Mono-telechelic Polymers by Catalytic Living Ring-Opening Metathesis Polymerization with Second-Generation Hoveyda–Grubbs Catalyst

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The second-generation Hoveyda–Grubbs (HG2) catalyst, which has a small initiation to propagation rate ratio \((k_i/k_p)\) in ring-opening metathesis polymerization (ROMP), was successfully used in a recently developed catalytic living ROMP. This proved that slow-initiating catalysts can enable ROMP in a living fashion to produce polymers with narrow dispersity and controlled molecular weight. The molecular weight control experiments show a linear relationship between polymer molecular weight and monomer to chain-transfer agent (CTA) ratio. Different norbornene-derivatives can be utilized as monomers. Di-block copolymers and tri-block copolymers can be synthesized either using the first polymer block as macro-CTA or continuously adding different monomers sequentially. Mono-telechelic polymers, with functional end groups such as protected carboxylic acid, alcohol and amine can also be achieved. All polymers were fully characterized using NMR, GPC and MALDI-ToF analytical techniques. This procedure provides access to well-defined end-functional polymers at lower cost and with reduced rare metal residues that might be of interest for biomedical, materials, industrial and academic use.

Introduction

Living ring-opening metathesis polymerization (ROMP) has become a very powerful tool in the construction of macromolecular complexes. This is because the absence of chain transfer and chain termination in living ROMP can result in good molecular weight control and narrow dispersity \((D)\) which offer control over the microstructure and properties of polymers. To achieve better control of living ROMP, many different catalysts have been developed over the past decades. However, as these complexes act as polymerization initiators stoichiometric amounts with respect to the number of polymer chains are required. This results in a high catalyst loading and metal residue in the final polymer, especially when aiming at low molecular weight polymers. Therefore, many methods have been developed to decrease the loading of transition metal complexes, which are all examples of catalytic ROMP. However, none of the reported catalytic ROMP methods are living as they typically rely on chain transfer agents to occur. Block copolymers can therefore not be synthesized via these methods and the dispersity of the obtained polymer is typically broad. Recently, we developed a catalytic living ROMP method through a degenerative reversible chain-transfer mechanism, in which only a catalytic amount of transition metal complex is required for living ROMP. Not only can this method be applied to the first and third generations Grubbs catalyst, also the

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second-generation Grubbs catalyst can produce well-defined living polymers with narrow dispersity (D < 1.5).

On the other hand, the second-generation Hoveyda–Grubbs catalyst (HG2) is a very “user-friendly” catalyst due to its chemical and thermal stability, long-term stability in storage, recyclability and high catalytic activity. However, similar to the second-generation Grubbs catalyst (G2), HG2 is not a general catalyst for controlled living ROMP because the slow initiation and small \( k_i/k_p \) typically leads to a loss of molecular weight control. Only few examples have been reported where the HG2 complex could be used for controlled metathesis polymerizations giving well-defined polymers.

An important characteristic of any living polymerization is a ‘fast and complete initiation’ typically achieved via a large \( k_i/k_p \). Both the first-generation Grubbs catalyst (G1) and third-generation Grubbs catalyst (G3) can achieve living ROMP by coordination of the activated 14e– catalyst species to ligands to form stable complexes with a 16e– or 18e– count. Such stabilization can slow down the propagation process, result in an increase of \( k_i/k_p \) and stabilize the catalyst species. Compared with these two generations of Grubbs catalysts, using the HG2 catalyst in living ROMP is challenging as there is no ligand to stabilize the highly active 14e– catalyst species once the propagation has started.

In 2004, Slugovc’s group polymerized \( \text{endo, exo-bis-ketone or -diester norbornene monomers} \) with HG1 and HG2 catalysts in a controlled manner through coordination of the \( \text{endo-carbonyl group} \) of the monomer to the catalyst in order to slow down the propagation rate and stabilize the catalyst. Four years later, Mingotaud’s group reported controlled ROMP using the HG2 catalyst in water. Later, Choi’s group reported a controlled living ROMP of tricyclo[4.2.2.0\(^2\),5]deca-3,9-diene and cyclopolymerization of 1,8-noradiynes with G2 and HG2 by coordinating the catalyst to the olefin in the monomer to increase \( k_i/k_p \) and stabilize the catalyst. They also isolated the propagating species during polymerization and confirmed their olefin-chelated structures. Recently, we succeeded using the second-generation Grubbs catalyst (G2) in catalytic living ROMP by adding the monomers slowly in order to slow down the rate of propagation. To our knowledge, no report on catalytic living ROMP with HG2 catalyst has been published. Here, we show that the highly stable HG2 catalysts can be used in catalytic living ROMP yielding narrow dispersity polymers.

