Macrocycle Polymerization

Entropically Driven Ring-Opening-Metathesis Polymerization of Macrocyclic Olefins with 21–84 Ring Atoms[**]

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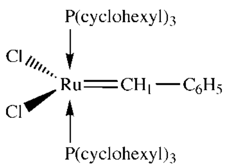
The ring-opening-metathesis polymerization (ROMP) of strained cyclic olefins has been studied extensively,[1,2] especially since Grubbs' catalyst **1**[3] and the more recently introduced "second-generation" Grubbs' catalyst **2**,[4] both of which are tolerant of many functional groups, became commercially available. The ROMP of strained cyclic olefins is mainly enthalpy-driven.



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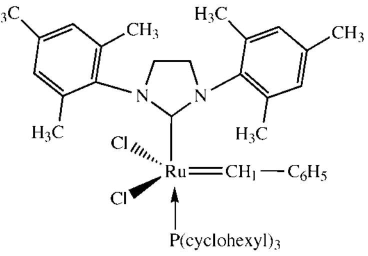

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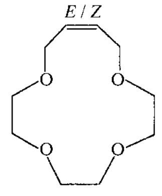

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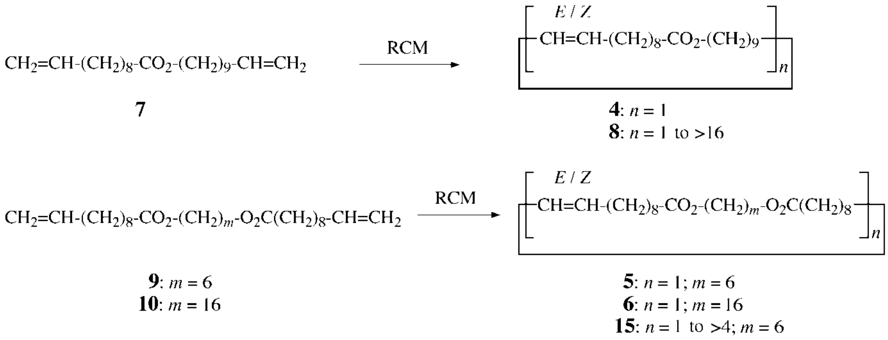
A relatively new type of ring-opening polymerization (ROP) exploits the well-known equilibria between cyclic oligomers and polymers[5–10] (Scheme 1). At high dilutions the equilibria lie heavily in favor of the cyclic oligomers, whereas at high concentrations they lie heavily in favor of the polymers. Thus, if one or more cyclic oligomers are taken neat as starting materials, and equilibrium is established, polymer synthesis results. The cyclic oligomers used as the feedstock are generally not strained, so the enthalpy change on polymerization is minimal. This type of polymerization is, therefore, mainly entropically driven, and so the process can be abbreviated ED-ROP. As a neat mixture the cyclic oligomers have relatively little translational entropy and the rings occupy limited conformations; conformational flexibility increases greatly upon conversion into polymers. Since ED-ROP is an equilibration process the polydispersity of the polymer is expected to have a value of 2.0. ED-ROP has been investigated for various types of macrocyclic oligomers,[11,12] but not for macrocyclic olefins.

$$\underbrace{(\mathrm{CycO})_n}_{\text{heavily favored by high dilution}} \quad + \quad \underbrace{\mathrm{P}_{x\text{-}n}}_{\text{or end groups}} \quad \underset{\text{CDP}}{\overset{\text{ROP}}{\rightleftharpoons}} \quad \underbrace{\mathrm{P}_x}_{\text{heavily favored by high concentration}}$$

Scheme 1. CycO = cyclic oligomer; P = polymer; CDP = cyclodepolymerization; "*x*" and "*n*" are degrees of polymerization.

Examples in which large, unstrained macrocycles (> 13 ring atoms) have been subjected to ROMP are rare,[2,13–15] and there only appear to be two examples in which the polymer has been formed in high yield, isolated, and characterized. The first was the ROMP of the 14-membered cyclic ether **3** in the presence of the catalyst **1**. This gave a polymer with $\bar{M}_n$ 65900 ($\bar{M}_n$ = number-average molar mass).[2] The second example was the ROMP of ambrettolide, an unsaturated macrolide with 17 ring atoms.[13] A neat sample of this compound was polymerized in the presence of a catalyst prepared from tungsten hexachloride and tetramethyltin to give a polymer in 95% yield with $\bar{M}_n$ 95000. Herein we show that when appropriate reaction conditions are used, unstrained macrocyclic olefins with up to 84, and possibly even more, ring atoms readily undergo entropically driven ROMP (ED-ROMP). Given that Grubbs and co-workers have recently reported an efficient method for the synthesis of very large macrocyclic olefins,[16] and that olefin-containing polymers are easily hydrogenated in the presence of decomposed metathesis catalysts,[17,18] ED-ROMP of large macrocyclic olefins is of more than theoretical interest.

