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ORIGINAL PAPER

Synthesis of PCL-*b*-PVAc block copolymers by combination of click chemistry, ROP, and RAFT polymerizations

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Abstract The synthesis of new poly(ε-caprolactone)(PCL)-*b*-poly(vinyl acetate)-(PVAc) block copolymers was investigated using different combinations of click chemistry, reversible addition-fragmentation transfer (RAFT), and ring opening polymerization (ROP) techniques. Two approaches, "coupling" and "macroinitiator" routes were studied. For the coupling approach, a chain transfer agent comprising an azide function was synthesized and used as initiator for the VAc polymerization. PCL containing an alkyne termination was obtained from a bifunctional initiator bearing an alkyne function and an hydroxyl group. These two functionalized precursors, PVAc and PCL, were coupled by a 1,3 cyclo addition reaction "click chemistry" in order to obtain the corresponding block copolymer. For the macroinitiator approach, PCL-*b*-PVAc block copolymers were synthesized using a two-step procedure: at first, a PCL macroinitiator with a xanthate end group was prepared by coordinated anionic polymerization of ε-caprolactone; then, the RAFT polymerization of VAc was initiated from the PCL, for the preparation of PCL-*b*-PVAc block copolymers. Whatever the method used, no detectable quantities of unreacted PVAc or PCL were observed. ^{1}H NMR and size exclusion chromatography analyses indicated successful synthesis of the block copolymers with well-defined structures.

Keywords RAFT · ROP · Click chemistry · Block copolymers · Poly(vinyl acetate) · Poly(ε-caprolactone)

Introduction

In recent years, biodegradable polymers have received increased attention due to their wide-spread application possibilities in pharmaceutical and biomedical fields.

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Poly(ε-caprolactone) (PCL) is a fully biodegradable, biocompatible, semi-crystalline thermoplastic polyester obtained from ε-caprolactone monomer through ring opening polymerization (ROP) [1, 2]. Compared to other biodegradable aliphatic polyesters, PCL has several advantageous properties, including high permeability to small drug molecules, slow erosion kinetics, and miscibility with various polymers. However, the rather high crystallinity of PCL decreases its compatibility with soft tissues and lowers its biodegradability [3]. Moreover, PCL has a lack of mechanical strength due to its low glass transition temperature (−60 °C) and low melting temperature (60 °C) [4]. These drawbacks can be overcome either by blending PCL with various polymers [5–7] or preferably by copolymerization of ε-caprolactone with other monomers as demonstrated for PCL-based block copolymers [8].

Mainly two synthetic pathways are available for the preparation of block copolymers comprising a PCL block. Each block can be prepared separately and connected by coupling of functional end groups, by the so-called "click" chemistry [9]. An alternative consists in preparing the first sequence of the copolymer with a chain end functionality suitable to initiate the polymerization of the second monomer.

Up to now, a variety of well-defined copolymers comprising PCL blocks have been synthesized by a combination of controlled/"living" polymerization methods, such as anionic or coordinated anionic for the PCL synthesis [10], atom transfer radical polymerization (ATRP) [11], nitroxide-mediated polymerization (NMP) [12], and ROP-Aldol-GTP for the synthesis of the second block [2].

"Click" reactions, as defined by Wu et al. [13], have been applied in polymer synthesis because of their quantitative yields, mild reaction conditions, and tolerance with a wide range of functional groups. The combination of various living/controlled polymerization techniques and click reaction was used to prepare a range of diblock copolymers, for example, PCL-*b*-PDMAEMA by ROP and ATRP [14], PCL-*b*-PVA by ROP and RAFT [15], and PnBA-*b*-PCL by NMP and ROP [16].

To the best of our knowledge, PCL-*b*-PVAc diblock copolymers have not yet been reported. Although, poly(vinyl acetate) (PVAc) could provide valuable properties to the system with its well-known adhesion properties and its partial miscibility with PCL, it could open new perspectives for the development of PCL-based materials with adjustable crystallinity and T_g values.

Diblock copolymers comprising a PVAc block were synthesized by different methods. Several groups [17, 18] reported the synthesis of PVAc-poly(meth)acrylic copolymers using PVAc-CCl_3 telomeres as ATRP initiator. Similar types of acrylic block polymers were obtained by transition-metal catalyzed living polymerization of VAc [19–22].

However, the synthesis of well-defined PVAc as precursor sequence of block copolymers containing PVAc is challenging, because vinyl acetate is a typical example of monomer that cannot be easily polymerized using controlled radical polymerizations. Recently, the first ATRP of vinyl acetate was achieved, however, with insufficient control of the molecular weight distribution [23]. The only way to obtain well-defined PVAc appeared to be RAFT polymerization using a xanthate as transfer agent [24].

