

Biodegradable block copolymers poly(ester)-co-poly(urethane-urea)s based on poly(ϵ -caprolactone): Synthesis and characterization

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Introduction

Nowadays there is a great interest to develop biodegradable polymers for important biomedical applications like temporary scaffolds that can facilitate tissue regeneration or matrices for controlled drug release [1-2]. The polymeric materials that have been using for this purpose are natural rubber, polyethylene, PVC, silicones, and polyurethanes. However, polyurethanes and poly(urethane-urea)s exceeds the mechanical and physical chemistry properties requires, because they can mimic the behavior of different tissues and have relatively good biocompatibility. Both polymers, polyurethane and poly(urethane-urea)s can be prepared from poly(ϵ -caprolactone) (PCL). PCL is a biodegradable polymer [3] and it is expected that its derivatives show similar properties. ϵ -caprolactone diols (PCLOH) are important derivatives as they can be used as 1) precursor of polyurethanes [4-6] or 2) macroinitiators in the synthesis of triblock copolymers [7-8].

Synthesis of HOPLCOH can be achieved by ring opening polymerization (ROP) of ϵ -caprolactone using a diol as initiator/chain transfer agent in the presence of a catalyst [9].

In this work, we report one route to obtain PCL diols (HOPCLOH) by ring opening polymerization of ϵ -caprolactone using ethylenediamine as initiator and decamolybdate anion or tin(II)-2-ethylhexanoate as catalysts. A ϵ -CL/catalyst molar ratio of 5000, 10000, 20000 and 40000 were used for decamolybdate anion and 1250, 2500 and 5000 for tin(II)-2-ethylhexanoate. The obtained molecular weight of the diols were approximately 530, 1250 and 2000 g/mol. Every

diol macromonomer HOPCLOH was successfully used to prepare poly(ester)-co-poly(urethane-urea)s in good yields.

Experimental conditions.

Materials.

ϵ -caprolactone monomer (Sigma-Aldrich) was dried over calcium hydride and distilled under vacuum before use. Ethylenediamine (Sigma-Aldrich) was used as received. Ammonium heptamolybdate tetrahydrate $(\text{NH}_4)_6[\text{Mo}_7\text{O}_{24}]\cdot 4\text{H}_2\text{O}$ (Fluka) was grounded in a mortar and passed through a 100 mesh sieve. The grounded catalyst was dried in an oven at 80°C overnight before use. Tin(II)-2-ethylhexanoate (Sigma-Aldrich) was used as received. 1,6-diisocyanate-hexane (Sigma-Aldrich) and L-Lysine ethyl ester dihydrochloride (Fluka) were used as received.

Synthesis.

Poly(ϵ -caprolactone) diol (HOPCLOH) macromonomer. Experiments were carried out in glass vials. In a typical run 1 mL of ϵ -CL (1.03g, 9.024mmol), ethylenediamine (74.1 μL , 1.096mmol for HOPCLOH of 530g/mol; 29.3 μL , 0.4328mmol for HOPCLOH of 1250 g/mol; and 18 μL , 0.2655mmol for HOPCLOH of 2000 g/mol) and catalyst (Ammonium heptamolybdate tetrahydrate $(\text{NH}_4)_6[\text{Mo}_7\text{O}_{24}]\cdot 4\text{H}_2\text{O}$ or Tin(II)-2-ethylhexanoate) were placed in many glass vials. Molar ratios of ϵ -CL /catalyst were 5000, 10000, 20000, and 40000 for $(\text{NH}_4)_8[\text{Mo}_{10}\text{O}_{34}]$ and 1250, 2500 and 5000 for Tin(II)-2-ethylhexanoate. The vials were stoppered at room temperature and placed in two thermostated baths at 120 °C and 150 °C. Vials were removed from the baths at different times beginning with 1, 2, 4, 6, 8, 10 and 24 hours. No inert atmosphere was used. Ammonium decamolybdate $(\text{NH}_4)_8[\text{Mo}_{10}\text{O}_{34}]$ was formed in situ at reaction temperature by thermal decomposition of ammonium heptamolybdate $(\text{NH}_4)_6[\text{Mo}_7\text{O}_{24}]\cdot 4\text{H}_2\text{O}$. The obtained polymer (HOPCLOH) was characterized by ^1H and ^{13}C NMR, and MALDI-TOF.

