Metathesis Catalysts

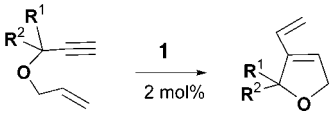
Alkenylcarbene Ruthenium Arene Complexes as Initiators of Alkene Metathesis: An Enyne Creates a Catalyst that Promotes Its Selective Transformation**

*Ricardo Castarlenas, Matthieu Eckert, and Pierre H. Dixneuf**

Alkene metathesis has become a powerful reaction in organic synthesis and polymerization as it allows new approaches for making crucial C–C bonds and thus reduces the number of steps in the synthesis to natural or biologically relevant compounds.[1] This is due to the discovery of well-defined alkylidene metal catalysts, of which those of ruthenium offer an especially good compromise between efficiency and tolerance to functional groups.[1d] The moderate stability of the coordinatively unsaturated ruthenium alkylidene catalytic species[2] can be compensated by high efficiency of the catalytic moiety, which allows transformation of a large quantity of substrate under mild conditions in a short time. Consequently, attempts are currently being made to generate highly active catalytic species in situ.[3,4]

Ruthenium arene complexes are effective precursors of catalytically active unsaturated alkylidene species.[3,5–8] Noels et al. showed that activation of $[\{RuCl_2(\eta^6\text{-}p\text{-cymene})\}_2]$ by addition of a bulky phosphane and (trimethylsilyl)diazomethane gives the highly active catalyst $[RuCl_2(=CHSiMe_3)(PCy_3)]$ for ring-opening metathesis polymerization (ROMP) of cycloolefins.[5] In situ introduction of a more electron-releasing N-heterocyclic carbene increases the catalytic performance.[6] Allenylidene ruthenium arene complexes promote alkene metathesis reactions,[1a,7] and their activity has been tremendously improved by protonation to generate a highly active indenylidene species.[8]

We now disclose the in situ generation of a new ruthenium alkene metathesis catalyst, namely, an alkenylcarbene ruthenium arene species generated from $[RuCl(\eta^6\text{-arene})(PCy_3)]X$ on activation of enynes. We show that the catalyst results from a metallo-retro-ene reaction involving a coordinated allyl or alkyl propargylic ether and allows the ring-closing metathesis (RCM) of enynes and dienes [Eq. (1)]. We present a remarkable example of a smart substrate: a propargyl ether that generates in situ a catalyst for its own selective transformation.



(1)

The 16-electron cationic complex $[RuCl(\eta^6\text{-}p\text{-cymene})(PCy_3)]CF_3SO_3$ (**1**), precursor of the allenylidene derivative $[RuCl(\eta^6\text{-}p\text{-cymene})(=C=C=CPh_2)(PCy_3)]CF_3SO_3$ (**2**),[7] does not show significant activity for the RCM of diallyl tosylamide (**3**; Table 1, entry 1). However, despite the fact that RCM of enynes is usually more difficult to perform than that of dienes, it was surprisingly found that complex **1** achieves excellent activity in the transformation of enynes into the corresponding alkenyl cycloalkenes under mild conditions [Eq. (1), Table 1, entries 2–6].[9] Thus, when allyl propargyl ethers **5–9** were treated with 2 mol% of **1** in CH_2Cl_2 at room temperature, alkenyl cycloalkenes **10–14** were selectively formed with a remarkable turnover frequency (TOF) of 12–47 h^{-1}. These results are just in the range of those obtained with other ruthenium-based olefin metathesis catalysts, as shown by Fürstner et al.[10] (1 mol% of catalyst, 80°C, 80–85% yield, 0.3–1 h) and Grela et al.[11] (1 mol% of catalyst, 0°C, 98% yield, 1 h). However, the lower catalytic activity for allyl propargyl tosylamide (**15**; Table 1, entry 7) confirms that allyl propargyl ethers play an important role.

