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Benzoic acid-organocatalyzed ring-opening (co) polymerization (ORO(c)P) of L-lactide and ε-caprolactone under solvent-free conditions: from simplicity to recyclability†

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The development of sustainable synthetic approaches to biodegradable and biocompatible polymeric materials represents a key challenge in polymer chemistry. A novel solvent-free and organocatalyzed ring-opening (*co*)polymerization (ORO(*c*)P) method utilizing benzoic acid(BA) as simple thermostable carboxylic acid-type catalyst is proposed to not only produce structurally well-defined aliphatic homopolyesters derived from L-lactide (L-LA) and ε-caprolactone (CL), but also and, unexpectedly, statistical copolyesters based on the two monomer units. RO(*c*)P reactions were conducted in bulk in a temperature range of 155–180 °C, in presence of alcohols as initiators. A triblock copolymer, namely, PLLA-*b*-PCL-*b*-PLLA, was also synthesized, attesting to the "controlled/living" character of this BA-OROP process. A bifunctional mechanism is proposed to operate, involving activation of both the monomer and the propagating hydroxyl by H-bonding. Very importantly, the BA organocatalyst could be readily recycled by simple sublimation and could be reused in further organocatalytic cycles.

Introduction

Poly(lactide) (PLA) and poly(ε-caprolactone) (PCL) are representative aliphatic polyesters that have received considerable attention in the past decades, as potential bio-sourced alternatives to petroleum-based polymeric materials.[1–3] Owing to their intrinsic biodegradable, nontoxic and biocompatible properties,[4,5] both PLA and PCL have found a growing interest in a wide panel of potential applications, including in biomedical and pharmaceutical,[4,5] electronic,[6] automotive[7] or packaging[8] fields. However, both polymers suffer from some drawbacks that still limit their widespread adoption in industry. For instance, PLA is a high Young modulus brittle material exhibiting poor elasticity,[9,10] high degradation rate[11] and poor drug permeability.[12] PCL shows opposite properties to PLA, with a good elasticity and permeability,[12] slow degradation rate,[11] but with poor mechanical properties.[10,13] Therefore, statistical aliphatic copolyesters based on LA and CL monomer units is often seek for to optimize thermo-mechanical and biodegradable properties of related materials and broaden their application scope.[14–20]

Synthesis of PLA and PCL is typically achieved by ring-opening polymerization (ROP), while statistical copolyesters can be obtained by ring-opening copolymerization (ROcP). Both ROP and ROcP reactions generally employ heavy metal-based complexes as catalysts providing high activity and selectivity.[1,13,21,22] However, the development of catalytic systems enabling statistical copolymerization of LA and CL is particularly challenging, owing to the highly differing reactivity between the two monomers in ROcP, LA being preferentially incorporated first, which generally results in the formation of gradient-type copolymers.[22]

Organocatalysts have been introduced in polymer synthesis as they offer many advantages over metallic catalysts, including a reduced toxicity and cost, and easier synthesis and storage. As organocatalysts lead to metal-free polymers, this is particularly relevant in specific applications, such as microelectronics, biomedical or cosmetics. A variety of small organic molecules, including Brønsted/Lewis bases and acids, have thus been employed to catalyze the polymerization of miscellaneous monomers.[23–29]

While in solution and at working temperatures generally low, LA is preferentially incorporated in ROP utilizing basic,

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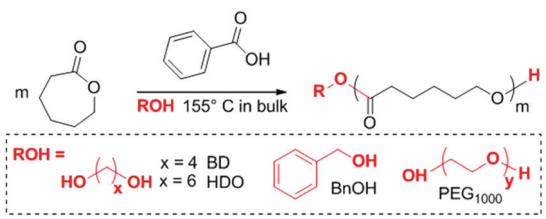
nucleophilic and/or bifunctionnal organocatalytic systems, the latter prove unstable under solvent-free conditions and/or at T > 150 °C. They can also generate some coloration and decrease the thermal properties of the final material.[30,31] Besides, only two strong organic acid catalysts, namely, trifluoromethane sulfonic acid (TfOH),[32,33] and diphenyl phosphate (DPP)[34] have been reported to control the ROP of LA, and only DPP has enabled the ROP of LA to be carried out in bulk at 130 °C; though, no detailed investigation into the control of the polymerization has been described.[34]

Basic organocatalysts can be employed for the ROP of CL when combined with a co-catalyst, *e.g.* a thiourea[35–38] or an urea[37,38] allowing for a fast and controlled process. Acidic organocatalysts, such as sulfonic[39] and phosphoric acid,[40–42] prove particularly efficient to trigger the organocatalyzed ROP (OROP) of CL.

Weaker acidic catalysts, namely, carboxylic acids, such as trifluoroacetic acid, and naturally occurring α-hydroxyacids, such as lactic acid, citric acid, mandelic acid, tartaric acid,[43–47] and other α-amino acids[46,48–50] have also attracted some interest in OROP of LA and CL over the last 15 years. This is due to their broad availability as well as their air, moisture and thermal stability. Interestingly, some carboxylic acids enable the ROP process to be performed under solvent-free conditions, which is of prime relevance in a context of green chemistry.[43–47] Complex polymer architectures, including star-[43] and dendrimer-like PCLs[44] or graft copolymers can even be obtained *via* such an organocatalyzed pathway. The carboxylic acid-OROP of CL can be typically performed in bulk at 120–160 °C.[43–47] Strangely enough however, the simplest aromatic carboxylic acid, namely, benzoic acid (BA), a highly thermally stable[51] and naturally occurring compound, has not been investigated as such in OROP. In contrast, stoichiometric combination of BA and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as superbase, despite forming a stable salt in solution, has proven efficient in controlling the ROP of LA in dichloromethane at r.t., with BnOH as initiator.[52] More recently, Guo *et al.* have resorted to BA derivatives featuring hydrogen bond donating substituents, *e.g.* 2,4-dihydroxybenzoic acid, *o*,*o*-bis (pivalamido)benzoic acid or 3-amino-1,2,4-benzothiadiazine-1,1-dioxide, for the OROP of cyclic esters in solution at r.t.[53–55]

Catalyst recycling represents another challenge that remains to be tackled in polymer synthesis by organocatalysis, and only a handful of reports have addressed this point.[44,46,56–58] In the present study, we describe the catalytic activity of BA towards OROP of CL and L-LA (LLA) carried out in bulk in a temperature range of 155–180 °C, and in presence of alcohols as initiators. The OROcP of LLA and CL is also reported as a means to achieve statistical copolyesters. Moreover, advantage of the capability for BA to sublimate is exploited to recycle and reuse it in further organocatalytic cycles, affording chemically pure PCL- and PLLA-based aliphatic (co)polyesters.



Scheme 1 BA-OROP of CL.

Results and discussion

Investigations into the BA-OROP of LLA and CL

The catalytic activity of BA was first assessed for the OROP of CL, reactions being performed at 155 °C in bulk in presence of 1,4-butanediol (BD), 1,6-hexanediol (HD), benzyl alcohol (BnOH) and poly(ethyleneglycol) (PEG_{1000}; M_n = 1000 g mol^{-1}) as initiators (Scheme 1, Table 1). Polymerizations were first evaluated with BD targeting a total degree of polymerization ($DP_{tot} = [CL]_0/[BD]_0$) from 25 to 100. The catalytic loading effect was also investigated for a DP of 25 with 2.5–10 mol% of BA rel. to CL (Scheme 1, entries 2 to 6). While no reaction took place in absence of BA (entry 1), quantitative conversions were reached within less than 7 h, demonstrating the catalytic ability of BA to promote OROP of CL at high temperature

Table 1 Results and conditions of the BA-OROP of CL in bulk initiated by different alcohols[a]

Entry	I	Cat[b] (%)	$[M]_0/[I]_0$	Time (h)	C_M[c] (%)	$M_{n,SEC}$[d] (g mol^{-1})	$Đ$[d]	DP_{th}[e]	DP_{exp}[f]
1	BD	0	25	22	—	—	—	—	—
2	BD	2.5	25	4.5	97	4340	1.17	24.3	23.8
3	BD	5	25	2	93	4170	1.12	23.2	21.3
4	BD	10	25	1.25	94	4180	1.14	23.5	23.0
5	BD	5	50	4	93	8230	1.23	48.3	43.3
6	BD	5	100	7	94	16 910	1.33	93.7	93.6
7	BnOH	5	25	3.8	89	4538[g]	1.25[g]	22.2	21.4
8	PEG	5	50	7.8	95	7780[g]	1.41[g]	47.6	n.a.

