

Immobilization of the Grubbs second-generation ruthenium-carbene complex on poly(ethylene glycol): a highly reactive and recyclable catalyst for ring-closing and cross-metathesis

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Abstract—A poly(ethylene glycol)-bound Hoveyda–Grubbs Ru catalyst derived from the Grubbs second-generation Ru carbene complex was synthesized and shown to be highly reactive in the ring-closing metathesis of a wide variety of diene substrates, yielding di-, tri-, and tetra-substituted carbocyclic and heterocyclic olefins. The immobilized catalyst also proved to be highly reactive and recyclable in cross-metathesis and ring-opening/cross-metathesis. In all cases tested, the catalyst exhibited a high level of recyclability and reusability.

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The advent of well-defined Ru carbene catalysts, most notably, the Grubbs-type Ru benzylidenes **1**^{1a} and **2**^{1b}

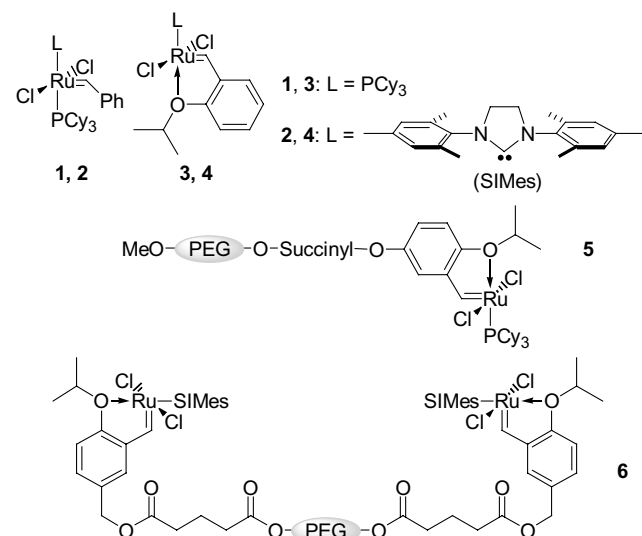


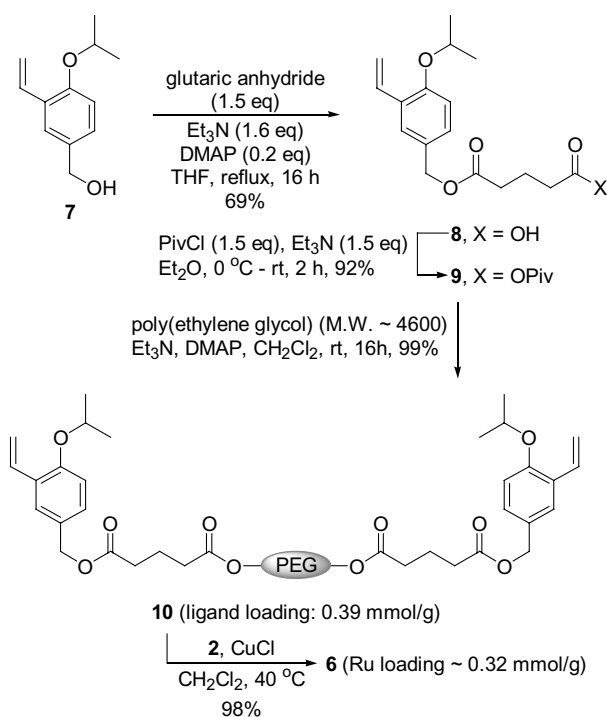
Figure 1. Ru catalysts for olefin metathesis.

Keywords: Catalyst immobilization; Grubbs catalysts; Olefin metathesis; Poly(ethylene glycol); Ruthenium.

