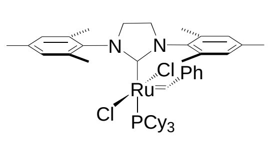
Synthesis of A,B-Alternating Copolymers by Ring-Opening-Insertion-Metathesis Polymerization**

Tae-Lim Choi, Isaac M. Rutenberg, and Robert H. Grubbs*

Alternating copolymers are normally formed by step growth polymerization of AA–BB monomers and in some special chain-growth reactions.[1] Although recent developments in ring-opening-metathesis polymerization (ROMP)[2] and acyclic-diene-metathesis polymerization (ADMET)[3] have extended the versatility of both chain-growth and step-growth reactions, these metathesis polymerization reactions have not provided a general solution to alternating copolymerization. Examples of alternating copolymers by ROMP are rare as a result of the difficulty of finding systems in which there is an alternation in the affinity of the propagating metal carbene for the monomers.[4] Although ADMET is a step-growth polymerization, examples of alternating copolymerization with two monomers by this mechanism have not been reported since most olefins studied have similar reactivity. Therefore, a general metathesis route toward A,B-alternating copolymers would open the way to the synthesis of new functional polymers.



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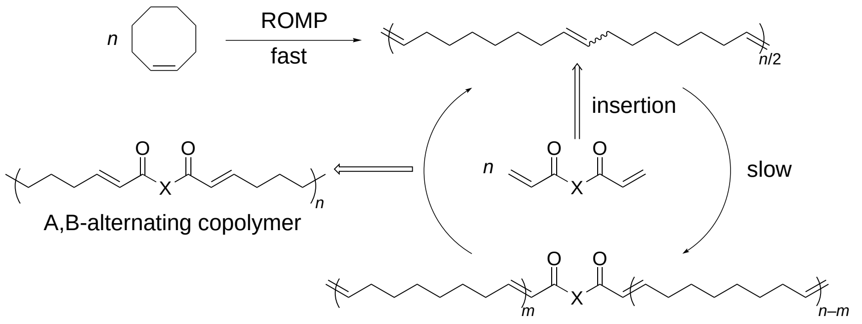
Although well-defined olefin-metathesis catalysts such as [((CF$_3$)$_2$MeCO)$_2$(ArN)−Mo=CH(*t*Bu)] (**1**) and [Cl$_2$(PCy$_3$)$_2$Ru=CHPh] (**2**) have proven useful for the synthesis of polymers, the highly active catalyst **1** is sensitive to some polar functional groups[5] and the highly functional-group-tolerant catalyst **2** shows decreased reactivity.[6] These disadvantages were recently addressed with the development of catalyst **3**, which exhibits high activity and remains tolerant of many functional groups.[7] Furthermore, catalyst **3** promotes ring-closing metathesis and selective cross metathesis (CM) of α,β-unsaturated carbonyl olefins with high conversions,[8] thereby expanding the scope of olefin metathesis in organic synthesis. This suggests that catalyst **3** should be able to produce polymers from α,β-unsaturated carbonyl olefins. Also, if the coupling between internal olefins and α,β-unsaturated carbonyl olefins is selective, as is the case in cross metathesis, diacrylate monomers should be selectively inserted into ROMP polyolefins to yield alternating copolymers (Scheme 1). Herein we report the development of a new method for synthesizing A,B-alternating copolymers by ring-opening-insertion-metathesis polymerization (ROIMP).



Scheme 1. Proposed mechanism for ROIMP.

Treatment of a 1:1 mixture of monomers A (diacrylates) and B (cycloalkenes) with catalyst **3**, indeed, yielded highly A,B-alternating copolymers in high yields. Examples of A,B-alternating copolymers from a variety of diacrylates and cycloalkenes are shown in Table 1. For example, with a total monomer/catalyst ratio of just 290:1, a 1:1 mixture of 1,4-butanediol diacrylate and cyclooctene gave a copolymer with up to 99 % A,B-alternation and a molecular weight of 90100 g mol^{-1} (Table 1, entry 1). It is important to match the stoichiometry of cyclooctene because any excess of cyclooctene results in oligocyclooctene blocks, which lowers the A,B-alternation.

