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A New Ru-Catalyzed Cascade Reaction Forming Polycyclic Cyclohexadienes from 1,6-Diynes and Alkenes

Jesús A. Varela, Silvia G. Rubín, Carlos González-Rodríguez, Luis Castedo, and Carlos Saá*

Departamento de Química Orgánica y Unidad Asociada al CSIC, Facultad de Química,
Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain

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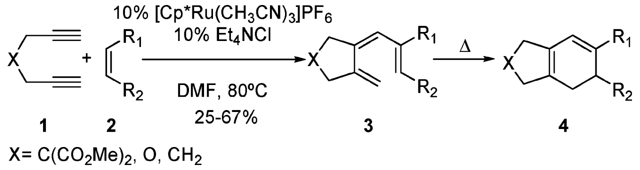
Modern organic synthesis strives for reactions that rapidly transform readily available starting materials into complex molecules.[1] Transition-metal-catalyzed cycloaddition can construct complex polycyclic molecules in a single step.[2] For carbocyclic systems containing six-membered rings, the inter- and intramolecular metal-catalyzed [2 + 2 + 2] cycloaddition reactions of alkynes are nowadays used to prepare numerous benzene and polycyclic benzene derivatives.[3] However, the analogous reactions of alkynes with alkenes[4] or enynes,[5] which afford functionalized bicyclic 1,3-cyclohexadienes, have received much less attention. Here we describe a new cascade reaction involving an Ru-catalyzed addition of alkenes to 1,6-diynes[6] followed by a thermal 6e$^-\pi$ electrocyclization (Scheme 1).

Scheme 1. Ru-Catalyzed Addition of Alkenes to 1,6-Diynes Followed by 6e$-\pi$ Electrocyclization



Slow addition of a solution of **1a** (X = $C(CO_2Me)_2$) in DMF to a heated mixture of DMF and methyl acrylate (**2a**) containing the catalytic mixture (10% $[Cp^*Ru(CH_3CN)_3]PF_6$ plus 10% Et_4NCl) afforded the cyclohexadiene **4a** (R_1 = CO_2Me, R_2 = H) in reasonably good yield (Table 1, entry 1, conditions A).[7] Other monosubstituted electron-deficient olefins [methyl vinyl ketone (**2b**), acrolein (**2c**), and acrylonitrile (**2d**)] gave the corresponding cyclohexadienes in moderate yields (33−51%, Table 1, entries 2−4), while the disubstituted olefin dimethyl maleate (**2e**) gave a 61% yield of the more functionalized cyclohexadiene **4e** (Table 1, entry 5). Substituted alkenes with metal-coordinating heteroatoms (ethers **2f**−**h** and alcohol **2i**) afforded quite good yields of the expected cyclohexadienes (Table 1, entries 6−9), but the more electron-rich vinyl propyl ether failed to react. Surprisingly, nonactivated olefins [1-heptene (**2j**) and vinyl trimethylsilane (**2k**)] also reacted with **1a**, affording cyclohexadienes **4j** and **4k** in 67 and 25% yields, respectively (Table 1, entries 8 and 9), and showing that the presence of a heteroatom in allylic position in the alkene is not required, as has been suggested,[4i,j] but it appears to be significant for better yields of cyclized products. Selected reactions performed using 10 equiv of alkenes **2** (conditions B) gave better yields (Table 1, entries 3, 6, 7, and 11).

Strikingly, the double bonds in cyclohexadienes **4** are not in the positions expected for a [2 + 2 + 2] cycloaddition reaction. This type of bond migration product **4** has previously been observed by Itoh[4i,j] when using benzyl allyl ether and was attributed to the occurrence of a 1,5-H shift after the expected [2 + 2 + 2] cycloaddition reaction. In the present case, isolation of the open trienes **3e** and **3f**[8] following reaction of **1a** with allyl ethers **2e** and **2f** at room temperature allowed the hypothesis of the mechanism shown in Scheme 2 (path A). When mixed with Et_4NCl, the cationic catalyst $[Cp^*Ru(CH_3CN)_3]PF_6$ probably generates the neutral complex Cp^*RuL_2Cl (**I**, L= CH_3CN), as is suggested by changes in the ^1H NMR spectrum.[7] Oxidative coupling of this complex with the diyne would form the ruthenacyclic species **II**, insertion of the alkene which would give complex **III**. β-Elimination, followed by reductive elimination, would then afford (*Z*)-hexatrienes **3**, which at 50 °C would undergo thermal disrotatory 6e$^-\pi$ electrocyclization to give cyclohexadienes **4**.

Table 1. Reactions of Diyne **1a** with Acyclic Alkenes **2a**−**k**

entry		alkene		cyclohexadiene	yield[a,b]
1	**2a**	$R_1 = CO_2Me$	$R_2 = H$	**4a**	62
2	**2b**	$R_1 = COMe$	$R_2 = H$	**4b**	51[c]
3	**2c**	$R_1 = CHO$	$R_2 = H$	**4c**	33[d] (60)
4	**2d**	$R_1 = CN$	$R_2 = H$	**4d**	46
5	**2e**	$R_1 = CO_2Me$	$R_2 = CO_2Me$	**4e**	61
6	**2f**	$R_1 = CH_2OEt$	$R_2 = H$	**4f**	52 (90)
7	**2g**	$R_1 = CH_2OPh$	$R_2 = H$	**4g**	66 (85)
8	**2h**	$R_1 = CH_2OTMS$	$R_2 = H$	**4h**	58
9	**2i**	$R_1 = CH_2OH$	$R_2 = H$	**4i**	66[e]
10	**2j**	$R_1 = C_5H_{11}$	$R_2 = H$	**4j**	67
11	**2k**	$R_1 = TMS$	$R_2 = H$	**4k**	25 (72)