**Results and discussion**

Different from the three generations of Grubbs catalysts, the Hoveyda derivatives have no ligand to re-coordinate to the 14e– ruthenium complex once the catalyst has initiated in ROMP. However, there are reports showing that heteroatoms such as N, O or S and olefins in the monomer structure can co-ordinate to the ruthenium complexes to affect the reactivity of the propagating carbene. In order to follow the intermediates formed during our catalytic living ROMP using HG2, time-resolved \(^1\)H NMR reactions were carried out. The HG2 catalyst was dissolved in CD\(_2\)Cl\(_2\) under argon with 10 equiv of the chain-transfer agent \( (E)-3-(2\text{-cyclopropylvinyl})cyclopent-1\text{-ene} \) (CTA). A \(^1\)H NMR spectrum was recorded, however, no new carbene peaks, differing from the pure HG2 complex, appeared even after 1 h.

![Fig. 2](http://doc.rero.ch)

**Fig. 2** \(^1\)H NMR spectroscopic comparison of the reaction between HG2 [3.2 mg, 1.0 equiv], CTA [6.7 mg, 10 equiv], MINI [50 mg, 56 equiv] and 3-chloropyridine [5.6 mg, 10 equiv]. All reactions were carried out in 0.75 ml degassed CD\(_2\)Cl\(_2\) under Ar. a) CTA was added to HG2, then MINI was added after 1 h. b) CTA and 3-chloropyridine were added to HG2 together, then MINI was added after 15 h. c) 3-Chloropyridine was added to HG2 first, next MINI was added after 10 min, CTA was added after another 10 min.
Then, 56 equiv exo-N-methyl norbornene imide (MNI) was added to this NMR tube and the 1H NMR spectrum was measured immediately. We observed that all MNI monomer was polymerized by the time the NMR spectrum was recorded (in less than 5 min), however, the propagating carbene proton could still not be detected (Figure 2a). This confirmed that the heteroatoms present in our monomer and the olefin in our CTA do not appear to coordinate to the HG2 ruthenium complexes to produce 16e− or 18e− detectable ruthenium complexes during the polymerization. The HG2 ruthenium complexes most likely retain the activated 14e− form during the whole polymerization process. This makes controlled living ROMP using the HG2 catalyst even more challenging because the unstabilized 14e− ruthenium complexes are highly reactive, easily decompose and can undergo side reactions. As far as we know, this is the first report of a controlled living ROMP using the HG2 catalyst in a 14e− form without any additive to stabilize the activated catalyst species.

To further understand the reaction rate of the HG2 catalyst with the CTA and monomer during catalytic living ROMP, 3-chloropyridine was added to the next 1H NMR reaction to coordinate to the reacted ruthenium complex. After mixing HG2 with 10 equiv of CTA and 3-chloropyridine, we detected the appearance of cyclopropyl methylidene species at 17.31 ppm even after 5 min. of reaction time (Figure 2b)17. However, the reaction rate was very slow. It took more than 15 h to completely convert the original HG2 carbene signal to a cyclopropyl carbene. Once all of the HG2 benzylidene signal had disappeared, 56 equiv of MNI was added to the NMR tube. Both propagating carbene peaks and cyclopoly carbene peaks were detected within 5 min. after monomer addition (Figure 2b). The propagating carbene peaks, however, disappeared within 10 min (Figure 2b) and only the cyclopropyl carbene signals remained. This could be explained by assuming that only a small amount of cyclopropyl carbene complexes initiated the propagation. This small amount of propagating carbene complex then converted to a cyclopropyl carbene once again by reacting with the CTA after all monomer had been consumed. Alternatively, all cyclopropyl carbene complexes initiated the propagation but most of the propagating carbene complexes had already converted back to the cyclopropyl carbene complex before the first 1H NMR was measured. To obtain further information with regard to the intermediates formed in this reaction a third 1H NMR experiment was carried out. The HG2 catalyst was first mixed with 10 equiv of 3-chloropyridine. We found that the HG2 benzylidene peak shifted from 16.50 ppm to 16.65 ppm in less than 5 min (Figure 2c). This shift is caused by the coordination of 3-chloropyridine to the HG2 catalyst carbene complex24. All coordinated HG2 catalyst carbene complexes initiated the polymerization immediately after 56 equiv of MNI was added to the NMR tube. These propagating carbene complexes (18.57 ppm) converted to cyclopropyl carbene complexes (17.31 ppm) following the addition of 10 equiv CTA in less than 5 min (Figure 2c). These results confirmed that a) the heteroatoms and the olefin in MNI and the CTA do not coordinate to the HG2 carbene complex, b) the HG2 benzylidene complex reacts with the CTA at a very slow rate, c) the propagating carbene complex of HG2 reacts with CTA in a very fast fashion. With this information in mind, we polymerized exo-N-methyl norbornene imide (MNI) with the HG2 complex in a ratio of MNI:HG2 = 300:1. We expected to get a polymer that had an average molar mass of 53100 g mol⁻¹ if this polymerization took place in a living fashion. As expected, only an insoluble gel of very high molecular weight was obtained which shows that HG2 cannot be employed in living ROMP using MNI directly. Next, we tried the catalytic living ROMP method using the HG2 complex in a ratio of HG2:CTA:MNI = 1:10:300. We first dissolved HG2 (3.2 mg, 0.005 mmol) and (E)-3-(2-cyclopropylvinyl)cyclopent-1-ene CTA (6.7 mg, 0.05 mmol) in 2 ml degassed methylene chloride (DCM). Then MNI (266 mg, 1.5 mmol in 20 ml degassed DCM, 0.075 mol/l) was added dropwise with a syringe pump at 5 ml/h. We obtained a polymer (polyMNI) with 9000 g mol⁻¹ molar mass and Đ = 1.26. We were delighted to find that these results match the molecular weight and dispersity control similar to those observed in a recently reported catalytic living ROMP17. We would like to emphasize at this point that no 3-chloropyridine was added to the polymerization experiment. 3-Chloropyridine helped in observing the metathesis reaction in 1H-NMR experiments (Figure 2), however, we observed in a previous study17 that the degenerate chain transfer mechanism of catalytic
living ROMP was insensitive to the carbene complex initiation rate. We therefore omitted 3-chloropyridine under catalytic living ROMP polymerization conditions.