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(Fig. 1) has fueled the widespread application of olefin metathesis.² Another significant advance in this area is the discovery by Hoveyda and co-workers of the robust and recyclable Ru catalysts **3** and **4**.³ The development of immobilized Ru catalysts for olefin metathesis has also attracted increasing interest since this would be expected to further increase the practicality and efficiency of the catalysts for this reaction. We⁴ and others⁵ have established that various polymeric and solid supports can be employed to immobilize these catalysts. In particular, the air stable poly(ethylene glycol) monomethyl ether (MeO-PEG)-immobilized Ru catalyst **5**^{4a} derived from the Grubbs catalyst **1** was shown to exhibit high activity in ring-closing diene metathesis (RCM) under homogeneous conditions. This catalyst can be conveniently recovered by precipitation with diethyl ether and repeatedly reused without significant loss of its activity, demonstrating the practical advantage of using MeO-PEG as a soluble polymer⁶ to immobilize Ru catalysts. We now wish to report the synthesis and application of the more reactive poly(ethylene glycol) (PEG)-immobilized Ru catalyst **6** derived from the Grubbs second-generation catalyst **2** bearing a nucleophilic carbene ligand (SIMes).

Catalyst **6** can be readily assembled as shown in Scheme 1. Based on our experience with the MeO-PEG-bound catalyst **5** that has a Ru loading of approximately 0.1 mmol/g, we envisaged that the use of poly(ethylene glycol) (PEG) that bears two OH groups on each



Scheme 1. Synthesis of the poly(ethylene glycol)-immobilized Ru catalyst **6**.

polymer chain would result in an increased overall catalyst loading on the polymer. The known isopropoxystyrene derivative **7**^{5h} was first treated with glutaric anhydride in the presence of Et₃N and DMAP to give the monoacid **8**. This material was then coupled to PEG, through the mixed acid anhydride intermediate **9**, to afford the PEG-bound ligand **10** in essentially quantitative yield based on 500 MHz ¹H NMR spectroscopic analysis as well as on the mass increase of the polymer. Treatment of **10** with catalyst **2** in the presence of CuCl^{3b} resulted in a clean and quantitative exchange of the styrene ligand as judged by ¹H NMR spectroscopy to give **6** as an air stable deep green powder in 98% yield (loading 0.32 mmol/g).

The activity of **6** was then evaluated with the two test dienes **11** (Table 1) and **13** (Table 2). As shown in Table 1, the disubstituted diene **11** underwent RCM in the presence of 2 mol % Ru of **6** in CH₂Cl₂ at 40 °C to give the cyclic olefin **12** in excellent conversion as indicated by 500 MHz ¹H NMR spectroscopy. As with the MeO-PEG-bound catalyst **5**, the recovery **6** from the reaction mixture can be achieved by precipitation with diethyl ether in air.⁷ Importantly, the recycled catalyst can be reused for up to 10 cycles with only a very slight decrease in activity after each recycling and reuse. The high level of recyclability of catalyst **6** was further established with the tri-substituted diene **13** (Table 2), which cyclized cleanly in the presence of 5 mol % Ru of **6**, with conversion still exceeding 90% even after 17 consecutive cycles. An average of less than 1% decrease in the conversion of the diene after each cycle points to a highly efficient, although not full, return of the catalytically active species (SIMes)Ru(Cl)₂=CH₂ to the PEG-bound isopropoxystyrene ligand **10**.⁸

Table 1. Recycling and reuse of PEG-bound Ru catalyst **6** in the RCM of test diene **11**^a

Cycle	1–4	5	6	7	8	9	10
(%) Conversion ^b	>98	97	97	95	95	92	90

^a All reactions were performed in refluxing CH₂Cl₂.

^b Determined by 500 MHz ¹H NMR spectroscopy.

Table 2. Recycling and reuse of PEG-bound Ru catalyst **6** in the RCM of test diene **13**^a

