A new type of self-supported, polymeric Ru-carbene complex for homogeneous catalysis and heterogeneous recovery: synthesis and catalytic activities for ring-closing metathesis†

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A novel 2nd generation Grubbs-type catalyst tethering an isopropoxystyrene has been synthesized and automatically polymerized in solution to form a self-supported polymeric Ru-carbene complex, which catalyzed ring-closing metathesis homogeneously, but was recovered heterogeneously.

Olefin metathesis has become one of the simplest and most effective synthetic methods for carbon–carbon double bond construction and is widely employed in a variety of fields of chemistry including natural products, pharmaceuticals, and polymer chemistry.[1] Much of the recent successful progress in olefin metathesis stems largely from the availability of several, well-defined ruthenium catalysts such as Grubbs-type ruthenium alkylidenes **1**[2] and Hoveyda/Grubbs-type ruthenium catalysts **2**,[3] which are easy to handle and are tolerant towards different kinds of functional groups (Fig. 1). Despite the general superiority offered by these Ru catalysts, they share some disadvantages associated with difficulties in the recovery and reuse of the expensive metal catalysts as well as product contamination caused by metal leaching. Hence, from an economic and environmental point of view, development of immobilization technology for recycling of the catalyst is of great importance.[4] A common approach for immobilization of homogeneous ruthenium catalysts is grafting of the catalyst, particularly Hoveyda/Grubbs-type **2** to supports such as polymers,[5] dendrimers,[6] or nanoparticles.[7] The use of tagged catalysts has also been employed as alternative immobilization methods for fluorous[8] or ionic liquid phase catalysis,[9] in which the tagged catalyst can be easily separated from untagged products by liquid–liquid partition.

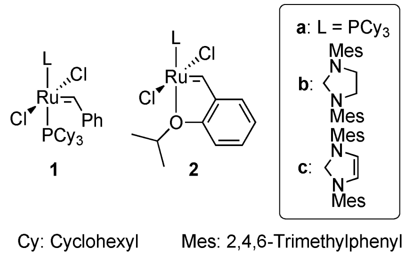

Fig. 1 Representative Ru-complexes for olefin metathesis.

Another promising and recent strategy involves heterogenization of the homogeneous catalysts or precursors by homocombination of multi-topic organic ligands to generate "self-supporting" metal–organic polymeric networks.[10] Compared to other methods, the self-supporting strategy can produce heterogeneous catalysts without using any supports with a high density of catalytically active units. However, these heterogeneous self-supported catalysts often have decreased catalytic activity compared to their homogeneous counterparts. Taking advantage of this self-supporting strategy, it could conceptually be possible to generate new types of self-supported catalysts or catalyst precursors to conduct catalysis homogeneously with heterogeneous recovery. We anticipated that the structural features and "release and return" metathesis mechanism could provide an excellent opportunity for the generation of a new type of self-supported Ru-complexes, allowing homogeneous catalysis and heterogeneous recovery.

Quite recently, we demonstrated for the first time the validity of this strategy for ring-closing metathesis with Ru-carbene catalyst **3** (type A in Fig. 2).[11] The catalytically active dimeric Ru-methylidene and dimeric isopropoxybenzylidene were dissociated from the polymer matrix, and after catalysis, could be re-associated to form the polymeric catalyst precursor **3**, which was recovered heterogeneously. In principle, homo-coupled, self-supported polymeric Ru-carbene complexes such as **4** (type B in Fig. 2) would also be possible, in which the catalytically active Ru-methylidene

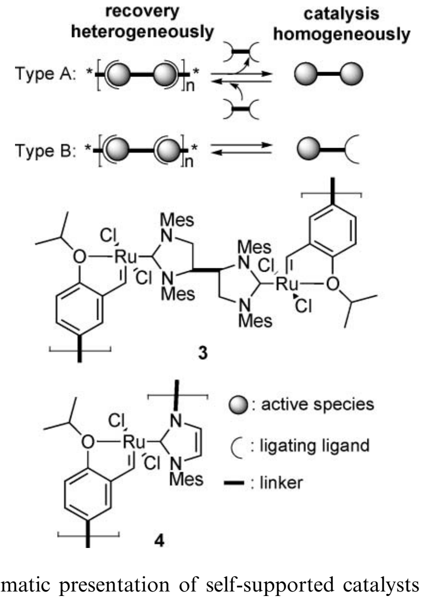

Fig. 2 Schematic presentation of self-supported catalysts for homogeneous catalysis and heterogeneous recovery.

