

EXPERIMENTAL STUDY OF HIGH PRESSURE FLUID PHASE BEHAVIOUR OF A TERNARY SYSTEM INVOLVING *L*-LACTIDE, CARBON DIOXIDE AND IONIC LIQUID

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1. INTRODUCTION

Ionic liquids (ILs) have attracted a significant and growing interest since 1980s. They have been studied extensively as green solvents thanks to their advantageous properties such as negligible vapour pressure; they are in their liquid state in a wide range of temperatures and pressures adequate for synthetic reactions, high thermal stability, high ionic conductivity, large electrochemical window and a high solvent power. The increasing use of the ILs is one of the goals of green chemistry because they create cleaner, sustainable and environmentally friendly synthetic and engineering processes.¹

Furthermore, biocatalytic approaches in polymer science are expected to further increase the diversity of polymeric materials. The application of enzymes in polymer synthesis and transformation is attractive due to their catalytic activity under mild conditions with high enantio- and regioselectivity.

Enzyme catalyzed polymerization reactions are generally performed in bulk or in non-aqueous solvents. The problem associated with the use of organic solvents is the possibility of deactivation of enzymes or the decrease in the reaction rate, especially when polar hydrophilic solvents are used. Surprisingly, the enzymes are very active in ILs media in a wide range of operational temperatures and this feature extends enzyme-catalyzed reactions to a solvent polarity range that was previously inaccessible.²

Since the discovery of the enzymatic activity in non-aqueous media,³ many biocatalytic processes have been investigated.⁴ The use of ILs media in biocatalytic reactions has gained increasing attention over the last decade and many ILs have been used as substitutes for the traditional organic solvents.

Poly(*L*-lactide) (PLLA) is one of the biodegradable and biocompatible aliphatic polyesters, which is used in surgical suture, drug delivery systems and piezoelectric materials.⁵

A recent work was carried out using ionic liquids for the effective enzymatic synthesis of the biocompatible poly-*L*-Lactic polymers through a ring opening polymerisation route.⁶ Adequate polymerisation yields and molecular weights were obtained using the 1-hexyl-3-

methylimidazolium hexafluorophosphate ([HMIM][PF₆]) as solvent in a mass ratio of 1,43 compared to *L*-lactide (LLA) and temperatures ranging between 65 and 90°C. In these conditions LLA was soluble in [HMIM][PF₆]. It was also observed that LLA polymerization may be carried out without enzyme addition. However, the whole experiments were halted by the increased solution viscosity bringing the reaction to an end.

Alternatively, high CO₂ solubility in some ILs was demonstrated, in particular with [HMIM][PF₆].⁷ The viscosity of the ILs media should be reduced by adding supercritical (SC) CO₂ and mass transfer of substrates should also be favoured. In addition, LLA solubility data in CO₂ are available in the literature.⁸ The isotherm phase diagram for LLA/CO₂ binary mixtures has been established in a temperature range from 60 to 75°C for a LLA concentration in a range from 3 to 9 mol LLA/100 mol CO₂ approximately.

The combination of the ionic liquid with SC CO₂ as solvent media is prompted as the solution to reduce the media viscosity, thus enhancing polymer propagation.

The present work is dealing with fluid phase equilibria measurements of the ternary system CO₂+ [HMIM][PF₆]+LLA. The no enzymatic polymerisation of LLA is considered and the bubble points have been determined under the same optimum experimental conditions of temperature and mass ratio ([HMIM][PF₆]/LLA) reported.⁶

2. EXPERIMENTAL

2.1. REAGENTS

L-Lactide (3S, (cis)-3,6-dimethyl-1,4-dioxane-2,5-dione (Aldrich, 98% purity) was purified by re-crystallization in absolute methanol (Aldrich, 99% purity). 1-Hexyl-3-methylimidazolium hexafluorophosphate ([HMIM][PF₆]) was purchased from Solvionic (99.5% purity). and used as supplied. CO₂ cylinder containing a dip tube was provided by Air liquide (99.7% purity).

