KU LEUVEN

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Halogen-free synthesis of 1,3-dialkylimidazolium ionic liquids

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Abstract

Ionic liquids (ILs) are a novel kind of compounds, they are solvents that consist entirely out of ion pairs. Imidazolium rings are popular cations in ionic liquids since they are aromatic and therefore stable cations. Ionic liquids are mildly toxic and have negligible vapor pressure. Therefore, they show great potential as substitutes for volatile and dangerous organic solvents in industrial processes and for toxic catalysts. Some ionic liquids show temperature-dependent miscibility with certain solvents (ideally water), causing them to phase separate or become homogeneous depending on the temperature of the mixture. The solubility of imidazolium ionic liquids can be altered by changing the anion or by changing the amount, length and functional groups of the substituents on the imidazolium cation. In this thesis, a versatile route towards substituted imidazolium compounds from standard molecules: aldehydes, diketones and amines was investigated. This was approached using the imidazole synthesis described in the Arduengo patent and the direct imidazolium synthesis from Zimmerman *et al*. In practice, both syntheses suffered from a severe amount of side-products when enolizable carbonyl compounds were used. Avoiding these products and an optimization of the synthesis resulted in the creation of an efficient platform of 1,3-dialkylimidazolium acetate ionic liquids. From these imidazolium acetate compounds, many other ionic liquids could be prepared using different metathesis strategies. These strategies were tested, introducing the following anions: Tf_2N^- (bis(trifluoromethylsulfonyl)imide), TsO^- (*p*-toluenesulfonate), $DEHP^-$ (bis(2-ethylhexyl)phosphate) and NO_3^- (nitrate). These ionic liquids were thus prepared using two simple and halogen-free synthetic procedures. The solubility of the ionic liquids with water was tested between 0 and 100 °C and one of the ionic liquids showed temperature-dependent miscibility with water: 1,3-dihexylimidazolium nitrate ([HHIM][NO_3]). The cloud point for a 1:1 mixture was determined to be 84.1 °C and the phase diagram was defined. The solubility of the IL in water was measured via quantitative ^{1}H NMR with a 1,4-dioxane standard: 5 wt% and the amount of water dissolved in the IL was 24 wt%. The discovery of the thermomorphic [HHIM][NO_3] is very interesting, since no other thermomorphic nitrate IL was ever reported. This IL can be a promising starting point for future research.

Samenvatting

Ionische vloeistoffen (ILs) zijn vloeistoffen die enkel uit ionen bestaan en een smeltpunt onder de 100 °C hebben. Deze ILs vertonen potentieel in het vervangen van industriële solventen en katalysatoren. Imidazolium ringen zijn populaire kationen voor ILs omdat hun aromaticiteit voor een stabiel kation zorgt. De meest gebruikte zijn 1-alkyl-3-methylimidazolium, dankzij de beschikbaarheid en gemakkelijke alkylatie van N-methylimidazool. In dit onderzoek werd een eenvoudige en veelzijdige synthese van imidazolium ringen met veel substituenten vanuit eenvoudige moleculen onderzocht. Het startpunt was het patent van Arduengo (US 6177575 B1), wat de synthese van imidazolen uit diketonen, aldehyden, amines en ammoniumzouten beschrijft. Deze neutrale imidazolen kunnen daarna gequaterniseerd worden met halo-alkanen, waardoor een IL verkregen wordt. Uitwisseling van het anion verandert de eigenschappen van de IL. Het doel is het synthetiseren van imidazolium ILs met temperatuursafhankelijke mengbaarheid met water, wat betekend dat het verwarmen van een mengsel een homogenisatie (UCST) of fasescheiding (LCST) van de twee stoffen teweegbrengt. Deze thermomorfe eigenschappen zijn gunstig bij extracties en vaak noodzakelijk voor industriële toepasbaarheid.

Het patent omschreef de synthese voor een zeer breed gamma van substituenten, maar het gebruik van enoliseerbare diketonen en aldehyden veroorzaakte veel onafscheidbare nevenproducten. Het gebruik van niet-enoliseerbare reagentia verminderde het aantal mogelijke substituenten drastisch. De compatibele substituenten waren ofwel toxisch (gefluoreerd), niet stabiel of reactief genoeg (quaternaire koolstof) of resulteerden in te hoge smeltpunten (aromatische substituenten). Een synthese met glyoxal, formaldehyde, 1.5 eq. azijnzuur en 2 eq. amine werd uitgevoerd, met als product 1,3-dialkylimidazolium acetaat. Deze acetaat IL werd gesynthetiseerd in een halogeenvrije *one-pot*-reactie en kon geïsoleerd worden via een eenvoudige extractie met di-ethylether. Grote hoeveelheden (± 25 g) van zeven acetaat ILs werden gemaakt, met verschillende substituenten: ethyl, butyl, isobutyl, hexyl, octyl, decyl en 2-ethylhexyl. De opbrengsten waren zeer hoog, al zorgde de toenemende hydrofobiciteit van het product voor lagere opbrengsten na de extractie (94% voor [EEIM][AcO] tot 47 % voor [DDIM][AcO]). Meerdere metatheses werden uitgevoerd, afhankelijk van de zuursterkte werd een zuur of zout van het nieuwe anion gebruikt. Het azijnzuur werd verwijderd via verdamping en de acetaatzouten door neerslag in apolaire solventen. Volgende anionen werden geïntroduceerd: Tf_2N^- (bistriflimide), TsO^- (*p*-toluenesulfonaat), $DEHP^-$ (bis(2-ethylheyl)fosfaat) en NO_3^- (nitraat). Deze ILs werden gemaakt in twee eenvoudige en halogeenvrije stappen, via een imidazolium acetaat platform vanwaar verschillende metatheses uitgevoerd kunnen worden. De oplosbaarheid in water

werd onderzocht tussen 0 en 100 °C om thermomorf gedrag op te sporen. De acetaat ILs waren allen volledig water oplosbaar, de DEHP en bistriflimide ILs waren volledig onoplosbaar. De tosylaat ILs met korte ketens waren oplosbaar, die met langere ketens onoplosbaar. Alle nitraat ILs waren onoplosbaar, uitgezonderd van 1,3-dihexylimidazolium nitraat. Het [HHIM][NO_3]:H_2O 1:1 mengsel had een troebelpunt bij 84.1 °C (UCST) en het volledige fasediagram werd bepaald. Een opmerkelijke ontdekking, aangezien geen enkele thermomorfe nitraat IL in de literatuur beschreven is.

Summary

Ionic liquids are a novel kind of compounds: they consist entirely out of ion pairs and are liquid below 100 °C. Their potential use in replacing solvents or catalysts in industrial processes has caused a lot of interest in ionic liquids (ILs). Imidazolium rings are popular cations for these ionic liquids, since their aromaticity results in a stable cation. The most used imidazolium compounds are 1-alkyl-3-methylimidazolium, due to the easy alkylation of commercially available N-methylimidazole. Imidazolium compounds with more and longer substituents are seldom used in ILs, due to more intensive synthetic procedures. In this project, a facile and versatile route yielding highly substituted imidazolium compounds from standard molecules is explored. The starting point for this synthetic route was the Arduengo patent (US 6177575 B1), which describes the synthesis of imidazoles from a diketone, an aldehyde, an amine and an ammonium salt. The neutral imidazoles can afterwards be quaternized with halo-alkanes resulting in an ionic liquid. Replacing the anion via metatheses, alters the properties of the ionic liquids. The goals is to obtain ILs with temperature dependent miscibility, which means that heating an IL-water mixture will cause homogenization (UCST) or phase separation (LCST) of the two compounds. These thermomorphic properties are beneficial for extractions and IL purification and are often required for industrial applicability.

The patent claimed to be applicable for a wide array of substituents, however, using enolizable diketones and aldehydes in the synthesis resulted in many side products which could not all be separated from the imidazole. Avoiding these enolizable carbonyl compounds limits the amount of substituents drastically. Most of the compatible substituents were either toxic (high fluorination), not reactive or stable enough (highly substituted carbon atoms) or resulted in high melting points (aromatic substituents) of the ILs. A synthesis was performed using glyoxal and formaldehyde, 1.5 eq. of AcOH and two amine eq., this resulted in the direct synthesis of quaternized 1,3-dialkylimidazolium acetate.

These acetate ILs were prepared in an efficient halogen-free and one-pot synthesis and could easily be purified by an extraction with diethyl ether. Large batches of seven different acetate ILs were prepared, with different alkyl substituents: ethyl, butyl, isobutyl, hexyl, octyl, decyl and 2-ethylhexyl. These products could be synthesized with excellent yields, however the extraction with diethyl ether caused the yield to drop, an effect that became more prominent for less hydrophilic ionic liquids (94% for [EEIM][AcO] to 47 % for [DDIM][AcO]). The acetate ILs were used in multiple metatheses, introducing various anions. Depending on the acidity, the acid or salt of the anion was used to remove the acetate. When using acids,

the expelled acetic acid could be easily removed via evaporation on the Schlenk line or extraction. Acetate salts were removed via extraction or precipitation in apolar solvents. Using these techniques, several metatheses were performed, resulting in the introduction of the following anions: TF_2N^- (bis(trifluoromethylsulfonyl)imide), TsO^- (*p*-toluenesulfonate), $DEHP^-$ (bis(2-ethylheyl)phosphate) and NO_3^- (nitrate). These various ILs were thus prepared in two easy and halogen-free (when no halogen anion is used) synthetic steps, with an imidazolium acetate platform from which several metatheses can be performed.

