

Volume 36, Number 9 May 6, 2003

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Communications to the Editor

Synthesis of Degradable Poly(methyl methacrylate) via ATRP: Atom Transfer Radical Ring-Opening Copolymerization of 5-Methylene-2-phenyl-1,3-dioxolan-4-one and Methyl Methacrylate

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Received January 8, 2003 Revised Manuscript Received March 3, 2003

Free radical ring-opening polymerization has been proposed as a useful route for the synthesis of polymers with various functional groups, such as ester, ether, ketone, amide, and carbamate, in their backbone.¹ The addition of unsaturated heterocycles to polymerization of commercial monomers could improve the properties of the resulting polymers, such as thermal stability, low volume shrinkage during polymerization, and degradability.^{2–4} When conventional radical initiators were used for such (co)polymerization reactions, the molecular weight of the resulting (co)polymers could not be controlled, and molecular weight distributions were quite broad.

Controlled/living radical polymerizations (CRP) provide well-defined (with predicted molecular weight, narrow molecular weight distribution, and high degree of end-functionalization) polymers.⁵ Among the various CRP methods, atom transfer radical polymerization (ATRP) is probably the most robust due to its ability to copolymerize a broad range of monomers with various functional groups and its tolerance to solvents of different polarity as well as to impurities often encountered in industrial systems.⁶

There have been several reports on the free radical ring-opening polymerization of cyclic ketene acetals

Chart 1



(Chart 1) using TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy radical)⁷ and ATRP.⁸ Since the cyclic ketene acetal is a relatively unreactive monomer, its copolymerization with conventional vinyl monomers is difficult, especially with a reactive monomer such as methyl methacrylate (MMA). The low reactivity of the cyclic ketene acetal is due to the presence of two electrondonating substituents which cannot stabilize the resulting radical. We considered that it would be interesting to replace one of them by a carbonyl group and generate a captodative system.⁹ Such a monomer has previously been considered for radical ring-opening polymerization.¹⁰ Therefore, 5-methylene-2-phenyl-1,3-dioxan-4one (MPDO; Chart 1, e) should be a highly reactive monomer due to the presence of a radical stabilizing α -ester group. The (co)polymer formed by radical ringopening polymerization of MPDO has a fully ringopened structure with α -keto ester groups in the backbone providing potential sites for biodegradability and photodegradability. The high reactivity of MPDO should enhance the probability for its incorporation into the backbone in copolymerization reactions with styrene and (meth)acrylates, and the resulting copolymers with α -keto ester groups randomly distributed along the chain should preserve the capability for both biodegradability and photodegradability.

MDPO was prepared according to the previously reported method,^{10a,b} with some modification.¹¹ The atom transfer radical copolymerization of MPDO with MMA was carried out in anisole using CuBr/CuBr₂/ PMDETA (*N*,*N*,*N*,*N'*,*N'*-pentamethyldiethylenetriamine) as a catalyst and ethyl 2-bromoisobutyrate as an initiator, as shown in Scheme 1.¹² The reaction conditions and the results of the copolymerization are listed in Table 1.

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Scheme 1



Table 1. Conditions and Results for Copolymerization of MPDO and MMA

| | temp (°C) | [MPDO]:[MMA] | time (min) | conv of MMA (%) ^{d} | conv of MPDO (%) ^{d} | $M_{ m n,th}^{e}$ | $M_{\rm n}({ m GPC})^f$ | PDI ^g |
|------------------------|-----------|--------------|---------------|---|--|-------------------|-------------------------|------------------|
| 1 ^a | 90 | 1:10 | 30 | 88 | 89 | 15 760 | 15 730 | 1.24 |
| 2a ^a | 70 | 1:10 | 90 | 85 | 91 | 15 360 | 15 420 | 1.21 |
| $\mathbf{2b}^{b}$ | 70 | 1:5 | 90 | 83 | 88 | 14 260 | 13 930 | 1.28 |
| 2c ^c | 70 | 1:3 | 90 | 81 | 86 | 15 790 | 16 810 | 1.31 |
| 3 ^a | 50 | 1:10 | 180 | 83 | 88 | 14 980 | 15 070 | 1.22 |
| | | | | | | | | |

^{*a*} Reaction conditions: $[I]_0/[CuBr_2]_0/[PMDETA]_0/[PMDETA]_0/[MPDO]_0/[MMA]_0 = 1/1/0.05/1.05/15/150. ^{$ *b* $} [I]_0/[CuBr_2]_0/[PMDETA]_0/[MPDO]_0/[MMA]_0 = 1/1/0.05/1.05/25/125. ^{$ *c* $} [I]_0/[CuBr_2]_0/[PMDETA]_0/[PMDETA]_0/[MPDO]_0/[MMA]_0 = 1/1/0.05/1.05/40/120. ^{$ *d*} Measured by gas chromatography. ^{*e*} Theoretical number-average molecular weight was calculated from the conversion of the monomers. ^{*f*} Determined by GPC using tetrahydrofuran as eluent with poly(methyl methacrylate) standards. ^{*g* $} Polydispersity index = <math>M_w/M_n$.



Figure 1. Relationship of $\ln[M]_0/[M]$ and conversion with polymerization time in the copolymerization of MPDO with MMA ([MPDO]:[MMA] = 1:10).

First, the ATRP copolymerization of MPDO and MMA ([MPDO]:[MMA] = 1:10) was carried out at 90 °C to produce poly(MDPO-*co*-MMA), **1**. Conversion of the two monomers reached ~90% within 30 min. The number-average molecular weight of the resulting copolymer **1**, measured by GPC, was $M_n = 15$ 730 g/mol, which is well matched with the theoretical value ($M_{n,th} = 15$ 760 g/mol), and the polydispersity index was $M_w/M_n = 1.24$.

