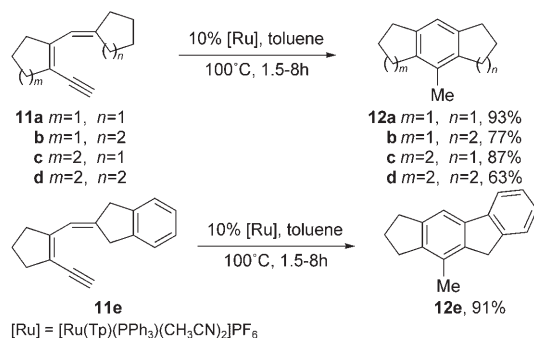
Scheme 5. Tungsten-catalyzed cycloisomerization of *o*-(iodoethynyl)styrenes **5** to iodonaphthalene derivatives **6**.

Recently, Liu and co-workers described the synthesis of highly substituted benzenes by electrocyclicization of 3,5-dien-1-yne by a metal-catalyzed reaction via the generation of a Ru-vinylidene intermediate.^[9] The novelty in the Liu's results is the regioselective 1,2-alkyl shift after the electrocyclicization reaction of cyclopropylidenyl and cyclobutylidenyl derivatives **7** and **8** in presence of a 10% of $[\text{Ru}(\text{Tp})(\text{PPh}_3)(\text{CH}_3\text{CN})_2]\text{PF}_6$ (Scheme 6). The observation of a 1,2-deuterium shift in the case of $[\text{D}]\mathbf{8}$ suggests the formation of a vinylidene intermediate.

Surprisingly, when the reaction is performed with cycloalkylidene derivatives **11**, polycyclic benzenes **12** containing an unexpected methyl group are obtained (Scheme 7). This



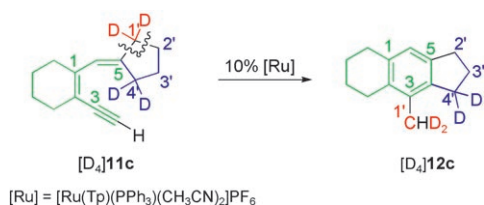
Scheme 6. Cyclization of 3,5-dien-1-yne to benzenes.



Scheme 7. Ruthenium-catalyzed methylene-transfer reaction.

transformation involves not only a regioselective 1,2-alkyl shift, but also a transfer of a methylene group.

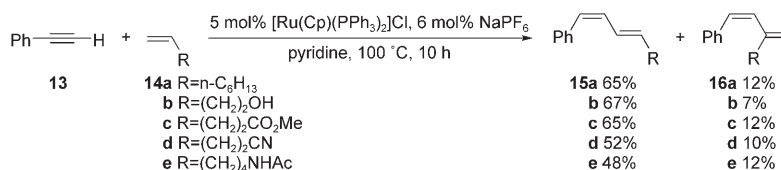
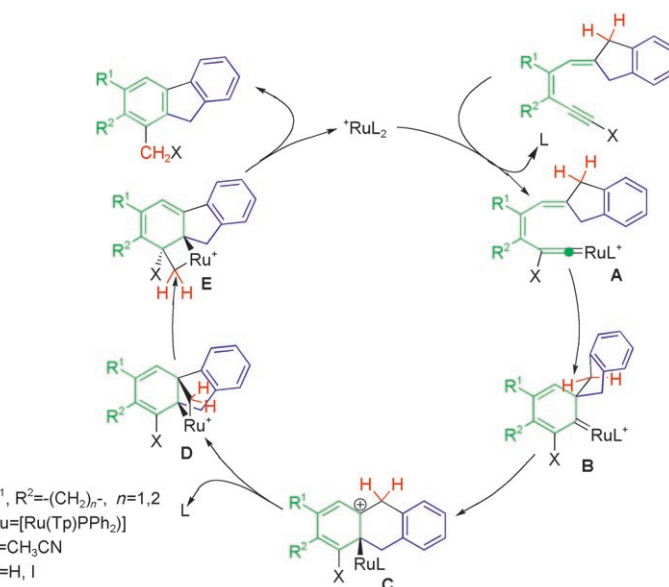
To get an insight into the operating mechanism for this transformation, the reaction was performed with isotopic-labeled compound $[\text{D}_4]\mathbf{11c}$ (Scheme 8).

Scheme 8. Ruthenium-catalyzed methylene-transfer reaction with isotopic labeled $[\text{D}_4]\mathbf{11c}$.

When tetradeuterated diene $[\text{D}_4]\mathbf{11c}$ was used, the benzene obtained, $[\text{D}_4]\mathbf{12c}$, confirmed the cleavage of the $\text{C1}'\text{-D}_2$ of the cyclopentylidene group and its link to the C3 carbon atom of the benzene, while the $\text{C2}'\text{-H}_2$ and $\text{C4}'\text{-D}_2$ units are linked to the C5 and C4 carbon atoms, respectively, of the benzene ring (Scheme 8).

