Block copolymerization of 2,2-dimethyltrimethylene carbonate with adipic anhydride catalyzed by lanthanum tris(2,6-di-tert-butyl-4-methylphenolate)

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Abstract: Tetrahydrofuran-soluble block copolymer of 2,2-dimethyltrimethylene carbonate with adipic anhydride [poly(DTC-b-AA)] containing 64.7/35.3 DTC/AA in molar ratio with \( M_n \) of \( 1.23 \times 10^4 \) and \( M_w/M_n \) of 1.64 was synthesized by lanthanum tris(2,6-di-tert-butyl-4- methylphenolate) catalyst at 25 °C in 32 min. The copolymer was characterized by SEC, \(^1\)H NMR and DSC. Copolymers with AA block from 8.5 % to 50.8 % were prepared by changing the solvent and feeding ratio of DTC/AA.

Introduction

Poly(adipic anhydride) (PAA) attracts increasing attention as a new biomaterial which has the advantage of rapid degradation rate [1]. Its half-degradation time is one to two weeks while that of polyesters such as polylactide (PLA), poly(ε-caprolactone) (PCL), poly(trimethylene carbonate) (PTMC) and poly(2,2-dimethyltrimethylene carbonate) (PDTC) are around one year or even longer [2,3]. However, PAA suffers low mechanical strength due to its low molecular weight usually less than 5000 g/mol and its hydrolytic sensitivity of moisture. Various catalysts or initiators for adipic anhydride (AA) polymerization have been reported including aluminum triisopropoxide [4], stannous octoate [5], triethylamine [3, 6, 7]; dibutylmagnesium [8], potassium poly(ethylene glycol)ate [9] and rare earth trisphenolates [10,11].

Ring-opening copolymerization of adipic anhydride with other cyclic esters is a feasible method to enhance PAA's mechanical strength and to adjust the degradation rate of polyesters. Block copolymer poly(CL-b-AA) (19,000-27,000) was synthesized after 40 h polymerization using Al(OiPr)\(_3\) as the initiator [4]. Potassium poly(ethylene glycolate) was reported as the initiator to prepare copolymers of PAA-PEG-PAA and PAA-PCL-PEG-PCL-PAA [12]. However, only PTMC/PAA blends were obtained instead of TMC-co-AA copolymers in their copolymerization attempts [6]. To the best of our knowledge, no reports were concerned about successful copolymerization of AA with cyclic carbonates. Our research group has reported high effective rare earth phenolate catalysts for polymerizations of DTC, TMC, CL and AA [13-17]. This paper describes the preparation of block copolymers of poly(DTC-b-AA) catalyzed by single component lanthanum tris(2,6-di-tert-butyl-4- methylphenolate) (La(OAr)\(_3\)) compound.
Results and discussion

Rapid termination and transfer reactions of inter- and intra-anhydride molecules during AA polymerization produce low molecular weight polymers. Furthermore, PAA is insoluble in toluene and THF, which formed a heterogeneous polymerization mixture and limited PAA chain growing. Similar results were also reported previously by Jérôme [4], Deng [9] and our group [10].

Homo- and sequential copolymerizations of DTC with AA catalyzed by La(OAr)₃ were successfully achieved as listed in Tab. 1. The copolymerization products were elastic solid granules, differing from homopolymers of PDTC (a crisp mass) and PAA (brittle white powder). The block copolymers of 2,2-dimethyltrimethylene carbonate with adipic anhydride [poly(DTC-b-AA)] initiated by La(OAr)₃ had high molecular weights (11.6~15.9×10⁴) and moderate Mₚ/Mₘ (1.50~1.77). In addition, DTC/AA (molar ratio) in the copolymer decreased with lowering DTC/AA molar ratio in the feed (Tab. 1).

Tab. 1. Homo- and copolymerization of DTC with AA catalyzed by La(OAr)₃.

