Communication

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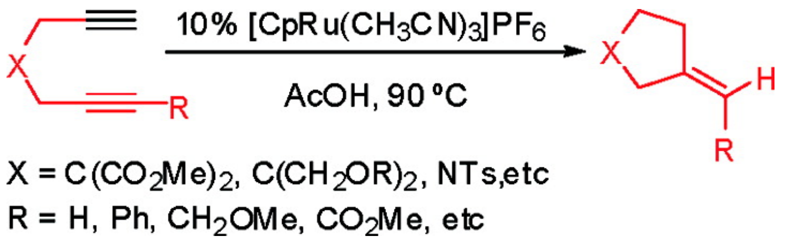

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# Ruthenium-Catalyzed Decarbonylative Cyclization of 1,6-Diynes

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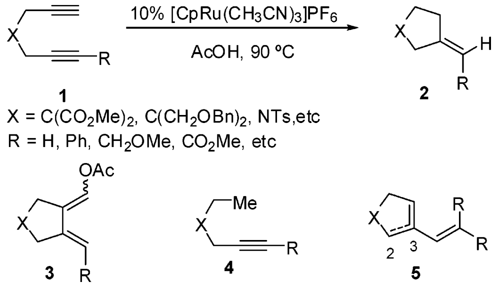
Ruthenium-catalyzed transformation is widely recognized as one of the most efficient means of alkyne functionalization.[1] Nonmetathetic ruthenium-catalyzed C−C bond formation between alkyne partners proceeds via ruthenacycle/*bis*-carbene[2] or vinylidene[3] intermediates, depending on the nature of the alkynes and the reaction conditions. The intramolecular version has recently been applied to the cycloisomerization of diynols via ruthenacycles[4] and the carboxylative cyclization of 1,6-diynes via catalytic Ru-vinylidenes.[5,6] In the course of work on metal-vinylidene-catalyzed C−C bond-forming reactions,[7] we have developed, and report here, a process that nicely complements the latter transformation, namely a ruthenium-catalyzed cyclization-decarbonylation of 1,6-terminal diynes **1** mediated by carboxylic acids[8,9] (Scheme 1).

***Scheme 1.*** Ru-Catalyzed Decarbonylative Cyclization of 1,6-diynes **1**



Heating the electron-poor 1,6-diyne **1a** (X = C(CO$_2$Me)$_2$, R = CO$_2$Me) in a 10 mol % solution of the catalyst [CpRu(CH$_3$CN)$_3$]PF$_6$ in AcOH afforded, after 24 h at 90 °C, the *exo*-methylenecyclopentane derivative **2a**, with one carbon less than **1a**, in good yield (Table 1, entry 1). Heating at 130 °C for 24 h led to some decomposition and a lower yield of **2a** (entry 2). However, the more electron-rich, sterically more demanding catalyst [Cp*Ru(CH$_3$CN)$_3$]PF$_6$ gave the dienylacetate **3a** in quite good yield (entry 3), through cyclization and intermolecular addition of AcOH.[10] The use of other Ru(II) catalysts, such as CpRu(PPh$_3$)$_2$Cl and ($\eta$5-indenyl)Ru(PPh$_3$)$_2$Cl, led to lower yields of **2a** (entries 4 and 5),[11] as did dilution of **1a** (entry 6). The reaction was indifferent to the identity of the carboxylic acid (entry 7).[11]

***Table 1.*** Ru-Catalyzed Cyclization of **1a** in Acetic Acid[a]

| entry | catalyst[b] | *t* °C | time | yield[c] | product |
|---|---|---|---|---|---|
| 1 | [CpRuL$_3$]PF$_6$ | 90 | 24 h | 66% | **2a** |
| 2 | [CpRuL$_3$]PF$_6$ | 130 | 12 h | 42% | **2a** |
| 3 | [Cp*RuL$_3$]PF$_6$ | 130 | 2 h | 70% | **3a**[d] |
| 4 | CpRu(PPh$_3$)$_2$Cl | 90 | 48 h | 22% | **2a** |
| 5 | ($\eta$5-In)Ru(PPh$_3$)$_2$Cl | 90 | 48 h | 11% | **2a** |
| 6[e] | [CpRuL$_3$]PF$_6$ | 90 | 24 h | 42% | **2a** |
| 7[f] | [CpRuL$_3$]PF$_6$ | 90 | 24 h | 58% | **2a** |

[a] [**1a**] = 0.1 M except for entry 6. [b] L = CH$_3$CN, In= indenyl. [c] Isolated yields. [d] Mixture of *Z*/*E* isomers 3:2. [e] [**1a**] = 0.05 M. [f] Acrylic or propanoic acid.

