Ru-Catalyzed Isomerization Provides Access to Alternating Copolymers via Ring-Opening Metathesis Polymerization

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Supporting Information

ABSTRACT: We describe an isomerization–alternating ROMP protocol that gives linear copolymers with rigorous sequence alternation. Bicyclo[4.2.0]oct-7-ene-7-carboxamides of primary amines are isomerized in the presence of (3-BrPyr)2Cl2(1H,1Mes)Ru−CHPh to the corresponding bicyclo[4.2.0]oct-1(8)-ene-8-carboxamides in which the olefinic bond is tetrasubstituted. The isomerized amides undergo alternating ring-opening metathesis polymerization with cyclohexene to provide soluble and linear copolymers with molecular weights up to ~130 kDa. This process provides efficient entry to strictly alternating copolymers that can display diverse functional groups.

Cyclobutene-1-carboxylic acid derivatives exhibit selective reactivities in ruthenium-catalyzed ring-opening metathesis.22,27,28 For example, the ROMP of the secondary amides of cyclobutene-1-carboxylic acid provides regioregular polymers that contain E-olefins and that have low molar mass dispersities.27,28

Although neither a cyclobutenecarboxylic acid ester nor a cyclohexene undergoes ROMP on its own, the two copolymerize to produce precisely alternating copolymers.22 This iterative process, initiated when the benzylidene Ru carbene undergoes ROM with the cyclobutene ester and enabled when the resulting enol Ru carbene undergoes ROM with cyclohexene, provides a perfectly alternating copolymer in a single reaction. We named this process AROMP, for alternating ring-opening metathesis polymerization.

The strict alternation obtained in cyclobutenecarboxylic acid ester/cyclohexene AROMP suggests interesting applications.29,30 However, because the lengths of the resulting linear polymers have been limited by intramolecular cross-metathesis (backbiting) reactions,22,31 we designed bicyclic olefinic esters as AROMP substrates.32 We found that methyl bicyclo[4.2.0]-oct-7-ene-7-carboxylic ester and cyclohexene provide linear, alternating copolymers without competing inter- or intra-molecular cross-metathesis reactions, although their length was limited by slow propagation.

Recognizing the interesting architecture of polymers that have rings fused to their backbones, we tested the corresponding bicyclo[4.2.0]oct-7-ene-7-carboxamides 1a−f in ROMP reactions with the Grubbs III catalyst 2 (Scheme 1). To

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Both GPCs were calibrated with poly(styrene) standards at 30 kDa exclusion limit, Phenomenex) on the same chromatography system constructed from a Shimadzu pump coupled to a Shimadzu UV detector. Methylene chloride served as the eluent with a flow rate of 0.700 mL/min. Molecular weights and molar mass dispersities of poly(1-alt-3), and poly(1b-alt-3), were measured on a Phenogel 5 μM XL C column (300 × 7.8 mm, 100 kDa exclusion limit, Phenomenex) on silica gel-60 (230–400 mesh), and Combi-Flash chromatography on RediSep normal phase silica columns (silica gel-600 mesh). Bruker Nanobay 400, Avance III 500, and Avance III 700 NMR instruments were used for analysis. Chemical shifts were calibrated from residual undeuterated solvents; they are denoted in ppm (δ).

Molecular weights and molar mass dispersities except poly(1c-alt-3), and poly(1b-alt-3), were measured on a Phenogel 5 μM 104EA LC column (300 × 7.8 mm, 500 kDa exclusion limit, Phenomenex) on the same chromatography system. THF served as the eluent with a flow rate of 1.00 mL/min. Both GPCs were calibrated with poly(styrene) standards at 30 °C.

our surprise, under ROMP conditions, each of the amides 1 isomerized to the bicyclo[4.2.0]oct-1(8)-ene-7-carboxamide 1’. None of the amides showed evidence of homopolymerization in the presence of catalyst 2. Notably, addition of cyclohexene 3 to isomerized amides 1’ in the presence of catalyst 2 provided a reaction manifold for the isomerized amides that led to linear, alternating copolymers, poly(1’-alt-3), of extensive length. Herein, we describe the AROMP of the isomerized monomers bearing functional groups, which provides long, soluble, and perfectly alternating copolymers.