<table>
<thead>
<tr>
<th>Run</th>
<th>Solvent</th>
<th>DTC/AA b (feeding)</th>
<th>Time c (min)</th>
<th>Yield (%)</th>
<th>DTC/AA d (polymer)</th>
<th>Mₘ e (10⁴)</th>
<th>Mₚ/Mₘ e</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₂Cl₂</td>
<td>0/100</td>
<td>30</td>
<td>82.4</td>
<td>0/100</td>
<td>0.15 g</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>toluene</td>
<td>0/100</td>
<td>30</td>
<td>71.5</td>
<td>0/100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>CH₂Cl₂</td>
<td>100/0</td>
<td>2</td>
<td>90.1</td>
<td>100/0</td>
<td>5.35 h</td>
<td>1.62</td>
</tr>
<tr>
<td>4</td>
<td>toluene</td>
<td>100/0</td>
<td>2</td>
<td>96.0</td>
<td>100/0</td>
<td>12.0</td>
<td>1.65</td>
</tr>
<tr>
<td>5</td>
<td>CH₂Cl₂</td>
<td>75.0/25.0</td>
<td>2+30</td>
<td>73.8</td>
<td>84.7/15.3</td>
<td>12.3</td>
<td>1.53</td>
</tr>
<tr>
<td>6</td>
<td>CH₂Cl₂</td>
<td>66.7/33.3</td>
<td>2+30</td>
<td>74.1</td>
<td>81.8/18.2</td>
<td>13.0</td>
<td>1.50</td>
</tr>
<tr>
<td>7</td>
<td>CH₂Cl₂</td>
<td>50.0/50.0</td>
<td>2+30</td>
<td>74.6</td>
<td>64.7/35.3</td>
<td>12.3</td>
<td>1.64</td>
</tr>
<tr>
<td>8</td>
<td>CH₂Cl₂</td>
<td>33.3/66.7</td>
<td>2+30</td>
<td>75.2</td>
<td>49.2/50.8</td>
<td>11.6</td>
<td>1.77</td>
</tr>
<tr>
<td>9</td>
<td>toluene</td>
<td>75.0/25.0</td>
<td>2+30</td>
<td>75.9</td>
<td>91.5/8.5</td>
<td>15.9</td>
<td>1.59</td>
</tr>
<tr>
<td>10</td>
<td>toluene</td>
<td>66.7/33.3</td>
<td>2+30</td>
<td>75.3</td>
<td>88.8/11.2</td>
<td>15.1</td>
<td>1.61</td>
</tr>
<tr>
<td>11</td>
<td>toluene</td>
<td>50.0/50.0</td>
<td>2+30</td>
<td>74.1</td>
<td>72.1/27.9</td>
<td>14.4</td>
<td>1.62</td>
</tr>
</tbody>
</table>

a Conditions: ([DTC]+[AA])/[La(OAr)₃] = 500, [DTC+AA] = 3.0 mol/L, 20 °C. b Molar ratio. c 2 min for DTC and then followed by 30 min for AA. d Molar ratio calculated from ¹H NMR. e SEC measurement. f [AA] = 1.0 mol/L. g Calculated from ¹H NMR. h [DTC]/[La(OAr)₃] = 250, [DTC] = 1.5 mol/L.

The percentages of AA in the copolymers obtained from methylene chloride were higher than those from toluene in the same conditions. The reason seemed that the insolubility of PAA segment in toluene led to precipitation, while methylene chloride was a preferable solvent for homogeneous AA polymerization [10]. Furthermore, DTC polymerization catalyzed by La(OAr)₃ proceeded via a coordination anionic mechanism and low polar solvent toluene was more appropriate than methylene chloride for the polymerization [13]. Therefore, the AA fraction of the copolymer could be easily adjusted by changing either the solvent or DTC/AA feeding ratio.

