JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
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Multiple Olefin Metathesis Polymerization That Combines All Three Olefin Metathesis Transformations: Ring-Opening, Ring-Closing, and Cross Metathesis

Ho-Keun Lee,[†] Ki-Taek Bang,[†] Andreas Hess,[†] Robert H. Grubbs,[‡] and Tae-Lim Choi*,[†]

[†]Department of Chemistry, Seoul National University, Seoul 151-747, Korea
[‡]Department of Chemistry, California Institute of Technology, Pasadena, California 91125, United States

Ⓢ *Supporting Information*

ABSTRACT: We demonstrated tandem ring-opening/ring-closing metathesis (RO/RCM) polymerization of monomers containing two cyclopentene moieties and postmodification via insertion polymerization. In this system, well-defined polymers were efficiently formed by tandem cascade RO/RCM reaction pathway. Furthermore, these polymers could be transformed to new A,B-alternating copolymers via a sequential cross metathesis reaction with a diacrylate. Additionally, we demonstrated the concept of multiple olefin metathesis polymerization in which the dicyclopentene and diacrylate monomers underwent all three olefin metathesis transformations (ring-opening, ring-closing, and cross metathesis) in one shot to produce A,B-alternating copolymer.

During the last two decades, the olefin metathesis reaction has been widely used as an efficient method to synthesize various molecules by forming new carbon−carbon double bonds.[1] Olefin metathesis transformation can be carried out by three main types metathesis: ring-opening metathesis (ROM), ring-closing metathesis (RCM), and cross metathesis (CM); these metathesis have become versatile tools in organic synthesis. Furthermore, the olefin metathesis reaction has been applied to various polymerizations such as ring-opening metathesis polymerization (ROMP),[2] cyclopolymerization[3] derived from RCM, and acyclic diene metathesis (ADMET) polymerization[4] derived from CM. These polymerizations have produced various polymers, including both conjugated and nonconjugated polymers, and in some cases, living polymerization is also possible.[3f,h,j,5,6]

The utility of the olefin metathesis reaction was further broadened when organic chemists discovered tandem olefin metathesis reactions in which two or more olefin metathesis transformations occur simultaneously in a single step. This cascade reaction allowed chemists to efficiently synthesize various complex organic molecules.[7] Various examples of natural product total synthesis using this cascade reaction method as a key strategy for the formation of the core skeletons have been reported, demonstrating the versatility of these tandem olefin metathesis reactions.[8]

Similar methods could be introduced to polymer synthesis, but combining two or more transformations tends to produce ill-defined polymers with a random microstructure due to the lack of control. As a result, almost all polymers prepared by olefin metathesis polymerization have been produced by a single type of olefin metathesis transformation, yielding polymers with simple repeat units.[2−4]

Over the past decade, a handful of examples have been reported detailing successful polymerizations produced by two different olefin metathesis transformations. The first example was the ring-opening insertion metathesis polymerization (ROIMP), a general method for synthesizing A,B-alternating copolymers by combining ROMP and highly selective CM in a one-pot synthesis.[9] Another example was the two-pot polymerization using ROMP and ADMET, wherein two metathesis reactions sequentially occurred (first ROMP and then ADMET) and produced branched polymers in an independent manner.[10] The most recent result was a simultaneous tandem ring-opening/ring-closing metathesis (RO/RCM) polymerization, reported by our group. This polymerization of monomers containing cycloalkenes and terminal alkynes proceeded via a relay-type mechanism in a living manner.[6] These attempts increased the complexity in the polymer microstructures accessible via olefin metathesis polymerization.

In our search to broaden the overall scope of polymerization, herein, we report a new tandem olefin metathesis polymerization methodology via a cascade RO/RCM polymerization of monomers containing two cyclopentenes.[5] The concept of multiple olefin metathesis polymerization (MOMP) entails combining a CM reaction to produce A,B-alternating copolymers in either two-step or one-shot methods. This is the first example of polymerization in which the combination of all three olefin metathesis transformations produced well-defined polymers via precise reaction pathways.