The miscibility of the ionic liquids in water was investigated between 0 °C and 100 °C to detect thermomorphic behavior. All the acetate ILs were completely soluble in water while the bistriflimide and DEHP ILs were all insoluble. The tosylate ILs with shorter alkyl chains (ethyl–isobutyl) were water soluble and with longer alkyl chains (hexyl–2-ethylhexyl) the ILs were insoluble. All nitrate ILs were insoluble in water except for 1,3-dihexylimidazolium nitrate, which showed UCST behavior with a cloud point at 84.1 °C for a $[HHIM][NO_3]$:H_2O 1:1 mixture. The complete cloud point curve was determined using different ratios of IL and water. The mutual solubility of the IL and water phases were determined. After homogenization, the water phase contained 5 wt% IL and the IL phase contained 24 wt% water. The discovery of the thermomorphic $[HHIM][NO_3]$ is quite remarkable. To our knowledge, no nitrate IL was ever reported to show thermomorphic behavior, which can be an interesting starting point for future research.

Thesis outline

Chapter 1 contains a literature study to introduce the reader into the matter of ionic liquids, imidazolium synthesis and the properties of ionic liquids (ILs). The focus lies on the synthesis of substituted imidazoles and the quaternization of these neutral imidazoles into positively charged imidazolium cations. Also the properties of imidazolium ILs will be investigated, including the solubility of these ILs in water.

In chapter 2, the used techniques and their theoretical principles are introduced. All the products were characterized using ^{1}H NMR, ^{13}C NMR, FTIR, CHN analysis and ESI-MS. The water content of the ILs was measured with Karl Fisher titration and the properties were determined using viscosimetry, DSC and TGA experiments.

Chapter 3 is the Health, Safety and Environment (HSE) chapter.

In chapter 4, the performed experiments are discussed in detail, as well as the motives behind these syntheses. The synthesis of the imidazoles and imidazolium compounds is described, as well as the metathesis reactions and metathesis strategies.

Chapter 5 deals with the results and discussion thereof. The syntheses and metatheses are discussed and the properties (melting points and viscosity) of the ILs are evaluated. A special section concerning the miscibility of the ILs with water is included.

To conclude, chapter 6 summarizes the conclusions and achievements of this master thesis. Suggestions for future research are also included.

List of abbreviations

Abbreviation/symbol	Represents
AcO^-	Acetate
AcOH	Acetic acid
AER	Anion exchange resins
BBIM	1,3-Dibutylimidazolium
C_nMIM	1-Alkyl-3-methylimidazolium
cP	Centipoise
DDIM	1,3-Didecylimidazolium
DEHP	Bis(2-ethylhexyl)phosphate
DSC	Differential scanning calorimetry
EEIM	1,3-Diethylimidazolium
EhEhIM	1,3-Di(2-ethylhexyl)imidazolium
ESI-MS	Electrospray ionization mass spectrometry
FTIR	Fourier transform infrared
HHIM	1,3-Dihexylimidazolium
iBiBIM	1,3-Diisobutylimidazolium
IL	Ionic liquid
LCST	Lower critical solution temperature
MsO^-	Methanesulfonate (mesylate)
NMR	Nuclear magnetic resonance
OOIM	1,3-Dioctylimidazolium
ppm / ppb	Parts per million / billion
REEs	Rare-Earth Elements
RTIL	Room temperature ionic liquid
Tf_2N^-	Bis(trifluoromethylsulfonyl)imide (bistriflimide)
TGA	Thermogravimetric analysis
TsO^-	*p*-Toluenesulfonate (tosylate)
TXRF	Total reflection X-ray fluorescence
UCST	Upper critical solution temperature
v	Wave number
wt%	Weight percentage
δ	Chemical shift (ppm)
η	Viscosity (cP)

1 Literature study

1.1 Ionic liquids

1.1.1 Definition

Ionic liquids (ILs) are a special kind of compounds, different definitions and comparisons have been made to describe these rather new structures. The most widely used definition of ionic liquids is: organic liquids that consist entirely out of ions and that are liquid below 100 °C.[1-3] In contrast to molecular solvents like water and dichloromethane, which consist of neutral molecules, ionic liquids consist entirely of cation and anion pairs. Ionic liquids differ from molten salts in their much lower melting temperature, since molten salts are only liquid at extremely high temperatures.

There is a high variety in both cations and anions, and most of the cations can be substituted and customized with a wide array of substituents.[4] This results in huge amounts of possible combinations for ionic liquids, which has been estimated at 10^{18}.[5] Due to this large amount, very specific ionic liquids can be designed for different purposes, each with a specific set of properties, therefore ionic liquids are often referred to as 'designer solvents'.[1]

Even though ionic liquids were discovered in the beginning of the 20th century, it is only in the last couple of decades that they became of high interest, due to their potential to replace molecular solvents and serve as catalysts. Due to the negligible vapor pressure and generally low toxicity of ionic liquids, their impact on the environment is drastically lower compared to molecular solvents, which are often volatile, flammable and toxic.[1,6] Ionic liquids show excellent properties for their use as solvents: they are liquid over a wide temperature range, show high solvating behavior while being weakly coordinating and have a negligible vapor pressure.[1,7-10] These environmentally friendly and tunable properties of ionic liquids also make them ideal homogeneous catalysts, especially biocatalysts, where the toxic nature of conventional catalysts is a major disadvantage.[11]

1.1.2 History of ILs

The synthesis of ethylammonium nitrate ($[EtNH_3][NO_3]$) is regarded as the first event in ionic liquid chemistry. Walden *et al*. synthesized ethylammonium nitrate by adding nitric acid to ethylamine in 1914.[12,13] This specific synthesis was carried out with the sole purpose of preparing ethylammonium nitrate with regard to its ionic properties. Therefore it is regarded as the first ionic liquid synthesis.

First-generation.

The interest in ionic liquids however, only emerged later on, around 1980, with the synthesis of the so called 'first-generation ionic liquids'.[11] These ionic liquids were composed of simple cations: 1,3-dialkylimidazolium and *N*-alkylpyridinium, combined with anions like chloroaluminate and, to a lesser extent, different metal halide anions. The first ionic liquids were made by mixing aluminum(III) chloride with 1,3-dialkylimidazolium and *N*-alkylpyridinium chloride, the most popular of which was the 1-ethyl-3-methylimidazolium chloroaluminate.[6,14] These first-generation ILs were popular due to the fact that they were liquid at room temperature and rather easy to synthesize, resulting in a large amount of research on ionic liquids. Nevertheless, there were some important drawbacks since the anions: chloroaluminate and metal halide anions are toxic and reactive with water. Therefore they had to be handled under inert atmosphere and could not be tested in any system that contained water or oxygen.[3] Regardless, they invoked a lot of interest in ionic liquids and resulted in studies towards air-stable ionic liquids.

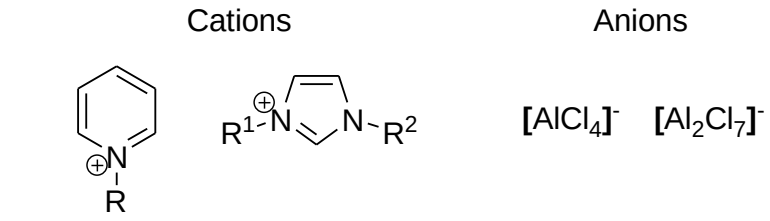
Second-generation

The second-generation ionic liquids tackled the problems regarding moisture and air sensitivity of the previous generation by changing the anions.[11] The new anions had to be environmentally stable while at the same time still result in low temperature ionic liquids. Anions fulfilling these requirements are: halides, tetrafluoroborate ($[BF_4]^-$), nitrate, sulfate, acetate, triflate, mesylate, etc.[11,15] Later on, more apolar anions were also designed to prepare hydrophobic ionic liquids: bis(trifluoromethylsulfonyl)imide ($[Tf_2N]^-$) and hexafluorophosphate ($[PF_6]^-$). Next to the existing cations (1,3-dialkylimidazolium and *N*-alkylpyridinium), ammonium and phosphonium were added. These discoveries led to a generation of air and moisture stable ionic liquids which caused a lot of interest in several fields towards different applications. The main drawbacks of these ionic liquids are the toxicity and cost of several starting products, especially when dealing with fluorinated anions.

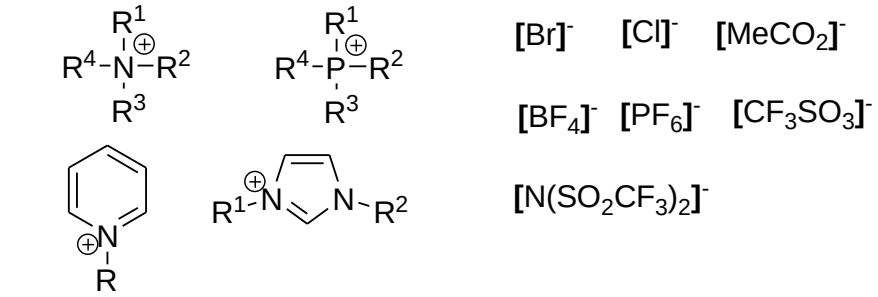
Third-generation.

The third-generation ionic liquids were designed to solve the main problems of the second generation: high cost and toxicity. Most of them are also designed towards specific applications including catalysis or solvents. The new anions are naturally occurring moieties like: saccharinate, amino acids, alkyl phosphates and alkyl sulfates. The new cations are: choline and betaine.[11,15] These ionic liquids are much cheaper and less toxic since most of them are naturally occurring compounds, the fact that they are biodegradable lowers their environmental impact even further.[11] Figure 1 lists an overview of the different ionic liquid generations and their most important components.

