Depolymerization of Poly[(*R*)-3-hydroxybutyrate] to Cyclic Oligomers and Polymerization of the Cyclic Trimer: An Example of Thermodynamic Recycling

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ABSTRACT: Biotechnologically produced poly[(*R*)-3-hydroxybutyrate] (PHB) was subjected to catalytic depolymerization in the melt and in solution. In the melt depolymerization yields crotonic acid beside linear oligomers according to an ester pyrolysis reaction independent of the catalyst used. In solution cyclic oligomers were obtained via back-biting reactions. Efficient catalysts for this reaction are dibutyltin dimethoxide and *p*-toluenesulfonic acid. The thermodynamic parameters of the depolymerization of PHB to yield (*R*,*R*,*R*)-4,8,12-trimethyl-1,5,9-trioxacyclododeca-2,6,10-trione (TBL) were determined from calorimetric measurements by Lebedev et al. as a function of temperature at standard pressure ($p = 101.325$ kPa) and are at $T = 400$ K: $\Delta H^\circ_{\text{depol}} = -43$ kJ·mol^{-1}, $\Delta S^\circ_{\text{depol}} = 66$ J·K^{-1} mol^{-1}, and $\Delta G^\circ_{\text{depol}} = -70$ kJ·mol^{-1}. The experimental results are in full agreement with these values. Polymerization of TBL in the melt with dibutyltin dimethoxide as initiator results in poly[(*R*)-3-hydroxybutyrate] (PHB′) of low molecular weight ($M_n = 5 \times 10^3$), the spectroscopic characteristics are identical with those of the biotechnologically produced material. The thermodynamic parameters of the polymerization were determined from calorimetric measurements by Lebedev et al. as a function of temperature; they are at standard pressure ($p = 101.325$ kPa) and a polymerization temperature of $T = 400$ K: $\Delta H^\circ_{\text{pol}} = 12$ kJ·mol^{-1}, $\Delta S^\circ_{\text{pol}} = -32$ J·K^{-1}·mol^{-1}, and $\Delta G^\circ_{\text{pol}} = 25$ kJ·mol^{-1}. These results contradict the polymerization experiment. The factors which may contribute to a decrease of $\Delta G^\circ_{\text{pol}}$ are discussed.

Introduction

The degradation of polymers with the aim to recover valuable monomers, e.g., cyclic monomers or oligomers, seems to present an intelligent method for the recycling of high-value polymers. From a thermodynamic point of view, depolymerization may occur at reaction conditions for which the free energy of polymerization is positive. Thus, for example, above the ceiling temperature of a polymer/monomer system, with both ΔH and ΔS being negative, depolymerization occurs after creating active centers. A number of polymers obtained by ring-opening polymerization exhibit a low ceiling temperature. These are the polymers derived from monomers with low ring strain, which are five-, six-, and seven-membered cycles containing heteroatoms. When the monomer is a three- or four-membered cycle with high ring strain, depolymerization leads to a mixture of higher cyclic oligomers.[1]

The ring-closing depolymerization of a polyester leads to the cyclic monomer, a lactone, or to cyclic oligomers; further ester pyrolysis may take place, yielding a linear unsaturated carboxylic acid. The probability of the latter reaction is high if the CC double bond is conjugated to the carbonyl group. This applies to the polyester of 3-hydroxybutyrate; ester pyrolysis results in crotonic acid and oligomers with crotonate end groups.

The naturally occurring polyester poly[(*R*)-3-hydroxybutyrate] is a high-value polymer because of the chirality of the repeating unit which originates from the "chiral carbon pool".

In the present paper we report experimental results on the depolymerization of poly[(*R*)-3-hydroxybutyrate] (PHB) and on the polymerization of the cyclic trilactone (*R*,*R*,*R*)-4,8,12-trimethyl-1,5,9-trioxacyclododeca-2,6,10-trione (TBL) yielding a low molecular weight poly[(*R*)-3-hydroxybutyrate] (PHB′). The experimental results are discussed in the light of the thermodynamic parameters of PHB depolymerization and TBL polymerization obtained from calorimetric measurements performed by Lebedev et al.[2]

Experimental Part

Materials. Biotechnologically produced poly[(*R*)-hydroxybutyrate] (PHB) (from ICI and ZENECA) was used without further purification. Dibutyltin dimethoxide ($Bu_2Sn(OMe)_2$) (from Merck), dibutyltin oxide (from Aldrich), *p*-toluenesulfonic acid monohydrate (from Merck), trifluoromethanesulfonic acid methyl ester (from Aldrich), and anhydrous ferric trichloride (Fluka) were used without further purification. 1-Chloro-3-ethoxytetrabutyldistannoxane $[Bu_4Sn_2Cl(O)OEt]_2$ was prepared according to the literature.[3]

Toluene was freshly distilled from a solution of *sec*-butyllithium before use; chloroform was refluxed with $CaCl_2$ and distilled.

Nitrogen (from Linde) was passed over molecular sieves 4 Å, finely distributed potassium on aluminum oxide, and BTS catalyst (from BASF) for purification.

Measurements. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Varian VXR 300 spectrometer at 300 MHz and 75.4 MHz, respectively. Deuteriochloroform was used as a solvent with tetramethylsilane as the internal standard.

Gel permeation chromatography (GPC) analyses were carried out using an ERC HPLC pump 64 with an ERMA 7515 A refractive index detector. For the separation a combination of two columns was applied (Jordi gel, length 500 mm, diameter 10 mm, pore width 100 and 1000 Å). Chloroform was the eluting solvent with a flow rate of 1.0 mL/min; calibration was achieved with polystyrene standards.

Optical rotatory data were obtained using a Perkin-Elmer polarimeter P24 at 365 nm with chloroform as a solvent at room temperature.

Thermodynamic Data. The thermodynamic data of TBL, PHB, and PHB′ were determined by Lebedev et al. at the Lobachevski State University Nizhny Novgorod (Russian Federation).[2] The isobaric heat capacity, melting temperatures, and melting enthalpies were determined in the tem-

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Table 1. Catalytic Depolymerization of PHB in the Melt: Dependence of Yield and Product Composition on Reaction Parameters

no.	catalyst	mol % catalyst[a]	T, °C	% yield	DP[b]	mol % hydroxybutyrate units	mol % crotonate units
1	NaOH	1	220	63	1.9	47.9	52.1
2	$Ti(OiPr)_4$	1	220	65	1.6	38.7	61.3
3	$Bu_2Sn(OMe)_2$	1	220	72	2.4	58.7	41.3
4	Bu_2SnO	1	220	84	2.6	61.4	38.6
5	$FeCl_3$	1	220	93	1.2	19.4	80.6
6	$CF_3SO_3CH_3$	1	220	81	1.0	1.9	98.1
7	*p*-TsOH·H_2O	1	220	77	1.9	46.2	53.8
8	*p*-TsOH·H_2O	5	220	68	2.8	63.6	36.4
9	*p*-TsOH·H_2O	5	280	91	3.3	70.1	29.9
10	*p*-TsOH·H_2O	5	320	93	3.1	67.9	32.1

[a] Amount of catalyst in mol % with respect to hydroxybutyrate monomeric units. [b] Number average degree of polymerization; DP = 1 ≅ crotonic acid.

Table 2. Catalytic Depolymerization of PHB in Refluxing Solvent ([PHB] = 5 wt %): Dependence of Yield and Product Composition on Reaction Parameters

solvent	bp of solvent, °C	amt of catalyst, mol %[a]	t, h	yield of depolymerization products, wt %
THF	67	5% $Bu_2Sn(OMe)_2$	48	0
$CHCl_3$	62	5% $Bu_2Sn(OMe)_2$	20	0
1,2-$C_2H_4Cl_2$	84	5% $Bu_2Sn(OMe)_2$	24	0
toluene	111	2−15% $Bu_2Sn(OMe)_2$	20	cyclic oligomers (16−95%)
toluene	111	10% $Ti(OiPr)_4$	24	cyclic + linear unsaturated oligomers
toluene	111	15% Bu_2SnO	24	0
toluene	111	25% *p*-TsOH·H_2O	17[b]	cyclic oligomers (77%)
toluene/1,2-$C_2H_4Cl_2$	≈100	22% *p*-TsOH·H_2O	22[b]	cyclic oligomers (80%)

[a] Amount of catalyst in mol % with respect to hydroxybutyrate monomeric units. [b] Afterward water is distilled off azeotropically during 4 h.

perature range from 5 to 340 K using a vacuum adiabatic calorimeter TAU-1. All relevant data are given in the reference. For the discussion it is necessary, however, to report some important steps.