Block copolymers poly(ester)-co-poly(urethane-urea). The products were obtained by a two steps procedure. Pre-polymer was formed in the first step from the diol (HOPCLOH, MW=2140 g/mol) (1.0g, 0.4664mmol), 1,6-diisocyanate-hexane (187.5 μL , 1.1682mmol), catalyst (Tin(II)-2-

ethylhexanoate) (1,5μL, 0.0047mmol), and 3mL of CH₃Cl. Reaction mixture was stirred until homogenization. The vial was stoppered at room temperature and placed in a thermostated bath at 80°C. Vial was removed from the bath after 3 hours of reaction. After this time, chain extensor L-Lysine ethyl ester dihydrochloride (LYS) (0.1729g, 0.6996mmol), triethylamine (292 μL, 2.09mmol) and 3mL of CH₃Cl were added to the mixture of reaction. After stirring for three more hours at 80 °C and overnight at room temperature, the resulting slurry was poured over water/ice, and precipitated polymer washed with water and dried at vacuum. Polymer film was obtained by casting in a leveled glass within a fume cupboard. The cast solution was putting in a box to protect it from dust and allowed to stand at ambient temperature for 24 hours. The film was then released. Samples for physical characterization were cut from films unless otherwise stated. Film thickness ranged from 50 to 250 μm.

Results and discussion.

Figure 1 shows the kinetic curves obtained from the reaction of poly(ε-caprolactone) diol ((HOPCLOH, 1250 g/mol). It is seen that kinetic rate increases at higher catalyst concentrations, but it is clear in the case of Ammonium decamolybdate (NH₄)₈[Mo₁₀O₃₄] that the best results are observed when a molar ratio ε-CL/catalyst of 20000. Ammonium decamolybdate (NH₄)₈[Mo₁₀O₃₄] is better catalyst than Tin(II)-2-ethylhexanoate because the polymerization system requires lower catalyst concentration to obtain high conversion in a shorter time, whereas Tin(II)-2-ethylhexanoate requires high concentration to get the same behavior.

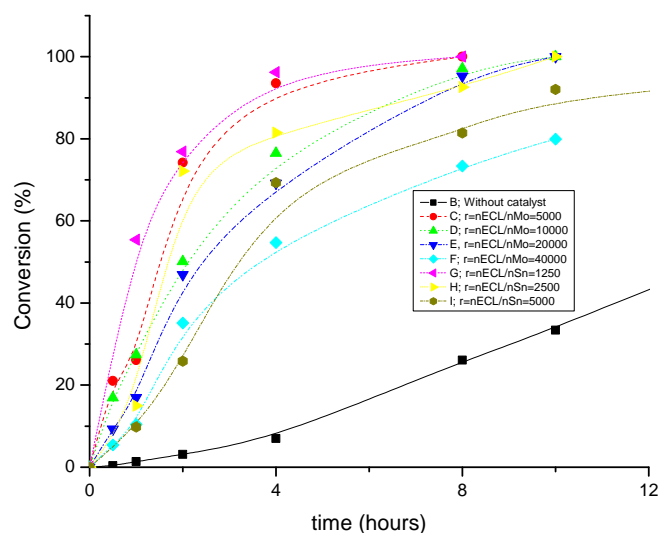


Figure 1. Different Kinetic curves obtained for the preparation of the 1250 g/mol PCL diols by variation catalyst concentration (ammonium decamolybdate $(\text{NH}_4)_8[\text{Mo}_{10}\text{O}_{34}]$ and Tin(II)-2-ethylhexanoate)

Conclusions.

PCL diols (HOPCLOH) with molecular weights of 530, 1250 and 2000 g/mol were prepared by ring opening polymerization of ϵ -CL. Ethylenediamine was successfully inserted onto the PCL chains. Ammonium decamolybdate $(\text{NH}_4)_8[\text{Mo}_{10}\text{O}_{34}]$ is better catalyst than Tin(II)-2-ethylhexanoate, because lower concentrations (molar ratio of ϵ -CL/catalyst=20000) are necessary to obtain high conversions in short reaction times. The HOPCLOH structure was verified by ^{13}C NMR. The different PCL diols were used successfully as macromonomer to obtain copolymers poly(ester)-co-poly(urethane-urea)s films. Crystalline degree, mechanical properties and biodegradability behavior are under evaluation.

6. References.

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