1636 *Macromolecules* 1990, *23*, 1636-1639

Thermodynamics of L-Lactide Polymerization. Equilibrium Monomer Concentration

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ABSTRACT: Thermodynamics of L-lactide [(3*S*,6*S*)-3,6-dimethyl-1,4-dioxacyclohexane-2,5-dione] polymerization in 1,4-dioxane solvent was studied. The equilibrium concentration of L-lactide, measured by gel permeation chromatography, decreased from 0.15 mol·L^{-1} at 406 K to 0.06 mol·L^{-1} at 353 K. The standard thermodynamic parameters, determined on the basis of the temperature dependence of the L-lactide $\rightleftharpoons$ poly(L-lactide) equilibrium position, were as follows: enthalpy, $\Delta H°_{ss} = -22.9$ kJ·mol^{-1}; entropy, $\Delta S°_{ss} = -41.1$ J·mol^{-1}·K^{-1} (at 1 mol·L^{-1}). Negative values of $\Delta H°_{ss}$ and $\Delta S°_{ss}$ lead to the existence of ceiling transition temperature, $T_c = 914$ K (value computed for the bulk polymerization). The relatively high value of polymerization enthalpy compared with that of other *six-membered* monomers was attributed to the bond oppositions and angle distortions in the skew-boat conformation of the L-lactide molecule.

Introduction

Lactides are six-membered cyclics, and the reversibility of their polymerization could be expected. In spite of the abundant literature on lactide polymerization (e.g., refs 1–12), mostly stemming from the increasing importance of the polymer in the medical applications (see refs 13–15 and references cited therein), there are no experimental data available on the thermodynamics of the propagation–depropagation steps. This is even more surprising, remembering that plateaus were observed in the published[7,8,15] monomer–conversion plots. The only paper we have been able to find on this subject dealt with the thermodynamic parameters of lactide polymerization determined by Lebedev et al.[16] on the bases of heats of combustion and heat capacities.

In the present contribution we report on the thermodynamic parameters of equilibrium polymerization of L-lactide (1, (3*S*,6*S*)-3,6-dimethyl-1,4-dioxacyclohexane-2,5-dione) in 1,4-dioxane solvent. We have also calculated enthalpy and entropy of polymerization from the experimental data of other authors[7] and compare these values as well as the parameters estimated by Lebedev et al.[16] with values derived from our data.

Experimental Section

Materials. Monomer. L-Lactide (1) was prepared from L-lactic acid (from Fluka AG, Buchs SG, Switzerland) according to the described procedure.[17] The crude monomer was purified twice by recrystallization from dry ethyl acetate and subsequently by sublimation in vacuo [70 °C (~10^{-2} mbar)] (mp 98 °C). It finally was distributed in vacuo into glass ampules equipped with break-seals and stored at -12 °C.

Initiator. Tin(II) 2-ethylhexanoate (2) (from Sigma Chemical Corp., St. Louis, MO) was distributed in vacuo (~10^{-3} mbar) into thin-walled phials.

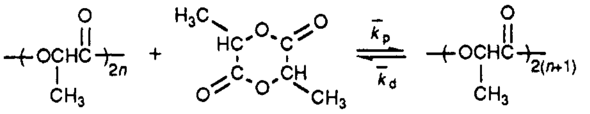
Solvent. 1,4-Dioxane (from PPH Polskie Odczynniki Chemiczne, Poland) was refluxed several days over sodium metal and then fractionated and condensed over Na/K liquid alloy in vacuo.

Polymerization. Polymerization mixtures were prepared using the standard high-vacuum technique. In all experiments the initial concentrations of both monomer ($[1]_0$) and initiator ($[2]_0$) were constant and equal: $[1]_0 = 1$ mol·L^{-1} and $[2]_0 = 2.4 \times 10^{-2}$ mol·L^{-1}. After mixing of monomer, initiator, and solvent at room temperature, ampules with the resulting polymerization mixture were placed in the thermostating bath at the given temperature. Samples were withdrawn at the desired times, up to the moment when monomer concentration reached constant level. The withdrawn samples were quenched in liquid N_2 and defrozen immediately before GPC measurements.

