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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*-carbene² or vinylidene³ 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 ruthenacycles⁴ and the carboxylative cyclization of 1,6-diynes via catalytic Ruvinylidenes.^{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).

Heating the electron-poor 1,6-diyne **1a** (X = C(CO₂Me)₂, R = CO₂Me) in a 10 mol % solution of the catalyst [CpRu(CH₃CN)₃]-PF₆ 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(CH₃CN)₃]-PF₆ 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(PPh₃)₂Cl and (η 5-indenyl)Ru(PPh₃)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

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-CO₂Me 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).

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(CH₃CN)₃]PF₆ 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.

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



Table 1. Ru-Catalyzed Cyclization of 1a in Acetic Acida

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	$(\eta 5-In)Ru(PPh_3)_2Cl$	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 = CH₃CN, In= indenyl. ^c Isolated yields. ^d Mixture of Z/E isomers 3:2. ^e [1a] = 0.05 M. ^f Acrylic or propanoic acid.

Table 2. Ru-Catalyzed Cyclization of 1,6-diynes 1a-I in Acetic Acid^a

entry	R	Х	diyne	product	yield% ^b
1	CO ₂ Me	C(CO ₂ Me) ₂	1 a	2a	66
2	CO ₂ Me	$C(CO_2Et)_2$	1b	2b	74
3	CO_2Me	$C(CH_2OBn)_2$	1c	2c	60
4	CO ₂ Me	NTs	1d	2d	55
5	Н	$C(CO_2Me)_2$	1e	2e	50
6	Н	NTs	1f	2f	43
7	TMS	$C(CO_2Me)_2$	1g	2e	53
8^c	Et	$C(CO_2Me)_2$	1ĥ	2h	36
9^d	CH ₂ OMe	$C(CO_2Me)_2$	1i	2i	60
10^{e}	CH ₂ OMe	$C(CO_2Me)_2$	1i	5i + 5i'	45
11	C(Me) ₂ OH	$C(CO_2Me)_2$	1j	$5\mathbf{j} + 5\mathbf{j}'$	40
12^{d}	Ph	$C(CO_2Me)_2$	1k	2k	60 ^f
13^d	3-Furyl	C(CO ₂ Me) ₂	11	21	53

^{*a*} Typical conditions: diyne **1** (0.1 M), 10 mol % [CpRu(CH₃CN)₃]PF₆, 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(CH₃CN)₃]PF₆.

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





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	Н	Me	85	0:1
2	6b	Et	Н	68	7.5:1
3°	6b	Et	Н	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. $E = CO_2Me$.





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 Ruhydride 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.
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