### EXPERIMENTAL METHODS

All metathesis reactions were performed under an N2 atmosphere. Solvents, e.g. CH2Cl2 and THF, were purified with Pure Process Technology (PPT). Deuterated solvents for all ring-opening reactions were degassed and filtered through basic alumina before use. Catalyst Cl2(H2IMes)(PCy3)Ru was purchased from Aldrich. Cyclohexene-D10 was purchased from CDN Isotope Inc. The synthesis of catalyst (3-Br-Pyr)2Cl2(H2IMes)Ru was performed according to the procedure of Love et al.33

**General Procedure for NMR Scale Isomerization Reactions.** Under an N2 atmosphere, a solution of the original amide and catalyst was prepared in the indicated solvent (600 μL) in an NMR tube, and NMR spectra were acquired at 35 °C. At the end of the isomerization reaction (after complete consumption or no further isomerization of amide as judged by the change of the olefinic proton resonance), each reaction was terminated with ethyl vinyl ether (100 μL) and stirred for 30 min. The solvent was evaporated, and the resulting residue was purified by silica chromatography to isolate the isomerized amide.

**i-[4.2.0] Amide 1a’.** Amide 1a (28 mg, 120 μmol, 20 equiv) and catalyst 2 (5.3 mg, 6 μmol, 1 equiv) were mixed in CD2Cl2 in an NMR tube for 16 h; during this time, the integral for the olefinic proton decreased to 10% of its original value. The mixture was concentrated, and the product was isolated by chromatography (100:1/CH2Cl2:MeOH) to yield 24 mg (80%) of i-[4.2.0] Amide 1a’ (δ = 5.3 Hz, 3H, CH3). 13C NMR (5.3 mg, 6 μmol, 1 equiv) were mixed in CD2Cl2 in an NMR tube for 1.5 h, when isomerization was complete. The mixture was concentrated, and the product was isolated by chromatography (100:1/CH2Cl2:MeOH) to yield 49 mg (85%) of 1a’. H NMR (500 MHz, CDCl3): δ = 5.3 Hz, 3H, CONH, 4.11 (dd, J = 5.3 Hz, 2H, side chain CH2), 3.78 (s, 3H, OCH3), 2.03 (m, 2H, CH2), 2.01 (m, 2H, CH2), 1.92 (m, 1H, CH2), 1.85 (m, 1H, CH2), 1.75 (m, 1H, CH2), 1.34 (m, 2H, CH2), 1.12 (m, 1H, CH2).

**i-[4.2.0] Amide 1b’.** Amide 1b (67 mg, 300 μmol, 50 equiv) and catalyst 2 (5.3 mg, 6 μmol, 1 equiv) were mixed in CD2Cl2 in an NMR tube for 8 h. The mixture was concentrated, and the product was isolated by chromatography (100:1/CH2Cl2:MeOH) to yield 58 mg (75%) of 1b’. H NMR (500 MHz, CDCl3): δ = 5.9 Hz, 3H, CONH, 4.11 (dd, J = 5.3 Hz, 2H, side chain CH2), 3.78 (s, 3H, OCH3), 2.03 (m, 2H, CH2), 2.01 (m, 2H, CH2), 1.92 (m, 1H, CH2), 1.75 (m, 1H, CH2), 1.34 (m, 2H, CH2), 1.12 (m, 1H, CH2).

**i-[4.2.0] Amide 1c’.** Amide 1c (58 mg, 300 μmol, 50 equiv) and catalyst 2 (5.3 mg, 6 μmol, 1 equiv) were mixed in CD2Cl2 in an NMR tube for 1.5 h, when isomerization was complete. The mixture was concentrated, and the product was isolated by chromatography (100:1/CH2Cl2:MeOH) to yield 49 mg (85%) of 1c’. H NMR (500 MHz, CDCl3): δ = 5.5 Hz, 3H, CONH, 4.11 (dd, J = 5.3 Hz, 2H, side chain CH2), 3.78 (s, 3H, OCH3), 2.03 (m, 2H, CH2), 2.01 (m, 2H, CH2), 1.92 (m, 1H, CH2), 1.75 (m, 1H, CH2), 1.34 (m, 2H, CH2), 1.12 (m, 1H, CH2).

