Protonation and Complexation Approaches for Production of Protic Eutectic Ionic Liquids

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Abstract: *4-formyl-N,N-dimethylbenzenaminium chloride (FDBC), carboxymethanaminium chloride (CMAC), 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium chloride (DHPC), (R)-1-carboxy-2-mercaptoethanaminium chloride (CMEC) and 1-methyl-2-oxopyrrolidinium chloride (MOPC) were synthesised and complexed with either urea or oxalic acid at different molar ratios to form protic eutectic ionic liquids (PEILs). The melting point of the PEILs was measured using differential scanning calorimetry (DSC). Based on the melting point results, MOPC complexed with oxalic acid ([MOPC][O]) at a 1:1 molar ratio and DHPC complexed with urea ([DHPC][U]) at a 1:2 molar ratio were regarded as room temperature ionic liquids (RTILs). The solubility study showed that [MOPC][O] was able to fully dissolve soluble starch and rice starch (10 wt%) and partially dissolve sago starch.*

Keywords: protic eutectic ionic liquids (PEILs), hydrochloride salts, complexation, protic ionic liquids, deep eutectic solvent

Abstrak: *4-formil-N,N-dimetilbenzenaminium klorida (FDBC), karboksimetana minium klorida (CMAC), 1,3-dihidroksi-2-(hidroksimetil)propan-2-aminium klorida (DHPC), (R)-1-karboksi-2-merkaptoetanaminium klorida (CMEC) dan 1-metil-2-oksopirrolidinium klorida (MOPC) telah disintesis dan dikompleskan dengan sama ada urea atau asid oksalik pada nisbah molar berbeza untuk menghasilkan bendalir ionik protik eutektik (PEILs). Takat lebur PEILs telah diukur menggunakan kalorimeter imbasan pembezaan (DSC). Berdasarkan keputusan takat lebur, MOPC yang dikompleskan dengan asid oksalik ([MOPC][O]) pada nisbah molar 1:1 dan DHPC yang dikompleskan dengan urea ([DHPC][U]) pada nisbah molar 1:2 dianggap sebagai bendalir ionik suhu bilik (RTILs). Kajian keterlarutan kanji menunjukkan [MOPC][O] mampu melarutkan sepenuhnya kanji larut dan kanji beras (10% berat) dan melarutkan sebahagian kanji sagu.*

Kata kunci: bendalir ionik protik eutektik (PEILs), garam hidroksida, pengkompleksan, bendalir ionik protik, pelarut eutektik dalam

1. INTRODUCTION

Salt melting below the boiling point of water (< 100°C) produces ionic liquids (ILs). The term room-temperature ionic liquids, or RTILs, is usually

reserved for ionic melts with melting points below room temperature. ILs form liquids that consist only of cations and anions. ILs are usually characterised by a reasonable ionic conductivity (similar to most non-aqueous electrolytes). ILs' extremely low vapour pressure is non-volatile, and ILs are highly polar, miscible with certain organic solvents and/or water, and have good solubility with organic and inorganic materials. They are also chemically inert, reusable and can be designed, nonflammable and thermally stable as well.[1–3] ILs is promising and environmentally benign, and have numerous reaction media which are expected to provide an attractive alternative to conventional volatile organic compounds (VOC). Nevertheless, in the last few years, they have become more attractive in other fields, such as catalysis,[4] basic electro-chemical studies of organic and inorganic compounds[5], formation of metal nanostructures,[6] analytical chemistry[7] including sensors,[8] bio-analytical chemistry,[9] and electro-chemical biosensors.[10]

