Differential Scanning Calorimetry Study of Phase Transitions in Poly(lactide)−Chloroform−Methanol Systems

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ABSTRACT: The phase separation processes occurring in poly(L-lactide) (PLLA)−chloroform−methanol mixtures and poly(DL-lactide) (PDLLA)−chloroform−methanol mixtures have been studied using differential scanning calorimetry, cloud point measurements, and optical microscopy. It is demonstrated that liquid−liquid demixing occurs in ternary solutions of PDLLA at sufficiently high methanol concentrations. For PLLA-containing solutions, both liquid−liquid demixing processes and solid−liquid demixing processes occur. The most important parameters for the phase separation process are the applied cooling rate and the polymer concentration. Nonequilibrium phase separation processes play an important role in the phase separation of ternary PLLA solutions. Due to the high activation energy needed for crystallization, liquid−liquid demixing will usually precede solid−liquid demixing even if solid−liquid demixing is favored thermodynamically. Only at low cooling rates and high polymer concentration does solid−liquid demixing take place without the interference of liquid−liquid demixing.

Introduction

Immersion precipitation has become an important technique for the preparation of porous membranes.[1] The technique consists of casting a polymer solution on an inert support and immersion of the cast solution in a nonsolvent bath. The nonsolvent in the coagulation bath induces precipitation of the polymer solution. Usually the porous structure of the membranes obtained by immersion precipitation is due to liquid−liquid demixing by nucleation and growth of a polymer poor phase. Gelation processes are held responsible for the formation of a dense top layer of the membranes and the fixation of the morphology of the phase-separated solution. Vitrification of concentrated polymer solutions as well as associations between the components in solution and crystallization of the polymer from solution has been mentioned as possible gel-inducing transitions.[2]

Up to now only few studies have been devoted to gel-inducing transitions in relation to immersion precipitation. Gaides *et al.* evaluated the importance of the glass transition for the membrane formation of solutions of poly(sulfone) in dimethylacetamide coagulated in water.[3] They demonstrated that for this system the glass transition intersects with the liquid−liquid miscibility gap. Berghmans and Keller and co-workers demonstrated for thermally induced phase separation of binary polymer solutions that this combination of phase transitions allows the formation of stable porous gels.[4−8] Examples of polymer solutions that form gels according to this mechanism are atactic polystyrene in decalin and atactic poly(methyl methacrylate) in 1-butanol.[4−6] Phase separation processes in ternary solutions containing crystallizable polymers have been studied using differential scanning calorimetry (DSC) and light transmission by Burghardt *et al.* and Smolders *et al.* for poly(2,6-dimethylphenylene oxide) and cellulose acetate in various solvent/nonsolvent mixtures.[9−11] However due to the small energy effects involved in the demixing process or to a too low sensitivity of the DSC equipment, no transitions due to liquid−liquid demixing could be detected. Transitions due to solid−liquid demixing could only be detected after reheating of concentrated polymer solutions aged for long times. Membranes prepared from these polymers have a cellular morphology and display a low level of crystallinity. This is in line with the low rates of crystallization of these polymers and indicates that liquid−liquid demixing processes are most important for the structure formation of the membranes.

Poly(L-lactide) (PLLA) is a rapidly crystallizing polymer suitable for the preparation of porous membranes for biomedical applications.[12−14] Previously it was shown that depending on the solvent/nonsolvent combination and the PLLA concentration of the casting solution membranes could be obtained with morphologies dominated by structures originating from solid−liquid demixing (leafy structures) and originating from liquid−liquid demixing (cellular structures). To understand the structure formation of these membranes, a detailed study of the phase separation processes occurring in these solutions is required.

Recently *in situ* film side and bath side video analysis techniques have been developed to study nonsolvent-induced phase separation.[15,16] Although these techniques can yield useful information on the solvent/nonsolvent exchange and phase separation processes, it is difficult to couple phase separation processes to the composition of the solution.

Differential scanning calorimetry is a technique suitable for studying phase separation processes as a function of temperature.[17,18] Advantages of DSC compared to *in situ* analysis are the controlled cooling rate and the fixed overall composition of the solutions. Further the possibility to reheat the samples again is advantageous. The transition temperatures obtained from heating scans can be expected to be located much closer to the equilibrium transitions than transition temperatures obtained from cooling scans. However the translation of these experiments to the immersion precipitation process should be performed with caution.

In this contribution phase, diagrams will be presented for solutions of poly(lactide)s in chloroform−methanol mixtures. Chloroform−methanol is a solvent/nonsol-

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vent combination frequently used for the preparation of hollow fibers.[12] DSC is used to study the kinetics of phase transitions occurring in these systems. In addition to the semicrystalline PLLA, also the amorphous poly(DL-lactide) (PDLLA) is studied.

