EDGE ARTICLE

Synthesis of poly(L-lactide) and gradient copolymers from a L-lactide/trimethylene carbonate eutectic melt†

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A 50 : 50 wt% mixture of L-lactide and trimethylene carbonate yields a eutectic at 21.3 °C. This mixture was exploited to prepare poly(L-lactide) homopolymers at r.t. without addition of extra solvent. The intrinsic kinetic behavior of the DBU organocatalyst also allowed for the sequential polymerization of both comonomers, leading to well defined gradient copolymers.

Introduction

Driven by an exponential demand for renewable (bio)sourced materials, consumption of bio-based lactic acid polymers has grown drastically over the past decade.[1] A plethora of reviews and patents deal with the ring-opening polymerization (ROP) process of lactide (LA) monomers, which represents the most controlled and easiest technique to produce poly(lactide) (PLA). Owing to its crystalline character, solubilization of LA in organic solvents (most of the time aromatic and/or chlorinated) or its melting is a prerequisite to allow for its ROP. This paradoxical situation to produce biodegradable PLA designed to decrease the environmental impacts and reduce the society dependence on imported oil stimulates our interest to ring-open and polymerize LA at room temperature (r.t.) without addition of any solvent. In this context, the possibility to create an organic eutectic between LA and a "green" molecule is of high interest.[2]

A eutectic composition represents a mixture of compounds for which the melting point is lower than for any other proportion. Although eutectic crystallization is often used and debated in the metallurgy field, it has also received attention for bio-macromolecules and low molecular weight chemical systems.[3] Based on the work of Smith and Pennings showing that a eutectic point occurs in an athermal polymer/diluent system,[4] different research groups have demonstrated unique crystallization morphologies of polymer blends at the eutectic composition.[5]

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Results and discussion

After a wide screening, we discovered that L-lactide (L-LA) and 1,3-dioxan-2-one (TMC) are able to generate a very fluid eutectic melt ($d \sim 1.059$) at 23 °C, temperature at which each monomer is solid (melting temperature of L-LA $\sim$ 98.3 °C and TMC $\sim$ 46.0 °C); a 50 : 50 wt% mixture leads spontaneously and in less than 10–15 min to a perfect eutectic melt (Fig. 1). Differential scanning calorimetry (DSC) analyses were performed to study the eutectic behavior of different mixtures of L-LA and TMC. Both melting points and enthalpies were recorded after pretreatment of all blends at 100 °C for 5 min.

As presented on Fig. 2a, at the exception of the pure products and the eutectic composition, mixtures are characterized by two melting points corresponding to both the eutectic mixture at around 21.3 °C and the noneutectic product (see Supporting Information†, Fig. S1). The exact eutectic composition can be obtained by plotting the relative intensity of the melting enthalpy of the eutectic ($\Delta H_{eutectic}/(\Delta H_{noneutectic} + \Delta H_{eutectic})$) as a function of the L-LA content. By using a second order fitting curve, we deduce that a composition in L-LA/TMC of around 39 : 61 molar% corresponds to the eutectic molar mixture (Fig. 2b).
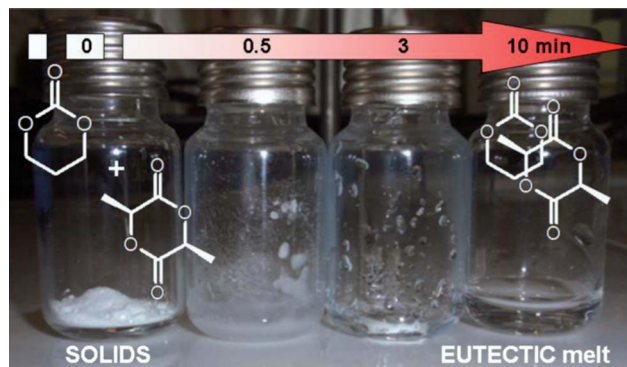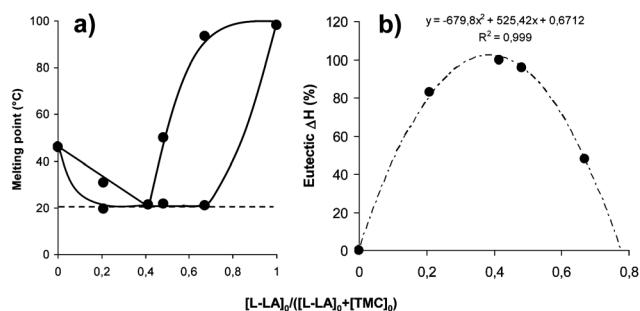

