Amorphous random copolymers of lacOCA and manOCA for the design of biodegradable polyesters with tuneable properties

Maxime Vagenende,1, Geert-Jan Graulus,1, Jasper Dellaey,1, Jasper Van Hoorick,1, Francis Berghmans,1 Hugo Thienpont,1 Sandra Van Vlierberge,1,*, Peter Dubruel,1,*

1Polymer Chemistry and Biomaterials Group, Department of Organic and Macromolecular Chemistry, Centre of Macromolecular Chemistry (CMaC), Ghent University, Krijgslaan 281 (Building S4), B-9000 Ghent, Belgium
2Vrije Universiteit Brussel, Department of Applied Physics and Photonics, Brussels Photonics (B-PHOT), Pleinlaan 2, B-1050 Brussels, Belgium

**ARTICLE INFO**

**Keywords:** Biodegradable polyesters; O-carboxyanhydrides; Ring-opening polymerisation; LacOCA; ManOCA

**ABSTRACT**

Biodegradable polymers derived from renewable resources can be interesting materials for a plethora of applications and have therefore gained increased interest over the last decades. We herein report for the first time the synthesis of random copolymers based on lactic and mandelic acid via ring-opening-polymerisation of their corresponding O-carboxyanhydrides (OCA). Copolymers with tailored glass transition temperature and degradation time were obtained by adjusting the co-monomer feed during copolymerisation. Molecular weight analyses of the obtained copolymers indicated lower molecular weights in comparison to the target values. Our hypothesis that keto-enol tautomerisation of the OCA-monomers was the cause for this anomaly was substantiated by a mechanistic study of the OCA-polymerisation reaction using lacOCA and manOCA as case study.

1. Introduction

Synthetic polymers derived from renewable resources have gained increasing attention over the last decades [1–4]. This is due to the large demand for environmentally degradable polymers (mainly polyesters) for applications such as (food) packaging, biomedical applications (e.g. degradable implants, drug delivery, tissue engineering, sutures, ...) and due to their decreasing production cost (approximately €2–10 per kg) and straightforward processability [5–10]. Depending on the targeted application, polymers with different characteristics are required. Examples thereof include the glass transition temperature (Tg), degradation time, mechanical properties, refractive index, .... The most common environmentally degradable polyesters, produced from renewable resources include poly(lactide) (PLA) and poly(lactide-co-glycolide) (PLGA), which have a maximal Tg of around 50 °C (in case of amorphous polymers) and a maximum degradation time of several weeks up to months, depending on the polymers’ chemical composition, the thickness and morphology of the polymer sample and the environment in which the polymer is applied [11–13]. For certain applications however, higher Tg’s or longer degradation times are required. Higher Tg polymers could be used to produce more thermally stable, biodegradable packaging materials or to produce implantable materials that do not suffer from poor dimensional stability due to a relatively low Tg [5,14]. Moreover, polymers with adjustable degradation times can be particularly interesting for example in the case of controlled-release drug carriers where among others, the degradation rate determines the drug-release profile [7,14]. To overcome the above mentioned problems, lactic acid analogues with more bulky side groups (e.g. mandelic acid) can be applied. It has already been reported in literature that poly(mandelic acid) (PMA) degrades about 100 times slower than poly(lactic acid) and that PMA shows a maximum Tg of 100 °C, which is substantially higher than the Tg of amorphous PLA (PDLLA) of 50 °C [11,15].

In this paper, we report for the first time on the synthesis of random amorphous copolymers containing mandelic and lactic acid via a controlled polymerisation process under relatively mild conditions. Lactic and mandelic acid were cyclised into their cyclic O-carboxyanhydride (OCA) derivatives (lacOCA and manOCA respectively) prior to ring-opening-polymerisation (ROP). We anticipate that copolymers of lactic- and mandelic acid will reveal Tg values between 50 °C and 100 °C. Furthermore, it is anticipated that the monomer ratio will also influence the degradation time of the final polymer ranging between that of PLA and PMA.

As it was previously reported that obtaining high molecular weight...
polymers using such OCA monomers can be troublesome [16–19], we will also compare these findings in the present work with the newly developed copolymers and study possible reasons for the observed findings.