Block copolymers having a PVAc block synthesized by RAFT were scarcely described and only recently the synthesis of well-defined copolymers containing a PVAc block has been achieved [25]. PVAc-*b*-PS have been synthesized by a combination of RAFT and ATRP by Tong et al. [26] using a difunctional initiator, as well as by Jeong et al. [27]. Stenzel et al. prepared block copolymers of vinyl acetate and methacryloyl mannose by combining RAFT and click chemistry [28]. Shipp et al. [29] obtained PtBA-*b*-PVAc and PMA-*b*-PVAc block copolymers by a combination of ATRP and RAFT.

Herein, we describe for the first time the preparation of well-defined PCL-*b*-PVAc diblock copolymers according to two methods. The first, by a click chemistry approach, consists in coupling an azide terminated PVAc, obtained by RAFT technique, with an alkyne functionalized PCL prepared by ROP. The second, by a macroinitiator technique, is based on the preparation of xanthate end-functionalized PCL acting as macroinitiator for the VAc polymerization. The respective advantages of these two preparation techniques are outlined.

Results and discussion

Part I: Synthesis of PCL-*b*-PVAc block copolymers using click chemistry

PCL-*b*-PVAc block copolymers could be synthesized either by coupling azide terminated PCL (PCL-N_3) with alkyne end-functionalized PVAc (PVAc-alkyne) or, on the opposite, by reacting PCL-alkyne with PVAc-N_3. From our preliminary tests, it turned out that the preferred reaction was the coupling of PCL-alkyne with PVAc-N_3. In fact, the synthesis of PCL-N_3 would require a two-step reaction, with at first the preparation of PCL bromide by a ROP process, followed by its transformation into PCL-N_3 in the presence of NaN_3.

Synthesis of alkyne terminated PCL

Similar to the preparation technique described by Xu et al. [30], alkyne-terminated PCL were prepared by ROP of CL initiated with 4-pentyn-1-ol as indicated in Scheme 1.

Scheme 1 Polymerization of ε-caprolactone initiated from 4 pentyn-1-ol

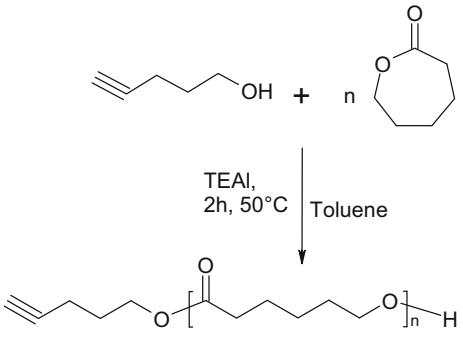


Table 1 Characteristics of the PCL-alkyne and PVAc-N_3 homopolymers

	M_n[a] (^{1}H NMR), g/mol	M_n[b] (SEC), g/mol	pdi
PCL-alkyne-1	3,450	3,700	1.16
PCL-alkyne-2	7,100	7,700	1.19
PCL-alkyne-3	11,400	11,600	1.13
PVAc-N_3-1	11,500	12,800	1.25
PVAc-N_3-2	4,500	5,210	1.23

[a] M_n ^{1}H NMR calculated from the DP_n determined by ^{1}H NMR

[b] $M_{n,SEC}$ after correction with the Mark–Houwink coefficients

The CL polymerizations were carried out at 50 °C in toluene. Tin trifluoroacetate claimed by Xu et al. as a catalyst was replaced by triethylaluminum (TEAl) recommended by Kricheldorf et al. [31] for its higher efficiency (better control of the polymerization and shorter reaction time). Well-defined PCL in the M_n range of 3,700 to 11,000 g/mol and low polydispersity indices (pdi = 1.13 – 1.19) were obtained. From Table 1, it appears further that the M_n values determined by SEC are in good agreement with those calculated by ^{1}H NMR. The alkyne end-functionality is clearly evidenced by the characteristic peak of the alkyne proton at 2 ppm.