Moreover, the MALDI-ToF mass spectrum of this polymer confirmed the assumed polymer structure with the end groups defined by the CTA (Figure 3). These results confirmed that the HG2 catalyst can be employed in catalytic living ROMP to generate polymers with controlled molecular weight and dispersity.

Encouraged by these results, we further explored the molecular weight control by HG2 for catalytic living ROMP. We previously reported that the polymer molecular weight was determined by the monomer:CTA ratio in catalytic living ROMP. Using HG2, we successfully synthesized different molecular weight polymers by changing the MNI:CTA ratio (polymers 3-7, see supporting information). The linear correlation between the molecular weight (Mn, GPC(chloroform)) and the MNI:CTA ratio fulfils the characteristics of a living polymerization (Figure 4). A dispersity of the resulting polymers lower than 1.5 further confirmed the living character. Moreover, the HG2:CTA ratio shows the advantages of catalytic living ROMP in that the same molecular weight polymers can be synthesized using as much as 100 times less catalyst than used in the traditional living ROMP (Figure 4). The polymer structures were verified using MALDI-ToF mass spectrometry and NMR spectroscopy. They match the assumed structures with cyclopropyl and cyclopentenyl end groups (see supporting information).

Different types of monomers such as exo-N-phenyl norbornene imide (PNI), exo-N-methyl oxanorbornene imide (OMNI), endo-5-norbornene-2,3-bis(trisopropyl)silylmethanol (NBSM) and exo-N-methyl-7-oxabicyclo[2.2.1]hept-4-yl-5-ene-2,3-dicarboximide (MOMNI) were explored in catalytic living ROMP using the HG2 catalyst (see supporting information). Similar results were obtained for MNI and PNI. Larger dispersities were observed when OMNI, NBSM and MOMNI were applied in catalytic living ROMP with HG2. Even 10 equiv of 3-chloropyridine added to the reaction solution did not improve the dispersities. This can result from the coordination of oxygen in these functional monomers with the ruthenium in the HG2 complex resulting in a slowing down of the chain-transfer rate while also slowing down the propagation rate \(^{24,31}\).

In support of this assumption, we observed a coordinated carbene peak in the \(^1\)H NMR reaction between HG2 and MOMNI (see supporting information, Figure S1). However, the MALDI-ToF mass spectrum confirmed that all polymers had the expected end groups and repeat units (see supporting information, Polymer 8-12). It is worth mentioning that when the bulky and slowly propagating MOMNI was used as the monomer, the polymerization could be carried out in one pot rather than by slow addition using a syringe pump \(^{17}\).

