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Vacuum effect on the lactide yield

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Abstract

The vacuum effect on the yield and purity of lactide obtained by catalytic lactic acid oligomer depolymerization was investigated. As raw material for the lactic acid oligomer synthesis the L-lactic acid aqueous solution was used. It was shown that the highest yield of raw-lactide takes place via distillation under a vacuum. The raw-lactide in all fractions was purified by recrystallization from dry ethyl acetate. The highest yield of raw-lactide is observed at a vacuum of 10 ... 15 mbar. The distillation process of raw-lactide is complicated with chemical reactions. Control of the reaction, raw materials and products was performed using DTA, gel permeation chromatography, infrared spectroscopy and high performance liquid chromatography.

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1. Introduction

Polymers play a leading role among packaging materials for many years. Therefore, in developed market economies there is a problem of environmental pollution, as the product from these polymers may stay unchanged in the natural conditions for hundreds years¹.

Nowadays, the main way to solve the problem of polymer waste is to create the production of polymers capable to rapid and complete biodeterioration in the natural conditions, with no release of toxic substances into the environment²⁻⁴.

One of the most perspective biodegradable plastic is polylactide, which is synthesized through lactide from lactic acid (LA) obtained from a renewable resource (glucose, corn, sugarcane)⁵. An important advantage of polylactide is

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the fact that it is a clear, colorless thermoplastic polymer which can be processed by all methods used for thermoplastics processing including 3D printing⁶.

Moreover, tailor-made polymer materials based on lactide and other hydroxy acids are widely used for the manufacture of medical products for general and reconstructive surgery, traumatology and orthopedics in order to restore the vital organs and tissues of human. Medical products based on biopolymers can cure diseases of the musculoskeletal system, injuries of different etiology, cardiovascular system diseases, promote the rapid healing of all kinds of tissue after surgery preventing the formation of post-surgical synechias. After predetermined time of operation biodegradable plastic products are excreted, degrading with the formation of the natural metabolism products⁷.

For high-biodegradable polylactide and its copolymers obtaining, the most common and effective method is the ring opening lactide polymerization in the presence of various catalysts and initiators⁸. In the stage of producing and purifying of lactide the most product loss is observed.

Previously the effect of catalyst type, temperature, pressure, initial LA oligomer molecular weight, impurities and other parameters on the yield and purity of the raw-lactide was studied. The importance of lactide purification and drying was shown as purer lactide, the higher molecular weight of polylactide may be obtained. Moreover, these parameters also affect the racemization process of lactide optical isomers⁹.

Therefore, the aim of this work was to investigate the effect of negative pressure on the raw-lactide yield with the catalytic (zinc oxide) LA oligomer depolymerization.

Nomenclature

LA	Lactic acid
LAO	Lactic acid oligomer
P	Pressure

2. Experiment

2.1 Materials

80% solution of L-LA produced by M.C.D. Import & Export Gmbh (Germany) was used. For the LA oligomerization stage zinc oxide with a mass fraction of the basic substance of 99.7% was used. For recrystallization of raw-lactide ethyl acetate with a mass fraction of the basic substance of 99.1% was used.

2.2 LA oligomer synthesis

Concentration and obtaining of AL oligomers was carried out on the rotary vacuum evaporator Heidolph Hei-VAP.

Into 500 ml round bottom flask 200 ml of LA was placed. The flask was 500 ml attached to the rotary vacuum evaporator. Reaction conditions are the following: temperature was 150 °C, the speed of the flask rotation was 60 rev/min, a vacuum was 30 ... 50 mbar, with vacuum being created immediately. After 1.5 hours the catalyst (ZnO) in an amount of 1.5% from weight of the oligomer was added in the reaction mixture. The total reaction time was 240 minutes.

After finishing the LA oligomerization process the oligomer was sampled to determine its molecular weight. Then, the resulting melt of LA oligomer was poured into 5 equal portions in 50 ml flasks. The weight of the obtained LA oligomers was 25.0 grams for each subsequent synthesis of raw-lactide.