2. Experimental

2.1. Materials

All chemicals mentioned in the current contribution were used as received unless stated otherwise. Chloroform (HPLC grade), diphenyl (trichloromethyl chloroformate), anhydrous pyridine, neohexanol (3,3-dimethylbutan-1-ol) and anhydrous dichloromethane were purchased from Sigma Aldrich (Diegem, Belgium). Calcium hydride, lithium lactate and mandelic acid were obtained from Acros Organics (Geel, Belgium). Neohexanol was distilled over calcium hydride and stored over molecular sieves (4 Å). Dry THF was obtained from a custom made solvent purification system, provided by J.C. Meyer (Laguna Beach, California, USA) using an aluminium oxide column provided by nitrogen as carrier gas and stored over molecular sieves (4 Å) until used. All NMR spectra were recorded in deuterated solvents obtained from Euriso-top (Saint-Aubin, France).

2.2. Methods

2.2.1. Synthesis of lacOCA

LacOCA was prepared following a slightly adapted procedure found in literature in order to guarantee the formation of 100% pure monomer [20]. In brief, 9.6 g (100 mmol) DL-lithium lactate was dissolved in 150 mL dry THF and was placed in an ice bath. A solution of 12.07 mL (100 mmol) trichloromethyl chloroformate in 25 mL of anhydrous THF was slowly added to the D,L-lithium lactate suspension over 20 min at 0°C. The suspension was stirred for 2.5 h at room temperature. After 2.5 h, THF was removed in vacuo. The collected liquid was carefully quenched with isopropanol. 50 mL diethyl ether was added to the residue to precipitate the Li-salts which were subsequently removed via filtration. The filtrate was concentrated in vacuo to approximately 10 mL in volume. The collected diethyl ether fraction was carefully quenched with isopropanol. The concentrated solution was layered with anhydrous hexane and placed in a freezer at −20°C overnight to induce crystallization. The supernatant liquid was removed via filtration and the formed crystals were thoroughly washed with hexane. Pure lacOCA was obtained with a yield of 66.7%.

2.2.2. Synthesis of manOCA

Unlike the typical synthesis method reported earlier for manOCA [21], manOCA was prepared following the same reaction procedure than lacOCA since similar yields were obtained compared to literature while following an easier work-up procedure (data not shown) [22]. In short, 15.22 g (100 mmol) of DL-mandelic acid was dissolved in 150 mL dry THF and was placed in an ice bath. A solution of 12.07 mL (100 mmol) trichloromethyl chloroformate in 25 mL dry THF was slowly added to the mandelic acid solution over 20 min at 0°C. The solution was stirred for 16 h at room temperature. The work-up of the reaction differed slightly from the work-up of the lacOCA monomer since for manOCA, no lithium salts needed to be removed after reaction with diphenyl. More specifically, after 16 h, THF was removed in vacuo until approximately 10 mL in volume was retained. The concentrated liquid was carefully quenched with isopropanol. The concentrated solution was layered with anhydrous hexane and placed in a freezer at −20°C overnight to induce crystallization. The supernatant liquid was removed via filtration and the formed crystals were thoroughly washed with hexane. Pure manOCA was obtained with a yield of 83.8%.

2.3. Synthesis procedures

2.3.1. Synthesis of lacOCA

2.3.2. Synthesis of manOCA

2.4. Polymerisation characterisation

Mechanical properties were determined using a TA Instruments’ Q2000 Dynamic Mechanical Analysis (DMA). Samples (5–10 mg) were placed in a platinum sample pan and automatically loaded into the DMA furnace. The samples were subsequently removed via filtration and the formed crystals were thoroughly washed with hexane. Pure manOCA was obtained with a yield of 83.8%.