The thermodynamic parameters ΔH°, ΔS°, and ΔG° were calculated from the isobaric heat capacity c°_p and the temperature dependence of c°_p at standard pressure ($p = 101.325$ kPa).

In order to determine the function $c^\circ_p(T) = \Delta Q/\Delta T$, the quantity of heat ΔQ absorbed in a certain temperature interval ΔT was determined as a function of temperature using a calorimeter. For TBL, PHB, and PHB′ this function was determined in a large temperature range (4.8−430 K for TBL, 10−490 K for PHB, 10−485 K for PHB′). For temperatures below the last experimental point, e.g. 5 K, till 0 K the value of $c^\circ_p(T)$ is extrapolated with a Debye function (D). The melting points (T_m), melting entalpies ΔH°_m, and melting entropies ΔS°_m are determined graphically from the c°_p vs T plot.

The thermodynamic functions $H^\circ(T) - H^\circ(0)$, $S^\circ(T)$, and $G^\circ(T) - G^\circ(0)$ are calculated from the following equations:

$$H^\circ(T) = \int c^\circ_p(T)\,\mathrm{d}T \Rightarrow H^\circ(T) - H^\circ(0) = \int_0^{5\mathrm{K}} nD(\theta/T)\,\mathrm{d}T + \int_{5\mathrm{K}}^{T_m} c^\circ_p(T)\,\mathrm{d}T + \Delta H^\circ_m + \int_{T_m}^{T} c^\circ_p(T)\,\mathrm{d}T \quad (1)$$

$$S^\circ(T) = \int \frac{c^\circ_p(T)}{T}\,\mathrm{d}T \Rightarrow S^\circ(T) = \int_0^{5\mathrm{K}} \frac{nD(\theta/T)}{T}\,\mathrm{d}T + \int_{5\mathrm{K}}^{T_m} \frac{c^\circ_p(T)}{T}\,\mathrm{d}T + \Delta S^\circ_m + \int_{T_m}^{T} \frac{c^\circ_p(T)}{T}\,\mathrm{d}T \quad (2)$$

$$G = H - TS \Rightarrow G^\circ(T) - G^\circ(0) = H^\circ(T) - H^\circ(0) - TS^\circ(T) \quad (3)$$

where D is the Debye function and n and θ are adjustable parameters.

From these equations the absolute entropies $S^\circ(T)$ are obtained directly when the entropy at 0 K is neglected. For the enthalpy $H^\circ(T)$ and the free enthalpy $G^\circ(T)$ the above equations give only differences $\Delta H^\circ = H^\circ(T) - H^\circ(0)$ and $\Delta G^\circ = G^\circ(T) - G^\circ(0)$. The calculation of the absolute values needs a reference point, e.g., as determined from energies of combustion. The molar energies of combustion $\Delta U^\circ_{\mathrm{comb}}{}^{298}$ were determined in a calorimeter with a static bomb at 298 K, and from these experimental results the molar enthalpy of combustion [$\Delta H^\circ_{\mathrm{comb}}{}^{298}$] was calculated according to

$$\Delta H^\circ = \Delta U^\circ + \Delta nRT \quad (4)$$

where Δn represents the change in moles of all gaseous products in the reactant and product. From the chemical equation of combustion, the enthalpy of formation (of TBL, PHB, and PHB′) is calculated since the enthalpy of combustion was experimentally determined and the standard enthalpies of formation (ΔH°_f) of O_2, CO_2, and H_2O are known. ΔH°_f corresponds to the absolute enthalpy at 298 K; with the knowledge of the enthalpy at this fixed point and the knowledge of $\Delta H^\circ = H(298) - H(0)$, $H(0)$ can be calculated and, as a consequence, the functions $H^\circ(T)$ and $G^\circ(T)$.

From the thermodynamic functions $H^\circ(T)$, $S^\circ(T)$, and $G^\circ(T)$ of the compounds the thermodynamic reaction parameters are derived from the differences, i.e., the polymerization parameters are calculated from eqs 5−7:

$$\Delta H^\circ_{\mathrm{pol}}(T) = H^\circ_{\mathrm{PHB'}}(T) - H^\circ_{\mathrm{TBL}}(T) \quad (5)$$

$$\Delta S^\circ_{\mathrm{pol}}(T) = S^\circ_{\mathrm{PHB'}}(T) - S^\circ_{\mathrm{TBL}}(T) \quad (6)$$

$$\Delta G^\circ_{\mathrm{pol}}(T) = G^\circ_{\mathrm{PHB'}}(T) - G^\circ_{\mathrm{TBL}}(T) \quad (7)$$

Depolymerization of PHB in the Melt. PHB [430 mg, 5 mmol of hydroxybutyrate repeating units (HB r.u.)] and a calculated amount of catalyst (1−10 mol % with respect to r.u.) are heated to a constant temperature. The volatile material is removed in a cold trap. The decomposition product is heterogeneous; liquid and crystalline reaction products were obtained. The yield of volatile material is between 63 and 95 wt % (cf. Table 1).

Depolymerization of PHB in Solution. A solution of PHB and catalyst in a solvent is heated to reflux (cf. Table 2). The solution in chloroform, 1,2-dichloromethane, or toluene is homogeneous but slightly opalescent, while in tetrahydro-

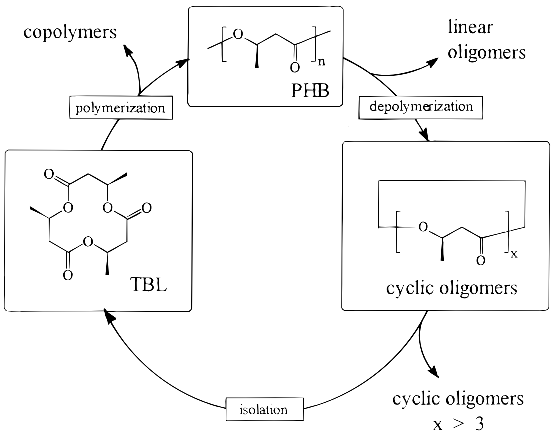


Figure 1. Concept of thermodynamic recycling in the system PHB/TBL.

furan the mixture remains heterogeneous. On use of *p*-toluenesulfonic acid monohydrate as a catalyst, the solution remains turbid until the water is removed by azeotropic distillation.

The product was isolated by evaporation of the solvent after the organic phase was extracted with a sodium carbonate solution, a 2 M solution of hydrochloric acid, and saturated sodium chloride solution. This material, which is a mixture of mainly cyclic oligomers was then subjected to distillation/sublimation, and the cyclic trimer TBL was isolated in a yield of 42−50 wt % as a white solid (mp 108.5 °C).

^{1}H NMR spectrum of TBL (300 MHz, $CDCl_3$): $\delta = 1.31$ (d, 9H, $J = 6.4$ Hz, 3CH_3), 2.43/2.58 (2 × d/d, 6H, $J = 13.5/2.4//13.5/11.1$ Hz, 3CH_2), 5.35 (m, 3H, 3HC−O) ppm. ^{13}C NMR spectrum of TBL (75.43 MHz, $CDCl_3$): $\delta = 20.75$ (CH_3), 42.12 (CH_2), 68.82 (CH), 170.0 (CO) ppm.

Polymerization of TBL (cf. Ref 4).

Results and Discussion

The principle of thermodynamic recycling applied to poly[(*R*)-3-hydroxybutyrate] is illustrated in Figure 1. Starting with the biotechnologically produced PHB, cyclic oligomers are obtained via catalytic ring-closing depolymerization; formation of linear oligomers is considered an undesired side reaction, since linear oligomers are eliminated from the closed circuit. The cyclic trimer is the main reaction product from ring-closing depolymerization; this material is isolated and used for polymerization experiments. On homopolymerization a stereochemically pure poly[(*R*)-3-hydroxybutyrate] is obtained (PHB′) which has a molecular weight much lower than the natural material. The cyclic trimer may be copolymerized with suitable monomers. It should be possible to use the whole mixture of cyclic oligomers as a starting material for the polymerization after purification. The linear oligomers but also the higher cyclic oligomers yield upon methanolysis a chiral building block: methyl (*R*)-3-hydroxybutyrate.

