Fast Tandem Ring-Opening/Ring-Closing Metathesis Polymerization from a Monomer Containing Cyclohexene and Terminal Alkyne

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Ⓢ *Supporting Information*

ABSTRACT: We report extremely fast tandem ring-opening/ring-closing metathesis polymerization of a monomer containing two rather unreactive functional groups: cyclohexene and a terminal alkyne. When a third-generation Grubbs catalyst was used at low temperature, this tandem polymerization produced polymers with controlled molecular weights and narrow polydispersity indices. To explain this extremely fast polymerization, its reaction mechanism was studied. This new type of controlled polymerization allowed for the preparation of block copolymers using other conventional living metathesis polymerizations. The diene on the backbone of the polymer was postfunctionalized by sequential Diels−Alder and aza-Diels−Alder reactions, which led to selective functionalization depending on the stereochemistry of the diene.

Figure 1. Monomers with low metathesis polymerization activities.

(a) Equilibrium between ROM and RCM

(b) Propagating carbene is sterically too hindered for polymerization

During the last two decades, the synthesis community has witnessed the power of olefin metathesis reactions, which provide a versatile means for preparing both small and large molecules. Various olefin metathesis polymerization methods, such as ring-opening metathesis polymerization (ROMP),[1] acyclic diene metathesis (ADMET) polymerization,[2] and cyclopolymerization,[3] have been widely used to synthesize both conjugated and nonconjugated polymers. For each polymerization process, a different strategy is adopted to achieve efficient polymerization. For example, ROMP proceeds because of the enthalpic gain resulting from the relief of ring strain in the monomers. Therefore, highly strained cycloalkenes such as norbornene and cyclooctadiene are frequently used as monomers. ADMET takes advantage of the entropic gain afforded by removal of ethylene gas to shift the equilibrium toward polymerization. Lastly, the driving force for cyclopolymerization is provided by the irreversible generation of stable conjugated polyenes from monomers containing diyne functional groups. In short, these polymerizations become efficient when the thermodynamics of the reactions favor polymerization over depolymerization. On the other hand, monomers without a thermodynamic driving force hardly undergo polymerization. For example, cyclohexene, a monomer with almost no ring strain, hardly undergoes ROMP because the monomeric state is favored at equilibrium (Figure 1a).[4] Furthermore, cyclopentenes with substitution at the 3- or 4-position show much lower ROMP activities than unsubstituted cyclopentene because substitution lowers the ring strain.[5] Other challenging monomers are terminal alkynes, which produce
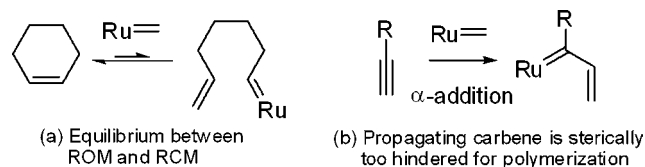
substituted polyacetylenes with low molecular weights in low yields.[6] Although enthalpic gains are expected to result from the formation of conjugated olefins from alkynes, propagating carbene complexes are not reactive enough to undergo polymerization, especially when ruthenium catalysts are used.[7] This is because a 1,1-disubstituted alkylidene is generated as an intermediate carbene complex via α-addition of the ruthenium catalyst, and the resulting bulky propagating carbene complex hinders polymerization (Figure 1b). Therefore, the polymerization of monomers with cyclohexene or alkyne functional groups remains challenging.

In the field of organic chemistry, various complex molecules have been synthesized by the tandem olefin metathesis reaction, which is an efficient method for preparing multiple rings in a single step.[8] Many natural product syntheses have been carried out by adopting this method as a key strategy for constructing their core skeletons.[9] Furthermore, the tandem-relay metathesis reaction has been used to promote ring rearrangement reactions via enyne ring-opening metathesis (ROM) and ring-closing metathesis (RCM) processes.[10] The lessons from the organic chemistry community have given new insights into the preparation of polymers with new structures and functions; otherwise, only polymers with simple microstructures would be expected from conventional metathesis polymerization. For example, tandem metathesis polymerization using ROM and cross-metathesis (CM) reactions, wherein the two metathesis reactions occur sequentially (first ROM, then CM) and independently of each other, provides a synthetic route for producing A,B-alternating copolymers and branched polymers.[11] Inspired by these continuous tandem-relay reactions, we envisioned that a unique polymerization, a simultaneous relay-type tandem RO/RCM (ring-opening/ring-closing metathesis) sequence, might produce polymers with novel structures. Herein we report for the first time the highly efficient and controlled tandem-relay polymerization of a monomer containing two ironically unreactive functional groups, cyclohexenyl and alkynyl, by using the third-generation
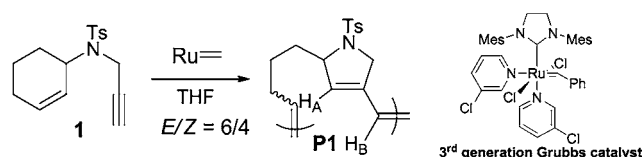
Grubbs catalyst, and we demonstrate the application of this polymerization in the preparation of new polymers with various architectures.