2.5. Data analysis

Data analysis was performed using TA Instruments’ Universal Analysis software and provided the glass transition for the studied materials.
2.3.3. Comparison of reaction kinetics for both lacOCA and manOCA

To compare the polymerisation kinetics of lacOCA and manOCA, both monomers were polymerised to an intended DP of 100. After the addition of 10 mmol of each monomer and 10 mL of DCM to two separate flame-dried Schlenk vials in an argon-filled glovebox, these vials were sealed with a rubber septum. Separate solutions of initiator and catalyst were prepared by diluting neohexanol and pyridine 10 times in DCM. Both monomer solutions as well as the catalyst and initiator solutions were removed from the glovebox and immediately frozen in liquid nitrogen to allow three subsequent freeze-pump-thaw (FPT) cycles. Appropriate amounts of initiator and catalyst solution (100 µmol) were added simultaneously to the monomer solution which was placed in a water bath at 25°C in order to start the reaction. At regular intervals, the reaction medium was sampled using dry and Ar-purged syringes for subsequent analysis via 1H NMR spectroscopy and SEC.

2.3.4. General procedure of the (co)polymerisation of lacOCA and manOCA

(Co)polymers of lacOCA and manOCA (target DP 100) were prepared by adding the appropriate amounts of all reagents (Table 1) in flame-dried Schlenk vials. Given the low required amounts of initiator and catalyst, 1:10 solutions in DCM were prepared. All reagents were added to the Schlenk vials in an argon-filled glovebox to prevent the enclosure of moisture. Subsequently, the vials were closed with rubber septa and removed from the glovebox. The reaction mixture was frozen by means of liquid nitrogen after which the vials were connected to the Schlenk line and three FPT cycles were performed to remove any remaining moisture and/or oxygen gas. After the final FPT-cycle, the vials were brought under Ar-atmosphere and placed in a water bath at 25°C. The solutions were stirred for 24 h. Subsequently, the obtained polymers were precipitated in cold methanol. The polymer was finally removed via filtration and dried in vacuo.

3. Results and discussion

The most commonly used biodegradable amorphous polyesters that can be produced from renewable resources are typically characterized by relatively low $T_g$ values (circa 50°C for amorphous PLA and PLGA). This implies that these polymers can only be used for applications with a limited temperature range, as at elevated temperatures (i.e. higher than 50°C), these polymers would start to deform. To overcome this limitation, we applied lacOCA and manOCA for the first time to synthesize degradable random copolymers that are based on renewable resources with tailored $T_g$ values and degradation times (vide infra).

3.1. Monomer synthesis

The synthesis of the OCA monomers was performed following a slightly modified procedure found in literature [22]. We observed that in the case of lacOCA, it was necessary to remove the precipitated Li-salts after the cyclisation step with diphosgene, through addition of diethyl ether and the subsequent filtration of the formed salts. Next, in order to obtain pure lacOCA, the filtrate required to be concentrated in vacuo to the point that crystallisation of the formed OCA monomer occurred, after which recrystallization with anhydrous diethyl ether and hexane allowed the formation of pure lacOCA (structure shown in Fig. 1) (confirmed through $^1$H NMR spectroscopy) with a yield of 66.7%.

In case of manOCA, no Li-salts were formed after cyclisation, therefore a slightly different purification protocol was used. After the cyclisation step with diphosgene, the reaction mixture was concentrated in vacuo until crystallisation occurred and recrystallized with anhydrous diethyl ether and layered with hexane allowed the formation of pure OCA (structure shown in Fig. 1) (confirmed through $^1$H NMR spectroscopy), with a yield of 83.8%.
3.2. Monomer stability study

Prior to the use of the lacOCA and manOCA for polymerisation experiments, their stability was assessed under different storage conditions. These experiments were performed with the aim to exclude the possible generation of α-hydroxy acids through spontaneous OCA ring-opening, which results in the formation of an alcohol functionality which can act as a nucleophile and therefore as additional initiator during the subsequent polymerisation, leading to a lowering of the resulting molecular weight. To this end, monomers were stored under different conditions and their stability was monitored via 1H NMR spectroscopy at regular intervals. For this study, monomers were stored in vacuo, under argon or nitrogen atmosphere and using phosphorus pentoxide as a drying agent. These conditions were compared at different temperatures (i.e. −20°C, 4°C and room temperature). The results of this study (included in the supporting information Figs. 1 and 2), indicated that under all conditions, spontaneous ring-opening of the monomers occurred. Moreover, it was shown that 30 to 100% of the lacOCA monomers were opened after 7 days depending on the storage conditions, whereas for manOCA this value ranged between 3 and 10%, depending on the exact storage conditions. This spontaneous ring opening which leads to the formation of lactic acid or mandelic acid should therefore be avoided to eliminate possible lowering of the molecular weight of the resulting polymers. It is thus crucial to perform the reaction immediately after the monomer synthesis.

