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Influence of storage conditions on the stability of lactide

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Abstract

The objective following of the present study was to investigate the effect of different storage time and conditions on the stability of lactide. In this study the samples of lactide with different purities were stored under three various storage conditions and the compound integration was monitored for a period of 2 weeks. The storage conditions selected were (1) in the desiccator, (2) in the glove box under argon and (3) under ambient atmosphere. The purity of samples was performed on HPLC and Karl Fischer titration during all period of storage. It was shown that the initial purity of the lactide has a significant bearing on the lactide degradation.

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1. Introduction

Lactide is a cyclic dimer of lactic acid. It is the main raw material for producing polylactide (PLA) and other biodegradable polymers based on lactic acid. PLA is a rigid thermoplastic polyester, biodegradable and made by a fermentation process with annually renewable resources, followed by both ring-opening polymerization of the cyclic lactide dimer or by direct condensation of lactic acid.

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Nomenclature

T	temperature, °C
P	pressure, mbar
[O ₂]	residual oxygen, ppm
W	residual moisture, ppm
T _m	melting temperature, °C

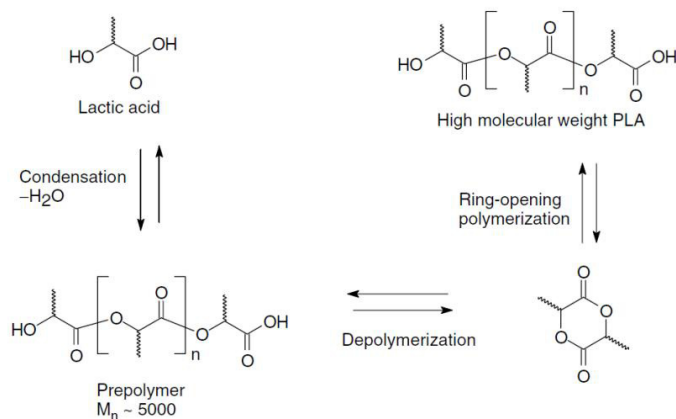


Figure 1. Schematic of PLA production via prepolymer and lactide

It is one of the most important bioresorbable and biodegradable polymeric material in a group of bioplastics. These polymers are transparent and their degradation can be controlled by adjusting the composition, and the molecular weight. Their properties are similar those of petroleum derived plastics. Some of the most important benefits of PLA include rapid degradation in the environment and the by-products are of very low toxicity, eventually being converted to carbon dioxide and water. Biopolymers that may be employed in packaging continue to receive more attention than those designated for any other application. PLA represents a good properties for its using in textile industries, food packaging, automotive and clinical applications due to its good mechanical properties and processability. The biopolymers used in medical applications must be compatible with the tissue they are found in, and may or may not be broken down after a given time period. PLA has also medical applications as sutures, orthopaedic implants, controlled drug release etc¹.

The ring opening polymerization (ROP) route includes polycondensation of lactic acid followed a depolymerisation into the cyclic lactide dimer, which can be ring opening polymerized to high molar mass polymers. It is necessary to use an extra pure lactide for ROP process. It is known that the impurities in the monomer have a significant effect on the molecular weight of PLA. Unfortunately, crystalline lactide is not stable during storage under the ambient conditions, which makes it unsuitable for further polymerization.

So, for example, the proposed crystals of lactide packed into sealed packages in an inert atmosphere and stored in a freezer (at a temperature below 12°C)². It is also reported that powdered lactide had been stored during one year at ambient temperature and at 4°C throughout the year in airtight bags and vapor barriers (including inner plastic bag and outer aluminum pouch). It has been shown that the lactide is unsuitable for further polymerization after 10 weeks storage³.

Crystalline lactide might be oxidized with the components of the environmental atmosphere (moisture, oxygen, acid contamination, etc.) and very rapidly decomposed in air. The rate of the lactide decomposition depends on a contact surface and the temperature. Therefore, most of the patents are report that this problem is solved by reducing the material surface. According to^{3,4} formation of the lactide flakes allows to store and transfer lactide at the ambient temperature without racemation, oxidation and hydrolysis processes. Formation of the tablets or granules from lactide powder is more effective when the surface-volume ratio of the particles is less than 3000 m⁻¹^{2,5}. It has been studied that the storage of the lactide in a sealed container at a temperature from 40 to 150°C at a pressure of 0.1 bar to 10 bar for seven days in an inert atmosphere allows to save its stability⁶.