Experimental Section

Materials. PLLA and PDLLA were synthesized from L-lactide and a racemic mixture of L- and D-lactide (Purac Biochem B.V., Gorinchem, The Netherlands), respectively, according to standard procedures.[19] The PLLA was optically inactive and had an intrinsic viscosity of 2.0 dL/g (chloroform, 25 °C). The PDLLA was optically inactive and had an intrinsic viscosity of 2.0 dL/g (chloroform, 25 °C). Using the Mark−Houwink relations given by van de Witte *et al.* for poly(lactide)s in chloroform (PDLLA, $[\eta] = 1.33 \times 10^{-4}\ MV^{0.79}$; PLLA, $[\eta] = 2.48 \times 10^{-4}\ MV^{0.77}$), the molecular weights of PLLA and PDLLA are 12 000 and 200 000 g/mol, respectively.[20] Polydispersities (M_w/M_n) as determined in chloroform with a GPC instrument equipped with a Viskotek differential viscometer were 2. DSC heating traces (heating rate 10 °C) of PLLA samples slowly cooled from the melt (10 °C/min) showed a glass transition at 60 °C and a melting endotherm ranging from 160 to 185 °C. The peak melting temperature was 178 °C, and the heat of fusion was 40 J/g. Using the value of Loomis *et al.* for the heat of fusion of 100% crystalline material (140 J/g), the crystallinity is 30%.[21] PDLLA is amorphous and has a glass transition at 55 °C. Methanol was of analytical quality (Merck-Schuchardt, Darmstadt, Germany). Chloroform was of spectroscopical quality (Lichrosolv, Merck-Schuchardt).

Methods: Differential Scanning Calorimetry. Solutions of the polymer in a solvent/nonsolvent mixture were prepared in sealed glass tubes and homogenized at 85 °C. The tubes were subsequently brought in liquid nitrogen and opened under a blanket of dry nitrogen. Pieces of around 40 mg were taken from the sample and hermetically sealed in stainless steel, volatile sample pans (Perkin Elmer). DSC scans were performed with a Perkin Elmer DSC-7 instrument equipped with TAS-7 software and a Perkin Elmer PE-7500 professional computer. Temperature calibration was performed with indium, gallium, and cyclohexane. Calibration of the heat of fusion was performed using the heat of fusion of indium. Runs were carried out with automatic baseline correction. The baseline was obtained by performing a cooling run with no sample or via reference pans using a scan rate of 10 °C/min. The curvature of the baseline was minimized for the chosen temperature range. Adjustment of the scan rate for the baseline to the different scan rates of the samples did not result in a major improvement of the results. To avoid degradation of the samples, the samples were homogenized at 85 °C as short as possible but long enough to destroy any structure that might have formed during the preparation of the sample or the preceding runs. Ten minutes appeared to be sufficient and was used in all experiments. An increase of the time of homogenization did not change the results. Repeating the first run after a series of runs with the same sample also gave the same results. Cooling rates were varied between 2 and 10 °C/min. Solvents were checked routinely for thermal transitions in the temperature range chosen.

Cloud Points. Homogenized polymer solutions in sealed glass tubes were cooled slowly at a cooling rate of 0.1 °C/min. Cloud points were obtained by measuring the laser light transmission (He−Ne laser) through the tubes as a function of temperature. These demixing temperatures were plotted as a function of polymer concentration for several solvent/nonsolvent mixtures. Cloud point compositions at 25 °C were obtained by extrapolation.

Melting Transitions. Solubility curves were determined in a similar way. Solutions with compositions located outside the liquid−liquid miscibility gap were slowly cooled to room temperature and reheated after aging for 1 day at a heating rate of 0.1 °C/min. The melting point was determined visually.

Optical Microscopy. Solutions prepared according to the procedures described for the cloud point determination were transferred to thin flat capillaries (microslides; Camlab Ltd., Cambridge, U.K.) and analyzed using a Mettler hot stage (FP82) and a Leitz Ortolux II pol-BK optical microscope equipped with a camera. The applied cooling rate was 1 °C/min.

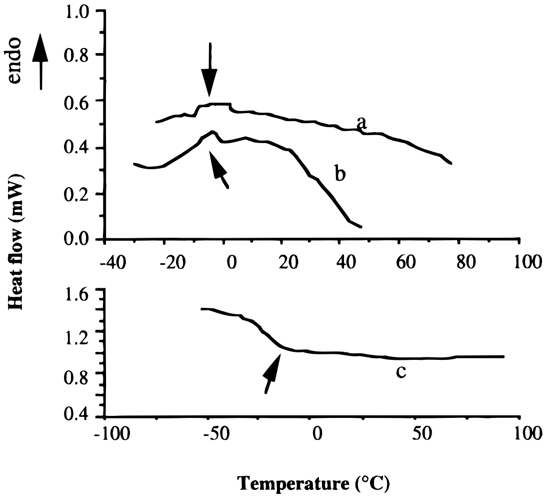


Figure 1. DSC scans of the solvents. Transitions are marked with an arrow. Cooling rate was 10 °C/min: (a) chloroform, (b) methanol, (c) sealing ring. Experiments a and b were performed with stainless steel sample pans; c was performed with aluminum sample pans.

Results and Discussion

DSC Scans of the Solvents. The DSC cooling traces of the solvents or solvent mixtures are depicted in Figure 1. In the DSC traces of chloroform and methanol, a small unexpected endothermic transition around 0 °C is observed.

Maderek *et al.* also reported unexpected transitions in DSC traces of solvents.[22] Pure solvents like isooctane, cyclopentane, *n*-hexane, and benzene gave unexpected exothermic transitions during heating as well as during cooling at temperatures usually 30 °C below the boiling point of the liquid. It was suggested that these steps were caused by microstreams induced by temperature differences in the samples. The heat effects encountered in our DSC traces were much smaller and of a different nature. Freezing of residual amounts of water can be excluded as a possible cause. The transition was endothermic instead of exothermic during cooling, and the amount of water detected in the solvents by gas chromatography was too low to explain the size of the peak. The only plausible explanation is that the Viton rubber ring present in the sample pans is responsible for the transition. Runs with aluminum sample pans containing the rubber sealing ring of the volatile sample pan did show a shift in the baseline in the same temperature range. Experiments using empty volatile sample pans containing the rubber ring did not show peaks. An explanation can be that the solvents in the sample pan shift or broaden the transition of the rubber ring. The temperature ranges of the transitions of the rubber ring in the sample pan and the rubber ring in the reference pan are slightly different, and a residual effect is obtained. In further discussions this small transition will be considered an artifact.

