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Polymerization of Lactic Acid Using Microwave and Conventional Heating

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Abstract

The polymerization of lactic acid (LA) has been investigated by two methods: conventional heating and under microwave irradiation. The reactions of polymerization have been carried out in two stages: at the beginning water is removed and oligomer is obtained; then, the catalysts/co-catalysts are added and reactions are carried out. Tin octoate, toluene sulfonic acid, 2-aminopropanoic acid (alanine) have been investigated as polymerization catalysts and the derivatives of 2,4,6,8- tetramethylol - 2,4,6,8- tetraazabicyclo[3.3.0]octane -3,7-dion (Tetraol), comprising atoms of Mg, Zn, Al have been synthesized for the first time. The structure of the synthesized catalyst has been investigated using the method of IR, ¹H NMR. It has been shown that the process of obtaining polylactic acid (PLA) by microwave irradiation proceeds hundreds of times faster. PLA samples synthesized by this method have the same optical characteristics as the PLA obtained by conventional heating.

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Keywords: lactic acid, microwave irradiation, tetraol, angles of optical rotation of PLA, polymerization.

1. Introduction

At present, the use of polylactic acid (PLA) and copolymers based on it is the most relevant in medicine: suture material, tissue engineering, implants, and carriers of drugs with controlled release.

The use of polylactic acid in medicine is due primarily to its unique properties such as excellent biocompatibility

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and biological degradation¹.

PLA can be synthesized in various ways using different catalysts.

A large number of catalysts were studied for the polymerization of lactic acid including biomedical applications¹⁻³. At present, there are more than 100 catalysts for polylactic acid obtaining. Usually, for these purposes organometallic compounds of tin, zinc, aluminum, magnesium² are used.

Polylactic acid is obtained by two methods: ring-opening polymerization of lactides and polycondensation of lactic acid⁴.

The most common catalyst for the synthesis of high molecular weight polylactic acid is tin octoate. Polymerization of lactide to ring opening in the presence of tin octoate is proceeded only in the presence of initiators - compounds containing hydroxyl groups (e.g., alcohols)⁴. The disadvantages of this catalyst are the duration of the polymerization process and the difficulty in removing a catalyst from the polymer. Traces of tin octoate are undesirable when polylactic acid is used for drug delivery, tissue engineering and other medical applications⁵.

Microwave activation in organic synthesis is one of the most rapidly developing areas. First of all, this is due to the multiple (tens, hundreds and thousands of times) reduction of the chemical reactions time⁶.

The aim of this research is to develop new effective methods of obtaining low molecular weight PLA, focused on the use for medical purposes.

In this work, we investigated the polymerization of lactic acid in the presence of tin octoate with various alcohols as co-catalysts; developed new catalysts (tetraol derivatives, containing atoms of Mg, Zn, Al); 2-aminopropanoic acid (alanine) and toluene sulfonic acid in conventional thermal conditions and under microwave irradiation.

2. Experiment

2.1. Chemicals and Reagents

We used L-lactic acid containing 12 wt% of water. Toluene, chloroform, ethyl acetate were used as a “pure for analysis” (analytical grade) qualification. Tin octoate, α - and β -alanine, p-toluenesulfonic acid were used as “chemically pure” qualifications.

Tetraol was synthesized by the known method⁷. For synthesis of tetraol derivatives, containing atoms of Mg, Zn, Al, an aqueous solution of tetraol was added to the aqueous solutions of $MgCl_2$, $ZnCl_2$ and $AlCl_3$ salts and reacted at 50°C for 2 hours. The obtained samples were crystallized, washed with isopropyl alcohol and chloroform, and then dried in vacuum at 50°C.

2.2. Polymerization of lactic acid

The polymerization of lactic acid was carried out in two stages (see Fig. 1):

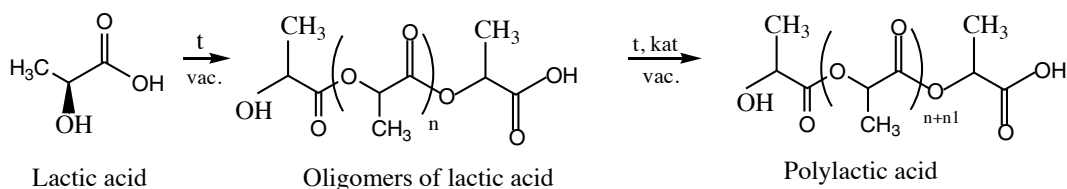


Fig.1. Scheme of the polylactic acid synthesis.