According to these results, the proposed mechanism would start with an electrocyclicization of the ruthenium-vinylidene **A** (Scheme 9). The 1,2-alkyl shift of the carbene **B** generated would afford the cationic intermediate **C**. Attack of the ruthenium center of species **C** at the remote benzyl carbon atom with a concomitant 1,2-phenyl shift would give rise to the cyclobutylruthenium species **D**. Then a [1,5]-sigmatropic alkyl shift would afford the cyclobutylruthenium **E**, which ultimately would give rise to the observed compounds (Scheme 9).

[2+2] Cycloadditions involving catalytic metal-vinylidenes: Catalytic Ru-vinylidenes also participate in [2+2] cycloadditions with unsaturated compounds, either inter- or intramolecularly. Thus, it has been described that the reaction of phenylacetylene (**13**) with several olefins **14** in the presence

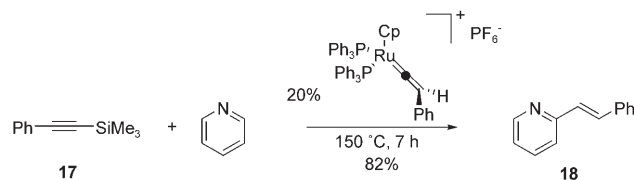
Scheme 10. Ru-catalyzed coupling of phenylacetylene (**13**) with olefins **14**.

Scheme 9. Proposed mechanism for the ruthenium-catalyzed methylene-transfer reaction.

of catalytic amounts of $[\text{Ru}(\text{Cp})(\text{PPh}_3)_2]\text{Cl}$ afford 1,3-dienes **15** and **16** (Scheme 10).^[10]

In the same way, pyridine can be regio- and stereoselectively alkenylated through ruthenium-mediated reactions.^[11] Treatment of (2-phenylethyn-1-yl)trimethylsilane (**17**) with

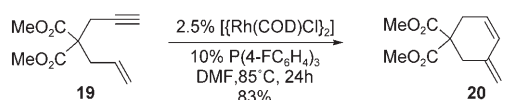
pyridine in the presence of catalytic amounts of an Ru-vinylidene complex, affords the alkenylated pyridine **18** in good yield (Scheme 11).



Scheme 11. Ru-mediated regio- and stereoselective alkenylation of pyridine.

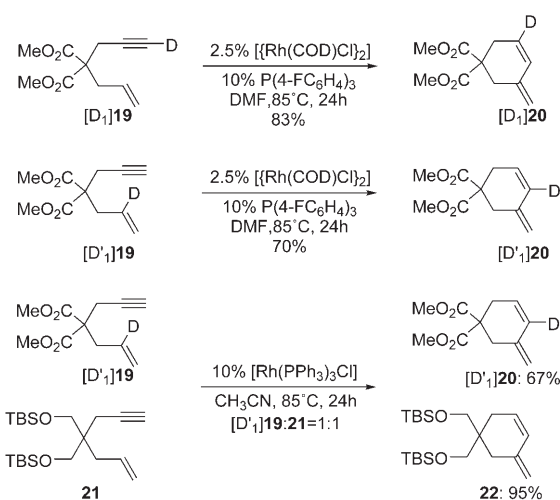
Recently, a new cycloisomerization reaction of unactivated enynes to give cyclohexenes by means of [2+2] cycloaddition with Rh-vinylidene complexes has been reported.^[12] Thus, treatment of 1,6-enyne **19** with $[\{\text{Rh}(\text{COD})\text{Cl}\}_2]$ as the catalyst and in the presence of a 10 mol % of $\text{P}(\text{4-FC}_6\text{H}_4)_3$ in

DMF at 85 °C for 24 h afforded the cyclohexene **20** in excellent yield (Scheme 12).



Scheme 12. Rh-catalyzed cycloisomerization of enynes.

To gain more insight into the mechanism reaction, a series of deuterium-labeling experiments were performed (Scheme 13).

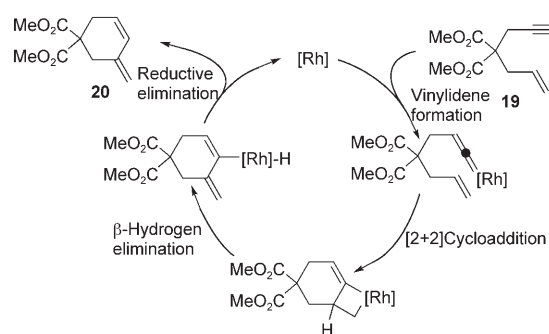


Scheme 13. Enyne cycloisomerization reaction with deuterated compounds.