In the following the thermodynamic parameters of TBL, PHB, and PHB′ as obtained from calorimetric measurements[2] will be presented followed by a discussion of the probability of the ring-closing depolymerization of PHB to form TBL as well as of the ring-opening polymerization of TBL to give PHB′ on the basis of these data. Finally, the predictions based on thermodynamic parameters obtained from calorimetric measurements are compared with experimental results, and conformity and inconsistency are discussed.

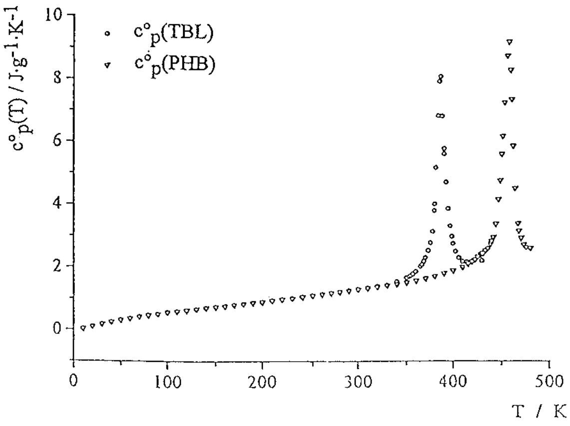


Figure 2. Experimental heat capacities c°_p of PHB and TBL.

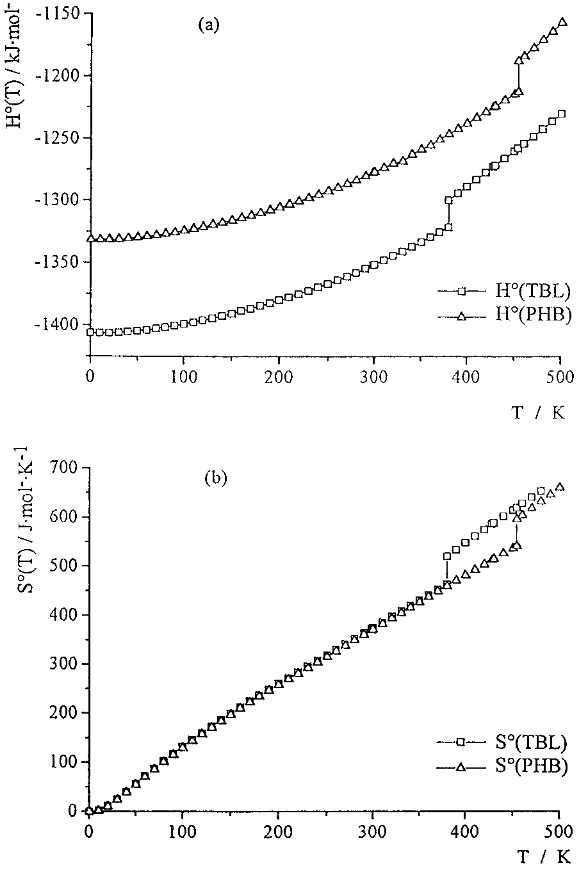


Figure 3. Thermodynamic functions of PHB and TBL: (a) enthalpy [$H°(T)$]; (b) entropy [$S°(T)$]; data obtained from calorimetric measurements.

Ring-Closing Depolymerization of PHB: Determination of the Thermodynamic Parameters. The isobaric heat capacities c°_p of PHB and TBL were determined experimentally (Figure 2). In the solid state the heat capacities of both PHB and TBL are identical within the accuracy of measurements. At the melting points (454 K for PHB and 380 K for TBL), however, a prominent increase of the c°_p values is observed; these measurements do not indicate a glass transition temperature. At temperatures above the melting point both PHB and TBL decompose (ester pyrolysis) and the c°_p values cannot be determined precisely. From the $c^\circ_p(T)$ values and the molar combustion enthalpies [$\Delta U^\circ_{\mathrm{comb}}{}^{298}$(PHB) = −6025 kJ/mol HB r.u. and $\Delta U^\circ_{\mathrm{comb}}{}^{298}$(TBL) = −5943 kJ/mol HB r.u.] the thermodynamic functions of PHB and TBL enthalpy $H°(T)$ and entropy $S°(T)$ were calculated (Figure 3). The trilactone TBL has a distinctly lower value of the enthaply over the whole temperature range studied as compared with

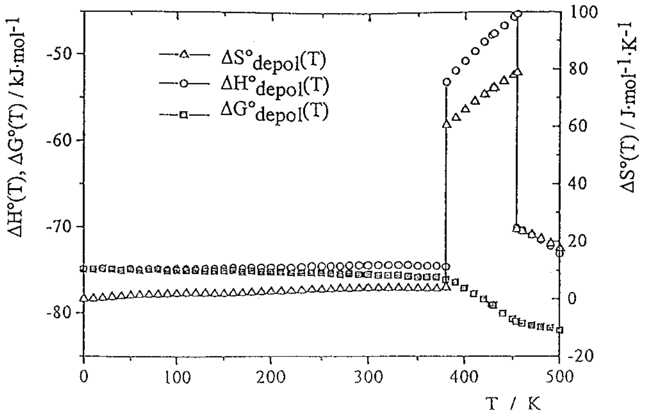


Figure 4. Enthalpy, entropy, and free energy of ring-closing depolymerization of PHB to TBL as a function of temperature (data obtained from calorimetric measurements).

the biotechnologically produced PHB. In the solid state this difference can be explained by the perfect crystalline order of the low molecular weight TBL compared to the partially crystalline PHB. In the liquid phase—the melt—the higher dipole moment of the r.u. in TBL as compared to PHB may cause the lower enthalpy value of TBL. (The higher dipole moment of the HB r.u. in TBL is caused by the parallel orientation of the three carbonyl groups in the twelve-membered ring of TBL).[5] In the temperature interval between the melting points of TBL and PHB ($380 < T/\mathrm{K} < 454$) the difference of the enthalpies of PHB and TBL shows a minimum because here the enthalpy of the melt of TBL is compared to that of semicrystalline PHB.

Analysis of the entropy of PHB and TBL as a function of temperature (Figure 3b) reveals no difference in entropy within the limits of accuracy of the measurement as long as both, PHB and TBL, are in the solid state. When both substances are in the melt, at $T > 454$ K, TBL exhibits a slightly higher entropy value than PHB. The difference between the entropies of TBL and PHB is highest in the temperature range $380 < T/\mathrm{K} < 454$ where TBL is in the molten state (high entropy) and PHB is in the semicrystalline state. In Figure 4 the thermodynamic functions of the ring-closing depolymerization of PHB to form TBL—$\Delta H°_{\mathrm{depol}}(T)$ and $\Delta S°_{\mathrm{depol}}(T)$ and the free energy of depolymerization $\Delta G°_{\mathrm{depol}}(T)$—as calculated from calorimetric measurements, are presented. In the entire temperature range studied $\Delta G°_{\mathrm{depol}}$ has a large negative value, showing a high probability of the depolymerization reaction. This large negative value of $\Delta G°_{\mathrm{depol}}$ is a result of the negative value of $\Delta H°_{\mathrm{depol}}$ and the positive value of $\Delta S°_{\mathrm{depol}}$ over the whole temperature range. From the discontinuous change of $\Delta H°$ and $\Delta S°$ at the melting points of TBL and PHB the enthalpy and entropy of fusion of both compounds was determined to be $\Delta H^{\circ}_{\mathrm{fus}}{}^{298}(\mathrm{TBL}) = 21.5$ kJ·mol^{-1}, $\Delta H^{\circ}_{\mathrm{fus}}{}^{298}(\mathrm{PHB}) = 24.8$ kJ·mol^{-1}, $\Delta S^{\circ}_{\mathrm{fus}}{}^{298}(\mathrm{TBL}) = 56.6$ J·mol^{-1}·K^{-1}, $\Delta S^{\circ}_{\mathrm{fus}}{}^{298}(\mathrm{PHB}) = 54.6$ J·mol^{-1}·K^{-1}.

As a conclusion, from a thermodynamic point of view, the depolymerization of naturally produced PHB to TBL should be possible in the whole temperature range studied.

