Published in final edited form as:

Chemphyschem. 2015 July 20; 16(10): 2219–2225. doi:10.1002/cphc.201500146.

Controlling the Formation of Ionic-Liquid-based Aqueous Biphasic Systems by Changing the Hydrogen Bonding Ability of Polyethylene Glycol End Groups

Prof. Dr. Jorge F. B. Pereira^{a,b,*}, Dr. Kiki A. Kurnia^c, Dr. Mara G. Freire^c, Prof. Dr. João A. P. Coutinho^c, and Prof. Dr. Robin D. Rogers^{a,d,*}

^[a]Department of Chemistry, The University of Alabama, Tuscaloosa, AL 35487, USA

^[b]Department of Bioprocess and Biotechnology, School of Pharmaceutical Sciences, UNESP – Univ Estadual Paulista, 14801-902 – Araraquara, SP, Brazil

^[c]Chemistry Department, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal

^[d]Chemistry Department, McGill University, Montreal, QC Canada H3A 0B8

Abstract

The formation of aqueous biphasic systems (ABS) when mixing aqueous solutions of polyethylene glycol (PEG) and an ionic liquid (IL) can be controlled by modification of the hydrogen bond ability of the polymer's end groups. It is shown that the miscibility/immiscibility on these systems stems from both the solvation of the ether groups in the oxygen chain and the ability of the PEG terminal groups to preferably hydrogen bond with water or the salt anion. The reduction of even one hydrogen bond in PEG can noticeably affect the phase behavior, especially in those regions of the phase diagram where all the ethylene oxide (EO) units of the polymeric chain are completely solvated. In this region, removing or weakening the hydrogen bond donating ability of PEG results in greater immiscibility, i.e., in a higher ability to form ABS, as a result of the much weaker interactions between the IL anion and the PEG end groups.

Keywords

aqueous biphasic systems; ionic liquids; polyethylene glycol; hydrogen bonding; polymers

1 Introduction

The search for more sustainable separation and purification processes has led to the use of aqueous biphasic systems (ABS) as an alternative to typical liquid-liquid extraction methods which frequently employ volatile and hazardous solvents.[1] ABS are water-rich systems combining two different compounds (polymer/polymer, polymer/salt, salt/salt, etc.) that above certain concentrations lead to an immiscible liquid-liquid region.[1] Although ABS combining different polymer/polymer or polymer/salt pairs have been studied and

*Corresponding Authors: J. F. B. Pereira, jfbpereira@fcfar.unesp.br, R. D. Rogers; robin.rogers@mcgill.ca.

characterized since the middle of the last century, renewed interest arose when a new type of systems was observed by the combination of two salts in aqueous solution.[2]

Salt/salt ABS using ionic liquids (ILs; salts with melting points lower than 100 °C) overcame some of the polarity limitations of the traditional polymer/polymer or polymer/salt ABS, allowing thus higher extraction yields and purification factors.[3] ILs have been a key in the development of new separation processes using ABS, since they exhibit interesting solvation and design properties, allowing the tailoring of an extraction process by proper cation-anion combinations.[4] While ABS composed of ILs and organic/inorganic salts have been described as platforms to enhance the extraction of diverse biomolecules from aqueous media,[5] in several cases selectivity between similar biomolecules couldn't be achieved.[6]

In order to overwhelm some of the limitations of ABS composed of ILs and conventional salts, we recently demonstrated the possibility of their formation using polyethylene glycol (PEG)-IL combinations.[7] The first evidence revealed that PEG-IL-based ABS are far more interesting and complex than initially admitted,[8] motivating additional experimental and simulation studies.[9] These works revealed that despite the hydration capability of the isolated ions in aqueous media, dominant in the salt-salt ABS, the interactions between the IL and the PEG are significant in ABS formation,[10] and additional important interactions must be considered, such as the interactions between cation-PEG, anion-PEG, cation-anion, water-anion, and cation-water.[11] More recently, cholinium carboxylate ILs have also successfully applied in the formation of ABS with PEG, and it was further highlighted the importance of the PEG-ILs interactions in the phase splitting mechanism.[12] Furthermore, the efficiency of PEG-IL ABS in separating different molecules such as antibiotics, antioxidants, alkaloids, and dyes, validated not only the applicability of these systems as efficient purification processes, but also as selective techniques further allowing the separation of similar molecules from aqueous media.[13]