The reaction of enyne **[D₁]****19** bearing an acetylenic deuterium label gave the diene **[D₁]****20** through translocation of the deuterium label exclusively to the adjacent carbon atom, suggesting the pertinence of a vinylidene mechanism. In the reaction of **[D'₁]****19**, almost complete migration of the vinylic deuterium label to the formerly terminal acetylenic carbon atom was observed. Moreover, no crossover of the deuterium took place in the reaction system employing a 1:1 mixture of the labeled and unlabeled enynes **[D'₁]****19** and **21**, respectively, indicating that a rhodium hydride or free radical mechanism is unlikely. All these observations support the proposed mechanism in which the catalytic cycle consists of formation of a rhodium–vinylidene complex followed by [2+2] cycloaddition with the alkene and ring-opening of the rhodacyclobutane (Scheme 14).

Other simple unactivated enynes give rise to the corresponding cyclohexenes derivatives using $[\text{Rh}(\text{COD})\text{Cl}]_2$ or $[\text{Rh}(\text{PPh}_3)_3\text{Cl}]$ as catalysts (Table 2).

Sigmatropic rearrangements involving catalytic metal–vinylidenes: Cycloisomerization of acylethynylcyclopropanes **23** with catalytic amounts of $[\text{Cr}(\text{CO})_5(\text{thf})]$ or $[\text{W}(\text{CO})_5(\text{thf})]$



Scheme 14. Proposed mechanism for [2+2] cycloadditions of Rh–vinylidenes.

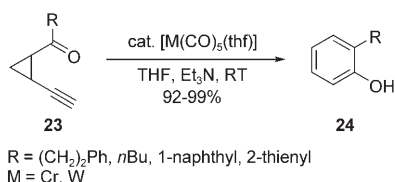
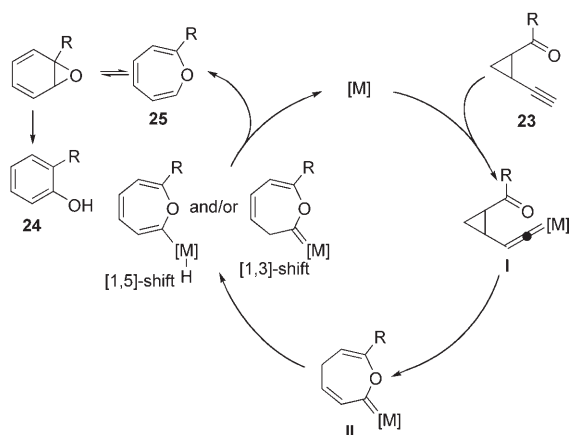
Table 2. Rhodium-catalyzed cycloisomerization of enynes.

Entry	Reactant	Product	Yield [%] ^[a,b]
1			80 (A), 77 (B)
2			90 (A), 90 (B)
3			99 (B)
4			67 (A)
5			54 (A)
6			58 (A), 53 (B)
7			98 (A), 95 (B)
8			77 (C)

[a] Conditions: A) 5 mol% of $[\text{Rh}(\text{COD})\text{Cl}]_2$; 25 mol% of $\text{P}(4\text{-FC}_6\text{H}_4)_3$; DMF (0.1 M); 85 °C; 24 h. B) 10 mol% of $[\text{Rh}(\text{PPh}_3)_3\text{Cl}]$; CH_3CN (0.1 M); 85 °C; 24 h. C) 20 mol% of $[\text{Rh}(\text{PPh}_3)_3\text{Cl}]$; 20 mol% of PPh_3 ; slow addition 10 h; final concentration = 0.1 M in CH_3CN . [b] Isolated yields.

in THF at room temperature gave phenols **24** in good yields (Scheme 15).^[13]

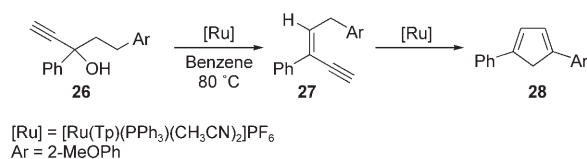
The proposed mechanism (Scheme 16) involves an [3,3]-sigmatropic rearrangement of the acylcyclopropylvinylidene **I**, initially formed from alkyne **23**, to 1-oxa-3,6-cycloheptadien-2-ylidene complex **II**. Then a [1,5]-H shift and/or a [1,3]-H shift from CH_2 in the seven-membered ring of **II** followed by reductive elimination of the metal species re-

Scheme 15. W- and Cr-catalyzed formation of phenols from acylethynyl-cyclopropanes **23**.

Scheme 16. Proposed mechanism for W- and Cr-catalyzed [3,3]-sigmatropic rearrangement of metal-vinylidenes.

sults in the initial formation of an oxepin **25**. The oxepin is then converted into a phenol **24** with the assistance of $\text{M}(\text{CO})_3$ as a Lewis acid under the reaction conditions.