[a] Isolated yields from reactions performed at 80 °C by slow addition, over 4 h, of 0.5 mmol of **1** in DMF to a mixture of 3 equiv of **2**, 10% Et_4NCl, and 10% $[Cp^*Ru(CH_3CN)_3]PF_6$ in DMF (conditions A). Dimer (10−15%) and trimer of **1a** (5%) are the only observed byproducts, and there are no traces of Diels−Alder adducts of cyclohexadienes **4**. [b] Yields in parentheses were isolated when using 10 equiv of **2** without slow addition of **1** (conditions B). [c] Solvent used: acetone, 46 °C. [d] A 6% yield of the benzene derivative was also isolated. [e] A 3:1 mixture of **4i** and its regioisomer **4i′** (R_1 = H, R_2 = CH_2OH) was isolated.

As expected, like Itoh,[4i,j] we found that addition of 2,5-dihydrofuran (**2l**) to diynes **1a**, **1b** (X = O), and **1c** (X = CH_2) afforded the tricyclic 1,3-cyclohexadienes **5l**, **5l′**, and **5l″** in good to excellent yields (Table 2, entry 1). Cyclic enones **2m** and **2o** and lactone **2n** behaved similarly, with relatively good yields (entries 2 and 3). Finally, like their acyclic analogues, nonactivated cycloalkenes **2p** and **2q** reacted, affording the expected tricyclic cyclohexadienes **5p** and **5q** although in low yields (entry 4).

With no cyclic alkene, we were able to isolate an intermediate analogous to hexatriene **3** (Scheme 2). We hypothesize that the conformation of the corresponding tricycloruthenacycle **III** is not suitable for β-elimination due to the steric restrictions imposed by the annelated ring, with reductive elimination being the favored pathway leading to the tricyclic cyclohexadienes **5** (Scheme 2, path B).[9]

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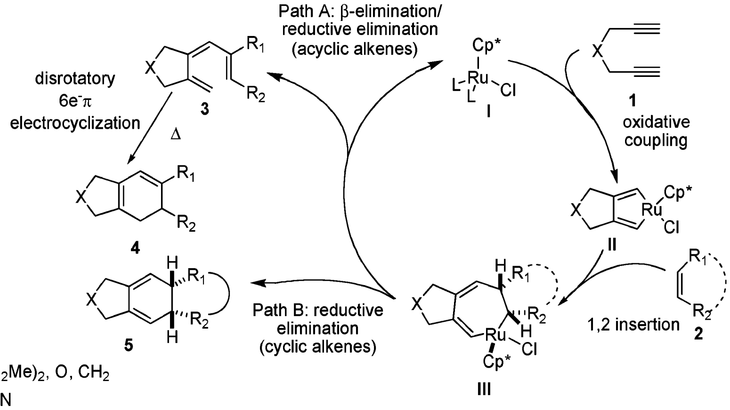
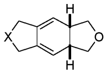
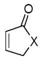
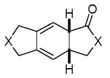
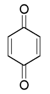
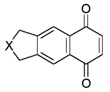
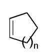
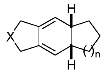
Scheme 2. Possible Mechanisms of the Ru-Catalyzed Preparation of Cyclohexadienes from 1,6-Diynes by Addition of Acyclic Alkenes (path A) or Cyclic Alkenes (path B)



X = C(CO$_2$Me)$_2$, O, CH$_2$
L = CH$_3$CN

Table 2. Reactions of Diynes **1** with Cyclic Alkenes **2l**−**q**, Giving Cyclohexadienes **5l**−**q**

entry	cyclic alkene	cyclohexadienes[b]	yield[a]
1	 **2l**	 **5l**, **5l'**, **5l''**	92, 95, 56
2	 **2m** X=CH$_2$ **2n** X=O	 **5m** X=CH$_2$ **5n** X=O	**5m** 37(12)[c] **5n** 60
3	 **2o**	 **5o**	53[d]
4	 **2p** n=1 **2q** n=2	 **5p** n=1 **5q** n=2	**5p** 29 **5q** 32

[a] Isolated yields following conditions A as in Table 1. Same byproducts are also observed. [b] X = C(CO$_2$Me)$_2$ except in **5l′** (X = O) and **5l″** (X = CH$_2$). [c] Solvent used: acetone, 46 °C. Yield of the benzene derivative in parentheses. [d] See ref 4f for aromatics from Ni/Zn-promoted cycloadditions of cyclic enones.

In conclusion, we have discovered a new cascade reaction involving two consecutive transformations: the Ru-catalyzed addition of acyclic alkenes to 1,6-diynes to give (*Z*)-hexatrienes followed by thermal 6e$^-\pi$ electrocyclization to afford bicyclic cyclohexadienes in which the double bonds have "migrated". Under the same reaction conditions, cyclic olefins afford tricyclic cyclohexadienes through [2 + 2 + 2] cycloaddition reactions.

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Supporting Information Available: A typical procedure for the Ru-catalyzed reaction and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) See Supporting Information for details.

(9) To ascertain why acyclic olefins **2** gave exclusively open triene **3** by β-elimination from ruthenacycle **III** (path A) and cyclic olefins to the cycloadduct **5** by reductive elimination (path B), we undertook DFT calculations using B3LYP/LANL2DZ. See Supporting Information for details.

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