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Precipitation polymerization of ε-caprolactone in water using metal triflates as catalysts

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Abstract   The precipitation polymerization of ε-caprolactone has been assessed in water using various commercial metal triflates as catalysts. The reaction is quantitative at 70 and 100 °C, leading to number-average molecular weights up to 5,400 g/mol and dispersities around 1.5–2.0. A polycondensation mechanism operating from in situ generated 6-hydroxyhexanoic acid is proposed. Among various salts, aluminum and tin(II) triflates lead to the higher molecular weight after 24 h reaction at 70 °C.

Keywords   Triflates · Poly(ε-caprolactone) · 6-Hydroxyhexanoic acid · Water

Introduction

Aliphatic polyesters are widely used as biocompatible and biodegradable materials. They are synthesized by the ring-opening polymerization of cyclic esters and by the polycondensation of hydroxy acids or dicarboxylic acids with diols. Poly(ε-caprolactone) is usually synthesized by the ring-opening polymerization of ε-caprolactone, as the corresponding hydroxy acid is scarcely isolable and rather expensive. The reaction is highly sensitive to moisture and water impurities, and

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requires the purification of the monomer prior to polymerization. The synthesis of polyester by polycondensation is in turn realized under vacuum at high temperature, in order to remove the water formed in the course of the reaction.

Polymerizations in dispersed media are of interest notably for the particles solution that can be obtained and the related applications. The use of harmless solvents is of particular interest in this regard. The synthesis of polyesters in water can be conducted in emulsion in the presence of a surfactant [1–4] starting from monomers that are not soluble in water. The water which is formed by the polyesterification is not soluble in the particles and is thus expelled out, leading to the displacement of the equilibrium toward the formation of esters. ε-Caprolactone is a water-soluble compound, and can thus not be used for such emulsion processes. The precipitation polymerization of ε-caprolactone in water using suitable water-stable catalysts may in turn open new leads.

Enzymes were reported to mediate the polymerization of lactones [5, 6] and the polycondensation of diacid with diols [7] in water, yielding low molecular weight oligoesters with yields around 50 %. The lipase-mediated polymerization of ε-caprolactone in water did not succeed [5, 6]. The enzymatic ring-opening polymerization of lactones was also reported in polymersomes in water, but the polymerization of ε-caprolactone did not succeed [8]. The polymerization of ε-caprolactone in water was never reported as far as we know. Triflate salts were reported as efficient Lewis acid catalysts for the ring-opening polymerization of ε-caprolactone [9, 10] and for polyesterification reactions [11, 12]. They are furthermore known as water-stable Lewis acids [13]. The aim of this study was to investigate metal triflates as catalysts for the precipitation polymerization of ε-caprolactone in water.

Experimental

Materials

ε-Caprolactone was purchased from Acros, while 6-hydroxyhexanoic acid was purchased from Alfa Aesar. Al(OTf)$_3$ (99,9 %), Sc(OTf)$_3$ (99 %), Sm(OTf)$_3$ (98 %), and Yb(OTf)$_3$ (99 %) were purchased from Aldrich and Sn(OTf)$_2$ (98 %), Cu(OTf)$_2$ (98 %), Zn(OTf)$_2$ (98 %), Y(OTf)$_3$ (99 %), La(OTf)$_3$ (99 %), Nd(OTf)$_3$ (99 %), and HOTf (99 %) were purchased from Acros. All chemicals were used as received.

Polymerization

The catalyst, water, and the monomer were added in a flask in this order. After a given reaction time, water was added in the flask, leading to a white precipitate. After 20–30 min stirring, the precipitate was recovered by filtration, and dried at room temperature under vacuum until constant weight.

Measurements

Size exclusion chromatography (SEC) was performed in THF as eluent at 40 °C using a Waters SIS HPLC-pump, a Waters 410 refractometer and Waters styragel column (HR2, HR3, HR4, HR5E) calibrated with polystyrene standards. The number-average molecular weight of poly(ε-caprolactone) measured with polystyrene standards was corrected by a factor of 0.56 [14]. NMR spectra were recorded on a Bruker Avance 300 Instrument at room temperature in $CDCl_3$. The chemical shifts were calibrated using the residual resonances of the solvent. MALDI-TOF–MS was performed on a Ultraflex II spectrometer (Bruker). The instrument was operated in either the reflector or linear mode. The spectra were recorded in the positive-ion mode. The samples were prepared by taking 2 μL of a THF solution of the polymer (10 mg/mL) and adding this to 16 μL of 1,8-dihydroxy-9(10H)-anthracenone (dithranol, 10 mg/mL in THF) to which 2 μL of CF_3SO_3Ag (2 mg/mL in THF) had been added. A 1 μL portion of this mixture was applied to the target and 50–100 single-shot spectra were accumulated. The given masses represent the average masses of the Ag+ adducts. The spectrometer was calibrated with an external mixture of angiotensin I, ACTH 18-39 and bovine insulin or PEG 1500.