Taken together, the previous works[11] suggested that if one could control the hydrogen bond donor or acceptor ability of PEG, by replacing the terminal –OH by –OMe or –NH₂ groups, this would allow tuning the capability of the PEG to interact with the IL and water and consequently control the size of the biphasic region. To explore this hypothesis, herein we investigate the phase behavior of aqueous combinations of two ILs with anions of different basicity, namely the weakly basic cholinium chloride ([Ch]Cl) and the strongly basic cholinium acetate ([Ch][OAc]), with PEGs of different molecular weight and with –OH (hydrogen bond donor and acceptor), –NH₂ (stronger hydrogen bond acceptor, weaker donor), and –OMe (hydrogen bond acceptor; virtually no donation) end groups, as shown in Figure 1.

2 Results and Discussion

2.1 Removing One Hydrogen Bond Donor from PEG

The alcoholic end groups in PEG molecules are the only source of strong hydrogen bond donating ability. We therefore began our investigation by removing hydrogen bond donation from the PEGs at one end by replacing an –OH group with –OMe. Polyethylene glycols with one hydroxyl and another end group alkylated with a methyl group of average

molecular weights 350 g mol⁻¹ (OH-PEG-350-OMe), 550 g mol⁻¹ (OH-PEG-550-OMe), and 750 g mol⁻¹ (OH-PEG-750-OMe) were combined with [Ch]Cl and [Ch][OAc] and their phase diagrams were compared with aqueous mixtures of PEG-600 and PEG-400. Aqueous solutions of [Ch]Cl (70 wt%) or [Ch][OAc] (90 wt%) and of each PEG (from 90 wt% to pure) were prepared and used for the determination of the binodal curves at 25 °C ($\pm$ 1 °C) and atmospheric pressure, according to literature procedures.[14] The experimental binodal curves in units of molality (mole of solute *per* kg of solvent) are shown in Figure 2 and detailed experimental weight fraction data are provided in Tables S1 and S2 in the Supporting Information.

It is apparent that for the methylated PEGs the MW trend usually observed in PEG-salt ABS is followed: polymers of higher MW require less salt to induce phase separation.[7],[11], [15] However, there is a small increase in the ability to form ABS (i.e., larger biphasic region) when one –OH end group is replaced by –OMe. For example, OH-PEG-OMe induces phase demixing at equivalent or lower polymer concentrations even with a lower MW: OH-PEG-350-OMe $\approx$ PEG-400 and OH-PEG-550-OMe > PEG-600. These trends are observed for both salts, although the differences in these polymer pairs are smaller for the ABS constituted by the more basic anion - [Ch][OAc]-based ABS.

To further probe the effects of hydrogen bonding, we choose to examine in more detail the phase diagrams of the IL with the stronger hydrogen bond acceptor anion, [Ch][OAc]. The phase diagrams were replotted in Figure 3 as the number of ethylene oxide (EO) units of each polymer *per* water molecule [mol of EO *per* mol of H₂O] *vs.* the ratio between the salt and the water [mol of salt *per* mol of H₂O] to emphasize any effects related to hydrogen bonding. In addition, two mixtures in the biphasic region for the three OH-PEG-OMe/[Ch][OAc] ABS were prepared at different molar ratios of H₂O:EO:[Ch][OAc].

The macroscopic appearance of the ABS at two different mixture compositions shown in Figure 3 suggests that changing the phase composition (higher or lower polymer content), or the respective OH-PEG-OMe MW, results in different partitioning of water between the co-existing phases. Analysis of the individual phases by ¹H NMR identified the top phase as the [Ch][OAc]-rich phase and the bottom phase as the OH-PEG-OMe-rich phase. For high polymer concentrations a change in the meniscus between the two phases is observed with increasing MW, which results from the increasing hydrophobicity difference between the phases. This effect is further enhanced when the systems have low concentrations of OH-PEG-OMe (*ca.* 1.25:1:5 EO:[Ch][OAc]:H₂O), for which the polymer-rich phase assumes a spheroid configuration suggesting that, in this phase, the water is fully surrounded by the polymer, and which results in a high hydrophobicity of the bottom phase and consequent high surface tension differences between the phases.