Fig. 1 Time evolution of a 50 : 50 wt% mixture of L-LA and TMC at r.t.: from pure solid products to eutectic melt.

Fig. 2 a) Melting points of different L-LA/TMC mixtures; b) relative percentage of the eutectic melting enthalpy recorded for different L-LA/TMC mixtures.

FT-IR concludes that the carbonyl groups of L-LA and TMC are not directly involved into the formation of the eutectic point in view of the absence of changes in their vibrational signature going from the pure products to the mixtures (data not shown here). However, ^{1}H NMR analysis of a 50 : 50 wt% (recorded in a minimum of CDCl$_3$ not to disrupt the molecular association) concludes that the two methyl groups of the L-LA structure are the most modified in terms of chemical environment in the mixture (Fig. S2†). It is worth noting that both cyclic monomers were not hydrolyzed or decarboxylated during their spontaneous eutectic formation.

Modelling the formation of a eutectic at the atomic scale is clearly a formidable task that would require extensive computations. In order to get a first insight into this process, we have checked whether the interaction energies in representative dimers vary going from reactants to products. In this simple model, the eutectic formation can be viewed as the breaking of the interactions within the homo-blends and their creation within two hetero-blends. For each system, we first performed molecular dynamics simulations with the Dreiding force field to determine the preferential orientation of the two molecules and next density functional theory (DFT) calculations with counterpoise corrections to evaluate the interaction energies. The interaction energies between pure L-LA, TMC, and complexes of L-LA/TMC have been estimated at the DFT level, using the wB97XD functional and a 6-31g(d,p) basis set. All technical details of the simulations are described in the SI†. Table 1 shows that the interaction energies within the TMC/TMC and L-LA/TMC complexes are almost identical while it is lower for L-LA/L-LA. The change in total energy associated with the eutectic formation is found to be negative (-0.46 kcal mol^{-1}), and hence consistent with the spontaneous eutectic formation.

We have repeated the same calculations for blends of TMC with glycolide (GLA) or mandelide (MA). Even though the latter two compounds do not differ much from L-LA, our simulations predict that mixtures of TMC/GLA should spontaneously form a eutectic while none should be observed for mixtures of TMC/MA (see Table SI1†). For the latter, the associated energy is positive (0.37 kcal mol^{-1}) while for the former, it amounts to -1.03 kcal mol^{-1}. Strikingly, these predictions are fully corroborated by experimental observations, thus suggesting that our crude model could prove very useful for a first screening of compounds. Calculations performed at a high level of theory (MP2/aug-cc-pvdz) on the smaller systems also yield negative values of -0.53 kcal mol^{-1} and -1.17 kcal mol^{-1} for L-LA/TMC and GLA/TMC mixtures, respectively, in good quantitative agreement with the DFT values.

To date, L-LA/TMC copolymers, commercially available under trademarks Resomer LT or Inion Optima, are mainly obtained by the use of metallic, potentially toxic, and hardly removable tin, aluminum, zirconium or lanthanide catalysts/initiators.[6] Despite the large difference between the reactivity ratios (r) of L-LA and TMC measured during their copolymerization ($r_{L-LA} = 13.0$; $r_{TMC} = 0.53$),[6f] perfect diblock copolymers (or even blocky) are rarely obtained since intensive redistribution of polymer segments (reshuffling) proceed along with the chain growth process.[6f] Kricheldorf et al. observed that when 2,2-dibutyl-2-stanna-1,3-dioxepane is used as initiator for the copolymerization of L-LA and TMC in chlorobenzene, both "classical" and "sequential" copolymerizations lead to poly(L-lactide) only. Such a result was hypothetically explained by the formation of a five-membered intramolecular complex between the tin alkoxide end-group and the carbonyl oxygen of the adjacent ester group limiting the reactivity towards the cyclic carbonate moeities.[6a]