Results and discussion

Entries representative of the polymerization of ε-caprolactone in water catalyzed by yttrium triflate are presented in Table 1. As ε-caprolactone is soluble in water, the reactive medium is homogeneous at the beginning of the reaction. A translucent phase appears as the reaction proceeds. This phase settles down as the stirring is stopped. A white precipitates appears as additional amounts of water are added in the flask at the end of the reaction. The yield is quantitative in most cases, and number-average molecular weights up to 5,400 g/mol are obtained. An experiment without catalyst was conducted, and led to short oligomers (entry 1). An increase in the concentration of the monomer leads to an increase of the molecular weight (entries 3–5). The equilibrium is reached after 24 h for small dilutions conditions (entry 5 vs. 6). Decreasing the amount of catalyst for average dilution conditions (entries 7–8) lead to an increase of the molecular weight, but to a decrease of the yield.

The MALDI-TOF analysis of a typical polymer (entry 3) is presented in Fig. 1. Two distributions can be noticed, corresponding to linear (main distribution) and cyclic macromolecules (filled circles). The corresponding chromatogram, that gives data in weight fraction, shows a shoulder at long retention times (Fig. 1). The hydrodynamic volume of cyclic polymers is lower than that of the corresponding linear polymer. The calibration that is done with linear polymer underestimates thus the number-average molecular weight of the cyclic fraction and that of the whole polymer as a consequence [15]. Number-average molecular weights have to be considered in this frame.

Table 1 Yttrium triflate catalyzed polymerization of ε-caprolactone in water. Reactions conducted with 1 g ε-caprolactone (8.8 mmol)

Entry	H$_2$O (mL)	εCL/H$_2$O (mol)	Y(OTf)$_3$ (mol%)	Time (h)	Temp. (°C)	Conv. (%)	M_n[a] (g/mol)	$Đ_M$[b]
1	0.99	0.16	–	24	100	67	n.d[d]	n.d[d]
2	0.93	0.17	1	24	100	99	1,000	1.6
3	0.59	0.27	1	24	100	97	3,500	1.9
4	0.32	0.5	1	24	100	91	4,300	1.8
5	0.12	1.34	1	24	100	98	4,800	1.7
6	0.13	1.25	1	72	100	93	4,700	1.7
7	0.61	0.26	0.1	48	100	67	5,400	1.8
8	0.28	0.56	0.1	48	100	63	4,900	2.0
9	0.51	0.31	1	24	70	99	2,700	1.8
10	0.50	0.32	1	72	70	100	4,400	1.7
11[c]	0.10	1.58	1	24	100	79	4,300	1.7

[a] Measured by size exclusion chromatography and corrected

[b] Measured by size exclusion chromatography

[c] 6-hydroxyhexanoic acid as the monomer

[d] Oligomers and solvent signals overlap
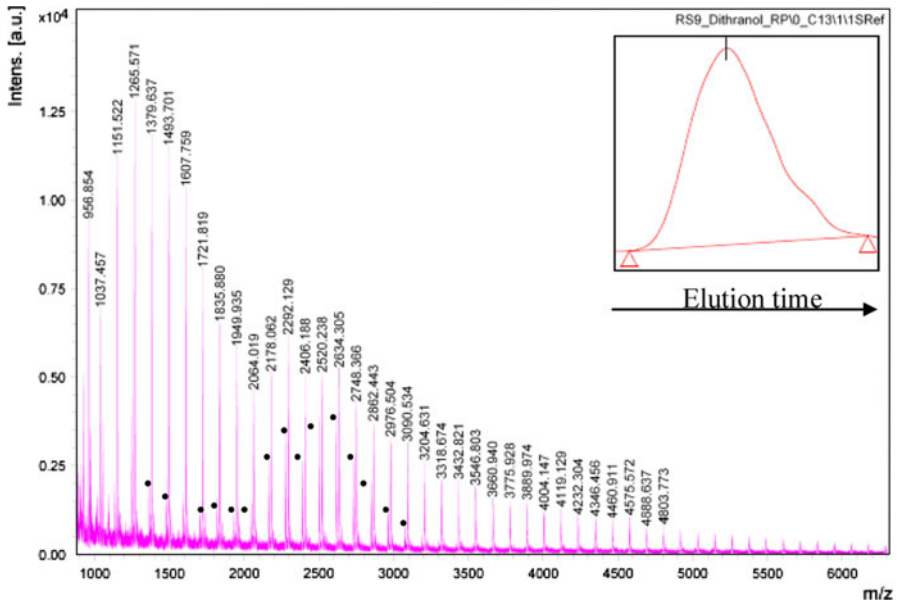
Fig. 1 MALDI-TOF spectra of entry 3 (*filled circle* shows the cyclic species) and corresponding chromatogram (*inset*)

