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Ring-opening metathesis polymerization with [2+2]-crosslinking to create new materials

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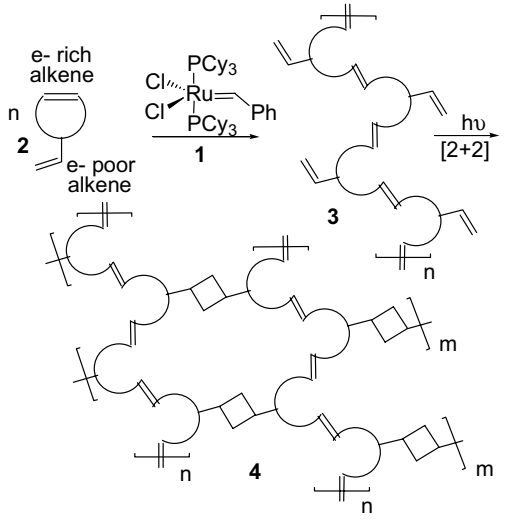
Abstract—There are almost no examples of Grubbs'-type ring-opening metathesis polymers that have been [2+2]-crosslinked. Two new monomers, **6** and **10**, were used to construct two novel linear soluble polymers **7** and **11**, bearing photochemically labile moieties for [2+2]-cycloaddition reactions. These soft polymers were photocrosslinked into very hard polymers, **8** and **12**. Potential advantages of these new bioinspired materials include: (1) ready processing into flat, round, and cylindrical shapes; (2) reasonably low toxicity due to trace amounts of catalyst needed; and (3) rapid rate of polymerization and crosslinking that avoids acids and bases.

The recent discovery of well-defined transition metal catalysts for the metathetical polymerization of olefinic compounds makes available a wide range of unique polymeric materials from soluble ROMP supports.[1] The most effective catalysts have been those derived from ruthenium such as **1** in Scheme 1; these have been developed and promulgated by Grubbs.[1a,2] Other catalyst systems include molybdenum-, rhenium-, and tungsten-based carbenoids.[3] ROMP has mostly found widespread use in the synthesis of new polymers.[1] Driven by the release of ring strain in a cyclic olefin, the overwhelming majority of polymerizations have involved the use of bicyclo[2.2.1]heptene systems such as norbornene and various oxo- and aza- and annulated congeners.[4] This chain polymerization is initiated by a reaction between metal alkylidene **1** and a cyclic olefin (i.e., **2**). Never examined as hard biomaterials, we believe these ROMP materials show great promise in biomedical applications.

This communication investigates the chemical synthesis of new materials using ring-opening metathesis polymerization (ROMP) to construct **3**[5] with a subsequent photochemically-mediated crosslinking to prepare **4**.[6] The new polymers discussed herein are designed to specifically harden under controlled and mild conditions with light. We wanted to investigate a photochemical [2+2]-cycloaddition with linear ROMP chains to avoid physiologically-incompatible acid- or base-mediated methods. Note that in the design of monomer precursor **1**, two different alkenes had to be devised. An electron-rich and cyclic alkene, strained in a norbornene ring system, would function as the ROMP alkene. The other alkene would be pendant and electron poor by activation with a conjugated ester carbonyl; this would be ideal for the [2+2].



Scheme 1. ROMP with [2+2]-photocrosslinking.

Keywords: ROMP; Photocycloaddition; Crosslink; [2+2].
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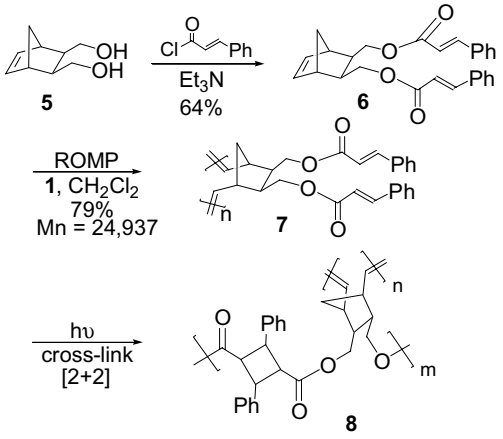
The two general cases studied in this report contained activated alkenes from cinnamates and coumarins that could be photochemically [2+2]-crosslinked. Of some importance to this work in the early stages was the lack of information in the literature because there was little known about a sequential ROMP reaction and a [2+2]-photocycloaddition.[7] A small handful of other ROMP/cycloadditions such as Diels–Alder reactions had been studied, however.[8] We hoped these studies would construct linear ROMP polymers with a thick 'toothpaste-like' consistency to fill irregular ectopic shapes in bones and teeth and, after filling the gaps, it can be treated with light to form a hard biomaterial for use as a temporary replacement.[9]