First generation:



Second generation:



Third generation:

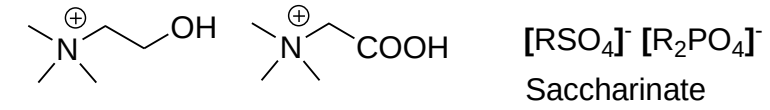


Figure 1: Overview of IL generations and main components.[15]

1.2 Imidazoles

1.2.1 Aromaticity

An imidazole ring is a five-membered aromatic ring containing two nitrogen atoms: in the 1- and 3-position (Figure 2). The imidazole molecule is aromatic due to the six π-electrons delocalized over the ring: two electron pairs from the double bonds and the third electron pair is the lone pair of the first nitrogen atom. Also the nitrogen atom in the 3-position contains a lone pair, but it does not contribute to the aromatic structure since it is located in an sp^2 orbital standing perpendicular to the π -conjugation.

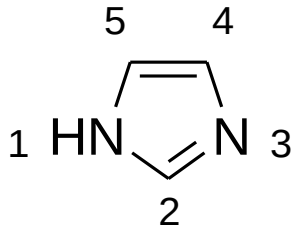
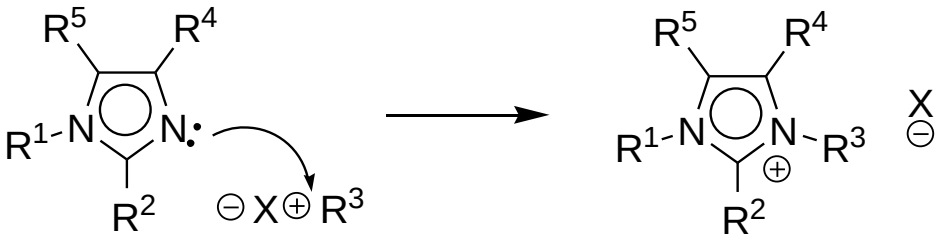


Figure 2: Structure of imidazole.

Since an IL consists solely of ions, a neutral imidazole cannot be a part of it. The charged cationic species of an imidazole ring is called imidazolium, which is used in ionic liquids. Imidazolium is most commonly prepared via quaternization of an imidazole ring using an alkyl chain with a good leaving group such as: chloride, bromide, tosylate, etc.[7,16] The lone pair on the nitrogen atom attacks the electrophilic alkyl chain, the aromaticity is retained since the lone pair forming the new bond was not part of the aromatic structure (Scheme 1). This persistence of the aromaticity causes the stability of the imidazolium cation and thus making it ideal for ionic liquids. Moreover, the positive charge is delocalized causing a decrease of the melting point due to a lower interaction with the anion.



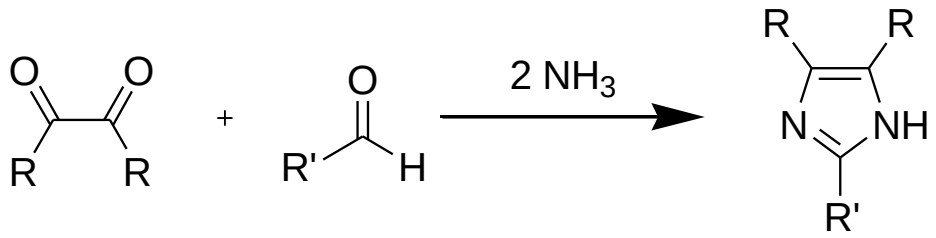
Scheme 1: Retention of aromaticity after quaternization of imidazoles.

The anionic leaving group stays bound to the imidazolium to ensure electronic neutrality, the anion can be exchanged with other anions by various mechanisms: metathesis reactions, anion exchange resins, etc.[17,18] Some syntheses directly prepare the quaternized imidazolium from basic molecules (not imidazole) and will be discussed later in section 1.3.3.[19,20]

1.2.2 Synthesis

Debus-Radziszewski method

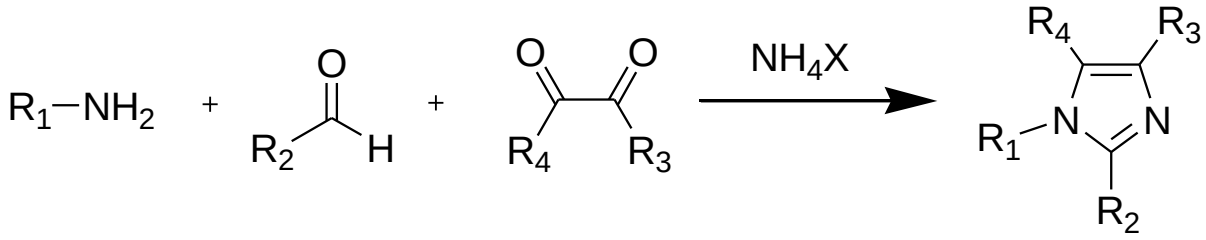
The oldest synthetic route to obtain imidazole is the Debus-Radziszewski method and was first described in 1858: a glyoxal molecule reacts with formaldehyde and two ammonia equivalents to form an imidazole ring.[21] This method works for other diketones and aldehydes as well and results in 2,4,5-trisubstituted imidazole rings (Scheme 2). The synthesis is described to be valid for any alkyl, aryl, or functionalized substituents as long as the functional groups do not interfere in the reaction. However, the Debus-Radziszewski method is mostly used with aromatic substituents. An example of this approach is the synthesis of lophine (2,4,5-triphenylimidazole) by Radziszewski.[22]



Scheme 2: Debus-Radziszewski method for making imidazole rings.[21]

Modified Debus-Radziszewski method

An improved version of the Debus-Radziszewski method is the modified Debus-Radziszewski method (Scheme 3) in which a tetrasubstituted imidazole ring is formed.[2] In this modification, one of the ammonia equivalents is replaced with an amine, this results in an extra substituent in the final imidazole product. An acid is added as a catalyst. To limit the amount of reagents and thus simplify the reaction procedure, the ammonia and acid are mostly added as one compound: an ammonium salt.



Scheme 3: Modified Debus-Radziszewski synthesis.[2]

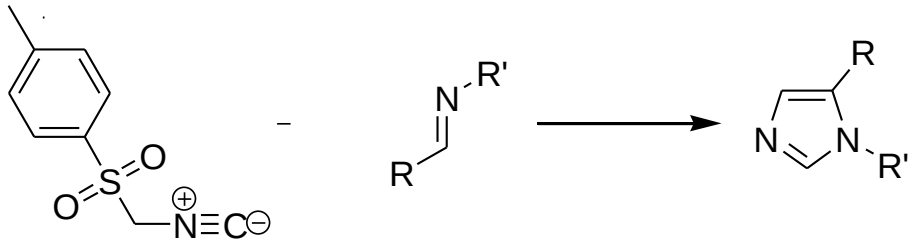
The reaction couples all five functionalities: primary amine, ammonium and three carbonyl groups, into an imidazole ring with four side chains. These side chains however, have some limitations. First of all, the side chains should not contain any functional groups which can react with the amines or carbonyl functions or which may interfere in the reaction. Also no selectivity is observed in the implementation of the diketone substituents, resulting in a mixture of imidazole rings with mirrored substitution of the diketone substituents: R_3 and R_4. This problem can easily be avoided by using symmetric diketone compounds with identical substituents, now the reaction yields only one imidazole compound.

This synthetic method for producing substituted imidazoles was patented by Arduengo *et al*.[2] The patent describes the synthesis to be valid for substituted hydrocarbyl substituents.

Van Leusen synthesis:

The Van Leusen imidazole synthesis is based on the special 'TosMIC' molecule. TosMIC or: *p*-toluenesulfonylmethyl isocyanide is a functional end group and consists of a tosylate group coupled to isocyanide.[23] This compound can be used in the synthesis of 5-membered

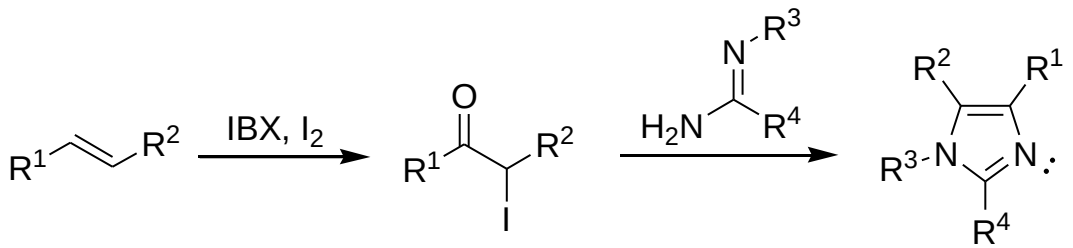
heterocyclic compounds including pyrroles, oxazoles and imidazoles.[24] TosMIC reacts with unsaturated bonds to form heterocyclic compounds (Scheme 4), when an imine is used, the product will be an imidazole. If TosMIC would react with carbonyl or alkene derivatives, oxazole and pyrrole will be formed respectively. Therefore, one must not use substituents on the imine which contain any of these functional groups or any other unsaturated bond. Not many imines are commercially available but they can be synthesized from the corresponding aldehyde and amine.[23] Since it is not possible to use substituents bearing unsaturated bonds, this method for making imidazoles is not favorable since many functional groups contain unsaturated bonds or need a precursor which contain double bonds. An additional disadvantage is the high price of the TosMIC reagent.