Ring-Closing Depolymerization of PHB: Experimental Results. Catalytic depolymerization of PHB was performed in the melt and in solution. The results, i.e., the nature of hydroxybutyrate oligomers, differ significantly; while from melt depolymerization linear oligomers are obtained, depolymerization in solution results in cyclic oligomers.

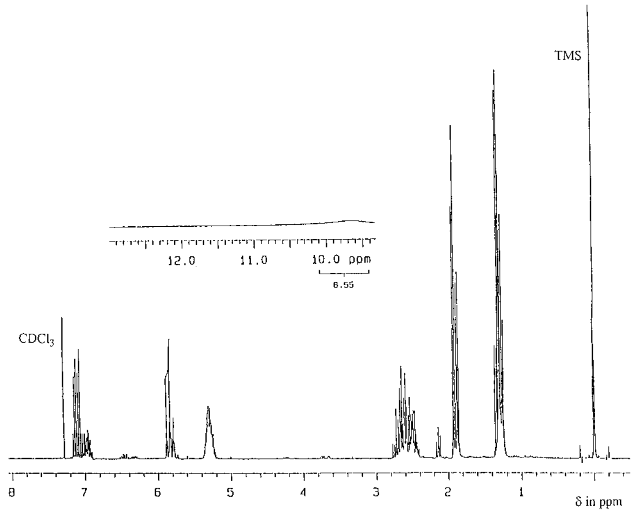


Figure 5. ^{1}H NMR spectrum of linear hydroxybutyrate oligomers obtained by catalytic depolymerization of PHB with 1 mol % Bu_2SnO in the melt at 220 °C.

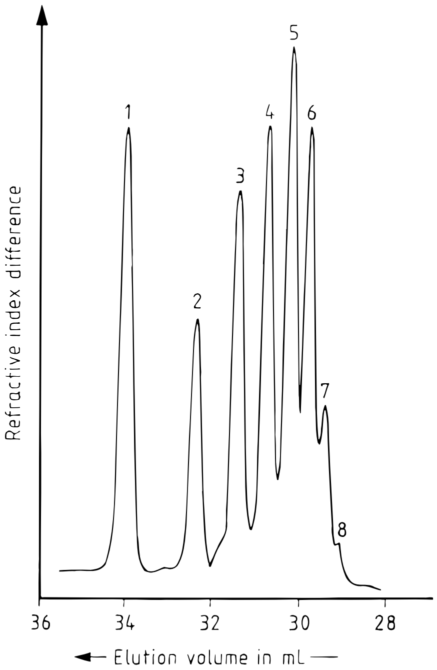


Figure 6. Gel permeation chromatography (GPC) trace of oligomers obtained by catalytic depolymerization of PHB with 1 mol % Bu_2SnO in the melt at 220 °C (No. 4 Table 1).

The catalytic depolymerization of high molecular weight, biotechnologically produced PHB in the melt results in linear oligomers with crotonate end groups and crotonic acid via an ester pyrolysis mechanism with different catalysts at 200−320 °C (cf. eq 8)

The ^{1}H NMR spectrum of the raw material (Figure 5) shows the characteristic signals of the hydroxybutyrate repeating units at 1.28 ppm (methyl protons), 2.46/2.60 ppm (methylene protons), and 5.26 ppm (methine protons). Corresponding to crotonic acid and to crotonate end groups, signals at 7.1/5.9 ppm and at 6.9/5.8 ppm are observed, respectively, as well as methyl protons of the unsaturated units at 1.86 ppm. A quantitative determination of the integrals of the resonances corresponding to methyl groups attached to sp^3 carbon atoms (at 1.28 ppm) and to sp^2 carbon atoms (at 1.86 ppm) yields the percentage of saturated and unsaturated C_4 units from which the average degree of polymerization (DP) can be calculated. Table 1 shows

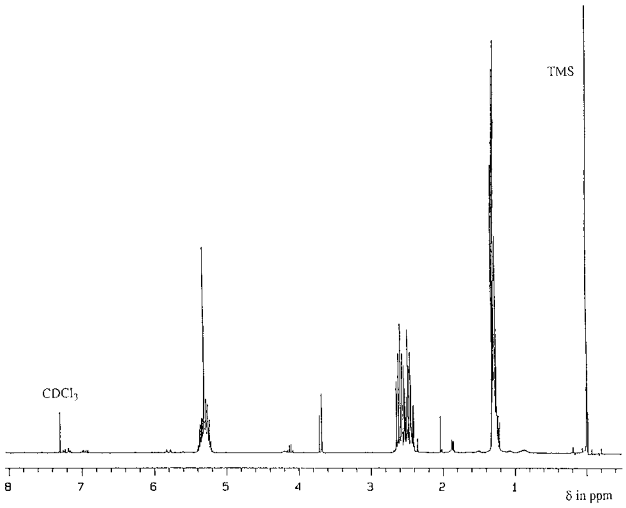


Figure 7. ^{1}H NMR spectrum of cyclic hydroxybutyrate oligomers obtained by catalytic depolymerization of PHB with $Bu_2Sn(OMe)_2$ in refluxing toluene solution; [PHB] = 5 wt %; $[Bu_2Sn(OMe)_2]/[HB\ r.u.] = 0.05$; $t = 24$ h.

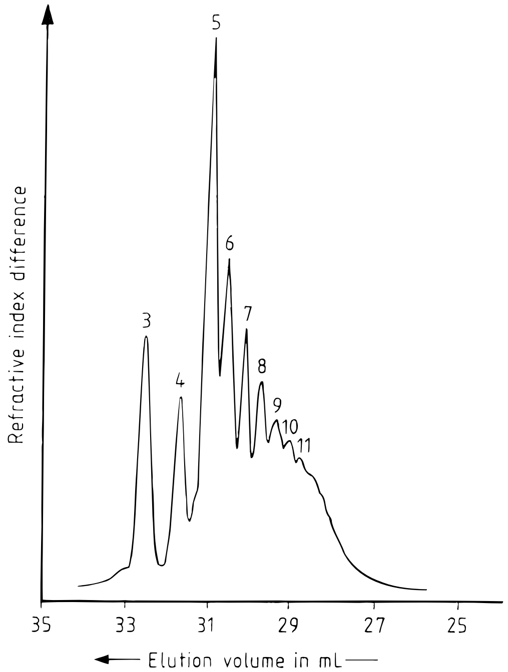
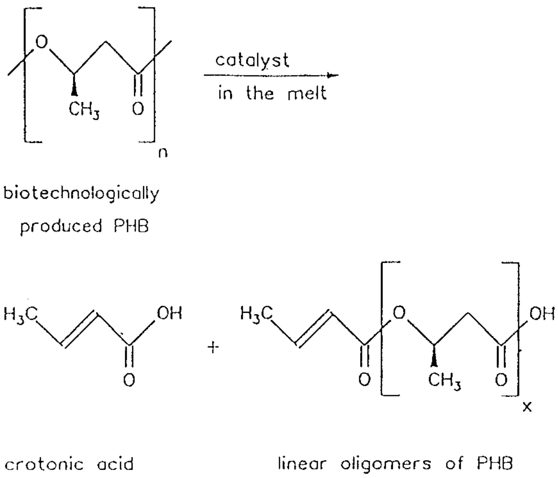


Figure 8. Gel permeation chromatography (GPC) trace of oligomers obtained by catalytic depolymerization of PHB with $Bu_2Sn(OMe)_2$ in refluxing toluene solution; [PHB] = 5 wt %; $[Bu_2Sn(OMe)_2]/[HB\ r.u.] = 0.05$; $t = 24$ h.

results of the catalytic depolymerization of PHB in the melt with various catalysts and at various temperatures. The extent of ester pyrolysis can be influenced by the reaction conditions; however, ester pyrolysis cannot be suppressed. A ring-closing depolymerization with formation of cyclic hydroxybutyrate oligomers, necessary for the realization of thermodynamic recycling, was not observed in any of the described examples. GPC of these products as given in Figure 6 shows a homologous series of linear oligomers, which are resolved up to the octamer (for a calibration plot of the linear oligomers cf. Figure 9). As the first member of this series of linear oligomers crotonic acid was identified.