Solutions Containing PDLLA. In Figure 2 the compositions of the PDLLA solutions used for DSC have been plotted in the phase diagrams. The line drawn through the points represents the cloud point curve at 25 °C. No transitions were found in the DSC traces of

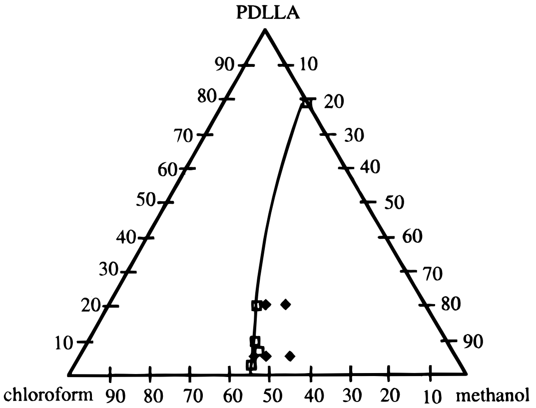


Figure 2. Isothermal phase diagram of the system PDLLA−chloroform−methanol at 25 °C (in wt %). Compositions of PDLLA solutions used in the DSC experiments are indicated (◆). The turbidimetrically determined cloud point curve at 25 °C is also given (□).

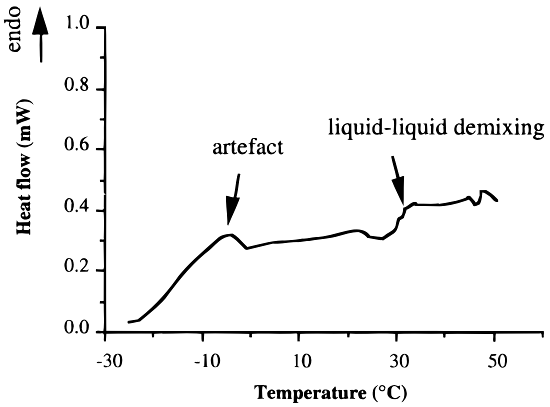


Figure 3. DSC cooling trace obtained with a 5%, w/w, PDLLA solution in a 53/47, w/w, chloroform−methanol mixture. Cooling rate was 10 °C/min. The onset of liquid−liquid demixing is indicated with an arrow. The artifact indicated in Figure 1 is also indicated in this figure.

solutions of PDLLA in chloroform. DSC traces for the system PDLLA−chloroform−methanol are given in Figures 3, 5, and 6. In Figure 3, the DSC cooling trace of a PDLLA solution with a composition close to the cloud point curve at 25 °C is given. Apart from the artifact at 0°, a very small exothermic transition is observed at approximately 32 °C. The heat effects are very small and start with a sharp exothermic step.

These transitions are most likely due to liquid−liquid demixing.[4,5,8] During reheating DSC traces with an endothermic transition were obtained (not shown). Optical microscopy confirmed that the solution started to phase separate at *ca.* 34 °C (Figure 4). The nucleation and growth of droplets can easily be identified. The absence of birefringence under crossed polarizers confirmed that no crystallites are present in the demixed solution in accordance with expectations.

The influence of the polymer concentration on the DSC cooling traces is given in Figure 5. The heat effect per milligram of sample increases strongly with the initial polymer concentration.

The temperatures of the onsets of the transitions were generally close to the expected cloud point temperatures (estimated cloud point temperatures: 5%, *ca.* 35 °C, 20%, *ca.* 35 °C). Because of the differences in scan rates and the poorer resolution of DSC, some deviations can occur. The demixing temperatures measured by DSC of the solutions of PDLLA with a chloroform−methanol ratio of 44/56 were slightly higher (*ca.* 45 °C) than the demixing temperatures of the solutions with PDLLA in solutions with a chloroform−methanol ratio of 50/50 (*ca.* 40 °C). From both the cloud point measurements and the DSC data, it can be concluded that the demixing temperatures of the polymer solutions are not much influenced by the polymer concentration and the solvent/nonsolvent ratio.