2.3 Lactide synthesis

Lactide synthesis was performed on a standard vacuum distillation installation provided with an air condenser. The heating of the reaction mixture was carried out using an electromagnetic stirrer IKA C-MAG HS 7. To create and maintain the desired value of the vacuum pumping station Vacuum brand PC 3001 VARIO was used. During

the lactide producing process vapor fractions were sampled at the temperature range of 100 ... 180 °C and at the selected vacuum ranged of 5 ... 30 mbar. The process of LA oligomer depolymerization into lactide lasted for 60 minutes.

The derived raw-lactide in all obtained fractions was purified by recrystallization from dried ethyl acetate¹⁰ and identified using IR spectroscopy.

2.4 Analytical control

Control under the reaction and purity of the derived products were performed using differential thermal analysis (2n / DSC / DTA), infrared spectroscopy (FT-IR spectrometer Nicolet 5700), gel permeation chromatography (Agilent Technologies 1260 Infinity chromatograph, calibrated by the standard polystyrene samples), high performance liquid chromatography (YoungLin Clarity YL9100 chromatography) and melting temperature (MeltingPointM-560).

IR spectra were recorded on a Nicolet 5700 spectrophotometer in the range from 400 to 4000 cm⁻¹ (KBr). TGA curves were recorded in argon atmosphere at the temperature range of 25 ... 330 °C. The molecular weight was determined by gel-permeation chromatography Agilent Technologies 1260 Infinity with refractometric detector (Column GPC/SEC-stiogel, length 300 mm, internal diameter of 7.5 mm, eluent rate - 1 ml/s, calibration by polystyrene standards with known molecular weight). The content of LA and lactide in sampled fractions was determined on HPLC YoungLin Clarity YL9100, equipped with a column Tracer 120 ODS-A C18 (250 × 4.6) mm with a particle size of 5 microns and a UV-detector (analysis conditions: working wavelength - 200 nm, sample injection amount - 20 mkl, the column oven temperature - 25 °C).

3. Results and discussion

Usually^{8, 11} the polylactide synthesis consists of the following stages: concentration and oligomerization of LA solution; catalytic depolymerization of LA oligomer in lactide; lactide purification; lactide polymerization/copolymerization; disposal of waste. To eliminate the multistage process LA of direct dehydration to lactide with heterogeneous catalyst (metal oxides) in the vapor phase¹²⁻¹⁵ was proposed, with the yield being at least 40%.

Previously the main factors affecting the yield of lactide and meso-lactide from the LA oligomer were identified⁹:

1. The temperature, since the reaction rate strongly depends on it: the higher the temperature, the higher the lactide vapor pressure above the reaction mixture. At the same time, as the temperature increases and the rate of lactide racemization also increases.
2. The pressure. Negative pressure of 10 mbar or less is used. Under higher pressure LAO depolymerization rate and lactide yield decrease.
3. LA oligomer molecular weight has less effect on lactide formation rate. With the increasing the initial molecular weight of LA oligomer of 1800 g/mol the yield of meso-lactide sharply increases.
4. Catalyst concentration. The more the catalyst amount, the higher the reaction rate. In practice, a linear dependence is observed due to the complications of heat and mass transfer conditions. With the increasing the concentration of several catalysts the meso-lactide yield increases.

Thus, the process of lactide obtaining is multi-stage and energy-intensive. At the same time a low yield, large losses in the lactide purification, large amount of waste take place. In addition at all the synthesis stages LA and lactide optical isomers transformation is noticed.

The stages of LA concentration and LA oligomer obtaining usually occur quite smoothly and with a good yield^{8, 11}. Therefore, in this work widely available and cheap catalyst (ZnO) and low pressure were used. Although sometimes for activation of these processes azeotropic distillation of water (saluted and condensation) in the presence of aromatic, organochlorine compounds, esters and paraffins is used^{16, 17}. Azeotropic distillation is also used for the direct production of polylactic acid with an average molecular weight (less than 100,000 g / mol) from aqueous LA solution, omitting the stage of lactide depolymerization to LA oligomer¹⁸.