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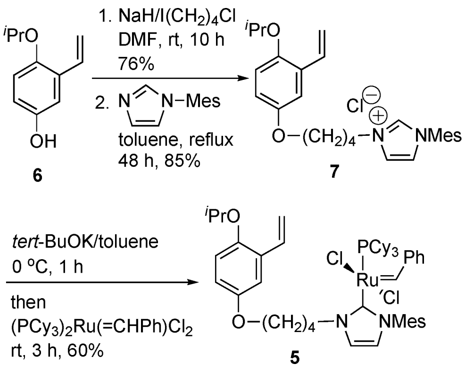
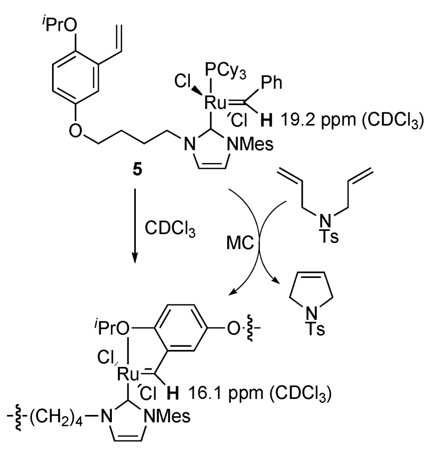
species, having a chelating isopropoxystyrene group, would be generated. Herein we report the synthesis of this new-type of 2nd generation Ru-carbene complex **5** tethering an isopropoxy styrene group, and its conversion to a self-supported polymeric Ru-carbene complex **4**, and their catalytic activity and reusability in ring-closing metathesis.

As a precursor for the homo-coupled, self-supported polymeric Ru-carbene complex **4**, the Grubbs' 2nd generation-type Ru-carbene complex **5**, tethering an isopropoxystyrene with a butyl linker, was designed and synthesized as shown in Scheme 1. The 5-hydroxy-2-isopropoxystyrene **6**[5d] was alkylated with 1-chloro-4-iodobutane, and the resulting chloride reacted with 1-mesitylimidazole[12] to form imidazolium chloride **7**. For the synthesis of complex **5**, the NHC-carbene was generated *in situ* by reaction of imidazolium chloride **7** with *t*-BuOK in toluene at 0 °C, then reacted with Grubbs' 1st generation catalyst at room temperature for 3 h. After short silica-gel chromatographic purification, the desired Ru-carbene complex **5**, bearing an isopropoxystyrene moiety linked with a butyl tether, was isolated in 60% yield.‡ In the ^{1}H NMR spectrum, the characteristic resonance signals of Ru=C*H*-Ph at 19.2 ppm and the free vinyl protons of styrene, $=CH_2$, at 5.69 ppm (dd, $J = 17.8$, 1.3 Hz) and 5.24 ppm (dd, $J = 11.1$ and 1.3 Hz) were observed.[2c] However, it was found that **5** was not stable in $CDCl_3$, and converted to the homo-coupled self-supported polymeric Ru-carbene complex **4**. As shown in Fig. 3, during the NMR measurement, the intensity of the Ru=C*H*– peak at 19.2 ppm (Fig. 3a) rapidly decreased, and a new Ru=C*H*– resonance peak at 16.1 ppm corresponding to the isopropoxybenzylidene Ru-complex appeared after 5 min (Fig. 3b). After 30 min, the resonance peak at 19.2 ppm was completely converted to the peak at 16.1 ppm (Fig. 3c). Moreover, disappearance of the vinyl proton resonance signals at 5.69 ppm and 5.24 ppm in **5** clearly indicated formation of complex **4** (see ESI for full scale spectrum†).



Scheme 1 Synthesis of Ru-carbene complex **5** tethering an isopropoxystyrene group.



Scheme 2 Synthesis of homo-coupled polymeric Ru-carbene complex **4**.

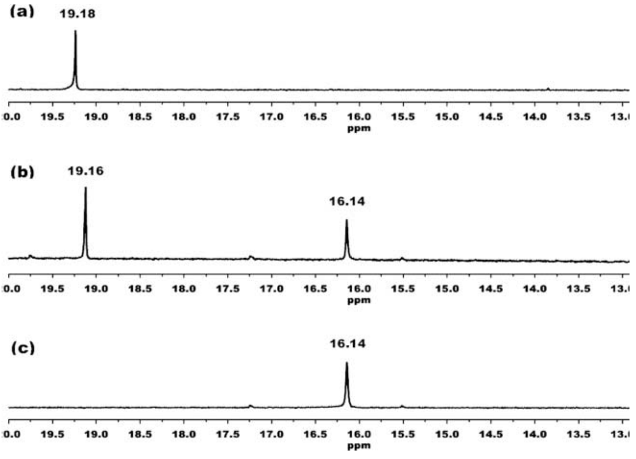


Fig. 3 ^{1}H NMR (250 MHz, $CDCl_3$) spectra of the Ru=C*H*– region of (a) **5**; (b) after 5 min; (c) after 30 min.