The extent of A,B-alternation could be easily determined by ^{1}H NMR spectroscopic analysis, since olefinic protons for A,B-alternating units have a distinct chemical shift from the starting materials and homocoupled units. *E*-Acrylate dimers produce a sharp singlet at $\delta = 6.9$ ppm (Figure 1 a), whereas polycycloalkenes display a multiplet at $\delta = 5.4$ ppm (Figure 1 c). On the other hand, A,B-alternating units produce a doublet of triplets at $\delta = 7.0$ ppm and a doublet at $\delta = 5.8$ ppm (Figure 1 b). Therefore, the extent of A,B-alternation can be easily calculated by integrating these peaks. The sharp coupling patterns demonstrate a highly uniform polymer structure with *E* olefin isomer ($J = 15.9$ Hz). ^{13}C NMR spectroscopic analysis also shows high A,B-alternation, displaying only two olefinic carbon peaks for carbon atoms α and β to the carbonyl group (Figure 1 d).

In support of the mechanism shown in Scheme 1, independently prepared polycyclooctene was treated with diacrylate and catalyst **3**, yielding A,B-alternating copolymer similar to the product of Table 1, entry 1. Furthermore, monitoring the reaction by ^{1}H NMR spectroscopy showed rapid and complete ROMP of cyclooctene followed by gradual appearance of peaks corresponding to A,B-alternating units. Furthermore, when a ROIMP reaction was terminated after 20 minutes, a polymer enriched in homopolycycloalkene olefin units was obtained. These results strongly suggest a

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[**] We thank the NIH and NSF for generous support of this research, and Dr. C. W. Lee, Dr. A. F. M. Kilbinger, Dr. J. P. Gallivan, O. A. Scherman, C. W. Bielawski, D. Benitez, and D. P. Sanders for helpful discussions.

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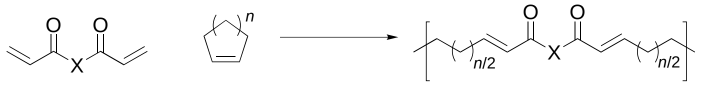
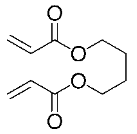
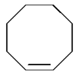
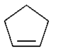
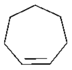
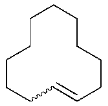
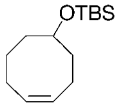
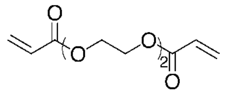
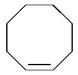
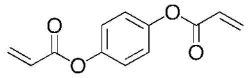
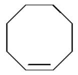
Table 1. Examples of ROIMP products, their A,B-alternations, molecular weights, and distributions.



Entry	Diacrylate	Cycloalkene[a]	M/C[b]	Conc. [M][c]	Yield [%][d]	A,B-alt. [%][e]	Mn/PDI [×10^{-3} g mol^{-1}][f]
1			290	0.2	84	99	90.0/1.73
2			125	0.4	75	96	20.3/1.58
3			125	0.4	93	97	14.0/1.80
4			200	0.5	91	94	26.1/1.71
5			250	0.4	69	94.5	21.4/1.43
6			200	0.2	99	98.5	26.5/1.80
7			100	0.1	98	97	25.2/2.06

[a] 1.0 Equivalents of cycloalkene was used, except for cyclopentene (1.3 equiv). [b] Total monomer/catalyst ratio. [c] Concentration with respect to diacrylate. [d] Yields of isolated products after precipitation into hexane or methanol. [e] Determined by ^{1}H NMR spectroscopic analysis. [f] Determined by CH_2Cl_2 GPC relative to polystyrene standards.

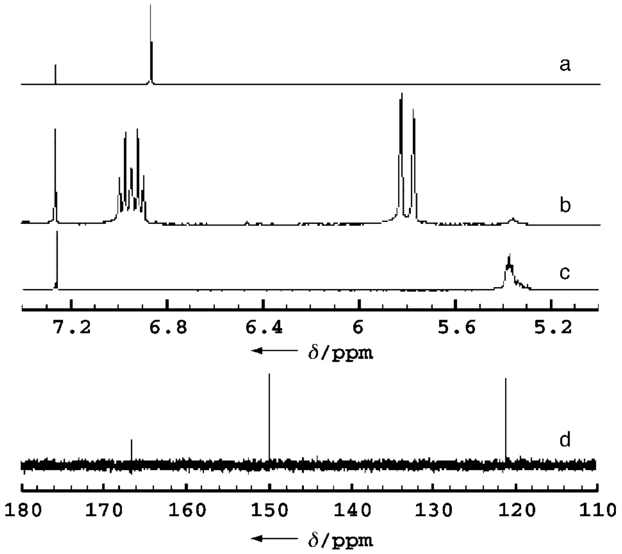


Figure 1. NMR spectra for a ROIMP product (Table 1, entry 1).

mechanism whereby ROMP of the cycloalkene initially produces an unsaturated polymer scaffold to which subsequent insertion of the diacrylate forms the final A,B-alternating structure.