3.3. Kinetic study for the polymerisation of lacOCA and manOCA

Following the monomer study, the polymerisation kinetics of lacOCA and manOCA were compared. To this end, both monomers were homopolymerised to a target degree of polymerisation (DP) of 100 in dichloromethane (DCM) at 25°C, using neohexanol as initiator and pyridine as catalyst. At regular intervals, an aliquot of each reaction mixture was collected, dissolved in deuterated chloroform and analysed using both 1H NMR spectroscopy and SEC analysis (SEC chromatograms are included in the supplementary information). For the SEC analysis of poly(lacOCA), a correction factor of 0.58 was applied to correct for the difference in hydrodynamic volume with the polystyrene standards whereas for poly(manOCA) no correction factors could be found in literature [23]. Note that with the above-mentioned OCA purification protocols, it was possible to start the reaction with pure monomers immediately after monomer synthesis to avoid spontaneous ring opening.

Only for lacOCA, the monomer conversion could be determined using 1H NMR spectroscopy due to overlap of the monomer and polymer methine signals in case of manOCA (5.7–6.1 ppm). The manOCA polymerisation was therefore only monitored via SEC. Fig. 2 indicates that the evolution of the molecular weight of poly(lacOCA) versus the polymerisation time closely matches the conversion rate as determined via 1H NMR spectroscopy. However, the data from Fig. 2 further reveal that the experimental molecular weight of both poly(lacOCA) and poly(manOCA) are substantially lower (approximately 40%) in comparison to the theoretical one (vide infra). However, dispersities of both homopolymers remain below 1.2, indicating controlled polymerisations. Fig. 3 shows the reaction kinetics for the polymerisation of lacOCA to be of first order.

3.4. Copolymerisation reactions of lacOCA and manOCA

After kinetic studies of the homopolymerization reactions of lacOCA and manOCA, both monomers were used in copolymerization experiments to assess the possibility of using both monomers to obtain random copolymers (see Fig. 1). For these copolymerization assays, 1H NMR analyses (see supporting information Fig. 4) indicated that both monomers were present in the copolymers’ backbone. Moreover, the ratios of the cocomomers determined via integration of the methine protons nicely correspond to the initial monomer feed in the copolymerization reaction mixtures. Furthermore, their chemical structure was confirmed via ATR-IR spectroscopy (see supporting information Fig. 3). Next, the polymers were analysed via size exclusion chromatography (SEC) to assess the obtained molecular weights and dispersities (Table 1). Dispersities (ĐM) of the obtained polymers are all.
lower than 1.2, indicating controlled polymerisations. Despite taking into account that the polymerisation reactions were performed immediately after the monomer synthesis and with pure monomers, the obtained molecular weights were observed to be 20–40% lower than anticipated, depending on the constitution of the copolymer. Therefore, it was hypothesized that this phenomenon could be attributed to a different effect, which was anticipated to be the result of the basicity of the catalyst (pyridine) which was used in combination with the acidity of the α-proton of the OCA monomers (vide infra).

### 3.5. Monomer racemisation

It has been reported in literature that during polymerisation, racemisation of OCA monomers can occur, depending on the applied catalyst [24,25]. It was hypothesized that this racemisation under the influence of a basic catalyst such as pyridine occurs via an enolic intermediate as depicted in Fig. 4 [25–27]. As an enol contains an alcohol moiety, which can act as an initiator for the ROP, the formation of enolic intermediates results in lower experimental molecular weights. The presence of the acidic α-proton in case of both manOCA and lacOCA allows for deprotonation in the presence of a basic catalyst, which results in the formation of the above mentioned enol species.