Measurements. Monomer concentrations were monitored by GPC using an LKB 2150 HPLC pump, a set of Waters ultrastyragel columns 1000, 500, and 100, and a Hewlett Packard 1031 A R5 detector. THF with 0.9 mL·min^{-1} flow rate was an eluent. The ratio of response coefficients (RI detection) due to poly(L-lactide) and L-lactide was 1:1.23.

Results and Discussion

Figure 1 shows kinetic curves of L-lactide polymerization, initiated with tin(II) 2-ethylhexanoate in 1,4-dioxane solvent. Concentration of monomer 1 ([1]) decreases during polymerization until a certain conversion is reached, ($[1]_{eq}$). Semilogarithmic anamorphoses of these curves (Figure 2) are linear, provided that kinetic equations include $[1]_{eq}$ and thus that $\ln [([1] - [1]_{eq})/([1]_0 - [1]_{eq})]$ is plotted as a function of time. It follows from Figure 1 that higher $[1]_{eq}$ values are observed at higher polymerization temperature. Thus, this system can be described by the simple kinetic scheme with reversible propagation, e.g.



(1)

(where $\bar{k}_p$ and $\bar{k}_d$ are propagation and depropagation rate coefficients). The dependence of $[1]_{eq}$ on temperature is shown in Figure 3. For a temperature range from 80 to 133 °C $[1]_{eq}$ changes from 0.058 to 0.152 mol·L^{-1}, respectively.

The standard thermodynamic parameters for L-lactide polymerization were then determined from the dependence of $\ln [1]_{eq}$ on the reciprocal of the absolute temperature (eq 2)[18] ($\Delta H°_{ss}$ and $\Delta S°_{ss}$ denote the standard enthalpy and entropy for the polymerization of 1 in solution).

$$\ln [1]_{eq} = \Delta H°_{ss}/RT - \Delta S°_{ss}/R \qquad (2)$$

Using the least-squares method to analyze the experimental data in terms of eq 2, we obtain $\Delta H°_{ss} = -22.9$ kJ·mol^{-1} and $\Delta S°_{ss} = -41.1$ J·mol^{-1}·K^{-1}.

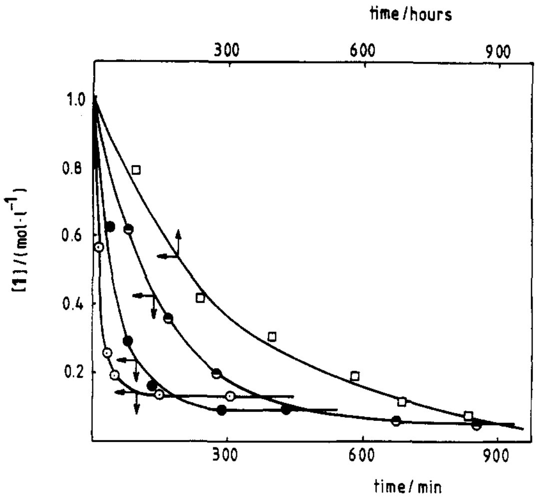


Figure 1. Conversion of L-lactide (1) during polymerization initiated with tin(II) 2-ethylhexanoate (2). Conditions of polymerization: $[1]_0 = 1$ mol·L^{-1}; $[2]_0 = 2.4 \times 10^{-2}$ mol·L^{-1}; solvent, 1,4-dioxane; temperature, (⊙) = 120.5 °C, (●) = 100 °C, (◒) = 80 °C, (□) ≅ 20 °C (rt).

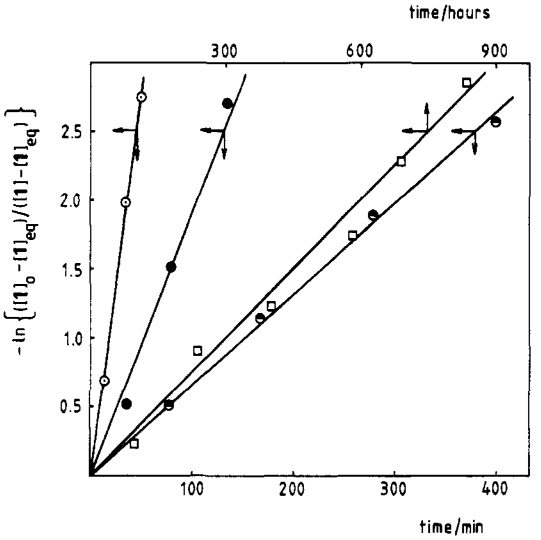


Figure 2. Semilogarithmic anamorphoses of the kinetic curves shown in Figure 1. Values of $[1]_{eq}$ for kinetics conducted at 120.5, 100, and 80 °C were directly measured by GPC. The value of $[1]_{eq}$ at room temperature was obtained by extrapolation of $\ln [1]_{eq} = f(1/T)$ plot (Figure 3) to room temperature.