Other cycloalkenes were also viable for ROIMP and yielded highly A,B-alternating polymers (Table 1, entries 2–4). However, substrates with particularly low ring strain, such as cyclopentene and cycloheptene, required a lower monomer/catalyst ratio (125:1) as a result of the slow rate of ROMP.[9] To obtain a high A,B-alternation (96%) with volatile cyclopentene (b.p. 44°C), a slight excess (1.3 equiv) of the cycloalkene relative to the diacrylate was used. Even with 2.0 equivalents of cyclopentene, a polymer with higher than 85% A,B-alternation was obtained. Also, treating an isolated polymer of lower A,B-alternation with catalyst **3** yielded a final polymer with higher A,B-alternation. These results suggest that the equilibrium for cyclopentene lies toward the cyclic form at 40°C; excess homopolycyclopentene units are degraded back to cyclopentene and lost from the system by evaporation.[10]

Notably, various functional groups can be incorporated into ROIMP copolymers. 5-*tert*-Butyldimethylsilyloxycyclooctene proved to be a viable monomer, comparable to the parent cyclooctene (Table 1, entry 5). In this way, free alcohol groups could be installed into alternating monomer units upon simple deprotection. Further variations such as ethylene glycol and phenyl groups can be substituted into diacrylate units (Table 1, entries 6 and 7). These results demonstrate that the regioselective incorporation of functional groups is possible by the appropriate choice of monomers A and B, thus opening up a new class of polymers that can be synthesized by ROIMP.

ROIMP exhibits remarkable conversion and selectivity. Compared to ADMET, where high vacuum and elevated temperatures are required to drive the polymerization to high

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conversion by removal of ethylene gas,[3] ROIMP gives high conversion under gentle reflux conditions for two reasons. First, ROMP of monomer B is efficient in making the initial homopolycycloalkene chains. Second, the formation of 1,2-disubstituted α,β-unsaturated carbonyl compounds is thermodynamically favored by more than 3 kcal mol^{-1} per bond.[11] These enthalpic factors, combined with the loss of ethylene, drive the reaction to high conversion. Furthermore, the unfavorable oligomerization of diacrylates, in which the intermediate is an unstable enoic carbene, leads to high A,B-alternation.[12] Therefore, ROIMP has benefits of both chain-growth and step-growth polymerization, leading to high molecular weight and high selectivity.

To optimize conversion, other polymerization conditions were investigated. It was found that 0.1–0.5 M solutions in CH_2Cl_2 at 40 °C give the best results. In contrast to ROMP, increasing the concentration beyond 0.5 M resulted in lower conversion. Switching to toluene or 1,2-dichloroethane as solvent also gave lower conversion at either 40 °C or 60 °C. Although there is precedence for CH_2Cl_2 being the best solvent for cross metathesis of functionalized olefins,[12] the concentration dependence for ROIMP is somewhat surprising, since concentrations of 0.1–0.5 M are considered dilute conditions for conventional step-growth-polymerization reactions.

Controlling the molecular weight of polymers is a very important issue since polymers with different molecular weights often exhibit different properties. For alternating copolymers produced by ROIMP, molecular weight can be roughly controlled by changing the relative stoichiometry of the two monomers. For example, using 0.96 equivalents of cyclooctene to 1.0 equivalent of hydroquinone diacrylate gave a copolymer of 17800 g mol^{-1} with 98 % A,B-alternation (PDI = 1.64), whereas a copolymer of 45200 g mol^{-1} and 95.5 % A,B-alternation (PDI = 1.69) was obtained by increasing the cyclooctene to 1.06 equivalents. These results show that when compared with the 1:1 case (Table 1, entry 7), an excess of hydroquinone diacrylate shortens the polymer chain, but an excess of cyclooctene gives higher molecular weight as a result of the oligomeric blocks of polycyclooctene.

In conclusion, we have demonstrated a new general method for synthesizing highly alternating copolymers by olefin metathesis. The high conversion and degree of alternation arise from the thermodynamically driven selective bond formation between diacrylates and cycloalkenes.

Experimental Section

Full procedures and characterization data are given in the Supporting Information.