[a] Reactions were performed in bulk at 155 °C under argon atmosphere with reaction conditions: m_{CL} = 200 mg. [b] Catalyst percent *related to* monomer. [c] CL conversions were determined by ^{1}H NMR analysis. [d] Uncorrected number average molar mass ($M_{n,SEC}$) and dispersity ($Đ$) of crude polymers as determined by SEC chromatography (polystyrene standards) at 313 K and THF as eluent. [e] Theoretical degree of polymerization $DP_{th} = \frac{[M]_0}{[I]_0} \times C_M$. [f] Experimental degree of polymerization calculated from PCL chain ends as determined by ^{1}H NMR. [g] Determined by SEC chromatography (polystyrene standards) at 308 K and THF/NEt_3 (2 wt%) as eluent. n.a.: not available.

under solvent-free conditions. Analyses by ^{1}H NMR spectroscopy evidenced the formation of α,ω-bis-hydroxy telechelic PCL's, irrespective of the initial experimental conditions (Fig. S1†). Of particular interest, colorless semi-crystalline compounds ($T_g \approx -60$ °C and T_m ranging from 50 °C to 58 °C, as determined by DSC, Fig. S2†) were obtained, attesting to the thermal stability of BA as organocatalyst. Exclusive initiation of the BA-OROP of CL by BD was supported by MALDI-ToF MS analysis. Fig. 2a shows the Gaussian-like distribution of a representative PCL with a major population, **A**, corresponding to the expected PCL structure [$m/z = 90(M_{BD}) + m \times 114(M_{CL}) + 23(M_{Na^+})$]. The other population, **B**, eventually corresponds to PCL chains cationized with Na_2I^+.

Polymer number average molar masses, as determined by SEC ($M_{n,SEC}$), showed excellent agreement with M_n values calculated from the initial $[CL]_0/[BD]_0$ ratio, with $M_{n,SEC}$ increasing linearly with monomer conversion (Fig. 1a and b) and dispersities remaining low ($1.12 < Đ < 1.33$; Fig. 2b, c and Fig. S3†), consistent with a "controlled/living" ROP process. This was also supported by a chain extension experiment, as follows (Table S1†). The BA-OROP of CL in presence of BD at 155 °C ($[CL]_0/[BD]_0/[BA]_0 = 25/1/1.25$) afforded a PCL precursor with $M_{n,SEC} = 3900$ g mol^{-1} and $Đ = 1.11$. Addition of 25 eq. of CL at 155 °C increased the molar mass to $M_{n,SEC} = 7600$ g mol^{-1} after 2 h, while maintaining a low dispersity ($Đ = 1.17$; Fig. 2d), confirming efficient re-initiation from the PCL precursor.

To further demonstrate the versatility of this BA-OROP method, benzyl alcohol (BnOH) and poly(ethylene glycol) (PEG) were evaluated as initiators (Table 1, entries 7–8).

Well-defined PCL samples were also obtained in both cases, as shown by the linear increase of molar masses with monomer conversion (Fig. S4†) and the observation of monomodal and symmetrical SEC traces from both initiators (Fig. S5 and 6†).

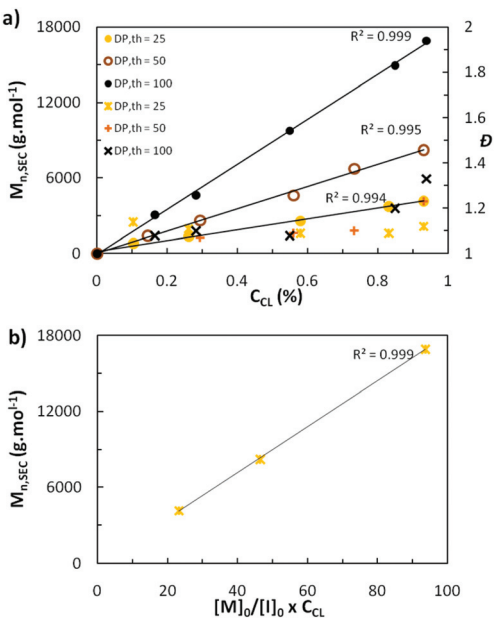


Fig. 1 (a) Evolution of uncorrected $M_{n,SEC}$ (●) and dispersity $Đ$ (×) with monomer conversion. (b) Evolution of the uncorrected $M_{n,SEC}$ with monomer-to-initiator ratios multiplied by the monomer conversion (entries 3–5–6, Table 1).

The potential of BA to trigger the OROP of LLA was also investigated. The same experimental conditions than those applied to the OROP of CL were first implemented with BD as initiator (Scheme 2, Table 2, entries 9–15). A reaction was also carried out at 180 °C (entry 13). Remarkably, such conditions enabled the synthesis of PLLA's of controlled molar masses, with a good concordance between experimental and theoretical values, for initial LLA/BD ratio in the range 25–75. Indeed, $M_{n,SEC}$ values were found to vary linearly with conversion whatever the targeted DP (Fig. 3a & b, S8†) and dispersities remained low ($Đ < 1.29$; Fig. 3a & 4a, b, S9†). As in the case of BA-derived PCL, ^{1}H NMR analysis of PLA samples showed diagnostic signals arising from the initiator. One initiator fragment per polymer chain was thus determined, attesting to the excellent agreement between DP_{th} and DP_{exp} and to the high end-group fidelity (Fig. S7†). MALDI-ToF MS analysis of a representative PLLA sample confirmed the incorporation of the BD initiator (Fig. S10†) with a distribution of peaks consistent with the formation of a α,ω-bis-hydroxy PLA (cationized with sodium), and a peak-to-peak mass increment of 144 g mol^{-1} corresponding to the molar mass of a LA monomer unit. Occurrence of transesterification, *i.e.* intermolecular chain transfer, was however evidenced to some extent, through the presence of signals apart by 72 Da, characteristic of PLA's obtained at high temperature.[30] However, while PLA's are generally coloured when synthesized in bulk from N-containing organocatalysts,[30,59] BA here led to colourless PLA's (Fig. 4d) even when performing the OROP reaction at 180 °C.

Chain extension experiments were then successfully achieved, in this case in presence of 3-phenylpropanol (PPA) as initiator and BA as organocatalyst. The bulk OROP of LLA at 155 °C ($[LLA]_0/[PPA]_0/[BA]_0 = 25/1/1.25$) first led to a PLLA with a final $M_{n,SEC} = 4690$ g mol^{-1} and $Đ = 1.34$ after 87 h, reaching 88% conversion (Table 2, entry 16). After purification, subsequent addition of LLA and BA ($[LLA]_0/[PLA]_0/[BA]_0 = 25/1/1.25$), and heating the reaction mixture to 155 °C, gave a final PLLA of increased molar mass after 55 h: $M_{n,SEC}$ of 7170 g mol^{-1} and a $Đ = 1.32$ (Fig. 4c, Table S2†).

After BA was demonstrated to efficiently trigger the OROP of the two monomers, reaction kinetics were investigated. Series of BD-initiated BA-OROP experiments were thus conducted at 155 °C using $[monomer]_0/[BD]_0 = 25$ at three catalytic loadings, namely, 2.5, 5 and 10 mol% rel. to the monomer. Resulting semi-logarithm plots (Fig. 5a–c) showed a pseudo first-order kinetic plot in the case of LLA monomer. As for the OROP of CL, kinetics revealed an inhibition period (Fig. 5d). To gain more insight into such kinetics, benzyl alcohol (BnOH) was selected as initiator, probing conversion of the latter by ^{1}H NMR analysis. Methylene protons of BnOH indeed showed a diagnostic signal at 4.68 ppm, while methylene oxycarbonyl-type protons, *i.e.* after initiation, shifted to 5.09 ppm (Table S3, Fig. S13†).

