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MgH₂/PEG initiating system for ring opening polymerization of lactone and lactide

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Abstract: Dihydroxy-terminated poly(ethylene glycol) and MgH₂ form an efficient initiating system for the ring opening polymerization of ϵ -caprolactone and L-lactide. Polycaprolactone-*block*-polyethylene glycol-*block*-polycaprolactone and polylactide-*block*-polyethylene glycol-*block*-polylactide were synthesized in bulk at 120 °C for 16 h under argon. MgH₂ provided a faster polymerization rate compared with other initiating systems based on non toxic metals used under vacuum.

Molecular weight of copolymers varied according to the monomer / ethylene oxide units ratio. The developed procedure led to easy polymerization with better control of the design, molecular weight and polydispersity of the final material. Copolymers were characterized by SEC, DSC, ¹H and ¹³C NMR and IR. Micelles in aqueous solutions were prepared by finding balance between hydrophobic polyester and hydrophilic polyethylene glycol blocks.

Interest for this method is the use of MgH₂ environmental chemical, absence of solvent and vacuum techniques, the possible recovery of solid material without further operation.

Keywords : block polymer; poly(ϵ -caprolactone); polylactide; poly(ethylene glycol).

Introduction

Aliphatic polyesters from lactone or lactide and their copolymers have attracted much interest as non toxic biodegradable polymers over the past years. Many publications and patents deal with related syntheses in wide range of applications [1-7].

Poly lactide (PLA), hydrolysable polyester known and used for a long time for medical applications, is one of the polymers widely accepted to play a major role as future packaging material, textiles and agriculture films [8]. This is mainly due to the good mechanical properties of PLA, which are comparable to today's standard packaging polymer, i.e. polystyrene [9-10]. PLA provides a closed natural cycle, being produced from plants and crops, polymerized and processed into packaging product and degraded after use into soil and humus.

Recently, polymeric micelles derived from copolymers of poly lactide or poly(ϵ -caprolactone) (PCL) and polyethylene glycol (PEG) have attracted attention because of their bioresorbability, improved biocompatibility and potential application in drug delivery [11,13]. Polyesters based on lactic and glycolic acids (PLA/GA) are the most investigated and advanced bioresorbable polymers. They now cover an extensive range of applications such as surgical sutures. Moreover, nanocomposites based on such polyesters attracted interest due to possible upgrading of biocompatibility and biodegradability with a large range of polymers [14].

Ring opening polymerization of lactone and lactide, for which various effective systems have been developed [15], provided a direct and easy access to the corresponding high molecular weight polyesters. Many catalysts have been used for ring opening polymerization, the most widely used catalysts are tin compounds. Particularly important is tin (II) ethylhexanoate (SnOct_2) because of both its efficiency and possible use as a food additive [6,7,16-18]. SnOct_2 like most other tin compounds possesses a high cytotoxicity against a broad variety of microorganisms and thus it is used as food stabilizer as well as antifouling additive in paints. However, this cytotoxicity is undesirable when SnOct_2 or other tin salts are present as impurities in polymers [19].

It is highly recommended to use non toxic catalysts in the synthesis of polymers intended for biomedical, pharmaceutical and agriculture applications since complete removal of catalyst residues from the polymer is often impossible. This situation has prompted several research groups to explore the usefulness of initiators based on rather non toxic metals, such as Fe [20-22], Zn [23-39], K [40], Ca, Mg and Bi [4,40-

51]. Calcium based catalysts may serve this purpose and are gaining lots of interest. However, calcium compounds, such as calcium oxide, carbonate and carboxylate have low catalytic activity towards ring opening polymerization in bulk and require temperatures up to 180 °C [52,53].

Polyglycolide homopolymers with high molecular weights and random copolymers of glycolide and ϵ -caprolactone were synthesized using calcium acetylacetonate as a catalyst but the molecular weight could not be controlled and the end groups were not identified [54]. Calcium catalyst developed by Union Carbide has long been used for the heterogeneous ring opening polymerization of oxiranes. The structure of the catalyst however is still unclear, owing to the poor solubility and the high reactivity towards most organic solvents [55].

Calcium ammoniate catalyst for the ring opening polymerization of olefin oxides appeared in early 1960s and it was modified in 1980s. It was also effective in the polymerization of ϵ -caprolactone (CL) and L-lactide (LA) but its catalytic mechanism has not been clear yet because calcium ammoniate cannot dissolve in any organic solvents and it is very unstable and sensitive to moisture.

The synthesis of PLA-*b*-PEG-*b*-PLA triblock copolymers using CaH₂ and Zn has been reported [56,57]. Although the residues were non toxic, the catalytic activity of such chemicals for ring opening polymerization was limited as evidenced by the high polymerisation temperature (140-150 °C) and long polymerization time (4-5 days). Moreover, the whole process is carried out under vacuum. These disadvantages make an industrial development of the synthesis technologically more difficult and less profitable.

Therefore, in this paper, an efficient magnesium alkoxide initiating system generated in situ under argon or nitrogen from magnesium hydride (MgH₂) and dihydroxy-terminated poly(ethylene glycol) has been developed. This new initiating system allowed us to synthesize PEG-based biodegradable triblock copolymers more rapidly than the similar systems based on Ca, Fe or Zn. PCL-*b*-PEG-*b*-PCL and PLA-*b*-PEG-*b*-PLA were characterized by NMR, SEC and DSC. Amphiphilic properties were also evaluated by the measure of the wettability and surface energy of cast film and by the determination of the critical micelle concentration of aqueous solutions.

Results and discussion

To demonstrate the efficiency of MgH_2 for preparing a magnesium alkoxide initiating system for ring opening polymerization, the reaction was carried out in presence of dihydroxy-terminated PEG and MgH_2 with various monomer / ethylene oxide units ratio (CL/EO and LA/EO) under rigorously anhydrous conditions and solvent free. PCL-*b*-PEG-*b*-PCL and PLA-*b*-PEG-*b*-PLA triblock copolymers were obtained.

1. Synthesis and triblock structure of PCL-*b*-PEG-*b*-PCL

Conversion degree of CL and structure of copolymers from NMR analyses

The kinetic of polymerization was followed by ^1H NMR and it was based on the disappearance of the monomer. This analysis made also possible to reach the molecular weight from the intensity of signals of protons attached to PCL blocks.

As a representative example for PEG 2000 (Figure 1), the intensity of the monomer peaks decreased in the course of polymerization indicating the consumption of CL monomer.