We intended to use degradable carboxylate side chains which eventually would become cinnamate and coumarin esters imbedded in the polymer. Once ROMPed and [2+2]-photocrosslinked, a hard polymer of almost any required dimensions is afforded.[12] These preliminary studies now show (vide infra) very hard disks (1×0.33 cm) or thin films can be formed, in addition, the polymer assumes the shape of almost any vessel. The advantage of using a metathesis-based strategy is the flexibility afforded by this mild polymerization and its ability to tolerate functional groups. In addition, only traces of the Ru catalyst **1** are used.[10] Also, better mechanical strength can be obtained by the linear (ladder like) crosslinking throughout the polymer chain length.

In order to obtain the described compounds, easily prepared nonbornene diol **5** was to be the precursor to the cinnamate ester polymers (Scheme 2).[11] To synthesize the dicinnamate monomer **6**, diol **5** was esterified with dicyclohexylcarbodiimide (DCC) and cinnamic acid to afford **6** in 53% yield.[12] In an effort to improve the yield of **6**, diol **5** was treated with cinnamoyl chloride in the presence of triethylamine and gave a 64% yield (Scheme 2). Thus, the second approach was subsequently always followed to synthesize **6**.

Grubbs' first-generation benzylidine catalyst **1** (5 mg) promoted the successful ring-opening metathesis polymerization of **6** (2.00 mmol) in CH_2Cl_2 (3.5 mL) in 2 min. The linear soluble polymer **7** (ca. 6:1 *trans*:*cis*) formed in 79% with a M_n of 25,000 and it had a toothpaste-like consistency. Next, the dicinnamate ROMP polymer **7**[13] was subjected to photocrosslinking using a 400 W Hanovia lamp to yield the hard off-white insoluble polymer **8** as a potential biomaterial in essentially quantitative yield.

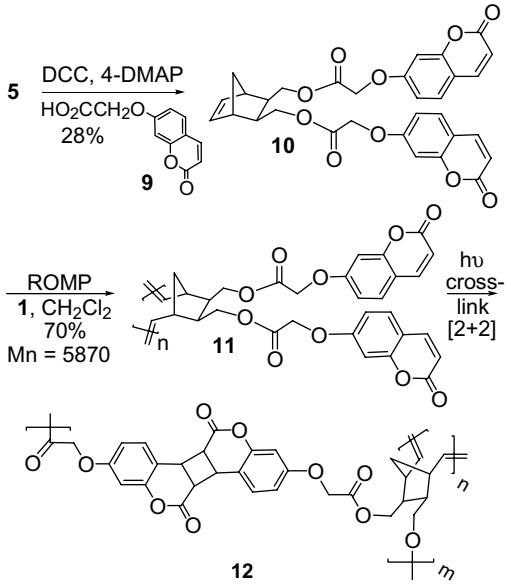


Scheme 2. ROMP and crosslinking of cinnamates.