2.2. HIGH-PRESSURE EXPERIMENTAL SET-UP

The phase equilibrium data of the CO₂+ [HMIM][PF₆]+LLA ternary system were determined through the so-called synthetic method.⁹ The phase transitions resulting from pressure variations are determined through direct visualisations without sampling. The high pressure experimental set-up used in this study is illustrated in Figure 1. It is mainly composed of a high pressure variable-volume view cell (Top industries S. A., France). Its volume can be adjusted from 4 to 12 cm³ by moving an internal piston. The cell is equipped with a magnetic stirrer, a double jacket connected to a thermostated bath and a sapphire window. Visualisations are insured by a video camera connected to a monitor.

Even if the visualisation method is chosen in this study because of its simplicity, the set-up used is also equipped with sampling lines at the top and the bottom of the high pressure cell.

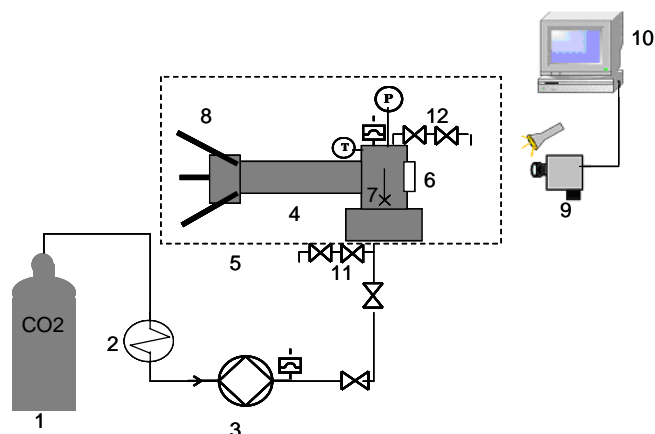


Figure 1 : Scheme of the high pressure experimental set-up

1 CO₂ bottle; 2 Cool bath; 3 Liquid pump; 4 High pressure cell; 5 Thermostated bath; 6 Sapphire window; 7 Magnetic stirrer; 8 internal piston; 9 Video camera; 10 Monitor; 11/12 sampling lines

2.3. EXPERIMENTAL PROCEDURE

In a typical experiment, the high pressure cell is first filled with LLA and IL in a mass ratio of 70 % wt_{LLA}/wt_{IL}. The desired quantity of CO₂ determined by double weighing of a high pressure cylinder is then added to the cell. After that, the system is set to the desired temperature; 90 °C (±0.2°C) and is magnetically stirred to insure a good homogenisation of the mixture. When the thermal equilibrium is reached, the pressure of the known composition biphasic mixture is increased gradually by moving the internal piston to reach a single phase system. In order to determine the bubble point pressure, the system is decompressed slowly until the apparition of a second phase. For delimiting precisely the transition pressure, the compression-decompression cycles are reproduced many times. At the end of the experiment, products are removed and the high-pressure cell was cleaned. As a consequence, each experiment was carried out for a 12 hours maximum time.

2.4. ¹H NMR ANALYSIS

NMR analyses were performed on some samples in order to determine their composition and check whether polymerisation occurred in high pressure media.

NMR structural identifications were performed on a Bruker Avance DRX500 spectrometer (1H-500.13 MHz) equipped with a 5 mm triple resonance inverse cryoprobe TXI (¹H-¹³C-¹⁵N), with z gradient. Spectra were recorded with 2.5 mm NMR tube in 100 μL of 100% DMSO-d₆ solvent (¹H 2.50 ppm - ¹³C 39.52 ppm) at 300 K. The pulse programs of all 1D/2D experiments (¹H, HSQCed and HMBC) were taken from the Bruker standard software library.

3. RESULTS

3.1. EXPERIMENTAL PHASE BEHAVIOUR RESULTS

The phase behaviour of the ternary system $\text{CO}_2 + [\text{HMIM}][\text{PF}_6] + \text{LLA}$ was determined by measuring its bubble point pressures at 90°C fixed temperature for several molar fractions of CO_2 ranging from 0.33 to 0.45 (c.f. Table 1).