As expected, higher OROP rates were observed upon increasing the concentration in BA. However, first order

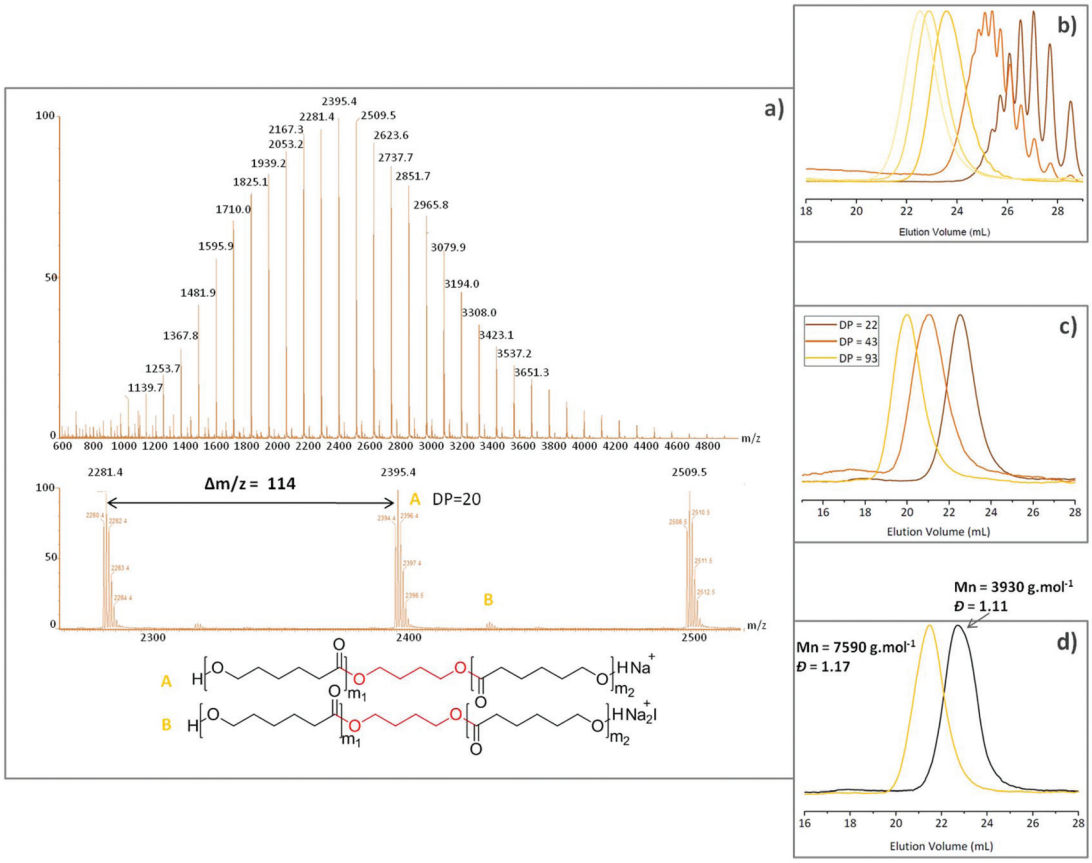
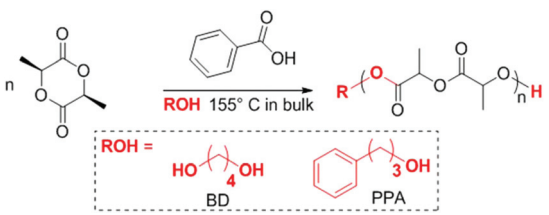


Fig. 2 (a) MALDI-ToF mass spectrum of BD-initiated BA-OROP-derived PCL (entry 3, Table 1) with M_{CL} = 114 g mol^{-1}; (b) SEC kinetic evolution (entry 3, Table 1); (c) SEC comparison between entries 3, 5 and 6; (d) chain extension experiments (see main text).



Scheme 2 BA-OROP of LA.

kinetic plots, ln([M]$_0$/[M]) *vs.* time, revealed an induction period that was ascribed to a relatively slow initiation (78% of BnOH was converted after 0.5 h, Fig. S14, Table S3†), linear evolution being eventually noted after nearly full conversion of BnOH (98%, after 1.25 h).

Overall, BA-OROP of CL proved faster than that of LLA, consistently with previous findings regarding acidic organocatalyts, namely, TFOH and DPP.[34,60] Model reactions consisting

Table 2 Results and conditions of BD-initiated BA-OROP of LLA in bulk[a]

Entry	I	Cat[b] (%)	[M]$_0$/[I]$_0$	Time (h)	C_M [c] (%)	$M_{n,sec}$ [d] (g mol^{-1})	$Đ$[d]	DP$_{th}$ [e]	DP$_{exp}$ [f]
9	BD	0	25	49	69	3660	1.09	17.2	16.5
10	BD	2.5	25	46	87	4750	1.17	21.8	23.4
11	BD	5	25	36.4	87	4620	1.12	21.8	20.7
12	BD	10	25	21	73	4050	1.09	18.2	17.8
13[g]	BD	5	25	10.1	87	4230	1.13	21.7	21.3
14	BD	5	50	69.5	83	8940	1.21	41.4	40.7
15	BD	5	75	110	87	14 540	1.29	65.2	66.6
16	PPA	5	25	87	88	4690	1.34	22	21.6

[a] Reactions were performed in bulk at 155 °C under argon atmosphere with reaction conditions: m_{LLA} = 200 mg. [b] Catalyst content *vs.* monomer. [c] LLA conversions were determined by ^{1}H NMR analysis. [d] Uncorrected average molar mass and dispersity ($Đ$) of crude copolymers determined by SEC (polystyrene standards), at 313 K and THF as eluent. [e] Theoretical degree of polymerization $DP_{th} = \frac{[M]_0}{[I]_0} \times C_M$. [f] Degree of polymerization calculated from the chain ends thanks to ^{1}H NMR. [g] Reaction performed at 180 °C.

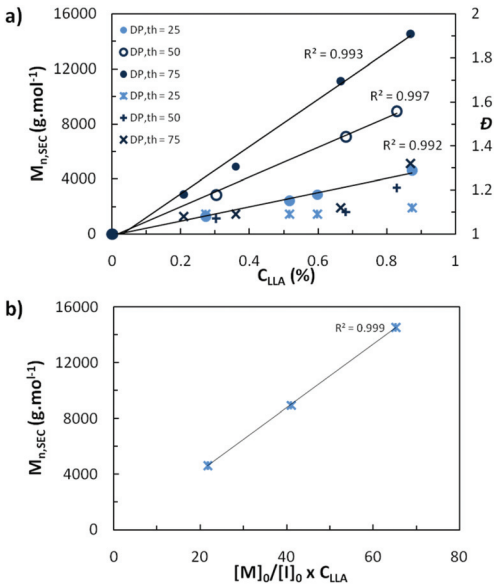


Fig. 3 (a) Evolution of uncorrected $M_{n,SEC}$ (●) and dispersity $Đ$ (×) of PLLA with monomer conversion; (b) evolution of $M_{n,SEC}$ of PLLA's with the monomer-to-initiator ratios multiplied by the monomer conversion (entries 11, 14 and15, Table 2).

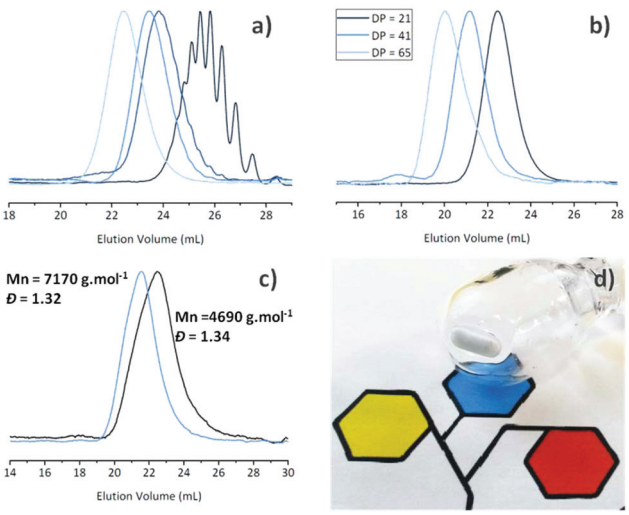


Fig. 4 (a) SEC kinetic evolution (entry 11, Table 2); (b) SEC comparison of entries 11, 14 and15, Table 2; (c) chain extension experiment initiated by PPA (see main text); (d) picture of a crude PLA obtained after 110 h of reaction at 155 °C (entry 15, Table 2).

in mixing equimolar amounts of BA and each of the two monomers were analysed by ^{13}C NMR in $CDCl_3$. A clear shift of the carbonyl carbon of CL, from 176.32 to 176.55 ppm, was detected, suggesting CL was activated by BA (Fig. S15a†). Chemical shift was less manifest in the case of LLA (167.51 ppm to 167.56 ppm; Fig. S15b†), confirming a higher efficacy of acidic catalysts towards OROP of CL. In addition, higher loadings in BA (5–10 mol% *vs.* 2.5 mol%) increased the apparent propagation rate constant (k_{app})of the BA-OROP of CL by a factor of 2–3, whereas under the same conditions, the increase of k_{app} was only 1.25 and 1.38 higher for the BA-OROP of LA.