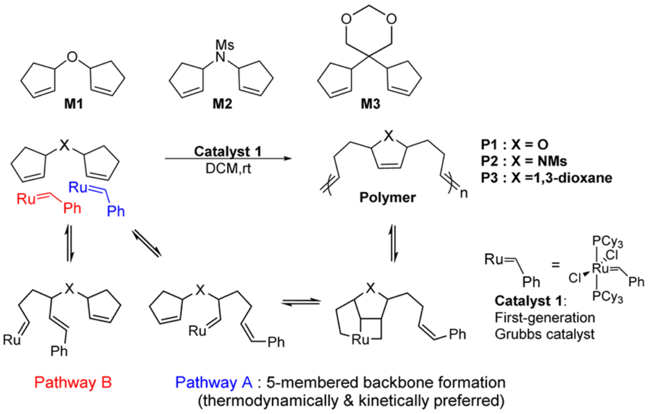
To achieve tandem RO/RCM polymerization, we designed novel monomers containing cyclopentene moieties, because monomers should be able to undergo both ring-opening and ring-closing metathesis reactions simultaneously. Consequently, we synthesized three monomers **M1−3**; in each, two cyclopentene moieties were connected by oxygen, nitrogen, or carbon linkers, respectively (Scheme 1a).

However, two issues need to be first overcome in order to achieve selective tandem RO/RCM polymerization from these new monomers containing two polymerizable cyclopentene moieties. The first issue was to determine whether these

Received: June 10, 2015
Published: July 17, 2015

DOI: 10.1021/jacs.5b06033
J. Am. Chem. Soc. 2015, 137, 9262−9265

Scheme 1. (a) Structure of the Dicyclopentene Monomers and (b) Reaction Scheme of the Tandem RO/RCM Polymerization and Proposed Polymerization Pathway for the Selective Formation of Five-Membered Ring Repeat Units



monomers having 3-substituted cyclopentene moieties would polymerize at all. The Grubbs group reported that the ROMP of 3-substituted cyclopentene derivatives always failed,[11] because the substituent at the 3-position increased the steric hindrance and decreased the ring strain, thereby preventing the ROMP. The second issue was to determine how to control the competing ROM and RCM equilibrium of the cyclopentene moieties in the monomer so that the desired, structurally well-defined polymers would be produced selectively (Scheme 1b). For example, if the ROMP became dominant, a cross-linked gel was produced. Even if the cascade RO/RCM reaction did occur, there were two possible pathways depending on the orientation of the approached catalyst. Only Pathway A was a productive pathway for the tandem polymerization, because the second RCM step was favored due to the proximity effect. On the other hand, in Pathway B, a new carbene underwent RCM back to the monomer (Scheme 1b). Thus, optimizing the polymerization condition to control the competing equilibrium between ROM and RCM was the key to the successful tandem polymerization.

Initially, to search for the most suitable catalyst, we screened various catalysts for the tandem RO/RCM polymerization of **M1**. Generally, a first-generation Grubbs catalyst (**Catalyst 1**) has lower activity than that of second- or third-generation Grubbs catalysts. In our system, however, **Catalyst 1** showed the best performance when comparing the monomer consumptions via ^{1}H NMR (Figure S1). Next, we screened the reaction concentration to determine the effect on the polymerization. At 0.1 M, **M1** with a monomer:catalyst ratio (M:C) of 50:1 was successfully polymerized into poly(2,5-disubstituted-2,5-dihydrofuran) with 87% conversion after 24 h. To shorten the reaction time, we increased the concentration up to 1 M, but an insoluble cross-linked gel formed within 10 min, meaning that the concentration reached its critical concentration at which the ROMP of the cyclopentene moiety became dominant. This finding was somewhat expected because the critical monomer concentration for the ROMP of the cyclopentene is 0.8 M at 25 °C.[12] On the other hand, at 0.5 M, full conversion was obtained after 12 h without any cross-linking, and simple precipitation in methanol produced a rubbery polymer with moderate yields. When decreasing the catalyst loading or increasing the M:C ratio to 150:1 and even 250:1, we achieved quantitative conversion under optimized conditions, producing **P1** with M_n of 13.8−52.3 kDa in proportion to the M:C ratio (Table 1, entries 1−3).