The catalytic depolymerization in a solution of biotechnologically produced PHB was performed in toluene or toluene/1,2-dichloroethane at reflux using various catalysts. Under these reaction conditions ring-closing depolymerization occurs and a ring–chain equilibrium is established (cf. eq 9). The ^{1}H NMR spectrum (Figure 7) of the raw material shows hydroxybutyrate units as the main product with minute amounts of unsaturated C_4 units. The resonances of the methyl, methylene, and methine protons of the hydroxybutyrate repeating units in the cyclic oligomers show values centered at 1.3, 2.5, and 5.3 ppm, respectively. (The resonance at 3.7 ppm originates from the catalyst used, Bu_2SnOMe_2.) On purification of the cyclic fraction or isolation of fractions containing different amounts of cycles by column chromatography the resonance at 3.7 ppm disappears as well as the signals derived from crotonate units. The ^{1}H NMR spectrum of a purified fraction of oligomers shows no end groups. Thus these oligomers are considered to be cyclic.



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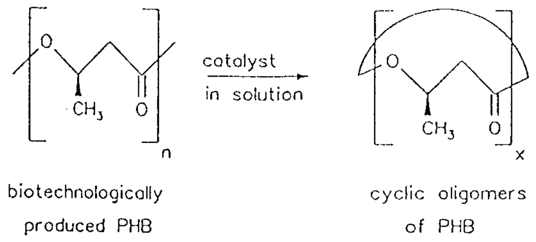

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Table 2 shows the results obtained on ring-closing depolymerization using various reaction conditions: various solvents having different boiling points, various catalysts at different concentrations and different reaction times. The best results are obtained in runs 4 and 8 of Table 2. The optimum conditions of run 4 are the following: polymer concentration of 5 wt %, catalyst concentration between 5 and 10 mol % with respect to hydroxybutyrate repeating units, and reaction time of 20 h. From the GPC trace of the cyclic oligomers (Figure 8) a linear calibration plot was obtained (Figure 9), showing that we deal with a homologous series of oligomers. The calibration plot of the cyclic oligomers differs from that of the linear oligomers; the cyclic oligomers show a larger elution volume than the linear oligomers of the same degree of oligomerization because of a smaller hydrodynamic volume. The assignment of the GPC peaks was made from the knowledge of the elution volume of the cyclic trimer TBL, which was isolated as a pure compound by distillation from the mixture of cyclic oligomers followed by recrystallization. The cyclic hydroxybutyrate oligomers are present in a ring–chain equilibrium with linear poly(hydroxybu-

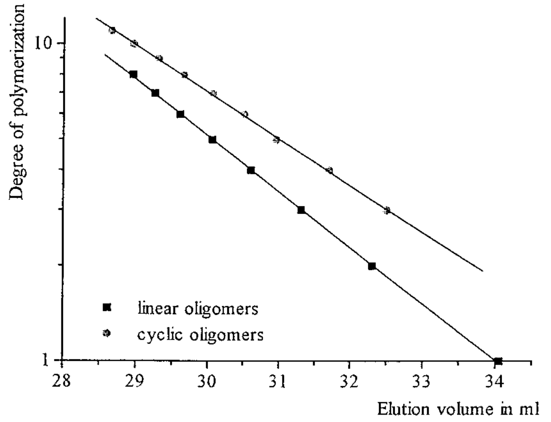


Figure 9. GPC calibration plot of linear and cyclic PHB oligomers.

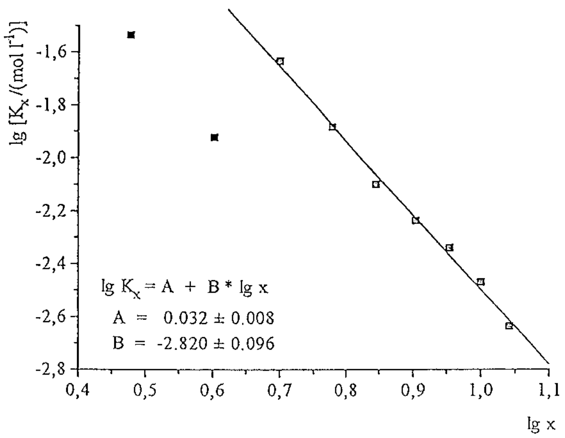


Figure 10. Jacobson–Stockmayer plot of cyclic hydroxybutyrate oligomers obtained by depolymerization of PHB with $Bu_2Sn(OMe)_2$ in refluxing toluene solution; [PHB] = 5 wt %; $[Bu_2Sn(OMe)_2]/[HB\ r.u.] = 0.05$; $t = 24$ h.

tyrate) (with K_x being the equilibrium constant) from which they are formed by ring-closing depolymerization (back-biting) reaction; the twelve-membered cycle (TBL) is the smallest ring obtained, however, in high concentration. The molar equilibrium concentration of the cyclic oligomers ($[M_x] \approx K_x$) with $x \geq 5$ is in agreement with the Jacobson–Stockmayer theory as applied to ring–chain equilibria (Figure 10);[6] the experimental points coincide with a straight line $\log K_x = A + B \log x$ (with $A = 0.032 \pm 0.008$ and $B = -2.820 \pm 0.096$). The deviation of the cyclic trimer and tetramer from the theoretical line is due to the fact that the number of bonds in their molecules is too small to guarantee Gaussian statistics of the conformation of the molecular chain. For the slope of the straight line the Jacobson–Stockmayer theory predicts a value of −2.5; however, scaling arguments lead to slopes of −2.5 to −2.9 depending on the solvent used.[7]

The explicit form of the Jacobson–Stockmayer equation (eq 10)

$$K_x = \left(\frac{3}{2\pi}\right)^{3/2} \frac{1}{N_A \sigma_R} (C n_o l^{-2})^{-3/2} x^{-5/2} \qquad (10)$$

in which K_x is the equilibrium constant of the formation of a cyclic oligomer with the degree of oligomerization x, n_o represents the number of bonds in the repeating unit, the symmetry number has the value 2 ($\sigma_R = 2$), and the average bond length $\sqrt{l^2} = 1.486 \times 10^{-9}$ dm allows the determination of the characteristic ratio C_∞ ($x > 5$) from the intercept of the linear Jacobson–Stockmayer plot. This value, which represents a measure of the stiffness of a polymer chain, was determined to be $C_\infty = 7.1 \pm 1$.

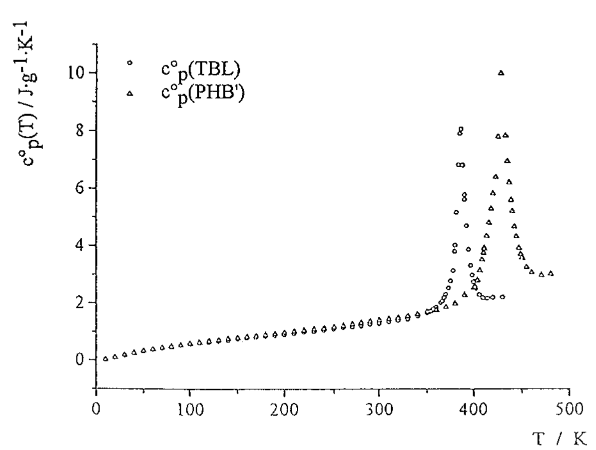


Figure 11. Experimental heat capacities $c°_p$ of TBL and PHB′.

Ring-Opening Polymerization of TBL: Presentation of the Thermodynamic Parameters. The isobaric heat capacities $c°_p$ of TBL were determined as a function of temperature (Figure 11). Up to the melting point of TBL the difference between $c°_p$ of PHB′ and $c°_p$ of TBL increases from 1% at $T = 30$ K to 9% at $T = 380$ K. (This difference is equal to the difference between $c°_p$ of PHB′ and $c°_p$ of PHB.) Above the corresponding melting points, PHB′ and TBL begin to decompose and no data on $c°_p(T)$ can be obtained. A glass transition temperature for PHB′ cannot be deduced from these data.

The calculated absolute enthalpy $H(T)$ of PHB′ in the solid state is always higher than the enthalpy of TBL but lower than the enthalpy of the biotechnologically produced PHB. Arithmetically, these differences result from the differences in the molar energies of combustion ΔU_{comb}^{298} of PHB′ (−5970 kJ/mol), TBL (−5943 kJ/mol), and PHB (−6025 kJ/mol). The larger negative values of the enthalpy of PHB′ as compared to that of PHB may point at a higher crystallinity or an improved crystalline order in PHB′. In the temperature range from 380 to 428 K (TBL liquide, PHB solid) the difference in enthalpy values of PHB′ and TBL is very small, but still the value for PHB′ is higher than that for TBL.