Both comonomers are also polymerizable by using more friendly 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)-based organocatalysts.[7] Whereas DBU alone is only active for the ROP of L-LA, the hydrogen bonding capabilities of added thiourea (TU) have been proved useful for ROP of TMC in a reasonable time.[7] Accordingly, we have exploited here DBU for the homopolymerization of L-LA from its eutectic L-LA/TMC melt at r.t. Moreover, the catalytic discrimination of L-LA versus TMC ROPs has also been exploited for the generation of poly(L-lactide-g-trimethylene carbonate) (P(LLA-g-TMC)) gradient copolymers.

Room temperature bulk polymerizations of L-LA from its eutectic melt ([LA]$_0$/[TMC]$_0$ = 41/59) for different targeted molar masses have been performed by using benzylic alcohol (BnOH) and DBU as initiator and catalyst, respectively (Table 2, Scheme 1). Since reactions are carried out in bulk at r.t., PLLA chains start to nucleate into the eutectic (at a time depending on the targeted M_n) and to crystallize out of the melt limiting the growing polymer to a pure PLLA homopolymer, as expected. The relatively high dispersities ($Đ_M$) obtained are attributed to the diffusion limitation during the very fast ring-opening process. ^{13}C NMR and, in a less extent, ^{1}H NMR analyses of crude samples are unambiguously attributed to the homo PLLA without any trace of TMC incorporation (Fig. 3a).[6e]

The sequential copolymerization of TMC has been performed in bulk at moderate temperatures and also in solution (Table 3). Practically, an initial [LA]$_0$/[TMC]$_0$/[BnOH]$_0$/[DBU]$_0$ ratio of 100/140/1/1 has been chosen ([LA + TMC]$_0$ ~ 3.3 M). When the PLLA sequence starts to crystallize out of the eutectic melt at r.t. (~30 s; M_nGPC PLLA = 15,500 g mol^{-1}), the medium is slightly

Table 1 DFT-calculated interaction energies (in kcal mol^{-1}) for the L-LA/L-LA, TMC/L-LA and TMC/TMC complexes

L-LA/L-LA	L-LA/TMC	TMC/TMC
11.52	12.03	12.07

Table 2 Molecular characterizations of PLLA obtained from L-LA/TMC eutectic ROP in bulk at r.t

Entry	[LA + TMC]/[BnOH]/[DBU]	Polym. time(min)	Conv. $_{LA/TMC}$(%)^a	M_nGPC (g mol^{-1})^b	$Đ_M$^{b}
1	240/1/1	0.5	95/0	15,500	1.33
2	1800/1/3	4	70/0	44,000	1.65

^{a} As determined by ^{1}H and ^{13}C NMR spectroscopies. ^{b} As determined by GPC in THF/NEt$_3$ at 35 °C using PS standard calibration.
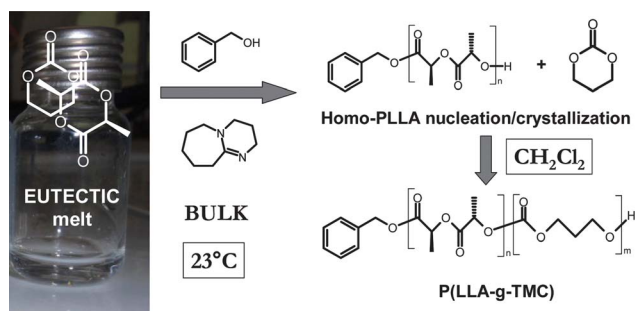
Scheme 1 Preparation of P(LLA-g-TMC) gradient copolymers from the eutectic melt of L-LA and TMC monomers.
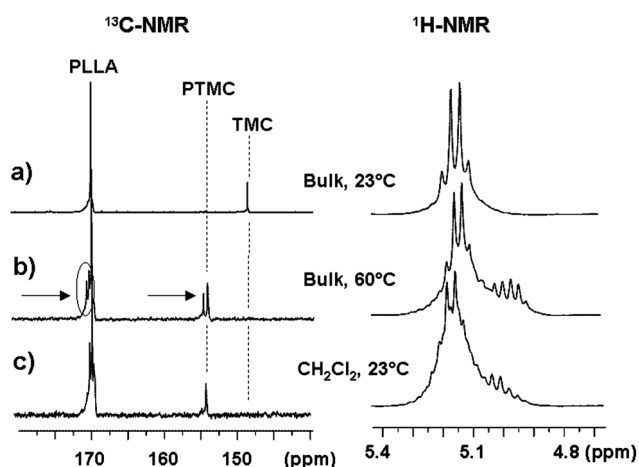
Fig. 3 ^{13}C NMR (140 to 180 ppm region) and ^{1}H NMR (4.7 to 5.4 ppm region) analyses of L-LA/TMC copolymers obtained in different conditions.