The behavior observed for the three OH-PEG-OMe polymers suggests that the [Ch][OAc]-H₂O interactions dominate those of OH-PEG-OMe-H₂O and/or OH-PEG-OMe-[Ch][OAc], and in agreement with the high basicity of the acetate anion. Such preferential ionic solvation would induce the dehydration of the OH-PEG-OMe and consequently results in a phase-volume reduction. However, at higher OH-PEG-OMe concentrations (*ca.* 7:1:7 EO:[Ch][OAc]:H₂O), preferential hydration of the polymer-rich phase is clearly observed with

the increase in volume of the OH-PEG-Me-rich phase and volumetric decrease of the IL-rich phase.

Additionally, in Figure 3, it is observed that the OH-PEG-550-OMe-ABS exhibits a different binodal shape than the other two PEGs at higher polymer concentrations. The OH-PEG-550-OMe binodal curve approaches that of OH-PEG-350-OMe for a high polymer content suggesting therefore that the effect of molecular weight is minimal in this region of the phase diagram. These deviations in the binodals curves were, however, accentuated by decreasing the MW of the polymer. The removal of one hydrogen bond donor from the PEG polymers with higher MW does not noticeably affect the phase behavior, where the solvation of the aliphatic chain plays the dominant task, while for low MW polymers the extremities seem to play an important role as well.

2.2 Changing the hydrogen bonding donor/acceptor balance of PEG

The analysis of the OH-PEG-OMe-based ABS suggested that the removal of a single hydrogen bond donating end group from PEG plays a significant role in ABS formation. To further test this hypothesis, ABS were prepared with di-substituted PEGs combined with [Ch][OAc]. Four different types of PEG polymers were chosen with approximately the same MW, including those with two hydrogen bond donor end groups (PEG-600), one hydrogen bond donor (OH-PEG-550-OMe), and no hydrogen bond donors (MeO-PEG-500-OMe). In addition, to study the hydrogen bond donor/acceptor balance, NH₂-PEG-600-NH₂ was studied, where the –OH groups on both ends of the PEG were replaced with –NH₂, a stronger acceptor and weaker hydrogen bond donor than –OH. The same cloud point titration methodology was used to determine the phase diagrams, at 25 °C and atmospheric pressure, and that are reported in Figure 4. The detailed weight fraction compositions are provided in the Supporting Information (Tables S3 and S4).

The binodal curves depicted in Figure 4 indicate that the ability to promote two phases follows the trend: NH₂-PEG-600-NH₂ > MeO-PEG-500-OMe >> OH-PEG-550-OMe ≈ PEG-600. Whereas the replacement of one –OH by one –OMe doesn't significantly change the ability of the polymer to induce ABS formation, the replacement of both –OH end groups of PEG by two –OMe or two –NH₂ results in major increases in the biphasic region meaning that lower concentrations of these polymers are needed to induce a phase separation.

The results for MeO-PEG-500-OMe are perhaps easier to rationalize. Removing both strong hydrogen bond donors (i.e., –OH) eliminates any hydrogen bonding from the PEG termini to the polymer itself, to other polymers, to water, and to the acetate anion. The terminal –OH groups would be the only way to hydrogen bond to the acetate anion or to any other PEG polymer, while water and the cholinium cation could still donate hydrogen bonds to the PEG ether oxygens. This could easily result in phase separation at lower polymer concentrations by making the PEG less compatible with water or IL.

The results for NH₂-PEG-600-NH₂ are somewhat more unexpected; while this polymer has a more hydrophilic character than PEG-600, it presents a biphasic region equivalent to MeO-PEG-500-OMe. To understand this phenomenon, one needs to better understand the nature