OROP reactions were then conducted by varying the concentration of BD at a constant catalyst concentration of 5 mol% rel. to the monomer. This allowed us to evidence that $\ln(k_{app})$ varied linearly with $\ln([I]_0)$ (Fig. S17 & S19, Table S4, S5†). In other words, the dependence in initiator for both BA-OROP's of CL and LA was first-order, which allowed us to express the following kinetic equation, where $k_{app} = k_p[BA]_0^r[BD]_0$ is the apparent rate constant and [M] the monomer concentration:

$$-\frac{d[M]}{dt} = k_{app} \times [M]$$

Furthermore, while k_{app} was found to evolve linearly with $[BA]_0$ in the case of the OROP of CL (Fig. 5e), a downward curvature was noted in the case of LLA (Fig. 5f). This could be rationalized by the occurrence of competitive interaction/deactivation of PLLA hydroxyl chain ends by BA for a high catalyst loading. Similar observations have been made by Bourissou *et al.* regarding the TfOH-OROP of CL in which the apparent rate constant decreased for high TfOH : initiator ratios.[39]

Model experiments involving this time mixtures of BA and BD in various proportions ($0.5 < [BA]_0/[BD]_0 < 5$) were monitored by ^1H NMR spectroscopy in $CDCl_3$. A progressive shift of the hydroxy proton of BD was noted as $[BA]_0/[BD]_0$ increased, demonstrating the existence of the H-bonding between the two components (Fig. S15c & d†).

All these results appear consistent with the occurrence of a bifunctional mechanism, where both the monomer and the initiator are activated by the organocatalyst, similarly to previous reports utilizing stronger organic acids in OROP of cyclic esters.[40,61,62] The mechanism would thus involve protonation of the carbonyl moiety of the monomer by BA and simultaneous deprotonation of the initiator by the conjugated base of BA enabling the nucleophilic attack (Scheme 3, (**1**)). Ring-opening would be assisted by BA (**2**) leading to a complex between the ring-opened monomer and the catalyst (**3**), as depicted in Scheme 3.

Catalyst and monomer recycling

Among challenges to address in the developing field of polymer synthesis by organocatalysis, there is still the need for further investigating the toxicity of organocatalytic systems in the one hand. Preliminary studies have shown, for instance, that residual thioureas,[63] phosphazenium salt[64] and 4-dimethylaminopyridine[65] (DMAP) exhibit some cytotoxicity. On the other hand, removing the catalyst from the final polymer may be required, as residual catalyst can induce premature degradation after polymerization, in particular during processing.[35,66,67] To prevent hazards due to potentially toxic catalytic species in the final polymers, a purification step is usually implemented – typically by precipitation utilizing a large excess of solvent–, which obviously adds to the cost of the synthesis process. It worth mentioning that Paluch *et al.* devel-

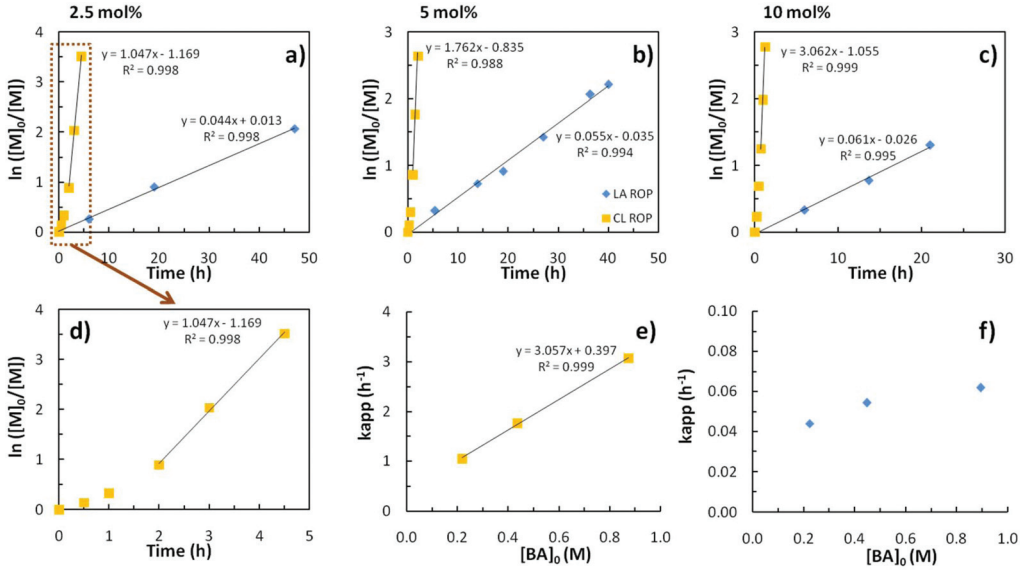
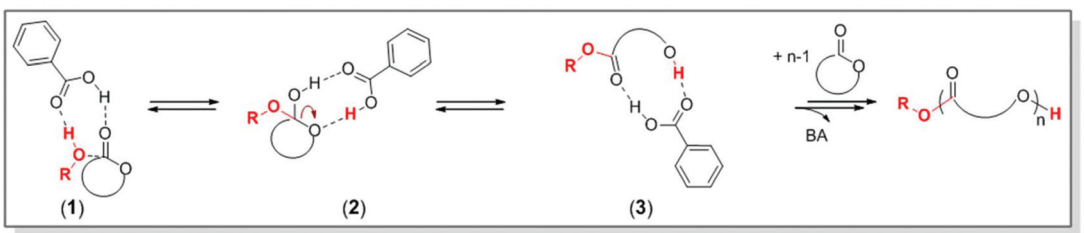


Fig. 5 Semi-logarithmic kinetic plot of the BA-OROP of CL (yellow squares) [entries 2 to 4, Table 1] and LA (blue diamonds) [entries 10 to 12, Table 2] using BD as initiator in bulk at 155 °C for $[M]_0/[I]_0$ = 25 and (a) 2.5 mol%, (b) 5 mol% and (c) 10 mol% of BA catalyst rel. to the monomer. (d) Semi-logarithmic kinetic plot of BA-OROP of CL using 2.5 mol% of BA catalyst. The plot of the k_{app} *vs.* the catalyst concentration $[BA]_0$ for the BA-OROP of (e) CL and (f) LA.



Scheme 3 Proposed bifunctional mechanism proposed for the ROP of a lactone catalyzed by benzoic acid (BA).

oped a solvent-free and catalyst-free ROP of CL under pressure.[68] Here we took advantage of the ability for BA to sublimate enabling its easy removal from the reaction mixture after OROP. As CL and LLA can be also readily removed, respectively, by evaporation and sublimation, this allowed us to achieve highly pure PLA, PCL and P(LA-*co*-CL) samples, *i.e.* free of any catalyst and monomer residues. The as-recovered BA could therefore be reused for subsequent organocatalytic cycles, and due to their easy removal, both monomers could be recycled too. The equipment we set-up for both organocatalyst and monomer recycling is displayed in Fig. 6a, and practical details are provided in the Experimental part. Hexane-1,6-diol (HDO) was also evaluated as a potential bio-based initiator for the BA-OROP of CL, using an initial $[CL]_0/[BA]_0/[HDO]_0$ ratio of 25/1.25/1. After reaction at 155 °C for 2 h (conv. = 91%) a crude PCL with $M_{n,SEC}$ = 4290 g mol^{-1} and $Đ$ = 1.12 was obtained. After the aforementioned purification step was implemented, a PCL sample free of monomer residues and containing less than 0.15 mol% of BA catalyst was recovered (Fig. 6c), the SEC trace of which nearly superimposed that of the crude compound ($M_{n,SEC}$ = 4250 g mol^{-1}, $Đ$ = 1.12, Fig. S20†), indicating absence of transesterification during the workup. Both recovered BA and unreacted CL proved chemically pure (Fig. 6b). Hence, they could be reused for a subsequent organocatalytic cycle that was performed under the same conditions by adding appropriate amounts of CL monomer and HDO initiator ($[CL]_0/[BA]_0/[HDO]_0$ = 25/1.25/1). The recycling procedure was thus repeated up to 5 times, providing a PCL always exhibiting very similar features ($3740 < M_{n,SEC} < 4290$ g mol^{-1} and $1.09 < Đ < 1.12$), as summarized in Fig. 6e. The slight decrease in the catalytic activity observed after the fifth cycle (Fig. 6d) is ascribed to some loss of BA after sublimation during purification. Nonetheless, these results demonstrate that BA can be readily recycled by sublimation and reused without significant loss of its organocatalytic activity. Furthermore, the process is particularly straightforward, fast (5 min) and does not employ any solvent. Not only could it be implemented for the controlled synthesis of PCL, but also for that of BA-derived P(LA-*co*-CL) copolymers (*vide infra*; see further).