Table 1. Bubble-point coordinates for various concentrations of CO_2 in the $\text{CO}_2 + [\text{HMIM}][\text{PF}_6] + \text{LLA}$ system. $T = 90^\circ\text{C}$, $\Delta P = \pm 0.1$ MPa.

P (MPa)	$x([\text{HMIM}][\text{PF}_6])$	$x(\text{CO}_2)$	$x(\text{LLA})$
6.95	0.274	0.329	0.397
8.38	0.260	0.364	0.376
9.83	0.236	0.422	0.342
10.50	0.217	0.447	0.337

Both CO_2 and LLA showed very good solubility in the IL-rich phase at moderate pressures. In fact, for the compositions studied homogeneous monophasic systems were observed for pressures lower than 12 MPa (c.f. Figure 2).

Furthermore, the equilibrium pressures of the ternary system $\text{CO}_2 + [\text{HMIM}][\text{PF}_6] + \text{LLA}$ are increased when the CO_2 concentration increased (isothermally).

In the proposed experimental conditions, the similar behaviour as the binary system $\text{CO}_2 + [\text{HMIM}][\text{PF}_6]$ ⁷ was observed. The bubble point pressures are also close (c.f. Figure 2). However, higher pressures were required to solubilize lower quantities of LLA in a CO_2 -rich phase.⁸ In fact, the phase transition pressures at 75°C vary from 14 to 24 MPa for molar ratios of LLA in CO_2 ranging from 0.03 to 0.09. Compared to literature data, LLA mole fraction was increased and CO_2 mole fractions were lowered in the present work (c.f. Table 1). Nevertheless, only a slight increase in bubble point pressures compared to the binary system $\text{CO}_2 + [\text{HMIM}][\text{PF}_6]$ data was observed.

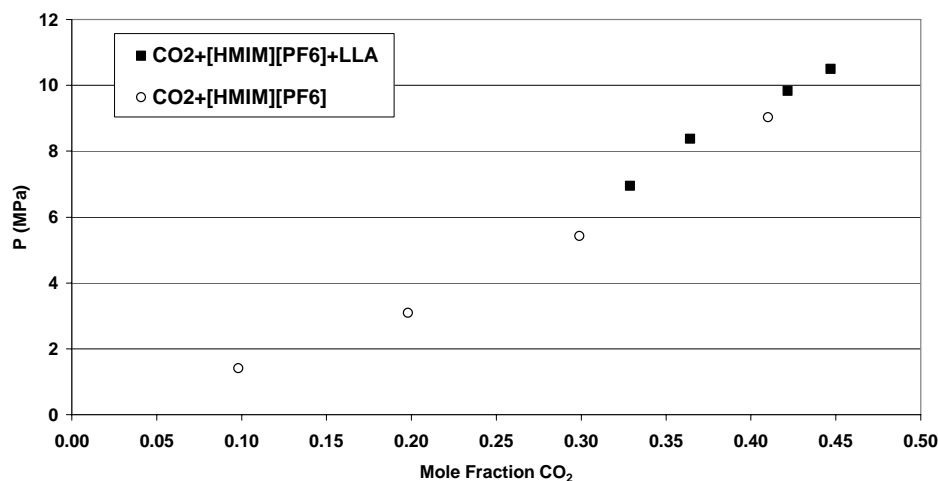


Figure 2. P-x diagram of the ternary system CO₂+ [HMIM][PF₆]+LLA. Comparison with literature data of the binary system CO₂+ [HMIM][PF₆]⁷. T= 90°C.

3.2. ¹H NMR ANALYSIS DATA

NMR analyses were carried out on the 42% CO₂ mass fraction mixture in order to qualitatively check whether the presence of SC CO₂ influences the polymerisation reactions. A sample of this mixture was withdrawn from the bottom sampling line and dissolved in a methanol bath. ¹H NMR spectrum on this sample (1H-0.42) shows the apparition of different CH₃-CHOH-C=O motifs as illustrated in Figure 3.

The quadruplet signals corresponding to the methine groups (CH) appear for chemical shifts ranging from 4 to 5.5 ppm. Doublet signals corresponding to the methyl (CH₃) groups appear for chemical shifts ranging from 1.3 to 1.6 ppm.