Synthesis of PVAc-N_3

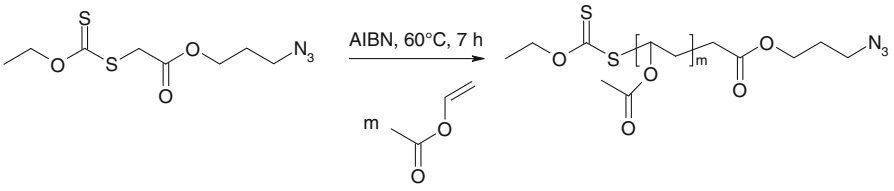
The RAFT methodology, described by Stenzel et al. [28] and more recently by Tong et al. [26], was applied to the synthesis of azide end-functionalized PVAc. The azido-dithiobenzoate used as transfer agent was prepared according to the procedure developed by Stenzel et al. [28]. Having confirmed that VAc was not polymerizable by RAFT in DMF solution, all the PVAc-N_3 samples were prepared in bulk under similar conditions, as described by Stenzel et al. and by Tong et al. [26]. From the reaction scheme (Scheme 2), it is worth noting that this RAFT procedure leads to a α,ω-functionalized PVAc with a thioester and an azide end group, respectively.

From the optimization of the reaction conditions at 60 °C, it appeared that in order to keep the polydispersity index below 1.3, the conversion has to be limited to about 20% and that 1/10 is the preferred AIBN/RAFT transfer agent molar ratio. Typical results are outlined in Table 1.

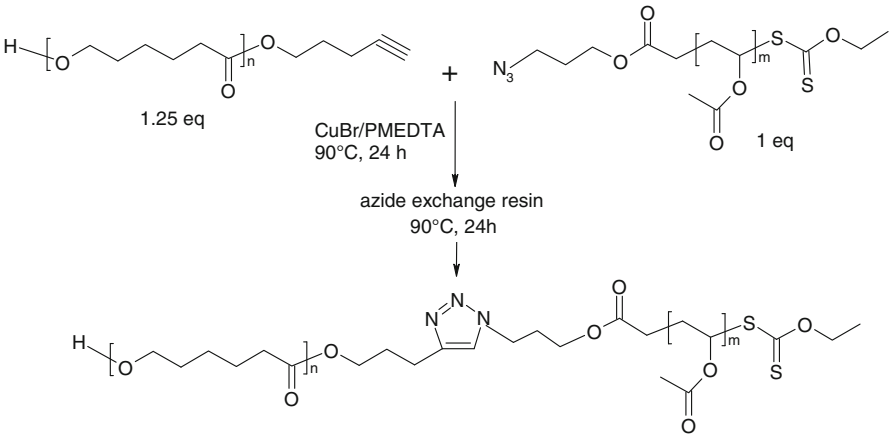
For the samples prepared under these optimized conditions, a fair agreement can be noticed for the M_n values determined by SEC and by ^{1}H NMR end group analysis. Well-defined functionalized PCL and PVAc homopolymers having molecular weights ranging from 3,450 to 11,400 g/mol and 4,500 to 11,500 g/mol, respectively, have been obtained for further click coupling.

"Coupling" reaction of PVAc-N_3 with PCL-alkyne by click chemistry

PCL-*b*-PVAc block copolymers, not reported up to now, were synthesized by coupling the alkyne terminated PCL with the azide terminated PVAc via "click chemistry," according to Scheme 3.



Scheme 2 RAFT polymerization of vinyl acetate



Scheme 3 Synthesis of PCL-*b*-PVAc block copolymers using "click chemistry"

The click chemistry reactions were carried out in DMSO, a common solvent for both PCL and PVAc, with copper bromide and PMDETA as catalyst, in the presence of a slight excess of PCL-alkyne (1.25 equiv. with respect to PVAc). PVAc having the molar mass of 4,500 g/mol has been chosen for the coupling with the different PCL-alkyne as we were interested in synthesizing block copolymers rich in PCL. After reaction, the excess of PCL-alkyne was eliminated with an azide exchange resin [32, 33]. A further purification step consists in the elimination of the Cu-PMDETA complex by reprecipitation in a citric acid/ammonium hydroxide buffer solution [9].

The SEC chromatograms of the purified samples show only one peak and no detectable quantities of unreacted PVAc or PCL were observed. The absence of residual PCL-alkyne and PVAc-N_3 indicates the effectiveness of the purification procedures and of the coupling reaction The NMR spectrum given in Fig. 1, corresponding to the PCL-alkyne-1/PVAc-N_3-2 coupling, shows the presence of a weak peak at 7.60 ppm which is characteristic of the triazole proton of the junction cycle. The NMR spectra show furthermore the characteristic peaks of both PCL and PVAc confirming the successfully coupling using click chemistry.

Well-defined PCL-*b*-PVAc block copolymers with different PCL lengths have been synthesized as shown in Table 2. The molecular weights of the block copolymers have been determined by summing the molecular weight of each block.