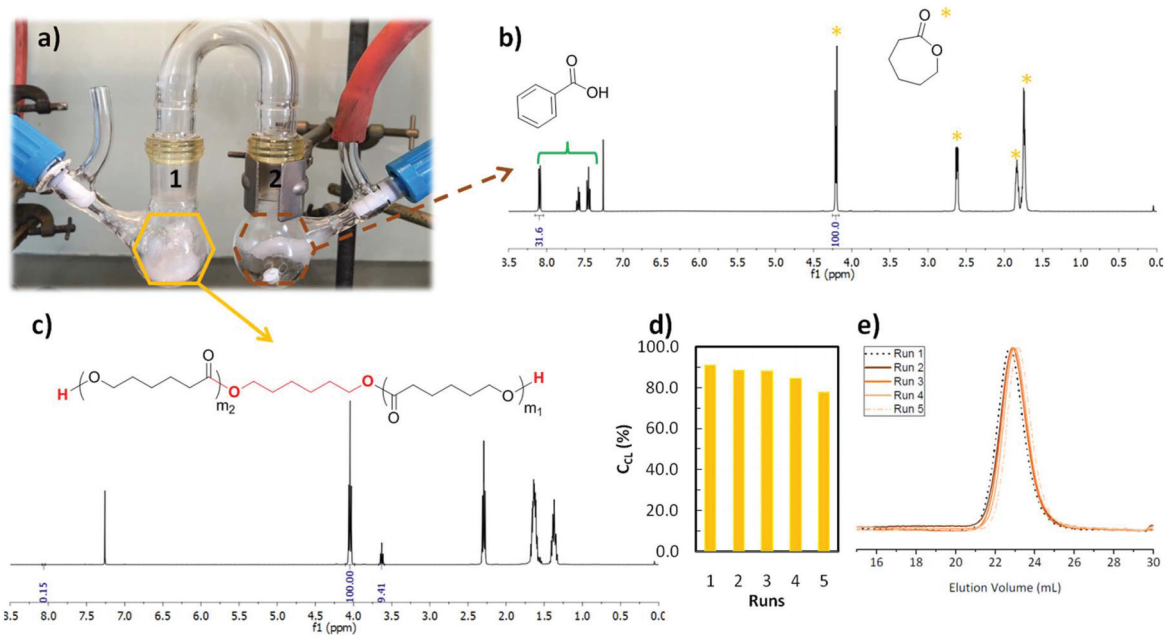
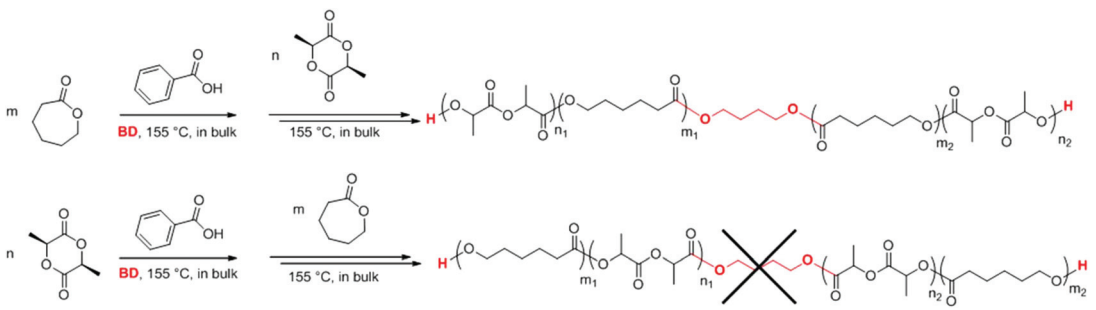


Fig. 6 (a) Picture of recycling setup; (b) ^{1}H NMR analysis performed of BA and CL recovered from vacuum treatment of Schlenk 1; (c) ^{1}H NMR analysis performed on the product purified by vacuum treatment: only PCL initiated from the 1,6-hexanediol; (d) bar graph showing the conversion of CL for each run; (e) normalized SEC traces from RI detector of pure PCLs (THF, 313 K, 1 mL min^{-1}).

Synthesis of block and statistical copolymers. As controlled synthesis of PCL and PLLA, utilizing BA as organocatalyst, was established, this prompted us to prepare both block and statistical copolymers based on PLLA and PCL. Synthesis of triblock copolymers was first investigated by sequential BA-OROP in presence of BD as initiator. As depicted in Scheme 4, monomers were introduced either by adding LLA and CL in this order or in the other, *i.e.* CL first then LLA (see Experimental). A very well-defined PLLA-*b*-PCL-*b*-PLLA triblock copolymer could be obtained as follows. An α,ω-bis-hydroxy PCL ($M_{n,SEC}$ = 4240 g mol^{-1}, $Đ$ = 1.12, entry 1, Table S6†) was isolated before BA-OROP of LLA ($[LA]_0/[BA]_0/[PCL]_0$ = 25/1.25/1) that was conducted at 155 °C for 26 h, reaching 75% conversion. Formation of the block copolymer was attested by a clear shift of its SEC trace to the higher molar masses, compared to that of the parent PCL diol ($M_{n,SEC}$ = 7730 g mol^{-1}; $Đ$ = 1.14; Fig. 7c, entry 1, Table S6†). Analysis by ^{1}H NMR confirmed the presence of both PLLA and PCL blocks, as illustrated in Fig. 7 showing the representative protons of both blocks, and protons of hydroxyl-methylene PCL end-groups at 3.6 ppm that totally vanished (Fig. 7a), in favor of hydroxyl-end protons in alpha position to the methine end-group of PLLA at 4.36 ppm (Fig. 7b). Furthermore, experimental molar masses were very close to theoretical values. Thus, triblock copolymer synthesis could be readily accomplished by sequential BA-OROP of CL and LA in this order, using BD as initiator. In contrast, attempts to reverse the order of the two monomers, *i.e.* by polymerizing LLA first to achieve a PCL-*b*-PLLA-*b*-PCL triblock copolymer met with limited success (entry 2, Table S6†). BA-OROP of CL from the α,ω-bis-hydroxy PLLA precursor ($M_{n,SEC}$ = 4200 g mol^{-1}; $Đ_M$ = 1.15) proved indeed extremely low (conv. = 27% after 2 h). This might be explained by a slow initiation of CL from the secondary OH end-groups of PLLA, as observed by NMR showing indeed a remaining signal due to



Scheme 4 Synthesis of triblock copolymers by BA-OROcP pathway (n = n_1 + n_2 and m = m_1 + m_2).

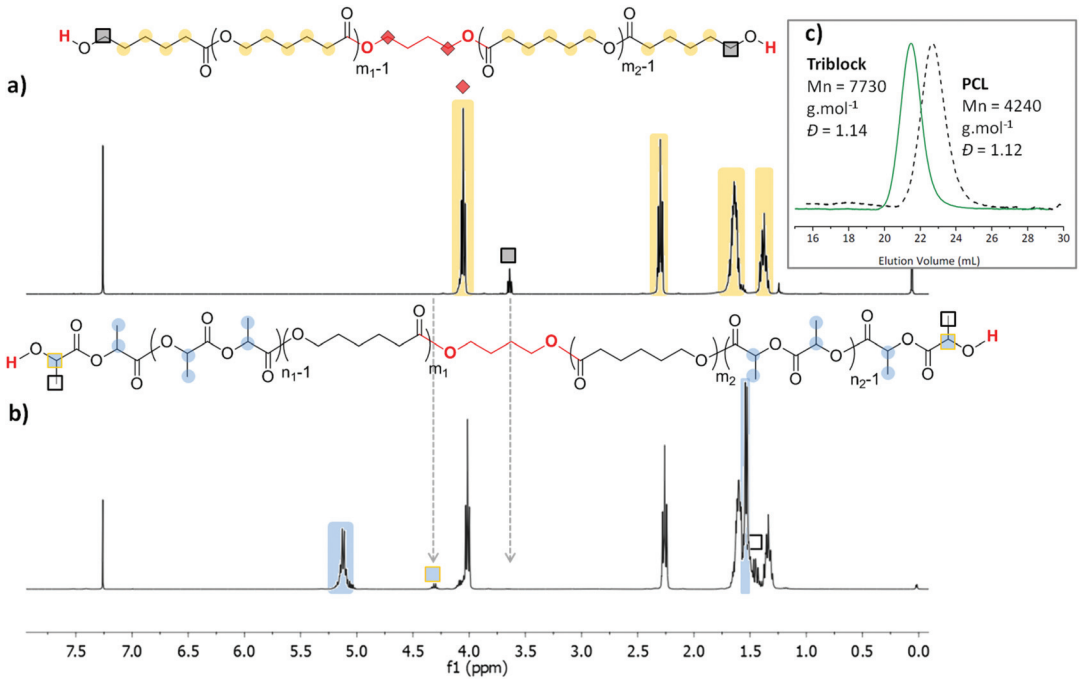
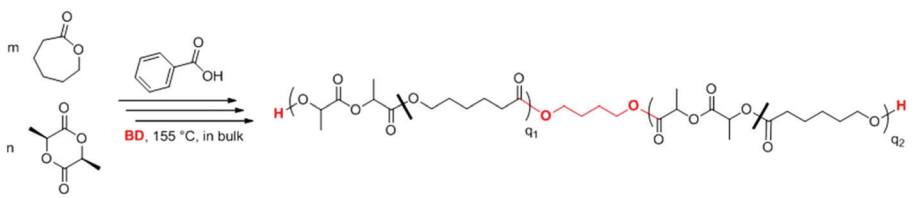


Fig. 7 ^{1}H NMR spectra comparing: (a) PCL macroinitiator and (b) PLA-*b*-PCL-*b*-PLA triblock [$CDCl_3$, 400 MHz]; (c) normalized SEC traces from RI detector of PCL (black dashed line) and corresponding triblock copolymer (uncorrected M_n determined by SEC in THF, 313 K, 1 mL min^{-1}, PS standards).

these protons (Fig. S24†). Such hypothesis has been confirmed by initiating the BA-OROP of CL at 155 °C from butane-2,3-diol for an initial monomer-to-initiator of 30 (Table S7†). As compared to the same reaction performed from a primary alcohol (Table S7,† entry 1), initiating the BA-OROP from a secondary alcohol reduces considerably the overall polymerization conversion while increases the PCL dispersity (Table S7, entry 2 and Fig. S25†).