Monomer **1** was tested for the RO/RCM tandem polymerization even though it appeared to be a poor monomer for two reasons. First, **1** contains a cyclohexenyl moiety with not just very low ring strain but also a substitution at the 3-position, making it sterically and thermodynamically unsuitable for polymerization.[5b] Second, **1** contains a terminal alkyne, which itself is resistant to polymerization. Ironically, we observed facile metathesis polymerization by the fusion of these two functional groups with unlikely reactivity. After optimization, we found that the third-generation Grubbs catalyst[12] polymerized 100 equiv of **1** in tetrahydrofuran (THF) with complete conversion in just 1 min at room temperature (Table 1, entry 1). This superb reactivity is comparable to that of

Table 1. Tandem Metathesis Polymerization of 1

entry	M/I	temp.	time (min)	M_n (g/mol)^a	PDI^a	conv (%)^b
1	100	r.t.	1	26000	1.86	100
2	100	−10 °C	2	31000	1.18	100
3	100	−30 °C	10	31000	1.18	100
4	30	−30 °C	3	8000	1.17	100
5	50	−30 °C	5	18000	1.18	100
6	150	−30 °C	20	41000	1.21	90

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

ROMP of norbornene, the most reactive monomer for metathesis polymerization.[13] The resulting polymer (**P1**) had a number-average molecular weight (M_n) of 26 000 g/mol with a polydispersity index (PDI) of 1.86. We then focused on narrowing the PDI for possible controlled/living polymerization. We reasoned that the broad PDI could not be attributed to the slow initiation of the catalyst[12] but rather had to result from an undesired chain-transfer reaction. This was a reasonable analysis since this ultrafast initiating catalyst should be reactive enough to undergo chain-transfer reactions with the resulting dienes at room temperature, which would broaden the PDI. Thus, to suppress the chain-transfer reaction, the reaction temperature was lowered to −10 °C, which reduced the PDI to 1.18 with completion of polymerization in just 2 min. To ensure controlled polymerization with a monomer-to-initiator ratio (M/I) greater than 100, the reaction temperature was further lowered to −30 °C. Regardless of the choice of catalyst, solvent, or temperature, an E/Z ratio of 6:4 for the newly formed olefins on the polymer backbone remained unchanged. This ratio was easily determined by crude ^{1}H NMR analysis because each peak corresponding to the E and Z isomers for olefinic H_A and H_B (with the correct coupling constants of 16 and 8 Hz for the E and Z isomers) was clearly resolved, allowing for reliable integration [see the Supporting Information (SI) for details].

Polymers having various molecular weights were synthesized by varying the M/I, and controlled polymerization with a degree of polymerization (DP) ranging from 30 to 135 was

achieved (Table 1, entries 3−6), resulting in a linear increase in the molecular weight (Figure 2). In addition, the PDI was controlled to be less than or equal to 1.2.[14]
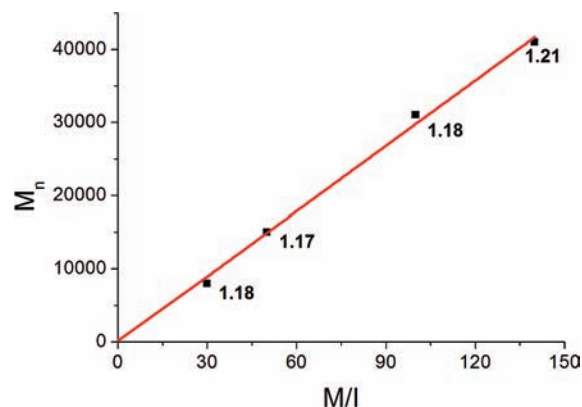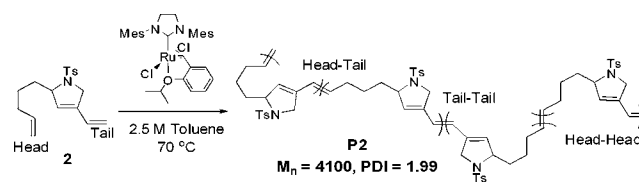

Figure 2. Plot of M_n vs M/I for **P1**. Numbers on the line indicate PDI values.