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Attempted Isomerization of Amide 4. Amide 4 (27 mg, 120 μmol, 10 equiv) and catalyst 2 (5.3 mg, 6 μmol) were mixed in CDCl3 in an NMR tube for 24 h, at which point the integral for the olefinic proton had decreased to 30% or 10% of its original value, respectively. Partial 1H NMR spectroscopy of the crude 4′ (600 MHz, CDCl3): δ 6.69 (s, 0.1H, ==CH), 6.31 (m, 0.1H, CONH), 6.09 (d, J = 6.9 Hz, 0.9H, CONH). Partial 1H NMR of the crude 1′ (600 MHz, CDCl3): δ 6.71 (s, 0.2H, ==CH), 6.36–6.26 (m, 0.3H, CONH), 6.11 (d, J = 6.9 Hz, 0.7H, CONH). Partial 1H NMR spectroscopic data are reported due to incomplete isomerization and significant overlap of 1H-1H with the new peaks from 1F-1F.

**General Procedure for NMR Scale AROMP Reactions.** All reactivity experiments were performed at least twice, and preparative polymerization experiments were performed three times. Under a N2 atmosphere, a solution of amide I in CD2Cl2 (300 μL) was added to the NMR tube. Then 300 μL of catalyst 2 solution was added to the NMR tube. After complete mixing of the solution, NMR spectra were acquired at 35 °C. Cyclohexene 3 was added after the amide was completely converted to its tetrasubstituted isomer as judged by the disappearance of the olefinic proton resonance around 6.7 ppm. This procedure was used for the preparation of polymers with up to 50 AB repeats. To ensure narrow dispersities, in the preparation of longer alternating polymers, the isomer 1′ was isolated and mixed with fresh catalyst 2 in CDCl3 or CDCl2. Cyclohexene 3 was added after catalyst 2 completely initiated as determined by the disappearance of the Ru alkylidene resonance at 19.1 ppm in the 1H NMR spectrum. When the propagation stopped or the isomerized amide disappeared as judged by a complete upfield shift of the amide N-H resonance from ~5.4 to ~6 ppm, the reaction was quenched with ethyl vinyl ether and stirred for 30 min. The solvent was evaporated, and alternating copolymer was purified by step chromatography (100% CH2Cl2 to remove contaminants, then 20:1 CH2Cl2:MeOH to elute copolymer). The theoretical Mw theor were calculated from the monomer:catalyst feed ratio.

**Poly(1′-alt-3)1a.** Amide 1a (14.2 mg, 60 μmol, 50 equiv), catalyst 2 (1.1 mg, 1.20 μmol, 1 equiv), and 3 (9.8 mg, 120 μmol, 100 equiv) were mixed in CDCl3 in an NMR tube. After 2 h, amide 1a was completely consumed. Flash column chromatography of the crude product yielded poly(1′-alt-3)1a (14.9 mg, 78% yield).

**Poly(1′-alt-3)1b.** Amide 1a (28.5 mg, 120 μmol, 1 equiv), catalyst 2 (1.1 mg, 1.20 μmol, 1 equiv), and 3 (19.6 mg, 240 μmol, 200 equiv) were mixed in CDCl3 in an NMR tube. After 6 h, amide 1a was completely consumed. Flash column chromatography of the crude product yielded poly(1′-alt-3)1b (26.8 mg, 70% yield).

**Poly(1′-alt-3)1c.** Amide 1a (40.2 mg, 180 μmol, 150 equiv), catalyst 2 (1.1 mg, 1.20 μmol, 1 equiv), and 3 (29.4 mg, 360 μmol, 300 equiv) were mixed in CDCl3 in an NMR tube. After 2.5 h, amide 1b was completely consumed. Flash column chromatography of the crude product yielded poly(1′-alt-bd)1c (34.0 mg, 62% yield).

**Poly(1′-alt-3)1d.** Amide 1b (40.2 mg, 180 μmol, 150 equiv), catalyst 2 (0.55 mg, 0.60 μmol, 1 equiv), and 3 (29.4 mg, 360 μmol, 300 equiv) were mixed in CDCl3 in an NMR tube. After 3.5 h, 90% of amide 1b was consumed. Flash column chromatography of the crude product yielded poly(1′-alt-d)1d (27.5 mg, 52% yield).

**Poly(1′-alt-3)1e.** Amide 1c (11.6 mg, 60 μmol, 10 equiv) and catalyst 2 (5.3 mg, 6 μmol) were mixed in CDCl3 in an NMR tube for 18 h. Only a 2% decrease in the intensity of the olefinic resonance was observed.
RESULTS AND DISCUSSION

Synthesis of Monomers. Bicyclo[4.2.0] and [3.2.0] esters were synthesized by a modification of Snider's approach as previously described. Basic hydrolysis provided the carboxylic acid (1c).