The majority of investigations have concentrated on imidazolium cations with discrete anions, such as BF_4^-, PF_6^- and $(F_3CSO_2)_2N^-$.[11] There are several simulations and experimental studies mainly concerning the structure of imidazolium-based ILs; the main conclusions are that those liquids are micro-biphasic systems composed of polar and non-polar domains.[12] However, the use of these types of ILs includes several disadvantages, such as toxicity and cost, making them somewhat impractical for larger industrial applications, such as metal electroplating, electrodeposition, and bio-catalyses. Therefore, the key challenges in the application research of ILs have been the availability and cost issues. Myriad issues, such as toxicity and availability, will limit ILs' practical uses for larger scale applications of other metals and bio-materials. Although a multitude of recipes has been published to carry out the synthesis of ILs, not all laboratories focused on applied research have the expertise, work practices and equipment necessary to carry out synthesis work due to the complicated synthetic processes that are involved. In addition, to prepare pure, dried ILs, or to execute post-synthesis purification, the steps are often challenging. On the other hand, the commercial availability of some ILs is restricted to small volumes, or the cost of many liquids is still unacceptable for applied engineering research.[13] The physical and chemical properties of ILs can be influenced significantly by small amounts of impurities. The catalytic activity and electro-chemical behaviour is highly dependent on the purity level of the ILs. The quality of ILs has become an important consideration in their use. Commercial producers try to make ILs of the highest quality achievable at reasonable cost. Typical impurities include organic starting materials and other volatiles, halide impurities, other ionic impurities from incomplete metathesis reactions, and water. Analysis and trace analysis of impurities in ILs is still a field of ongoing fundamental research.[14]

During our investigations, we have found that the synthesis and applications of primary and tertiary ammonium halide salts is much less than the information concerning the hydrochloride salts that are related to the preparation

of ILs. For that reason, the concept of hybrids protonation, and the complexation of nitrogen-based organic compounds, have been utilised. From economic and environmental points of view, the protonation of nitrogen-based organic compounds has attracted great attention from a wide range of organic chemists over the last two decades. Altering insoluble nitrogen-based compounds into hydrochloride salts is a common way to make them water- and acid-soluble substances that are usually used in medications. Combinations of hydrochloride salt and complexing agents to form ILs have never been reported before. In this study, we produced protic eutectic ionic liquids (PEILs), a subgroup of the ILs family that is a protic eutectic mixture of hydrochloride salts and complexing agents (hydrogen bond donors like urea or oxalic acids) in a specific molar ratio. PEILs are air and water stable and have the high conductivity needed for electrochemical applications. Here as a part of our study on environmentally friendly ILs synthesis, we would like to report an operationally simple, inexpensive and efficient preparation of novel PEILs. Aminobenzaldehyde, amino acids, hydroxymethyl amine, amino acid thiol side chains and cyclic amide reactants offer an attractive alternative for studying the ability to generate ILs that are cost effective.

In a comparison with the traditional ILs synthesised by metathesis or ion exchange,[15,16] PEILs were prepared by means of protonation and complexation, making them more flexible alternatives to conventional ILs. It was reported[17] that urea and oxalic acid-based ILs complexed with anions including chloride or iodide seem to be promising for the low melting point ILs that incorporate complexing agents. The idea exploited here is using hydrochloric acids as proton-rich electrolytes for proton carrying media. Without a doubt, PEILs are potential candidates for non-volatile ILs based on electrolyte syntheses, since they possess many benefits that traditional ILs, based on imidazolium salts, do not have. Moreover, they are easy to synthesise; the components of the eutectic can be easily mixed and converted to ILs without further purification. Besides, they are very cheap due to the low cost of raw materials. Its most important features, which make it a suitable IL for large-scale applications, are its low cost and ease of preparation as compared to other air- and water-stable ILs based on imidazolium or pyridinium salts. Moreover, as compared to conventional ILs, they share many characteristics; only ionic mixtures, not ionic compounds, are known to be less toxic, air- and moisture-stable, biodegradable and economically viable for large-scale processes. In this study, thermal characterisation conducted by differential scanning calorimetry (DSC) and solubility tests consumed bio-polymer like starch were also studied.

2.   EXPERIMENTAL

2.1   Materials

4-dimethylaminobenzaldehyde, 2-aminoacetic acid, tris(hydroxymethyl)-aminomethane, (2R)-2-amino-3-sulfanyl-propanoic acid and 1-methylpyrrolidin-2-one were supplied by Sigma Aldrich (USA). Hydrochloric acid (HCl) was purchased from R&M Chemicals (fuming ~ 37%). Urea and oxalic acid were also obtained from Sigma Aldrich (USA). All of the chemicals' purity exceeded 99% and the chemicals were used as they were received. The chemical structure of the reactants is shown in Figure 1.