Indeed, this hypothesis was confirmed via four experiments. In a first experiment, manOCA was dissolved in CDCl₃ to which 3 equivalents of TAIC and varying amounts of pyridine were added. The pyridine amount ranged between 0 and 5 equivalents relative to the amount of manOCA. The ¹H NMR spectra of these TAIC experiments are shown in Fig. 6 and reveal the disappearance of the α-proton peak due to the formation of this enolic intermediate and the reaction with TAIC, resulting in the disappearance of the initial C-H signal. Note that for each analysed sample, the same NMR sample was analysed at different time points in order to make a correct comparison. Furthermore, comparing different amounts of pyridine present in the reaction mixture, it can be observed that, the more pyridine present, the faster the C-H peak is disappearing, with full disappearance of the α-proton peak after three days in all cases, except for the reference sample that did not contain any pyridine. In a last experiment, pyridine was replaced by 2-cyano-pyridine, which has a lower pKa value (~0.3) than pyridine (5.3). It was anticipated that less enolic intermediate would be formed due to the lower basicity of this pyridine derivative. Indeed, the ¹H NMR spectra show that there was no decrease in intensity of the α-proton peak after 3 days. ¹³C NMR spectroscopy experiments (results included in supplementary information Fig. 5) result in a similar conclusion. Indeed, the disappearance of the α-carbon peak together with the simultaneous appearance of the associated quaternary carbon peak in the presence of pyridine indicates the formation of the TAIC-manOCA adduct as presented in Fig. 5. Moreover, this effect could not be observed for the experiments in the absence of pyridine or in case the less basic pyridine-derivative, i.e. 2-cyano-pyridine was used, implying that in the latter case, no keto-enol formation occurred. Therefore, it is anticipated that by using less basic catalysts, the issue with obtaining polymers with lower experimental molecular weight could be resolved. Preliminary polymerisation experiments using 2-cyano-pyridine as catalyst were however not able to elevate the molecular weights (data not shown). It is therefore anticipated that an alternative suitable catalyst with a low basicity should be selected for each OCA monomer used for polymerisation reactions. This is however beyond the scope of the current work, albeit necessary to increase the molecular weights obtained herein.

In a second experiment, the above-mentioned hypothesis was substantiated by the molecular mass analysis of the copolymers listed in Table 2 based on ¹H NMR spectroscopy. Table 2 provides a comparison between the experimental and the theoretical DP of the lacOCA-manOCA copolymers. The results indicated that the copolymers showed lower DP’s than would be theoretically expected with the highest contrast observed for the polymers containing the highest lacOCA content. It is anticipated that the instability of the lacOCA monomer (see supporting information Fig. 1) is resulting in spontaneous ring opening of the monomer, leading to the in situ formation of lactic acid. The α-hydroxyl functionality on this lactic acid can act as an additional initiator for the ROP, resulting in a lowering of the obtained molecular weights.

Thirdly, the hypothesis that monomer racemisation is leading to lowering of the resulting molecular weight was confirmed in a third experiment during which homopolymerisation reactions of manOCA with different target molecular weights were compared. In Table 3, the theoretical (200, 500 and 1000) and experimental DP’s are shown for three different homopolymerisation reactions, using pyridine as a catalyst, ethylene glycol as a bifunctional initiator (which was selected since it contains two alcohol moieties in an attempt to double the molecular weight of the resulting polymers and thus half the amount of initiator was used compared to the experiments in which a monofunctional initiator was used, vide supra) and DCM as a solvent. It can be observed that the discrepancy between the theoretical and the experimental DP is higher, for higher targeted DP. This effect can be explained by the principle of Le Chatelier [28]. Considering the equilibrium reaction depicted in Fig. 4, each time an enolic intermediate is consumed as an initiator during a ROP reaction, the equilibrium will reinstate, forming new enolic product that can again initiate a polymerisation reaction. Therefore, the higher the targeted DP, the more this enolic product will be formed and the lower the experimental DP compared to the theoretical DP.