Poly(1c-alt-3)-100 Amide 1c (11 mg, 60 μmol, 50 equiv) and catalyst 2 (1.1 mg, 120 μmol, 1 equiv) were mixed in CDCl3 in an NMR tube. Upon completion of isomerization, 3 (9.8 mg, 120 μmol, 100 equiv) was added, and after 2 h, amide 1c was completely consumed. Flash column chromatography of the crude product yielded poly(1c-alt-3)-100 (14 mg, 74% yield). 

1H NMR (500 MHz, CDCl3): δ 7.45–7.27 (m, 5H, Ph), 6.40–5.57 (m, 97H, CH and CONH), 5.09 (m, 49H), 2.34 (m, 50H, CH2), 2.58 (m, 46H), 2.39 (m, 44H), 2.29–1.90 (m, 368H, 1H, 700H), 1.04–0.87 (m, 150H, CH3). M_n = 14 500. M_w/GPC = 9400. M_p/GPC = 17 000. D_M = 1.8.

Poly(1c-alt-3)-200 Amide 1c (23.2 mg, 120 μmol, 100 equiv) and catalyst 2 (1.1 mg, 120 μmol, 1 equiv) were mixed in CDCl3 in an NMR tube. After 2 h, amide 1c was completely consumed. Flash column chromatography of the crude product yielded poly(1c-alt-3)-200 (24 mg, 85% yield). 

1H NMR (500 MHz, CDCl3): δ 7.26 (m, 20H, Ph), 7.10 (m, 10H, Ph), 3.67 (m, 10H), 2.63 (m, 10H), 2.48 (m, 10H), 2.29 (m, 10H). M_n = 20 500. M_w/GPC = 24 400. D_M = 1.4.

Poly(1d-alt-3-D)100 Amide 1d (13.7 mg, 60 μmol, 10 equiv) and catalyst 2 (5.3 mg, 60 μmol, 1 equiv) were mixed in CDCl3 in an NMR tube. Monomer 3 (9.8 mg, 120 μmol, 20 equiv) was added upon completion of isomerization. After 1 h, amide 1d was completely consumed. Flash column chromatography of the crude product yielded poly(1d-alt-3-D)100 (13 mg, 68% yield). 

1H NMR (500 MHz, CDCl3): δ 7.36 (m, 5H, Ph), 6.44–5.65 (m, 74H, CH and CONH), 5.22–4.99 (m, 424H, CH), 3.33–3.13 (m, 871H, CH2), 2.55 (m, 447H), 2.48–2.33 (m, 390H, 131H, 1H, 111H, 1.04–1.15 (m, 612H), 1.06–0.82 (m, 1522H), 1H NMR (126 MHz, CDCl3): δ 169.8, 141.8, 136.9, 134.4, 120.8, 43.7, 143.3, 31.3, 30.0, 28.8, 28.3, 28.1, 26.9, 23.0, 11.3. M_n = 137 700. M_w/GPC = 111 600. M_p/GPC = 130 900. D_M = 1.2.

Poly(1d-alt-3-D)120 Amide 1d (13.7 mg, 60 μmol, 10 equiv) and catalyst 2 (5.3 mg, 60 μmol, 1 equiv) were mixed in CDCl3 in an NMR tube. After 6 h, 85% of amide 1c was consumed. Flash column chromatography of the crude product yielded poly(1d-alt-3-D)120 (13 mg, 46% yield). 

1H NMR (500 MHz, CDCl3): δ 7.36 (m, 5H, Ph), 6.44–5.65 (m, 74H, CH and CONH), 5.22–4.99 (m, 424H, CH), 3.33–3.13 (m, 871H, CH2), 2.55 (m, 447H), 2.48–2.33 (m, 390H, 131H, 1H, 111H, 1.04–1.15 (m, 612H), 1.06–0.82 (m, 1522H), 1H NMR (126 MHz, CDCl3): δ 169.8, 141.8, 136.9, 134.4, 120.8, 43.7, 143.3, 31.3, 30.0, 28.8, 28.3, 28.1, 26.9, 23.0, 11.3. M_n = 137 700. M_w/GPC = 111 600. M_p/GPC = 130 900. D_M = 1.2.