4-dimethylaminobenzaldehyde

2-aminoacetic acid

tris(hydroxymethyl)aminomethane

(2R)-2-amino-3-sulfanyl-propanoic acid
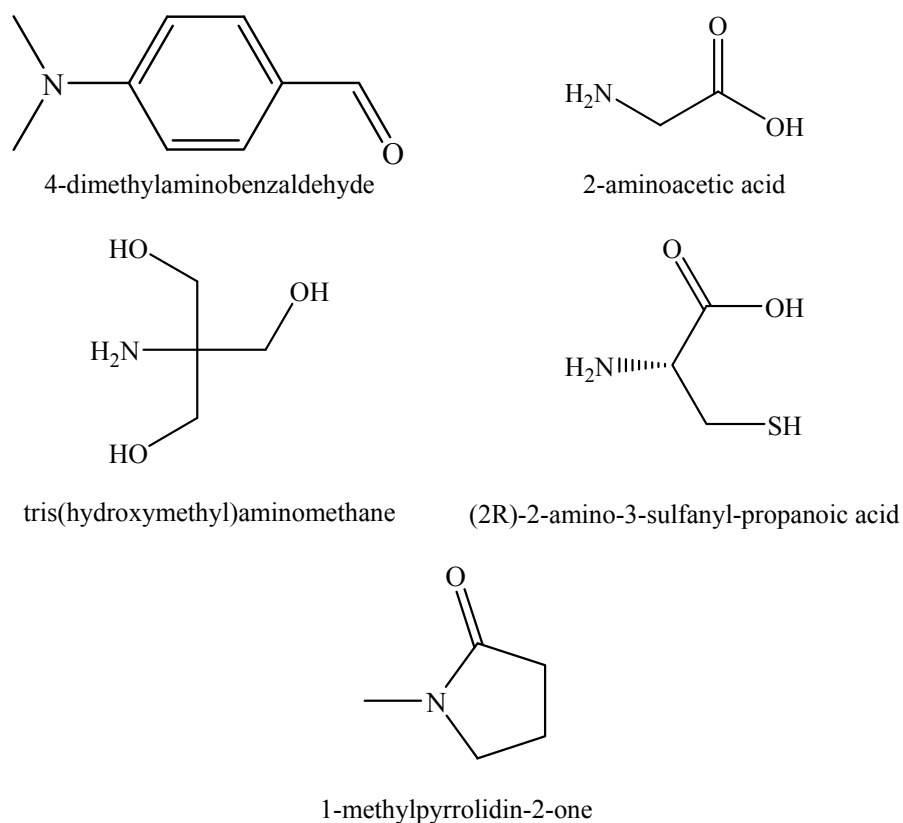
1-methylpyrrolidin-2-one

Figure 1: Reactants used for preparing PEILs.

2.2   Preparation of Hydrochloride Salts

4-dimethylaminobenzaldehyde, 2-aminoacetic acid, tris(hydroxymethyl)-aminomethane, (2R)-2-amino-3-sulfanyl-propanoic acid and 1-methylpyrrolidin-