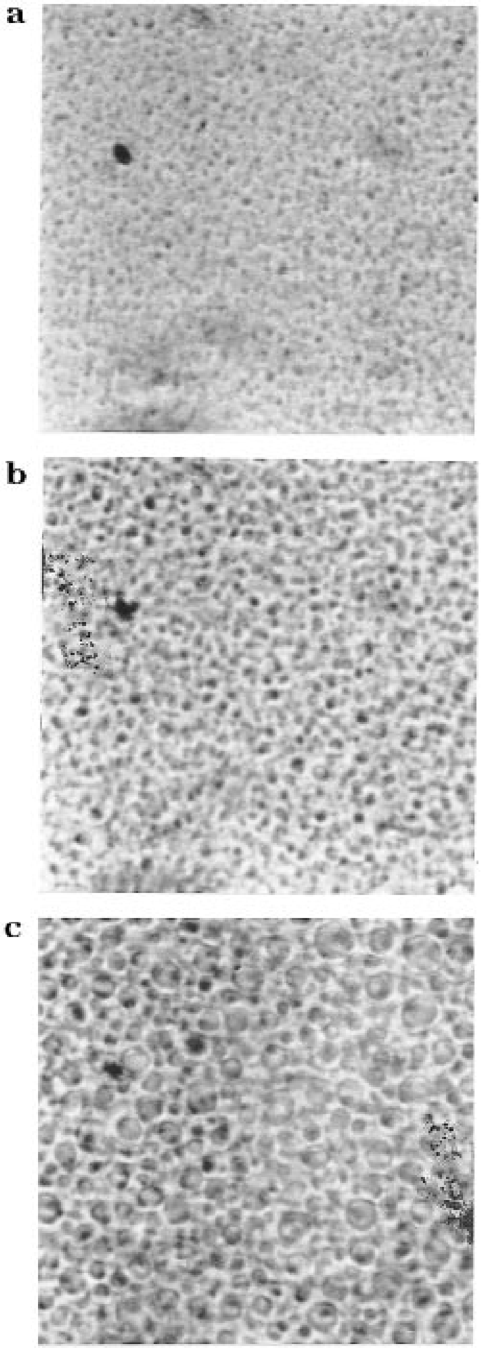


Figure 4. Micrographs of the liquid−liquid phase separation process on a 5%, w/w, PDLLA solution in a 53/47, w/w, mixture of chloroform and methanol (compare Figure 3). Magnification is 250× (reproduced at 70% of original size). Temperatures: (a) 33.6 (b), 32.2, and (c) 30.9 °C.

The onset temperature of the exotherm due to liquid−liquid demixing is independent of the cooling rate, and the magnitude of the initial step is proportional to the cooling rate (Figure 6). This feature may be used to distinguish liquid−liquid demixing from solid−liquid demixing. Usually crystallization processes in polymer solutions are accompanied with a symmetric exothermic

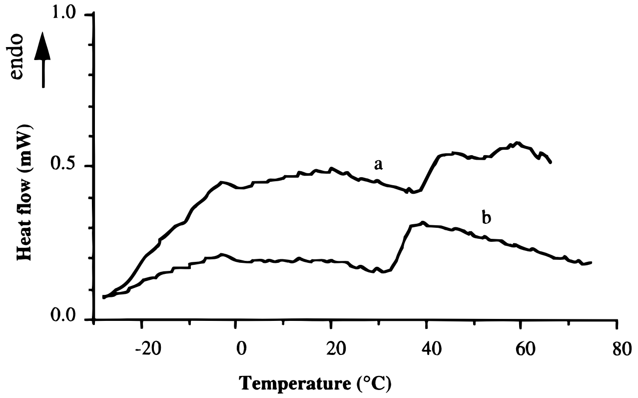


Figure 5. Influence of the initial polymer concentration on the DSC trace obtained with a PDLLA solution in a 50/50, w/w, chloroform−methanol mixture. Cooling rate was 10 °C/min. All transitions are due to liquid−liquid demixing: (a) polymer concentration, 5%, w/w; sample mass, 76 mg; (b) polymer concentration, 20%, w/w; sample mass, 29 mg.

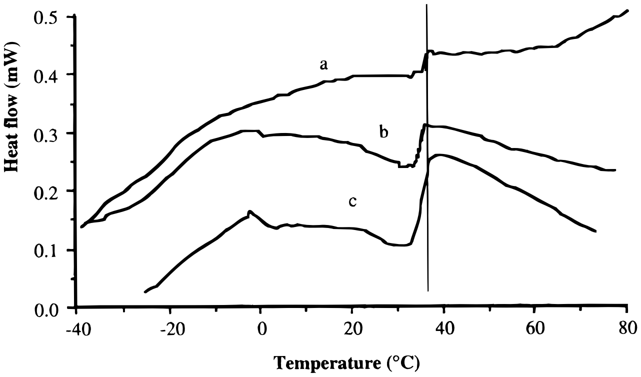


Figure 6. Influence of the cooling rate on the DSC trace obtained with a 20%, w/w, PDLLA solution in a 50/50, w/w, chloroform−methanol mixture. Cooling rates: (a) 2, (b) 5, and (c) 10 °C/min. All transitions are due to liquid−liquid demixing. The magnitude of the initial step part of the transition is proportional to the cooling rate. The line connects the onsets of the transitions. The temperature at the onset of the transition is independent of the cooling rate.

peak in the DSC rate.[17,18,23] Due to the much higher activation energies necessary for crystallization, the onset of this transition strongly depends on the cooling rate in contrast to liquid−liquid demixing.

No transitions are observed in the DSC traces that can be attributed to vitrification. Berghmans *et al.* showed that in binary solutions of atactic polystyrene or poly(methyl methacrylate) liquid−liquid demixing can be followed by vitrification of the polymer rich phase. Both transitions showed up in their DSC thermograms.[4,6] The glass transition temperatures of PLLA and PDLLA are 60 and 55 °C, respectively. Triolo *et al.* showed that *ca.* 30% solvent is sufficient to decrease the glass transition of the polymers to −40 °C.[24] Considering the high swelling of poly(lactide)s in methanol, it is not expected that in the solutions used in our experiments the polymer concentrations during the liquid−liquid demixing process will raise high enough to reach the glass transition.

Solutions Containing PLLA. In contrast to the cloud point curve of PDLLA, the cloud point curve for PLLA bends toward the polymer/solvent axis (Figure 7). At room temperature PLLA crystallizes from chloroform at polymer concentrations >25−35%, w/w. This indicates that solid−liquid demixing can be responsible for at least the cloud points at higher polymer concentrations. Solutions that phase separate by liquid−liquid demixing can be distinguished from solutions that phase separate by solid−liquid demixing by the rate of increase of the turbidity of the phase-separating solution. Liquid−liquid demixing results in an instantaneous turbidity, while solid−liquid demixing results in a slow whitening of the solution. From this analysis it appears that the cloud points at high polymer concentrations correspond to solid−liquid demixing, and the cloud points at low polymer concentrations correspond to liquid−liquid demixing. The solubility curves are located at lower methanol concentrations than the cloud point curves indicating that crystallization is favored thermodynamically over liquid−liquid demixing. If no undercooling effects occur, the crystallization curve should coincide with the melting curve.