of the hydrogen bond donating and accepting ability of the amine compared to –OH. To achieve this understanding, we turned our attention to the use density functional theory (DFT) through computational techniques, namely electrostatic potential-derived (CHelpG) and CONductor-like Screening Model for Real Solvents (COSMO-RS). The CHelpG method calculates the charge point of individual atom composing the studied PEG and its derivatives, on the other hand, through COSMO-RS allows us to investigate the ability of individual atom to act either as hydrogen-bond donor (Hb_don3) or hydrogen-bond acceptor (Hb_acc3). The details description of CHelpG calculation, Hb_don3, and Hb_acc3 can be found in the literature.[16] Together, these methods permit us to investigate the charge distribution of the studied PEG and its derivatives and, ultimately, their ability to interact with water or [Ch][OAc]. The CHelpG[17] charges of atoms composing various functionalized PEG-400 molecules were calculated using Gaussian 03, Revision D.02 at TZVP level of theory.[18] The HB_don3 and HB_acc3[19] were also calculated at the same level of theory using COSMOthermX program using the parameter file BP_TZVP_C20_0111 (COSMOlogic GmbH & Co KG, Leverkusen, Germany). In addition, we also calculated the CHelpG charges and Hb_bond3 and Hb_don3 of water. The detail CHelpG and COSMO-RS calculations is given in the Supporting Information. The atom coordinates, CHelpG charges, HB_don3, and HB_acc3 for all atoms are also given in the Supporting Information (Tables S10-S16).

Simple water molecules that consist of three atoms – 2 hydrogens and an oxygen – have the capacity to act as both hydrogen-bond donor and acceptor. Detail analysis on Table S10 in the Supporting Information reveals that water ability to act as hydrogen-bond donor arise from its hydrogen atoms, meanwhile the oxygen atoms contribute to its strong ability as hydrogen-bond acceptor. Comparing with PEG molecule, which might be “considered” as water molecule by substituting hydrogen atom with bulky polyethylene glycol, the polymer has improved capacity as hydrogen bond acceptor that can be addressed due to presence of multiple oxy-ether. It is, however, should be noted that changing the terminal group of the PEG from OH – to NH₂ and to O-CH₃, lead to the change of their hydrogen-bond capacity. In this respect, the more hydrophilic character of the NH₂-PEG-400-NH₂ results from the enhanced hydrogen bond accepting ability of the N atom (of the –NH₂ groups) when compared to the O atom (of the –OH groups) in conventional PEGs, as shown in Table 1 and Figure S1 in Supporting Information, where higher partial negative charges on the N compared to the O atom are observed. Higher hydrogen bonding energies to the amine (O-H···N 29 kJ mol⁻¹) are present when compared with the hydroxyl groups (O-H···O 21 kJ mol⁻¹).[20] As a result of these differences, there will be stronger interactions between water and the –NH₂ groups making the dehydration of the polymer more difficult.

The dominant interactions of the PEG terminal groups were also previously shown to result from a competition for their solvation between the water and the IL anion. [21] While the hydroxyl group can act as a good hydrogen bond donor or acceptor, and thus favorably interacts with the acetate or chloride anions, the amine group, due to its stronger hydrogen bond acceptor and weaker hydrogen bond donor character, does not interact as strongly with the acetate anion (also a hydrogen bond acceptor). The much weaker interaction between the IL acetate anion and the amine group makes this more hydrophilic PEG derivative less

soluble in the cholinium acetate, as observed experimentally and confirmed by the infinite dilution activity coefficients reported in Table 2, thus leading to an easier formation of ABS (larger biphasic region).

2.3 The keys to PEG-IL-ABS formation

The results described above reveal the importance of hydrogen bonding, particularly hydrogen bond donation from the PEG to the anion, in the formation of PEG-based ABS, and demonstrate how even small changes in the polymer chemical structure can affect the phase separation. In particular, while the data confirms the importance of hydration of the ethylene oxide units, it emphasizes the relevance of the hydrogen bond donor ability of the PEG end groups when the balance of competitive hydrogen bonding interactions can readily alter phase formation.

Figure 4 indicates that changing both end groups will increase the biphasic region, but that the mechanism for this depends on the type of functionalization. In an attempt to further explore the relative importance of hydrogen bonding and functionalization of PEGs in ABS formation, two additional phase diagrams combining [Ch][OAc] and OH-PEG-350-OMe and MeO-PEG-350-NH₂ were determined and are compared in Figure 5. These polymers (Figure 1) are distinguished by having only one hydrogen bonding end group that can be either a stronger donor (–OH) or a stronger acceptor (–NH₂). In order to compare the respective binodal curves with the previous ones, and to obtain more information on the molecular level interactions, the binodal curves were plotted both in units of molality [mol of solute *per* kg of solvent] (Figure 5a) and in mol of PEG ethylene oxide (EO) units *per* mol of H₂O (Figure 5b) *vs.* mol of salt *per* mol of H₂O. The detailed weight fraction data are presented in Table S9 of the Supporting Information.