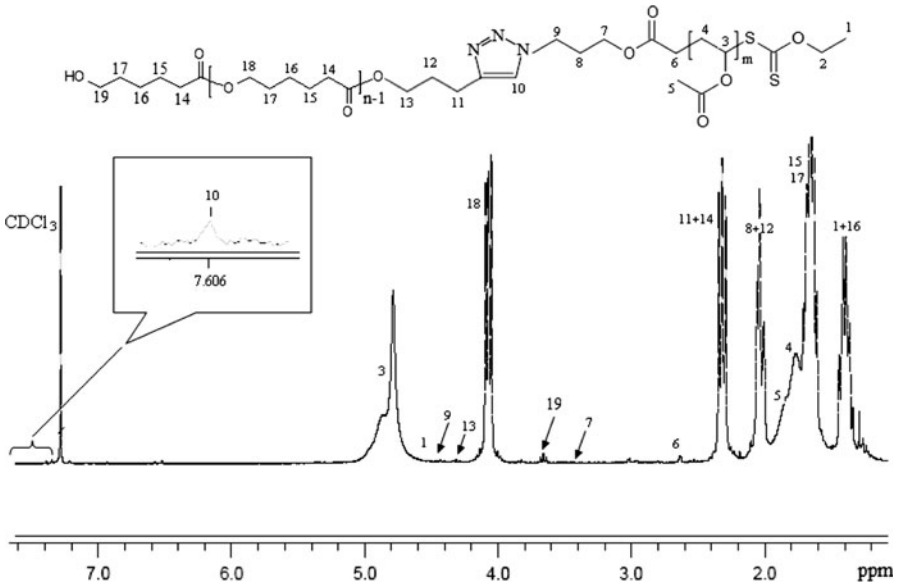


Fig. 1 ^{1}H NMR spectrum of a PCL-*b*-PVAc block copolymer synthesized using "click chemistry"

Table 2 Characteristics of PCL-*b*-PVAc diblock copolymers obtained by "coupling"

M_n[a] PVAc (^{1}H NMR), g/mol	M_n[b] PCL (^{1}H NMR), g/mol	%Molar PCL (^{1}H NMR)	% Molar PVAc (^{1}H NMR)	M_n[c] PCL-*b*-PVAc, g/mol	M_n[d] PCL-*b*-PVAc (SEC), g/mol	pdi
4,500	3,450	40	60	7,950	11,400	1.43
	7,100	52	48	11,600	18,000	1.46
	11,400	67	33	15,900	19,800	1.12

[a,b] M_n, ^{1}H NMR see Table 1

[c] M_n(PCL-b-PVAc) = $M_{n\ ^{1}H\ NMR}$(PCL) + $M_{n\ ^{1}H\ NMR}$(PVAc)

[d] M_n determined by SEC, calibrated with PS standards

In fact, for block copolymers it is well known that SEC, calibrated with PS standards, does not provide direct access to their molar mass. In the present case, it appears that the SEC M_n values, given in Table 2 for comparative reasons, are overestimated with respect to those obtained by summing up the M_n values of the precursor sequences.

The click chemistry coupling is especially well adapted for the preparation of copolymers in the molar mass range up to about 20,000 g/mol. It requires, however, several purification steps in order to remove, not only the copper complex catalyst, but also the slight excess of alkyne terminated precursor block.

The presence of a xanthate function at the end of the copolymer chain could be either eliminated as indicated by Tong et al. [15] or it opens the possibility to initiate another RAFT polymerization in order to synthesize triblock copolymers.

Part II: Synthesis of PCL-*b*-PVAc block copolymers using the "macroinitiator" method

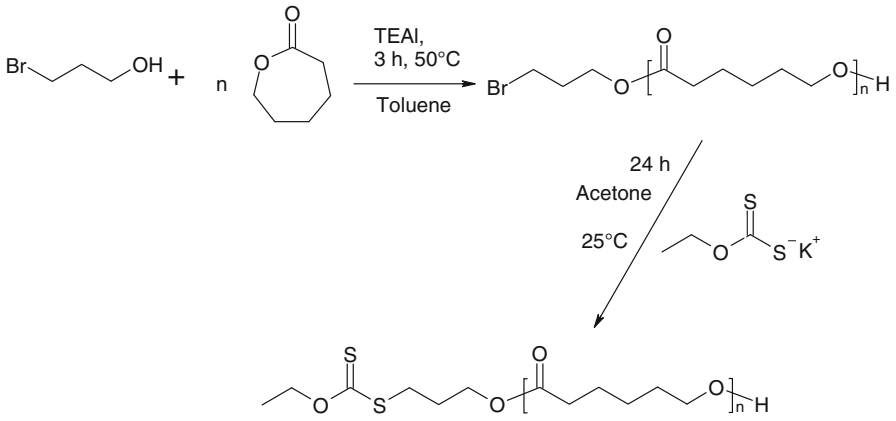
PCL-*b*-PVAc block copolymers were obtained according to the "macroinitiator" method, preparing at first a xanthate end-functionalized PCL able to control the synthesis of the second block PVAc by RAFT polymerization.