The entropy of PHB′ is—under the same physical conditions and neglecting the entropy at absolute zero—higher than the entropy of TBL (Figure 12b); but for molten TBL and solid PHB′ ($380 < T/\mathrm{K} < 428$), however, the entropy of PHB′ is obviously smaller, altogether the differences in entropy are small. For PHB the entropy is also smaller than that of PHB′; this can be explained by the much higher molecular weight of the biotechnologically produced material ($M_n = 9 \times 10^5$) as compared to the molecular weight of PHB′ ($M_n = 4 \times 10^3$).

From the above mentioned absolute values of the thermodynamic parameters of TBL and PHB′, the thermodynamic functions of the polymerization $\Delta H°_{pol}(T)$, $\Delta S°_{pol}(T)$, and $\Delta G°_{pol}(T)$ were calculated (Figure 13). The polymerization enthalpy first increases smoothly with temperature from 30 to 35 kJ·mol^{-1}. At the melting point of TBL ($T = 380$ K) a sudden decrease of $\Delta H°_{pol}$ to values below 10 kJ·mol^{-1} is observed; at the melting point of PHB′ $\Delta H°_{pol}$ increases again to values >45 kJ·mol^{-1}. The differences in the enthalpies observed at the respective melting points represent the

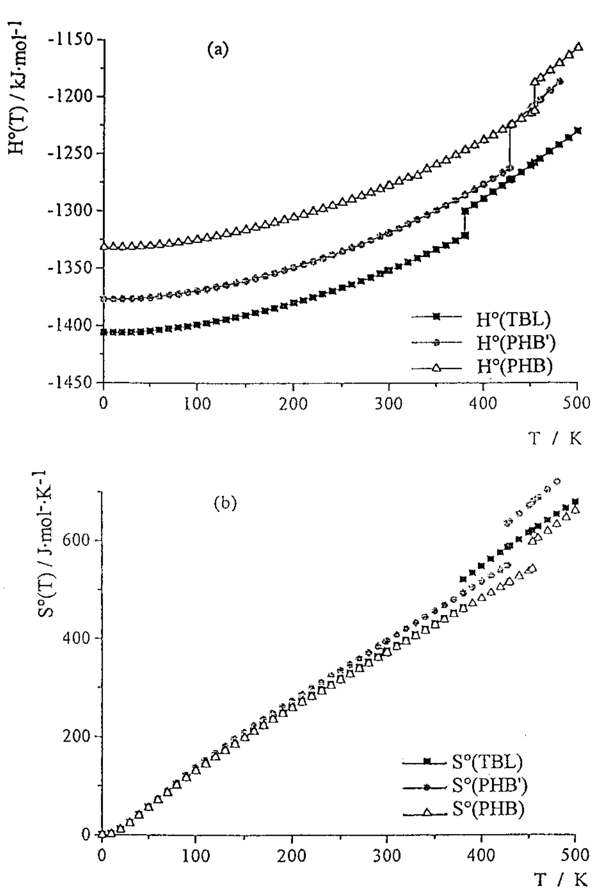


Figure 12. Thermodynamic functions of TBL, PHB′, and PHB: (a) enthalpy [$H°(T)$]; (b) entropy [$S°(T)$]. Data obtained from calorimetric measurements.

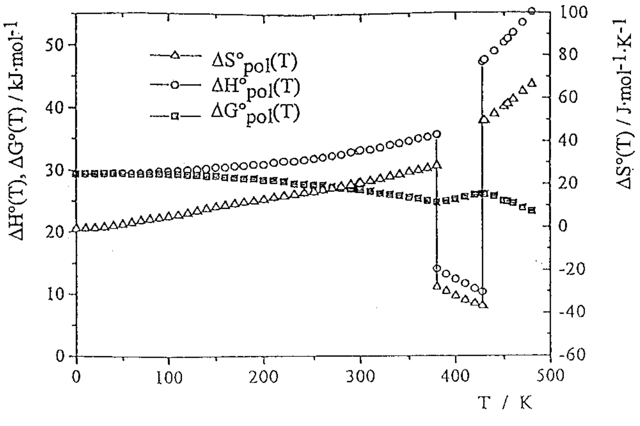
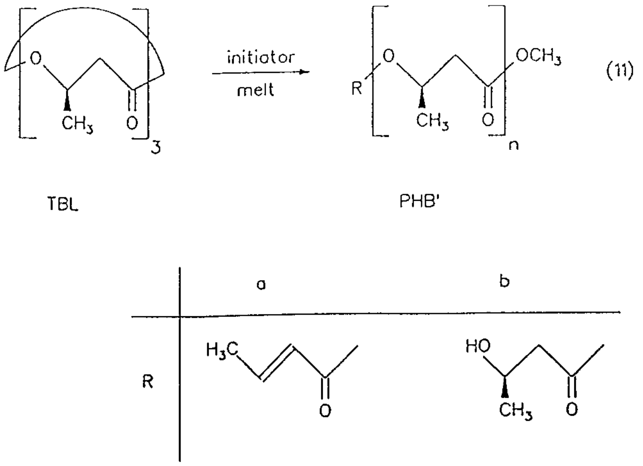


Figure 13. Enthalpy, entropy, and free energy of ring-opening polymerization of TBL to PHB′ as a function of temperature (data obtained from calorimetric measurements).

corresponding enthalpies of fusion ($\Delta H^{\circ}_{fus}{}^{298}$(TBL) = 21.5 kJ·mol^{-1}; $\Delta G^{\circ}_{fus}{}^{298}$(PHB′) = 36.7 kJ·mol^{-1}). In the same temperature range the entropy of polymerization $\Delta S°_{pol}$ shows a behavior analogous to that of the enthaply of polymerization. (The corresponding entropies of fusion were determined to be $\Delta S^{\circ}_{fus}{}^{298}$(TBL) = 56.6 J·mol^{-1} K^{-1}, and $\Delta S^{\circ}_{fus}{}^{298}$(PHB′) = 86.0 J·mol^{-1} K^{-1}). For the free energy of polymerization $\Delta G°_{pol}(T)$, however, only small changes are observed as a function of temperature. In the whole temperature range studied $\Delta G°_{pol}(T)$ has a positive value with a minimum between 350 and 400 K ($+23 < \Delta G°_{pol}$/kJ·mol^{-1} $< +30$). This means that from a thermodynamic point of view—in an ideal system—the ring-opening polymerization of TBL to PHB′ is impossible.

Ring-Opening Polymerization of TBL: Experimental Results. As reported earlier, the ring-opening polymerization of TBL to PHB′ can be achieved in the melt with tin- or titanium-based catalysts (eq 11, Table 3).[4] The best results with respect to conversion and polymer yield are obtained with $Bu_2Sn(OMe)_2$ as a catalyst at 120 °C. The polymer fraction insoluble in methanol was considered for further characterization. The highest molecular weight (M_n = 5000) was achieved at a polymerization temperature of 100 °C with 1 mol % $Bu_2Sn(OMe)_2$ and a reaction time of 144 h. With distannoxane $[Bu_4Sn_2Cl(O)OEt]_2$ and Ti(O*i*Pr)$_4$ as catalyst, both the molecular weight and the polymer yield were lower as compared to $Bu_2Sn(OMe)_2$. At this point attention should be paid to a comparison of properties of the biotechnologically produced PHB and PHB′ obtained from ring-opening polymerization of TBL.



The IR and ^{13}C NMR spectra of both polymers are virtually identical; the ^{1}H NMR spectrum of PHB′ shows resonances of low intensity due to end groups, e.g., OCH_3, $CH_3CH{=}CH{-}CO$, and $CH_3CH(OH)CH_2CO$ (as a consequence of the low molecular weight of these samples). The uniform configuration at the chiral center of the polymers, is responsible for many polymer properties, e.g., crystallinity, thermal properties, and biological degradability. The biotechnologically produced PHB has an isotactic structure with (*R*)-configuration at the stereogenic centers.[8] The isotactic structure of PHB′ was proven by IR spectroscopy, DSC measurements, and ^{13}C NMR spectroscopy.[4] The absolute configuration at the stereogenic centers of the hydroxybutyrate repeating units was determined by means of ORD spectroscopy (Figure 14, for comparison, the ORD spectrum of PHB is also presented). The equal shape of the two curves and especially the equal orientation are proof of the same configuration. The differences in the absolute values of $[\alpha]_{\lambda}^{298}$ and in the wavelength for $[\alpha] = 0°$ are explained by the different lengths of the helical chain segments which are expected due to the great differences in molecular weight of PHB′ and PHB.[9]

As a result, PHB′ is identical in structure with PHB but with a much lower molecular weight and different end groups.