To investigate the "living" nature of the copolymerization and monomer conversion behavior, copolymerization ([MPDO]:[MMA] = 1:10) was also carried out at 70 and 50 °C. Comonomer conversion greater than 80% was reached within 90 min at 70 °C and required 180 min at 50 °C. As shown in Figure 1, plotting $\ln[M]_0/[M]$ against polymerization time afforded straight lines for both MPDO and MMA, demonstrating the constant concentration of the growing radicals. The ratio of monomer consumption for MPDO and MMA is almost constant regardless of time, as shown in Figure 1. The linear molecular weight–conversion profile (Figure 2) indicates that that the molecular weight can be simply controlled by polymerization time. The number-average molecular weights of the resulting polymers, **2a** and **3**,



Figure 2. Dependence of M_n and M_w/M_n on conversion in the copolymerization of MPDO with MMA ([MPDO]:[MMA] = 1:10).

measured by GPC are close to theoretical values, and the polydispersity indexes are reasonably narrow (about 1.2). These results confirmed that the copolymerization of 10 mol % MPDO with MMA is well-controlled under ATRP conditions.

The copolymerization reaction was also carried out with different ratios of MPDO and MMA. Conversion reached over 80% within 90 min at 70 °C regardless of the monomer ratio ([MPDO]:[MMA] = 1:5 (**2b**) and 1:3 (**2c**)). The number-average molecular weights of the resulting polymers were measured by GPC and were well matched with theoretical values, and the polydispersity indexes were in the range 1.2-1.3. The linear kinetic plots for consumption of monomers indicated a constant concentration of growing radicals, and the monomer consumption ratio of MPDO and MMA was similar regardless of the initial ratio of MPDO to MMA.

The structure of the copolymer was examined by ¹H NMR spectroscopy (Figure 3). The ¹H NMR spectrum of MPDO monomer shows a peak at 6.6 ppm, corresponding to the acetal proton, but this peak entirely shifts to 5.9 ppm, corresponding to a methine proton next to the ester oxygen of the ring-opened unit in the



Figure 3. ¹H NMR spectra of MPDO and poly(MPDO-stat-MMA) 1 (CDCl₃, 300 MHz; *: solvent and residual THF peaks).



^a Reaction conditions: (A) KOH (10 equiv), 2-propanol/2-butanone, 30 °C, 18 h; (B) UV light, 40 °C, 2 h.



Figure 4. GPC curves of the polymers: (a) copolymer **1**, (b) after hydrolysis of **1**, (c) after photolysis of **1**.

spectrum of the corresponding polymer, which indicates essentially complete ring opening of MPDO during the reaction. The ¹H NMR spectrum of the polymer shows peaks at 7.4 and 2.0-2.7 ppm, corresponding to aromatic and aliphatic protons of the MPDO units, respectively. Also, it shows all of the peaks corresponding to the protons of MMA units. From the ¹H NMR measurement, it is confirmed that MPDO is successfully incorporated to the copolymer with a ring-opened structure.

Additional evidence for the random incorporation of MPDO by ring-opening copolymerization is obtained by hydrolysis and photolysis of the polymer. To examine the copolymerization behavior and degradability of the copolymer, hydrolysis was carried out under basic conditions¹³ and photolysis by photoirradiation,¹⁴ as shown in Scheme 2. After hydrolysis the molecular weight of copolymer **1** was reduced to $M_n = 1620$ g/mol (about 10 times lower than the original polymer), with polydispersity index $M_w/M_n = 1.89$; after photolysis, $M_n = 1480$ g/mol and the polydispersity was 1.96 (Figure

4). This means that MPDO with a ring-opened structure was randomly incorporated into the PMMA chain.

In conclusion, a photodegradable and hydrolytic (i.e., also biodegradable) degradable PMMA with low polydispersity index were synthesized by copolymerization of MMA and MPDO by ATRP. The rate of incorporation of MPDO and MMA into the copolymer was the same regardless of the polymerization temperature and monomer feed ratio under typical ATRP conditions.

Acknowledgment. Financial support from the members of the CRP Consortium at Carnegie Mellon University, National Science Foundation (DMR-00-90409), and Korea Science and Engineering Foundation (KO-SEF) for postdoctoral fellowship support (I.S.C.) is acknowledged. We thank Professor H. Hall and Professor T. Endo for many stimulating discussions.

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- (11) The cyclic acrylate was synthesized by the reaction of β -chlorolactic acid with benzaldehyde in 45% yield, followed by dehydrochlorination with diisopropylamine in ether in almost quantitative yield. The crude product was purified by distillation: bp 83–84 °C (0.1 mmHg). The polymerization was carried our immediately after purification of the monomer. The ¹H NMR spectrum of the monomer shown in Figure 3 indicates that the monomer is stable in solution. However, it polymerized spontaneously when exposed to air.
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- (13) The hydrolysis was carried out with potassium hydroxide (10 equiv) in 2% w/v 2-propanol/2-butanone (v/v = 50/50) solution (solute, 100 mg; solvent, 5 mL) at 30 °C for 18 h.
- (14) The irradiation was carried out with 2% w/v anisole solution (solute, 100 mg; solvent, 5 mL) in a Rayonet photochemical chamber reactor equipped with 12 RPR-254 nm lamps at 40 $^\circ$ C for 2 h.

MA034029+