Table 1. Tandem RO/RCM Polymerizations of M1−3

entry	monomer	M:C	conc. (M)	time (h)	M_n[a] (k)	PDI[a]	conv[b] (%)
1	M1	50:1	0.5	12	13.8	1.79	100
2	M1	150:1	0.5	12	38.0	1.91	100
3	M1	250:1	0.5	12	52.3	1.83	100
4	M2	50:1	1.5	24	25.9	1.53	100
5	M2	150:1	1.5	24	66.2	1.91	97
6	M2	250:1	1.5	48	114.5	2.14	98
7	M3	50:1	1.5	24	29.9	1.48	100
8	M3	150:1	1.5	48	62.9	1.70	97
9	M3	250:1	1.5	48	114.4	1.90	95

[a]Determined by THF SEC calibrated using polystyrene standards. [b]Conversion was determined by crude ^{1}H NMR analysis

The structure of purified **P1** was characterized with NMR (Figure 1, Figure S2), which clearly confirmed the formation of a low ring-strained, five-membered, 2,5-dihydrofuran backbone. Also, an internal olefin with an *E*:*Z* ratio of 5:1 for the acyclic olefin was observed. Interestingly, **M1** was polymerized at concentrations <0.1 M despite possessing the low-strained cyclopentene and the substitution at the 3-position. This finding was in sharp contrast to the case of cyclopentene, which was seemingly a more reactive monomer but did not undergo ROMP at concentrations <0.8 M.[12] Instead, at concentrations below the critical monomer concentration for the ROMP, the cascade RO/RCM occurred to produce the polymer with a rearranged backbone with the 2,5-dihydrofuran moiety, implying that the 2,5-dihydrofuran backbone moiety in **P1** was thermodynamically more stable than the cyclopentene in the monomer. Also, due to the substitutions at the 2- and 5-positions on dihydrofuran, the reverse reaction or depolymerizion would be slower than chain propagation.

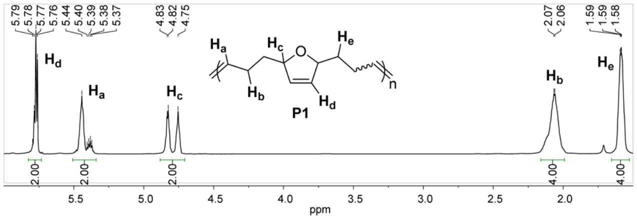
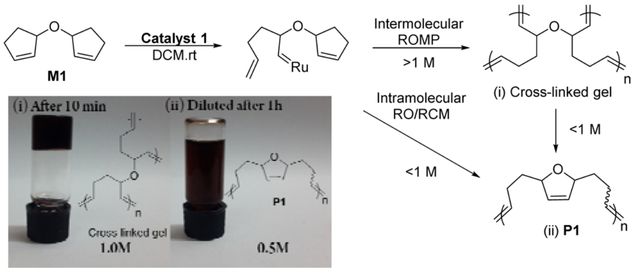


Figure 1. ^{1}H NMR spectrum of **P1**.

To broaden the monomer scope, we investigated the tandem polymerization of **M2** and **M3** in which two cyclopentenes were connected by nitrogen and carbon, respectively. Unlike **M1**, the analogous polymerizations of **M2** and **M3** at 0.5 M did not achieve full conversions, but qualitative tandem polymerization without any cross-linking occurred when the concentration increased to 1.5 M. It seems that the ring-strain and the competing equilibrium between ROM and RCM for **M2** and **M3** were slightly different than those for **M1**. Regardless, both monomers efficiently underwent the tandem polymerization even with low catalyst loading with M:C ratios of 250:1, and the M_n value of the resulting **P2** and **P3** were roughly controlled and proportional to the M/C ratios (Table 1, entries 4−9), and structures of purified **P2** and **P3** were also characterized by NMR (Figures S3, S4, S9, and S10) However, in all three cases, the polydispersity index (PDI) values were broad due to chain-transfer reactions.