Moreover, in a fourth experiment, manOCA was synthesised starting from the enantiopure R-mandelic acid which was subsequently polymerised to investigate racemisation in the polymer. Upon polymerisation of the enantiopure monomer, an isotactic polymer would be expected. However, analysis of the methine region of the resulting ¹H NMR spectrum (depicted in Fig. 7), did not show the singlet signal that would be expected for an isotactic polymer but rather a peak pattern that is associated with the formation of atactic polymer as reported earlier in literature [29]. These results were confirmed via ¹³C NMR spectroscopy experiments (as evidenced in Fig. 6 which is included in the supplementary information). These experiments clearly show the appearance of a second α-carbon signal at approximately 75 ppm due to the racemisation of R-manOCA into S-manOCA.
3.6. Thermal analyses

3.6.1. Thermogravimetric analyses

Despite the above-mentioned hurdles that were encountered with respect to obtaining high molecular weight polymers, thermal analysis of the synthesized lacOCA-manOCA copolymers was conducted. First, thermogravimetric analyses (TGA) were performed to determine their thermal stability. The results are shown in Fig. 8. Onset temperatures of the five copolymers were comparable, with a maximum difference of 46°C. Moreover, all copolymers exhibited degradation onset temperatures that exceed 310°C, showing excellent thermal stability. The residue at 800°C increased with increasing manOCA content in the copolymers, with values ranging from 0.35 to 3.92%. This increase can be attributed to the presence of the mandelic acid's aromatic moieties which result in char formation at elevated temperatures [30].

3.6.2. Differential scanning calorimetry

One of the main aims of this study was to design random copolymers with a tailored $T_g$. Therefore, the $T_g$ values of the studied copolymers were determined using DSC. In Fig. 9, the $T_g$ values are shown as
a function of the manOCA content. The Tg values increase as the manOCA content in the monomer feed rises, proving our hypothesis that the presence of aromatic side-group-containing monomer would increase the Tg of the resulting copolymer which is assumed to be the result of π-π stacking. Furthermore, it is anticipated that these values can further increase when obtaining higher molecular weights as reported earlier for poly(D,L-lactic acid) and poly(D,L-mandelic acid), revealing maximum Tg values of respectively 50 and 100 °C as plateau values once a sufficiently high molecular weight is reached [11,15]. Nevertheless, copolymers of lacOCA and manOCA containing 25 mol% of manOCA already exhibit a Tg value close to 60 °C. Moreover, as from 50 mol% or higher, this value of 60 °C can easily be surpassed. Moreover, by further increasing the manOCA content, a maximum Tg value of 90 °C could be obtained. These results indicate that by carefully controlling the monomer feed during polymerisation, polymers can be synthesized where the Tg can be altered from 42 °C up to 90 °C, depending on the targeted application. Furthermore, for each polymer only one Tg can be observed, leading to the conclusion that random copolymers were formed instead of block-copolymers for which two Tg values would be observed. Moreover, the lack of melting or crystallisation peaks in the DSC thermogram prove the presence of amorphous random copolymers.

3.7. Degradation assays

In a last part, the degradation of the synthesized copolymers in PBS buffer (pH 7.4) was monitored via SEC over a time period of 100 days.

Table 2
Comparison between the theoretical and experimental DP (via SEC and 1H NMR spectroscopy) for the obtained copolymers of lacOCA and manOCA.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>DPtheo</th>
<th>DPexp</th>
<th>DP1HNMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly(lacOCA)</td>
<td>100</td>
<td>73</td>
<td>57</td>
</tr>
<tr>
<td>Poly(lacOCA-co-manOCA) 75:25</td>
<td>100</td>
<td>81</td>
<td>60</td>
</tr>
<tr>
<td>Poly(lacOCA-co-manOCA) 50:50</td>
<td>100</td>
<td>77</td>
<td>58</td>
</tr>
<tr>
<td>Poly(lacOCA-co-manOCA) 25:75</td>
<td>100</td>
<td>71</td>
<td>99</td>
</tr>
<tr>
<td>Poly(manOCA)</td>
<td>100</td>
<td>63</td>
<td>75</td>
</tr>
</tbody>
</table>

The results of the degradation profiles for the five copolymers is shown in Fig. 10. The results indicate that increasing the manOCA content in the copolymer, results in a lower molecular weight loss, proving our hypothesis that the relative monomer ratio would influence the degradation rate of the copolymers.