heated or quickly solubilized in CH$_2$Cl$_2$. Different conditions have been used for the sequential copolymerization of TMC in bulk: at 46 °C ($\sim T_m$ TMC), 52 °C (onset of PLLA T_g) and 60 °C (offset of PLLA T_g) to either improve the diffusion of the TMC monomer to the active site or to make more accessible the PLLA active end-group to the TMC units.

While a 46 °C treatment of the PLLA/TMC does not allow improving the sequential ROP of the cyclic carbonate from the lactidyl/DBU active site (Table 3, entry 1), a slight increase of the temperature up to the PLLA T_g highly improves its incorporation (entries 2–3). However, in both cases, ^{13}C and ^{1}H NMR analyses highlight the appearance of chain reshuffling reactions (Fig. 3b & 4). In contrast, by performing the TMC ROP in solution (entry 3), a very low level of polymer segment redistribution is detected even after 16 h (Fig. 3c & 4). Very specific signal assignment in the carbonyl and methylene carbons regions of the ^{13}C NMR spectra to appropriate comonomer sequences of L-LA and TMC-based copolymers were realized in details by Kasperczyk in 2006.[6f] Fig. 4 represents the zoom of the carbonate carbonyl carbon range (153 to 156 ppm) of both Fig. 3b and c. While both spectra are characterized by a peak showing up at 154.12 ppm attributed to a carbonate/lactide/carbonate triad also visible at 5.05 ppm in the ^{1}H NMR spectrum, the clear assignment of transesterification reactions is only visible in Fig. 3b (*at circa* 154.84 ppm) since the peak around 154.29 ppm is referred to the polycarbonate sequence.
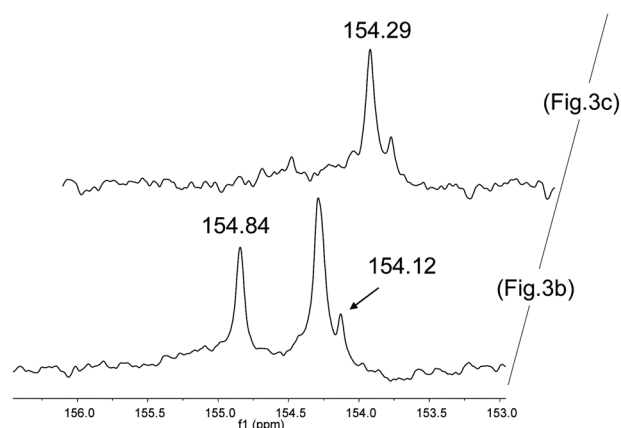
Fig. 4 Comparison of ^{13}C NMR spectra (153 to 156 ppm region) of L-LA/TMC copolymers obtained in different conditions as referring from Fig. 3b and c.