Representative procedure (Table 1, entry 1): Catalyst **3** (2.7 mg) and cyclooctene (65 μL, 0.45 mmol) were added to a flask charged with 1,4-butanediol diacrylate (90 mg, 0.45 mmol) in CH_2Cl_2 (2 mL). Quick degassing by dynamic vacuum was conducted and the flask was fitted with a condenser and heated at reflux under argon for 6 h. The product (108 mg, 84 %) was precipitated into methanol. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.93 (dt, J = 7.2, 15.9 Hz, 1 H), 5.77 (d, J = 15.9 Hz, 1 H), 4.13 (br s, 2 H), 2.12 (m, 2 H), 1.73 (m, 2 H), 1.43 (m, 2 H), 1.30 ppm (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 149.6, 121.3, 64.0, 32.5, 29.3, 28.2, 25.8 ppm.

Received: June 5, 2002 [Z19471]

[1] a) G. Odian, *Principles of Polymerizations*, Wiley, New York, **1991**; b) E. Drent, P. H. M. Budzelaar, *Chem. Rev.* **1996**, *96*, 663.

[2] For recent reviews on ROMP, see: a) K. J. Ivin, J. C. Mol, *Olefin Metathesis and Metathesis Polymerization*, Academic Press, San Diego, **1997**; b) R. H. Grubbs, E. Khosravi, *Mater. Sci. Technol.* **1999**, *20*, 65; c) M. R. Buchmeiser, *Chem. Rev.* **2000**, *100*, 1565.

[3] For a recent report using catalyst **3**, see; S. E. Lehman, K. B. Wagener, *Macromolecules* **2002**, *35*, 48, and references therein.

[4] a) B. A. Samak, A. G. Carvill, J. G. Hamilton, J. J. Rooney, J. M. Thompson, *Chem. Commun.* **1997**, 2057; b) B. A. Samak, V. Amir-Ebrahimi, D. G. Corry, J. G. Hamilton, S. Rigby, J. J. Rooney, J. M. Thompson, *J. Mol. Catal.* **2000**, *160*, 13; c) M. F. Ilker, E. B. Coughlin, *Macromolecules* **2002**, *35*, 54.

[5] R. R. Schrock, *Acc. Chem. Res.* **1990**, *23*, 158.

[6] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100.

[7] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953.

[8] a) A. K. Chatterjee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 1751; b) A. K. Chatterjee, J. P. Morgan, M. Scholl, R. H. Grubbs, *J. Am. Chem. Soc.* **2000**, *122*, 3783; c) T.-L. Choi, A. K. Chatterjee, R. H. Grubbs, *Angew. Chem.* **2001**, *113*, 1317; *Angew. Chem. Int. Ed.* **2001**, *40*, 1277; d) A. K. Chatterjee, T.-L. Choi, R. H. Grubbs, *Synlett* **2001**, 1034; e) T.-L. Choi, R. H. Grubbs, *Chem. Commun.* **2001**, 2648; f) C. W. Lee, T.-L. Choi, R. H. Grubbs, *J. Am. Chem. Soc.* **2002**, *124*, 3224.

[9] C. W. Bielawski, R. H. Grubbs, *Angew. Chem.* **2000**, *112*, 3025; *Angew. Chem. Int. Ed.* **2000**, *39*, 2903.

[10] R. R. Schrock, K. B. Yap, D. C. Yang, H. Sitzmann, L. R. Sita, G. C. Bazan, *Macromolecules* **1989**, *22*, 3191.

[11] The number was obtained by AM1 calculation from Spartan v. 1.1, Wavefunction.

[12] T.-L. Choi, C. W. Lee, A. K. Chatterjee, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 10417.

Polymerase Recognition of Unnatural Base Pairs**

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The storage and replication of genetic information requires bases that pair stably and selectively in duplex DNA and are also good substrates for DNA polymerases. Though the four natural bases pair by hydrogen bonding, there is no reason to assume that the pairing of two unnatural bases could not be driven by other intermolecular interactions, for example, those based on hydrophobicity.[1,2] To investigate this issue, a wide variety of hydrophobic base pairs has been characterized.[3,4] For example, ICS (see Figure 1) and its derivative PICS, with a propynyl group at C7, form self-pairs in duplex DNA that are as stable as natural base pairs. The unnatural triphosphates are also inserted opposite themselves in the

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[**] This work was funded by the National Institutes of Health (GM 60005 to F.E.R) and by the Skaggs Institute for Chemical Biology (F.E.R. and P.G.S.)

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