It was first thought that the good catalytic activity observed was due to the fact that terminal enynes can react with **1** to form vinylidene species, as vinylidene ruthenium intermediates are moderate olefin metathesis initiators.[12]

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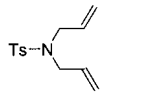
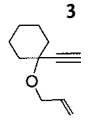
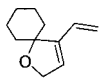
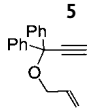
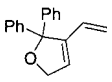
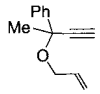
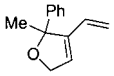
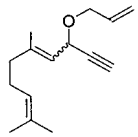
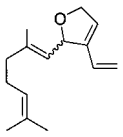
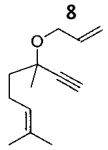
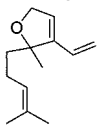
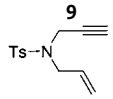
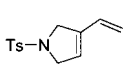
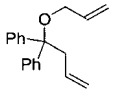
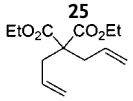
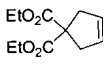
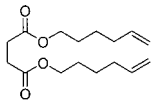
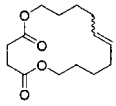
Table 1: Diene and enyne RCM reactions promoted by **1** at room temperature.[a]

Entry	Substrate	Product	*t* [h]	Conv. [%][b]	TOF [h^{-1}]
1	 **3**	 **4**	20	3	0.07
2	 **5**	 **10**	1	95	47.5
3	 **6**	 **11**	2.5	60	12.0
4	 **7**	 **12**	1	90	45.0
5	 **8**	 **13**	2	87	21.7
6	 **9**	 **14**	3	93	15.5
7	 **15**	 **16**	24	70	1.5

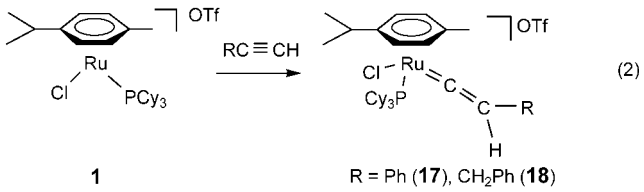
[a] [Monomer]/[Ru] = 50. [b] Determined by GC.

Table 2: Diene RCM reactions with 2% mol catalyst at room temperature.

Entry	Catalyst	Substrate	Product	*t* [h]	Conv. [%][a]	TOF [h^{-1}]
1	**17**	**3**	**4**	20	40	1
2	**18**	**3**	**4**	20	35	0.87
3	**20**	**3**	**4**	20	22	0.55
4	**21**[b]	**5**	**10**	1	99	49.50
5	**21**[b]	**3**	**4**	0.25	99	198
6	**24**[b]	**3**	**4**	0.25	95	190
7	**21**[b]	 **25**	 **28**	4	99	12.37
8	**21**[b]	 **26**	 **29**	2	99	24.74
9	**21**[b]	 **27**	 **30**	1	99	49.50

[a] Determined by GC. [b] Catalyst prepared in situ from **1** and **22** or **23**.

With the aim of confirming this hypothesis, new vinylidene derivatives [RuCl(η⁶-*p*-cymene){=C=CH(R)}(PCy_3)]CF_3SO_3 (R = Ph (**17**), CH_2Ph (**18**)) were synthesized from **1** and phenyl acetylene and benzyl acetylene, respectively [Eq. (2)].



1 R = Ph (**17**), CH_2Ph (**18**) (2)

Complexes **17** and **18** are unstable at room temperature but were characterized at −30 °C. In the $^{13}C\{^1H\}$ NMR spectrum, the most interesting feature is the low-field doublets that appear at 358.3 ($^2J_{C,P}$ = 20.1 Hz, **17**) and 345.0 ppm ($^2J_{C,P}$ = 19.3 Hz, **18**), which correspond to the Ru=C carbon atom of the vinylidene moiety. However, **17** and **18** only slightly promote the RCM of diallyl tosylamide (TOF 0.87–1 h^{-1}, Table 2, entries 1 and 2) and therefore cannot explain the excellent catalytic activity displayed by complex **1** in the RCM of enynes **5**–**9**.

