Room temperature ionic liquids (RTILs) based on amino acids

Graveney School

Overview

In a previous project, students from Graveney synthesised a number of RTILs based on (i) 1-R-3-methylimidazole cations with different alkyl groups and (ii) the hexafluorophosphate anion.

Our aim, ultimately, is to synthesise and characterise a range of RTILs in which the anion differs rather than the cation. Various groups have reported the synthesis of RTILs with amino acids as anions. Amino acids are non-toxic, cheap, readily available and exhibit a broad range of chemical properties depending on their side chains (see above).

Here we report on first steps in the preparation of RTILs in our laboratory as part of this project.

Research aims

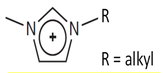
- To create a range of ionic liquids based on the imidazole cation and anions based on readily available amino acids.
- To determine the properties of these substances via experimentation.
- To analyse products using spectroscopic methods.

Summary

Ionic substances are often thought of as having high melting and boiling points due to strong electrostatic forces of attraction between ions of opposite charge. For example, table salt (NaCl) has a melting point of 801°C and a boiling point of 1,465°C. Coulomb's law states that this force of attraction (ionic bonding) depends on the magnitude of the charges involved and the distance between them. By selecting large cations and large anions with low charges, it is possible to synthesise ionic substances that are liquids at room temperature – room temperature ionic liquids ("RTILs").

RTILs are of interest because of a range of properties:-

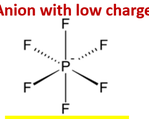
- Their inherent conductivity makes them suitable for a wide range of electrochemical applications such as electroplating and battery development;



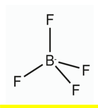
Big Cations with low charge
This has an R group that can be changed to give different properties

1-R- 3-methylimidazole

Big Anion with low charge



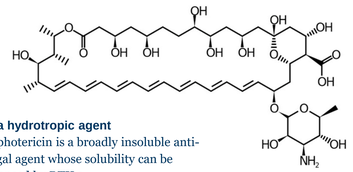
Hexafluorophosphate



Tetrafluoroborate

The big, weakly charged anions and cations have weak ionic bonds and produce ionic compounds with low melting points.

The principle behind room temperature ionic liquids



As a hydrotropic agent
Amphotericin is a broadly insoluble anti-fungal agent whose solubility can be enhanced by RTILs

As a novel solvent
The first lady of Finland wears a dress made from cellulose recovered using RTILs

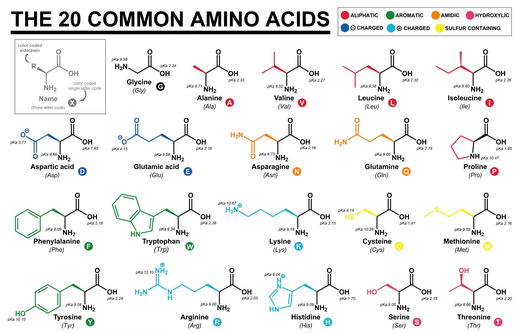
- They have proved to be powerful alternative catalysts - for example, in the catalytic cracking of crude oil;
- They are used as novel solvents - for example, to recover cellulose from timber, which can then be used as a low environmental impact polymer;
- They have been shown to have *hydrotropic* effects – for example, increasing the solubility of drugs without forming micelles, thereby increasing their bioavailability.

Background information

The possible number of RTILs is enormous because of the range of potential cations and anions available. The properties of a given RTIL will depend on the nature of both the cation and the anion. Such a framework presents an opportunity to seek to "tune" RTILs to meet given requirements.

Human beings use 20 different amino acids in synthesising a vast array of proteins and peptides. Amino acids are zwitterions containing both proton donating (-COOH) and proton accepting ($-NH_2$) groups. As such, they have the potential to form both anionic and cationic species in RTILs (see figure right). The 20 amino acids' side chains fall into various categories: aliphatic, aromatic, amidic, hydroxylic, charged and sulfur containing (see figure above). This offers a ready made palette of ions with different properties with which to design RTILs.