In the following section we will try to give an answer to the question why the molecular weight of PHB′ obtained by ring-opening polymerization of TBL is limited to values of $M_n \approx 5000$. The following points will be discussed: (i) ester pyrolysis reactions, (ii)

Table 3. Polymerization of TBL in the Melt with Different Initiators

initiator	[I], mol %[a]	T, °C	t, h	% conversion[b]	% yield[c]	$10^{-3}M_n$[d]	M_w/M_n[e]
$Bu_2Sn(OMe)_2$	1.0	110	120	66	60	4.8	1.7
$Bu_2Sn(OMe)_2$	1.0	120	120	82	63	4.3	1.5
$[Bu_4Sn_2Cl(O)OEt]_2$	1.0	110	120	60	33	2.6	1.8
$[Bu_4Sn_2Cl(O)OEt]_2$	1.0	120	196	67	35	3.3	1.4
$Ti(OiPr)_4$	1.0	110	52[f]	51	43	2.0	1.5

[a] Initiator concentration in mol % with respect to hydroxybutyrate monomeric units. [b] Determinated by means of ^{13}C NMR spectra by integration of carbonyl peaks [c] Methanol insoluble fraction [d] Number average molecular weight determinated from end groups (^1H NMR) [e] Polydispersity index determined by gel permeation chromatography using polystyrene standards. [f] No further increase in yield and number average molecular weight with longer reaction times.

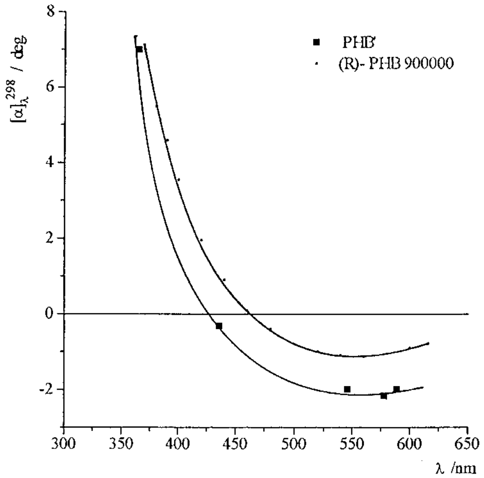


Figure 14. ORD spectrum of PHB′ (room temperature, [PHB′] = 3.0 wt % in chloroform) obtained by ring-opening polymerization of TBL with $Bu_2Sn(OMe)_2$ as initiator at 100°C in the melt; $[Bu_2Sn(OMe)_2]/[HB\ r.u.] = 0.05$; $t = 144$ h.

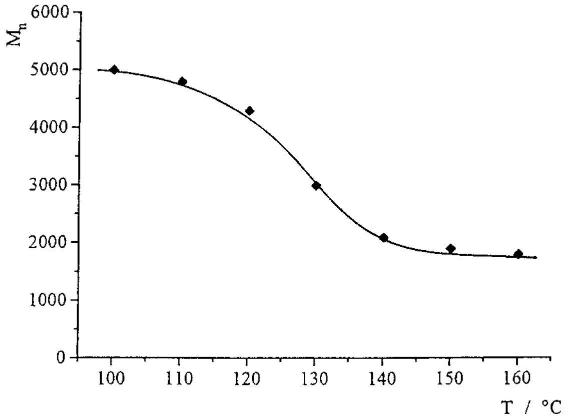


Figure 15. Number average molecular weight (M_n) of PHB′ obtained by polymerization of TBL with $Bu_2Sn(OMe)_2$ in the melt as a function of the polymerization temperature; $[Bu_2Sn(OMe)_2]/[HB\ r.u.] = 0.01$.

precipitation of PHB′ from the TBL melt, (iii) transesterification reactions.

(i) From the ^1H NMR spectrum of PHB′ we have deduced that crotonate end groups are present in the polymer. At this point it should be mentioned that M_n values determined from end group analysis correspond to the M_n values obtained by GPC measurements. These groups might be the result of ester pyrolysis reactions taking place during the chain growth reaction. We studied the dependence of the number average molecular weight (M_n) on the reaction temperature (Figure 15) and found that with increasing temperature the molecular weight of the polymer decreases. This is a strong indication that ester pyrolysis causes the formation of inactive polymer chains. From the literature[8b] it is known, that this degradation reaction

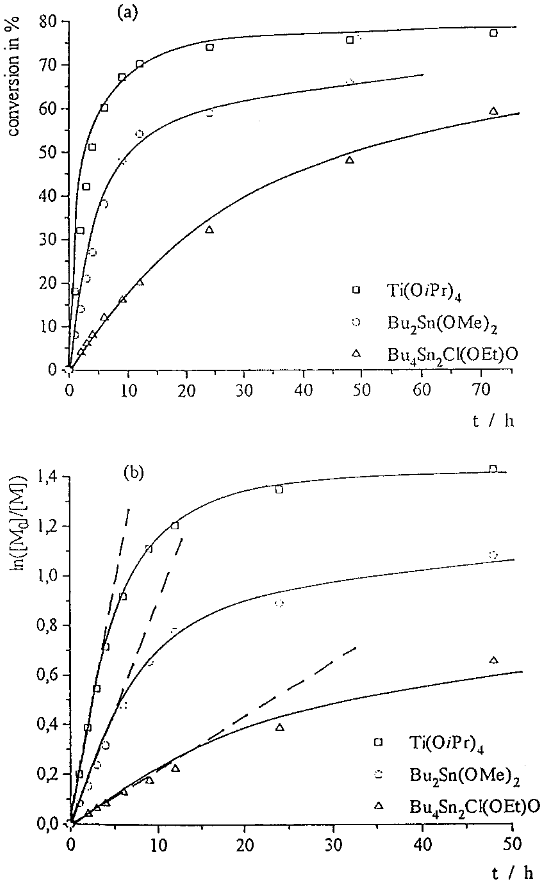


Figure 16. (a) Time conversion plots for the polymerization of TBL in the melt with different initiators. (b) First-order plots for the polymerization of TBL in the melt with different initiators. $[I]/[HB\ r.u.] = 0.01$.

takes place in the absence of a catalyst with a high rate at temperatures >200 °C, although at lower temperatures the rate is still measurable. In the presence of a catalyst this reaction is strongly favored and competes successfully with the chain growth reaction even at temperatures between 100 and 150 °C. From these results it is expected that at lower polymerization temperatures PHB′ samples with higher molecular weights are obtained.

(ii) Observation of the polymerization reaction revealed that after a certain time a precipitate is formed in the melt. It was suggested that the polymer having reached a certain molecular weight is not soluble in the melt of TBL and precipitates. Time–conversion plots of TBL polymerization in the melt at 120°C with various initiators (Figure 16a) show that with $Ti(OiPr)_4$ as initiator after 24 h no further increase of conversion is observed, while with distannoxane the reaction is much slower (even after 70 h an increase of conversion is observed). From the first-order plot (Figure 16b) it is seen that up to a conversion of 35–45% a linear

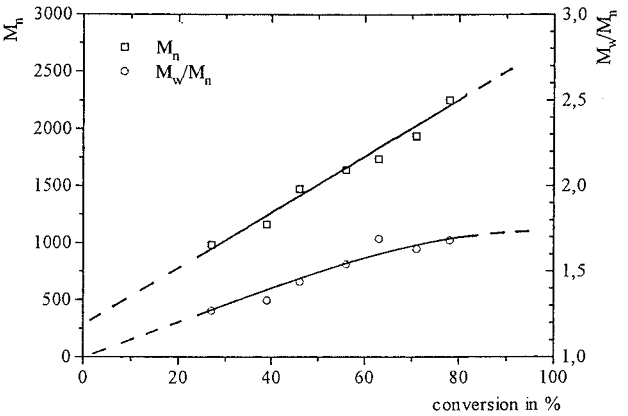


Figure 17. Number average molecular weight (M_n) and polydispersity index (M_w/M_n) of PHB′ obtained by polymerization of TBL with $Bu_2Sn(OMe)_2$ in the melt as a function of TBL conversion. $[Bu_2Sn(OMe)_2]/[HB\ r.u.] = 0.01$.

relationship of $\ln([M]_0/[M])$ vs time is observed; above this value the reaction slows down. At this conversion the reaction mixture becomes heterogeneous, which leads to a decrease in concentration of active species in the melt. Polymerization experiments with a polymerization time ≫70 h show that in the solid state no further increase in molecular weight is obtained. As a consequence, the molecular weight of PHB′ is limited by its insolubility in the TBL melt at a certain molecular weight.