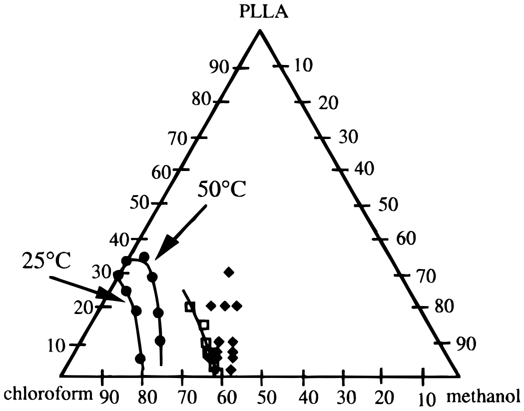


Figure 7. Isothermal phase diagram of the system PLLA−chloroform−methanol at 25 °C (in wt %). Compositions of PLLA solutions used for the DSC experiments are indicated (◆). The turbidimetrically determined cloud point curve at 25 °C is also given (□). Melting transitions for two temperatures (solubility curves) are indicated (●).

Also for 7%, w/w, PLLA solutions in chloroform, no transitions were observed in the DSC traces. The compositions of the ternary solutions used for the DSC experiments are presented in the ternary phase diagram of the system PLLA−chloroform−methanol.

In Figure 8 optical micrographs of the phase separation process of a 10%, w/w, PLLA solution in a 61/39, w/w, chloroform−methanol mixture are presented. Under these conditions phase separation indeed takes place by crystallization of the polymer. No indications for liquid−liquid demixing were observed. During reheating of the phase-separated solution, the crystals formed melted at *ca.* 55 °C. For solutions with lower PLLA concentrations, phase separation initially took place by liquid−liquid demixing. In a later stage of the demixing process, birefringent entities confirmed the presence of crystallites.

In Figure 9 DSC cooling traces for polymer solutions with different polymer concentrations and a fixed chloroform−methanol ratio (61/39, w/w) are presented. At temperatures of 25−35 °C, steplike transitions are found for all polymer concentrations. The DSC trace obtained with the solution with 10% polymer contained only transitions due to liquid−liquid demixing. This seems to be in contradiction with our microscopic observations. However the much lower cooling rate used with the hot stages apparatus is most likely the reason for this disagreement (cooling rates: hot stage, 1 °C/min; DSC, 10 °C/min). The influence of the cooling rate will be discussed in more detail later.

At a polymer concentration of 20%, w/w, the DSC cooling trace differs from the cooling traces of the

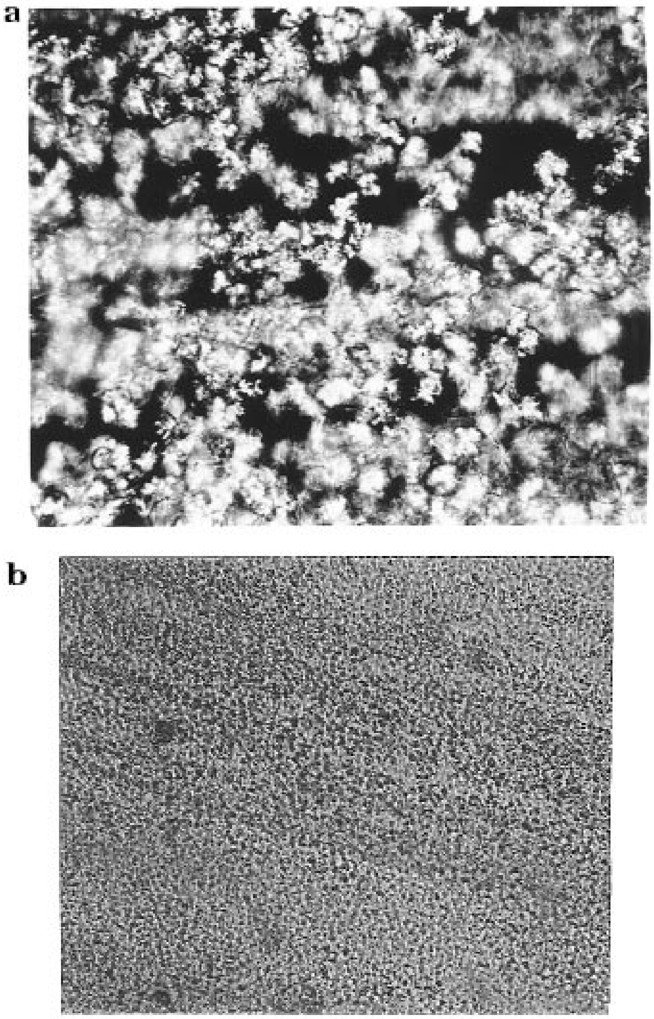


Figure 8. Optical micrographs of the solid−liquid demixing process of a 10%, w/w, PLLA solution in a 61/39, w/w, mixture of chloroform and methanol. Temperatures: (a) 30 °C, polarization micrograph magnification 100× (reproduced at 60% of original size); (b) 30 °C, unpolarized light, magnification 250× (reproduced at 60% of original size).