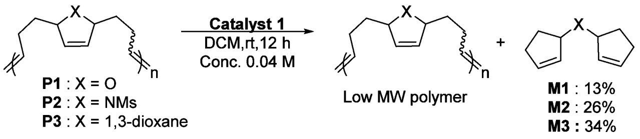
As we previously observed, the polymerization of **M1** at concentrations over that of the critical monomer concentration produced cross-linked gel due to the dominant intermolecular ROMP process. However, by diluting the solution containing this cross-linked gel to 0.5 M, the gel completely disappeared after 6 h, mainly yielding a soluble polymer containing the same dihydrofuran backbone. This result was obtained because the dilution led to the reversible decross-linking via the intramolecular RO/RCM process to produce **P1** (Scheme 2).

Scheme 2. Concentration-Dependent Polymerization



Since the entire polymerization was in thermodynamic equilibrium, the isolated polymers could also be depolymerized to the corresponding monomers via the reverse tandem intramolecular RO/RCM process. Each purified **P1−3** was redissolved into a 0.04 M CH_2Cl_2 solution, and fresh **Catalyst 1** was added. After 12 h, 13% of **M1**, 26% of **M2**, and 34% of **M3** were observed with ^{1}H NMR, implying that even depolymerization indeed occurred in dilute conditions (Scheme 3). These results demonstrated that by understanding the equilibrium, the direction of the ROMP or RO/RCM processes could be predicted depending on the concentration.

Scheme 3. Depolymerization of P1−3



To broaden the utility of this tandem polymerization, we experimented to determine if the resulting polymers could undergo postmodification with a second-generation Grubbs catalyst. If the coupling between internal olefins on **P1−3** and *α,β*-unsaturated carbonyl olefins on diacrylate monomers proceeded with high conversion and high selectivity, as in the case of CM,[13] the diacrylates could be selectively inserted into the polymers to yield A,B-alternating copolymer containing *α,β*-unsaturated carbonyl olefins. To test this idea, the purified polymers (**P1−3**) were treated with 1,4-butandiol-diacrylate and **Catalyst 2** under optimized conditions (Scheme 4).

After the backbiting of the catalyst into the acyclic olefins on the polymers, a series of exclusive CMs occurred selectively with the diacrylate,[13] and this process converted **P1−3** into thermodynamically more stable **P4−6**, respectively, containing *α,β*-unsaturated carbonyl olefin with moderate molecular weights (Table 2).

Scheme 4. MOMP Reactions with P1−3

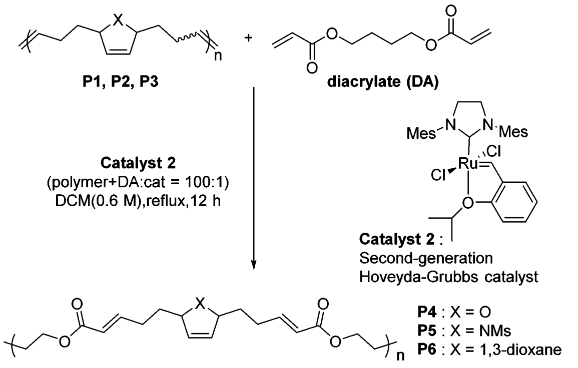


Table 2. Analysis of MOMP Products

polymer	A,B-alt. (%)[a]	M_n[b] (k)	M_w[b] (k)	PDI[b]
P4	97.5	10.6	22.0	2.09
P5	94.3	7.3	13.5	1.82
P6	94.2	16.4	30.7	1.87
P4′	95.5	9.3	19.8	2.11

[a] Determined by ^{1}H NMR spectroscopic analysis. [b] Determined by THF SEC calibrated using polystyrene standards.