Table 1. Isomerization of Amides Effected by Catalyst 2

| entry | 1 | 1/[2]/[3] | cat/additive | time (h) | % conv |
|-------|---|---------|--------------|---------|--------|
| 1     | 1a | 20.1"   | 2            | 16       | 90     |
| 2     | 1b | 50.1"   | 2            | 8        | 95     |
| 3     | 1c | 50.1"   | 2            | 1.5      | 100    |
| 4     | 1d | 20.1"   | 2            | 0.3      | 100    |
| 5     | 1e | 50.1"   | 2            | 6        | 100    |
| 6     | 1f*| 10.1"   | 2            | 24       | 70     |
| 7     | 1f*| 10.1"   | 2            | 24       | 90     |
| 8     | 1e | 10.1"   | 2            | 14       | 100    |
| 9     | 1e | 2/3-Br-pyridine | 20 equiv | 14       | 35     |
| 10    | 1e | 5.1"    | 2            | 1        | 100    |
| 11    | 1e | 5.1"    | (Cl)2(C=CH)3 | 14       | 5      |
| 12    | 1e | 10.1"   | 2            | 24       | 65     |

"[cat.] = 0.01 M, CD2Cl2, 35 °C, % conv was determined by monitoring the monomer alkenes resonances in 1H NMR spectra. [cat.] = 0.005 M, CD2Cl2, 35 °C.

Figure 1. 1H NMR spectra of the alkene and aromatic regions of amide, isomerized amide, and AROMP product. (a) Monomer 1c in CDCl3. (b) Formation of the tetrasubstituted isomer 1c in the presence of catalyst 2 in CDCl3. (c) Purified alternating copolymer poly(1c-alt-3)-100 in CDCl3. (CDCl3 was used to avoid overlap with aromatic proton signals and to allow their integration.) The two alkene signals correspond to H1 and H4 of poly(1c-alt-3)-100 (see Scheme 1 for structure).
materials. The spectroscopic signatures of 1c’ and 1d’ were distinct from those of 1c and 1d, indicating that isomerization had occurred. Relative to the 1H NMR spectra of the starting materials, those of 1c’ and 1d’ contained one more methylene proton signal, one fewer methine signal, and no olefinic proton resonance (Figure 1 and Figure S1). Further spectroscopic characterization of 1c’ by HSQC NMR spectroscopy indicated that it retains the unsaturated bicyclic structure of 1c but that the double bond had migrated (Scheme 1 and Figures S2 and S3).

Typically, tetra-substituted olefins are not obtained with catalyst 2.46−49 However, the isomerization of amide 1 to amide 1′ is less surprising when viewed in the context of the Pd(II)-catalyzed isomerization of the parent system cis-bicyclo[4.2.0]-oct-7-ene, analogous to 1, to the 2-ene, which presumably proceeds through the 1(8)-ene, analogous to 1′ (Scheme 2).

Scheme 2. Proposed α-Allylic Isomerization of Amides 1 to 1′

\[
\begin{align*}
\text{cis-bicyclo[4.2.0]oct-7-ene} & \quad \rightarrow \quad \text{bicyclo[4.2.0]oct-1(8)-ene} \\
\text{cis-bicyclo[4.2.0]oct-2-ene} & \quad \rightarrow \quad \text{bicyclo[4.2.0]oct-1(8)-ene}
\end{align*}
\]

“From the calculations of Curran et al.40

Calculations by Curran, Risse, and co-workers suggest that the 1(8)-ene is 3.7−5.0 kcal/mol more stable than the 7-ene.40 In our system, further isomerization to the cis-bicyclo[4.2.0]oct-2-ene-8-carboxamide is unfavorable because in this compound the alkene is not in conjugation with the amide. Results from the Curran group with the [3.2.0] system are also consistent with our observation that the bicyclo[3.2.0] system 4 does not undergo appreciable isomerization. Their calculations show the bond migration from the 6-position to the 1(7)-position is endothermic by more than 9 kcal/mol.40 As noted above, regiosomer 4′ is not formed upon addition of catalyst 2 to amide 4 is not isomerized by catalyst 2.

**Mechanism of Isomerization.** Control experiments support the role of species 2 as the isomerization catalyst. No isomerization was observed upon incubation of 1c in CH₂Cl₂ at 35 °C for 16 h in the absence of catalyst 2. Over the course of our experiments, we utilized four different batches of 2. All four preparations of 2 catalyzed isomerization to the same extent and at the same rate. Furthermore, addition of 50 equiv of 3-bromopyridine to amide 1e and catalyst 2 reduced the percentage of isomerization 3-fold over a 14 h time period as compared to isomerization in the absence of exogenous 3-bromopyridine \((\text{[2]} = 0.005 \text{ M, Table 1, entry 8 vs 9). Likewise, we found that 20 mol % of (Cl)₂(H₂IMes)(PCy₃)ᵢRu=CHPh, for which PCy₃ ligand dissociation is less favored, catalyzed less than 5% isomerization of amide 1e in 14 h as compared to 100% conversion with 20 mol % catalyst 2 within 1 h (Table 1, entry 10 vs 11). These experiments indicate that coordination of the substrate to the Ru catalyst is required for isomerization.