Cycle	1	2–6	7–10	11–14	15	16	17
(%) Conversion ^b	100	99	98	96	94	94	94

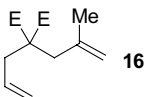
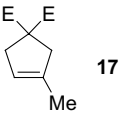
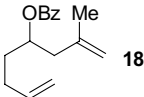
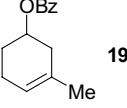
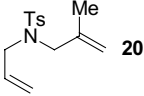
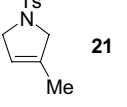
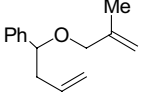
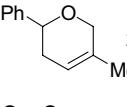
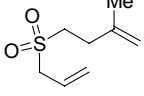
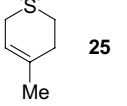
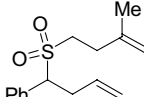
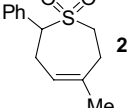
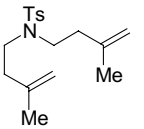
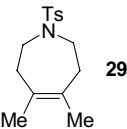
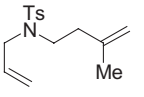
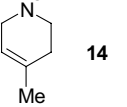
^a All reactions were performed in refluxing CH₂Cl₂.

^b Determined by 500 MHz ¹H NMR spectroscopy.

To examine the scope of catalyst **6**, we next focused on its performance in the RCM of a variety of other tri- and tetra-substituted dienes as well as in cross-metathesis. As shown in Table 3, the activity of different batches of catalyst **6** was uniformly high in the formation of tri-substituted carbocyclic (batch A) and heterocyclic olefins (batch B) with various ring sizes. These dienes underwent clean and high yielding RCM using either a freshly prepared or recycled catalyst. The catalyst (batch C) also proved highly active even with the tetra-substituted diene **27**. As it could be expected, an extended reaction time was necessary to achieve a high conversion of the diene. Nevertheless, the catalyst was clearly recyclable (cycles 1–3) even in the case of this demanding diene and remained active after the third cycle as tested with diene **13** (cycle 4).

Finally, the reactivity and recyclability of **6** were scrutinized by testing its performance in the cross-metathesis (CM) reactions shown in Table 4. CM involving Ru enoic carbene complexes^{9a,b} has been reported only recently with catalysts **2**^{9b,c} and **4**.¹⁰ Grubbs has shown^{9a,b} that these Ru carbenes are highly reactive but are quite unstable and have much shorter lifetimes than other alkylidene or benzylidene complexes. In the absence of any information regarding the recyclability of the parent catalyst **4** in these reactions,^{10,11} we wondered whether or not the formation of an unstable Ru enoic carbene from **6** would be detrimental to its regeneration. To our delight, the CM dimerization of *tert*-butyl acrylate proceeded uneventfully in the presence of only 2.5 mol % Ru of **6** (Table 4, cycle 1). The recycled catalyst showed essentially equal efficacy in the CM dimerization of *n*-butyl acrylate (cycle 2) as well as in the

Table 3. Activity and recyclability of PEG-bound Ru catalyst **6** in the RCM of various dienes^a

Catalyst batch	Cycle	Diene	Product	Time	(%) Conversion ^b (yield ^c)
1A (3.2 mol% Ru)	1	 16	 17	14	1>98 (97)
	2	15	16	4	96 (93)
	3	 18	 19	2	92 (89)
	4	18	19	2	90 (87)
B (3.2 mol% Ru)	1	 20	 21	3	>98 (95)
	2	 22	 23	3	>98 (96)
	3	 24	 25	3	97 (92)
	4	 26	 27	3	>98 (95)
C (5 mol% Ru)	1 ^d	 28	 29	6.5	39 (37)
	2 ^d	28	29	18	96 (93)
	3 ^d	28	29	18	82 (79)
	4 ^e	 13	 14	3	86 (83)

^a Unless otherwise noted, all reactions were performed in CH₂Cl₂ (0.05 M) at reflux.

^b Determined by 500 MHz ¹H NMR spectroscopy.

^c Refers to isolated, pure products after silica gel chromatography.

^d Performed in CH₂Cl₂ (0.4 M) at reflux.