Scheme 4: Reaction of TosMIC with imine to form imidazole.[24]

Hantzsch synthesis

The Hantzsch synthesis is method for the preparation of substituted pyridines.[25] Many modifications of this synthesis exist, yielding other aromatic and nitrogen containing structures like imidazoles and thiazoles.[26] The regioselective synthesis of imidazoles can be achieved by using a α-iodoketone, which can be synthesized from an alkene. The alkene is treated with *o*-iodobenzoic acid (IBX) and molecular iodine (I_2) which generate hypoiodous acid (IOH). This *in situ* generated hypoiodous acid generates the α-iodoketone from the alkene.[27] By addition of an amidine, imidazole is formed, which is regioselective regarding the R^1, R^2 and R^3 substituents as a result of using an α-iodoketone instead of diketones.[26]



Scheme 5: Regioselective (Hantzsch) imidazole synthesis using α-iodoketones.[26]

1.3 Imidazolium

Imidazolium compounds can be made in two different ways: the quaternization of imidazoles (commercial or synthesized) or the direct synthesis of imidazolium cations.[20,28-30] The quaternization has the advantage of a higher possible variety in substituents, while the direct synthesis requires less synthetic steps.

1.3.1 Protonation of imidazoles

The pK_a of protonated imidazoles is roughly 7, so using strong acids results in an easy protonation of imidazoles (Figure 3).[31] Using the acid corresponding to the desired anion, a specific IL can be synthesized.

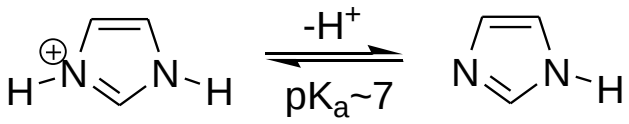


Figure 3: Protonation of imidazoles.

However, this way of preparing ionic liquids is not popular due to this rather low pK_a, which is not beneficial since many products can deprotonate the imidazolium, resulting in the destruction of the ionic liquid. Also, the easy quaternization of the commercially available N-methylimidazole offers a much better alternative for preparing imidazolium ionic liquids compared to simply protonating imidazoles.

1.3.2 Quaternization of imidazoles

Imidazoles can be easily quaternized using haloalkanes (e.g. MeI, chlorohexane,…) as described in Scheme 1. Both the imidazole and the haloalkane are dissolved in a suitable solvent, mostly acetonitrile or dimethylformamide (DMF) and refluxed for the required amount of time. [28,29,32] The choice of haloalkane depends on several factors: the substituent, the reactivity of the imidazole and the desired anion. Depending on the substituent that needs to be placed on the imidazole, the available haloalkanes are selected. If high reactivity is required, iodides and bromides are preferred. If the reactivity is already high enough, due to certain substituents on the imidazole or haloalkane, chlorides can be used as well. The halogen leaving group will form the anion of the imidazolium ionic liquid, this can be an extra criterion with the eye on future metatheses. A polar aprotic solvent is used to promote the S_N2 reaction. When the used products are less reactive and thus high temperatures are required, a solvent with a high boiling point is needed.[16,28,29]

The ease and popularity of this quaternization reaction is represented by the huge amount of 1-alkyl-3-methylimidazolium (C_nMIM) cations, some examples are displayed in Figure 4.[33,34]

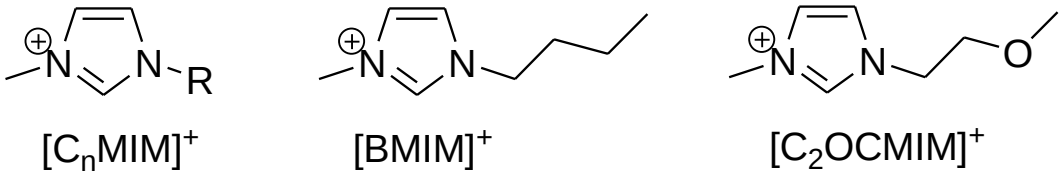
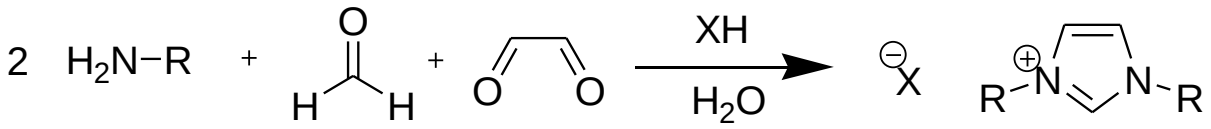


Figure 4: Examples of $[C_nMIM]^+$ cations: the universal 1-alkyl-3-methylimidazolium, 1-butyl-3-methylimidazolium and 1-(2-methoxyethyl)-3-methylimidazolium.[33]

This large variety of these imidazolium compounds originates from the commercial availability of N-methylimidazole and easy and versatile alkylation by various reagents. [20,29] The substituents are not limited to simple alkanes, many functionalities like oligoethers and aromatic structures can be introduced as well.[8,12,34-40]

1.3.3 Direct imidazolium synthesis

The direct synthesis of imidazolium compounds can be performed as well, this is done by replacing the ammonium salt by another amine equivalent. This synthesis was described by Zimmerman *et al.*, glyoxal and formaldehyde are used as aldehyde and diketone respectively in the reaction with the two amine equivalents (Scheme 6).[20,41] The acid used in the synthesis does not act as a catalyst anymore, since the conjugate base will become the anion required by the imidazolium cation, forming an actual ionic liquid.



Scheme 6: Direct synthesis of quaternized 1,3-dialkylimidazolium ionic liquids.[20,23]

Only one amine can be used since using a mixture of amines would result in a statistical mixture of three different imidazolium salts. This way, homosubstituted 1,3-dialkylimidazolium is formed, losing the control of one substituent. A huge advantage however, is that the resulting synthesis directly yields quaternized imidazolium ionic liquids in one reaction, which on top of that can be performed halogen-free if the correct acid is chosen.[20]

1.4 Metatheses

The metathesis or 'anion metathesis' is the synthetic procedure in which the current anion of an IL is exchanged with a new anion. This results in a new IL with different characteristics

and other properties regarding physical appearance or chemical applications. This metathesis can be performed in several ways.

1.4.1 Anion alteration

The oldest one is the addition of a Lewis acid ($AlCl_3$) to existing chloride ionic liquids and is in fact not a metathesis.[3] It is the chemical alteration of the anion but without a real exchange of the anion. It is listed in this chapter since it is an alteration of the anion with the intent of changing the properties of the ionic liquid. The Lewis acid ($AlCl_3$) is added to the halide salt ([EMIM][Cl]), resulting in a new ionic liquid. The new anion is dependent on the ratio of Lewis acid added, as shown in Scheme 7.[3]

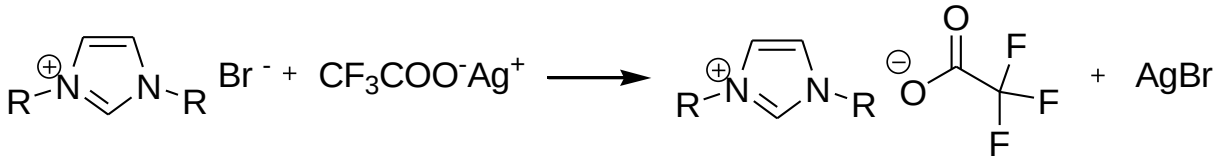
$$[EMIM][Cl] + AlCl_3 \rightleftharpoons [EMIM]^+[AlCl_4]^-$$

$$[EMIM]^+[AlCl_4]^- + n\ AlCl_3 \rightleftharpoons [EMIM]^+[Al_{n+1}Cl_{3n+4}]^-$$

Scheme 7: Anion modification by addition of a Lewis acid to a halide salt.[3]

1.4.2 Anion metatheses

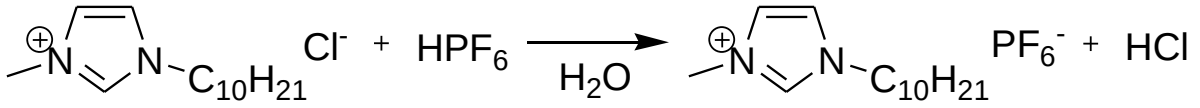
Later on, actual metathesis reactions were performed which used salts of the new anion in order to replace the anion of the ionic liquid.[3,42] This was done by using silver salts to replace the halide anion of imidazolium ionic liquids. If the synthesis was performed in aqueous medium or in a polar solvent, the very low solubility of silver halide salts (AgX) allowed for the isolation of the new ionic liquid.[3] This synthetic strategy is visualized in Scheme 8.[42]



Scheme 8: Metathesis reaction using silver salts to replace halogen anions.[42]

The elimination of the inorganic halide salts is not always as complete as expected. The high solvating power of ionic liquids makes it difficult to completely remove certain halide salts via extraction. After metathesis reactions or purification, the halide content can be measured using a TXRF, indicating any necessity of an extra purification step. Care must be taken since the yield can decrease significantly when too many extraction steps are required. Therefore other exchange methods might be more interesting in some cases, like metatheses using acids or anion exchange resins.[17]

Acids can also be used to exchange the anions of ionic liquids. If sufficiently strong acids are used, the protonation of the starting anion is complete, resulting in a new and pure ionic liquid, after removal of the newly formed acid. Many fluorinated acids can be introduced with this strategy, since many of them have low pK_a values: hydrogen bistriflimide (superacid), trifluoromethanesulfonic acid, (pK_a = -12), tetrafluoroboric acid (pK_a = -0.4), hexafluorophosphoric acid (pK_a = -8), etc.[43] An example is the synthesis of 3-decyl-1-methylimidazolium hexafluorophosphate from its chloride precursor (Scheme 9), described by Gordon *et al*.[44]



Scheme 9: Synthesis of 3-decyl-1-methylimidazolium hexafluorophosphate.[44]

Hofmeister series

When performing metathesis reactions in water, the Hofmeister series is a useful instrument in predicting the possibility and completeness of metathesis reactions.[45,46] The Hofmeister series is an experimentally observed order for cations and anions which ranks them according to their tendency to promote or oppose the dissolution of compounds. This order can be used in the metatheses of ionic liquids as well. When an ionic liquid is dissolved in water and another salt is added, the completeness of the anion exchange reaction will depend on the position of the two anions in the Hofmeister series.[46,47] When the new anion is placed higher in the series (more hydrophobic), the metathesis will be successful with increasing efficiency for higher placed anions. If the anion is placed lower in the series, the metathesis reaction will be incomplete or even non-existent.