(iii) Transesterification is another reaction influencing the course of polymerization which is vizualized by the increase in polydispersity index with conversion (time) (Figure 17). The polydispersity index reaches a maximum value of $M_w/M_n \approx 1.7$, which is lower than that of a most probable distribution ($M_w/M_n = 2$). This is explained by the fact that crystallization of PHB′ occurs before the transesterification equilibrium is reached. The plot of M_n vs conversion (Figure17) (at a given temperature) shows a linear relationship, indicating that the number of polymer chains remains constant, in other words indicating that no chain transfer reactions take place. ("Termination reactions", i.e., precipitation, are reflected by the increase in polydispersity index.)

Discussion of the Experimental Results on the Basis of the Thermodynamic Parameters. From the calorimetric measurements of PHB ($M_n \approx 10^5$), TBL, and PHB′ ($M_n = 4000 \pm 500$) the free enthalpy of the depolymerization of PHB to form TBL was calculated to be -70 ± 1 kJ·mol^{-1} and the free enthalpy of polymerization of TBL to form PHB′ was calculated to be $+25 \pm 1$ kJ·mol^{-1} (in the temperature range from 370 to 420 K, the temperature interval of interest for preparative work). The catalytic depolymerization of PHB to TBL is correctly predicted by the thermodynamic data; however, the successful polymerization of TBL to PHB′ is in apparent contradiction with the thermodynamic results. In fact, this means that at least in the temperature range where $\Delta G°_{pol}(T)$ has a minimum (but is still positive), in the real system ΔG_{pol} must be negative. This contradiction can be solved, if the influence of the reaction parameters on the free enthaply in a real system is taken into consideration.

In the following some of the factors which have an influence on the free polymerization enthalpy ($\Delta G°_{pol}$) and are relevant from an experimental point of view will be discussed.

(i) The influence of temperature on $\Delta G°_{pol}$ (Figure 13) was discussed earlier; a minimum in $\Delta G°_{pol}$ was found between 90 and 160 °C.

(ii) The free energy of polymerization depends on the ratio of the activity of the polymer (a_P) and the monomer (a_M) according to eq 12.

$$\Delta G_{pol} = \Delta G°_{pol} + RT \ln(a_P/a_M) \qquad (12)$$

The deviation from the standard free enthalpy of polymerization ($\Delta G°_{pol}$; $a_P = a_M = 1$) is high at low and high monomer conversions since then $a_P \neq a_M$. For the TBL polymerzation this means that in the beginning of the polymerization (when $a_P \ll a_M$) the term $RT \ln(a_P/a_M)$ is negative, thus enhancing polymerization; with increasing conversion the contribution of the term decreases, and at high conversion ($a_P > a_M$) the term is positive.

(iii) The thermodynamic data obtained from calorimetric measurements do not consider the interactions between polymer and monomer. In the real system these interactions occur since the monomer melt is also solvent for the polymer and solvation effects are to be considered. This effect again is most important in the beginning of the polymerization, when the monomer concentration is highest. With increasing polymer concentration the influence of the solvation effect decreases; polymer–monomer interactions are replaced by polymer–polymer interaction which finally lead to crystallization of the polymer melt. The interactions of polymer and monomer in the melt/solution can be estimated according to Flory[10] by the calculation of the activity of the polymer a_P and the monomer a_M using the Flory–Huggins parameter χ (eqs 13 and 14):

$$\ln a_P = (1/P_n) \ln \phi_P + (1/P_n - 1)(1 - \phi_P) + \chi(1 - \phi_P)^2 \qquad (13)$$

$$\ln a_M = \ln \phi_M + (1 - 1/P_n)\phi_P + \chi\phi_P{}^2 \qquad (14)$$

where P_n is the number average degree of polymerization and ϕ_P and ϕ_M are the volume fractions of the polymer and monomer, respectively. With eqs 13 and 14, eq 15 can be rewritten

$$\Delta G_{pol} = \Delta G°_{pol} - RT[\ln \phi_M + 1 - (1/P_n)(\ln \phi_P + 1) + \chi(\phi_P - \phi_M)]$$
$$\approx \Delta G°_{pol} - RT[\ln \phi_M + 1 + \chi(\phi_P - \phi_M)] \qquad (15)$$

Solving this equation for a temperature of 400 K and using for χ the value of a good solvent ($\chi = 0.3$–0.5) a decrease of $\Delta G°_{pol}$ of 2–3 kJ·mol^{-1} is obtained at low conversions (at high monomer concentrations); at high monomer conversions an increase of $\Delta G°_{pol}$ of 10 kJ·mol^{-1} is obtained. This result again proves that at low conversions the polymerization is preferred compared to the situation at high conversions.

(iv) The contribution of the degree of crystallinity to the free enthalpy of polymerization can hardly by estimated quantitatively; however, qualitatively higher crystallinity of the polymer should give a negative contribution to the free enthalpy, thus enhancing polymerization.

All these contributions together lead to a decrease of the free enthalpy of polymerization which for the reaction TBL → PHB′ ($\Delta G°_{pol} = +25$ kJ·mol^{-1}) is high enough to make the reaction possible but cannot compensate for the high value of $\Delta G°_{pol} = +70$ kJ·mol^{-1} necessary to produce high molecular weight PHB. This result implies that on polymerization of TBL the molecular weight of the resulting polymer influences strongly the monomer/polymer equilibrium. The reason for this peculiar behavior is not known; the concentration of end groups may play an essential role, which for PHB′ is 250 times higher than for PHB, as well as the crystallinity of the samples, which is higher for PHB′ than for PHB.

The difference between $\Delta G°_{pol}$(TBL→PHB) and $\Delta G°_{pol}$(TBL→PHB′) is rather high (50 kJ·mol^{-1}). The more favorable value for the polymerization of TBL corresponds to the polymer of lower molecular weight ($\Delta G°_{pol}$(TBL→PHB′) = +25 kJ·mol^{-1}, with increasing molecular weight $\Delta G°_{pol}$ becomes more positive reaching a value of $\Delta G°_{pol}$(TBL→PHB) = +70 kJ·mol^{-1}).

The energy balance of the polymerization seems to be more favorable for shorter chains, even at the expense of monomer conversion. This, however, does not mean that the chain growth reaction is hindered beginning with a certain chain length; the reason might be the establishment of a (dynamic) equilibrium upon transesterification reactions that is characterized by a certain average molecular weight and monomer conversion.

Finally, the estimation of errors and the cause for errors in the determination of the thermodynamic data should be addressed. The large difference in the free enthalpy of polymerization $\Delta G°_{pol}$(TBL→PHB) − $\Delta G°_{pol}$(TBL→PHB′) cannot arise from (i) the calorimetric measurements (limit of inaccuracy is ±2.5%) or (ii) the purity of TBL, PHB, and PHB′ (which is very high as demonstrated by their analytical data). The largest error may arise from the inaccuracy of the zero point entropy estimate. For TBL with 100% crystallinity the zero point entropy is zero according to the third law of thermodynamics. For PHB and PHB′ a residual entropy even at 0 K is expected because of their amorphous part. According to Temperly[11] an amorphous polymer has a zero point entropy of not more than $3k-4k$ per repeating unit (k = Boltzmann constant), or 25−33 J·mol^{-1}·K^{-1} (per mol repeating unit). For a partially crystalline polymer these values are reduced due to its degree of crystallinity. On the basis of these considerations the difference of the molar entropies of polymerization is ≤30 J·mol^{-1}·K^{-1} and the influence of the zero point entropy on the free entropy of polymerization at 400 K is 14 kJ·mol^{-1}.

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