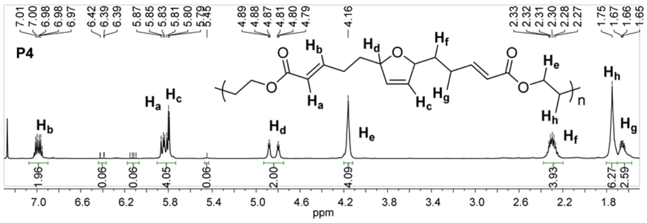


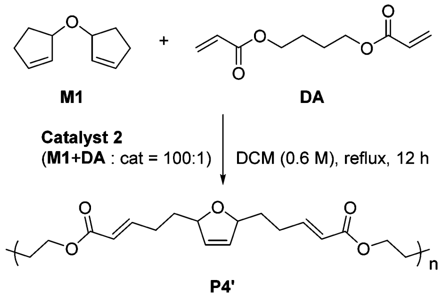
Figure 2. ^{1}H NMR spectrum of **P4**.

The structural features of these well-defined A,B-alternating copolymers (**P4−6**) were explicitly confirmed with ^{1}H NMR analysis (Figure 2 and Figures S11 and S12). First, the internal olefins near 5.5 ppm on P1 disappeared (Figure 1, **P1 H$_a$**), and new peaks corresponding to the *α,β*-unsaturated carbonyl olefins appeared at 7.0 and 5.8 ppm (Figure 2, **P4 H$_a$** and **H$_b$**, respectively). In particular, the newly formed olefin was 100% *E* isomer with a coupling constant of 16 Hz (Figure S13−1). Furthermore, the signal from the cyclic olefin (Figure1, **P1 H$_d$**) still remained at 5.8 ppm (Figure 2, **P4 H$_c$**). A,B-alternations of the polymers were calculated by comparing the ratio of newly formed *α,β*-carbonyl olefins and the remaining internal olefins on the original homopolymers; in all cases, significant alternations were observed (97.5% for **P4**, 94.3% for **P5**, and 94.2% for **P6**, Table 2). These structural analyses demonstrated the successful preparation of well-defined A,B-alternating copolymers via the sequential CM reaction.

We expected that it would also be possible to obtain the identical A,B-alternating copolymer via the one-shot polymerization method instead of the two-step sequential method described above. **M1** with the diacrylate was polymerized with **Catalyst 2** under the same conditions as those of the previous sequential method (Scheme 5). After 12 h of polymerization, the identical A,B-alternating copolymer **P4′** was obtained and confirmed with ^{1}H NMR (Table 2, Figure S13−2). This result provides the first example of MOMP, wherein all three types of olefin metathesis transformations (ring-opening, ring-closing, and cross metathesis) were combined in an orderly manner to produce just one uniform polymer microstructure via precisely controlled pathways.

In conclusion, we investigated the tandem RO/RCM polymerization of monomers containing two polymerizable

Scheme 5. MOMP via a One-Shot Method



cyclopentene moieties with a first-generation Grubbs catalyst. This tandem RO/RCM polymerization was carried out efficiently without side reactions such as cross-linking or depolymerization, because with the appropriate concentration, the precisely controlled cascade reaction occurred exclusively to produce a well-defined polymer microstructure. Furthermore, these resulting polymers successfully transformed to new A,B-alternating copolymers by insertion polymerization via sequential cross metathesis with a diacrylate using a second-generation Hoveyda−Grubbs catalyst. Finally, the one-shot polymerization of **M1** and diacrylate successfully produced the identical A,B-alternating copolymer. This report covers the first example of multiple olefin metathesis polymerization in which all three types of olefin metathesis transformations were used simultaneously with precise control to yield well-defined polymers.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, NMR data for polymers, and SEC traces for polymers. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b06033.

■ AUTHOR INFORMATION

Corresponding Author

*tlc@snu.ac.kr

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Authors dedicate this paper to Prof. Kwan Kim on his lifelong achievements in research and education at SNU and his retirement. We are grateful for financial support from Basic Science Research and Nano-Material Technology Development through NRF of Korea.

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