In the present work the monomers **4**, **5**, and **6**, which have 21-, 28-, and 38-membered rings, respectively, were prepared



by ring-closing metathesis (RCM).[2,19–21] The monomer **4** had been synthesized previously by RCM in 70% yield.[20] In a similar procedure, the α,ω-diolefinic ester **7** and Grubbs' catalyst **1** (3 mol%) were slowly added over 24 h to dichloromethane at 25 °C to give a final concentration of 0.01 M. A mixture of cyclic oligomers **8** was thus produced in 76% yield. The cyclic structures were identified from the ^{1}H NMR spectrum of the product mixture, which indicated the absence

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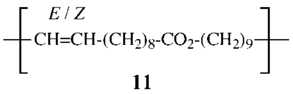
of vinyl groups, and the MALDI-TOF mass spectrum, in which the only series of peaks were attributable to cyclic oligomers. Analytical gel-permeation chromatography (GPC) showed that the cyclic monomer **4** made up 52% of the mixture. Chromatography afforded **4** as an oil in 25% yield. ^{13}C NMR spectroscopic analysis showed that both geometric isomers were present (*E*/*Z* 55:45). Similar RCM of the α,ω-diolefinic diesters **9** and **10**, but at final olefin concentrations of just 0.006 M, gave the cyclic monomers **5** and **6**, respectively, each in 67% yield and with an *E*/*Z* ratio of 80:20.

The ED-ROMP of the monomer **4**, with 21 ring atoms, was carried out by treating a 40% w/v solution in dichloromethane under a stream of nitrogen at 40 °C with Grubbs' second-generation catalyst **2** (1 mol%; Table 1, entry 1). The dichloromethane was allowed to evaporate into the nitrogen stream over 12 h and the polymer **11** was formed in 96% yield together with a mixture of cyclic oligomers (4%; see Scheme 1). The end groups of the polymer are derived from the catalyst. Once the system has reached equilibrium its composition should not change. However, the catalyst could be destroyed if necessary by reaction with methyl vinyl ether.[2] The presence of cyclic oligomers in the final mixture is to be expected, as even when neat monomers are used the final equilibrium position typically corresponds to approximately 2–3% of cyclic oligomers. Interestingly, 1) these recovered cyclic oligomers were a mixture and not just the cyclic monomer **4**, which indicates that they had also been involved in the equilibration, and 2) both the *E* and *Z* monomers reacted. The polymer formed had $\bar{M}_n$ 37000 and $\bar{M}_w$ 67500 ($\bar{M}_w$ = mass-average molar mass), based on GPC analysis (relative to a polystyrene standard). The FT-IR and ^{1}H NMR spectra were as expected for the polymer **11**. Note that the repeat units in the polymer **11** may be linked head-to-head, head-to-tail, or tail-to-tail.

Table 1: ED-ROMP of various cyclic olefins with the metathesis catalyst **2** (1 mol%) at 40 °C.[a]

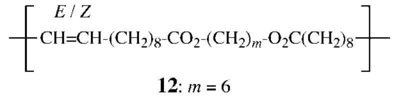
Entry	Monomer	*t*	Product ratio[b] c.o.[c]/polymer	Polymer	M_n ($\times 10^3$)[b]	M_w ($\times 10^3$)[b]
1	**4**	12 h	4:96	**11**	37.0	67.5
2	**8**	12 h	3:97	**11**	22.0	44.0
3	**5**	10 min	6:94	**12**	55.0	105.0
4	**6**	10 min	4:96	**13**	80.4	159.0
5	**5** + **6**[d]	10 min	10:90	**14**	74.4	135.0
6	**6**[e]	10 min	10:90	**13**	94.0	181.7
7	**15**	10 min	5:95	**12**	21.9	40.3

[a] See Experimental Section and main text for details of the procedure. [b] Based on GPC analysis. [c] Cyclic oligomers. [d] equimolar mixture. [e] Polymerized as a film on a microscope slide.