Synthesis of PCL-xanthate

PCL-xanthate was synthesized in two steps, by initiating at first the CL polymerization with 3-bromo-1-propanol, followed by the reaction of potassium O-ethyl xanthate on the PCL-Br precursor (Scheme 4).

Synthesis of bromine terminated PCL The experimental procedure of the synthesis of PCL-Br was identical to that used for the synthesis of PCL-alkyne, 4-pentyn-1-ol being replaced by 3-bromo-1-propanol. The presence of the bromine function on the initiator implies a slightly increase of the polydispersity indices, due to interactions between bromine and TEAl. Nevertheless, PCL-Br with relatively low polydispersity indices varying from 1.22 to 1.43 were obtained, as shown in Table 3. A fair agreement between the molecular weights determined using NMR analysis and those determined using SEC analysis after correction with the Mark–Houwink parameters can be noticed.

Modification of the PCL end Xanthates are good transfer agents for the RAFT polymerization of VAc according to Ting et al. [28], who studied a series of xanthates with different Z-groups and found that the O-ethyl xanthate was the most suitable. Therefore, O-ethyl xanthate was used to end-cap PCL and also to mediate the radical polymerization of VAc.



Scheme 4 Synthesis of PCL-xanthate

Table 3 Characteristics of the PCL-Br

PCL-Br	M_n[a] (^{1}H NMR), g/mol	M_n[b] (SEC), g/mol	pdi
PCL-Br 1	5,700	5,800	1.22
PCL-Br 2	11,400	11,200	1.43

[a] M_n ^{1}H NMR calculated from the DP_n determined by ^{1}H NMR

[b] $M_{n,SEC}$ after correction with the Mark–Houwink coefficients

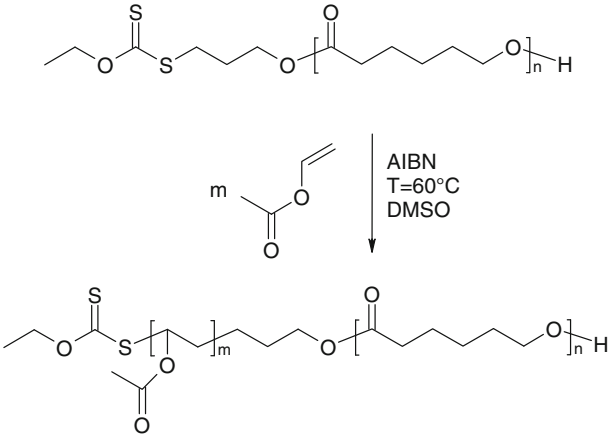
The PCL-xanthates were obtained by reaction of potassium O-ethyl xanthate with PCL-Br according to Scheme 4. ^{1}H NMR analysis of the PCL-xanthates thus obtained showed the total disappearance of the CH_2-Br peaks at 3.45 ppm and the appearance of the characteristic peaks of O-ethyl xanthate (at 4.6 ppm, for example). The quantitative agreement between the two chain ends is the proof that the reaction was complete. No degradation of PCL was observed as the SEC chromatograms of the polymers before and after reaction were identical.

Synthesis of PCL-b-PVAc block copolymers

The second possibility explored for the preparation of PCL-*b*-PVAc block copolymers was to use xanthate end-capped PCL samples as macroinitiators for the RAFT polymerization of VAc according to Scheme 5. The polymerization of vinyl acetate was achieved in the presence of AIBN at 60 °C in DMSO as a common solvent of PCL and PVAc.

From preliminary tests, it turned out that the optimum conditions for the RAFT polymerization were a molar ratio AIBN/PCL-xanthate of 1/10 and a reaction time of 24 h. Reproducibility of the synthesis has been verified, as shown in Table 4.