2-one were dissolved in distilled water and stirred. Equimolar amounts of HCl and the reactant solution were allowed to react during the stirring process for one hr in a rotary evaporator at an ambient temperature, followed by at an elevated temperature (85ºC). Distilled water was then removed by distillation under reduced vacuum pressure. The unreacted HCl was evaporated and any unreacted reactant was removed under a vacuum from the solid, which obtained a yield of over 80%. The hydrochloride salts were then collected and kept dry in a vacuum oven at 85ºC overnight. The products are 4-formyl-N,N-dimethylbenzenaminium chloride (FDBC), carboxymethanaminium chloride (CMAC), 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium chloride (DHPC), (R)-1-carboxy-2-mercaptoethanaminium chloride (CMEC) and 1-methyl-2-oxopyrrolidinium chloride (MOPC) hydrochloride salts. All of the hydrochloride salts were recrystallised from ethanol and then rigorously dried in the vacuum oven and kept under silica gels prior to use. The chemical structure of the synthesised hydrochloride salts is shown in Figure 2.
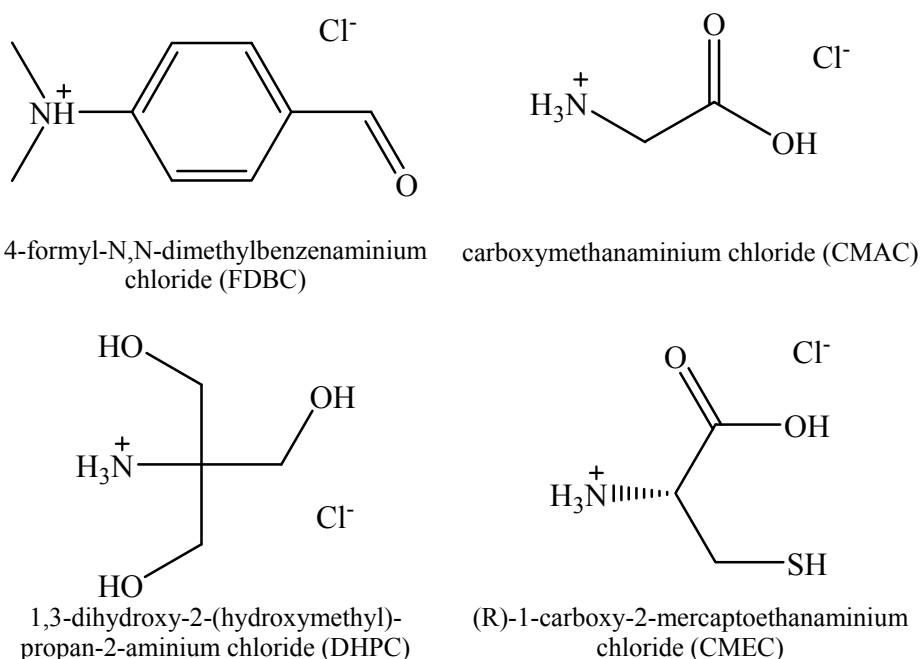

4-formyl-N,N-dimethylbenzenaminium chloride (FDBC)

carboxymethanaminium chloride (CMAC)

1,3-dihydroxy-2-(hydroxymethyl)-propan-2-aminium chloride (DHPC)
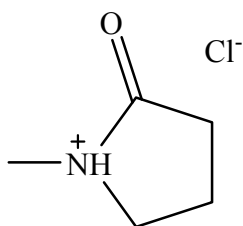

(R)-1-carboxy-2-mercaptoethanaminium chloride (CMEC)

Figure 2: Hydrochloride salts prepared by protonation *(continued on next page)*.

1-methyl-2-oxopyrrolidinium chloride (MOPC)

Figure 2: *(continued).*

2.3   **Preparation of Protic Eutectic Ionic Liquids (PEILs)**

The PEILs were prepared using a typical preparation procedure: intact FDBC, CMAC, DHPC, CMEC or MOPC was placed into a rotary evaporator flask and mixed slowly with urea or oxalic acid at a 0.5, 1, 2 and 3 molar ratio. The mixture was kept under rotating conditions by heating with an elevated temperature (85ºC) under vacuum pressure until a homogeneous liquid appeared. If no liquid appeared, heating and rotating were continued up to an additional period of seven hours. Then, the reaction mixture was dried overnight at 85°C in a vacuum oven to obtain the final product prior to differential scanning calorimetry (DSC) thermal analysis. The resultants, FDBC, CMAC, DHPC, CMEC and MOPC, when complexed with urea acid abbreviated as [FDBC][U], [CMAC][U], [DHPC][U], [CMEC][U], and [MOPC][U] and when complexed with oxalic acid is abbreviated as [FDBC][O], [CMAC][O], [DHPC][O], [CMEC][O] and [MOPC][O]. The PEILs were dried in a vacuum oven prior to use.

2.4   **Characterisation**

DSC analysis was conducted on a Mettler Toledo DSC822[e] apparatus under nitrogen flow using the Software Tools for Academics and Researchers (STAR) analysis software. The samples were tightly sealed in aluminium pans. All of the samples were subjected to the following procedures. The samples were first heated to 100°C to eliminate their thermal history. The experiments were carried out in a temperature range of –60°C to 450ºC with a cooling and heating rate of 10°C/min to obtain the melting point, T_m, which was determined from the DSC thermograms during the programmed reheating steps. The temperatures that are reported from the DSC data are curved peaks; melting points being endothermic upon heating. All of the samples were dried in a vacuum oven for at least 24 hr prior to the DSC measurements.