The data in Figure 5a reveal that there is an inversion in the ability of the two polymers to form ABS that occurs at *ca.* 3 mol kg^{–1} of [Ch][OAc]. Furthermore, the data plotted in Figure 5b show a change in the relative ability to induce the biphasic region at 0.5 mol EO unit *per* mol of H₂O (equivalent to 2 moles of H₂O per EO), suggesting that a reversal in the ABS formation ability occurs when the EO units are saturated with hydrogen bonds.[22] A change in behaviour between the region above/below 0.5 mol of EO *per* mol of H₂O is also observed in Figure 3 for the ABS composed of [Ch][OAc] and OH-PEG-OMe with higher MW, namely OH-PEG-750-OMe and OH-PEG-550-OMe. Above on average 2 moles of water *per* EO unit, MeO-PEG-350-NH₂ becomes fully solvated and exhibits a higher capability to phase separate than OH-PEG-350-OMe (below this value the trend is the reverse).

The relative ability of these polymers to form ABS with [Ch][OAc] seems to change with the relative content of the phase-forming components in solution from high polymer concentrations to high salt concentrations. The phase diagrams in Figure 5a reveal that making one end group more hydrophilic (exchanging –OH by –NH₂) enhances, as expected, the polymer solubility in the aqueous phase, decreasing therefore its ability to create an immiscible region when the concentration of polymer is high and the concentration of [Ch][OAc] is below 10 mol %. In this region, ABS formation seems to be controlled by the polymer-water solvation as the concentration of [Ch][OAc] is small. Conversely, when the

concentration of water is higher than 2 moles of H₂O *per* EO and the [Ch][OAc] concentration is higher than 10 mol %, the phase diagrams show an inversion in the phase behavior and the MeO-PEG-NH₂ becomes less soluble than OH-PEG-OMe enlarging the two-phase region. This suggests a change in the phase separation mechanism that is no longer dominated by the water solvation of the polymer, but by the mutual interactions between the polymer and the [Ch][OAc].

As discussed in the previous section, interactions between the acetate anion and the –NH₂ terminal groups of the PEG are not as favourable as with –OH, as shown by their infinite dilution activity coefficients, since both the acetate anion and the –NH₂ group are preferentially hydrogen bond acceptors. The change observed here is thus related to a situation where one moves from a system with high polymer and low salt concentrations, where the phase separation is dominated by the water solvation of the polymer, towards a system with high [Ch][OAc] and low polymer concentration, where the phase separation is dominated by the [Ch][OAc]-polymer interactions. In this region, the replacement of –OH by –NH₂ will invert the dominant interactions from more favorable with water (–NH₂-H₂O > –OH-H₂O) to less favorable with acetate (–NH₂-OAc < –OH-OAc) leading to an inversion in the phase behavior.

Previously, we demonstrated[10] for PEG/IL ABS, that in the region with a low content of water (close to the binary mixture PEG/IL) the hydroxyl groups of PEG and the anion interact strongly, and by addition of water these interactions are disrupted inducing the liquid-liquid demixing. However, herein the differences in the ABS formation ability were observed in the regions close to the two other binary systems: PEG/water (with low salt content) and IL/water (with low PEG content). The results here reported suggest that for each binary mixture a different mechanism is acting: the PEG solvation by the water will dominate the demixing close to the PEG/water binary mixture while the interaction balance between the IL anion/water and PEG will control the demixing close to the IL/water binary mixture. A schematic phase diagram representing each favourable mechanism *vs* the ternary phase region is depicted in Figure 6. Ongoing work should provide more details about these mechanisms.

3 Conclusion

In summary, this innovative study was aimed at understanding the polymers solvation in aqueous salt solutions. The formation of the related ABS was ascertained through the changing of the hydrogen bonding donor or acceptor capabilities of the polymer terminal groups (functionalized with –OH, –OMe, or –NH₂). All the phase diagrams reported here demonstrate the complexity of PEG-IL-ABS, where the immiscible region is a result of a delicate balance of interactions between the various compounds present in the system. It is shown that the miscibility/immiscibility on these systems stems not only from both the solvation of the ether groups in the polymer chain, as previously admitted, but also from the capability of the PEG terminal groups to preferably hydrogen bond with water or with the salt anion. The reduction of even one hydrogen bond from the PEG molecule can noticeably affect the phase behavior; especially in those regions of the phase diagram where the EO units of the polymeric chain are completely solvated. In this region of the phase diagrams,

removing or weakening the hydrogen bond donating ability of the PEG results in greater immiscibility as a result of the much weaker interactions between the IL anion (here acetate) and the PEG end group (e.g., $-\text{NH}_2$). Thus, by the proper control of the donor/acceptor character of the PEG terminal groups it is possible to control the biphasic region within a rather wide range.