The comparison of intensity of CH signals of CL monomer at 4.25 ppm and CH signals of PCL blocks at 4.04 ppm led to the determination of the conversion degree. Complete conversion of monomer and 90 % yield were obtained for 16 h reaction time under argon. The use of MgH_2 provided a faster polymerization rate compared with CaH_2 under vacuum reported by Li and al [57]. So, all polymerizations were carried out with the most suitable reaction conditions following: in bulk at 120°C, in a glove box under dry argon atmosphere for 16 h (Table 1).

The polymerization was stopped by bring back product at room temperature, dissolution in chloroform, precipitation in methanol and drying under vacuum. Increasing the monomer concentration resulted in an increase in the molecular weight of copolymers. All copolymers exhibited CL/EO ratio close to the corresponding feed compositions.

A typical ^1H NMR spectrum of PCL-*b*-PEG-*b*-PCL (from PEG 2000, $M_n = 12000 \text{ g mol}^{-1}$) as well as the detailed assignment of the different peaks is shown in Figure 1. The peaks at 1.30, 1.55, 2.25 and 4.04 ppm were assigned to the methylene proton atoms of PCL units and peak at 3.60 ppm was attributed to the methylene carbon atoms ($\text{O-CH}_2\text{-CH}_2\text{-}$) of PEG block.

The number molecular weight of triblock copolymer was calculated from the area ratio of the ^1H NMR peaks by equation (1).

$$M_{n \text{ NMR}} = M_{n \text{ PEG}} + (M_{n \text{ PEG}} / 44 \times 114 \times 2 \times I_{\text{CH}_2(\text{CL})} / I_{\text{CH}_2(\text{PEG})}) \quad (1)$$

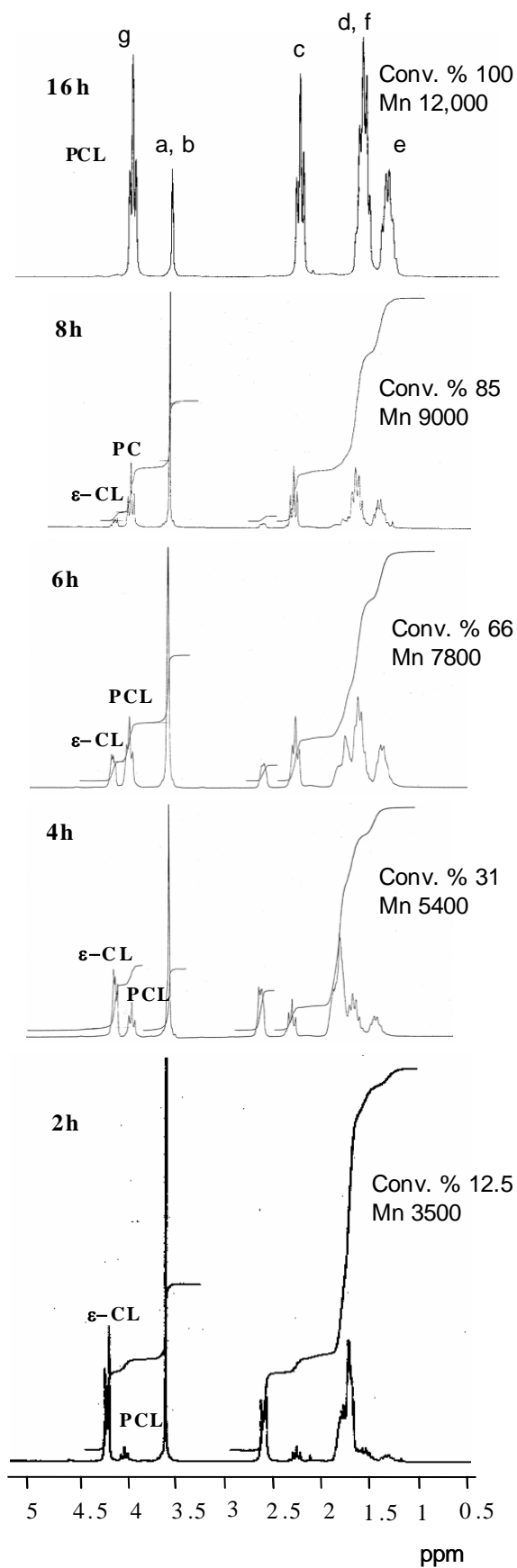
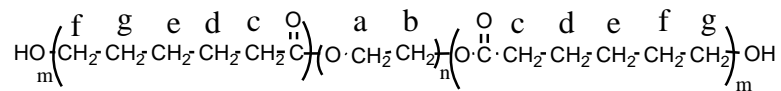


Fig. 1. ¹H NMR spectrum of PCL-*b*-PEG-*b*-PCL. Kinetic of polymerization from 2 to 16 h at 120 °C under argon, conversion degree (conv. deg.) and number molecular weight (M_n) of copolymer (PEG molecular weight 2000 g mol⁻¹).

Tab. 1. Molecular weights, compositions and T_g and T_m of PCL-*b*-PEG-*b*-PCL triblock copolymers synthesized under argon at 120 °C for 16 h with MgH₂ as catalyst.

Samples	$M_{n,PEG}$	CL/EO in feed _a	CL/EO in product _a	$M_{n,theor}$ _b	$M_{n,NMR}$ _b	$M_{n,SEC}$ _b	I_p	second heating T_g (°C)	T_m (°C)
1	2000	0.6	0.6	4800	5500	5100	1.4	-62	57
2	2000	1.2	0.1	7700	7000	7200	1.2	-58	53
3	2000	2.22	2.3	13,400	14,000	12,000	1.2	-58	54
4	2000	4.44	5.1	25,000	28,800	26,500	1.2	-56	53
5	2000	6.66	5.8	36,200	37,500	28,000	1.2	-53	52
6	2000	8.8	8.8	45,500	47,900	33,000	1.2	-51	57
7	10,000	0.2	0.15	15,700	13,700	13,400	1.3	-59	52
8	10,000	0.33	0.32	18,500	18,400	17,500	1.2	-58	50
9	10,000	0.44	0.44	24,000	21,800	12,500	1.2	-62	43
10	10,000	0.88	0.9	32,800	30,000	28,200	1.2	-61	43
11	10,000	1.76	1.7	44,200	45,000	44,000	1.2	-59.5	50
12	10,000	2.2	2.04	67,000	63,000	62,000	1.2	-54.5	52

^a ϵ -caprolactone (CL) and ethylene oxide (EO) unit ratio. CL/EO in the block copolymer was determined from the area ratio of the ¹H NMR peaks at 4.08 ppm (PCL blocks) and 3.65 ppm (PEG block)

^b Number molecular weight of copolymers. M_n was calculated from NMR spectra by $M_{n,NMR} = M_{n,PEG} + (M_{n,PEG} / 44 \times 114 \times 2 \times I_{CH_2(CL)} / I_{CH_2(PEG)})$ and estimated by SEC in chloroform with polystyrene standards.