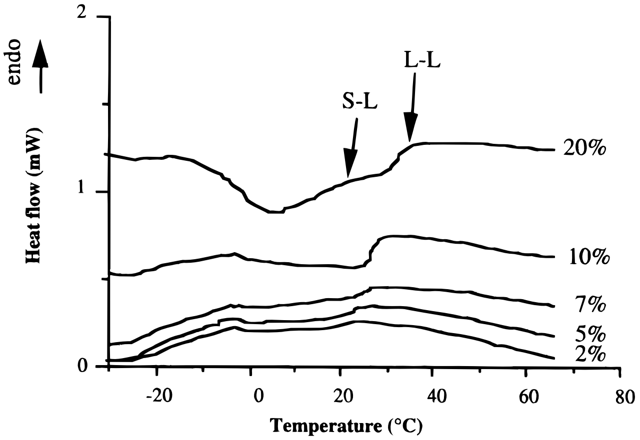


Figure 9. Influence of the polymer concentration on the DSC cooling traces obtained with solutions of PLLA in a chloroform−methanol (61/39, w/w) mixture. Cooling rate: 10 °C/min. For the polymer concentration of 20%, w/w, the onsets of liquid−liquid demixing and solid−liquid demixing are indicated with arrows. The transitions at lower polymer concentrations are due to liquid−liquid demixing.

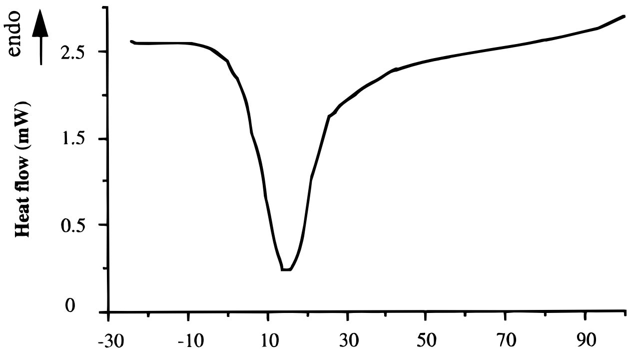


Figure 10. Cooling trace of a 30%, w/w, PLLA solution in a 61/39, w/w, chloroform−methanol mixture. Only a transition due to solid−liquid demixing is observed.

Table 1. Comparison of Demixing Temperatures Obtained by Cloud Point Measurements and DSC

PLLA (%, w/w)	onset of DSC transition (°C)	cloud point (°C)
2	22	26
5	25	22
7	26	30
10	29	33
20	35	45

solutions with lower polymer concentrations. Directly after the initial exothermic step, a second exothermic transition is found. It is likely that this extra transition is due to solid−liquid demixing processes. A DSC trace of a solution with a polymer concentration of 30% is presented in Figure 10. For this solution no exothermic step is found but only an exothermic peak typical for crystallization. It should be noted that in the case of high polymer concentrations the large exotherm due to solid−liquid demixing can mask the transition due to liquid−liquid demixing.

Generally only small differences exist in the demixing temperatures obtained by DSC and light transmission. Some examples are presented in Table 1. The agreement between the results obtained with both methods becomes worse at polymer concentrations between 10% and 20%, w/w. The reason for these deviations is the difference in cooling rate used for the experiments. Low cooling rates will favor the occurrence of solid−liquid demixing prior to liquid−liquid demixing.

The obtained results point to a gradually changing demixing mechanism with increasing polymer concentrations. At low polymer concentrations, only liquid−liquid demixing takes place during cooling. At a polymer concentration of 20%, liquid−liquid demixing is immediately followed by crystallization, and at still higher concentrations, mainly crystallization takes place during cooling.

In Figure 11 the DSC heating traces of solutions of PLLA in 61/39, w/w, chloroform−methanol aged for 10 min at −40 °C are presented. A melting endotherm is found in the DSC traces of all solutions. It is clear that during aging at low temperatures crystallization takes place in all solutions. The melting point of the crystallites in the demixed solutions increases with increasing polymer concentrations. For the solutions with polymer concentrations higher than 7%, w/w, exotherms due to crystallization during heating are clearly visible. Apparently the rate of crystallization at −40 °C is rather slow, and incomplete crystallization takes place. During reheating the rate of crystallization increases again, and crystallization takes place before melting.

In the DSC traces of solutions with concentrations higher than 7%, multiple or shouldered melting endotherms can be detected. The origin of these multiple melting endotherms is not clear yet but may be related

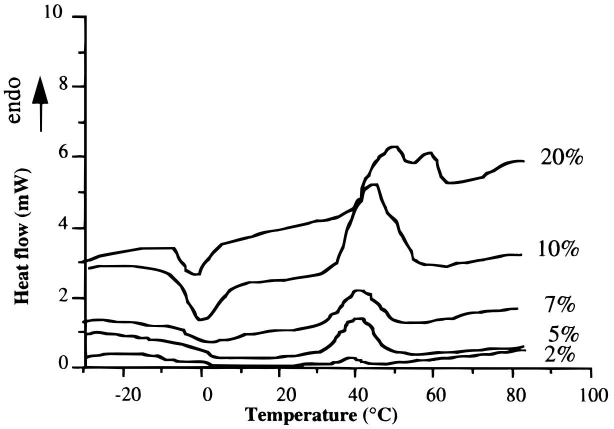


Figure 11. Influence of the polymer concentration on the DSC heating traces obtained with solutions of PLLA in a chloroform−methanol (61/39, w/w) mixture. DSC thermograms were obtained during reheating (10 °C/min) of solutions previously cooled from 85 to −40 °C (10 °C/min). Aging time at −40 °C was 10 min.