The tailoring of PEG-IL ABS has previously been accomplished[9],[12] by the judicious choice of the IL's ions, but here it is shown that the same level of control can be achieved by controlling the nature of the terminal groups of the PEG. Moreover, the most interesting phenomenon observed, is the possibility to switch the ability of the polymer to form ABS by modifying the polymer to both interact better with water and worse with the IL or *vice-versa*. Although the study reported here has helped us to better understand the formation of PEG-IL ABS for various types and compositions of PEG or ILs, and to define the potential to tailor these liquid-liquid extraction systems, further studies are still required, such as the evaluation of speciation effects and the investigation of the formation of preferential polymer-water hydration shells. The next challenge will be to use this knowledge for the selective extraction of complex biomolecules that are only stable under specific conditions (e.g., proteins and biopharmaceuticals) while envisaging their pharmaceutical and biotechnological applications.

4 Experimental Section

Full experimental details are disclosed in the Supporting Information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank the Novartis-Massachusetts Institute of Technology (MIT) Center for Continuous Manufacturing (CCM) for financial support. Jorge F. B. Pereira acknowledges the financial support (process reference 2014/16424-7) from FAPESP (São Paulo Research Foundation Brazil). Mara G. Freire acknowledges the European Research Council (ERC) for the Starting Grant ERC-2013-StG-337753. The authors thank the Parker D. McCrary for the help on the synthesis of PEG-amines-based polymers.

References

- [1]. (a) Albertsson, PÅ. Partition of cell particles and macromolecules. 3rd edn. Wiley; New York: 1986. (b) Zaslavsky, BY. Aqueous Two-Phase Partitioning. Marcel Dekker Incorporated; New York: 1995.
- [2]. Gutowski KE, Broker GA, Willauer HD, Huddleston JG, Swatoski RP, Holbrey JD, Rogers RD. J Am Chem Soc. 2003; 125:6632–6633. [PubMed: 12769563]
- [3]. (a) Gutowski KE, Broker GA, Willauer HD, Huddleston JG, Swatoski RP, Holbrey JD, Rogers RD. J Am Chem Soc. 2003; 125:6632–6633. [PubMed: 12769563] (b) Freire MG, Cláudio AFM, Araújo JMM, Coutinho JAP, Marrucho IM, Canongia Lopes JN, Rebelo LPN. Chem Soc Rev. 2012; 41:4966–4995. [PubMed: 22692625]
- [4]. Freire MG, Cláudio AFM, Araújo JMM, Coutinho JAP, Marrucho IM, Canongia Lopes JN, Rebelo LPN. Chem Soc Rev. 2012; 41:4966–4995. [PubMed: 22692625]
- [5]. (a) Shahriari S, Tome LC, Araújo JMM, Rebelo LPN, Coutinho JAP, Marrucho IM, Freire MG. RSC Adv. 2013; 3:1835–1843. (b) Freire MG, Louros CLS, Rebelo LPN, Coutinho JAP. Green