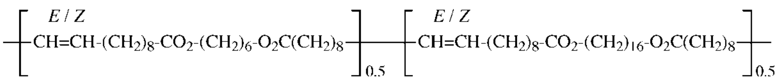
$$\left[\overset{E/Z}{\mathrm{CH{=}CH}}\mathrm{-(CH_2)_8-CO_2-(CH_2)_9} \right]$$

11



$$\left[\overset{E/Z}{\mathrm{CH{=}CH}}\mathrm{-(CH_2)_8-CO_2-(CH_2)_{\mathit{m}}-O_2C(CH_2)_8} \right]$$

12: *m* = 6
13: *m* = 16



$$\left[\overset{E/Z}{\mathrm{CH{=}CH}}\mathrm{-(CH_2)_8-CO_2-(CH_2)_6-O_2C(CH_2)_8} \right]_{0.5} \left[\overset{E/Z}{\mathrm{CH{=}CH}}\mathrm{-(CH_2)_8-CO_2-(CH_2)_{16}-O_2C(CH_2)_8} \right]_{0.5}$$

14

The cyclic monomers **5** and **6** (with 28 and 38 ring atoms, respectively) were polymerized under similar conditions, but with a reaction time in this case of just 10 min, to give the polymers **12** and **13**, respectively (Table 1, entries 3 and 4). The copolymer **14** was prepared by ED-ROMP of a mixture of the cyclic oligomers **5** and **6** (Table 1, entry 5). The monomer **6** was also polymerized by casting a film containing the metathesis catalyst **2** (1 mol%) from chloroform onto a microscope slide, followed by heating at 40 °C (Table 1, entry 6). After 10 min the polymer **13** could be peeled off as a selfstanding film. GPC analysis showed it to have $\bar{M}_n$ 94000 and $\bar{M}_w$ 181700.

The feedstock for ED-ROMP need not be a pure monomer: a mixture of cyclic oligomers will suffice, but only cyclic compounds may be present. An alternative method to RCM for the synthesis of a mixture of cyclic oligomers is cyclodepolymerization (CDP).[2,22] This is simply the reverse of ED-ROP and it has been suggested that such reactions could form a basis for methods for recycling condensation polymers[12] (see Scheme 1). CDP involves the treatment of polymers in dilute solution, typically 2% w/v,[12] with a catalyst that will reversibly cleave the linkages between the polymer repeat units. As a result of the low concentration, the ring–chain equilibrium is shifted in favor of the cyclic oligomers. This method of cyclic-oligomer synthesis produces a cleaner product than RCM because very few end groups are present in the CDP system. Thus, the CDP product contains very few linear species. CDP is best carried out using the second-generation catalyst **2**. Treatment of the polymer **11** with **2** (1 mol%) in dichloromethane at 40 °C for 2 h gave a mixture of cyclic oligomers **8** in 51% yield. GPC analysis showed the mixture **8** to consist of the cyclic monomer **4** (52%), cyclic dimer (30%), cyclic trimer (7%), cyclic tetramer (4%), and higher cyclic oligomers (7%). When these were polymerized under similar conditions to those used for the monomer **4**, the polymer **11** was produced in 97% yield with $\bar{M}_n$ 22000 and $\bar{M}_w$ 44000 (Table 1, entry 2). It was clear that the cyclic monomer, dimer, and trimer had undergone polymerization, which indicates that ED-ROMP occurs successfully with 21-, 42- and 63-membered macrocycles. The CDP of the polymer **12** under similar conditions to those used with the polymer **11** gave the cyclic oligomers **15** in 93% yield. GPC analysis showed the mixture to be composed of the cyclic monomer **5** (48%), cyclic dimer (17%), cyclic trimer (8%), and cyclic tetramer (5%). When the cyclic oligomers **15** were subjected to ED-ROMP under the standard conditions, the polymer **12** was reformed in 95% yield (Table 1 entry 7). GPC analysis of the product indicated that less than 2% of the cyclic dimer remained. Thus, ED-ROMP can be carried out successfully with a mixture of monomer, dimer, and trimer, thus showing that up to 84-membered rings can take part in ROMP.

To determine the effect of concentration on the yield of polymer, the monomer **4** was treated at various concentrations in dichloromethane with the second-generation catalyst **2** at 40 °C for 12 h, and the equilibrated mixture was analyzed by GPC. The results are summarized in Table 2. It is apparent from these experiments that the balance between cyclic oligomers and polymer is still heavily in favor of the latter at a concentration of 50% w/v. This observation suggests it may be possible to polymerize solid monomers in concentrated solutions at 40 °C.

Table 2: Distribution of cyclic oligomers and polymer obtained from equilibrations of **6** in dichloromethane at 40 °C with the catalyst **2** (1 mol%).