Table 2. Melting Points (*T*) and Heats of Fusion (Δ*H*) of PLLA Solutions in Chloroform−Methanol (C/M) Mixtures[a]

polymer concentration (%, w/w)	C/M ratio 61/39, w/w *T* (°C)[b]	Δ*H*[c]	57/43, w/w *T* (°C)[b]	Δ*H*[c]
2	46	0.1	60	0.6
5	53	1.2	63	1.6
7	53	1.7	65	3.3
10	58	3	66	3.2
20	65	4.7	81	7.5
30	103	10.1		

[a] Values correspond to solutions cooled to −40 °C (10 °C/min) and reheated after 10 min (10 °C/min). [b] *T*: end point of melting endotherm. [c] Δ*H*: heat of fusion in J/g of solution.

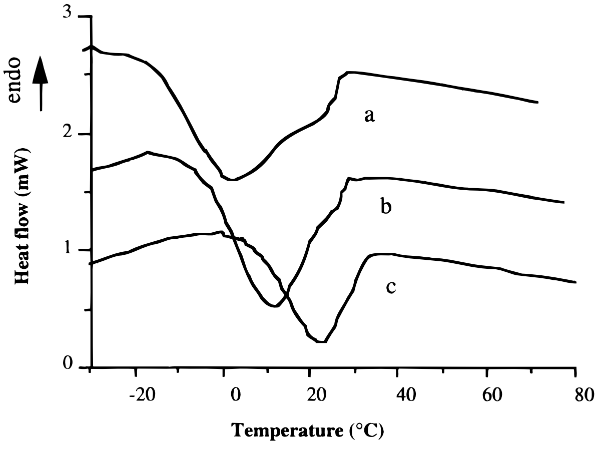


Figure 12. Influence of cooling rate on the heat effects obtained with solutions of 20%, w/w, PLLA in 65/35, w/w, chloroform−methanol mixtures: (a) cooling rate, 10 °C/min; (b) cooling rate, 5 °C/min; (c) cooling rate, 2 °C/min.

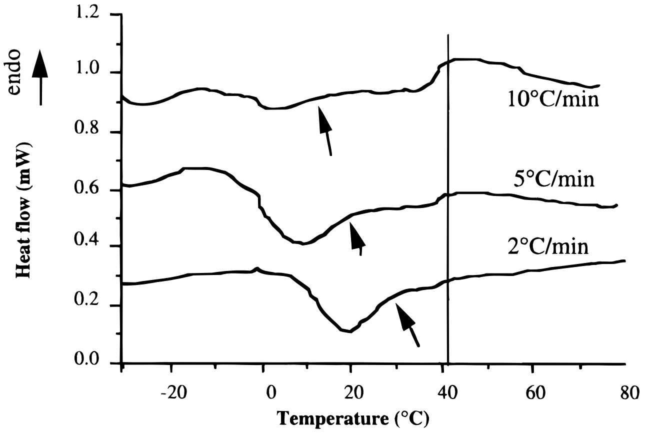


Figure 13. Influence of cooling rate on heat effects obtained with 10%, w/w, PLLA in 57/43, w/w, mixtures. The importance of solid−liquid demixing processes increases with decreasing cooling rates. Arrows indicate the onset of solid−liquid demixing, and the line indicates the onset of liquid−liquid demixing.

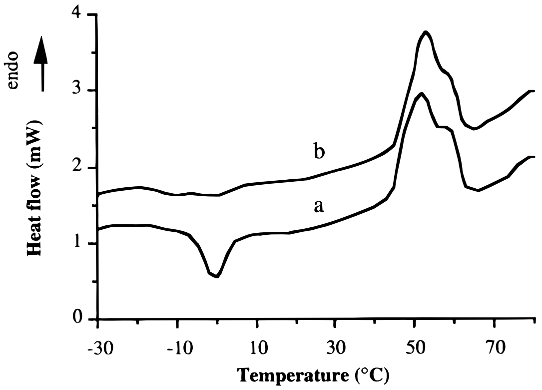
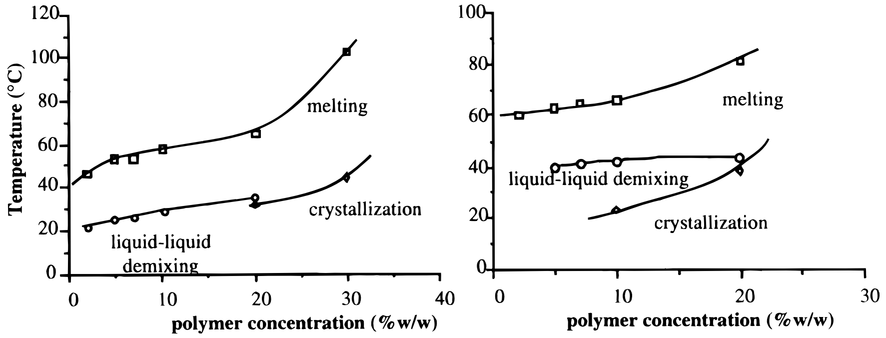


Figure 14. Influence of cooling rate applied for the cooling scan on the heat effects obtained with solutions of 20%, w/w, PLLA in 57/43, w/w, chloroform−methanol mixtures during subsequent reheating: (a) reheating, 10 °C/min after cooling 10 °C/min; (b) reheating, 10 °C/min after cooling 5 °C/min.

to size differences in the crystals or to compositional differences in the demixed solution. The melting point of the crystals of the 10% solution of PLLA in a 61/39, w/w, mixture of chloroform−methanol obtained by DSC (58 °C) is in good agreement with the results obtained by polarization microscopy (55 °C). When the chloroform−methanol ratio is changed to 57/43, w/w, exotherms due to crystallization are already obtained during cooling of solutions containing 7%, w/w, polymer (cooling rate 10 °C/min). The liquid−liquid demixing transition is shifted to a slightly higher temperature than for corresponding solutions with a chloroform−methanol ratio of 61/39, w/w (DSC traces not shown). Also the heat effects involved in the melting of the crystallites during reheating of the solutions are larger (Table 2). In most cases the heat of fusion of the crystallites in solution per gram of polymer varies between 20 and 40 J. These values are of comparable magnitude to the heat of fusion of melt-cooled films and correspond to crystallinities of 15−30%.