The utility of photopolymerizable coumarin functionalities was also studied in Scheme 3. The precursors for the coumarin ester polymer were diol **5**[11] and coumarin acid **9**.[14] The acid was then subjected to DCC esterification with diol **5**, constructing coumarin ester monomer **10** in a modest 28% yield.[15]

The coumarin ester monomer **10** was polymerized using Grubbs' catalyst **1** in CH_2Cl_2 as solvent. The total reaction time was 3–5 min. The linear soluble polymer **11** (ca. 8:1 *trans*:*cis*) [16] was formed in 77% from **10** with a M_n of 6000. Next, polymer **17** was subjected to photocrosslinking using a 400 W Hanovia lamp to yield the off-white insoluble polymer **12** as a potential bone scaffold. Coumarin families can undergo [2+2]-cycloaddition reactions when they are irradiated with a wavelength of UV light from 290 nm to 310 nm, respectively. The cyclobutane ring in **8** and **12** is known to be cleaved by a retro-[2+2] to regenerate cinnamate and coumarin when irradiated below 253 nm.[17] Hence a faster artificial degradation of these biomaterials may be possible if the natural process is too slow. The cinnamate ester precursor was also easier to synthesize than the coumarin ester precursor and gave better yields; hence, the cinnamate ester precursor may be a more promising biomaterial.

In conclusion, two novel monomers, **6** and **10**, and two novel linear soluble polymers, **7** and **11**, both bearing photochemically labile moieties were successfully synthesized. These linear soluble polymers were photocrosslinked into insoluble hard polymers **8** and **12**.



Scheme 3. ROMP and crosslinking of coumarins.

Advantages of these photopolymerizable materials include easy processing into complex shapes, relative nontoxicity, ease of polymerization, and fast crosslinking times.

Acknowledgements

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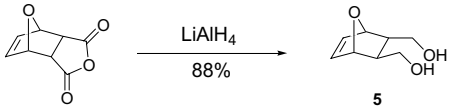
10. Any traces of Ru metal complexes are probably removed when polymers are precipitated during purification.
11. Diol **5** was prepared by known procedure, see: Millward, D. B.; Sammis, G.; Waymouth, R. M. *J. Org. Chem.* **2000**, *65*, 3902–3909,



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12. **Compound 6**: mp = 134.5–136.0 °C ^{1}H NMR ($CDCl_3$): δ 7.60–7.70 (d, 2H), 7.20–7.50 (m, 10H), 6.34–6.42 (d, 2H), 6.28–6.34 (s, 2H), 4.80 (s, 2H), 4.30–4.40 (dd, 2H), 4.10–4.20 (dd, 2H), 2.0–2.10 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 166.4, 145.0, 135.4, 134.0, 130.1, 129.0, 128.0, 118.0, 80.3, 63.7, 39.2. IR 1712.0, 1265.5. Anal. Calcd for $C_{26}H_{24}O_5$: C, 74.98; H, 5.81; Found: C, 74.64; H, 5.91.
13. **Compound 7**: ^{1}H NMR ($CDCl_3$): δ 7.56–7.70 (d, 2H), 7.20–7.50 (m, 10H), 6.30–6.48 (d, 2H), 5.60–5.85 (d, 2H), 4.60–4.80 (s, 2H), 4.20–4.44 (d, 4H), 2.50 (s, 2H). GPC (M_n = 25,000; Disp = 1.41).
14. Coumarin ester derivative **9** was synthesized as reported by Saegusa, T.; Sada, K.; Chujo, Y. *Macromolecules* **1990**, *23*, 2693–2697.
15. **Compound 10**: mp = 164.2–165.0 °C. ^{1}H NMR ($CDCl_3$): δ 7.66 (d, 2H), 7.43 (d, 2H), 6.90–6.88 (dd, 2H), 6.78 (d, 2H), 6.35 (s, 2H), 6.29 (d, 2H), 4.74 (s, 6H), 4.46 (dd, 2H), 4.21 (dd, 2H), 2.05 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 167.6, 161.0, 161.0, 156.0, 143.1, 135.5, 129.0, 113.7, 113.3, 113.0, 101.0, 80.2, 65.2, 64.8, 39.2. MS, *m/z* (M + H): calculated for $C_{30}H_{24}O_{11}$ 560 + 1 = 561 and found 561.
16. **Compound 11**: ^{1}H NMR ($CDCl_3$): δ 7.56 (2H), 7.26–7.30 (4H), 6.66–6.78 (4H), 6.17 (2H), 5.58–5.73 (2H), 4.67 (4H), 4.38–4.26 (4H), 2.44 (2H). GPC (M_n = 6000; Disp = 1.03).
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