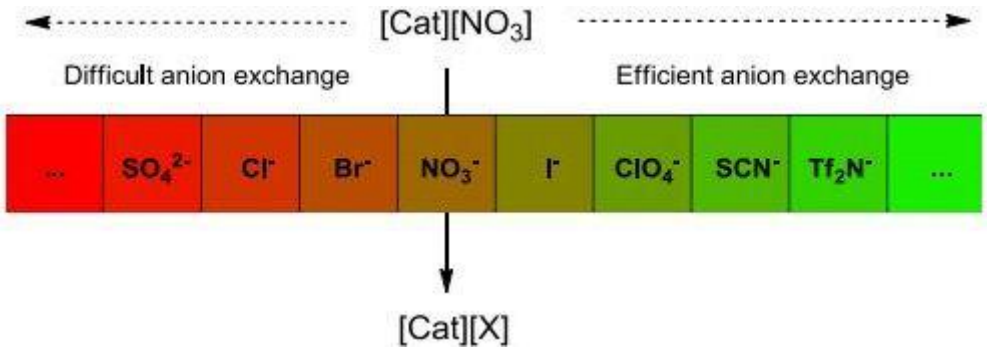


Figure 5: Influence of the Hofmeister series on metathesis reactions for ILs.[47]

1.4.3 Anion exchange resins (AER)

Anion exchange resins are columns packed with a material, often polymers, to which immobilized cations are bound. To retain electrical neutrality, an equal amount of anions

must be present in the cationic matrix. These anions are not immobilized and can therefore be exchanged with products added to the column, hence: 'anion exchange' columns. Opposite columns exist as well: cation exchange resins, in which the anion instead of the cation is immobilized, but these materials are obviously not interesting for replacing the anions of ionic liquids.

A popular AER for imidazolium ionic liquids is Amberlite®, which is composed of immobilized quaternary ammonium cations and hydroxide anions.[17] These hydroxide anions can be treated with other salts or acids in order to equip the column with desired anions, these can then later be introduced in the ionic liquid. A versatile procedure for the anion exchange of 1-butyl-3-methylimidazolium iodide and bromide ([BMIM][I] and [BMIM][Br]) was investigated by Dinarès *et al*.[18] The AER was treated with acids of the new anions, resulting in water formation and the introduction of the new anion on the column. The same strategy was performed with ammonium salts of the new anion instead of the acid, resulting in the formation of ammonium hydroxide, which is mostly dissociated into ammonia and water. The use of lithium or potassium salts is not possible since LiOH and KOH are strong bases and OH^- displaces the anion on the resin. An overview is given in Figure 6, the acid route is more effective for organic anions (MsO^-, BzO^-, BF_4^-,…) and the ammonium route for inorganic anions (X^-, HSO_4^-,…).

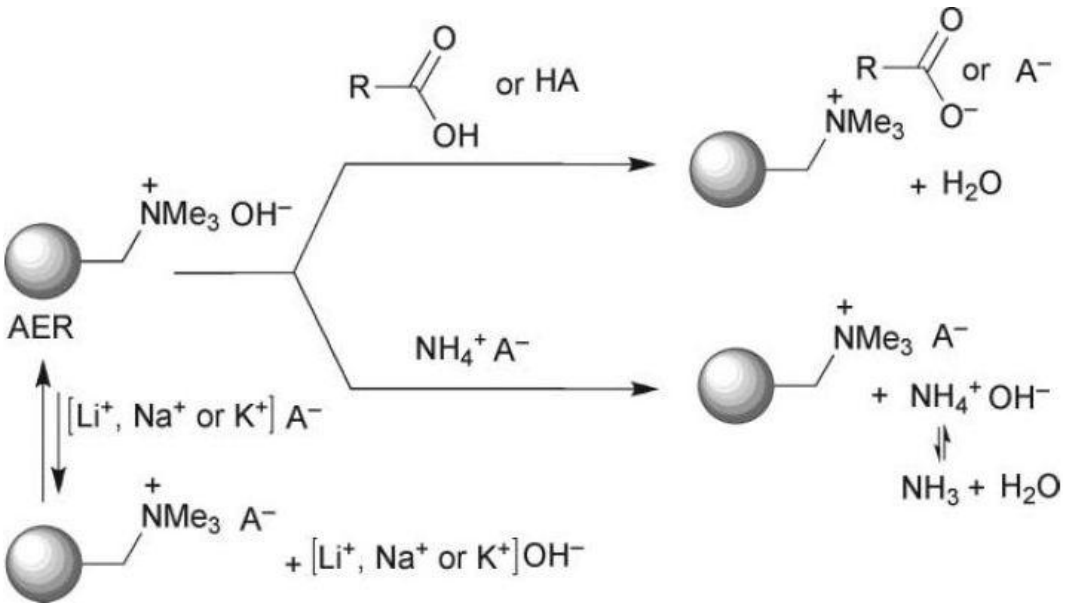


Figure 6: Loading of AER with new anions in Amberlite® resins.[18]

These 'activated' columns are then used to replace the bromide and iodide from the $[BMIM]^+$ ionic liquids. This is done by dissolving the ionic liquids in methanol and pouring them over the column, the eluate can then simply be gathered at the bottom of the column and the new

ionic liquids are isolated by removal of the solvent. This technique can be used to replace a wide variety of anions, as displayed in Figure 7.[18]

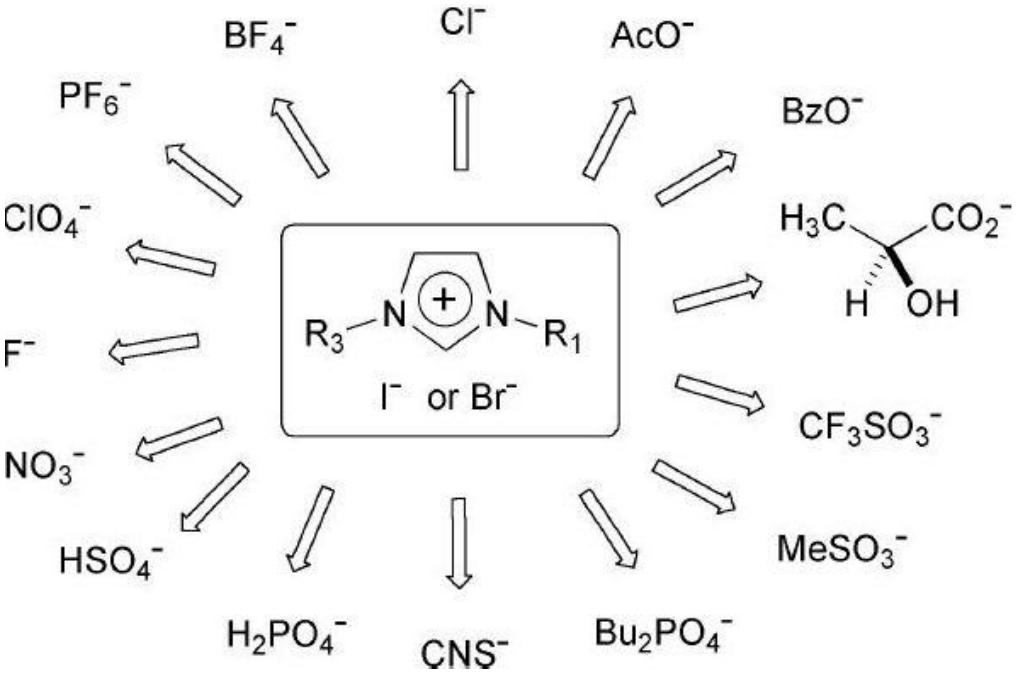


Figure 7: Possible metatheses for [BMIM][I/Br] using Amberlite® AER.[18]

Some disadvantages of anion exchange resins are that they have rather limited capacities, take a lot of time due to long elution times and are rather expensive.

1.5 Properties of imidazolium ionic liquids

The effect of the anion and substituents on the imidazolium cation can be really significant. However the very limited amount of highly functionalized imidazolium ionic liquids makes it difficult to determine the effect of all these substituents on the properties of the imidazolium ionic liquids. There has been extensive research on 1-alkyl-3-methylimidazolium ionic liquids ([C_nMIM][X]), due to their easy synthesis for many different substituents.[8,12,34-40] These data can be used to determine the effect of varying one substituent on the imidazolium cation. The effects of highly substituted imidazolium cations can therefore be derived from the combined effects of all the substituents on the cation.