2.5   Solubility Test

To characterise the capability of PEILs of being able to dissolve organic compounds, especially bio-polymers (such as starch), three types of bio-polymers that is soluble starch, rice starch and sago starch were dissolved into prepared PEILs. The solubility was measured using mixed starches with PEILs in a 100 ml rotavapor flask. The flask was immersed in a water bath at 70ºC and rotated for at least 3 hr. The starch and PEILs were fixed to a 10 wt% of starches, with the rest being PEILs. The solution was observed visually, and, if the solution appeared unsatisfactory, heating and stirring was continued up to 12 hr.

3.   RESULTS AND DISCUSSION

3.1   Physical Appearance

Table 1 shows the appearance profiles of the hydrochloride salts at room temperature (25°C). All of the prepared hydrochloride salts are solid at ambient temperature, corresponding to the physical properties of simple salts. Table 2 shows the appearances of the PEILs, where the numbers represent the molar ratio of the hydrochloride salts and the complexing agent binary system.

Because the hydrochloride salts are composed of organic cations and chloride ions, they appear to form a liquid at elevated temperatures with the appropriate molar ratio of the complexing agent. It seems that the complexation reaction occurred in which urea or oxalic acid completed complexation with the chloride ions. As can also be seen in Table 2, the protic eutectic of hydrochloride salt with a 2:1 molar ratio of urea to oxalic acid content was in the liquid state. However, as the content of the complexing agent reached either less or more than those molar ratios, the solid state appeared. Hydrogen bonding between the chloride ions with the complexing agent causes the liquid state to appear.[17]

Table 1: Appearances of hydrochloride salts at room temperature (25°C).

Hydrochloride salt	Appearance
FDBC	Yellow to green solid
CMAC	Pale green solid
DHPC	White solid
CMEC	White solid
MOPC	Yellow solid

Table 2: Appearance of PEILs with several molar ratio at 85°C.

PEIL	Ratio (complexing agent:PEIL)		Appearance	
	Urea	Oxalic acid	Urea	Oxalic acid
FDBC	0.5:1	0.5:1	Solid	Solid
	1:1	1:1	Solid	Liquid
	2:1	2:1	Liquid	Solid
	3:1	3:1	Solid	Solid
CMAC	0.5:1	0.5:1	Solid	Solid
	1:1	1:1	Solid	Solid
	2:1	2:1	Liquid	Solid
	3:1	3:1	Solid	Solid
DHPC	0.5:1	0.5:1	Solid	Solid
	1:1	1:1	Liquid	Liquid
	2:1	2:1	Liquid	Solid
	3:1	3:1	Solid	Solid
CMEC	0.5:1	0.5:1	Solid	Solid
	1:1	1:1	Liquid	Solid
	2:1	2:1	Liquid	Solid
	3:1	3:1	Solid	Solid
MOPC	0.5:1	0.5:1	Solid	Solid
	1:1	1:1	Solid	Liquid
	2:1	2:1	Liquid	Liquid
	3:1	3:1	Solid	Solid

3.2   DSC Thermal Analysis

DSC is a well known technique which gives an exhaustive overview of the relevant thermal analysis.[18] Table 3 shows the melting points of the reactants that were supplied by Sigma Aldrich MSDS (USA). Table 4 shows the melting points of the complexing agents, which were also supplied by Sigma Aldrich MSDS, which are solid at ambient temperature. The calorimetric data were obtained by heating and cooling the hydrochloride salts sample as shown in Table 5. Each melting point of the DSC traces represents a crystalline melting point for the hydrochloride salts. It can be observed that the melting points of the hydrochloride salts are significantly lower than the melting points of the reactants due to the higher decomposition potential of the reactants substance at high temperatures. Nevertheless, in this study, many of these hydrochloride salts have a melting point above 150°C. Mostly, the nitrogen constituent was protonated with the hydrogen ion so as to produce nitrogen ions bound with the hydrogen itself. In protonation, the nitrogen constituent phenomenon by strong acid neutralises the compound, and it created positive and negative ions that are regarded as protic ILs.[19]

Table 3: Reactant melting points as determined from literature data.