Thermal LA oligomer depolymerization to lactide flows at high temperature and in a sufficiently viscous media. This significantly complicates the conditions of heat and mass transfer in the reaction mixture, and leads to a decrease in the lactide yield. To increase the yield and purity of the raw-lactide it can be used the following: a

reactor with a thin film of LA oligomer melt¹⁹; tubular reactors²⁰; bubbling of inert gases and vapors of organic substances (nitrogen, argon, carbon monoxide or carbon dioxide, acetone, toluene, cumene, xylene and paraffins C₁ - C₁₀) through the LA oligomer melt²¹⁻²³;

It is difficult to consider and monitor the parameters and conditions in the above methods, leading to lactide yield increase. Therefore, to study the effect of negative pressure on the lactide yield it was used a simple way with a small load of LA oligomer to a distillation flask of vacuum distillation installation at a constant heat from the electromagnetic stirrer.

The use of this method of lactide producing from the LAO also includes several options: batching of LA oligomer; heating and holding the reaction mixture with followed reduction of the pressure to the desired value; cyclic lowering and raising the vacuum in the system; heating the oligomer at the desired vacuum value.

In the given work a variant of the LAO heating at the required vacuum was used. Vacuum value selecting usually carried out in a sufficiently wide range, for example, 10 torr or lower^{20, 25}, 7.5 to 14 torr²⁶ 13 ... 25 torr²⁷, the reaction is started at 100 - 110 torr and then reduced to 0.01 to 0.1 torr to obtain the raw-lactide²⁸. At low concentrations of catalyst (SnO) and changing the vacuum from 1 to 10 torr the yield of meso-lactide is increased insignificantly. In this case, after an induction period reaction product distillation is observed.

L-lactide obtained by LAO depolymerization, typically contains the following impurities: LA, water, meso-lactide, dimers, trimers and other low molecular weight linear LA oligomers.

It has previously been shown²⁹ that with increasing LAO molecular weight (from 690 to 3100 g/mol) in the obtained raw-lactide the LA content decreases in three times, but the meso-lactide content increases twice. Therefore, in this work as the raw material for lactide LA oligomer with a molecular weight equal to 650 g / mol (gel permeation chromatography) was used.

L (+) lactic acid has a boiling point 82°C at 0 torr and 122°C at 14 torr³⁰. Meso-lactide in vacuum from 6 to 80 mbar has the boiling temperature, which 10 ... 20 °C less than the boiling temperature of D, L-lactide and other LA isomers³¹. Low molecular weight linear LA oligomers have a higher boiling point compared to lactide. Therefore, in this work three fractions of the LAO depolymerization were sampled. It should be noted that while sampling the clear boundary between fractions based on the substance vapor temperature was not observed. In this regard, while sampling the external characteristics of the distillate were taken into account.

The obtained data of the number of fractions, melting points and the results of the first recrystallization of fraction are shown in Table 1.

Table 1. Distillation and raw-lactide purification data

P, mbar	Distillation			After recrystallization	
	Fraction vapour temperature, °C	Fraction yield, %	Melting point, °C	Yeild, %	Melting point, °C
5	104-120	10	88	3	91
	120-140	29	90	31	85
	140-170	44	85	49	91
	170-180	17	82	17	85
10	120-130	15	87	5	87
	130-140	41	94	43	94
	140-150	44	86	52	87
15	120-135	26	92	17	91
	135-145	50	89	65	81
	145-155	24	93	18	116
20	130-145	28	88	16.4	94
	145-155	35	93	43.3	94
30	155-165	37	89	40.3	90
	120-135	22	91	14	95

135-147	20	87	25	92
148-165	58	108	61	119

Table 1 shows that the vacuum strongly influence the number and composition of the fractions during the LA oligomer depolymerization. Maximum value of raw-lactide is formed at 10 ... 15 mbar. Therefore, the lactide at 12 mbar (table 2) was also synthesized. In this case, the total value of the obtained lactide in fractions correlates with the earlier data³².