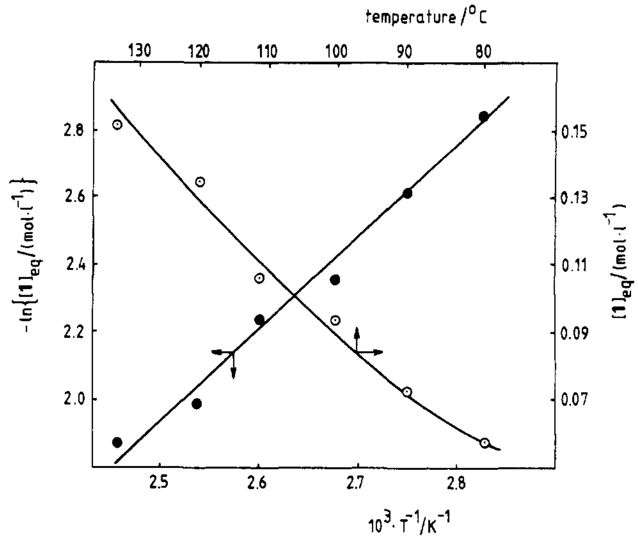


Figure 3. Dependence of the equilibrium concentration of L-lactide on the temperature.

In the ring-opening polymerizations, conducted at constant pressure, the change of enthalpy is mostly due to the monomer ring strain energy, if monomer–polymer–solvent specific interactions can be neglected.[19-22] Thus, 1 belongs to medium-strained cyclic monomers.[19,23]

The three- and four-membered rings are highly strained, and the enthalpy decrease is a major driving force of polymerization. Moreover, polymerization of these monomers is accompanied by the entropy decrease. In spite of that, the enthalpic contribution into free energy prevails ($\Delta H_p < 0$, $\Delta S_p < 0$, $|\Delta H_p| > -T\Delta S_p$ in eq 3). For

$$\Delta G_p = \Delta H_p - T\Delta S_p \tag{3}$$

larger cycles, the energy of ring strain diminishes (passing eventually through a local maximum) and ΔS becomes more positive.[24,25] It is known that the large majority of the six-membered rings are not polymerizable, because of the low ring strains, whereas the five-membered cycles are classified as medium-strained. We found in this work relatively high ring strain of L-lactide that should be explained.

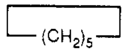
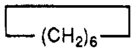
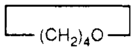
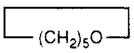
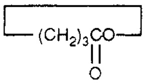
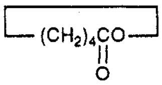
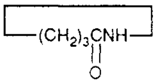
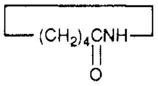
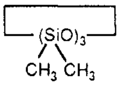
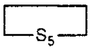
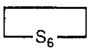
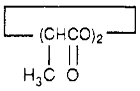
Some thermodynamic data for the five- and six-membered monomers are given in Table I. In all examples given, the entropic contribution into free energy is positive, like in the majority of polymerizations, and thus the monomer–polymer conversion is possible if the negative enthalpic contribution can outweigh the entropic factor.