¹³C NMR spectrum (Figure 2) showed the carbonyl region of the PCL blocks around 173 ppm, the methylene carbon atoms of PCL units at 64.0, 33.9, 28.2, 25.4, 24.4 ppm and the methylene carbon atoms (–O–CH₂–CH₂–) at 70.4 ppm.

Two additional weak peaks at 69.1 and 32.2 ppm were attributed to the linkage groups of block copolymer: the methylene carbon atom of the PEG block that is bonded directly to the PCL block via an ester linkage at 69.1 ppm and the methylene carbon atom of the PCL block adjacent to the PEG block at 32.2 ppm.

¹H NMR and ¹³C NMR spectra confirmed the PCL-*b*-PEG-*b*-PCL triblock structure of the copolymers. The central block came from the PEG used while the other two from the ring-opening polymerization of ϵ -caprolactone. The neighboring blocks were connected through an ester linkage. Therefore the PEG served as a macromolecular

initiator for the polymerization of ϵ -caprolactone. Thus the above copolymerization can be depicted as in scheme 1.

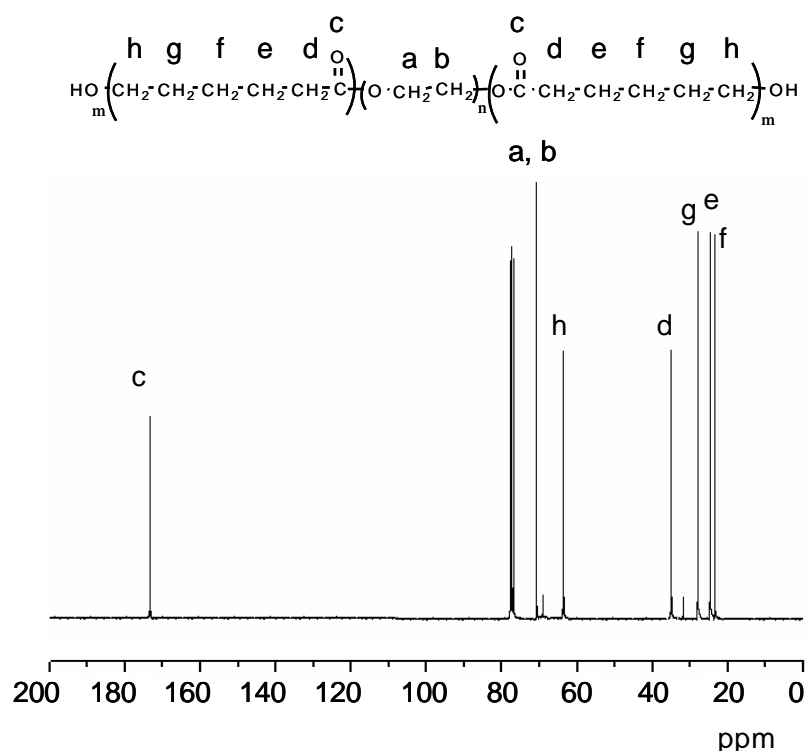
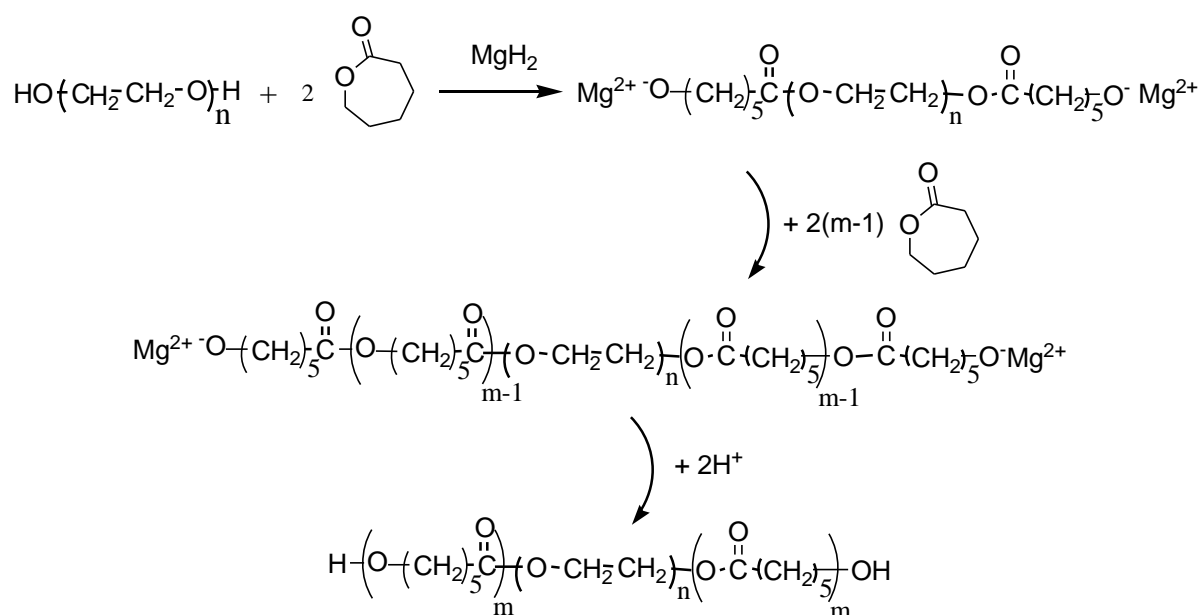


Fig. 2. ^{13}C NMR spectrum of PCL-*b*-PEG-*b*-PCL.



Scheme 1. Proposed mechanism for the formation of the PCL-*b*-PEG-*b*-PCL triblock copolymer. Mg divalent metal could lead to the possible formation of 2 initiating systems from 2 dihydroxy-terminated poly(ethylene glycol). Similar mechanism from

HO-PEG-OH and lactide explains the formation of the PLA-b-PEG-b-PLA triblock copolymer.