Table 2. Data of LA synthesis at negative pressure of 12 mbar

Parameter	Distillation fractions		
Fraction vapour temperature, °C	120-130	130-140	140-150
Fraction yield, %	16.4	59.2	24.4
Raw-lactide melting point, °C	89-90	91-92	86-88
LA content, % wt	63.1	21.6	9.4
Lactide content, % wt	43.9	65.6	70.1

It should be noted that in all these cases of catalytic LAO depolymerization product distillation there is no order of distillation by boiling points at a given vacuum. During the lactide obtaining two processes occur parallel: chemical reaction of catalytic LA oligomer depolymerization and physical process of reaction product distillation. Both processes occur at high temperature. Moreover, the high temperature of the reaction mixture significantly complicates the process of distillation. The findings suggest that the rate-determining step of the overall process is a chemical reaction. LAO depolymerisation, probably, proceeds according to series-parallel ways, as on the serial way maximum in time of intermediates and product yield are commonly observed. Probably for this reason, low-boiling LA (122°C at 14 torr³⁰) is presented in considerable quantities in all sampled distillation fractions from 105 to 180 °C (table. 2). The same is observed with meso-lactide.

Thus, the lactide production reaction combined with reaction product distillation is not an efficient process in terms of substance separation process.

Therefore, a variant of distillation of reaction products during the LA oligomer depolymerization with condensation and collecting in a single receiver was used. The obtained mixture of lactide and byproducts was subjected to fractional distillation. In this case (table 3), it is observed a clear fractions boundary of boiling points, compared with the first option, but there is still no close-cut separation of substances. Probably, it is also connected with chemical reaction (LA condensation, the lactide decomposition and others).

Table 3. Raw-lactide distillation data

Parameter	Distillation fractions		
Fraction vapour temperature, °C	120-130	130-140	140-150
Fraction yield, %	23	50	27
Raw-lactide melting point, °C	91-92	93-94	89-90
LA content, % wt	35.8	30.4	10.4
Lactide content, % wt	67.8	69.9	84.6

Previously, it was observed²⁹ that during the raw-lactide distillation increasing of LA oligomer content in the column cube is associated with the containing of the acidic impurities in the distillation column feed. Also it was shown that the flow of lactide and LA oligomer racemization is particularly noticeable in the presence of a catalyst.

In practice, it is recommended to subject product vapors to fractional condensation after lactide synthesis in the reactor and then sent raw-lactide to distillation or rectification^{33, 34}. It is also practiced the variant of using two distillation columns³⁵ or the variant with intermediate washing of lactide vapors³⁶.

Conclusion

In lactide obtaining by LAO depolymerization the highest yield of raw-lactide is observed at a vacuum of 10...15 mbar. At the same time there is no clear sequence of substance stripping by boiling points at a given vacuum. The findings suggest that the rate-determining step of the overall process is a chemical reaction. Secondary distillation of raw-lactide is also complicated by secondary chemical reactions.