An experiment was conducted with 6-hydroxyhexanoic acid in order to get insight into the polymerization mechanism, as metal triflates are known to catalyze ring-opening polymerizations [9, 10] as well as polyesterifications [11, 12]. The results are shown in Table 1, entry 11. It can be seen that the polycondensation of 6-hydroxyhexanoic acid efficiently occurs under these conditions. Protic species such as water are known to open cyclic esters in the presence of a Lewis acid leading to the corresponding hydroxy acid. The mechanism represented in Scheme 1 can thus be proposed. In the first step, ε-caprolactone coordinates onto the Lewis acid via its carbonyl group, leading to a cationic complex. The electrophilic attack onto H_2O leads to the formation of 6-hydroxyhexanoic acid, which can further polycondense into poly(ε-caprolactone). Up to a certain molecular weight, poly(ε-caprolactone) becomes insoluble in water and aggregates into domains, resulting in the expelling of the water formed in the course of the polycondensation. This expelling displaces the esterification equilibrium toward the formation of the ester, and results in the formation of poly(ε-caprolactone) with number-average molecular weights of several thousand observed here.

The influence of various triflate derivatives on the polymerization of ε-caprolactone in water is presented in Table 2. The experimental conditions of entry 9 have been selected for this purpose, as the equilibrium is not reached after 24 h at 70 °C. The polymerization is quantitative in all cases, with dispersities in the range 1.5–2.0. Triflic acid leads to a modest number-average molecular weight under these conditions. The highest number-average molecular weights are obtained using tin(II) and aluminum derivatives. Similar trends were reported in the bulk polycondensation of 1,6-hexanediol and succinic anhydride [12]. The MALDI-TOF spectra of the polyesters obtained using $Al(OTf)_3$ and $Sn(OTf)_2$ were found to be similar to that obtained using $Y(OTf)_3$ (Fig. 1), i.e., showing two distributions corresponding to linear (main) and cyclic macromolecules.
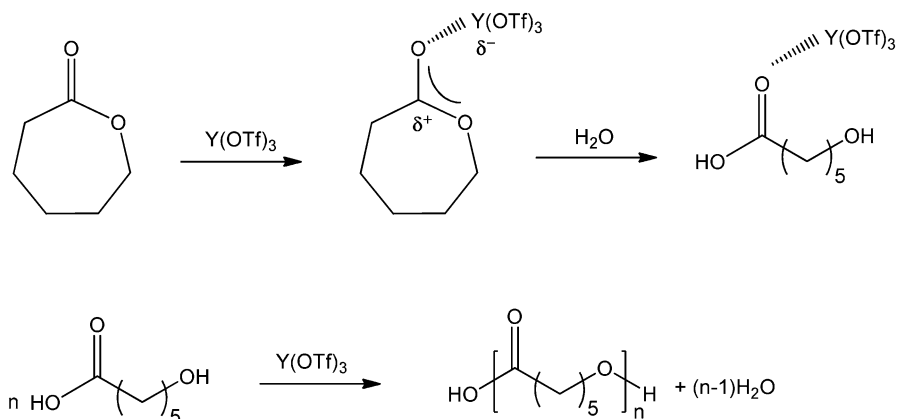
Scheme 1 Proposed polymerization mechanism

Table 2 Metal triflates and triflic acid as catalysts for the polymerization of ε-caprolactone in water

Entry	Catalyst	Yield (%)	M_n[a] (g/mol)	$Đ_M$[b]
12	HOTf	98	2,400	1.5
13	Sc(OTf)$_3$	92	3,000	1.9
14	Y(OTf)$_3$	99	2,700	1.8
15	La(OTf)$_3$	100	2,800	1.7
16	Sm(OTf)$_3$	100	2,700	1.7
17	Nd(OTf)$_3$	95	2,100	1.7
18	Yb(OTf)$_3$	100	3,100	1.9
19	Cu(OTf)$_2$	93	3,400	1.9
20	Zn(OTf)$_2$	97	2,200	1.8
21	Al(OTf)$_3$	99	4,600	2.0
22	Sn(OTf)$_2$	100	4,800	2.0

Experimental conditions: 70 °C, 24 h, 1 g ε-caprolactone (8.8 mmol), 0.5 mL water (27.8 mmol, ε-CL/H$_2$O = 0.32), catalyst 1 mol%

[a] Measured by size exclusion chromatography and corrected

[b] Measured by size exclusion chromatography

Conclusion

ε-Caprolactone can be efficiently polymerized in water at 70 and 100 °C using metal triflates as catalysts. Quantitative yields with number-average molecular weights up to 5,400 g/mol are obtained. Among various triflate salts, aluminum and tin(II) lead to the highest molecular weight after 24 h reaction at 70 °C. This is to our knowledge the first example of a precipitation polymerization of ε-caprolactone in water. The results reported here may pave the way toward the dispersion polymerization of ε-caprolactone (i.e., 6-hydroxyacid) in water using similar systems in combination with a suitable stabilizer [16], affording the straightforward formation of useful poly(ε-caprolactone) particles by polycondensation. Work in this direction is currently under progress.

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