It understood that the reaction of polymerization came to the stage of chain propagation. The CL monomer was inserted into the magnesium alkoxide active centers to form the two PCL blocks. Therefore the two PCL blocks should be identical and they were generated by two active centers which have the same chemical activity. Finally, the propagation was terminated by hydrolysis of the active centers to form the -OH end groups.

IR analysis

IR spectra (not shown), of course, cannot be taken as evidence for the graft polymers structure but can confirm and reveal different characteristic functions of the copolymer obtained: ester bond vibration at 1727 cm^{-1} and OH vibration at 3683 , 3622 and 3455 cm^{-1} of OH end PCL, thus confirming the presence of both PCL and PEG units.

SEC analysis

SEC curves (not shown) of the block copolymers were unimodal and showed narrow molecular weight distribution, the molecular weight of PCL block linked to PEG followed a linear relationship with monomer conversion.

The data shown in Table 1 were used to calculate the predicted values of M_n which were compared with those obtained by ^1H NMR and SEC. It should be noted the very close values observed between the theoretical and the experimental values. Values showed a relatively low polydispersity.

The value of M_n depended on the CL/EO ratio when the concentration of the catalyst was kept constant. An increase in the concentration of monomer, CL/EO ratio, led to an increase in M_n of the copolymer as it has been shown by both NMR and SEC.

The molecular weight with a known molar ratio of the monomer to the catalyst determined by SEC was very close to the ones obtained by ^1H NMR, within the expected experimental error.

Nevertheless, molecular weight of block copolymers determined by SEC using linear polystyrene standards in chloroform, was slightly smaller than the predicted value, it was particularly underestimated in the cases of samples 5, 6 and 9 in Table 1. Similar

result was already reported for block copolymers based on PEG and PCL or poly(δ -valerolactone) (PVL) [58]. In contrast, the molecular weight of PCL and PLA aliphatic polyesters determined by SEC with polystyrene calibration is typically overestimated, it is generally higher than the predicted value [59] because of a difference between polystyrene and aliphatic polyesters hydrodynamic volumes at the identical molecular weight. A better swelling of aliphatic polyesters in chloroform compared with copolyesters could be responsible for the variation in hydrodynamic volumes and the molecular weight determination. Perhaps, the presence of PEG hydrophilic block disturbs the extension of hydrophobic PCL chains in the same triblock or between neighbouring triblocks and limits the solvation of PCL chain segments.

The suitable agreement between the calculated values of M_n and those determined by NMR and SEC indicated that the HO-PEG-OH blocks were incorporated during the initiation step and that the polymerization proceeded exclusively by acyl-oxygen cleavage of ϵ -caprolactone. The molecular weight of copolymer increased proportionally with an increasing molar ratio of CL to PEG. This implies, on one hand, that the ring opening polymerization of CL is driven from the hydroxy tail of HO-PEG-OH and, on the other one, that HO-PEG-OH plays the role of the initiator for the ring opening polymerization of ϵ -caprolactone in presence of MgH_2 . The perfect control over molecular weight and low polydispersity indicated that the mechanism is a living polymerization nature.

DSC and WAXD analyses

PEG 2000 homopolymer showed glass transition temperature ($T_g = -62.3^\circ\text{C}$) and single melting peak ($T_m = 58.2^\circ\text{C}$) while the corresponding temperatures of PCL 20,000 were located at $T_g = -50.8^\circ\text{C}$ and $T_m = 54.5^\circ\text{C}$. We did not observe any crystallization peak for both polymers. We noticed that also both homopolymers had comparable glass transition and melting temperatures. The DSC curves of the PCL-*b*-PEG-*b*-PCL triblock copolymers exhibited only two temperatures, T_g varying from -62 to -50°C and T_m varying from 43°C to 59.6°C with molecular weight (Table 1). The PCL blocks were comparably long with respect to the length of PEG block. Similar results were observed for PEG 10,000. Therefore it is difficult to conclude that phase separation takes place in these triblock copolymers to form interconnected PCL domain and PEG domain.

While basing on the analyses carried out, we can consider that the melting peak of the copolymer corresponds to PCL blocks, and that PEG is in an amorphous state.

To consolidate these assertions, analyses of X-rays diffractions were carried out. WAXD spectra of PCL-*b*-PEG-*b*-PCL triblock copolymers, PEG and PCL homopolymers are shown in figure 3.

The crystalline pattern of PEG block was not observed in all triblock samples, WAXD measurement presented only two crystallization rays at 10.5 ° and 11.9 ° which are characteristic of the peaks of crystallization of PCL [60]. Thus we can conclude that only the PCL block is in a crystalline state in the copolymer and that the melting point recorded on the DSC thermogram corresponds to PCL block.

These results prove the presence of the separated microdomains in the triblock copolymers. The thermograms and diffractograms of various triblock copolymers are similar, thus confirming the phase separation for all the synthesized block copolymers.