We were also curious to examine the result of a BA-OROcP of the two monomers as a means to access PLLA-*stat*-PCL statistical copolymers. As emphasized above, developing efficient catalysts for that purpose is demanding.[22,35,41,60,69–72] Although CL is usually polymerized faster than LA in homopolymerization, the opposite situation is eventually observed in ROcP of both monomers, LA being incorporated faster than CL, which leads to the formation of gradient-type copolymers rather than statistical ones.[22] In this context, use of organocatalysts in ROcP reactions has received very little attention.[35,41,60,69–72] To the best of our knowledge, only two acidic organocatalysts have enabled to trigger random-like ROcP, including TfOH and dibenzoylmethane.[60,71,73] With basic organocatalysts, such as phosphazenes,[69] N-heterocycliccarbenes,[70,72] or 1,5,7-triazabicyclo[4.4.0]dec-5-ene[35] guanidine, only LA was inserted impeding statistical copolymer synthesis.

In a preliminary study, BA was here tested for the OROcP of CL and LLA under the same conditions described above for homopolymerization reactions of each monomer, *i.e.* at 155 °C under solvent-free conditions and using the following molar ratios: $[LA]_0/[CL]_0/[BA]_0/[BD]_0$ = 25/25/2.5/1 (Scheme 5). Monitoring the reaction by ^{1}H NMR revealed, to our delight, that both monomers were simultaneously inserted in the copolymer chain (Fig. S26†). The ^{1}H NMR spectrum of a purified copolymer allowed us to determine an overall composition in full agreement with proportions in co-monomers used in the feed ratio (Table S8, $f_{CL} = F_{CL}$; Fig. S27†). Very importantly, the presence of both homo- and heterodiads was unambiguously detected, with an estimated proportion of CL–CL homosequences of 1.2 times higher than that of CL–LA hetero-



Scheme 5 Synthesis of random-like copolyesters by BA-OROcP of CL and LLA (q = q_1 + q_2 = m + n).

sequences. In addition, the controlled character of OROcP process was evidenced both through (i) a linear evolution of $M_{n,SEC}$ values with monomer conversion (Fig. S28†), (ii) formation of copolyesters of narrow molar distribution ($D < 1.16$), and (iii) experimental DP values matching theoretical ones (Table S8†). DSC analysis was performed on the copolymer revealing a glass transition temperature of −11.6 °C, which agreed well with that calculated from the Fox equation (−11.8 °C). Such result is thus consistent with a statistical structure of the copolymer, and appears in agreement to the literature data (Fig. S29†).[74] Last but not least, recyclability of both monomers and of the BA organocatalyst was also possible in this case (see Experimental), since up to 5 recycling could be executed, though with a slight loss of catalytic activity after the fourth and fifth cycles (Fig. S21†).

A detailed investigation into this BA-mediated OROcP process, including determination of reactivity ratios and calculations by density functional theory will be the topic of a forthcoming publication.

Conclusions

This study reports for the first time the use of benzoic acid (BA) as simple, naturally occurring, cheap, thermally stable and readily recyclable weak acid organocatalyst for the metal-free synthesis of (co)polyesters based on poly(L-lactide) (PLLA) and poly(ε-caprolactone) (PCL). BA is shown to promote the organocatalyzed ring-opening polymerization (OROP) of both ε-caprolactone (CL) and L-lactide (LLA) in bulk at a rather high working temperature (155–180 °C), in presence of various alcohols as initiators, with an appreciable degree of control over molar masses and dispersities of the resulting aliphatic polyesters. A bifunctional mechanism involving activation by H-bonding of both the monomer and the alcohol initiator is proposed to operate. The controlled character of this BA-OROP process can be exploited to synthesize triblock copolymers by sequential OROP, though only by adding CL and LLA in this order to achieve, for instance, PLLA-*b*-PCL-*b*-PLLA triblock copolymers, using a diol as initiator. In addition, and particularly interestingly, use of BA enables to tackle a difficult challenge in polymer chemistry by an organocatalytic pathway, namely, statistical copolymer synthesis from CL and LLA, making BA a very versatile organocatalyst to engineer PLLA and PCL in different architectures. Finally, advantage of the capability for BA to sublimate was taken to recycle and reuse it in further organocatalytic cycles, without using any solvent, affording highly chemically pure PCL-and PLLA-based aliphatic (co)polyesters. Overall, these investigations broaden the scope of organocatalysis in macromolecular synthesis, by providing an alternative and green synthetic method to biodegradable, biocompatible and aliphatic (co)polyesters based on PLA and PCL free of any catalyst and monomer residues. This can be accomplished through the use of BA as weak acid-type organocatalyst combined with a straightforward purification procedure of the crude (co)polymers.

Experimental

Materials

L-Lactide (L-LA, 98%, TCI) was recrystallized three times from toluene and dried under vacuum for two days. ε-Caprolactone (CL, 99%, ACROS), benzyl alcohol (BnOH, 99%, ACROS), butane-1,4-diol (BD, 99%, VWR) and 3-phenylpropanol (PPA, 99%, Alfa aesar) were dried over CaH_2 for 48 hours prior to their distillation under reduced pressure and were stored on molecular sieves. Poly(ethylene glycol) (PEG_{1000}) (Fluka, M_w ~1000 g mol^{-1}) and hexane-1,6-diol (HDO, 97%, Alfa aesar) were dried *via* three azeotropic distillations of tetrahydrofurane (THF). Benzoic acid (BA, 99%, ACROS) was recrystallized once and dried *via* two azeotropic distillations using toluene. Compounds were stored in a glove box ($O_2 \leq 6$ ppm, $H_2O \leq 0.5$ ppm). Tetrahydrofurane solvent was dried using a MBraun Solvent Purification System (model MB-SPS 800) equipped with alumina drying columns. Toluene was dried using a SPS from Innovative technology and stored over polystyrylithium.

Methods

NMR spectra were recorded on a Bruker Avance 400 (^{1}H, ^{13}C, 400.2 MHz and 100.6 MHz respectively) in $CDCl_3$. Molar masses were determined by size exclusion chromatography (SEC) in THF (1 ml min^{-1}) with trichlorobenzene as a flow marker at 313.15 K, using refractometric (RI) detector. Analyses were performed using a three-column TSK gel TOSOH (G4000, G3000, G2000). The SEC device was calibrated using linear polystyrene (PS) standards. Positive-ion MALDI-Mass Spectrometry (MALDI-MS) experiments were recorded using a Waters QToF Premier mass spectrometer equipped with a Nd:YAG (third harmonic) operating at 355 nm with a maximum output of 65 μJ delivered to the sample in 2.2 ns pulses at 50 Hz repeating rate. Time-of-flight mass analyses were performed in the reflectron mode at a resolution of about 10 000. All samples were analyzed using *trans*-2-[3-(4-*tert*-butylphenyl)-2-methylprop-2-enylidene]malononitrile (DCTB) as matrix, which was prepared as a 40 mg mL^{-1} solution in $CHCl_3$. This solution (1 μL) was applied to a stainless-steel target and air-dried. Polymer samples were dissolved in THF to obtain 1 mg mL^{-1} solutions and 50 μL of 2 mg mL^{-1} NaI solution in acetonitrile was added to the polymer solution. Therefore, 1 μL of this solution was applied onto the target area already bearing the matrix crystals, and air-dried. For the recording of the single-stage MS spectra, the quadrupole (rf-only mode) was set to pass all the ions of the distribution, and they were transmitted into the pusher region of the time-of-flight analyzer where they were mass analyzed with 1 s integration time. Data were acquired in continuum mode until acceptable averaged data were obtained. Differential scanning calorimetry (DSC) measurements were carried out with a DSC Q100 LN2 apparatus from TA Instruments under helium flow. The PCL samples were heated for the first run from −130 to 100 °C, then cooled again to −130 °C and heated again for the third run to 100 °C (heating and cooling rate 10 °C min^{-1}). While PLA samples undergo 3 runs between −40 °C and

200 °C and P(LA-*co*-CL) between −70 to 200 °C. Glass transition temperatures (T_g) and melting temperatures (T_m) were measured from the second and first heating run respectively.