To elucidate the mechanism of tandem metathesis polymerization, the synthesis of **P1** by ADMET polymerization was attempted for comparison (Scheme 1). Monomer **2**, a product
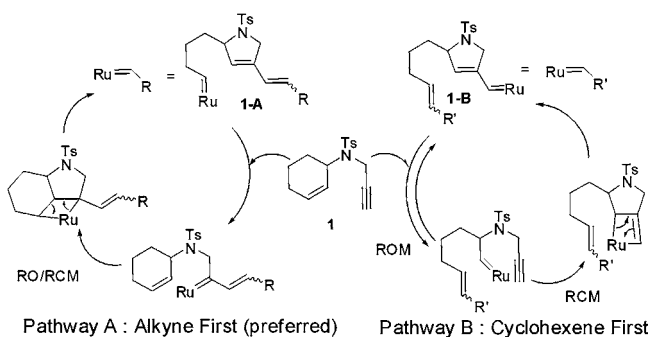
Scheme 1. ADMET Polymerization of Monomer 2

of the ring rearrangement reaction of **1** with ethylene gas, was subjected to ADMET polymerization, which yielded **P2** with low molecular weight (M_n = 4100 g/mol, PDI = 1.99) in 83% yield. In this process, new alkene signals that were not present in **P1** were observed by ^{1}H NMR analysis. These signals could be attributed to a regiorandom cross-coupling reaction occurring in this process (see the SI for details). As the catalyst reacted with two different terminal alkenes with low selectivity, ADMET polymerization gave all of the possible mixtures of head-to-head, head-to-tail, and tail-to-tail junctions, whereas only the regioregular head-to-tail junction was observed for **P1**. In addition, only *trans*-alkenes were obtained by ADMET polymerization because this polymerization, which is essentially the repetition of the CM reaction, produced thermodynamically more stable *trans*-olefins, while the regioregular polymer obtained by the kinetically controlled process contained olefins with an E/Z ratio of 6:4. Lastly, when the regioregular polymer was treated with the catalyst at a high temperature (70 °C) for 4 h, ∼30% of the head-to-tail olefin junction was transformed into the regiorandom structure by a secondary metathesis reaction on the regioregular polymer. These observations indicated that regioregular **P1** resulting from tandem polymerization was formed by a single kinetically controlled reaction pathway.

On the basis of the above conclusion, two possible mechanisms were proposed for tandem polymerization: "alkyne-first" and "cyclohexene-first" mechanisms (Scheme 2). In the alkyne-first mechanism, the catalyst would react with the terminal alkyne, after which the RO/RCM reaction involving

Scheme 2. Possible Mechanisms for Tandem Metathesis Polymerization

Pathway A : Alkyne First (preferred)   Pathway B : Cyclohexene First

Scheme 3. Block Copolymerization via Tandem Polymerization by (a) ROMP or (b) Cyclopolymerization

the adjacent cyclohexene would occur, generating the propagating carbene complex **1-A** (pathway A). In the cyclohexene-first mechanism, the catalyst would open the cyclohexene ring, and this ring opening would be followed by the enyne RCM reaction involving the adjacent terminal alkyne, generating **1-B** as a propagating carbene complex (pathway B). On the basis of the three reasons that supported fast polymerization, pathway A would be more plausible. First, the terminal alkyne is kinetically more accessible than the 3-substituted cyclohexene containing a hindered disubstituted olefin. Second, a recent report suggested that the Grubbs catalyst with an N-heterocyclic carbene ligand reacts more favorably with alkynes than with alkenes.[15] Finally, initial reaction of the catalyst with the alkyne would irreversibly form a diene, while the initial ring-opening of the cyclohexene through pathway B would be in equilibrium with the reverse RCM reaction, which would slow the polymerization. With this information, we could further explain why monomer **1** showed ultrafast tandem metathesis polymerization despite having two rather unreactive functional groups. First, the generation of **1-A** would be fast because of the facile α-insertion of the catalyst into the terminal alkyne and the facile RO/RCM reaction involving the proximal cyclohexene. Second, the transformation to **1-A** is thermodynamically driven by the formation of a stable conjugated diene and a pyrrolidine moiety with low ring strain. Furthermore, the resulting pyrrolidine contains a sterically hindered trisubstituted olefin, leaving no possibility for a reverse reaction.[16] After all, **1-A** containing a sterically unhindered carbene complex would propagate readily and irreversibly, resulting only in productive metathesis polymerization. Therefore, even in the absence of a large driving force such as the relief of ring strain in norbornene, this unidirectional tandem polymerization can occur rapidly, as in the case of ROMP.