Figure 12 shows the influence of the cooling rate on the DSC trace of a 20%, w/w, solution of PLLA in a 65/35, w/w, mixture of chloroform−methanol. The highest cooling rates give an exothermic transition starting with an exothermic step and immediately evolving in a peak. The maximum of the peak shifts to a higher temperature with decreasing cooling rates. At the lowest cooling rate (2 °C/min), only a peak due to crystallization is found. The onset of the peak due to crystallization has shifted to a higher temperature than the onset of the peak due to liquid−liquid demixing. Even more striking is the effect of the cooling rate on the DSC traces of the 10%, w/w, solution in a chloroform−methanol 57/43, w/w, solution (Figure 13). At all cooling rates both transitions are observed. For increasing cooling rates the difference in temperature between the onset of liquid−liquid demixing and solid−liquid demixing becomes larger. The magnitude of the exotherm becomes



(A) (B)

Figure 15. Binary representation of end points and onsets of phase transitions for the systems with PLLA as a function of polymer concentration and solvent/nonsolvent ratio. Cooling rate and heating rate are 10 °C/min: (A) chloroform−methanol, 61/39, w/w; (B) chloroform−methanol, 57/43, w/w.

smaller with increasing cooling rates. These trends were observed in all solutions for which two transitions could be observed in the DSC cooling trace. These observations confirm the criteria used for the assignment of transitions to liquid−liquid demixing and solid−liquid demixing. The effect of the applied cooling rate is also clear in subsequent reheating runs (Figure 14). In contrast to a cooling rate of 10 °C/min, no recrystallization is found in the heating run after cooling for 5 °C/min. In Figure 15 the transition temperatures obtained during cooling (10 °C/min) and reheating (10 °C/min) are collected.

For the phase separation mechanism and the structure formation in solution, the onset of the transition during cooling is most important, while for equilibrium considerations, end points of transitions obtained during reheating have more significance. In Figure 15 the onsets of transitions in cooling traces have been given as well as the end points of heating traces.

As pointed out earlier the liquid−liquid demixing transition is not very sensitive to the polymer concentration of the solution. The maximum in the cloud point curve is difficult to recognize but seems to be located at concentrations higher than 10%, w/w. It should however be kept in mind that the representation in Figure 15 is a quasibinary representation of a ternary solution (strictly spoken it is a multicomponent system because of the polydispersity of the polymer). The compositions of equilibrium phases do not have the same solvent/nonsolvent ratio as the homogeneous solution and are located outside of this plane of representation. The multicomponent nature of the solutions is most likely the reason for the absence of a clear maximum.[25]

From Figure 15 it becomes clear that in all cases the end point of the melting endotherm is located at higher temperatures than the onset of liquid−liquid demixing during cooling. For liquid−liquid demixing the temperature of homogenization is approximately the same as the temperature of demixing. This proves that solid−liquid demixing is thermodynamically favored over liquid−liquid demixing. Because of the lower activation energy for nucleation, liquid−liquid demixing can precede solid−liquid demixing even in cases where solid−liquid demixing is favored thermodynamically. Lee *et al.* and Chiu *et al.* also observed this phenomenon.[26,27] Lee *et al.* studied the competition between liquid−liquid demixing and solid−liquid demixing in solutions of isotactic poly(propylene) in dialkyl phthalates. By increasing the length of the alkyl groups from 4 to 10, the solvent quality could be changed from poor to good. The liquid−liquid miscibility gap shifted from above the melting temperature to below the crystallization temperature. Similar effects were observed by Chiu for the influence of molecular weight on the phase diagram of poly(ethylene) in dodecanol.

The DSC results are in line with the phase diagram for the system PLLA−chloroform−methanol (see Figure 7). The cloud point curve is located at higher nonsolvent concentrations than the solubility curve indicating that crystallization is thermodynamically favored over liquid−liquid demixing for the entire composition range.

Despite the differences associated with nonsolvent-induced demixing and temperature-induced demixing, these results well explain the morphological features of the membranes obtained with these systems.

Conclusions

The phase separation of ternary solutions of the amorphous PDLLA in chloroform−methanol mixtures proceeds slowly via liquid−liquid demixing. For ternary solutions of PLLA, both liquid−liquid and solid−liquid demixing processes play a role in the phase separation. At low polymer concentrations, liquid−liquid demixing processes precede solid−liquid demixing processes, while at high polymer concentrations, solid−liquid demixing processes become more important. The lower the cooling rate the more pronounced the solid−liquid demixing processes. Thermodynamically solid−liquid demixing is preferred over liquid−liquid demixing over the entire composition range used in this study. The results of the experiments show that even in cases in which liquid−liquid demixing is not favored thermodynamically this transition can still be of considerable importance during the phase separation of the solutions.

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