1.5.1 Vapor pressure

As already mentioned, ionic liquids show no or negligible vapor pressure.[3,9,10] This is a great contribution to their 'green character', and important in their potential to replace the current volatile, flammable and toxic organic solvents. The vapor pressure of some ionic liquids was examined by Bier *et al*., as indicated in Figure 8.[10] Besides the bistriflimide and dicyanamide (DCA) ionic liquids, the vapor pressure of some common solvents (water and benzene) and

inorganic fused salts was measured. Figure 8 shows a logarithmic plot of the vapor pressure of these compounds as a function of the temperature, it is clear that the vapor pressure of the RTIL is virtually non-existent, especially at moderate temperatures.

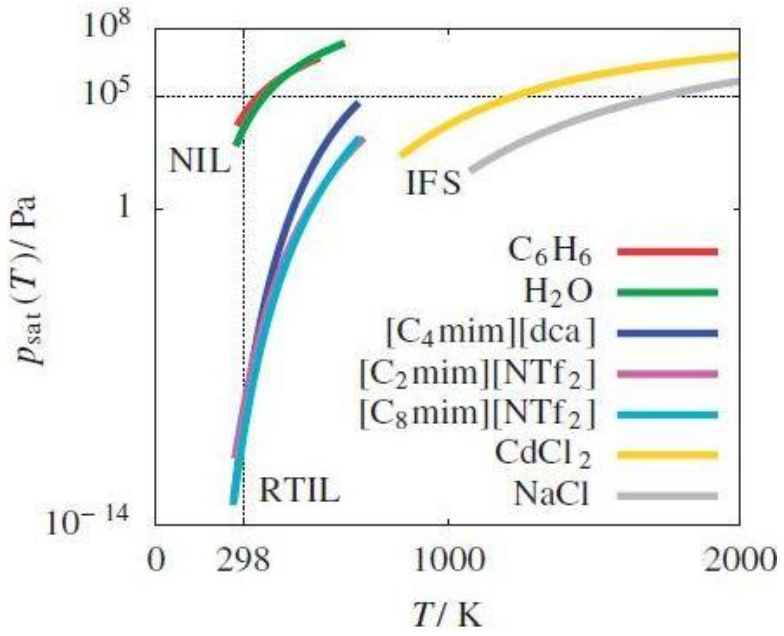


Figure 8: Vapor pressure of some room temperature ionic liquids (RTIL), non-ionic liquids (NIL) and inorganic fused salts (IFS) and their temperature dependence.[10]

1.5.2 Melting point

The melting temperatures of highly substituted imidazolium compounds have not been studied, although there have been extensive studies on the more available $[C_nMIM]^+$ ILs, which can predict the effect of varying a single substituent on the melting point.[34,48,49] However, these observations are not always easy due to the high degree of supercooling with many of these ionic liquids.[49] These studies have shown that various effects of the alkyl chain influence the melting temperature: alkyl chain length, degree of branching and symmetry of the substituent.[34,48,49] The effect of the alkyl chain length on the T_m as described by Holbrey *et al*. is displayed in Figure 9.

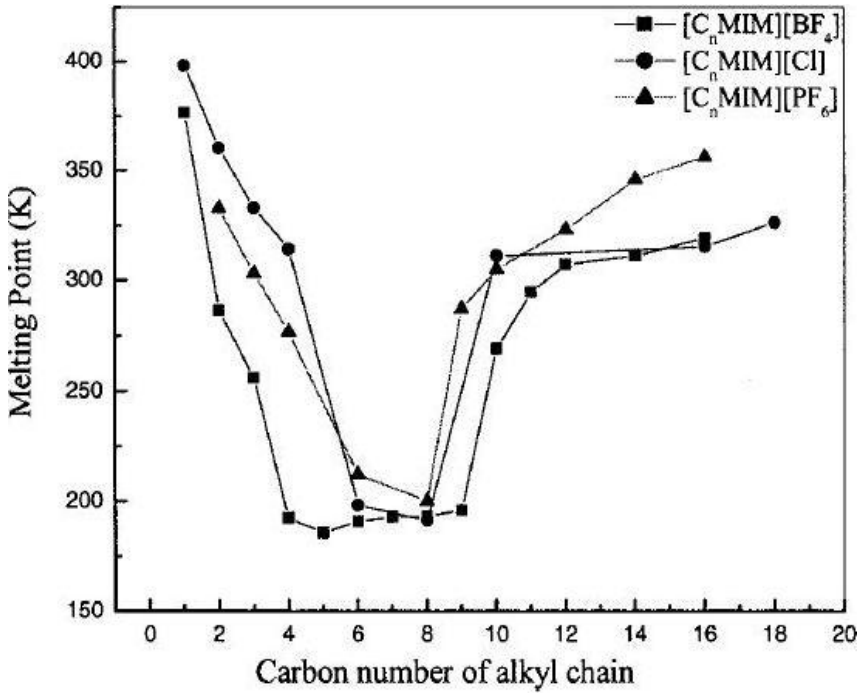


Figure 9: Effect of the alkyl chain length on the melting point of [C_nMIM][X] ionic liquids.[33]

For shorter alkyl chains (2 < n < 5), the melting point decreases due to an increase in the degrees of freedom.[49] For longer alkyl chain lengths (9 < n), the melting point increases again, this is a result of the increasing inter-cation interactions by Van der Waals forces. This increase stabilizes and slowly vanishes for even longer alkyl chains (12 < n < 18).[34] If the substituents are branched, the melting point will increase due to a smaller degree of free rotation volume causing a more efficient crystal packing.[3,48] The melting points of ILs will increase with increasing symmetry, this can be achieved in two ways: the alkyl substituents on the cation can be identical or the substituents themselves are symmetrical. This increase in symmetry will result in a more efficient crystal packing and therefore a higher melting temperature.[3,49]

The effect of the anion on the melting point is not as straightforward, although the largest influence is the strength of the cation-anion interaction.[48] This strength is mostly influenced by the charge distribution, the hydrogen bonding capacities of the anions and their size.[3] The charge distribution will influence the extent of the cation-anion attraction, which increases when there is a low charge distribution across the anion. This results in higher Coulombic attraction and therefore higher melting points.[48] An additional effect is the size of the anion, the smaller the anion, the better it can be implemented in the crystal lattice.[3] The capacity of the anion to engage in hydrogen bonding is directly related to the melting point, these additional attractive interactions will result in a higher cation-anion attraction and therefore

even higher melting points. The replacement of hydrogen atoms by fluorinated atoms diminishes the hydrogen bonding capacities, resulting in lower melting points, this is why fluorinated anions are often used to obtain RTILs.[48] The low melting point of bistriflimide ($[N(SO_2CF_3)_2]^-$) ionic liquids can therefore be explained: it is a large anion with an excellent charge distribution containing a large number of fluorine atoms.

1.5.3 Viscosity

A downside of ionic liquids compared to organic solvents is their high viscosity. The viscosity of toluene at RT is only 0.6 cP, while the viscosity of [BMIM][BF_4] is 448 cP and even 7826 cP for [HMIM][Cl] at room temperature.[50,51] This high viscosity of ionic liquids is a drawback for their use in industrial processes, since a high viscosity is accompanied by difficult stirring and slow heat and mass transfer. Knowledge of the viscosity and the parameters influencing the viscosity of ionic liquids are therefore essential.

Anion and cation

The effect on the viscosity of the substituents on the imidazolium cation and the anion are rather similar compared to the melting point, however there are important differences. Besides the effect of the anion and cation, the temperature also has a large influence on the viscosity of ionic liquids, which tends to decrease significantly with increasing temperature.[52]

Comparable to the melting points, the viscosity of ILs increases with increasing interaction between the anions and cations. On the other hand, the size of the ions has a different effect on the viscosity compared to the melting point. Where large anions and cations resulted in low melting temperature due to inefficient stacking, they increase the viscosity of imidazolium ionic liquids. Due to this effect, the viscosity increases continuously with increasing alkyl chain length, unlike the melting point, which showed a decrease for the shorter alkyl substituents (see Figure 9). The sole exception to this trend is the 1,3-dimethylimidazolium cation, which shows higher viscosities compared to the 1-ethyl-3-methylimidazolium cation.[40,50] The effect of the anion depends on its charge delocalization, size and rigidity. Poorly delocalized anions induce strong anion-cation interactions, resulting in high viscosities. Obviously, the viscosities increase when using large and rigid anions.

In general, increasing the size, rigidity and charge density of cations and anions results in larger viscosities.

Temperature dependence

Since many industrial processes are conducted at elevated temperatures, it is necessary to investigate the temperature response of the viscosity.

The viscosity of ionic liquids decreases with increasing temperature, this effect has been extensively investigated by several research groups.[35,40,52] The viscosity not only decreases with rising temperature, also the existing viscosity differences between ionic liquids decrease. This is shown in Figure 10, displaying the logarithmic plot of η as a function of T^{-1} for several bistriflimide ionic liquids. The plot confirms the order of viscosity for $[C_nMIM]^+$ cations with increasing alkyl chain length and demonstrates that ionic liquids with lower viscosities show a lesser decrease upon heating compared to more viscous ionic liquids.