Cyclobutenes are sensitive to acid-catalyzed decomposition and/or reaction. In order to exclude the possibility that substrates 1 were being converted to isomers 1′ by adventitious acid, we repurified the monomers by passing them through dry basic alumina before subjecting them to catalyst 2. The isomerization rates and product distributions were unchanged.

Ruthenium catalysts are known to promote olefin isomerization. Previous reports41−44 have proposed that either a Ru hydride species or a π-allyl Ru complex is responsible. The Ru hydride can form upon decomposition that occurs with extended reaction times or extreme reaction conditions.42,43 The rapid isomerization rates we observe are inconsistent with the formation of a Ru hydride species through decomposition of 2. Moreover, we never observed Ru hydride resonances at the expected upfield region between 0 and −30 ppm in the 1H NMR spectra of the above reactions. Addition of 1,4-benzoquinone, which has been reported to oxidize Ru hydride species and prevent olefin isomerization,53 to our amide 1e did not suppress isomerization. Therefore, a reduced, electron-rich species is unlikely to be responsible for initiation of isomerization (Table 1, entry 8 vs 12).

Alcohols can act as ruthenium reducing agents to enhance Ru hydride formation.50 However, their coordination with Ru can suppress isomerization that proceeds via a π-allyl mechanism.51,54,55 Therefore, we tested isomerization of 1c with and without methanol in the presence of 10 mol % catalyst 2. The 1c isomerization reaction containing 8% methanol in CD₃Cl₂ proceeded much more slowly than the reaction without methanol; only 65% isomerization was observed over 24 h as compared to complete isomerization in 1.5 h in the absence of methanol (Table 1, entry 13 vs 14). Our observations are consistent with isomerization via a π-allyl Ru complex formed upon coordination of amide 1 with catalyst 2 (Scheme 2). Evidence in hand does not distinguish between direct formation of this species from amide 1 or its formation by a “ring-walking” mechanism.40

The relative rate of isomerization depends on the nature of the amide nitrogen substituent: 1d > 1c > 1e > 1b > 1a > 1f/1f*. Amides of α-substituted amines and of amines that include an ester in the alkyl chain isomerize slower than primary alkyl or aryl amides.

To investigate further the electronic influence on isomerization, we undertook a control experiment to establish the amount of isomerization with the corresponding methyl bicyclo[4.2.0]oct-7-ene-7-carboxylate. When subjected to catalyst 2 (2 mol %) at 50 °C for 2 days, the ester underwent ROM without isomerization as judged by the disappearance of the catalyst alkylidene proton signal and the remaining signals for the ester starting material. Therefore, the amide moiety assists rapid equilibration of isomers of 1 in the presence of 2.

The reactivity data taken together with the structure−activity data strongly support a mechanism in which equilibration of regiosomers takes place via initial coordination involving the amide functional group and subsequent formation of a transient Ru π-allyl species (Scheme 2).

**Alternating Ring-Opening Metathesis Polymerization of Isomerized Amides.** We monitored the isomerization of
amide 1e to amide 1e′ in the presence of 1 equiv of catalyst 2 by 13C NMR spectroscopy. In addition to the growth of the signals corresponding to the formation of amide 1e′, remarkably we observed the appearance of new peaks at 322.3 and 178.5 ppm, presumably representing the carbene carbon and the amide carbon respectively in the [Ru]=[C(R)CONHR] species. We also observed a peak at 315.5 ppm, representing a second ruthenium carbene species. On the basis of this experiment, we concluded that ROM occurs upon formation of 1′ despite the tetra-substitution of the alkene monomer. Unlike the ruthenium carbenes from amide-substituted cyclobutenes, previously studied in our laboratory,27,28 the amide-substituted carbene derived from 1 does not undergo metathesis with remaining monomer, as noted above.