To elucidate the active species, a stoichiometric reaction between complex **1** and enyne **5** was carried out. After 5 min at room temperature, **5** was transformed into diene **10**, whereas cationic complex **1** apparently remained unchanged. This suggested that only a small amount of complex **1** was activated by **5** to form an undetectable highly active species that promotes RCM of the enyne. To increase the chances of observing the intermediate, the counteranion in **1** was exchanged with tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BAr^{F-}_4) to give the new cationic complex [RuCl(η⁶-*p*-cymene)(PCy_3)]BAr^F_4 (**19**; Scheme 1). The reaction of **19** with 1 equivalent of **5** was monitored by NMR spectroscopy at −30 °C. A new signal at δ = 48.1 ppm appeared in the $^{31}P\{^1H\}$ NMR spectrum showing the formation of a new complex which, on the basis of ^1H, ^{13}C, $^1H,^1H$ COSY, and $^1H,^{13}C$ HMQC and HMBC correlation experiments, was identified as alkenylcarbene complex [RuCl(η⁶-*p*-cymene){=CH−CH=$C(C_5H_{10})$}(PCy_3)]BAr^F_4 (**20**). Accompanying the signals for **20**, three multiplets at δ = 9.51, 6.25, and 6.10 ppm were observed and shown to correspond to the presence of acrolein.

A rational mechanism for the formation of the alkenylcarbene complex is proposed in Scheme 1. From the initially formed vinylidene species, a pericyclic retro-ene cleavage[13] generates the alkenylcarbene complex and acrolein. It has been shown that thermolysis of propargyl ethers at 350–450 °C leads to allenes and carbonyl compounds by a retro-ene transformation.[14] Mediation of a transition metal is expected to reduce the activation energy for the metallo-retro-ene reaction[15] and thus allow it to occur at low temperature (−30 °C).

The catalytic activity of the relatively stable BAr^{F-}_4-containing complex **20** in the transformation of diene **3** into **4** remains moderate (Table 2, entry 3), likely owing to the inhibition by BAr^{F-}_4. Indeed, the nature of the escorting anion

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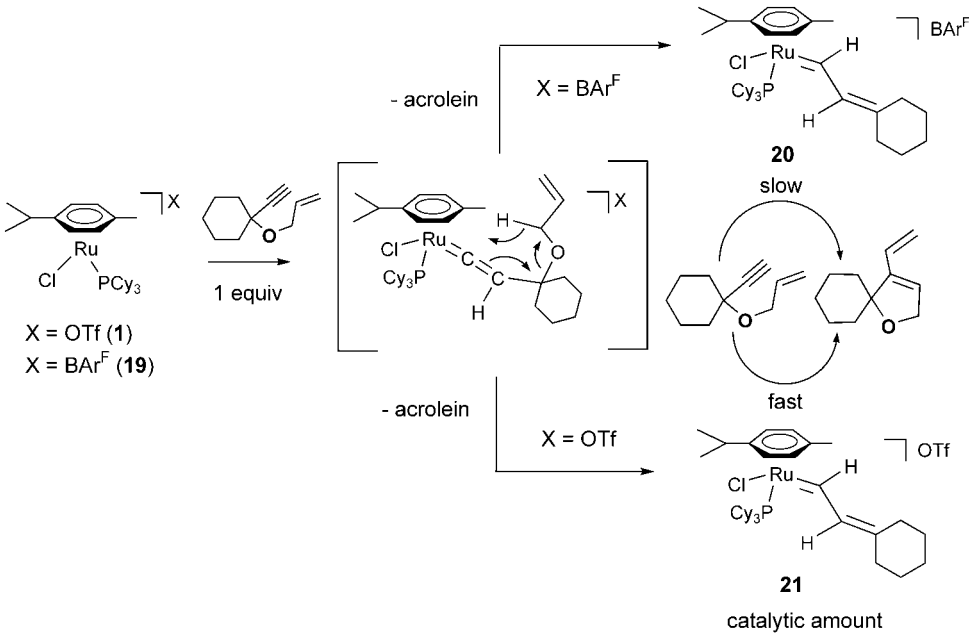
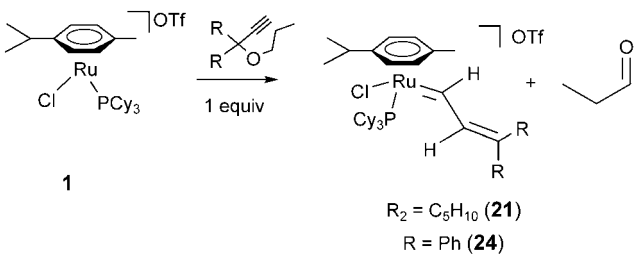