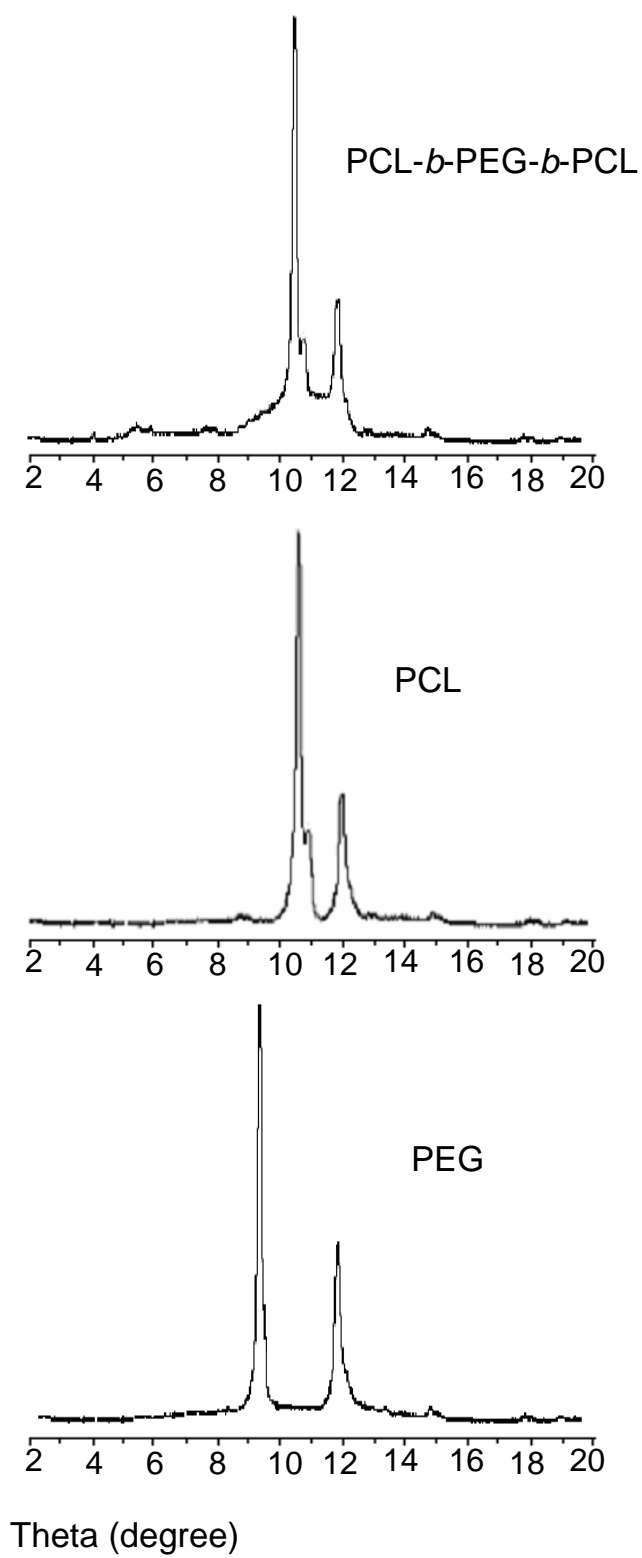


Fig. 3. X-ray diffraction patterns of PEG, PCL and PCL-*b*-PEG-*b*-PCL.

*2. Synthesis and triblock structure of PLA-*b*-PEG-*b*-PLA*

Same procedure described above was used for the preparation of PLA-*b*-PEG-*b*-PLA triblock copolymers from L-lactide and dihydroxy-terminated PEG, $M_n = 2000$ and 10,000. Copolymers with different molecular weight were prepared by varying the initial L-lactide concentration with MgH_2 kept constant. Results are reported in Table 2.

Tab. 2. Molecular weights, compositions and T_g and T_m of PLA-*b*-PEG-*b*-PLA triblock copolymers synthesized under argon at 120 °C for 16 h with MgH_2 as catalyst.

Samples	M_n PEG	LA/EO in feed a	LA/EO in product a	M_n theor b	M_n NMR b	M_n SEC b	I_p	second heating T_g (°C)	T_m (°C)
1	2000	1.2	1.5	5600	7000	6100	1.2	0	-
2	2000	2.3	2.4	9200	10,000	10,400	1.2	14	-
3	2000	3.4	2.8	12,800	11,000	11,000	1.3	28	120
4	2000	4.44	4.12	16,400	15,600	13,500	1.2	30	128
5	2000	6.66	5.8	30,800	29,900	28,000	1.2	36	140
6	2000	8.8	8.8	45,200	39,000	43,000	1.2	41	142
7	10,000	0.4	0.3	17,200	14,800	13,200	1.3	-35	-
8	10,000	0.66	0.6	20,800	20,000	19,700	1.2	-20	-
9	10,000	0.88	0.9	25,000	25,000	28,200	1.2	-10	100
10	10,000	1.7	1.65	38,800	37,000	38,200	1.2	-9	134
11	10,000	2.6	2.3	53,000	48,000	49,000	1.2	17	136
12	10,000	3.4	3.6	67,600	67,000	66,800	1.2	42	140

^a Lactide (LA) and ethylene oxide (EO) unit ratio. LA/EO in the block copolymer was determined from the area ratio of the 1H NMR peaks at 1.45 ppm (PLA block) and 3.65 ppm (PEG block)

^b Number molecular weight of copolymers. M_n was calculated from NMR spectra by $M_n \text{ NMR} = M_n \text{ PEG} + (M_n \text{ PEG} / 44 \times 72 \times 4 \times I_{CH_3(LA)} / I_{CH_2(PEG)})$ and estimated by SEC in chloroform with polystyrene standards.

NMR analysis

As an illustrative example, 1H NMR spectrum of a PLA-*b*-PEG-*b*-PLA triblock copolymer (sample 2 in Table 2) is shown in Figure 4.

The analysis allowed the characterization of the specific linkages due to the block copolymer architecture. The number molecular weight of copolymers was calculated from the 1H NMR peaks by the equation (2).

$$M_n \text{ NMR} = M_n \text{ PEG} + (M_n \text{ PEG} / 44 \times 72 \times 4 \times I_{CH_3(LA)} / I_{CH_2(PEG)}) \quad (2)$$

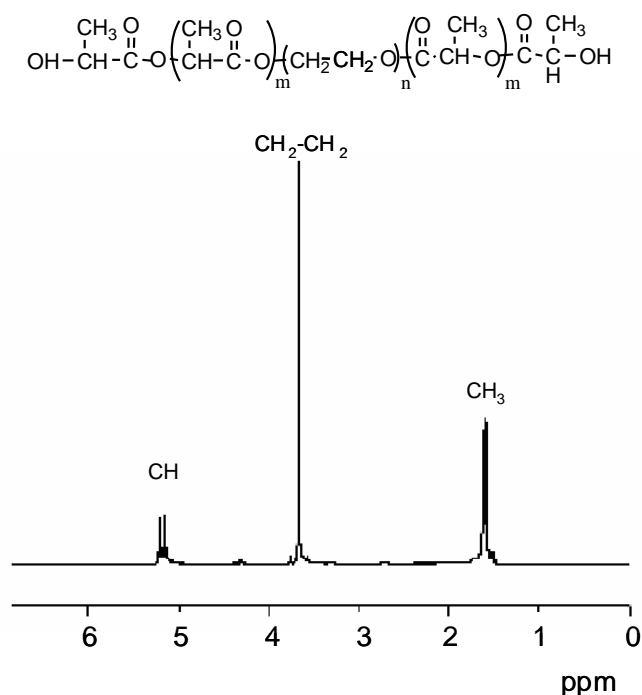


Fig. 4. ^1H NMR spectrum of PLA-*b*-PEG-*b*-PLA.

The multiplet around 4.3 ppm is assigned to the methylene signal corresponding to the junction between PEG and PLA blocks (PLA-COO-CH₂) [42].