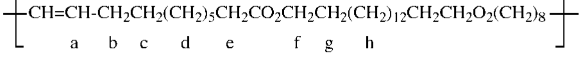
Entry	Initial conc.[a] [g/100 mL]	Product ratio[b] c.o.[c]/polymer	M_n ($\times 10^3$)[b]	M_w ($\times 10^3$)[b]
1	neat	4:96	36.8	67.4
2	50	3:97	33.4	60.1
3	2.0	57:43	16.2	25.5
4	0.5	100:0	–	–

[a] Initial concentration. [b] Based on GPC analysis. [c] Cyclic oligomers.

In conclusion, the range of cyclic olefins that can undergo ROMP can be increased substantially by using high monomer concentrations and ED-ROMP can be carried out successfully with macrocycles that have up to 84, and possibly even more, ring atoms. The $\bar{M}_n$ values obtained were as high as 94000 with polydispersities close to 2.0. Finally, when RCM is carried out in organic synthesis in the presence of very active metathesis catalysts, it should be borne in mind that equilibration of the cyclic monomer to give a series of cyclic oligomers may occur, that any polymer formed may be converted back into cyclic compounds by CDP, and that at high concentrations the cyclic oligomers may take part in ED-ROMP.

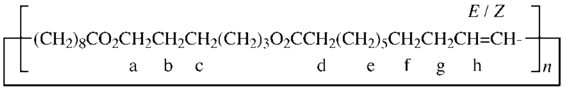
Experimental Section

Typical ED-ROMP: The cyclic oligomer **6** (100 mg, 0.179 mmol) was dissolved in dichloromethane (0.25 mL). The catalyst **2** (1.51 mg, 1 mol%) was then added and the mixture was stirred magnetically at 20 °C under a stream of nitrogen. The dichloromethane evaporated within 4 h to leave the polymeric product as a gum. A small portion of the product was analyzed by GPC (see Table 1 for results) and the rest was dissolved in dichloromethane and precipitated with methanol to give **13** (80 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$–1.40 (m, 44H, H-d and H-h), 1.58–1.70 (m, 8H, H-c and H-g), 1.94–2.04 (m, 4H, H-b), 2.30–2.38 (m, 4H, H-e), 4.04–4.14 (t, $J = 6.59$ Hz, 4H, H-f), 5.36–5.42 ppm (m, 2H, H-a).



$$\left[\underset{a}{\overset{E/Z}{\mathrm{CH{=}CH}}}\text{-}\underset{b}{\mathrm{CH_2}}\underset{c}{\mathrm{CH_2}}\underset{d}{\mathrm{(CH_2)_5}}\underset{e}{\mathrm{CH_2CO_2}}\underset{f}{\mathrm{CH_2}}\underset{g}{\mathrm{CH_2}}\underset{h}{\mathrm{(CH_2)_{12}}}\mathrm{CH_2CH_2O_2(CH_2)_8}\right]$$

CDP of **12:** The polymer **12** (200 mg, 0.474 mmol) was dissolved in dichloromethane (20 mL), and **2** (4.02 mg, 1 mol%) was added. The resulting mixture was stirred at 40 °C under nitrogen for 2 h. The solvent was then evaporated rapidly under vacuum and the product was purified by column chromatography (alumina, dichloromethane as eluent). This gave the mixture **14** as a gray, waxy solid (186 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$–1.50 (m, 24H, H-c and H-e), 1.58–1.74 (m, 8H, H-b and H-f), 1.94–2.10 (m, 4H, H-g), 2.26–2.36 (m, 4H, H-d), 4.00–4.20 (m, 4H, H-a), 5.35–5.45 ppm (m, 2H, H-h); MALDI-TOF mass spectrum of the product (doped with Na^+ in the form of NaBr, dithranol matrix) showed a series of mass peaks corresponding to a mixture of products, from the cyclic monomer (445, [monomer+Na]$^+$) to the cyclic hexamer (2558, [hexamer+Na]$^+$). The GPC analysis is given in the main text.



$$\left[\mathrm{(CH_2)_8CO_2}\underset{a}{\mathrm{CH_2}}\underset{b}{\mathrm{CH_2}}\underset{c}{\mathrm{CH_2(CH_2)_3}}\mathrm{O_2C}\underset{d}{\mathrm{CH_2}}\underset{e}{\mathrm{(CH_2)_5}}\underset{f}{\mathrm{CH_2}}\underset{g}{\mathrm{CH_2}}\underset{h}{\overset{E/Z}{\mathrm{CH{=}CH}}}\text{-}\right]_n$$

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