Reactants	Melting point, T_m (°C)
4-dimethylaminobenzaldehyde	72–75[a]
2-aminoacetic acid	240[a]
tris(hydroxymethyl)aminomethane	167–172[a]
(2R)-2-amino-3-sulfanyl-propanoic acid	>240[a]
1-methylpyrrolidin-2-one	−24[a]

Note: [a] obtained from Sigma Aldrich

Table 4: Melting points of complexing agent as determined from literature data.

Complexing agent	Melting point, T_m (°C)
Urea	132–135[b]
oxalic acid	189.5[b]

Note: [b] obtained from Sigma Aldrich

Table 5: Hydrochloride salts melting point as determined from DSC data.

Hydrochloride salt	Melting point, T_m (°C)
FDBC	44.60
CMAC	180.23
DHPC	157.41
CMEC	251.46
MOPC	50.17

The DSC data for the PEILs were taken for appropriate molar ratios of the complexing agent (two for urea and one for oxalic acid) owing to the appearances of the PEILs that, overall, were dilute liquids at 85ºC. All of the melting points corresponding with the peaks of DSC traces are listed in Table 6. It is important to relate the structure of the mixture to the physical properties of the compound; in the hydrochloride salts phase, the Coulomb interactions between cations and anions are generally stronger. As a result, compounds in these structures tend to have higher melting points than those between the atomic cations and anions of the PEILs compound. In the PEIL phase, an eutectic compound forms due to hydrogen bonding interactions between the complexing agent and the anions. Because it consists of nitrogen cations and anions, these structures separate cations from anions owing to the large radius ratios and these structures also provide weak interactions. Therefore, enhanced quantities of nitrogen cations and anions are produced with complex species. The increased stabilisation of the liquid state also decreased the kinetics of the crystallisation process, and, in this system, it leads to the possibility of lower melting points given the low temperature of molten salts.

Table 6:   PEILs melting points as determined from DSC data for 1:2 molar ratio of hydrochloride salt:urea and 1:1 molar ratio of hydrochloride salt:oxalic acid.

PEILs	Melting point, T_m (°C)
[FDBC][U]	39.25
[FDBC][O]	103.10
[CMAC][U]	86.62
[CMAC][O]	164.91
[DHPC][U]	18.72
[DHPC][O]	65.07
[CMEC][U]	61.14
[CMEC][O]	150.20
[MOPC][U]	87.23
[MOPC][O]	−14.08

Note: U = urea, O = oxalic acid

In addition, PEILs' melting points also decrease with the larger, more asymmetric nitrogen cations, in which the highest melting points are observed for the more symmetric nitrogen cations. The highest melting point exists for CMEC, with the primary nitrogen cation that has the thiol side chain. With the thiol side chain, the melting point increases to a value above that observed for the hydrochloride salt. The lower melting point is observed with [MOPC][O] due to the larger size of the cations providing greater degrees of freedom and asymmetry. The hydrochloride salts containing the cyclic cation have lower melting points for the PEILs, as compared to the other primary or tertiary cations investigated. The ring hydrochloride salts display greater ILs, probably due to the presence of the methyl group in one position in the MOPC ring which enhances the asymmetry of the cation.[20] Furthermore, it has been proposed that the anion in the ILs entity is the chloride ions complexed by the hydrogen bond donor that leads to a charge delocalisation, effectively decreasing the melting point.[21]

Apart from that, PEILs show clear endothermic activity, indicating a melting point below 200°C. When a complexing agent was added, the endothermic activity shifted to lower temperatures. When the hydrochloride salts were either DHPC or MOPC, as was appropriate for the complexing agent and the molar ratio, the melting point rapidly shifted to a lower room temperature. In contrast, on complexation with urea or oxalic acid, which increases the molar ratio, no obvious low melting point was observed in this temperature range when the complexing agent content was over two for molar ratio of urea, and one for molar ratio of oxalic acid. The existence of this transparent liquid may indicate that the liquids are homogenous, whereas they are otherwise indicated as heterogeneous. The liquids were found to be homogeneous mixtures of the two components, and precise hydrogen bonding formed through the complexation reaction.