Table 3
Comparison between three different target DP's during homopolymerisation reactions of manOCA and their influence on the experimental DP.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Eq Glycerol</th>
<th>Eq Man(OCA)</th>
<th>Mntheo [g mol⁻¹]</th>
<th>Mnthreo [g mol⁻¹]</th>
<th>Mnexp [g mol⁻¹]</th>
<th>Mwexp [g mol⁻¹]</th>
<th>Dm</th>
<th>DPexp</th>
<th>Dptheo</th>
<th>DPexp/DPtheo [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly(manOCA) DP200</td>
<td>1</td>
<td>200</td>
<td>8500</td>
<td>26,900</td>
<td>9600</td>
<td>2400</td>
<td>1.13</td>
<td>320</td>
<td>31.5</td>
<td>63</td>
</tr>
<tr>
<td>Poly(manOCA) DP500</td>
<td>1</td>
<td>500</td>
<td>2100</td>
<td>67,200</td>
<td>2400</td>
<td>116</td>
<td>1.11</td>
<td>16</td>
<td>500</td>
<td>3.2</td>
</tr>
<tr>
<td>Poly(manOCA) DP1000</td>
<td>1</td>
<td>1000</td>
<td>2500</td>
<td>134,200</td>
<td>2800</td>
<td>1.13</td>
<td>18</td>
<td>1000</td>
<td>1.8</td>
<td>100</td>
</tr>
</tbody>
</table>
degradation time of the resulting copolymers. Indeed, poly(lacOCA) showed a total molecular weight loss of 94% after 100 days, while this was only 18% for poly(manOCA), with intermediate degradation times observed for the lacOCA-manOCA copolymers. By carefully controlling the molecular composition of the copolymer, a suitable polymer can be synthesized with a desired degradation profile, depending on the envisaged application.

4. Conclusions

In the present study, lacOCA and manOCA were used to obtain random copolymers of lactic and mandelic acid via ring-opening polymerisation with the aim to synthesize biodegradable polymers based on natural resources that allow control over both the $T_g$ values and the degradation time of the resulting copolymers. The polymers were synthesized under relatively mild conditions and with high reaction control, resulting in polymers with $D_M$ values below 1.2. Moreover, it was shown that the $T_g$ value of these copolymers could be adjusted by controlling the lacOCA and manOCA monomer feed during copolymerisation. In this way, $T_g$ values ranging from 42 °C up to 90 °C could be obtained, rendering these polymers particularly interesting for applications that require polymers with structural rigidity at elevated temperatures such as for example in (food) packaging or as implantable materials. Next to their tuneable $T_g$, it was also shown that degradation times could be increased with increasing manOCA content in the copolymer, ranging from 94% molecular weight loss for poly(lacOCA) to only 18% molecular weight loss for poly(manOCA) after 100 days. Furthermore, these copolymers were used as a case study to prove that OCA monomer racemisation which is induced by the basicity of the applied catalyst is the reason for the consistently lower experimental molecular weights. This is an effect that is generally observed when using OCA monomers for ROP.

With the aim to obtain higher molecular weight polymers in the future, catalysts need to be carefully selected for each type of OCA monomer in order to limit the degree of racemisation during polymerisation and its effect on the resulting molecular weight. This is however beyond the scope of this research, yet interesting to be assessed in the future.

Acknowledgements

The Research Foundation Flanders (FWO) is acknowledged for financially supporting this research through projects G.0084.13 and G048915N. Jasper Van Hoorick and Jasper Delaey hold a FWO-SB grant from the research foundation Flanders (FWO, Belgium). Mr. Tim Courtin is acknowledged for recording the $^{13}$C NMR spectra and Mr. Bernhard De Meyer for recording the SEC spectra. Furthermore, Veerle Boterberg is acknowledged for her continuous efforts in keeping the lab and all its devices up and running.

Data availability

The raw/processed data required to reproduce these findings cannot be shared at this time due to legal or ethical reasons.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eurpolymj.2019.06.036.

References


Fig. 10. Degradation profile for the five copolymers over time, expressed as molecular weight percentage relative to their initial molecular weight at day 0.