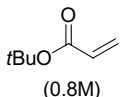
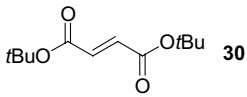
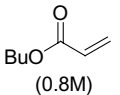
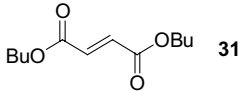
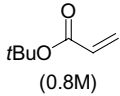
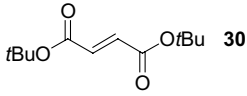
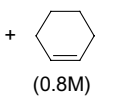
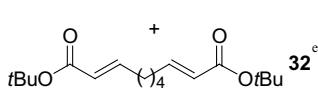
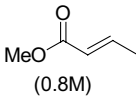

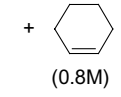
^e Performed with 3 mol% Ru relative to **13** in CH₂Cl₂ (0.05 M) at reflux.

ring-opening/cross-metathesis of the unstrained and thermodynamically stable cyclohexene with either *tert*-butyl acrylate (cycle 3¹²) or methyl fumarate (cycle 4).

In summary, we have shown that the poly(ethylene glycol)-bound Ru carbene complex **6** can be conveniently prepared and exhibits high reactivity, compara-

ble to the paradigmatic Grubbs second-generation catalyst **2** and the Hoveyda–Grubbs second-generation catalyst **4**, in a broad range of olefin metathesis reactions. Notable attributes of this new PEG-bound Ru catalyst include its high level of recyclability and reusability as well as its easy accessibility from commercially available polymer and catalyst precursor.

Table 4. Activity and recyclability of Ru catalyst **6** in cross-metathesis^a

Cycle	Olefins (concn)	Product	Yield ^b (%)
1 ^c	 (0.8M)	 30	88
2 ^c	 (0.8M)	 31	91
3 ^d	 (0.8M)	 30^c	18
	+  (0.8M)	 32^c	81
4 ^d	 (0.8M)	 33	68
	+  (0.8M)		

^a All reactions were performed in refluxing CH₂Cl₂ with 2.5 mol% Ru of catalyst **6**.

^b Refers to isolated, pure products after silica gel chromatography.

^c Reaction time: 6 h.

^d Reaction time: 4 h.

^e See Ref. 12.

Acknowledgements

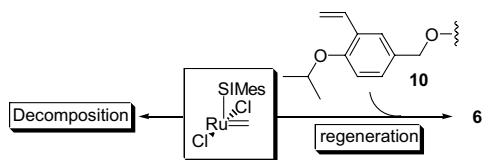
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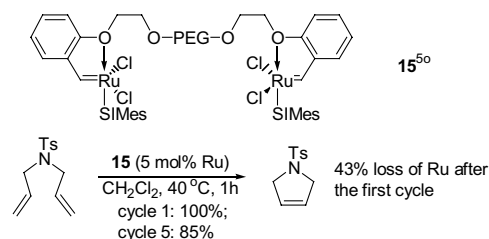
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- All operations including concentration of the reaction mixture, precipitation, filtration, and washing of the PEG-bound catalyst with reagent grade diethyl ether were carried out in vessels open to the air.
- Although the exact nature of the decomposition of the catalytically active species $(\text{SiMes})\text{Ru}(\text{Cl}_2)=\text{CH}_2$ is not clear at this time and a determination of metal leaching has not been attempted, the high level of recyclability of **6** indicates that the return of $(\text{SiMes})\text{Ru}(\text{Cl}_2)=\text{CH}_2$ to the PEG-bound ligand **10** occurs much faster than its decomposition:



It is also informative to compare **6** with the PEG-bound catalyst **15** that was previously reported by Lamaty and co-workers⁵⁰ and found to suffer significant decomposition upon recycling:



The difference in the stability and recyclability between **6** and **15** reflects the subtle electronic and steric requirements for the alkoxy ligand. Hoveyda has previously established that substitution of the isopropoxy group by a smaller and less electron-donating methoxy group leads to less stable Ru catalysts (see Ref. 3a).

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- Blechert and co-workers has previously reported the CM of electron-deficient olefins and terminal olefins using a recyclable Ru catalyst immobilized on Wang resin. However, it is mechanistically unlikely for a $[\text{Ru}]=\text{COR}$ carbene to be involved in these reactions (see Ref. 5i).
- Both products were isolated by silica gel chromatography as a mixture and individual yields were calculated based on 500 MHz ^1H NMR integration of the olefinic protons.