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Room Temperature Ionic Liquids from 20 Natural Amino Acids

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Room temperature ionic liquids (RTILs)[1] are attracting considerable attention as reaction solvents,[2] extraction solvents,[3] and electrolyte materials[4] as a result of their remarkable properties, including a negligibly small vapor pressure, high thermal stability, and high ionic conductivity. RTILs are now expected to be designer liquids with controllable physical and chemical properties or even specific functions.[3a,4b,5] Although there have been extensive studies of RTILs, relations between their structure and physicochemical properties have not yet been summarized.[6] RTILs have mostly been designed using a series of cationic derivatives[4,9] due to their convenient chemical modification, but there is much less information about the effect of anion structure. We have been developing novel task-specific RTILs by focusing on the amino acids because such RTILs can behave as anions with various characteristics. With this approach, we can analyze the effects of anion structure on the properties of the corresponding salts. Moreover, various functional groups on amino acids should be valuable for designing RTILs for a wide range of tasks. Here, we describe novel RTILs that are prepared by coupling the imidazolium cation with 20 different natural amino acids.

The common way of preparing RTILs is by the anion exchange of halide salts with metal salts. However, this method seems to be unsuitable for preparing pure and various RTILs due to contamination of halide salts and the limited variety of commercially available metal salts. Furthermore, because amino acids coordinate transition metal ions, pure amino acid RTILs cannot be obtained using the conventional method with metal salts.[7] Thus, we used a different method that involves preparing imidazolium hydroxide to neutralize a series of amino acids.[8]

Among several onium cations that we tested, 1-ethyl-3-methylimidazolium cation exhibited an excellent ability to form RTILs with amino acids. All of the resulting amino acid ionic liquids we obtained were transparent, nearly colorless liquids at room temperature (Figure 1). The structure of these amino acid ionic liquids was confirmed using ^{1}H NMR (JEOL α-500) and elemental analysis (see Supporting Information). Although these amino acid ionic liquids were insoluble in ethers, as are typical ionic liquids, they were miscible with various organic solvents, such as methanol, acetonitrile, and chloroform. Some RTILs prepared from amino acids containing two carboxyl groups, such as [emim][Glu] and [emim][Asp], were insoluble in chloroform. This miscibility, which has never been found in native amino acids, may allow amino acids to be used in many new applications. The miscibility of RTILs with organic solvents was dependent upon the side-chain structure of the corresponding amino acid anion. In addition, we found that these amino acid ionic liquids dissolved amino acids; for example, at least 2 wt % of L-valine dissolved in [emim][Val] at 25 °C. Studies have shown that RTILs have a strong hydrogen bonding ability that is useful for dissolving biomaterials, such as DNA, cellulose,[9] and other carbohydrates.[10] Thus, in various fields, such as industrial chemistry and pharmaceutical chemistry, these amino acid ionic liquids should provide a variety of applications, such as intermediates for peptide syntheses,[11] chiral solvents,[12] functional materials, and biodegradable ionic liquids.[13]

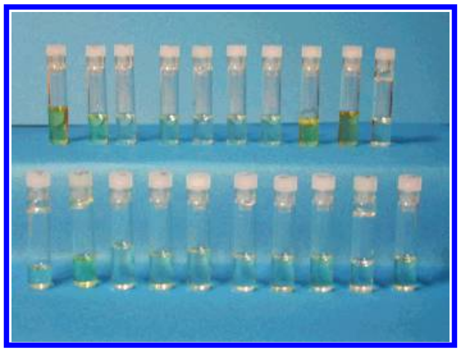

Figure 1. Prepared amino acid ionic liquids. Upper side (left to right): [emim][Leu], [emim][Lys], [emim][Met], [emim][Phe], [emim][Pro], [emim][Ser], [emim][Thr], [emim][Trp], [emim][Tyr], and [emim][Val]. Lower side (left to right): [emim][Ala], [emim][Arg], [emim][Asn], [emim][Asp], [emim][Cys], [emim][Gln], [emim][Glu], [emim][Gly], [emim][His], and [emim][Ile].

Differential scanning calorimetric measurements showed that these amino acid ionic liquids had no melting point, but a glass transition temperature (T_g) ranging from −65 to 6 °C (Table 1). Also, thermal gravimetric analysis revealed that, except for the decomposition of [emim][Cys] at 173 °C, all liquids were stable at temperatures of at least 200 °C. The T_g of these amino acid ionic liquids depended on the side-chain structure of the amino acid. [emim][Ala], [emim][Val], [emim][Leu], and [emim][Ile] had T_g values lower than those of other liquids. An increase of the alkyl side-chain length coincided with a gradual increase of T_g, probably due to an increase of the van der Waals force between alkyl side chains. By comparing the salt pair of [emim][Asn] and [emim][Gln] with the salt pair of [emim][Asp] and [emim][Glu], we found the alkyl chain length to have the dominant influence on T_g, regardless of the functional group. On the other hand, RTILs with a carboxyl and an amide group had a T_g higher than that of other amino acid ionic liquids. In particular, [emim][Asp] and [emim][Glu] had the highest T_g values at 5 and 6 °C, respectively. As a comparison of amino acid ionic liquids with different functional side groups, the T_g values of these three salts have the following sequence: −47 °C ([emim][Lys]) < −12 °C ([emim][Gln]) < +6 °C ([emim][Glu]). Thus, the T_g of [emim][Glu] is 50 °C higher than that of [emim][Lys] although Lys has a longer hydrocarbon side chain. On the other hand, [emim][Met] showed unique characteristics. It has relatively low T_g, due to its thioether unit. Introduction of ether units into substituents of the onium cation is known to lower the T_g of the corresponding RTILs.[14] A similar effect can be expected in [emim][Met] to lower its T_g.