SEC analysis of the block copolymers showed an increase in the molar mass of the block copolymers as compared to their PCL-xanthate precursors, proof of the



Scheme 5 Polymerization of vinyl acetate from end-capped PCL-xanthate

Table 4 Characteristics of PCL-*b*-PVAc obtained with the "macroinitiator" approach

PCL-ccc*b*-PVAc	M_n[a] PCL (^{1}H NMR), cg/mol	M_n PVAc[b] expected, g/mol	M_n[c] PVAc (^{1}H NMR), g/mol	Conversion (%)	M_n[d] PCL-*b*-PVAc, g/mol	M_n[e] PCL-*b*-PVAc (SEC), g/mol	pdi
PCL-*b*-PVAc-1	5,700	3,500	3,200	91	8,900	10,300	1.23
PCL-*b*-PVAc-2	5,700	3,500	3,000	86	8,700	9,600	1.24
PCL-*b*-PVAc-3	5,700	17,200	16,300	95	22,000	23,300	1.33
PCL-*b*-PVAc-4	11,400	9,500	8,600	91	20,000	23,100	1.30

[AIBN]/[RAFT agent] = 0.1/DMSO/60 °C/24 h

[a] ^{1}H NMR molar masses of PCL-xanthate are the same as those obtained for PCL-Br (Table 3)

[b] M_n PVAc expected = [VAc]/[PCL-xanthate] × 86

[c] Determined by ^{1}H NMR of the block copolymer

[d] M_n(PCL-*b*-PVAc) = M_n PCL(^{1}H NMR) + M_n PVAc(^{1}H NMR)

[e] M_n SEC determined by SEC, calibrated with PS standards

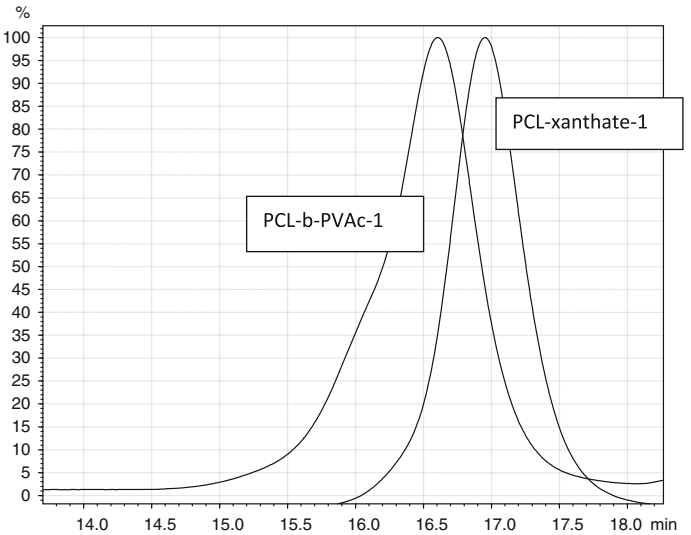


Fig. 2 SEC chromatograms of PCL-xanthate and PCL-*b*-PVAc

initiation of the VAc polymerization starting from the PCL block (Fig. 2). The shoulder observed for the block copolymer traces can be explained by a loss of control for such advanced conversion. The size of the PVAc block can be estimated as a function of the VAc/PCL ratio and conversions. These expected M_n values, at a conversion of around 90%, are in fair agreement with those determined by ^{1}H NMR analysis.

The block copolymers have been analyzed by ^{1}H NMR, and typical signals of PVAc and PCL were clearly observed. Knowing the molar mass of the PCL macroinitiator and assuming the quantitative initiation from the PCL-xanthate precursor, the molar masses of the copolymers have been determined from peak

intensity ratios of CH_2 of PCL chains and CH of PVAc. The determination of the optimum conditions for polymerization allowed the synthesis of well-defined block copolymers as indicated by the polydispersity indices (pdi = 1.23–1.33) of the SEC analysis.

The macroinitiator RAFT methodology was successfully applied to the synthesis of well-defined PCL-*b*-PVAc block copolymers without detectable PCL or PVAc residual chains.

Experimental

Materials

ε-Caprolactone (CL, 99%, Aldrich 24,129-6), 4-pentyn-1-ol (97%, Aldrich 53900-04-05), and 3-bromo-1-propanol (97%, Aldrich 627-18-9) are preserved under nitrogen, on molecular sieves (3 Å). Triethylaluminum (TEAl, 1.0 M in pure hexane, Aldrich 25, 266-2), azo-bis-isobutyronitrile (AIBN, 98%, Aldrich 441090), CuBr (99.999%, Aldrich 7787-70-4), bis (2-dimethyl aminoethyl) (methyl) amine (PMDETA, 99%, Aldrich 36, 949-7), azide exchange resin (Aldrich 36,834-2), aluminum oxide (Aldrich 19,944-3), and copper (I) bromide (98%, Aldrich 21,286-5) were used as received. Toluene was distilled over CaH_2 and preserved under nitrogen, on molecular sieves (3 Å). Vinyl acetate was purified by passing over a column of basic alumina and subsequently distilled prior to use.

