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Ammonium ionic liquids as green solvents for drugs

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ABSTRACT

A high solubility of antituberculosis antibiotic drugs: isoniazid and pyrazinecarboxamide in ammonium ionic liquids shown in this work, demonstrates the promising perspectives in the drug processing. Solid–liquid equilibrium (SLE) measurements have been made using a dynamic (synthetic) method. Thermophyscial properties such as melting point, enthalpy of fusion, temperatures of phase transitions and corresponding enthalpies for both isoniazid and pyrazinecarboxamide as well as for three ammonium salts were acquired using differential scanning calorimetry (DSC). The solubility of isoniazid in analysed ILs was found to be higher than that of pyrazinecarboxamide. Considering ammonium salts examined in this work, didecyldimethylammonium nitrate is the best solvent for both antibiotics. The solid–liquid phase equilibria were described using six different correlation equations which revealed a relatively good description with an acceptable standard deviation temperature range.

1. Introduction

Quaternary ammonium salts are well known compounds and have widespread industrial utilisation due to their surface activity and other interesting properties e.g. bioactivity and high antimicrobial activity [1].

Ionic liquids, ILs, are compounds which structures can be easily modified to allow for tailoring physico–chemical properties of ILs to meet the requirements for a specific task or application [2,3] such as organic reaction media [4], including combination with supercritical fluids [5], functional materials [6], extractive media [7], and as active pharmaceutical ingredients [8]. They have advantageous thermal stability [9,10] and solvent power [3,11–16]. Due to the high interest in the application of ILs, quaternary ammonium-based ionic liquids were synthesised as a novel and economic class of ILs [1]. Recently, their low lipophilicity advantageous in terms of its environmental impact [17] in comparison with other pyridinium and pyrrolidinium-based ionic liquids was reported. As consequence they possess low toxic effect towards the organisms [18]. Ammonium-based ILs were presented as air- and moisture-stable compounds with high thermal stability, especially those with the $[NTf_2]^-$ anion. They were reported to exhibit anti-bacterial and anti-fungal activities and to act as wood preservatives. Those accompanied by $[NO_3]^-$, $[NO_2]^-$ and $[BF_4]^-$ anions were successfully utilised for disinfection. When considering practical application and production costs, the ammonium-based ILs with $[NO_3]^-$ were found to be the most promising among other ILs, and they may be regarded as cheap, hydrophobic and multifunctional ILs [1]. They were used in liquid–liquid extraction to recover glycols commonly used in chemical industry from aqueous streams as an energy efficient alternative to technologies instead of the evaporation of water [19].

The solid–liquid (SLE) and liquid–liquid (LLE) phase equilibria measurements of ILs systems based on ammonium cations have attracted increased attention for applications in liquid–liquid extraction [20–23]. The present work is a continuation of our systematic study on the solubility of tuberculosis antibiotic drugs in ionic liquids [11,24]. The aim of this work was to present new experimental SLE phase diagrams for antibiotics (pyrazinecarboxamide or isoniazid) and ammonium ionic liquids. We were interested to see if the comparison of present and previously reported results with imidazolium ionic liquids could allow choosing the most promising type of ILs as future pharmaceutical solvents for the investigated antibiotics. In this work ammonium ionic liquids containing two methyl groups were studied. In particular, didecyldimethylammonium nitrate (IUPAC name: N-decyl-N, N-dimethyldecan-1-aminium nitrate) [DDA][NO_3]; (benzyl)dimethylalkylammonium nitrate, where alkyl is [$C_{12}H_{25}$ (w = 0.4) or $C_{14}H_{29}$ (w = 0.6)] (IUPAC names: N-benzyl-N,N-dimethyldodecan-1-aminium nitrate and N-benzyl-N,N-dimethyltetradecan-1-aminium nitrate, respectively) [BA][NO_3]; ethyl(2-hydroxyethyl) dimethylammonium bis(trifluomethylsulfonyl)amide (IUPAC

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