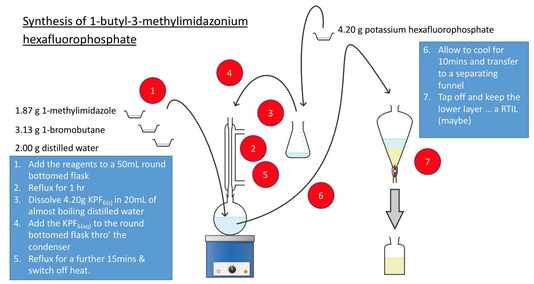
Often researchers seek to use a series of different cations to produce RTILs with a range of properties. Our aim is to use readily available, non-toxic and cheap amino acids as anions in a range of imidazolium based RTILs.



Background information (continued)

Amino acid based RTILs are potentially attractive because environmental and toxicity concerns have been expressed about fluorine containing anions often used in the production of ionic liquids - for example PF_6^- . Amino acids are biocompatible and environmentally benign and are therefore potentially more suitable for roles such as hydrotropic agents for increasing the solubility of drugs.

Our intention is to synthesise a range of RTILs based on amino acids and to characterise them by reference to a range properties, for example viscosity and thermal stability, and using an array of techniques.



Synthesis of 1-butyl-3-methylimidazonium hexafluorophosphate
A Chemix graphical representation of the experimental method

Experimental Method

Synthesis of 1-butyl-3-methylimidazonium hexafluorophosphate

- Weigh out: 1.87 g 1-methylimidazole; 3.13 g 1-bromobutane; 2.00 g distilled water
- Add the reagents to a 50 mL round bottom flask. Make a note of the appearance of the reaction mixture at this stage.
- Clamp the flask around the neck, and fit with a water condenser and place in the heating mantle. Attach water pipes to the condenser and set the water rate to a slow trickle.
- Begin heating by turning the dial on the heating mantle to 7. The reaction mixture should begin boiling in around 5 minutes. If the reaction mixture does not boil, check the positioning of the flask in the mantle. You may need to turn up the heat but do so cautiously.
- Heat under reflux for 1 hour. Make notes of any changes to the reaction mixture during heating. During reflux, weigh out 4.20 g potassium hexafluorophosphate. Dissolve in 20 mL of distilled water and heat to dissolve. The water must be close to boiling to dissolve all the KPF_6 .
- After 1 hour, switch off the heating mantle and remove the flask from the heat by raising the flask. Move the flask away from the hot mantle. Add the KPF_6 solution to the reaction mixture by pouring down the condenser using a funnel. Return to the heating mantle and heat to reflux again for 15 minutes.
- After 15 minutes, remove the flask from the heat as before, and leave for 10 minutes to cool. If white solid is present in the flask, add distilled water and swirl to dissolve. The flask now contains two layers. The upper layer is water with dissolved KBr. The lower layer should be slightly yellow in colour and is the ionic liquid.
- To separate the layers, pour the mixture into a separating funnel, remove the bottom layer (the ionic liquid) into a clean container.

Results

Approximately 0.5cm³ of a yellow liquid was recovered from the separating funnel.

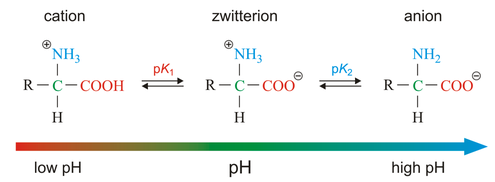
Students examine the products following reflux
The products formed two layers, the lower layer being an opaque yellow liquid

The product
1-butyl-3-methylimidazolium hexafluorophosphate

Conclusions & next steps

We have prepared a sample of an RTIL based on an imidazolium cation which is a key step in realising our aim to synthesise and characterise a group of RTILs based on an imidazolium cation and a range of amino acid anions.

The next steps in the project are to characterise the RTIL using spectroscopic techniques that are used at UCL's laboratories including ultra violet – visible spectroscopy (UV-Vis), infrared spectroscopy (FT-IR), mass spectrometry and nuclear magnetic resonance spectroscopy (NMR).



The zwitterionic character of amino acids

Our thanks to Mike Grocott and Neil Garrido at IRIS and Professor Robert Palgrave at UCL for their time and support.