We reasoned that the amide-substituted carbene derived from 1′ might undergo ring-opening cross-metathesis with cyclohexene 3, in a reaction analogous, but not identical, to the reaction of Ru enoic carbenes in our previous AROMP work.22,27,29,32 Indeed, copolymer was rapidly formed upon addition of cyclohexene 3 (Table 2). The copolymerization of monomer 1c′ or 1d′ with 3 yields a 50-AB-mer in approximately 2 h. Remarkably, in light of the steric hindrance in the system, this AROMP is faster under similar conditions than that of the less hindered 1-cyclobutene carboxylic methyl ester/cyclohexene AROMP which yields a 50-AB-mer in 3 h22 and that of the corresponding bicyclo[4.2.0]oct-7-ene-7-carboxylic ester which yields a 50-AB-mer in 8 h.32

Table 2. Alternating Copolymerization (AROMP) of Bicyclic Amides 1 or 1′ and Cyclohexenes 3 Catalyzed by Catalyst 2*

| entry | A/B | [A]:[3]:[2] | [2] (M) | time (h) | % conv | DP_{AB} | M_n^{GPC-d} (kDa) | M_w^{GPC-d} (kDa) | M_{D} | M_{n}^{theor} (kDa) |
|-------|-----|-------------|---------|----------|--------|---------|-----------------|-----------------|------|---------------------|
| 1     | 1c/3| 10:20:1     | 0.01    | 1.5      | 100    | 10      | nd             | nd              | nd   | nd                  |
| 2     | 1c/3| 50:100:1    | 0.002   | 2        | 100    | 50      | 17.0           | 9.4             | 1.8  | 14.5                |
| 3     | 1d/3| 50:100:1    | 0.002   | 1        | 100    | g       | 16.0           | 10.1            | 1.6  | 15.6                |
| 4*    | 1a/3| 50:100:1    | 0.002   | 2        | 100    | 50      | 15.1           | 12.5            | 1.2  | 15.8                |
| 5*    | 1a/3| 100:200:1   | 0.002   | 6        | 100    | 100     | 30.7           | 29.1            | 1.1  | 31.9                |
| 6*    | 1b/3| 150:300:1   | 0.002   | 2.5      | 100    | 140     | 40.3           | 34.0            | 1.2  | 45.7                |
| 7*    | 1b/3| 300:600:1   | 0.001   | 3.5      | 90     | 260     | 80.9           | 69.6            | 1.2  | 91.0                |
| 8*    | 1c/3| 100:200:1   | 0.002   | 2        | 100    | 100     | 28.4           | 20.5            | 1.4  | 28.1                |
| 9*    | 1c/3| 500:1000:1  | 0.0004  | 6        | 85     | 420     | 130.9          | 111.6           | 1.2  | 137.7               |

*All preparative polymerization experiments were performed three times. Representative molecular weight data are presented from a single polymerization. 1Conversion was determined by monitoring the disappearance of the amide resonance in 1 or 1′. 2Degree of polymerization (DP) was determined for the AB repeat by integration of polymer resonances relative to the styrene end group. We estimate the integration error to be within 5%. M_n = weight-average molecular weight; M_w = number-average molecular weight, determined by GPC. 3Theoretical M_w calculated from the monomer:catalyst feed ratio. 4Not determined. 5The DP could not be determined because of spectroscopic overlap and was estimated from the feed ratio of 1d and catalyst 2. 6Isomerized amide was isolated and fresh 2 added before AROMP in CDCl_3. 7Isomerized amide was isolated and fresh 2 added before AROMP in CD_2Cl_2.

In the cases of 1a, 1b, 1c, and one of the diastereomers of 1f/1f′, we obtained mixtures of starting materials and alternating polymers. In these systems, then, the rate of isomerization is slower than or similar to the rate of ROM. Owing to their fast isomerization, amides 1c′ and 1d′ were selected initially for further characterization of their AROMP products.

Analysis of poly(1d′-alt-3)_{50} by 1H NMR, 13C NMR, APT, and HSQC spectroscopy revealed that the polymer backbone has four alkene carbons and two alkene hydrogens corresponding to C1−C4 and H1 and H4 (Scheme 1 and Figure S5). HSQC spectroscopy confirmed that the amide-substituted olefin is a single stereoisomer; there is a single H1 signal at 6.29 ppm that correlates with C1 at 136 ppm (Figure 2). On the basis of comparison of the H1 alkene chemical shift with model compounds,27,56 we conclude that the conjugated alkene is of E-configuration. A single H4 signal at 5.11 ppm correlates with C4 at 121 ppm. Because of peak broadening in the polymer, we could not determine if the C3−C4 alkene is stereoregular.