Recently, a [1,5]-sigmatropic rearrangement of *cis*-enynes catalyzed by Ru-vinylidenes has also been reported.^[14] Heating a solution of 1-ethynyl-3-ol **26** in benzene with $[\text{Ru}(\text{Tp})(\text{PPh}_3)(\text{CH}_3\text{CN})_2]\text{PF}_6$ gave a mixture of cyclopentadiene **28** and enyne **27** in 51 and 40% yields, respectively (Scheme 17). Heating either the enyne **27** or the 1-ethynyl-



Scheme 17. Ru-catalyzed dehydrating cycloisomerization of 1-ethynyl-3-ols.

3-ol **26** alone under the same conditions for 12 h afforded exclusively the diene **28** in 80% yield. Thus, the ruthenium catalyst has dual roles in catalytic activities: dehydration of 1-ethynyl-3-ols and cyclization of *cis*-enyne.

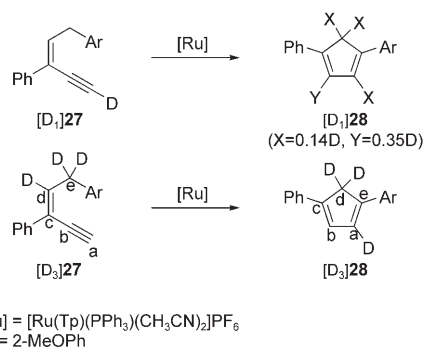
According to this methodology various 1-ethynyl-3-ols and *cis*-enynes can be converted into the corresponding cyclopentadienes (Table 3). The value of this cyclization is highlighted by its applicability to the activation of a nonbenzylic C–H bond (Table 3, entries 3, 5 and 6).

Table 3. Ruthenium-catalyzed cyclization of 1-ethynyl-3-ols and *cis*-enynes.^[a]

Entry	Reactant	Product	Yield [%]
1			70
2			62
3			71
4			80
5			71
6			79

[a] 10% of $[\text{Ru}(\text{Tp})(\text{PPh}_3)(\text{CH}_3\text{CN})_2]\text{PF}_6$ [substrate] = 0.15 M, benzene, 80 °C, 12 h.

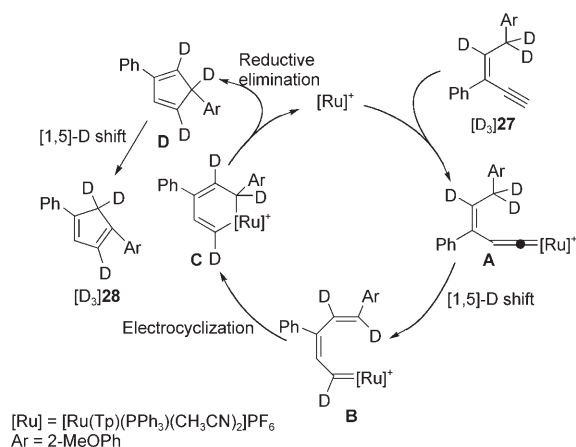
When the reaction was performed by using monodeuterated enyne $[\text{D}_1]\mathbf{27}$, the diene $[\text{D}_1]\mathbf{28}$ was obtained bearing only 21% deuterium excess at the $\text{CH}=\text{CPh}$ carbon atom. The remaining three diene protons of $[\text{D}_1]\mathbf{28}$ contained a total 0.42D. When a highly deuterated enyne $[\text{D}_3]\mathbf{27}$ was used the diene $[\text{D}_3]\mathbf{28}$ was obtained (Scheme 18).



Scheme 18. Ruthenium-catalyzed cycloisomerization of enynes with isotopic-labeled compounds.

A plausible mechanism (Scheme 19) to rationalize the deuterium-labeling experiments started with the formation of the ruthenium-vinylidene **A** followed by a [1,5]-deuterium shift of the benzylic position affording the ruthenium-carbene **B**. Then $6e^- \pi$ electrocycloisomerization of **B** gives rise to ruthenacyclohexadiene **C**, which undergoes a subsequent reductive elimination producing cyclopentadiene **D**, and, ultimately, yields the most stable regioisomer $[\text{D}_3]\mathbf{28}$ by means of a [1,5]-deuterium shift.

The above transformations show the ability of catalytic metal-vinylidenes to participate in pericyclic reactions. The



Scheme 19. Proposed mechanism for the cycloisomerization of enynes through [2+2] Ru-vinylidene cycloaddition.

easy formation of vinylidenes from terminal alkynes in the presence of catalytic amounts of metals makes this methodology a powerful tool for getting new valuable compounds. Inherent advantages of this methodology rely on the atom economy of the process, the use of catalytic amounts of metals, and the rich versatility to make quite complex transformations.

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