Based on these observations, we anticipated that the polymeric Ru-complex **4** could be prepared during ring-closing metathesis (RCM) with monomeric Ru-complex **5** (Scheme 2). Thus, the RCM of the benchmark substrate, *N,N*-bisallyl *p*-toluenesulfonamide, was carried out in methylene chloride at 40 °C in the presence of 5.0 mol% of **5**, and the reaction was complete in 4 h with >98% yield (entry 1 in Table 1). After RCM, complex **5** was converted to polymeric complex **4**, which could be recovered *via* precipitation using ethyl acetate, as previously observed in hetero-coupled, self-supported polymeric Ru-carbene complex **3**.[11] Inductive coupled plasma atomic emission spectroscopic (ICP-AES) analysis of isolated **4** showed 18 wt% incorporation of Ru into the polymer matrix. The recovered polymeric Ru-carbene complex showed slightly decreased catalytic activity compared to monomeric **5** (entry 2). The decreased catalytic activity of **4** could be ascribed to the slow dissociation of the catalytically active Ru-species from the polymer matrix. The recovered **4** can be reused 2 more times without loss of catalytic activity (entries 3 and 4). However, ICP-AES analysis indicated significant amounts of Ru

Table 1 Catalyst recycling in ring-closing metathesis of *N,N*-bisallyl *p*-toluenesulfonamide using Ru-carbene complexes **4** and **5**[a]

Entry	Catalyst	Time/h[b]	Yield (%)[c]	Ru leaching[d]
1	**5**	4	>98	
2[e]	**4**	6	>98	25 ppm
3[e]	**4**	6	>98	20 ppm
4[e]	**4**	6	>98	—
5[e]	**4**	8	>98	—
6[e]	**4**	12	>98	—

[a] Reactions were carried out using 5.0 mol% of Ru at 40 °C in methylene chloride (0.5 M). [b] Time for completion. [c] Determined by ^{1}H NMR analysis. [d] Determined by ICP-AES analysis of the ethyl acetate layer. [e] Recovered catalyst from previous entry was used.

leached out into the ethyl acetate layer in each cycle, thus requiring longer times to complete the reaction from 5th (entry 5) and 6th runs (entry 6). Although reusability of the polymeric Ru-carbene complex was not sufficiently high, this approach might provide an alternative way to generate self-supported recoverable Ru-catalysts for metathesis.

In summary, we have synthesized a new type of Grubbs' 2nd generation Ru-carbene complex **5** tethering an isopropoxystyrene moiety, which was rapidly converted to the homo-coupled, self-supported polymeric Ru-carbene complex **4**. Polymeric Ru-carbene complex **4** catalyzed ring-closing metathesis homogeneously and was recovered heterogeneously. Further studies on the impact of a linker on both structure of assemblies and their catalytic performance are under way.

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Notes and references

‡ Synthesis of **5** and its polymeric Ru-carbene complex **4** *via* RCM. A solution of imidazolium salt **7** (0.12 g, 0.26 mmol) in toluene (10 mL) was treated with ^{t}BuOK (29.5 mg, 0.26 mmol) and (PCy$_3$)$_2$Cl$_2$Ru=CHPh (0.18 g, 0.22 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 3 h under N$_2$. The suspension was filtered and the solvent was evaporated by vacuum. The resulting residue was purified by silica gel chromatography using EtOAc–hexane (1 : 3) as the eluent to afford **5** (0.075 g, 0.13 mmol, 60%). ^{1}H NMR (CDCl$_3$, 250 MHz) δ 19.24 (s, 1H), 7.41 (m, 2H), 7.16–6.99 (m, 6H), 6.81 (m, 4H), 6.47 (br s, 1H), 5.74 (dd, 1H, J = 1.3, 17.8 Hz), 5.27 (dd, 1H, J = 1.3, 11.1 Hz), 4.82 (t, 2H, J = 7.2 Hz), 4.38 (sept, 1H, J = 6.1 Hz), 4.07 (t, 2H, J = 5.7 Hz), 2.41–2.34 (m, 6H), 2.04 (m, 2H), 1.93 (m, 8H), 1.63 (m, 24H), 1.32 (d, 6H, J = 6.1 Hz), 1.25–1.21 (m, 6H). A 10 mL oven-dried round-bottom flask equipped with a reflux condenser was charged with polymeric Ru-catalyst **5** (13.5 mg, 0.014 mmol). The flask was evacuated and filled with N$_2$. *N*,*N*-Diallyl-*p*-toluenesulfonamide (120.0 mg, 0.279 mmol) and anhydrous CH$_2$Cl$_2$ (5.0 mL) were added, the flask was then heated to gentle reflux for 6 h, and the solvent was evaporated. Ethyl acetate (5 mL) was added to the residue, and the precipitated polymeric Ru-complex **4** was recovered by filtration and washed with ethyl acetate (5 mL × 2). After evaporation of the ethyl acetate, ^{1}H NMR analysis of the crude residue revealed complete conversion, and the product was isolated by flash chromatography (*n*-hexane–EtOAc = 3 : 1) to afford pure product as a white crystalline solid (61 mg, 99%). A second run of the metathesis using the recovered polymeric Ru-complexes **4** was conducted in the same way as described for the first run. This reaction was repeated, each time using the catalyst recovered from a previous cycle. The results are listed in Table 1.

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