In contrast, the existence of the solid may suggest that the yield is partially distributed despite the crystallisation of the liquids. From this result, the melting point of [DHPC][U] and [MOPC][O] in the complexing agents is different from the melting point of DHPC and MOPC. The DSC results appear to relate to the appearance differences among each resultant liquid. In other words, the highest of the melting points may suggest the existence of strong ion coupling in the mixture. Improved chemical stability for the liquid is possible because of the increased thermodynamic stability of the anion complexes, which are generally held together by strong chemical bonds.[22]

Additionally, the hydrogen groups of the two hydrogen bond donor complexing agents are attached to a relatively more electronegative atom than the chloride ion of the hydrochloride salts, which should favour their complexation. The complexation of hydrochloride salts is driven by a relatively strong hydrogen bond between the chloride ion and the hydrogens in the complexing agent, in particular with the relatively protic ones. When the complexing agent either exceeded or was less than those compositions, crystallisation was achieved, and the efficiencies of forming liquids were lower. However, in the [DHPC][U] and [MOPC][O], by increasing the amount of the complexing agent, compounds that tended to be solid were limited, and only caused the substance to become more viscous. Thus, the optimum composition of the complexing agent is evidently one of the key factors which determine the ideal complexation reaction. For this reason, this study indicated the feasibility of using the urea and oxalic acid as complexing agents for the development of ILs.

3.3   Solubility Test

Recently, ILs have been shown to dissolve and stabilise proteins[23] and to be soluble in cellulose.[24] From Table 7, the solubility test results showed that the low melting points of PEILs were very significant in dissolving the starches, even in a partial state. The results exposed that [FDBC][U] and [DHPC][U] were partially solubilised in the soluble starch (5 wt% starches), but could not be dissolved in the rice starch and the sago starch. [MOPC][O] was able to be fully solubilised in the soluble and rice starches, and partially solubilised in the sago starch. The solubility test also indicated that the presence of heat dramatically improved solubility. Even though the room temperature PEILs could not be dissolved in the cellulose, the [MOPC][O] is a potential solvent for solubilised starch, as compared to common organic solvents.

Table 7: Solubility of starches in PEILs as determined visually.

PEILs	Soluble starch	Rice starch	Sago starch
[FDBC][U]	Partially	No	No
[FDBC][O]	No	No	No
[CMAC][U]	No	No	No
[CMAC][O]	No	No	No
[DHPC][U]	Partially	No	No
[DHPC][O]	No	No	No
[CMEC][U]	No	No	No
[CMEC][O]	No	No	No
[MOPC][U]	No	No	No
[MOPC][O]	Fully	Fully	Partially

4.   CONCLUSION

Five types of nitrogen-based organic compounds—aminobenzaldehyde, amino acid, hydroxymethyl amine, the amino acid thiol side chain and cyclic amide—were used in this study. FDBC, CMAC, DHPC, CMEC, and MOPC were synthesised using HCl to produce hydrochloride salts. Then, either urea or oxalic acid were used as complexing agents to form PEILs.

From the DSC results, [MOPC][O] (MOPC complexed with oxalic acid in a 1:1 molar ratio) with a melting point of −14.08°C, and [DHPC][U] (DHPC complexed with urea in a 1:2 molar ratio) with a melting point of 18.72°C, were considered as room temperature ionic liquids (RTILs). The molar ratios of the complexing agent reveal that a double molar ratio of urea and an equimolar of oxalic acid produced PEILs. PEILs were successfully formed by using combinations of hydrochloride salts and complexing agents. HCl acts as a protonater to produce protic hydrochloride salts. It has been shown that hydrochloride salts could form complexes with hydrogen bond donors (urea or oxalic acid). Based on the dissolution of starch, [MOPC][O] was the best compound to dissolve starch as compared to the others. The appropriate molar ratio of the complexing agents created the proper nitrogen-based organic compounds to form PEILs, further complexing the agents' content, and, thus, the solid appearance were observed. The ILs were successfully produced by protonation and the complexation technique for aminobenzaldehyde, hydroxymethyl amine and cyclic amide systems. The physical and chemical properties of PEILs are congruent to those of the traditional ILs, but the range of structures for PEILs is likely to be different from that of ILs which are constituted only by discrete ions. Hence, this study can be applied economically to large-scale processes for commercial and inexpensive ILs and can therefore be used for industrial application.

5.   ACKNOWLEDGEMENT

6.   REFERENCES

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