All polymerization reactions were carried out in Schlenk tubes under argon.

Measurements

Size exclusion chromatography (SEC) was carried out using a Shimadzu LC-20AD liquid chromatograph equipped with two Varian PL gel 5 μ MIXED-columns (column, injection, and refractometer temperature: 30 °C, injection volume: 100 µL, solvent: tetrahydrofuran at 1 mL min^{-1}) and a refractive index detector (Shimadzu RID-10A). Size exclusion chromatography was calibrated with PS standards. ^{1}H NMR spectra were recorded on a 400-MHz spectrometer (Brucker AC 400) using $CDCl_3$ or DMSO-d as solvents.

Synthesis of PCL-*b*-PVAc block copolymers by "coupling"

Synthesis of PCL-alkyne

PCL-alkyne-1 To a Schlenk tube equipped with a magnetic stirring bar were added under argon 0.5 mL (5.42 mmol) of 4-pentyn-1-ol in 100 mL of toluene. 0.54 mL of TEAl (0.54 mmol) was then introduced, followed by 20 mL (0.18 mol) of CL. The polymerization was allowed to process for 2 h at 50 °C. The reaction mixture was concentrated, and the polymer precipitated into cold methanol, filtered, and dried to provide a white powder.

M_n (SEC) = 3,700 g/mol and pdi = 1.16, after correction using the Mark–Houwink coefficients $K = 13.95.10^{-3}$ mL g^{-1} and $a = 0.786$ for the PCL [34], $K = 14.10^{-3}$ mL g^{-1} and $a = 0.70$ for PS [35]. Yield = 91% for CL. M_n (^{1}H NMR) = 3,450 g/mol. ^{1}H NMR ($CDCl_3$ at 20 °C): 2 ppm (1H, t, CH≡), 3.65 ppm (2H, t, OH–CH_2), 4.2 ppm (2H, t, CH_2O–), 4.08 ppm (2H, t, CH_2–O), 2.33 ppm (2H, t, C=O), 1.64 ppm (4H, m, CH_2-CH_2), 1.40 ppm (2H, m, CH_2). These spectroscopic data are in agreement with those indicated by Xu et al. [30].

Synthesis of the azide terminated RAFT transfer agent

The synthesis of azido-dithiobenzoate was carried out according to the procedure developed by Quénemer et al. [25].

Synthesis of PVAc-N_3

PVAc-N_3-1 To a Schlenk tube equipped with magnetic stirring bar were added 100 mL (1.07 mol) of vinyl acetate, 28 mg (0.17 mmol) of AIBN, and 0.44 g of azido-dithiobenzoate (1.7 mmol). The reaction mixture was deoxygenated by three freeze–pump–thaw cycles and back filled with argon. The tube was then placed in an oil bath thermostated at 60 °C for 7 h. The polymer was isolated by evaporating off the residual monomer under vacuum followed by solubilization in DMSO and precipitation in hexane. Then, the product was recovered and dried under vacuum. M_n (^{1}H NMR, $CDCl_3$) = 11,500 g/mol, M_n (SEC) = 12,800 g/mol, and pdi = 1.25. Yield = 21% for VAc.

The obtained molecular weights were corrected for PVAc via the universal calibration using the Mark–Houwink coefficients. $K = 15.6.10^{-3}$ mL g^{-1} and $a = 0.704$ for the PVAc [36] and $K = 14.10^{-3}$ mL g^{-1} and $a = 0.70$ for PS [35].

Synthesis of PCL-*b*-PVAc copolymers using "click chemistry"

PCL-b-PVAc-2

To a Schlenk tube were introduced under argon 0.5 g (0.11 mmol) of PVAc-N_3 (M_n = 4,500 g/mol), 0.98 g (0.13 mmol) of PCL-alkyne (M_n = 7,100 g/mol), 0.09 g (0.625 mmol) of CuBr, 0.13 mL (0.625 mmol) of PMDETA, and 10 mL of DMSO. The reaction was allowed to continue for 24 h at 90 °C. After 24 h of reaction, 1 g of azide exchange resin was added to the reaction mixture under argon, in order to fix the PCL-alkyne in excess. The reaction was maintained under these conditions for 24 h. The product was then filtered to eliminate the resin, recovered, and vacuum freeze-dried.

In order to eliminate the Cu complex, the reaction product was dissolved in THF and then passed through a column of aluminum oxide. Trace amounts of copper salts in the product were removed by washing with an ammonium hydroxide/citrate aqueous buffer.