Ring strain in cyclopentane is due to the oppositions of the eclipsed C–H bonds. In cyclohexane this strain is released because, in the most probable chair conformation, the C–H bonds are staggered. The lone electron pairs of the sp^3-hybridized oxygen atoms act similar to the C–H bonds of methylene groups. Ring strains of cyclopentane and THF or cyclohexane and THP do not differ very much. Changing, however, one CH_2 group for the carbonyl group reduces, in the five-membered rings, the number of bond oppositions[30] and therefore γ-butyrolactone does not polymerize at normal conditions. In the six-membered δ-valerolactone the ester group cannot adopt the planar conformation, without introducing ring strain, due to the eclipsed conformations of the C–H bonds. Similar comparison can be made for the five- and six-membered amides. In the almost flat hexamethylcyclotrisiloxane molecule (D_3) the Si–O–Si and O–Si–O bond angle distortions provide considerable polymerization enthalpy.[31,32] Also in the homonuclear *cyclo*-hexasulfur, with bond angles and bond lengths close to the unperturbed bond dimensions, certain angle distortions exist.[24,33]

According to the X-ray crystallographic data,[34] D-lactide [(3*R*,6*R*)-3,6-dimethyl-1,4-dioxacyclohexane-2,5-dione] assumes irregular skew-boat conformation with approximately C_2 symmetry, in which two ester groups can adopt planar conformations. The mirror image molecule of L-lactide should adopt the same conformation. Assuming further that the boat conformation is the most probable one also in the liquid state or in solution, one can conclude that the relatively high value of $\Delta H°_{ss}$ is due to the ring strain, caused by bond oppositions and possibly by the bond angle distortions.

Negative values of both $\Delta H°_{ss}$ and $\Delta S°_{ss}$ for 1 lead to

Table I
Standard Thermodynamic Parameters of Polymerization of the Selected Five- and Six-Membered Cyclic Monomers

monomer	monomer and polymer states[a]	ΔH°_p, kJ·mol^{-1}	ΔS°_p, J·mol^{-1}·K^{-1}	refs
	lc	-21.8	-42.7	18, 19
	lc	2.9	-10.5	18, 19
	ls	-19.1	-74.0	26
	gg	1.7	<0	18, 19
	lc	~0	<0	19
	lc	-27.4	-65	27
	ll	-9.9	-13	27
	lc	0.4	-30.5	19, 28
	lc	-7.1	-27.6	19, 28
	ll	-23.4	-3.0	29
	ll	-34.9	-27.2	24
	ll	-8.2	-2.6	24
 [b]	ss	-22.9	-25.0	this work
	ll	-29.1	-40.7	this work

[a] l = liquid, c = condensed, g = gas, s = solution. [b] L-Lactide.

the existence of the ceiling temperature (T_c):

$$T_c = \frac{\Delta H^\circ_{ss}}{\Delta S^\circ_{ss} + R \ln [1]_0} \tag{4}$$

For $[1]_0 = 1$ mol·L^{-1}, $T_c = 557$ K. Tentatively assuming that in bulk polymerization ΔH°_{ll} and ΔS°_{ll} are equal to these determined in 1,4-dioxane solvent, we obtain T_c (bulk) equal to 913.6 K. (T_c(bulk) was calculated taking standard conditions at weight fraction $C_1 = 1$; in this case $\Delta S^\circ_{ll} = -25.03$ J·mol^{-1}·K^{-1} and $\Delta H^\circ_{ll} \approx -22.9$ kJ·mol^{-1}.)

As we indicated in the introduction, experimental data of other authors allowed us to compute ΔH°_p and ΔS°_p. Thus, Jamshidi et al.[8] polymerized 1 from 120 to 220 °C in bulk. On the conversion–time curves, particularly above 140 °C, maxima were observed, suggesting that apart from the propagation–depropagation equilibrium 1 some other reactions were present, leading to the poly(1) destruction. Nevertheless, using the maximum conversion values (C_1), obtained at the given temperature, and plotting values of $\ln C_1$ vs T^{-1} (Figure 4), we calculated $\Delta H^\circ_{ll} = -29.10$ kJ·mol^{-1}, $\Delta S^\circ_{ll} = -40.74$ J·mol^{-1}·K^{-1} and $T_c = 714$ K. These parameters are close to those we computed from the data of our own.

Leenslag and Pennings[7] reported T_c(bulk) = 548 K for polymerization of 1, obtained by linear extrapolation of the dependence of the viscosimetric average molecular weight ($\bar{M}_v$) of the resulting poly(1) versus polymerization temperature. This would mean that above 548 K 1 should not polymerize, and it does not seem realistic. This value of T_c is in fact much lower than T_c computed from the data of Jamshidi et al. and of our own. This discrepancy may result from the oversimplified assumption that $\bar{M}_v$ is a linear functon of a temperature. $\bar{M}_v$ is not a thermodynamic parameter and depends on the actual polymerization conditions. Even assuming living polymerization, i.e.