The presence of this multiplet is indicative of PLA-PEG linkage. The peak at 3.7 ppm was assigned to the methylene group of PEG block and peaks at 1.7 and 5.2 ppm to methyl and methine proton atoms of PLA block respectively. Thus the above copolymerization can be depicted as in scheme 1 (with LA instead of CL).

^{13}C NMR spectrum of PLA-*b*-PEG-*b*-PLA (Figure 5) showed peaks at 169.3 and 174.30 ppm attributed to the carbonyl group of the polyester blocks and peaks at 17.3 and 69.5 ppm attributed respectively to methyl and methine carbon atoms. First investigations based on ^{13}C NMR analysis also indicated that the stereochemistry of the chiral carbon atom of the L-lactide monomer CO- $\underline{\text{C}}\text{H}(\text{CH}_3)\text{-O}$ was unchanged during the polymerization leading to the formation of stereoregular sequence as P(L-LA).

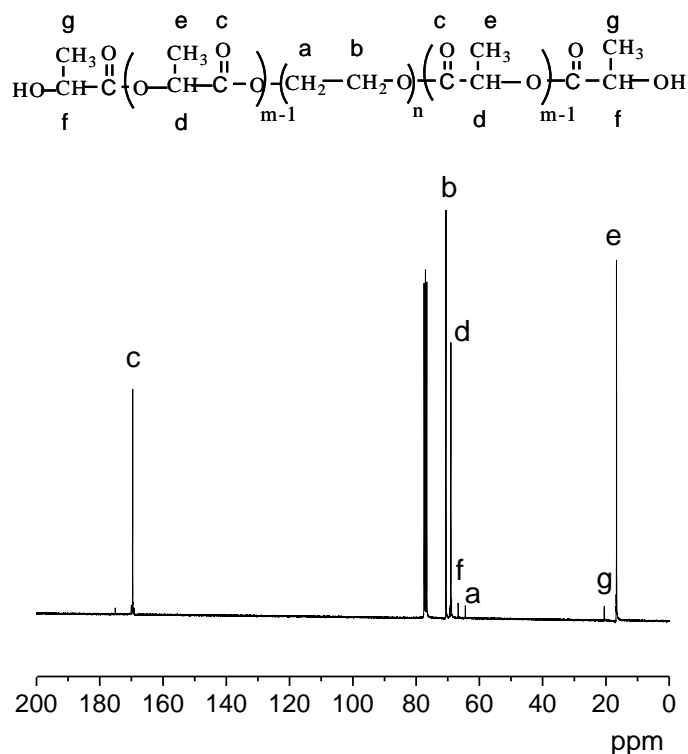


Fig. 5. ^{13}C NMR spectrum of PLA-*b*-PEG-*b*-PLA.

This means that no racemization happened during the polymerization, which would generate other sequences such as P(DL-LA) or P(D-LA). However detailed works are currently developed to specify the stereochemistry of PLA blocks under definite conditions.

IR analysis

IR spectrum (not shown) was similar to that of PCL-*b*-PEG-*b*-PCL. Ester bond vibration was situated at 1738 cm^{-1} .

SEC analysis

SEC curves of block copolymers were unimodal with a narrow molecular weight distribution. Copolymers had relatively low polydispersity and the number molecular weights estimated by SEC were very close to the ones determined by ^1H NMR. All copolymers exhibited ratios of LA/EO close to the corresponding feed composition,

moreover $M_{n\text{ SEC}}$ and $M_{n\text{ NMR}}$ were very close to the theoretical M_n value (Table 2), $M_{n\text{ SEC}}$ are slightly smaller than $M_{n\text{ NMR}}$ as discussed for PCL-PEG-PCL triblock. The good agreement between experimental and calculated M_n values indicated that the HO-PEG-OH block was incorporated to the triblock structure.

M_n depended on LA concentration when the concentrations of PEG and MgH_2 were kept constant. An increase in the concentration of monomer, led to an increase in M_n of the block copolymer. Such results allowed to conclude that the polymerization presents a living character.

DSC analysis

PLA 20,000 homopolymer showed glass transition temperature at $T_g = 46.6\text{ }^\circ\text{C}$ and single melting point at $T_m = 140\text{ }^\circ\text{C}$. DSC curves of PLA-*b*-PEG-*b*-PLA triblock copolymers exhibited only two temperatures, T_g varying from -35 to $43\text{ }^\circ\text{C}$ and T_m varying from 100.1 to $134.1\text{ }^\circ\text{C}$ according to the composition of the copolymer and the length of PEG and PLA blocks (Table 2). In very few cases, a crystallisation temperature at about 91°C was detected.

The glass transition temperatures have also been calculated following the Fox equation (3)

$$1 / T_g = \omega_1 / T_{g1} + \omega_2 / T_{g2} \quad (3)$$

where T_g is the glass transition temperature of the copolymer, $T_{g1} = -62.3\text{ }^\circ\text{C}$ is the glass transition temperature of PEG and $T_{g2} = 46.6\text{ }^\circ\text{C}$ for PLA; ω_1 and ω_2 are the weight fractions of EO units and LA units in the copolymer.

The calculated values indicated a disagreement with the experimental values determined by DSC. This seems to indicate that the copolymers may contain non compatible blocks, as we observed a T_g between those of the corresponding pure homopolymers as well as non relationship between T_g and weight fractions of PLA and PEG blocks.

WAXD spectra of PEG, PLLA homopolymers and PLA-*b*-PEG-*b*-PLA triblock copolymers are shown in figure 6.

The crystalline pattern of PEG block was not observed in all samples, the spectra presented only two crystallization rays at 8.5 ° and 9.7 ° attributed to the crystallization of PLA. The intensity of rays was dependent on LA / EO ratio, it

increased with the length of PLA blocks but the diffraction angle did not change, showing that PEG blocks are excluded from the crystallized PLA blocks.

These results confirm the presence of microdomains in triblock copolymers and non miscibility between PEG and PLA blocks.

3. Micelles preparation and characterization

The increase of hydrophilic nature of PCL and PLA by introducing PEG block to form copolymer would allow the formation of micelles in aqueous media [60-64]. The possibility of micelle formation depends on the hydrophilic/hydrophobic balance of copolymers which is characterized by the wettability, the surface energy and the critical micelle concentration (CMC).

Water contact angle (θ_{H_2O}) of polymer films increased gradually according to the length of hydrophobic blocks. θ_{H_2O} globally varied from about 15 ° for PEG 2,000 and 10,000 to 84 ° and 75 ° for PCL-*b*-PEG-*b*-PCL and PLA-*b*-PEG-*b*-PLA films with same molecular weight about 70,000 g mol⁻¹.