Table 3 Molecular characterizations of L-LA/TMC copolymers obtained by ROP from L-LA/TMC eutectic melt

| Entry	Conditions	TMC polym. time (h)	Conv. $_{LA/TMC}$ (%)^a	M_nGPC (g mol^{-1})^b	$Đ_M$^{b}
1	Bulk/46 °C	7	99/3	16,000	1.41
2	Bulk/52 °C	5	98/35	19,700	1.63
3	Bulk/60 °C	4	99/45	17,700	1.75
4	CH$_2$Cl$_2$/23 °C	16	97/63	22,000	1.64

^{a} As determined by ^{1}H and ^{13}C NMR spectroscopies. ^{b} As determined by GPC in THF/NEt$_3$ at 35 °C using PS standard calibration.

Combination of results tends then to indicate that the microstructure of the 41 molar% TMC-based copolymer obtained after TMC ROP from a PLLA/DBU chain and performed at r.t. in solution is referred to a gradient structure:
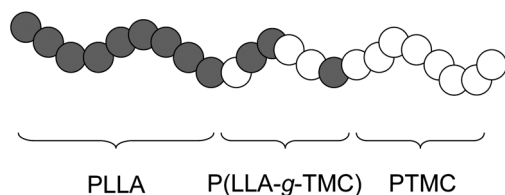
In full line with the state-of-the-art,[6f] after careful removal of the DBU catalyst[8] and by preventing the PLLA thermal degradation, DSC analysis of such gradient copolymer exhibits a single T_g at 19.2 °C attesting its amorphous form.

Acknowledgements

Notes and references

1 *Bioplastics MAGAZINE*, 2011, **6**, pp. 16–17.
2 The "green" term is used in reference to the following paper: B. M. Bhanage, S.-i. Fujita, Y. Ikushima and M. Arai, *Green Chem.*, 2003, **5**, 429–432.
3 (*a*) H. N. Joshi and N. Shah, *Am. Pharm. Rev.*, 2005, **8**, 120–129; (*b*) F. Lacoulonche, A. Chauvet, J. Masse, M. A. Egea and M. L. Garcia, *J. Pharm. Sci.*, 1998, **87**, 543–551; (*c*) D. Law, W. Wang, E. A. Schmitt and M. A. Long, *Pharm. Res.*, 2002, **19**, 315–321.
4 P. Smith and A. J. Pennings, *J. Polym. Sci.*, 1977, **15**, 523.
5 For example: (*a*) P. Smith and A. J. Pennings, *Polymer*, 1974, **15**, 413–419; (*b*) R. J. Zwiers, S. Gogolewski and A. J. Pennings, *Polymer*, 1983, **24**, 167–174; (*c*) J. Y. Kim, S.-T. Noh and Y. C. Bae, *Polymer*, 1998, **39**, 3473–3477; (*d*) J. Liu, N. Hameed and Q. Guo, *J. Polym. Sci., Part B: Polym. Phys.*, 2009, **47**, 1015–1023.
6 (*a*) H. R. Kricheldorf and A. Stricker, *Macromol. Chem. Phys.*, 1999, **200**, 1726–1733; (*b*) J. Yang, J. Yu, Q. Li, Y. Li and A. Cao, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 373–384; (*c*) L. Zhou, H. Sun, J. Chen, Y. Yao and Q. Shen, *J. Polym. Sci., Part A: Polym. Chem.*, 2005, **43**, 1778–1786; (*d*) Y. Nakayama, H. Yasuda, K. Yamamoto, C. Tsutsumi, R. Jérôme and Ph. Lecompte, *React. Funct. Polym.*, 2005, **63**, 95–105; (*e*) S. Agarwal, M. Puchner, A. Greiner and J. H. Wendorff, *Polym. Int.*, 2005, **54**, 1422–1428; (*f*) P. Dobrzynski and J. Kasperczyk, *J. Polym. Sci., Part A: Polym. Chem.*, 2006, **44**, 3184–3201.
7 M. K. Kiesewetter, E. J. Shin, J. L. Hedrick and R. M. Waymouth, *Macromolecules*, 2010, **43**, 2093, 2107.
8 O. Coulembier, S. Moins, J.-M. Raquez, F. Meyer, L. Mespouille, E. Duquesne and Ph. Dubois, *Polym. Degrad. Stab.*, 2011, **96**, 739–744.