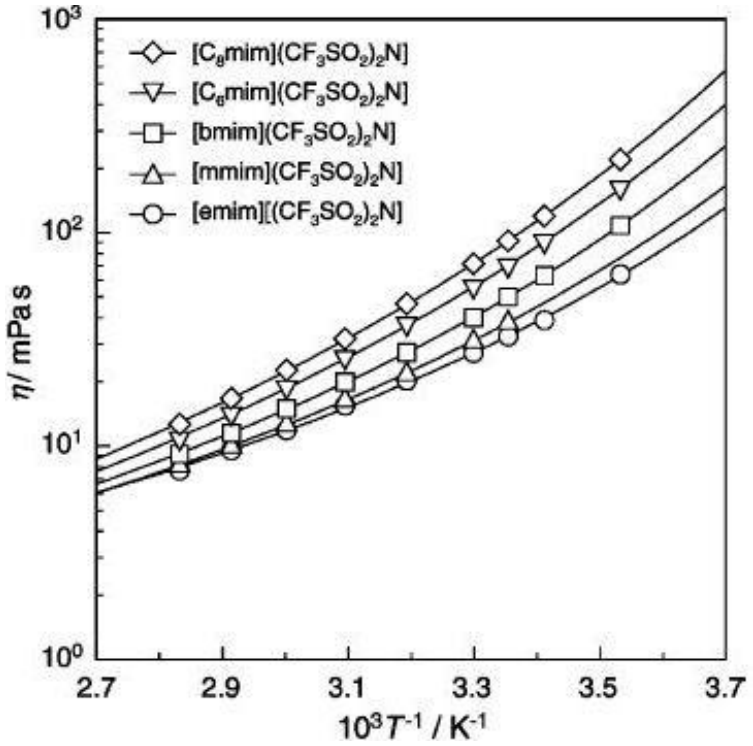


Figure 10: Temperature-dependent viscosity of certain $[C_nMIM][Tf_2N]$ ionic liquids.[40]

1.6 Temperature-dependent miscibility of imidazolium ionic liquids with water

1.6.1 Introduction

The use of ionic liquids as extractants in other non-ionic solvents is an increasing field of interest. If the ionic liquids can be used in a combination with water, two non-toxic compounds can lead to successful extractions.[1] However, ionic liquids are highly viscous, which limits their efficiency in dynamic properties regarding mass and heat transfer and results in intensive stirring processes.[50,51] These problems can be avoided if the ionic liquids form a homogeneous phase with the water solution. However, this eliminates the possible separation of the IL and the water, since they do not form a biphasic mixture. Using

thermomorphic ionic liquids combines the advantages and eliminates the disadvantages of the two systems (homogeneous and heterogeneous). These thermomorphic ionic liquids have temperature-dependent miscibility with other molecular solvents, meaning that if the temperature is altered the solution might turn from a biphasic state to a homogeneous solution or vice versa. The homogeneous state can then be established to ensure good mixing conditions and the biphasic system can be used to separate the IL from the solvent. Two phase transitions induced by temperature changes are described for IL and solvent mixtures: an upper critical solution temperature (UCST) and a lower critical solution temperature (LCST) phase transition. In the former (UCST) a biphasic mixture becomes homogeneous with increasing temperature, in the latter case (LCST) a homogeneous mixture will phase separate upon increasing the temperature (Figure 11).

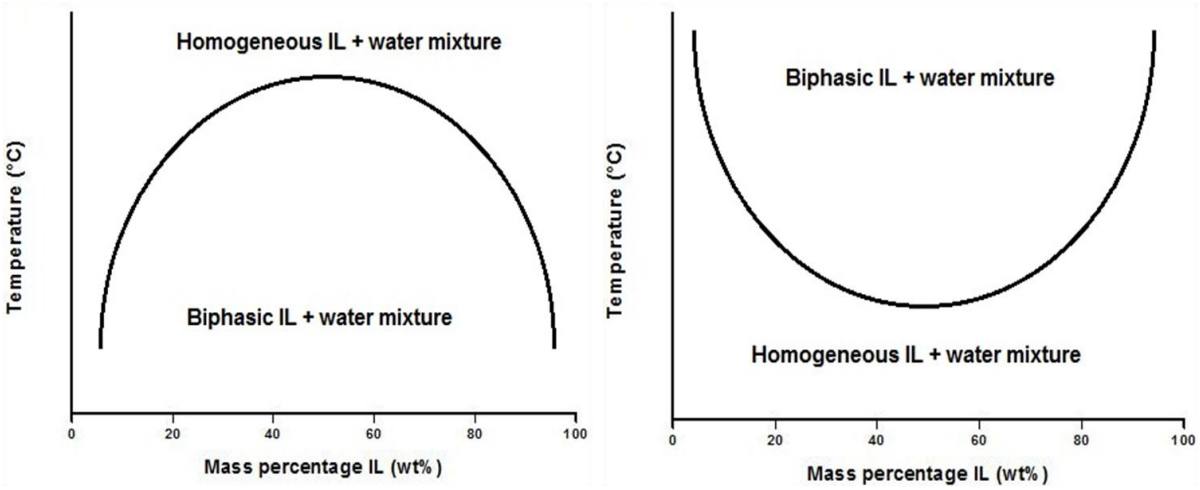


Figure 11: UCST (right) and LCST (left) behavior of binary IL + water mixtures.

Even though the IL and water might form two phases, they can still be mutually soluble, meaning that some water is dissolved in the IL and vice versa.[53] Knowing the extent of this mutual solubility is important, since this implies that IL is lost during extractions. This loss of IL requires for its separation from the water phase after extraction steps.

The temperature at which homogenization or phase separation occurs (cloud point temperature) can be measured in several ways. It can be done visually, which is straightforward but time consuming and susceptible for human errors, or by means of different apparatuses using transmission techniques, which are more correct but not available to every research group. The most simple and commonly used method is the visual observation: a mixture is placed in a viewing cell, stirred and slowly heated or cooled until the cloud point is reached. This point is visible by the transition from a clear homogeneous solution to a cloudy and turbulent mixture. This cloudy mixture will, when the stirring is ceased, phase separate into two different phases. The cloud point can also be determined

automatically by a detector which measures the decrease in light intensity caused by the transition. A laser is directed through the mixture and the light intensity is measured as a function of the temperature, when the cloud point is reached, the light will be scattered and this decrease in intensity is measured.[38]

1.6.2 IL-water mixtures with UCST behavior

Very little mixtures of pure imidazolium ILs and water have been reported to show UCST behavior, some of which are 1-butyl-3-methylimidazolium tetrafluoroborate and 1-octyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF_4] & [C_8MIM][BF_4]).[39,53,54] The liquid-liquid equilibrium phase diagram of [BMIM][BF_4] is displayed in Figure 12.

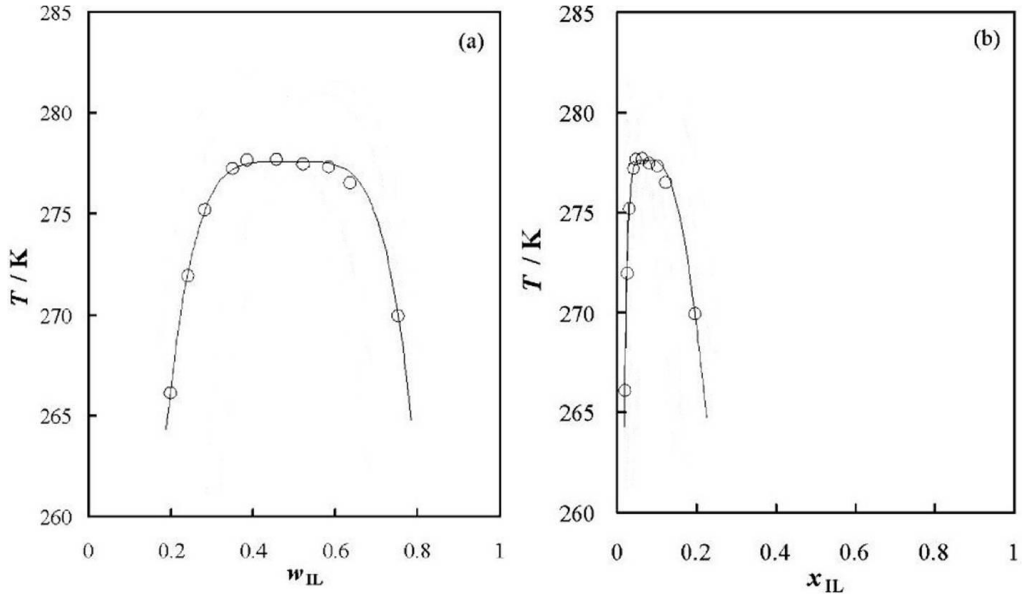


Figure 12: UCST phase diagram of [BMIM][BF_4] and water, (a) as a function of weight fraction IL and (b) as a function of molar fraction IL.[39]

The thermomorphic properties of ionic liquids can be altered by several factors. They can for instance be altered by the addition of salts, these can increase or decrease the solubility of ILs in the water phase. Salts that increase the water solubility of ILs are called 'salting-in' compounds, those that decrease the solubility 'salting-out' compounds.[45] The latter can for instance be used to recover the ILs lost to the water phase during extractions by decreasing their solubility in water.[47] The thermomorphic behavior of ionic liquids can also be altered by adding conventional organic solvents to the water phase. This was done by Najdanovic-Visak *et al*. where they used [BMIM][PF_6], this IL shows thermomorphic behavior in both EtOH and water.[55] Both of these solvents were mixed in a 1:1 ratio, resulting in a drastic decrease in cloud point temperature for IL solutions. This decrease reached up to 120 K compared to pure water mixtures and 37 K compared to pure ethanol mixtures.[55] The phase diagrams of all three IL solutions (water, EtOH and a 1:1 mixture) are presented in Figure 13.