At the beginning water was removed and an oligomer was obtained. Then, the polymerization of the oligomer was carried out in the presence of a catalyst. The syntheses were performed in a glass reactor under vacuum while bubbling with nitrogen. The tin octoate was added in a solution of toluene. Other catalysts were dissolved in the oligomer of lactic acid.

2.2.1. Polymerization of lactic acid by heating

The removal of water was carried out at a temperature of 120-140°C for 4 hours under vacuum while bubbling with nitrogen. 20 wt% of toluene was added in lactic acid for a more complete removal of water. After removal of 28 wt% of water a viscous oligomer of lactic acid suitable for further polymerization was obtained. The oligomer added to the catalyst pre-dissolved in lactic acid, and the polymerization was carried out in the presence of a catalyst at 160 °C.

2.2.2. Polymerization of lactic acid under microwave irradiation

The polymerization of lactic acid under microwave irradiation was carried out using devices developed in Karaganda State Technical University.

The water removal was carried out under microwave irradiation with power (W) of 350-500 W for 5-10 min. under vacuum while bubbling with nitrogen. It was removed more than 28 wt% of water.

The polymerization of oligomer was carried out in the presence of the catalyst/co-catalyst dissolved in the oligomer under microwave irradiation of 100-350 W.

2.3. Instrumentation

The melting point of the synthesized compounds was determined using a device “METTLER TOLEDO”. The IR spectra were recorded by an IR spectrometer “Agilent Resolutions Pro”.

The molecular weight of the obtained samples of polylactic acid (PLA) was determined by gel permeation chromatography using a device “Agilent 1200” (a refractometric detector with a chromatography column GPC/SEC (stirogel), eluent velocity - 1ml/s).

The angle of the optical rotation of polylactic acid was determined in a chloroform solution at 25 °C.

¹H NMR spectra were recorded by a Fourier spectrometer “Avance AV 300 Bruker” in a solution of deuterated water.

3. Results and Discussion

3.1. Tetraol derivatives, containing atoms of Mg, Al, Zn

Physico-chemical properties of the synthesized crystalline substances I - V are presented in Table 1.

The synthesized samples I – V of tetraol derivatives, containing metal atoms, are not melted but destroyed without melting at temperatures above 200 °C, while tetraol is melted at 134.6 °C.

The samples I – V were analyzed by IR and ¹H NMR spectroscopy.

The results of ¹H NMR studies are presented in Table 1. In ¹H NMR spectra of the compounds I - IV, the value of the chemical shift intensities of the CH₂ and CH (I_{CH₂(OH)}/I_{CH}) groups varies in the range of 3.95 – 4.06.

The reaction of metal chlorides with tetraol was assessed by the change in the intensity of absorption bands in IR-spectra. In the IR spectra of tetraol the absorption bands with a maximum at 1441 cm⁻¹, 1262 cm⁻¹ and 1205 cm⁻¹ (see Fig. 2), which could be attributed to bending vibrations of O-H groups⁹ were observed. After the reaction with MgCl₂ those absorption bands in the IR spectra were not observed, which might indicate the substitution of hydroxyl groups of tetraol.

In the IR spectra the displacement of the characteristic vibrations of the carbonyl group C = O from 1694 cm⁻¹ to 1684 cm⁻¹ was observed, that suggested the formation of new tetraol derivatives.

The IR spectra of the compounds I, II and III differ in the intensity of the broad absorption bands with a maximum of 3300±35 cm⁻¹. This band belongs to the stretching vibrations associated with O-H groups⁸.

With increasing content of Mg atoms in the compounds I – III the intensity of the absorption bands with a maximum of 3300±35 cm⁻¹ increases. We have suggested that these variations may be due to the stretching vibrations of O-H groups, coordination-bonded to water molecules Mg atom.

Table 1. Physico-chemical properties of tetraol derivatives containing atoms of Mg, Zn, Al.