- Chem. 2011; 13:1536–1545.(c) Freire MG, Neves CMSS, Marrucho IM, Canongia Lopes JN, Rebelo LPN, Coutinho JAP. Green Chem. 2010; 12:1715–1718.(d) Passos H, Sousa ACA, Pastorinho MR, Nogueira AJA, Rebelo LPN, Coutinho JAP, Freire MG. Anal Methods. 2012; 4:2664–2667.(e) Ventura SPM, Santos-Ebinuma V, Pereira JFB, Teixeira MS, Pessoa A, Coutinho JAP. J Ind Microbiol Biotechnol. 2013; 40:507–516. [PubMed: 23455697] (f) Ventura SPM, de Barros RLF, de Pinho Barbosa JM, Soares CMF, Lima ÁS, Coutinho JAP. Green Chem. 2012; 14:734–740.
- [6]. (a) Freire MG, Neves CMSS, Marrucho IM, Lopes JNC, Rebelo LPN, Coutinho JAP. Green Chem. 2010; 12:1715–1718.(b) Ferreira AM, Coutinho JAP, Fernandes AM, Freire Mara G. Sep Purif Technol. 2014; 128:58–66.
- [7]. (a) Freire MG, Pereira JFB, Francisco M, Rodriguez H, Rebelo LPN, Rogers RD, Coutinho JAP. Chem Eur J. 2012; 18:1831–1839. [PubMed: 22223510] (b) Pereira JFB, Kurnia KA, Cojocar OA, Gurau G, Rebelo LPN, Rogers RD, Freire MG, Coutinho JAP. Phys Chem Chem Phys. 2014; 16:5723–5731. [PubMed: 24522511] (c) Pereira JFB, Rebelo LPN, Rogers RD, Coutinho JAP, Freire MG. Phys Chem Chem Phys. 2013; 15:19580.
- [8]. Freire MG, Pereira JFB, Francisco M, Rodriguez H, Rebelo LPN, Rogers RD, Coutinho JAP. Chem Eur J. 2012; 18:1831–1839. [PubMed: 22223510]
- [9]. (a) Tomé LIN, Pereira JFB, Rogers RD, Freire MG, Gomes JRB, Coutinho JAP. Phys Chem Chem Phys. 2013; 16:2271–2274.(b) Tomé LIN, Pereira JFB, Rogers RD, Freire MG, Gomes JRB, Coutinho JAP. J Phys Chem B. 2014; 17:4615–4629.(c) Pereira JFB, Kurnia KA, Cojocar OA, Gurau G, Rebelo LPN, Rogers RD, Freire MG, Coutinho JAP. Phys Chem Chem Phys. 2014; 16:5723–5731. [PubMed: 24522511]
- [10]. (a) Tomé LIN, Pereira JFB, Rogers RD, Freire MG, Gomes JRB, Coutinho JAP. Phys Chem Chem Phys. 2013; 16:2271–2274.(b) Tomé LIN, Pereira JFB, Rogers RD, Freire MG, Gomes JRB, Coutinho JAP. J Phys Chem B. 2014; 17:4615–4629.
- [11]. Pereira JFB, Kurnia KA, Cojocar OA, Gurau G, Rebelo LPN, Rogers RD, Freire MG, Coutinho JAP. Phys Chem Chem Phys. 2014; 16:5723–5731. [PubMed: 24522511]
- [12]. Mourão T, Tomé LC, Florindo C, Rebelo LPN, Marrucho IM. ACS Sustainable Chem Eng. 2014; 2:2426–2434.
- [13]. (a) Pereira JFB, Vicente F, Santos-Ebinuma VC, Araújo JM, Pessoa A, Freire MG, Coutinho JAP. Process Biochem. 2013; 48:716–722.(b) Pereira JFB, Ventura SPM, e Silva FA, Shahriari S, Freire MG, Coutinho JAP. Sep Purif Technol. 2013; 113:83–89.(c) Pereira JFB, Rebelo LPN, Rogers RD, Coutinho JAP, Freire MG. Phys Chem Chem Phys. 2013;19580–19583. [PubMed: 24145792] (d) Mourão T, Tomé LC, Florindo C, Rebelo LPN, Marrucho IM. ACS Sustainable Chem Eng. 2014; 2:2426–2434.
- [14]. Pereira JFB, Lima AS, Freire MG, Coutinho JAP. Green Chem. 2010; 12:1661–1669.
- [15]. (a) Zaslavsky, BY. Aqueous two-phase partitioning, physical chemistry and bioanalytical applications. Academic Press; New York: 1995. (b) Zafarani-Moattar MT, Sadeghi R. Fluid Phase Equilib. 2001; 181:95–112.(c) Taboada ME, Asenjo JA, Andrews BA. Fluid Phase Equilib. 2001; 180:273–280.
- [16]. (a) Breneman CM, Wiberg KB. J Comp Chem. 1990; 11:361–373.(b) Klamt, A. COSMO-RS from quantum chemistry to fluid phase thermodynamics and drug design. Amsterdam, The Netherlands: Elsevier; 2005.
- [17]. Breneman CM, Wiberg KB. J Comp Chem. 1990; 11:361–373.
- [18]. University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, TURBOMOLE V6.1; 2009. p. 1989-2007.25 GmbH, since 2007; available from <http://www.turbomole.com>.
- [19]. Eckert, F., Klamt, A. COSMOtherm, Version C3.0, Release 13.01. COSMOlogic GmbH & Co. KG; Leverkusen, Germany: 2013.
- [20]. (a) Markovitch O, Agmon N. J Phys Chem A. 2007; 111:2253–2256. [PubMed: 17388314] (b) Larson JW, McMahon TB. Inorganic Chem. 1984; 23:2029–2033.(c) Emsley J. Chem Soc Rev. 1980; 9:91–124.
- [21]. (a) Rodriguez H, Francisco M, Rahman M, Sun N, Rogers RD. Phys Chem Chem Phys. 2009; 11:10916–10922. [PubMed: 19924326] (b) Tomé LIN, Pereira JFB, Rogers RD, Freire MG, Gomes JRB, Coutinho JAP. J Phys Chem B. 2014; 17:4615–4629.