Other 4-carbon or 4-aza substituted electron-poor 1,6-diynes **1b**−**d** behaved similarly, affording quite good yields of cyclopentylidenes **2b** and **2c** and pyrrolidine **2d**, respectively (Table 2, entries 2−4). Yields were lower without the 1-CO$_2$Me group (Table 2, entries 5 and 6), but the 1-silylated 1,6-diyne **1g** interestingly gave a slightly better yield of desilylated **2e** than its parent, **1e** (Table 2, entries 7 and 5).[12] By contrast, ethyl-substituted 1,6-diyne **1h** gave a mixture of **2h** and alkyne **4h** in 2.5:1 ratio (entry 8).

***Table 2.*** Ru-Catalyzed Cyclization of 1,6-diynes **1a**−**l** in Acetic Acid[a]

| entry | R | X | diyne | product | yield%[b] |
|---|---|---|---|---|---|
| 1 | CO$_2$Me | C(CO$_2$Me)$_2$ | **1a** | **2a** | 66 |
| 2 | CO$_2$Me | C(CO$_2$Et)$_2$ | **1b** | **2b** | 74 |
| 3 | CO$_2$Me | C(CH$_2$OBn)$_2$ | **1c** | **2c** | 60 |
| 4 | CO$_2$Me | NTs | **1d** | **2d** | 55 |
| 5 | H | C(CO$_2$Me)$_2$ | **1e** | **2e** | 50 |
| 6 | H | NTs | **1f** | **2f** | 43 |
| 7 | TMS | C(CO$_2$Me)$_2$ | **1g** | **2e** | 53 |
| 8[c] | Et | C(CO$_2$Me)$_2$ | **1h** | **2h** | 36 |
| 9[d] | CH$_2$OMe | C(CO$_2$Me)$_2$ | **1i** | **2i** | 60 |
| 10[e] | CH$_2$OMe | C(CO$_2$Me)$_2$ | **1i** | **5i** + **5i′** | 45 |
| 11 | C(Me)$_2$OH | C(CO$_2$Me)$_2$ | **1j** | **5j** + **5j′** | 40 |
| 12[d] | Ph | C(CO$_2$Me)$_2$ | **1k** | **2k** | 60[f] |
| 13[d] | 3-Furyl | C(CO$_2$Me)$_2$ | **1l** | **2l** | 53 |

[a] Typical conditions: diyne **1** (0.1 M), 10 mol % [CpRu(CH$_3$CN)$_3$]PF$_6$, AcOH, 90 °C, 8−24 h. [b] Isolated yields. [c] Alkyne **4h** (14%) was also obtained. [d] Alkynes **4i** or alkynes **4k,l** were also obtained (<10%). [e] Reaction performed at 130 °C. [f] **2k** (55%), catalyst [Cp*Ru(CH$_3$CN)$_3$]PF$_6$.

Interestingly, although the propargyl ether **1i** afforded the corresponding cyclopentylidene **2i** at 90 °C (Table 2, entry 9), heating **1i** at 130 °C for 24 h gave a 45% combined yield of dienes **5i** and **5i′** ($\Delta^{2,3}$) (R = H) through loss of MeOH (Table 2, entry 10),[4] and similar yields of dienes **5j** and **5j′** (R = Me) were obtained on heating the tertiary alcohol **1j** at 90 °C (Table 2, entry 11).[4] However, aryl-substituted diynes **1k** and **1l** gave the corresponding cyclopentylidenes **2k** and **2l** in quite good yields even when [Cp*Ru(CH$_3$CN)$_3$]PF$_6$ was used as catalyst (Table 2, entries 12 and 13).

When 1,7-disubstituted 1,6-diyne **1m** was subjected to typical reaction conditions, dienylacetate **3m** was obtained in an excellent 95% yield (Scheme 2).[4] This result clearly indicates that only a terminally unsubstituted yne unit will lose its terminal carbon in the cyclization process.

Not unexpectedly, carboxylative cyclization occurred when the reaction was performed with 1- or 8-unsubstituted 1,7-diynes **6**. This afforded dienylacetate **8a** or the regioisomeric dienylacetates **7b** and **8b** in quite good yields (Scheme 3 and Table 3), probably through formation of ruthenacycle intermediates followed by addition of AcOH.[4,2c]

Scheme 4 shows a mechanism that would account for the above observations.[13] Following the formation of ruthenium vinylidene **A**,[8] nucleophilic addition of AcOH would afford the acyclic vinyl Ru-hydride **B**, which through a [3+2]-type cycloaddition would

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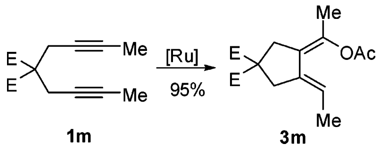
***Scheme 2.*** Ru-Catalyzed Cyclization of **1m** in AcOH