Consequently, the wettability and surface energy (γ_s) gradually decreased, mainly due to the decrease of polar component (γ_s^p), from about 70 mJ m⁻² to 42-46 mJ m⁻² (Figure 7 as a representative graph).

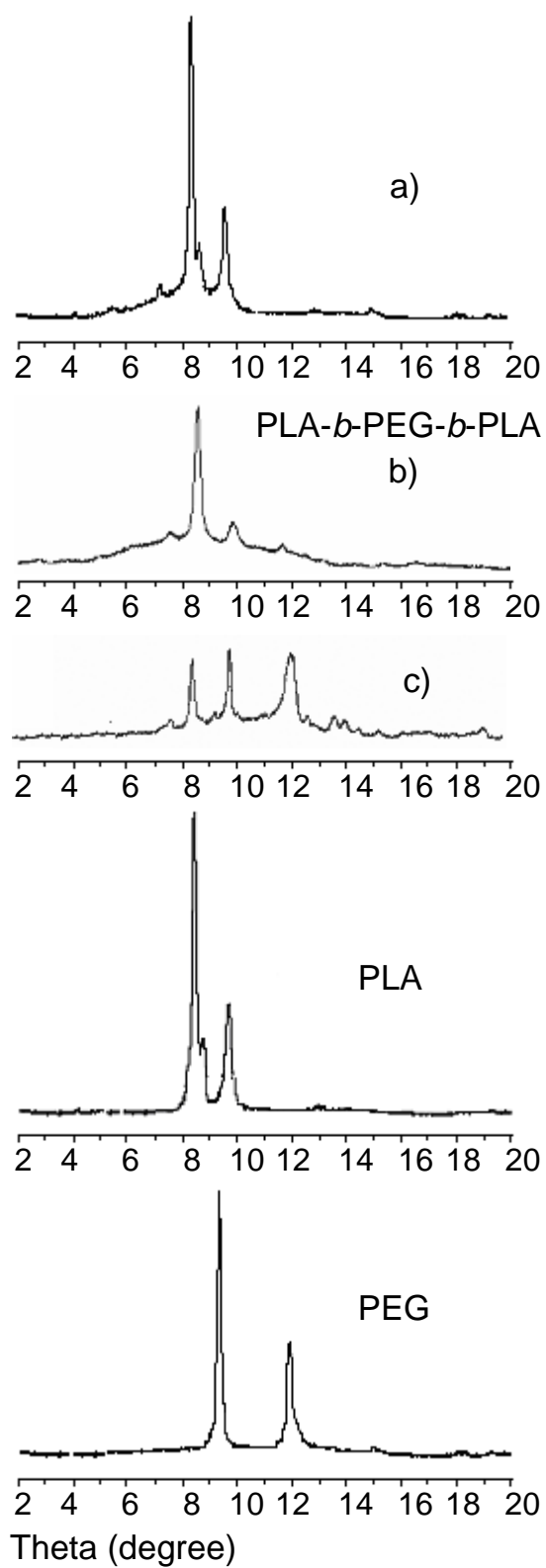


Fig. 6. X-ray diffraction pattern of PEG, PLLA and PLA-*b*-PEG-*b*-PLA. A), b), c) respectively sample 6, 4, 9 in Table 2.

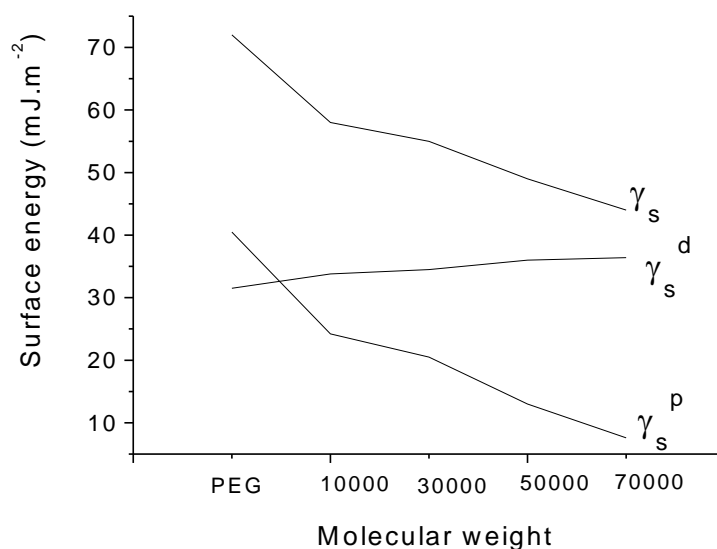


Fig. 7. Variation of the surface energy (γ_s), polar (γ_s^p) and dispersive (γ_s^d) components of PLA-*b*-PEG-*b*-PLA film with the increase of PLA block length (PEG 2000 g mol⁻¹). Similar graphs were obtained for PLA-*b*-PEG-*b*-PLA and PCL-*b*-PEG-*b*-PCL with PEG 10,000 g mol⁻¹.

The optimization of the formation of micelles is closely related to the research of best ratio between the number average polymerization degree of the central hydrophilic PEG block and that of the side hydrophobic PCL or PLA blocks. The hydrophobic blocks aggregate from the core and the hydrophilic blocks form the outer shell. Micelles were prepared via the addition of THF solution of copolymers in water. CMC was deduced from the graph of surface tension of aqueous solution of copolymers versus the polymer concentration. Surface tension decreased with increasing the concentration below CMC and it is nearly constant above CMC. CMC was then taken as the change in slope of the graph. CMC was in 0.2-0.9 g L⁻¹ range for PCL-*b*-PEG-*b*-PCL and PLA-*b*-PEG-*b*-PLA aqueous solutions and it decreased according to the increase of length of hydrophobic blocks (Figure 8).

It is found that the diameter of the micelles indeed increased with the increase of the length of hydrophobic blocks, the number of micelles increased with the increase of concentration and these micelles are of unimodal size distribution.