Compound	Value of initial reagents, mol	Chemical shift ^1H NMR, ppm		Value, $I_{\text{CH}_2}/I_{\text{CH}}$	Note
		CH- group	CH ₂ - group		
Tetraol	TO	4.69-4.94	5.53-5.66	4.04	$T_{\text{melt.}} - 134.6$ °C, crystal., white, soluble in water, ethanol, DMSO
Compound I	2TO : MgCl_2	4.68-4.95	5.65	4.06	Crystal., yellowish, hygroscopic, destroyed without melting at temperatures above 200 °C
Compound II	TO : MgCl_2	4.62-4.83	5.43-5.56	3.95	
Compound III	TO : 2MgCl_2	4.66-4.76	5.43-5.56	3.97	Crystal., yellowish, hygroscopic, decomposes in air in 20 days
Compound IV	2TO : ZnCl_2	4.64-4.84	5.54	4.05	Crystal., yellowish, decomposes in air in 40 days
Compound V	2TO : AlCl_3	4.44- 4.67	5.19-5.38	2.23	Crystal., yellowish, destroyed without melting at temperatures above 200 °C

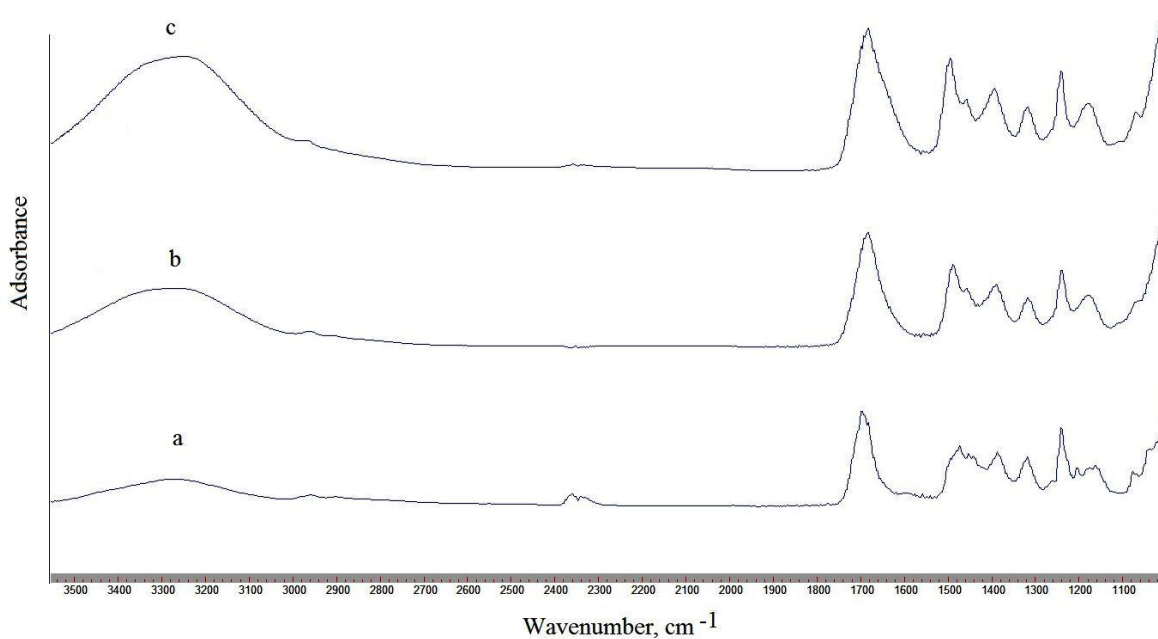


Fig.2. IR spectra of tetraol (a) and synthesized tetraol derivatives: compound I (b) and compound II (c).

Based on the obtained data it has been suggested that the reaction of interaction tetraol with magnesium chloride proceeds according to the following scheme:

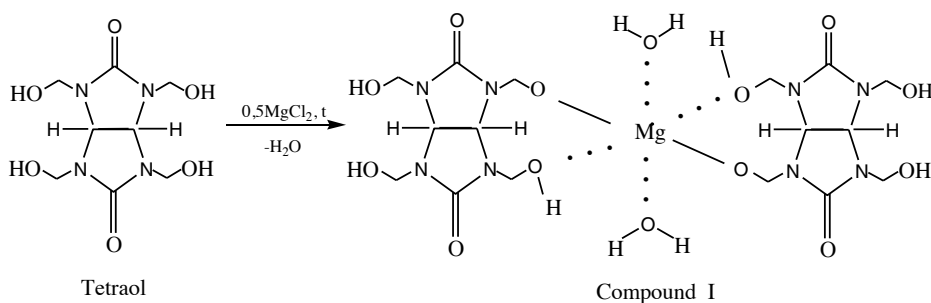


Fig.3. Scheme of the tetraol derivatives synthesis.