Since the tandem metathesis polymerization promotes living polymerization, block copolymers can also be prepared by this method. To demonstrate this, we combined tandem metathesis polymerization with conventional living ROMP and cyclopolymerization (Scheme 3). First, a diblock copolymer was prepared using **1** as the first block and ROMP monomer **3** as the second block. The diblock copolymer structure was confirmed by the total shift of the size-exclusion chromatography (SEC) trace from the first block of **1** (M_n = 12 kg/mol, PDI = 1.25) to a high molecular weight while retaining the narrow PDI (M_n = 35 kg/mol, PDI = 1.18). Similarly, another diblock copolymer, in which the second block was prepared by the cyclopolymerization of **4** at −10 °C, was successfully
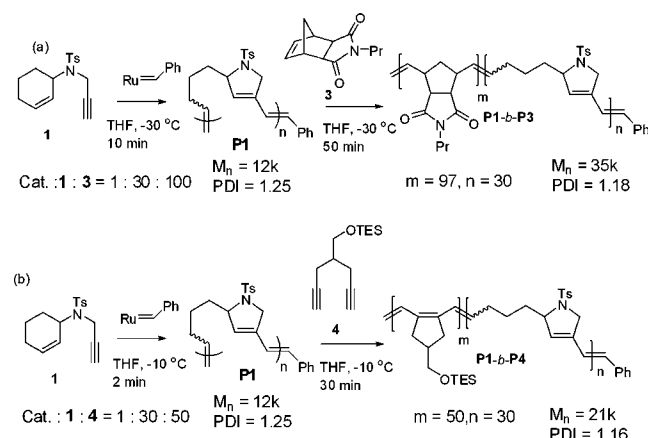
synthesized and characterized by SEC analysis (M_n = 21 kg/mol, PDI = 1.16; see Figure S1 in the SI).

Another unique feature of tandem metathesis polymerization is the generation of a 1,3-diene moiety in the polymer backbone. **P1** could be further functionalized by the Diels−Alder reaction.[17] In an initial attempt at such postmodification, we observed that different diene stereoisomers (E/Z = 6:4) showed vastly different reactivities toward the dienophile tetracyanoethylene (**5**) (Scheme 4). The diene containing the

Scheme 4. Diels−Alder and aza-Diels−Alder Reactions of P1[a]
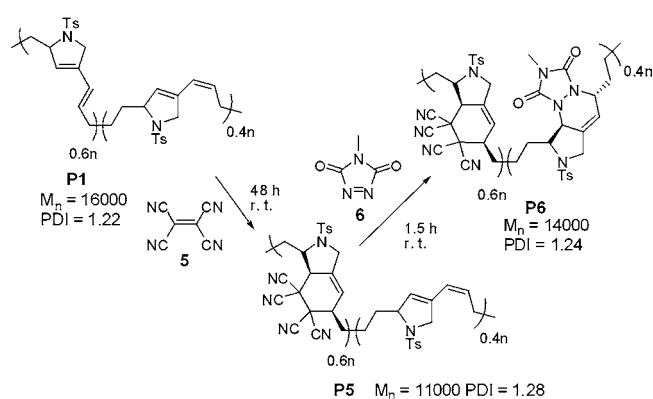
[a]Because of the low solubility, the PDI and M_n were determined by CHCl₃ SEC calibrated with polystyrene standards.

trans-alkene was fully consumed in the cycloaddition reaction after 48 h at room temperature, but the diene containing the *cis*-alkene did not react at all with **5**. This reduced activity was the result of steric hindrance for the Diels−Alder reaction due to the cis isomer; moreover, this reactivity did not change even at higher temperatures (up to 100 °C). However, a more reactive dienophile, 4-methyl-1,2,4-triazole-3,5-dione (**6**), underwent a facile aza-Diels−Alder reaction[18] with the remaining cis isomers in **P5**, resulting in the quantitative conversion of all of the dienes in **P1**. In both cases of postmodification, the narrow PDIs of the polymers **P5** and **P6** were maintained (see Figure S2), implying that the integrity of the original polymer was preserved.[19]

In conclusion, a monomer containing cyclohexene and a terminal alkyne was rapidly polymerized by a relay-type tandem

RO/RCM reaction. This reaction showed a high polymerization rate that was counterintuitive for these unreactive functional groups, but their combination showed a very intriguing synergistic effect that facilitated polymerization. This tandem polymerization could even proceed in a controlled manner to enable the synthesis of diblock copolymers in conjunction with other metathesis polymerizations, such as ROMP and cyclopolymerization. The resulting polymer was successfully modified further via cycloaddition reactions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, NMR data for polymers, and SEC traces for polymers. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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