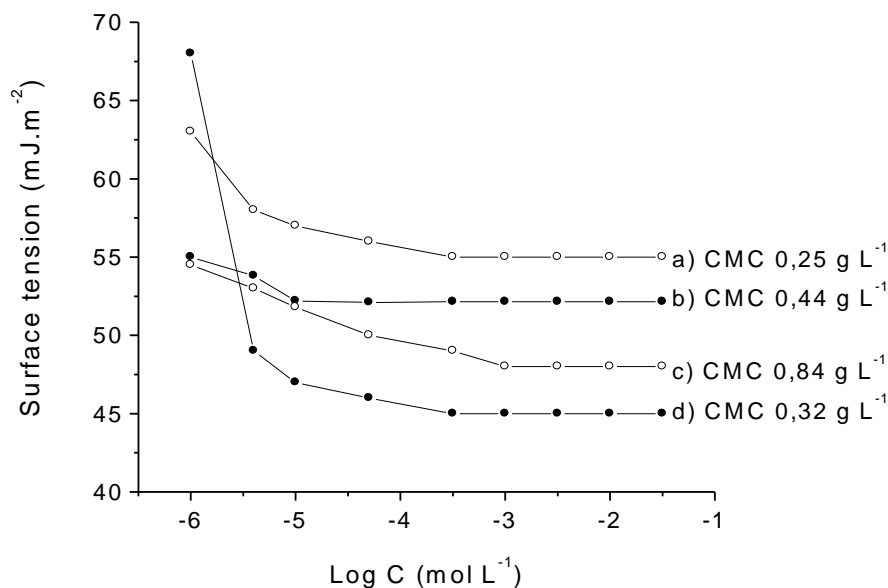


Fig. 8. Variation of the surface tension of aqueous solution of block copolymers with the concentration: PLA-*b*-PEG-*b*-PLA (°) a) $M_n = 25000 \text{ g mol}^{-1}$ c) $M_n = 15000 \text{ g mol}^{-1}$ and PCL-*b*-PEG-*b*-PCL (■) b) $M_n = 14000 \text{ g mol}^{-1}$ d) $M_n = 18400 \text{ g mol}^{-1}$.

Conclusions

MgH₂ led to the formation of an alkoxide system with PEG that initiated the ring opening polymerization of ϵ -caprolactone and L-lactide. The formation of block copolymers between PEG and PCL or PLA was confirmed by several characterization techniques.

Copolymers PCL-*b*-PEG-*b*-PCL and PLA-*b*-PEG-*b*-PLA were synthesized in bulk under argon. Interest for this method is the use of an environmental system, absence of solvent and vacuum techniques, and possible recovery of solid material without further operation. The operative conditions and yield were better than those already reported; they are in favour of a possible development on a works scale.

The synthesis is efficient, easy to control and no transesterification reaction has been detected.

DSC results indicated that the variation in physical properties is adjusted by the variation in copolymer compositions; the copolymers obtained contain non compatible blocks, as we observe by WAXD analysis.

The curves of distribution were unimodal with a narrow polydispersity around 1.2. The average molecular weight calculated by ^1H NMR and obtained by SEC is almost identical. The conversion products are about 100% and yields reach 90%.

The developed procedure enables polymerization with better control of the design, molecular weight, and polydispersity of the final material.

The wettability study showed the variation in the hydrophobic nature of the copolymer while the polyester blocks increased. We succeeded to obtain micelles in aqueous solution by finding balance between hydrophobic polyester blocks and hydrophilic PEG block.

These synthesized biodegradable block copolymers are interesting as materials for biodegradable drug delivery systems, among others.

Experimental part

Materials

ϵ -caprolactone (CL) (Sigma Aldrich) was purified by drying over CaH_2 , followed by a distillation under vacuum and finally stored under argon atmosphere. L-lactide (LA) (Sigma Aldrich) was purified by crystallization from dried toluene and sublimated. Dihydroxy-terminated poly(ethylene glycol) (PEG) with number average molecular weight 2000 and 10,000 g/mol (Sigma Aldrich) were purified by dissolution in chloroform and precipitation in diethyl ether, followed by drying under high vacuum more than one week just before use. Chiral L-LA monomer was selected for investigation into the stereochemistry of the polymerization. Complete results will be published shortly. In this article, polylactide block is called PLA without reference to the possible stereoregularity of the polymer chain. Magnesium hydride (MgH_2) (Sigma Aldrich) was used as received. X rays analysis of MgH_2 gave in at %, after deducting oxygen from analysis under air: Mg 99.38, Ca 0.1, Al 0.38, Si 0.12, Fe 0.01. Commercially available solvents were used as received without further purification.

Synthesis of copolymers

The systems modelled in this study are the ring opening polymerization of CL and LA with MgH_2 and PEG as the initiating complex. PEG was used to represent both the initiating hydroxyl functionality and the propagation of polyester chain.

As an illustrative example: in a glove box purged by dry argon, weighed amount of PEG, finely grinded MgH_2 at a proportion of 0.069 mole of MgH_2 per terminal hydroxyl of PEG and 6.9 mmole of CL or LA were introduced in a dry tube equipped with a magnetic stirrer. The tube was closed with a serum cap under argon and immersed in a silicon oil bath at 120°C for 16 hours. The copolymer thus obtained was purified by dissolution in chloroform and precipitation in methanol (two times). The solid product was dried under reduced pressure until constant weight was obtained.

Characterization

^1H NMR and ^{13}C NMR were recorded with a Bruker spectrometer, at 400 and 100 MHz respectively, in CDCl_3 solution at 25°C . Chemical shifts are given in ppm downfield from TMS. Differential Scanning Calorimetry (DSC) measurements were carried out on Mettler DSC 30 instrument, in sealed aluminium pans under nitrogen atmosphere, at $10^\circ\text{C}/\text{min}$ heating rate, calibrated with indium standards. SEC analysis was conducted with a Waters 2410 apparatus equipped with Styragel HR3, HR4 and HR5 columns and analyzed with an RI detector (Waters 2410) with chloroform as eluent at a flow rate of $0.5\text{ mL}/\text{min}$, using a Waters 515 pump at 35°C . Molecular weights were calibrated with polystyrene standards. Wide-angle X-ray diffraction (WAXD) was performed using a Philips diffractometer with Ni-filtered $\text{Cu K}\alpha$ radiation.

Wettability of copolymer films

Wettability and surface energy were determined by contact angle measuring. Films were obtained from copolymer solutions in CHCl_3 which were cast on a glass plate. After solvent evaporation, films were dried at 40°C for 4 hours. The contact angle measuring was made 5 s after the drop was deposited and the surface energy was calculated by the Owens and Wendt method using water and diiodomethane [65].

Micelle preparation

To prepare an aqueous solution, the copolymer solution in tetrahydrofuran (THF) with various concentrations, was added dropwise to doubly distilled water under stirring and then THF was removed using a rotary evaporator at 25°C for 2 h.

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