Integration of the poly(1′-alt-3)_{n} alkene signals relative to side chain signals demonstrated that an equal incorporation of
the two monomers had occurred. An AA or BB dyad would be formed upon backbiting. Additional alkene proton resonances in the 5 ppm region of the 1H NMR spectrum which would indicate formation of BB dyad were not observed. In the isomerized amide AROMP product, the AA dyad does not possess an alkene proton. Therefore, we inspected the 13C NMR spectra of poly(1d′-alt-3)30 and poly(1c′-alt-3)30 for the presence of AA dyad alkene resonances, specifically, a C= resonance between 160 and 145 ppm, and found none (Figure S6). Further evidence for the equal incorporation of monomers 1d′ and 3 was obtained with experiments with cyclohexene-D10. The 1H NMR spectra of the deuterium-labeled copolymer poly(1d′-alt-3-D10)30 show a complete loss of the alkene resonances at 6.3 and 5.1 ppm as expected for an alternating AB polymer (Figure S7).

We explored the utility of alternating copolymerization by testing the maximal length of alternating copolymer that could be prepared. When cyclohexene 3 was added directly to a completed isomerization reaction of 1c′ or 1d′, poly(1c′-alt-3)30 or poly(1d′-alt-3)30 was obtained (Table 2). However, the dispersities exceeded those expected from the monomer-catalyst ratio for a ruthenium-catalyzed polymerization, presumably because of loss of catalyst during isomerization. Therefore, in order to facilitate characterization of polymers longer than 100 AB dyads, to maximize their purity, and to minimize their dispersity, we isolated amides 1b′ before initiation of the AROMP reaction and added fresh catalyst.

In the case of amides 1a′ and 1b′, the AROMP reactions provided maximal lengths of 100 AB dyads and 260 AB dyads, respectively, with modest $D_M = 1.1$–1.2. Higher monomer feed ratios did not provide longer copolymers. In contrast, when amide 1c′ was mixed with catalyst 2 in a ratio of 500:1 with 1000 equiv of cyclohexene 3, we reproducibly obtained alternating copolymer with more than 400 AB dyads (Figure 1c) and a modest molecular weight distribution ($D_M = 1.2$). Although the isomerization of 1d′ to 1d′ was facile, the length of the copolymers obtained was limited to 50 AB dyads regardless of whether amide 1d′ or 1d′ was used to initiate propagation. Finally, amides 1e′ and 1f′ provided only short alternating copolymers that were not characterized further. Overall propagation efficiencies in order are $1c′ > 1b′ > 1a′ > 1d′ > 1e′ > 1f′$. Thus, the maximal length of copolymer obtained depends on the degree of steric congestion $α$ to the amide. Moreover, the presence of an aromatic ring in the amide substituent (1d′ or 1e′) significantly reduced propagation efficiency.

**CONCLUSIONS**

Bicyclo[4.2.0]oct-7-ene-7-carboxamides of primary amines are quantitatively isomerized to bicyclo[4.2.0]oct-1(8)-ene-8-carboxamides in the presence of catalyst 2. Moreover, reaction of compound 1d to give 1d′, which is complete within 15 min, is by far the fastest ruthenium-catalyzed olefin isomerization reported to date. This isomerization of an internal olefin in a bicyclic system provides a facile approach to synthesize tetra-substituted bicyclo[4.2.0]oct-1(8)-ene-8-carboxamides.

Remarkably, bicyclic tetra-substituted $αβ$-unsaturated amides are excellent AROMP substrates for the preparation of long, alternating copolymers. Isomerized unsaturated amides 1a′, 1b′, 1c′, and 1d′ undergo alternating ROMP with cyclohexene 1.5–4 times more rapidly than previously studied 1-cyclobutene carboxylic acid esters or bicyclo[4.2.0]oct-7-ene-7-carboxylic esters. The isomerized amide AROMP reaction is compatible with a variety of amides that provide functional group handles. This facile sequence, isomerization followed by alternating ring-opening cross-metathesis of A and ring-opening cross-metathesis of B, provides an efficient entry to well-controlled architectures, enables the production of linear, soluble, and impressively long (greater than 100 and up to 400 AB units) alternating polymers with superior monomer economics, and unlocks the prospect of employing functionalized alternating and sequence-specific copolymers in multiple applications.

**ASSOCIATED CONTENT**

Supporting Information

Experimental methods to prepare amides 1 and 56 figures (Figures S1−S56) with additional experimental data and spectra. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.5b01058.

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Notes

The authors declare no competing financial interest.

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