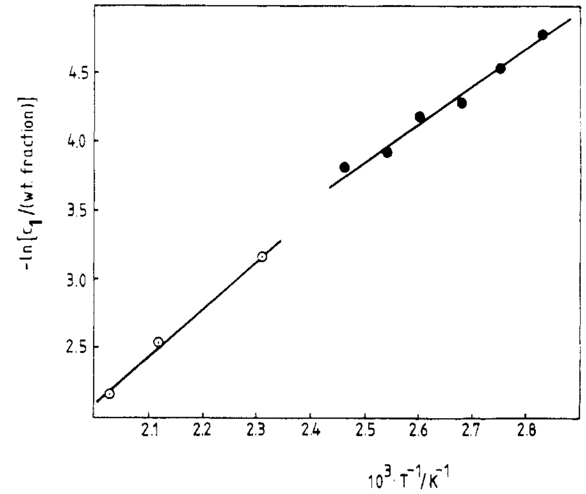


Figure 4. Logarithm of the equilibrium concentration of 1 versus reciprocal of absolute temperature. Comparison of the bulk polymerization ((◎) Jamshidi et al.[17]) with polymerization in 1,4-dioxane solution ((●) this work).

$$\overline{\mathrm{DP}}_n = \frac{1}{[2]_0}([1]_0 - [1]_{eq}) \tag{5}$$

the dependence of the average molecular weight (or polymerization degree, $\overline{\mathrm{DP}}_n$) is not a linear function of the polymerization temperature:

$$\overline{\mathrm{DP}}_n = \frac{1}{[2]_0}\left\{[1]_0 - \exp\left(\frac{\Delta H^\circ_p}{RT} - \frac{\Delta S^\circ_p}{R}\right)\right\} \tag{6}$$

This follows directly from eqs 2 and 5.

Tunc et al.[15] obtained a series of unreacted lactide concentration ($[1]_{un}$) versus temperature relations, for various $[1]_0/[2]_0$ ratios. For lower $[1]_0/[2]_0$ ratios (e.g., 10^4) $[1]_{un}$ increased with increasing temperature, as usually was observed. For higher ratios of monomer to the initiator concentration in the feed (e.g., $[1]_0/[2]_0 = 3 \times 10^5$) the reversed dependences were obtained; i.e., $[1]_{un}$ decreased when the temperature was increasing, at least at temperatures from 105 to 170 °C. This "abnormal" relation was obtained because, in our opinion, $[1]_{un}$ values were measured before the real thermodynamic equilibrium was reached in the system. Therefore, in the discussed case $[1]_{un} > [1]_{eq}$. The highest differences were obtained for highest $[1]_0/[2]_0$ ratios (i.e., lowest initial initiator concentrations) and lowest temperatures, due to the extremely low polymerization rates. There is no proof indeed that the measured values are related to the equilibrium concentration in any way. Fortunately, no further calculations based on these data were attempted.

Lebedev et al.[16] measured calorimetrically heat capacities and enthalpies of combustion, of another lactide, a racemic DL-lactide, and of its oligomer. The resulting enthalpy and entropy of polymerization were as follows: $\Delta H^\circ_{ll} = -27.0$ kJ·mol^{-1}, $\Delta S^\circ_{ll} = -13.0$ J·mol^{-1}·K^{-1} at 400 K. One can expect a similarity of ΔH°_p for L- and LD-lactide polymerization. As we have shown recently, these values for polymerization in 1,4-dioxane are practically identical (to be published elsewhere). Therefore, enthalpy of equilibrium 1 for L-lactide in bulk, calculated in the present paper, can be, in principle, compared with enthalpy for DL-lactide estimated by Lebedev et al. Both values are close to each other (within approximately 20% of the measured values). The origins of discrepancy between the $\Delta S°_p$ values are not clear.

Acknowledgment. We acknowledge the support of the Grant 01.14 of the Polish Academy of Sciences.

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Registry No. 1, 4511-42-6; tin(II) 2-ethylhexanoate, 301-10-0.