The effect of temperature on the block copolymerization of DTC with AA was investigated, and the results are listed in Tab. 2 (run 1, 3 and 4). The copolymerization yield, molecular weight and composition of the copolymer (molar ratio of DTC/AA) showed no distinct relation to the copolymerization temperature (in the range of 2 to 40 °C), which might be that both DTC and AA polymerizations were fast and little affected by temperature. However, Mₚ/Mₘ of the copolymer tended to be broader at high temperature. Similar results were reported in DTC polymerizations [18]. Catalyst concentration ([DTC]+[AA])/[La(OAr)₃] had little effect on the copolymerization of DTC with AA (run 1, 2, 4 and 5 in Tab. 2). La(OAr)₃ also exhibited high catalytic activity.
toward the copolymerization with \([\text{[DTC]}+\text{[AA]}]/\text{[La(OAr)}_3] = 800\).

**Tab. 2.** Copolymerization of DTC with AA at various temperatures and \([\text{[DTC]}+\text{[AA]}]/\text{[La(OAr)}_3] \) ratios.\(^a\)**

<table>
<thead>
<tr>
<th>Run</th>
<th>Temperature (°C)</th>
<th>([DTC]+[AA])/[La(OAr)] (_3)</th>
<th>Yield (%)</th>
<th>DTC/AA (^b) (polymer)</th>
<th>(M_n) (^c) ((10^4))</th>
<th>(M_w/M_n) (^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>500</td>
<td>78.1</td>
<td>66.0/34.0</td>
<td>10.6</td>
<td>1.38</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>800</td>
<td>75.8</td>
<td>64.3/35.7</td>
<td>11.3</td>
<td>1.37</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>500</td>
<td>74.6</td>
<td>64.7/35.3</td>
<td>12.3</td>
<td>1.64</td>
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<tr>
<td>4</td>
<td>40</td>
<td>500</td>
<td>78.7</td>
<td>64.5/35.5</td>
<td>13.4</td>
<td>1.76</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>800</td>
<td>76.1</td>
<td>66.4/33.6</td>
<td>14.6</td>
<td>1.52</td>
</tr>
</tbody>
</table>

\(^a\) Conditions: [DTC+AA] = 3.0 mol/L, DTC/AA = 50/50 (molar ratio), (2+30) min in CH\(_2\)Cl\(_2\). \(^b\) Molar ratio calculated from \(^1\)H NMR. \(^c\) SEC measurement.

The SEC curves of the copolymer (Fig. 1) showed a single peak indicating the presence of one kind of growing chains, though a slight shoulder implied a small proportion of the remaining PDTC homopolymers. Comparing the SEC results of the PDTC block with the final poly(DTC-b-AA) copolymer, we found that the molecular weight of the poly(DTC-b-AA) copolymer increases from \(5.35 \times 10^4\) to \(12.3 \times 10^4\) and \(M_w/M_n\) retains, which proved that the macro-initiator of PDTC living chain had initiated the ring-opening polymerization of AA. The fact that molecular weights of copolymers in Tab. 1 are higher than that calculated by monomer yield and composition is the result of the differences between the DTC and AA segments and standard polystyrene calibrated in SEC measurement. In addition, copolymers of poly(DTC-b-AA) could easily dissolve in THF while homopolymer PAA could not. Therefore, copolymers were obtained rather than polymer blends.

![Fig. 1. SEC curves of the PDTC block (run 3 in Tab. 1) and the final poly(DTC-b-AA) copolymer (run 7 in Tab. 1).](image)

It is interesting that the average molecular weight of the PAA block in the poly(DTC-b-AA) was much higher than that of the homopolymer (PAA, \(M_n\approx 2,000\) \(^{10}\)). It could be presumed that the long block-copolymerized PDTC segment availed the stability of PAA living center and prevented its termination and chain-transfer reactions.
Similar results were also found in block copolymerizations of CL with AA [4].