- [22]. Pochylski M, Aliotta F, Blaszcak Z, Gapinsky J. J Phys Chem B. 2006; 110:20533–20539.
[PubMed: 17034240]

Figure 1.
Chemical structure of the studied polymers and ionic liquids.

Figure 2.

Experimental solubility data at 25 °C and atmospheric pressure for ABS composed of [Ch]Cl (left) or [Ch][OAc] (right) ionic liquids with OH-PEG-OMe of molecular weights: (●) 350 g mol⁻¹; (□) 550 g mol⁻¹; and (▲) 750 g mol⁻¹ (compared with PEG-400 (○)[11] and PEG-600 (◆)[11]).

Figure 3.

Experimental solubility data for ABS composed of OH-PEG-OMe + [Ch][OAc] + H₂O at 25 °C and atmospheric pressure for different OH-PEG-OMe molecular weights: (●) 350 g mol⁻¹; (□) 550 g mol⁻¹; (▲) 750 g mol⁻¹ and two different mixture points for each ternary system ((O) 350 g mol⁻¹; (■) 550 g mol⁻¹; () 750 g mol⁻¹). Methyl eosin dye was added to facilitate visual analysis.

Figure 4.

Experimental solubility data at 25 °C and atmospheric pressure for ABS composed of [Ch] [OAc] with (■) MeO-PEG-500-OMe; (□) OH-PEG-550-OMe; (♦) PEG-600; and (▼) NH₂-PEG-600-NH₂.

Figure 5.
Experimental solubility data at 25 °C and atmospheric pressure for ABS composed of [Ch]
[OAc] with (▲) OH-PEG-350-OMe and (●) MeO-PEG-350-NH₂.

Figure 6. Schematic phase diagram representing the favorable mechanisms that control the ABS formation. The binodal curve used as example is from the ternary system composed of OH-PEG-350-OMe + [Ch][OAc] + water at 25 °C.

Table 1

HB_don3 and HB_acc3 of functionalized PEG-400 molecules retrieved from COSMO-RS using the BP_TZVP_C30_1301 parameterization.

Compounds	HB_don3	HB_acc3
PEG-400	4.03	27.63
OH-PEG-400-NH ₂	2.07	30.07
NH ₂ -PEG-400-NH ₂	0.09	30.47
OH-PEG-400-OMe	2.00	26.28
MeO-PEG-400-OMe	0.00	24.71
MeO-PEG-400-NH ₂	0.06	28.58

Table 2

Activity coefficients at infinite dilution of functionalized PEG-400 molecules in H₂O and [Ch][OAc] at 25 °C estimated by COSMO-RS using the BP_TZVP_C30_1301 parameterization.

Compounds	$\ln \gamma^\infty$	
	H ₂ O	[Ch][OAc]
PEG-400	-5.31	-2.09
OH-PEG-400-NH ₂	-7.56	-0.63
NH ₂ -PEG-400-NH ₂	-9.38	0.07
OH-PEG-400-OMe	-4.23	-0.62
MeO-PEG-400-OMe	-2.80	0.93
MeO-PEG-400-NH ₂	-7.20	0.42