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References

1. Tarasyuk VT. Relevance and perspectives of biopolymers in food industry. *Konservnaya promishlennost segodnya: tehnologii, marketing, finansi* 2011; 3 p:55-63.
2. Fomin VA, Guzeev VV. Biodegradable polymers, the state and prospects of use. *Plasticheskie massi* 2001;2:42-46.
3. Tasekeev MS, Eremeeva LM. *Biopolymers production as one of the solutions to the problems of ecology and APC: Analiticheskii obzor*. Almaty, NTZNTI..
4. Requirements for packaging recoverable through composting and biodegradation – Testing scheme and evaluation criteria for the final acceptance of packaging. *The European Standard EN13432*
5. Zhan Ying Zhang, Bo Jina, Joan M.K. Production of lactic acid from renewable materials by *Rhizopus* fungi. *Biochemical Engineering Journal* 2007; 35. p. 251-263
6. Rengier F, Mehndiratta A, von Tengg-Kobligk H, et. al. *Int. J. CARS*. 2010; 5:335-341.
7. Dumitriu EdS., Dekker M. *Polymeric biomaterials*. Inc; 2002. p. 1183.
8. Garlotta DA. Literature Review of Poly(Lactic Acid). *Journal of Polymers and the Environment* 2001; 9: 2 p. 63-84.
9. Gruber P.R, Hall E S, Kolstad J.J. et. al. Continuous process for manufacture of a purified lactide. *Patent US 5274073*,1993.
10. Glotova VN, Zamanova MK, Izhnebina TN, Novikov VT. Lactide purification by recrystallization. *Izv. VUZov. Himiya i himicheskaya tehnologiya*. 2014;57 :11. p. 63-65.
11. Auras R. et. al. Poly(lactic acid) Synthesis, Structures, Properties, Processing, and Applications. *John Wiley & Sons*, 2010.
12. Dong WHwang, Jong San Chang. Method for preparing lactide directly from lactic acid, and catalyst used therein. *Patent WO 2014030820 A1* 2014.
13. Benecke HP., Cheung A, Cremeans GE, et. al. Process for the production of cyclic esters from hydroxy acids and derivatives thereof. *Patent EP 0632807 B1* 1998.
14. Hölderlich W, Venschott M. Process for continuous preparation of lactide directly from concentrated lactic acid. *Patent WO 2013160485 A1* 2013.
15. Benecke HP, Markle RA, Sinclair RG, Catalytic production of lactide directly from lactic acid. *Patent US5332839* 1994.
16. Cockrem MCM, Kovacs I. Azeotropic distillation Of cyclic esters of hydroxy organic acids. *Patent US 2002/0157937 A1* 2002
17. Cockrem MCM., Kovacs I. Azeotropic distillation of cyclic esters of hydroxy organic acids. *Patent US 6984293 B2* 2001.
18. Bastioli C, Grzebieniak K, Niekraszewicz A, Perego G. A process for the production of poly(lactic acid). *Patent WO 1994003522 A1* 1994.
19. Bhatia KK, Lin K, Nash RS, Stambaugh. TW. Thin film depolymerization to dimeric cyclic esters. *Patent CA 2113799 A1* 1993.
20. Drysdale NE, Lin K, Stambaugh T. Continuous reduced pressure dimeric cyclic ester production. *Patent US 5288881* 1994.
21. Bhatia KK. Continuous process for rapid conversion of oligomers to cyclic esters. *Patent. US 5023349 A* 1991.
22. Shvetz VF, Kozlovskii RA, Schastlivaya SV, Varlamova ES, Makarov MG, Staroverov DV, Suchkov Yu.P. A method of lactide producing. *Patent RU2301230* 2007.
23. Bhatia K.K. Process for rapid conversion of oligomers to cyclic esters. *Patent US 5091544* 1992.
24. Zenya Shiiki, Yukichika Kawakami. Preparation process and purification process of dimeric cyclic ester of hydroxycarboxylic acid. *Patent US 5830991* 1998.
25. Masayuki KamikaWa, Toshiaki Matsuo, Kenichiro Oka, Naruyasu Okamoto, Ryuji Kaziya. Method and apparatus for producing polyhydroxy carboxylic acid. *Patent US 7723540 B2* 2010.
26. Kazuomi Kubota, Yoichi Murakami. Process for producing lactides and process for purifying crude lactides. *Patent US 5463086 A* 1995.
27. Muller M. Process for the preparation of lactide. *Patent US 5053522* 1991.
28. Idage BB, Idage BS, Swaminathan S. Improved process for the preparation of l-lactide of high chemical yield and optical purity. *Patent EP 2539332 A1* 2013
29. Benson RD, Borchardt RL., Gruber P.R. et. al. Continuous process for the manufacture of lactide and lactide polymers. *Patent EP 0893462 B1* 2010.
30. Narayanan N., Roychoudhury PK., Srivastava AL Lactic acid fermentation and its product polymerization. *Electronic Journal of Biotechnology* 2004; 7:2. p.167-179.
31. Muller M, Hess J, Schnell W-G. Meso-lactide, Processes for preparing it and polymers and copolymers produced there from. *Patent US4983745* 1991.
32. Yoshiaki Yamaguchi, Tomohiro Arimura. Method for purification of lactide. *Patent EP 0657447 B1* 1997

33. Gruber PR, Hall ES, Kolstad J J. et. al. Continuous process for manufacture of lactide polymers with purification by distillation. *Patent US 5357035* 1994.
34. Drysdale N, Stambaugh TW, Hmkessin JV. Solventless dimeric cyclic ester distillation process. *Patent US 5236560* 1993.
35. Rafler G, Rafler J, Windsperger A., Edlauer R, Gaß J. Verfahren zur Reinigung zyklischer Diester der L- bzw. D-Milchsäure. *Patent EP 2128 152A1* 2009.
36. Hagen R., Myul'bauer U, Tehlin V. A method for process streams purifying in the dilactide or polylactide production. *Patent RU 2471791* 2011.