![Image](image_url)

**Fig. 2.** $^1$H NMR spectrum of poly(DTC-b-AA) (run 7 in Tab. 1).

Fig. 2 shows the $^1$H NMR spectrum of the copolymer of run 7 in Tab. 1. Four groups of peaks are found: the single peaks at 1.0 and 4.0 ppm are attributed to $H^a$ and $H^b$ in PDTC block, respectively. The signals at 2.5 ppm and 1.75 ppm are assigned to $H^c$ and $H^d$ in PAA block. The signal at 2.40 ppm ($H^e$) is attributed to the overlap of $\alpha$-carboxyl methylene end group and $\alpha$-carbonyl methylene in the first AA unit next to PDTC block [9, 10]. The molar ratio of DTC/AA in the copolymer is about 64.7:35.3 (Fig. 2, run 7 in Tab. 1) calculated by the ratio of the signal intensities of $H^a$ to $H^d$ (Eqn. 1).

$$\frac{DTC}{AA} = \frac{I(H^a)}{I(H^d)}$$

(1)

The signals of $H^a'$ and $H^b'$ assigned to the hydrogen atoms of DTC monomers remained. The quotient between the intensities of $H^b'$ and $H^b$ reveals the DTC conversion of 92.3 % which coincides with the data of PDTC block of run 3 in Tab. 1. All $^1$H NMR spectra of poly(DTC-b-AA)s show $H^c$ and $H^d$ signals which are absent in PAA analyses.

It should be mentioned that no copolymers were obtained either in simultaneous copolymerization by feeding DTC and AA intended to prepare random copolymer or in sequential copolymerization by feeding AA before DTC intended to prepare poly(AA-b-DTC) block copolymer. Instead, both cases produced very low $M_n$ homo-PAA. As a result, lanthanum alkylxide of PDTC living chains are active species for initiating AA polymerization and forming poly(DTC-b-AA), as shown in Scheme 1. On the contrary, carboxyl lanthanum (>La–OOCCH$_2$CH$_2$CH$_2$CH$_2$CO–) being the end group of the PAA shows no catalytic activity toward the polymerization of DTC in the mild condition. Therefore, the remaining DTC monomer cannot polymerize any more after AA being added. The increase of copolymer molecular weight after AA monomer being added is due to the AA units growing on living PDTC chain.
Scheme 1. The copolymerization of AA with DTC.

DSC analysis in the second heating scan eliminates the thermal history of polymers precipitated from petroleum ether. Fig. 3 compares the thermal behavior of poly(DTC-b-AA) with that of PDTC and PAA. PDTC displays a $T_m$ at about 109 °C, while PAA shows three $T_m$s at 51, 65 and 109 °C. The DSC curve of poly(DTC-b-AA) exhibits three melting peaks at 56, 65 and 103 °C. The peaks at 56 and 65 °C may be attributed to the PAA block, while the peak at 103 °C affected by the copolymerization of DTC with AA is assigned to the interaction of the PAA segment and the PDTC segment.

The poly(DTC-co-AA) block copolymers are expected to be a candidate for drug release and delivery.

Fig. 3. DSC curves of poly(DTC-b-AA), PAA and PDTC in the second heating scan.

Experimental part

The preparations of AA, DTC and La(OAr)$_3$ were the same as reported [10, 13]. All polymerizations were carried out in previously flamed and argon purged glass ampoules. As a typical block copolymerization procedure, first, DTC (0.780 g, 6.00 mmol) solution was reacted with La(OAr)$_3$ (24.00 μmol) for 2 min, and then AA (0.768 g, 6.00 mmol) was added and allowed another 30 min polymerization. The product was dissolved in methylene chloride, precipitated in petroleum ether, filtrated, and dried to a constant weight in vacuum at room temperature.
$^1$H NMR spectra were recorded on a Bruker Avance DMX500 spectrometer in CDCl$_3$ with tetramethylsilane as inner standard. Size exclusion chromatographic (SEC) measurements were carried out on a Waters 208 apparatus with Waters 2410 RI detector in tetrahydrofuran (THF) (1.5 mL/min) at 30 °C. The molecular weights were calibrated with polystyrene standards. Thermal behaviors were determined on a Perkin Elmer DSC-7 apparatus. The melting temperatures were measured by the second heating scan to eliminate the thermal history of the polymer samples: heated up to 180 °C, cooled down to room temperature, kept for 5 min, and then heated to 180 °C. The heating and cooling rates were 10 °C/min and 30 °C/min, respectively.

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**References**