Therefore, the aim of this study was to investigate changes in the properties of lactide under laboratory storage conditions at the short period of time for further synthesis of PLA.

2. Experimental

As previously mentioned the aim of this study was to investigate the effects of the real storage conditions on the physical and chemical properties of the different purity lactide.

2.1. Materials

L-Lactic acid was purchased from Purac, with a monomer concentration 80% in water. Butylacetate (REAHIM, Russia) was used for recrystallisation. Ultrapure water for HPLC eluent was prepared using a Laboratory water purification system ADRONA Crystal-B (Latvia). Acetonitrile was supplied by Cryochrom chemical company (Russia).

2.2. Synthesis of lactide

Cyclization of lactic acid were conducted in a 1 L round bottom flask equipped with an electromagnetic stirrer (IKAC-MAGHS7) and a reflux condenser connected to an inline cold trap and a vacuum pump. ZnO was used as cyclization catalyst. A thermometer was used to measure an internal temperature of the solution in the reactor. The reactor pressure was measured by a transducer and monitored by a computer. The pressure in the reactor was lowered incrementally using a vacuum pump. The temperature and pressure during the process were precise. The reaction was carried out for 2 hours at 180-240°C and vacuum 40 mbar.

The obtained crude lactide was divided in two parts. First part of crude lactide was used for investigation directly. Second part of crude lactide was purified with recrystallization from butylacetate in the ratio 1:3 (lactide:butylacetate), and then dried to a melting temperature of 96°C in a vacuum oven (MemmertVO) at 45°C using a shallow vacuum 300 mbar.

2.3. Storage conditions

In this article, a study was designed to compare three different storage conditions that are frequently applied in an usual laboratory for this monomer.

The overall duration of the experimental storage study was two weeks. Variations of the conditions were based on a storage place and with using or not the inert atmosphere (argon). Finally, the following three storage conditions were chosen for the research:

1. Storage in the dessicator filled with silica gel, zeolite and calcium chloride in a 1:1:1 ratio
2. Storage in the glove box LABstarGloveBoxWorkstation, under argon
3. Storage under ambient atmosphere

Each sample was stored in the closed Petri dishes under selected conditions. In addition to the regular sample analyses (once in three days), the first measurement was done at the time point 0 ($t = 0$) to assess the initial compound integrity. The operating modes in the glove box are shown in Table 1.

Table 1. Operating modes used in the glove box

Parameter	Column A (t)
T, °C	23-24
P, mbar	1-1.9
[O ₂], ppm	0.5
W, ppm	0.5

2.4. Analytical methods

The lactide analyses were carried out by reverse phase chromatography on a Tracer Excel ODSA-120 column (4.6 mm × 250 mm particle size 5.0 μm) using an YL Clarity HPLC system (YoungLin Clarity, South Korea) equipped with a UV detector set at 210 nm. The mobile phase was a water-acetonitrile (Cryochrom, sort O) mixture at isocratic concentration, acidified with phosphoric acid 0.3% mass (Merck). This acid pH was chosen to preserve the efficiency of the column and to provide a good selection of the analytes. The column oven temperature was maintained at 40°C and the mobile phase flow rate 1 mL/min. The isocratic elution water-acetonitrile with the ratio of 88:12 v/v was chosen as a mobile phase. RSD of the lactic acid is 1-2.2%, RSD for lactide is 0.2-1.5%.

A melting point was determined by using MeltingPointM-560 instrument. The content of the water (ppm) in the samples was determined by titration according to Karl Fischer's KF Titrimplusmetrohm device 870.

3. Results and discussions

In case of direct polycondensation of the lactic acid the received polymer has a low molecular weight, because water is released in this reaction, and it doesn't allow to obtain a polymer with the required quality. Therefore, the PLA with a high molecular weight and other copolymers of LA are prepared by ROP with lactide according to Figure 1. For this process the purity of lactide plays the main role. It might be not less than 99.9%⁷.

Water and lactic acid are undesirable impurities in the lactide, these components reduce significantly the molecular weight of the synthesized polymer. It is strongly recommended to use lactide with water content less than 100 ppm, and lactic acid less than 50 ppm. Crude lactide might be purified by distillation⁸, melt crystallization⁷, recrystallization from various solvents. After that, the obtained lactide should be dried. Thus, it is recommended to polymerize the obtained lactide after purification immediately because it is unstable during laboratory storage conditions.