Synthetic procedures

General procedure for homopolymerization of CL or LLA. In a glove box, previously flamed 10 mL Schlenks were charged with the monomer CL or LLA (0.2 g), BA catalyst (2.5, 5 and 10 mol% as compared to the monomer) and a stir bar. Then the initiator (BnOH, BD, PPA or PEG_{1000}) was added *via* a 5 or 10 μL syringe. Schlenks were carefully sealed before being immersed in an oil bath preheated at the desired temperature (155 °C–180 °C). From time to time, one Schlenk was removed from the oil bath to follow the kinetic of polymerization by ^{1}H NMR and the average molar mass (M_n) and dispersity ($Đ$) by SEC. The purification consists in applying vacuum to the Schlenk at 155 °C with a high stirring rate. The CL monomer can be evaporated while BA catalyst and LA monomer are sublimated.

General procedure for block copolymerization of LLA and CL. In a glove box, previously dried 10 mL Schlenks were charged with the first monomer LLA (0.2 g, 1.4 mmol) or ε-CL (0.2 g, 1.75 mmol), the BA catalyst (5 mol% *vs.* monomer) and a stir bar. Then the BD initiator (DP_{th} = 25) was added *via* a 10 μL syringes. The Schlenks were carefully sealed before being introduced in an oil bath preheated at 155 °C. After 2 h or 36 h of polymerization for CL or LLA monomers, respectively, the Schlenk is introduced in the glove box in order to collect a sample to estimate the conversion *via* ^{1}H NMR and to determine the average molar mass (M_n) and dispersity ($Đ$) by SEC. The polymers were then purified by applying vacuum to the Schlenk at 155 °C with a high stirring rate. The Schlenk is again introduced in the glove box in order to add again the catalyst (5 mol%) and a certain amount of second monomer to target DP_{th} = 25. The polymerization is restarted by immersing the Schlenks in the oil bath for 2 or 26 hours in the case of CL and LLA OROP, respectively.

General procedure for random copolymerization of LLA and CL. In a glove box, previously dried 10 mL Schlenks were charged with an equimolar ratio of LLA (0.2 g, 1.4 mmol) and CL (0.158 g, 1.4 mmol), the BA catalyst (16.9 mg, 1.39×10^{-1} mmol) and a stir bar. Then the BD initiator (4.9 μL, 5.54×10^{-2} mmol) was added *via* a 10 μL syringe. Schlenks were carefully sealed before being introduced in an oil bath preheated at 155 °C. From time to time, one Schlenk was removed from the oil bath to follow the kinetic of polymerization by ^{1}H NMR. The polymers were then purified by applying vacuum to the Schlenk at 155 °C with a high stirring rate and the average molar mass (M_n) and dispersity ($Đ$) were analyzed by SEC.

General procedure for purification by vacuum. In a glove box, a previously flamed 20 mL Schlenk was charged with the monomer CL (1 g, 8.76 mmol), BA catalyst (53.5 mg, 4.38×10^{-1} mmol), the initiator HDO (41.4 mg, 3.5×10^{-1} mmol) and a stir bar. The Schlenk was then introduced in an oil bath preheated at 155 °C for 2 hours. After the polymerization, the mixture was cooled down and the Schlenk 1 is reintroduced in the glove box in order to collect a sample for ^{1}H NMR and SEC analyses and is then connected *via* a bridge to another flamed Schlenk 2. Schlenk 1 containing the crude polymer was then introduced in an oil bath preheated at 155 °C while vacuum (0.1–0.2 mbar) was applied to Schlenk 2 and cooled thanks to liquid nitrogen. After heating the bridge with a heat gun, a high stirring rate (800 rpm) was applied to the Schlenk 1 in order to collect in Schlenk 2, the unreacted CL monomer, the BA catalyst. Overall, the vacuum treatment in the oil bath at 155 °C lasted 5 minutes with some interruptions in order to heat again the bridge. The pure polymer is then cooled down and the assembly is introduced in the glove box. Schlenk 2 containing the unreacted monomer and the catalyst was charged with HDO (41.4 mg, 3.5×10^{-1} mmol) and the difference of monomer in order to reach 1 g (calculated thanks to the conversion by ^{1}H NMR). Finally, Schlenk 2 was introduced in the oil bath preheated at 155 °C for 2 h. The cycle was repeated 5 times.

The same procedure was applied for the copolymerization with the following conditions: LLA (0.6 g, 4.163 mmol), CL (0.475 g, 4.163 mmol), BA (51 mg, 4.16×10^{-1} mmol) and BD (15 mg, 1.67×10^{-1} mmol). The ROcP was conducted for 27 hours.

Conflicts of interest

There are no conflicts to declare.

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References

1 A. P. Gupta and V. Kumar, *Eur. Polym. J.*, 2007, **43**, 4053–4074.
2 T. Buntara, S. Noel, P. H. Phua, I. Melián-Cabrera, J. G. de Vries and H. J. Heeres, *Angew. Chem., Int. Ed.*, 2011, **50**, 7083–7087.
3 S. Wedde, P. Rommelmann, C. Scherkus, S. Schmidt, U. T. Bornscheuer, A. Liese and H. Gröger, *Green Chem.*, 2017, **19**, 1286–1290.
4 E. Castro-Aguirre, F. Iñiguez-Franco, H. Samsudin, X. Fang and R. Auras, *Adv. Drug Delivery Rev.*, 2016, **107**, 333–366.