Starting from [emim][Ala], we explored the effects of substituents on the T_g of the corresponding salts. When we added a hydroxyl group ([emim][Ser]), T_g increased by 8 °C, whereas introduction of carboxylate ([emim][Asp]) increased T_g by 62 °C. Although these values are not universal, they can act as a guide to the functional

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Table 1. Thermal Properties and Ionic Conductivity of 20 Kinds of Amino Acid Ionic Liquids

salt	T_g (°C)	σ_i (S/cm) at 25 °C	salt	T_g (°C)	σ_i (S/cm) at 25 °C
[emim][Gly]	−65	5.7×10^{-4}	[emim][Trp]	−31	9.1×10^{-9}
[emim][Ala]	−57	6.4×10^{-4}	[emim][His]	−24	1.0×10^{-7}
[emim][Met]	−57	2.4×10^{-4}	[emim][Tyr]	−23	4.0×10^{-8}
[emim][Val]	−52	8.8×10^{-5}	[emim][Cys]	−19	3.5×10^{-5}
[emim][Ile]	−52	6.9×10^{-5}	[emim][Arg]	−18	9.0×10^{-7}
[emim][Leu]	−51	8.1×10^{-5}	[emim][Asn]	−16	1.1×10^{-6}
[emim][Ser]	−49	6.5×10^{-4}	[emim][Gln]	−12	1.7×10^{-7}
[emim][Lys]	−47	7.8×10^{-5}	[emim][Asp]	5	1.7×10^{-9}
[emim][Thr]	−40	1.0×10^{-4}	[emim][Glu]	6	5.0×10^{-7}
[emim][Phe]	−36	6.0×10^{-5}	[emim][Pro]	−48	1.6×10^{-4}

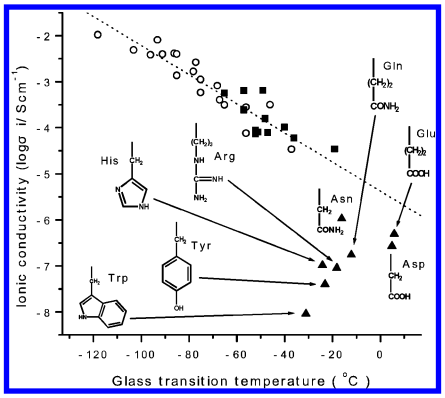

Figure 2. Relation between ionic conductivity (25 °C) and glass transition temperature (T_g) of amino acid ionic liquids (▲ and ■, amino acid ionic liquids; ○, imidazolium-type ionic liquids prepared by the neutralization in our laboratory).

groups of uninspected RTILs. For [emim][Phe], T_g is −36 °C, which is 21 °C higher than that of [emim][Ala] due to the stacking interaction of the phenyl groups. Introduction of a hydroxyl group to this Phe anion increased T_g as in the previous case (see [emim][Tyr] in Table 1; $T_g = -23$ °C). Therefore, these substituents are a kind of "T_g indicator" for uninspected RTILs containing functional groups.

The ionic conductivity of these amino acid ionic liquids ranges from 10^{-9} to 10^{-4} S/cm at 25 °C. Figure 2 shows the relation between the ionic conductivity at 25 °C and T_g for these liquids. In this figure, the open circles (○) are data for imidazolium-type ionic liquids prepared in our previous studies.[6] The ionic conductivity of previously synthesized RTILs is closely related to their T_g. This strong correlation indicates that the ionic conductivity of a given number of carrier ions is governed mainly by their mobility. In this study, the major amino acid ionic liquids followed a linear relationship between T_g and ionic conductivity (Figure 2, ■). However, the correlation is not so strong for other amino acid ionic liquids (Figure 2, ▲); moreover, the ionic conductivities are less than those for major amino acids of the same T_g. In particular, the relatively low ionic conductivities of amino acid ionic liquids, such as [emim][His] and [emim][Glu], may be due to hydrogen bonding or some other ion interaction that is expected through their side chains.

In summary, we synthesized new ionic liquids from a series of amino acids. The amino acid ionic liquids were miscible with organic solvents and could dissolve native amino acids. From the trends found in this study, one can estimate the glass transition temperature, the ionic conductivity, and the miscibility with organic solvents based on the structure of the side chains on the component ions. These findings should be useful for designing suitable ionic liquids for specific applications.

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Supporting Information Available: The details of the characterization of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) General procedure for amino acid ionic liquids. 1-Ethyl-3-methylimidazolium hydroxide ([emim][OH]) aqueous solution was prepared from 1-ethyl-3-methylimidazolium bromide using anion exchange resin (AMBERLITE IRA400CL (Aldrich) or AMBERLITE IRA400OH (SUPELCO)). An [emim][OH] aqueous solution was added dropwise to a slightly excess equimolar amino acid aqueous solution. The mixture was stirred under cooling for 12 h. Then water was evaporated at 40−50 °C. To this reaction mixture were added 90 mL of acetonitrile and 10 mL of methanol, and it was stirred vigorously. The mixture was then filtered to remove excess amino acid. Filtrate was evaporated to remove solvents. The product was dried in vacuo for 2 days at 80 °C. Structure of the resulting amino acid ionic liquid was confirmed by ^{1}H NMR spectroscopy (JEOL α-500) and elemental analysis. The water content of most amino acid ionic liquids, determined with a Karl Fischer moisture titrator (MKS-210; Kyoto Electronics Co.), was less than 0.2 wt %. Those of salts composed of Glu and Asp were around 0.4 wt %.
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