Under the influence of such factors such as moisture, temperature, oxygen in the air lactide undergoes to hydrolysis, oxidation and racemation reactions. For example, the absorption of atmospheric moisture leads to a lactide ring-opening, causing a conversion of lactide to lactic acid and lactyllactic acid. Availability of lactic acid and/or acid substance lactyllactic acid supplied to the final polymerization step leads to the formation of low-molecular weight polymer³.

But sometimes it is necessary to store or to transport the lactide. For this purpose, a great variety of ways discussed above are used. They all are provide the avoiding the contact of lactide with ambient atmosphere and keep the lactide in stable during a few weeks or months.

Therefore, it was studied the behavior of crystalline lactide with different purity when stored in a fume hood, a desiccator (with desiccant) and in glove box under an argon atmosphere.

It should be noted that the lactide samples weren't purified specially according to the literature melting point (98°C) and to the high purity (99.95%). The investigated lactide samples and crude lactide were like a crystalline powder with the melting point 95-96°C and 78-89°C, respectively, these samples had different content of impurities.

Samples of crude lactide and lactide were stored under the following conditions:

1. Storage in the dessicator filled with silica gel, zeolite and calcium chloride in a 1:1:1 ratio
2. Storage in the glove box LABstarGloveBoxWorkstation, under argon
3. Storage under ambient atmosphere

The melting point was used as a simple and a reasonable method for observing changes in the lactide samples during storage, which decreases typically with increasing quantities of impurities in the material. The results are shown in Table 2.

Table 2. Observed T_m of all samples by storage conditions and time

Sample	Storage conditions	Time, days				
		0 (initial)	4 th	7 th	11	14
Lactide	Glove box	95	95,5-96,5	96,3-97,4	94,7-96,5	94,5-96,2
	Ambient	95	96-97	96-97,1	95-97	93,7-95,7

	atmosphere					
	Dessicator	95	95,5-97	96,7-97,5	91-94	90-92
Crude lactide	Glove box	87	86,5-89,5	85,5-86,5	82-89,5	80-87
	Ambient atmosphere	87	85,5-87,5	85,5-87	78-85,5	73-84
	Dessicator	87	86-89	83-86	79-86	75-83

As a result, the T_m of lactide decreases during storage and average of melting temperature grows up. It should be noted that sampling of the lactide stored in the desiccator had been done under ambient atmosphere and this can be reason for the sharp decreasing of the T_m . Changes in the T_m of crude lactide are more noticeable than for crystalline lactide, which contains a small amount of impurities. Thus, the high content of impurities in the lactide considerably reduces the period of storage.

The presence of water in air could lead to the LA formation in lactide samples during storage. HPLC method was carried out for determination of the LA content (Table 3).

Table 3. Observed content of the lactic acid (% mass.) in the lactide samples

Sample	Storage conditions	Time, days		
		0 (initial)	4 th	7 th
Lactide	Glove box	0.28	0,38	1,13
	Ambient atmosphere	0.28	0,72	1,87
	Desiccator	0.28	0,75	1,25
Crude lactide	Glove box	27.00	12.95	28.10
	Ambient atmosphere	27.00	3.68	25.6
	Desiccator	27.00	13.10	17.36

The experimental data shown in Table 3 indicate that the lactide storage follows to accumulation of LA in the lactide. Actually after one week storage, the content of LA increases so much that doesn't allow to obtain a PLA with high molecular weight. The results show that the changes in lactide kept in the glove box were less than one kept under ambient conditions. The crude lactide was unstable under these conditions. There has been a dramatical decrease in the content of LA in the crude lactide samples in 4th day, but then it grew considerably over 3 days. We can't explain the occurrence of these sharp changes yet and it will be studied in the further researches. After storage the crude lactide samples did not succumb for purification.

4. Conclusions

In this paper, the storage degradation of lactide samples was studied with using the HPLC analysis, melting point measurements and Karl Fisher's titration. The lactide samples with different purity degree were decomposed under various storage conditions.

It was established that the storing the lactide under an inert atmosphere with minimal content of the oxygen and moisture reduces the T_m of the substance and follows to conversion of lactide to the LA.

It was investigated that the integration in the lactide kept under ambient conditions occurred notably faster than one kept in the glove box under argon, and these modifications followed to the further unsuitability of monomer for polymerization. It was shown that the initial purity of the lactide has a significant effect on the lactide degradation.

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