The polymer was precipitated from an excess of methanol, collected by filtration and then dried under vacuum.

M_n (^{1}H NMR, DMSO-D) = 11,600 g/mol, M_n (SEC) = 18,000 g/mol, and pdi = 1.46.

Synthesis of PCL-*b*-PVAc block copolymers using the "macroinitiator" method

Synthesis of bromine terminated PCL

PCL-Br-1 To a Schlenk tube equipped with a magnetic stirring bar were added under argon 0.5 g (7.81 mmol) of 3-bromo-1-propanol in 100 mL of toluene. 0.78 mL of TEAl (0.78 mmol) was then introduced, followed by 34.3 mL (0.39 mol) of CL. The reaction mixture was stirred at 50 °C for 3 h under argon.

PCL-Br: M_n (SEC) = 5,800 g/mol, pdi = 1.22 (after correction, using the Mark–Houwink coefficients). M_n (^{1}H NMR, $CDCl_3$) = 5,700 g/mol; yield = 100%.

Synthesis of PCL-xanthate from PCL-bromine

To a Schlenk tube were added 0.7 g (4.36 mmol) of potassium O-ethylxanthate, 6.3 g (1.10 mmol) of PCL-Br (5,700 g/mol), and 50 mL of distilled acetone. The reaction mixture was stirred at room temperature for 24 h under argon. The obtained PCL was precipitated in 100 mL of methanol and recovered by filtration, washed three times with water/methanol (50/50, v/v) to remove the excess of o-ethylxanthate, and freeze-dried under vacuum.

^{1}H NMR ($CDCl_3$ at 20 °C): 2.2 ppm (m, 2H, –CH_2S–); 3.65 ppm (t, 2H, OH–CH_2); 4.2 ppm (m, 2H, –CH_2O–); 4.6 ppm (q, 2H, –CH_2OC=S–), 4.08 ppm (t, 2H, CH_2–O), 2.33 ppm (t, 2H, C=O), 1.64 ppm (m, 4H, CH_2–CH_2), 1.40 ppm (m, 2H, –CH_2).

Synthesis of PCL-b-PVAc

PCL-b-PVAc-3 To a Schlenk tube were introduced under argon 1 g ($1.75.10^{-4}$ mol) of PCL-Xanthate (M_n = 5,700 g/mol), 0.003 g ($1.75.10^{-5}$ mol) of AIBN, 3 mL (0.035 mol) of VAc, and 10 mL of DMSO. The reaction mixture was stirred for 24 h at 60 °C under nitrogen. The block copolymer obtained was precipitated in water, recovered by filtration, and dried.

M_n (^{1}H NMR, DMSO-D) = 22,000 g/mol. M_n (SEC) = 23,300 g/mol and pdi = 1.33 (calibrated with PS standards).

Conclusion

"Coupling" and "macroinitiator" methods were successfully used to synthesize PCL-*b*-PVAc with controlled molecular weights and narrow polydispersity indices, on the one side by click chemistry and on the other by a combination of ROP and RAFT techniques.

PCL terminated by an alkyne group was obtained from a bifunctional initiator bearing an alkyne function and an hydroxyl group, whereas the azide functionalized

PVAc was synthesized by RAFT using a specific transfer agent. These two reaction products, PVAc and PCL, were coupled by a 1,3-cyclo addition "click chemistry" reaction to obtain the corresponding block copolymer. The use of alkyne terminated PCL and azide end-functionalized PVAc is a suitable approach for the synthesis of PCL-*b*-PVAc diblock copolymers of precise molar mass and composition, which are determined by the characteristics of the precursor blocks

For the "macroinitiator" method, the PCL-*b*-PVAc copolymers were obtained by a two-step procedure: first, PCL macroinitiators having a xanthate end group were prepared by ROP of ε-caprolactone; then, polymerization of VAc was initiated from the PCL. ^{1}H NMR and SEC analysis indicated successful synthesis of the block copolymers which were obtained with well-defined structures.

The polydispersity indices of the PCL-*b*-PVAc obtained via the "macroinitiator" method are similar to those of the copolymers prepared by a coupling reaction. The "macroinitiator" technique has the advantage that copolymers of relatively high molar mass are accessible. The corresponding values, however, can only be determined indirectly by combination of SEC and NMR, with the assumption of complete end-functionalization of the PCL precursor block and by neglecting trace amounts of PVAc homopolymer directly initiated by the primary free radicals.

Taking into account these minor limitations, well-defined PCL-*b*-PVAc diblock copolymers could be obtained for the first time, as well by "click chemistry" as by a "macroinitiator" process.

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