Scheme 1. Formation of ruthenium alkenylcarbene complexes by a metallo-retro-ene reaction.

in ruthenium allenylidene complex **2** drastically influences its catalytic activity in alkene metathesis according to the sequence $OTf^- > PF_6^- > BPh_4^- > BAr_4^{F-}$.[7]

Analogously to the formation of **20** from **19**, the reaction of triflate-containing complex **1** with enynes **5**–**9** is thus expected to generate ruthenium alkenylcarbene triflate catalyst **21**, which is much more active than the BAr_4^F analogue **20** (Scheme 1). In fact, in this case the ruthenium alkenylcarbene **21** could not be isolated or characterized from the reaction of **1** with enyne **5**. To prove that the vinylcarbene intermediate can be generated by a retro-ene reaction independent of the enyne substrate, stoichiometric activation of the propyl propargyl ethers of type $CH_3CH_2CH_2OCR_2C{\equiv}CH$ ($R^2 = C_5H_{10}$ (**22**), R = Ph (**23**)), which cannot give rise to enyne RCM reactions, was attempted with **1**. At −30 °C in dichloromethane the reaction led in this case to formation of propanal and the triflate-containing alkenylcarbene complexes $[RuCl(\eta^6\text{-}p\text{-cymene})(=CH{-}CH{=}CR_2)(PCy_3)]CF_3SO_3$ ($R^2 = C_5H_{10}$ (**21**), R = Ph (**24**), Scheme 2). Both complexes **21** and **24** decompose at room temperature but could be characterised at −30 °C by NMR experiments. Note that



Scheme 2. Triflate alkenylcarbene catalysts generated from **1** and propyl propargyl ethers.

complexes **21** and **24** could not be observed on reaction of **1** with enynes **5** or **6** owing to their high catalytic activity toward these enynes.

Addition of enyne **5** to a catalytic amount of **21**, generated in situ by reaction of **1** and **22**, led over 1 h at room temperature to complete formation of **10** (Table 2, entry 4) and confirmed the formation of **21** from **1** and **5**.

These in situ generated catalyst systems **21** and **24** tremendously increase olefin metathesis activity for formation of **4** from diene **3** in comparison with parent complex **1** (Table 1, entry 1 versus Table 2, entries 5 and 6). Moreover, dienes **25**–**27**, which are almost inert in the presence of **1**, are completely converted into **28**–**30** by addition of 2 mol % of **21** at room temperature (Table 2, entries 7–9).

These new 18-electron, ionic alkenylcarbenes $[RuCl(\eta^6\text{-}p\text{-cymene})\{=CH{-}CH{=}CR_2\}(PCy_3)]X$ strongly differ in their nature and synthesis with the neutral, 16-electron $[RuCl_2(=CH{-}CH{=}CPh_2)(PCy_3)_2]$ complex arising from diphenyl cyclopropene[16] and diphenyl propargylic chloride.[17]

The above simple reaction of ruthenium complex **1** with allyl or propyl propargylic ethers is a simple and novel method of preparing ruthenium alkenylcarbene complexes and involves a metal-assisted retro-ene reaction. The catalytic transformation of allyl propargylic ethers is a remarkable example of a substrate that transforms in situ an inert ruthenium complex into an active catalyst that is then able to convert the parent enyne into a highly reorganized alkenylcycloalkene. This new method of generating an active alkene metathesis initiator from alkyl propargylic ethers has potential for the catalytic transformation of a variety of substrates by simple variation of propargyl ethers and electron-donor ligands in complex **1**.

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Experimental Section

Full experimental details and spectroscopic data are available in the Supporting Information. Coupling constants are given in Hz.