Block copolymers are very important owing to their ability to self-assemble in solution and in the solid state \(^{32}\). At the same time, they are also important structures to prove the living character of a polymerization technique. Linear ABC tri-block copolymers are more challenging to synthesize than diblock copolymers and show more complex solution and solid state structures \(^{31}\). Therefore, we explored the ability of HG2 in catalytic living ROMP to synthesize ABC tri-block copolymers. MNI, OMNI and PNI were added to the HG2:CTA (1:10) reaction solution sequentially. The GPC (chloroform) traces showed a monomodal molecular weight distribution and shift in molecular weight after each monomer addition which supported the formation of an ABC tri-block copolymer polyMNI-b-polyOMNI-b-polyPNI (Polymer 13, Figure 5). These results further proved the living character of the polymerization technique using HG2. Moreover, AB di-block copolymers were also synthesized by catalytic living ROMP with HG2 using a macro-CTA...
which is synthesized by catalytic living ROMP with the HG2 catalyst. PolyMNI was first prepared by adding MNI to an HG2/CTA solution (HG2:CTA:MNI = 1:10:300) with a syringe pump at a speed of 0.83 ml/h. After precipitation, evaporation and analysis, polyMNI was used as macromolecular chain transfer agent for catalytic living ROMP of PNI and HG2 to produce polyMNI-b-polyPNI (Polymer14). The shift of the monomodal GPC traces from polyMNI (Mn_gpc (chloroform) = 7300 g mol⁻¹, Đ = 1.33) to polyMNI-b-polyPNI (Mn_gpc (chloroform) = 21000 g mol⁻¹, Đ = 1.45) confirmed the synthesis of an AB di-block copolymer (See supporting information Figure S61).

Mono-end functional and telechelic polymers are important and industrially relevant materials. To expand the applications of catalytic living ROMP, we investigated the possibility to synthesize telechelic polymers by catalytic living ROMP using HG2. We therefore polymerized MNI/CTA/HG2 (300:10:1) in DCM by adding MNI into CTA/HG2 mixture solution slowly. After all monomer had been consumed we added an excess (30 equiv with respect to CTA) of symmetrical cis-oct-4-ene to the reaction solution expecting a terminal cross-metathesis reaction with the cyclopentenyl end groups of polymer chains. To our surprise, no butenyl end-functionalized polymer could be detected in MALDI-ToF mass analysis. The only signal that was detected was the unreacted cyclopentenyl end-functionalized polymer. We assumed that the high dilution conditions of catalytic living ROMP were responsible for the low reactivity of the terminal cross metathesis reaction. In a second experiment, after addition of excess amounts of symmetrical cis-oct-4-ene, the reaction mixture was concentrated by evaporating the solvent and stirring overnight. After precipitation, the MALDI-ToF mass spectra and NMR analysis confirmed the successful exchange of the cyclopentenyl end group into a butenyl end-functionalized polymer (see supporting information Polymer 15).

Subsequently, t-butyl-protected trans-hex-3-enedioic acid, triisopropylsilyl (TIPS-) protected trans-hex-3-ene-1,6-diol and tertiobutyloxycarbonyl (Boc-) protected amine were used as functional symmetrical chain-transfer agents (SCTA) to synthesize carboxylic acid-, hydroxyl- and amino-functionalized mono-telechelic polymers via catalytic living ROMP. The matched MALDI-ToF mass and NMR spectra demonstrated that the carboxylic acid-, hydroxyl- and amino-functionalized mono-telechelic polymers were synthesized successfully by catalytic living ROMP with HG2 (see supporting information Polymer 16-18). These results also proved that not only the cis- symmetrical chain-transfer agents can be used in the cross metathesis of polymer end-groups, but also the trans- configuration. Moreover, these results once more confirmed that the polymer end groups remain reactive towards either propagation or cross metathesis reactions.

Conclusions
In conclusion, the user-friendly, stable and highly active second-generation Hoveyda-Grubbs (HG2) catalyst can be employed in catalytic living ROMP. The molecular weight can be controlled by changing the monomer:CTA ratio. Different substituted norbornene derivatives can be employed in this method. AB di-block copolymers and ABC tri-block copolymers can be synthesized using catalytic living ROMP either using a macromolecular-CTA or adding different monomers sequentially. Different end-group-functionalized mono-telechelic polymers are also accessible via a terminal cross metathesis reaction. These results will further expand the applications of catalytic living ROMP as a method for low cost polymers with low amounts of metal impurities. This can be particularly attractive for applications where low toxicity levels need to be achieved such as for biomedical functional polymeric materials.

Conflicts of interest
There are no conflicts to declare.

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Notes and references

4 K. Nomura, M. M. Abdellatif, Precise synthesis of polymers containing functional end groups by living ring-opening metathesis
polymerization (ROMP); efficient tools for synthesis of block/graft copolymers. Polymer 2010, 51, 1861.
Mono-telechelic polymers and triblock copolymers were synthesized by catalytic living ROMP with unstabilized 14e $^{14}$HG2 catalyst.