3.2. Polymerization of lactic acid

From the data presented in Table 2 we can see that the process of obtaining polylactic acid under thermal conditions is a long process and requires elevated temperatures. The process of removing water and producing oligomer under conventional heating is more than 6 hours.

Polymerization reactions of lactic acid oligomer under the effect of catalysts proceed only in the presence of co-catalysts (in this case, alcohols).

Table 2. PLA synthesis with different catalyst/co-catalyst under heating.

Catalyst/Initiator	LA/C/C-C	T reaction, °C	Reaction time., hours	Mw, Da	Mn, Da	Mw/Mn	$[\alpha]^*$, $\frac{\text{deg}}{\text{dm} \cdot \text{g}/\text{cm}^3}$
Tin octoate / isoamyl alcohol	1000:3:3	160	16	2178	1549	1.4	-158
α -alanine /isoamyl alcohol	1000 : 2:2	160	6	1210	964	1.3	-153
Compound I / isoamyl alcohol	1000 : 2:2	160	6	2150	1838	1.2	-148

LA/C/C-C – value of lactic acid/catalyst/co-catalyst in mass parts

$[\alpha]^*$ – specific optical rotation angle of polylactic acid (determined in chloroform at 25°C)

The results of lactic acid oligomer polymerization under microwave irradiation in the presence of various catalysts are presented in Table 3. Tin octoate, alanine, p-toluenesulfonic acid, synthesized tetraol derivatives were used as catalysts.

The polymerization reactions of lactic acid oligomer in the presence of the studied catalysts precede only with a co-catalyst, in this case - alcohol.

In case of conducting the reaction in the presence of tetraol salts simultaneously with the polymerization of lactic acid oligomers lactide is formed, as evidenced by the appearance of white crystals, leaving the reaction space. Thus, in this case, the polymerization conditions should be chosen so as to shift the equilibrium in the desired direction.

The PLA molecular weight increases when tert-butanol is used as a co-catalyst. The optical rotation angles of the synthesized polylactic acid samples significantly depend on whether the polymerization reaction proceeds at conventional heating or under microwave irradiation.

Table 3. PLA synthesis with different catalyst/co-catalyst under microwave irradiation

Catalyst/Initiator	LA/C/C-C	Power, W	Reaction time., min	Mw, Da	Mn, Da	Mw/Mn	$[\alpha]^*$, $\frac{\text{deg}}{\text{dm} \cdot \text{g}/\text{cm}^3}$
Tin octoate/isoamyl alcohol	1000:3:3	350	10	4012	2972	1.35	-153
Tin octoate/tert-Butanol	10000:3:3	350	10	3550	2573	1.38	-151
Tin octoate/isoamyl alcohol	10000:3:3	350	10	1750	1250	1.4	-153
Compound I / isoamyl alcohol	1000 : 2:2	200	5	4156	2770	1.5	-143
Compound III / isoamyl alcohol	1000 : 2:2	200	10	1950	1345	1.45	-135
Compound IV / isoamyl alcohol	1000 : 2:2	200	10	1990	1354	1.47	-140
Compound V / isoamyl alcohol	1000 : 2:2	200	10	1850	1225	1.51	-133
Compound II / tert-Butanol	1000 : 2:2	200	10	3120	2094	1.49	-152
p-toluenesulfonic acid / tert-Butanol	1000 : 2:2	200	10	3880	2798	1.39	-146
α -alanine / tert-Butanol	1000 : 2:2	200	10	3980	2843	1.4	-148

4. Conclusion

In this study the polymerization of lactic acid oligomers in the presence of various catalysts/co-catalyst in conventional heating and under microwave irradiation has been investigated.

It has been found that the process of removing water and the polymerization reactions proceeding under microwave irradiation are tens or hundreds of times faster than while conventional heating.

The possibility of using newly synthesized derivatives of tetraol containing atoms of Mg, Zn, Al as catalysts of polylactic acid polymerization has been shown. The development and implementation of methods for the synthesis under microwave irradiation can be an indispensable technology in the synthesis of PLA for medical purposes, as well as in the research and synthesis of new compounds.

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