***Scheme 3.*** Ru-Catalyzed Carboxylative Cyclization of 1,7-diynes

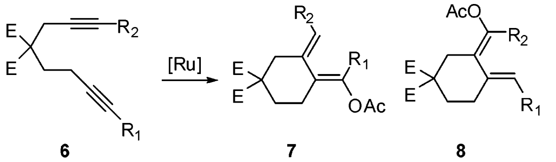
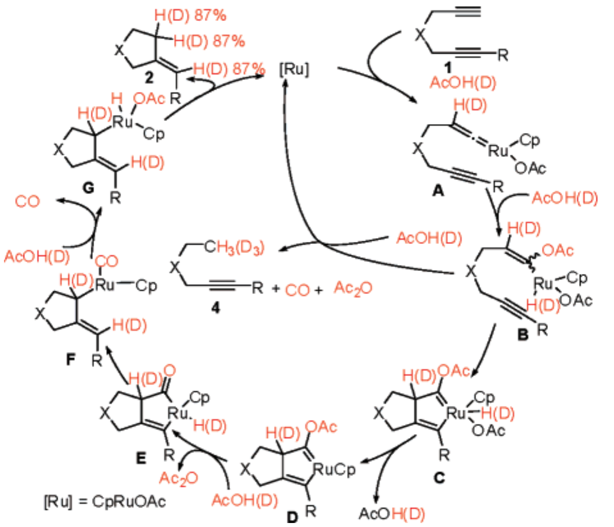


***Table 3.*** Ru-Catalyzed Carboxylative Cyclization of 1,7-diynes **6a**,**b**[a]

| entry | diyne | $R_1$ | $R_2$ | yield%[b] | 7/8 |
|---|---|---|---|---|---|
| 1 | **6a** | H | Me | 85 | 0:1 |
| 2 | **6b** | Et | H | 68 | 7.5:1 |
| 3[c] | **6b** | Et | H | 39 | 4:1 |

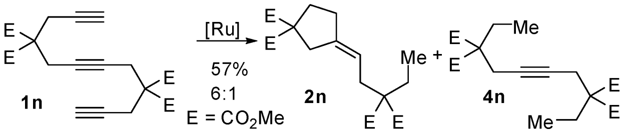
[a] Typical conditions were as in Table 2. [b] Isolated yields. [c] Heating **6b** at 130 °C favors formation of the homologue of uncyclized alkyne **4** (R = Et) in 39% yield. E = $CO_2Me$.

***Scheme 4.*** Proposed Mechanism for the Ru-Catalyzed Tandem Cyclization-Decarbonylation of 1,6-Terminal Diynes **1**



lead to cyclic carbene Ru-hydride **C**. Reductive loss of AcOH of **C** would give the cyclic carbene **D**, which undergoes another nucleophilic attack by AcOH to the acyl Ru-hydride **E**. Reductive opening of the ruthenacycle of **E** followed by oxidative addition of AcOH with concomitant decarbonylation of **F** led to the Ru-hydride **G**.[14] Finally, reductive elimination would then afford the observed cyclopentylidene **2**.[15] Analogous evolution of **B** would give alkyne **4** as a minor product. This mechanism would also account for 87% of the three hydrogens incorporated in **2a** being deuterium when the reaction of **1a** was carried out in AcOD.

In an attempt to insert a second alkyne in the ruthenacycle **C**, the reaction of the symmetrical triyne **1n** was investigated. Unfortunately, cyclopentylidene **2n** (49%) and uncyclized alkyne **4n** (8%) were the only products observed.



In conclusion, we have developed a ruthenium-catalyzed tandem cyclization−decarbonylation whereby 7-unsubstituted 1,6-diynes give *exo*-alkylidenecyclopentanes. The starting point of this process is likely to be the formation of an Ru−vinylidene complex. This new reaction is expected to open up further opportunities for the development of catalytic alkyne functionalization.

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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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(10) This type of nucleophile addition has been observed before: (a) for diynes, see ref 4b; (b) for alkynes, see ref 2b.

(11) For comprehensive screening results, see Supporting Information.

(12) Most likely, desilylation of the putative silylated cyclopentane **2g** occurred under the reaction conditions.

(13) We thank a reviewer for valuable suggestions.

(14) (a) Le Paih, J.; Rodriguez, D. C.; Derien, S.; Dixneuf, P. H. *Synlett* **2000**, 95. (b) No carbonylated product was observed when reaction of **1e** was performed under an atmosphere of CO. See Supporting Information for details.

(15) The *Z* geometry of **2** was determined by NOE experiments (see Supporting Information for details).

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