5 T. K. Dash and V. B. Konkimalla, *J. Controlled Release*, 2012, **158**, 15–33.
6 X. Wu, Y. Ma, G. Zhang, Y. Chu, J. Du, Y. Zhang, Z. Li, Y. Duan, Z. Fan and J. Huang, *Adv. Funct. Mater.*, 2015, **25**, 2138–2146.
7 A. Bouzouita, C. Samuel, D. Notta-Cuvier, J. Odent, F. Lauro, P. Dubois and J.-M. Raquez, *J. Appl. Polym. Sci.*, 2016, **133**, 43402–43410.
8 R. Auras, B. Harte and S. Selke, *Macromol. Biosci.*, 2004, **4**, 835–864.
9 O. Martin and L. Avérous, *Polymer*, 2001, **42**, 6209–6219.
10 K. Van de Velde and P. Kiekens, *Polym. Test.*, 2002, **21**, 433–442.
11 C. G. Pitt, M. M. Gratzl, G. L. Kimmel, J. Surles and A. Schindler, *Biomaterials*, 1981, **2**, 215–220.
12 C. G. Pitt, A. R. Jeffcoat, R. A. Zweidinger and A. Schindler, *J. Biomed. Mater. Res.*, 1979, **13**, 497–507.
13 M. Labet and W. Thielemans, *Chem. Soc. Rev.*, 2009, **38**, 3484–3504.
14 S. H. Kim, S. H. Kim and Y. Jung, *J. Controlled Release*, 2015, **206**, 101–107.
15 D. W. Grijpma, G. J. Zondervan and A. J. Pennings, *Polym. Bull.*, 1991, **25**, 327–333.
16 Y. Jung, M. S. Park, J. W. Lee, Y. H. Kim, S.-H. Kim and S. H. Kim, *Biomaterials*, 2008, **29**, 4630–4636.
17 J. I. Lim, S. il Kim and S. H. Kim, *Colloids Surf., B*, 2013, **103**, 463–467.
18 K. J. Cha, E. Lih, J. Choi, Y. K. Joung, D. J. Ahn and D. K. Han, *Macromol. Biosci.*, 2014, **14**, 667–678.
19 L. Calandrelli, A. Calarco, P. Laurienzo, M. Malinconico, O. Petillo and G. Peluso, *Biomacromolecules*, 2008, **9**, 1527–1534.
20 M. Rizzuto, A. Mugica, M. Zubitur, D. Caretti and A. J. Müller, *CrystEngComm*, 2016, **18**, 2014–2023.
21 A. Arbaoui and C. Redshaw, *Polym. Chem.*, 2010, **1**, 801–826.
22 E. Stirling, Y. Champouret and M. Visseaux, *Polym. Chem.*, 2018, **9**, 2517–2531.
23 M. K. Kiesewetter, E. J. Shin, J. L. Hedrick and R. M. Waymouth, *Macromolecules*, 2010, **43**, 2093–2107.
24 N. E. Kamber, W. Jeong, R. M. Waymouth, R. C. Pratt, B. G. G. Lohmeijer and J. L. Hedrick, *Chem. Rev.*, 2007, **107**, 5813–5840.
25 M. Fèvre, J. Pinaud, Y. Gnanou, J. Vignolle and D. Taton, *Chem. Soc. Rev.*, 2013, **42**, 2142–2172.
26 C. Thomas and B. Bibal, *Green Chem.*, 2014, **16**, 1687–1699.
27 W. N. Ottou, H. Sardon, D. Mecerreyes, J. Vignolle and D. Taton, *Prog. Polym. Sci.*, 2016, **56**, 64–115.
28 S. Naumann and A. P. Dove, *Polym. Int.*, 2016, **65**, 16–27.
29 A. P. Dove, *ACS Macro Lett.*, 2012, **1**, 1409–1412.
30 L. Mezzasalma, A. P. Dove and O. Coulembier, *Eur. Polym. J.*, 2017, **95**, 628–634.
31 H. Li and L. Gu, *J. Polym. Sci., Part A: Polym. Chem.*, 2018, **56**, 968–976.
32 D. Bourissou, B. Martin-Vaca, A. Dumitrescu, M. Graullier and F. Lacombe, *Macromolecules*, 2005, **38**, 9993–9998.
33 M. Baśko and P. Kubisa, *J. Polym. Sci., Part A: Polym. Chem.*, 2008, **46**, 7919–7923.
34 T. Saito, Y. Aizawa, K. Tajima, T. Isono and T. Satoh, *Polym. Chem.*, 2015, **6**, 4374–4384.
35 B. G. G. Lohmeijer, R. C. Pratt, F. Leibfarth, J. W. Logan, D. A. Long, A. P. Dove, F. Nederberg, J. Choi, C. Wade, R. M. Waymouth and J. L. Hedrick, *Macromolecules*, 2006, **39**, 8574–8583.
36 P. P. Datta, J. U. Pothupitiya, E. T. Kiesewetter and M. K. Kiesewetter, *Eur. Polym. J.*, 2017, **95**, 671–677.
37 K. V. Fastnacht, S. S. Spink, N. U. Dharmaratne, J. U. Pothupitiya, P. P. Datta, E. T. Kiesewetter and M. K. Kiesewetter, *ACS Macro Lett.*, 2016, **5**, 982–986.
38 B. Lin and R. M. Waymouth, *Macromolecules*, 2018, **51**, 2932–2938.
39 S. Gazeau-Bureau, D. Delcroix, B. Martín-Vaca, D. Bourissou, C. Navarro and S. Magnet, *Macromolecules*, 2008, **41**, 3782–3784.
40 D. Delcroix, A. Couffin, N. Susperregui, C. Navarro, L. Maron, B. Martin-Vaca and D. Bourissou, *Polym. Chem.*, 2011, **2**, 2249–2256.
41 X. Zhou and L. Hong, *Colloid Polym. Sci.*, 2013, **291**, 2155–2162.
42 K. Makiguchi, T. Satoh and T. Kakuchi, *Macromolecules*, 2011, **44**, 1999–2005.
43 F. Sanda, H. Sanada, Y. Shibasaki and T. Endo, *Macromolecules*, 2002, **35**, 680–683.
44 P. V. Persson, J. Casas, T. Iversen and A. Córdova, *Macromolecules*, 2006, **39**, 2819–2822.
45 P. V. Persson, J. Schröder, K. Wickholm, E. Hedenström and T. Iversen, *Macromolecules*, 2004, **37**, 5889–5893.
46 J. Casas, P. V. Persson, T. Iversen and A. Córdova, *Adv. Synth. Catal.*, 2004, **346**, 1087–1089.
47 J. Xu, J. Song, S. Pispas and G. Zhang, *J. Polym. Sci., Part A: Polym. Chem.*, 2014, **52**, 1185–1192.
48 H. Li, S. Zhang, J. Jiao, Z. Jiao, L. Kong, J. Xu, J. Li, J. Zuo and X. Zhao, *Biomacromolecules*, 2009, **10**, 1311–1314.
49 C. Wang, H. Li and X. Zhao, *Biomaterials*, 2004, **25**, 5797–5801.
50 E. Oledzka, M. Sobczak, M. Kolakowski, B. Kraska, W. Kamysz and W. Kolodziejski, *Macromol. Res.*, 2013, **21**, 161–168.
51 E. Lindquist and Y. Yang, *J. Chromatogr. A*, 2011, **1218**, 2146–2152.
52 D. J. Coady, K. Fukushima, H. W. Horn, J. E. Rice and J. L. Hedrick, *Chem. Commun.*, 2011, **47**, 3105–3107.
53 J. Xu, J. Liu, Z. Li, X. Li, C. Chen, C. Zhao, S. Xu, X. Pan, J. Liu and K. Guo, *Polym. Chem.*, 2016, **7**, 1111–1120.
54 J. Xu, K. Yang, Z. Li, J. Liu, H. Sun, S. Xu, H. Wang, T. Guo, H. Dong and K. Guo, *Polym. Chem.*, 2017, **8**, 6398–6406.
55 H. Sun, S. Xu, Z. Li, J. Xu, J. Liu, X. Wang, H. Wang, H. Dong, Y. Liu and K. Guo, *Polym. Chem.*, 2017, **8**, 5570–5579.
56 Y. Jin, Y. Ji, X. He, S. Kan, H. Xia, B. Liang, J. Chen, H. Wu, K. Guo and Z. Li, *Polym. Chem.*, 2014, **5**, 3098–3106.

57 M. Liras, E. Verde-Sesto, M. Iglesias and F. Sánchez, *Eur. Polym. J.*, 2017, **95**, 775–784.
58 G. W. Nyce, T. Glauser, E. F. Connor, A. Möck, R. M. Waymouth and J. L. Hedrick, *J. Am. Chem. Soc.*, 2003, **125**, 3046–3056.
59 G. Nogueira, A. Favrelle, M. Bria, J. P. Prates Ramalho, P. J. Mendes, A. Valente and P. Zinck, *React. Chem. Eng.*, 2016, **1**, 508–520.
60 M. Baśko and P. Kubisa, *J. Polym. Sci., Part A: Polym. Chem.*, 2006, **44**, 7071–7081.
61 N. Susperregui, D. Delcroix, B. Martin-Vaca, D. Bourissou and L. Maron, *J. Org. Chem.*, 2010, **75**, 6581–6587.
62 D. J. Coady, H. W. Horn, G. O. Jones, H. Sardon, A. C. Engler, R. M. Waymouth, J. E. Rice, Y. Y. Yang and J. L. Hedrick, *ACS Macro Lett.*, 2013, **2**, 306–312.
63 A. Nachtergael, O. Coulembier, P. Dubois, M. Helvenstein, P. Duez, B. Blankert and L. Mespouille, *Biomacromolecules*, 2015, **16**, 507–514.
64 Y. Xia, J. Shen, H. Alamri, N. Hadjichristidis, J. Zhao, Y. Wang and G. Zhang, *Biomacromolecules*, 2017, **18**, 3233–3237.
65 D. V. Sweet, *Regist. Toxic Eff. Chem. Subst*, 1985.
66 O. Coulembier, S. Moins, J.-M. Raquez, F. Meyer, L. Mespouille, E. Duquesne and P. Dubois, *Polym. Degrad. Stab.*, 2011, **96**, 739–744.
67 Y. Fan, H. Nishida, Y. Shirai, Y. Tokiwa and T. Endo, *Polym. Degrad. Stab.*, 2004, **86**, 197–208.
68 A. Dzienia, P. Maksym, M. Tarnacka, I. Grudzka-Flak, S. Golba, A. Zięba, K. Kaminski and M. Paluch, *Green Chem.*, 2017, **19**, 3618–3627.
69 H. Alamri, J. Zhao, D. Pahovnik and N. Hadjichristidis, *Polym. Chem.*, 2014, **5**, 5471–5478.
70 Y. Wang, J. Niu, L. Jiang, Y. Niu and L. Zhang, *J. Macromol. Sci., Part A: Pure Appl.Chem.*, 2016, **53**, 374–381.
71 M. Baśko and P. Kubisa, *J. Polym. Sci., Part A: Polym. Chem.*, 2007, **45**, 3090–3097.
72 L. Zhang, N. Li, Y. Wang, J. Guo and J. Li, *Macromol. Res.*, 2014, **22**, 600–605.
73 L. Mezzasalma, J. De Winter, D. Taton and O. Coulembier, *J. Polym. Sci., Part A: Polym. Chem.*, 2018, **56**, 475–479.
74 N. Nomura, A. Akita, R. Ishii and M. Mizuno, *J. Am. Chem. Soc.*, 2010, **132**, 1750–1751.