Furthermore, when adding a drop of the initial L-Lactide solution to the studied sample, the NMR spectrum (1H-0.42+L-lactide) shows the apparition of a new CH₃-CHOH-C=O motif, corresponding to the cyclic form of the monomer.

These results show that an open form of the monomer and/or oligomer and/or polymer forms were obtained within the solution in less than 12 hours in the high pressure cell.

Under atmospheric pressure, and in the same temperature and mass composition conditions, the polymerisation of LLA takes at least three days. This result shows that the polymerisation reaction is enhanced in the presence of SC CO₂. Further investigations on the evolution of the reaction yield in the presence of SC CO₂ are worth studying.

Furthermore, the appearance of these new forms of L-lactide in the mixture should modify the phase behaviour. Therefore, in further studies, phase behaviour studies would be carried out at lower temperature (~65°C). Indeed, it has been shown that at this temperature, polymerisation can not take place without the presence of enzyme catalysts.⁶

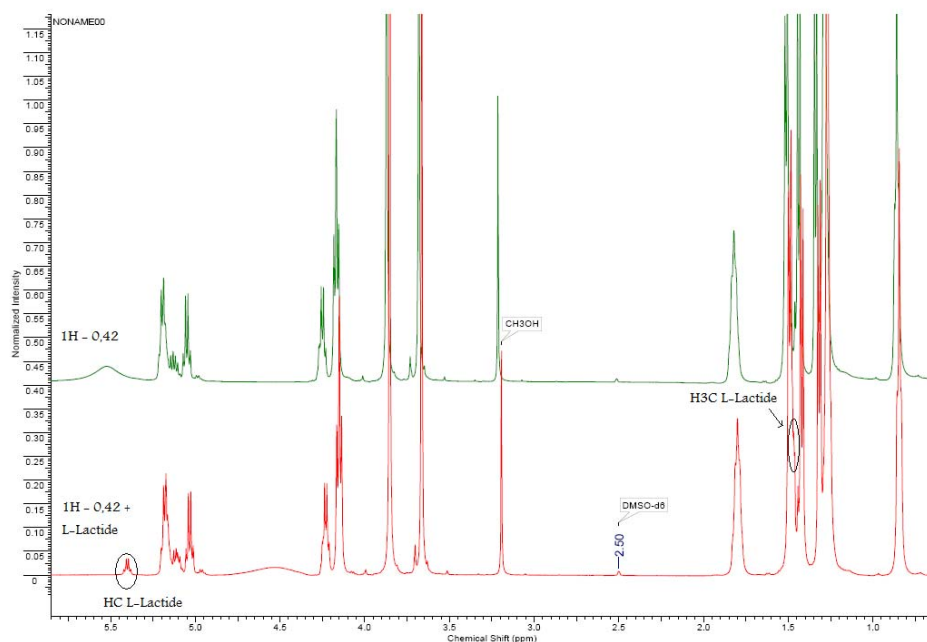


Figure 3 : ¹H NMR analysis spectra of the samples 1H – 0,42 and samples 1H – 0,42 + L-Lactide.

4. CONCLUSIONS

The ternary system CO₂+[HMIM][PF₆]+LLA was studied by experimental determination of bubble point pressures at fixed temperature. Similar behaviour between the ternary system and the binary system CO₂+[HMIM][PF₆] was observed.

CO₂ enrichment of the ternary system CO₂+[HMIM][PF₆]+LLA may lead to very high bubble point pressures although media dilution may be also favoured. So, optimal CO₂ enrichment may be investigated to the benefit of both mass transfer and LLA polymerisation.

Furthermore, NMR analyses show that the presence of CO₂ seems to favour polymerisation reaction. In fact, in less than 12 hours the appearance of new forms of LLA (oligomers or polymers) was observed.

In further work, phase behaviour will be studied at lower temperatures, in order to avoid polymerisation reactions that can influence the equilibrium results. Besides, computation work may be also carried out to study the influence of experimental parameters (temperature, LLA concentration, among others of interest) on the ternary system.

Product (monomer, polymer and IL) separation using SC CO₂ as a solvent may be considered in further work towards a fully green polymerisation process.

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