17, **18**: An orange solution of **1** (50 mg, 0.071 mmol) in CD_2Cl_2 (0.5 mL) in an NMR tube under argon atmosphere at 213 K was treated with phenylacetylene (9 μL, 0.081 mmol) or benzylacetylene (11 μL, 0.088 mmol). The color changed immediately to dark orange, and, after sealing the NMR tube, measurements were made. Selected data for **17**: ^{1}H NMR (300 MHz, CD_2Cl_2, 243 K): $\delta = 5.93$ ppm (s, 1H, =C=CH). ^{13}C{^{1}H} NMR (75.4 MHz, CD_2Cl_2, 243 K): $\delta = 358.3$ (d, $J_{C,P} = 20.1$, Ru=C), 118.4 ppm (s, Ru=C=*C*). Selected data for **18**: ^{1}H NMR (300 MHz, CD_2Cl_2, 243 K): $\delta = 5.17$ (dd, $J_{H,H} = 9.9$, 6.8, 1H, =C=CH), 3.95 (dd, $J_{H,H} = 14.6$, 6.8, 1H, =C(C*H*$_2$Ph)), 3.60 ppm (dd, $J_{H,H} = 14.6$, $J_{H,H} = 9.9$, 1H, =C(C*H*$_2$Ph)). ^{13}C{^{1}H} NMR (75.4 MHz, CD_2Cl_2, 243 K): $\delta = 345.0$ (d, $J_{C,P} = 19.3$ Hz, Ru=C), 112.1 ppm (s, Ru=C=*C*).

20: A violet solution of **19** (300 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) at 243 K was treated with allyl 1-ethynylcyclohexyl ether (40 mg, 0.24 mmol), and the reaction mixture was stirred for 2 h. The resulting orange solution was evaporated to dryness below 243 K, and the residue was washed three times with cold pentane/diethyl ether (5/1 mL). The yellow solid was dried under vacuum (270 mg, 84% yield). Selected NMR data: ^{1}H NMR (300 MHz, CD_2Cl_2, 243 K): $\delta = 16.28$ (d, $J_{H,H} = 14.1$, 1H, Ru=CH), 8.12 ppm (d, $J_{H,H} = 14.1$, 1H, Ru=CH–C*H*=). ^{13}C{^{1}H} NMR, (75.4 MHz, CD_2Cl_2, 243 K): $\delta = 302.3$ (d, $J_{C,P} = 18.7$, Ru=C), 173.8 ppm (s, =*C*(C$_5$H$_{10}$)), 146.3 ppm (s, C–*C*H=C).

21, **24**: An orange solution of **1** (50 mg, 0.071 mmol) in CD_2Cl_2 (0.5 mL) in an NMR tube under argon atmosphere at 213 K was treated with propyl 1-ethynylcyclohexyl ether (**22**; 12 mg, 0.072 mmol) or propyl 1,1-diphenylethynyl ether (**23**; 18 mg, 0.072 mmol). Measurements were made immediately. Selected data for **21**: ^{1}H NMR (300 MHz, CD_2Cl_2, 243 K): $\delta = 16.12$ (d, $J_{H,H} = 13.8$, 1H, Ru=CH), 8.10 ppm (d, $J_{H,H} = 13.8$, 1H, Ru=CH–C*H*=). ^{13}C{^{1}H} NMR (75.4 MHz, CD_2Cl_2, 243 K): $\delta = 299.9$ (d, $J_{C,P} = 17.4$, Ru=C), 172.5 (s, =*C*(C$_5$H$_{10}$)), 147.2 ppm (s, C–*C*H=C). Selected data for **24**: ^{1}H NMR (300 MHz, CD_2Cl_2, 243 K): $\delta = 15.28$ (d, $J_{H,H} = 13.7$, 1H, Ru=CH), 8.56 ppm (d, $J_{H,H} = 13.7$, 1H, Ru=CH–C*H*=C). ^{13}C{^{1}H} NMR (75.4 MHz, CD_2Cl_2, 243 K): $\delta = 300.1$ (d, $J_{C,P} = 19.5$, Ru=C), 159.2 (s, =*C*Ph$_2$), 146.4 ppm (s, C–*C*H=C).

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