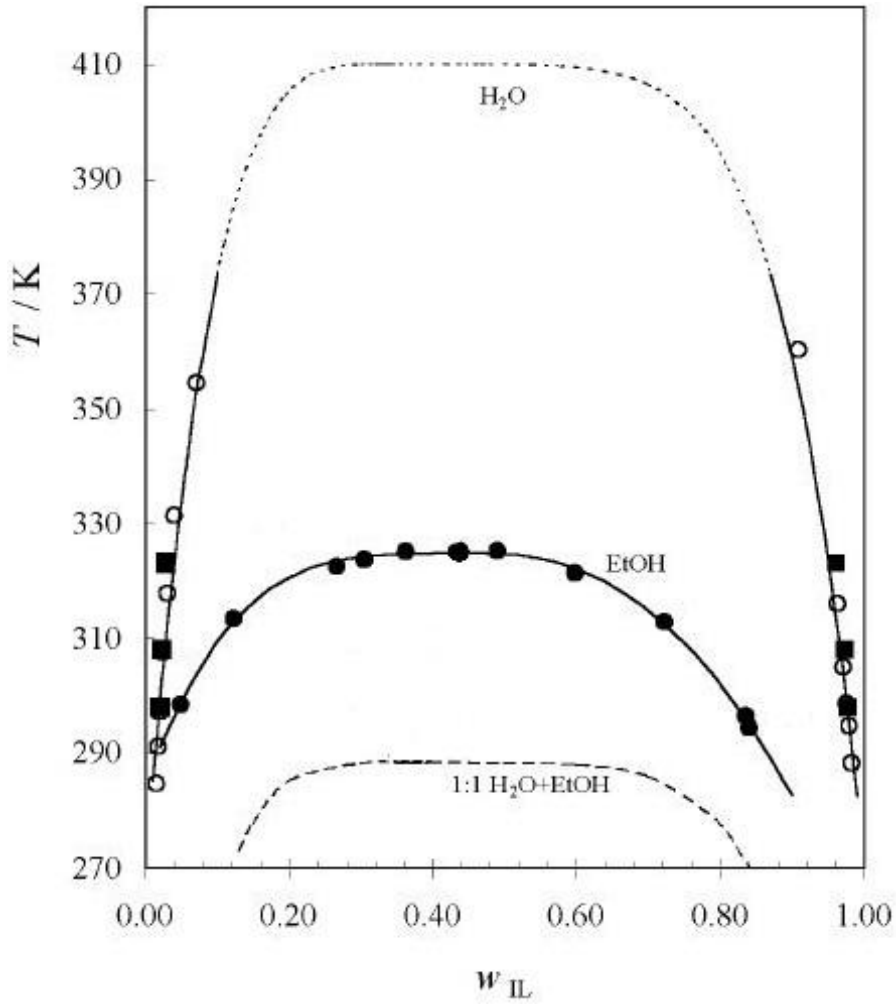


Figure 13: Phase diagrams of binary mixtures of [BMIM][PF_6] in water (open circles and full squares), pure ethanol (full circles) and water:EtOH 1:1 (dashed line).[55]

1.6.3 IL-water mixtures with LCST behavior

Also LCST behavior is only rarely observed for pure imidazolium ILs and water, the only known example is [BMIM][$FeCl_4$].[56,57] This tetrachloroferrate IL can be simply prepared by mixing equimolar amounts of its chloride analogue and iron trichloride ($FeCl_3$).[58] The resulting 1-butyl-3-methylimidazolium tetrachloroferrate shows reversible LSCT behavior with water in mixtures with weight fractions of IL below 35 wt%. A mayor disadvantage however, is that roughly 40 % of the iron is lost to the water phase after homogenization of the two phases has occurred.[57]

1.6.4 Thermomorphic behavior of ILs with organic solvents

Other imidazolium ILs show temperature-dependent miscibility with other solvents than water. These are almost always ILs which are insoluble in water since they consist of very hydrophobic anions. Popular organic solvents are for instance alcohols, for their capability in

hydrogen bonding, chloroform and aromatic or aliphatic hydrocarbons.[56] Of course their potential use in industrial processes will not be justified by the green character of the ionic liquids, since they are used in a combination with toxic and volatile organic solvents. A short list with some examples is given in Table 1.[36,55,56,59,60]

Table 1: Examples of imidazolium ILs mixtures with organic solvents showing thermomorphic behavior.[36,55,56,59,60]

IL	Organic solvent	Phase behavior
[BMIM][X] X=PF_6^-, BF_4^-, Tf_2N^-	Alcohols	UCST
[C_6OCMIM][TF_2N]	Aromatic hydrocarbons	UCST
[C_4MIM][TF_2N] & [C_5MIM][TF_2N]	Chloroform	UCST + LCST
[BMIM][PF_6]	Trifluoromethane	LCST

1.6.5 Targeting thermomorphic imidazolium ILs

Although temperature-dependent miscibility cannot be predicted, it can be targeted by using the proper substituents on the imidazolium cation and by choosing the right anion. Varying the anion and the chain length of the imidazolium ionic liquid can be applied to change its solubility in water. Using more hydrophobic anions and longer alkyl substituents on the imidazolium cation will result in a lower solubility in water. This was investigated by Anthony *et al*., they showed that the mutual solubility of [BMIM][PF_6] and water increased when the anion was changed to BF_4^- and decreased when the cation was substituted with the longer octyl chain, resulting in [OMIM][PF_6].[54] This technique can be used to prepare ionic liquids which are barely (or not) soluble in water, which increases their chance to show temperature dependent miscibility with water solutions.

2 Used techniques

2.1 Nuclear Magnetic Resonance Spectroscopy

^{1}H and ^{13}C NMR were used to determine the structure of synthesized products, to check the purity and to determine product and contaminant ratios. All measurements were performed on a Bruker Avance 300 spectrometer (operating at 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR). All the products were diluted in deuterated solvents: $CDCl_3$ (chloroform), DMSO-d_6 (dimethyl sulfoxide) or D_2O (water). Smaller sample amounts were used for ^{1}H NMR (5 mg) compared to ^{13}C NMR (30 mg) due to increased interference for ^{1}H NMR. To measure the amount of ionic liquid dissolved in water phases, a 1,4-dioxane standard was added to the samples.

Nuclear magnetic resonance spectroscopy uses the magnetic properties of certain nuclei (^{1}H, ^{13}C, ^{14}N, ^{19}F, ^{23}Na, ^{31}P, …) to discriminate them according to their chemical environment. This allows one to determine the nature and quantity of the nuclei and therefore identify the molecules and their relative abundances. The principle behind NMR spectroscopy is that the sample is placed in an external magnetic field, this results in an energy difference between the spin states. Transitions between these spin states can occur when they interact with electromagnetic radiation, hence 'NMR spectroscopy'. When the energy of the pulsating magnetic field matches the energy difference, interactions occur that can be measured. The energies vary for each nuclei and for each chemical environment, this results in several signals which can be contributed to a certain set of nuclei. Since the response signal is proportionate to the amount of nuclei undergoing a transition, NMR spectroscopy can be used to determine the relative abundances of these nuclei. The resonance frequencies are converted to a simpler number: the 'chemical shift', described in ppm values. This chemical shift is calculated from the frequency of the sample and the frequency of a certain standard, in most cases tetramethylsilane (TMS).

Since scanning an entire range of magnetic frequencies is very time consuming, another technique is used during actual measurements: 'Fourier Transform NMR'. Here the sample is exposed to all the relevant magnetic frequencies at once and all the nuclei are disrupted. Now they all undergo relaxation at once, but their relaxation time depends on their chemical environment. The signals are now measured versus the time they need to relax, this signal-time spectrum has to be converted to a signal-frequency spectrum. This is done by Fourier transformation using specific algorithms.

2.2 Attenuated Total Reflectance - Fourier Transform Infrared Spectroscopy

Fourier transformed infrared spectroscopy was used to determine the presence or absence of functional groups in the products, for instance phosphate and sulfate groups from DEHP or tosylate anions. All spectra were recorded with a Bruker Vertex 70 spectrometer, attenuated total reflectance techniques were used to directly analyze the spectra using OPUS software.

Infrared spectroscopy measures the interaction of electromagnetic radiation with molecules, causing the bonds to vibrate and/or bend. The same principles for normal UV-vis spectroscopy hold, but since bending and vibrations have energies within the infrared region, only this part of the spectrum is covered. The interaction frequencies are mostly determined by the mass of the atoms and the interactive forces between them. This results in a very specific set of peaks for each functional group, these can act as a fingerprint allowing one to determine the presence of certain functional groups in a sample.

Fourier transformed IR is used to reduce the measuring time by eliminating the need to scan the entire IR spectrum one wavelength at a time. A polychromatic beam of IR frequencies is split into several paths before being focused through the sample, one path is reflected by a fixed mirror, the other path is reflected on a moving mirror. The result is an interferogram which represents the light intensity as a function of the mirrors' position, this is Fourier transformed into a wavelength dependent spectrum as a function of the reciprocal length (v/cm^{-1}).

2.3 Electrospray Ionization Mass Spectrometry

Mass spectrometry was performed on certain products to identify compounds or to detect the presence of targeted molecules. It was used as an extra characterization technique besides NMR and FTIR spectroscopy. All measurements were performed on a Thermo Finnigan LCQ Advantage LC/MS/MS. Since training is required to operate this mass spectrometer, the measurements were performed with the help of authorized people.

Electrospray ionization mass spectrometry requires compounds to be dissolved in a volatile solvent, therefore methanol is used, since it is rather volatile and dissolves a large array of compounds. The solution passes through a small capillary tube over which a large potential is applied. At the end, a fine mist of small and charged droplets is expelled from the tube. These droplets contain the charged sample, which is ionized due to the huge potential. The fine droplets are accelerated by a pressure and potential gradient, which causes them to

move towards the detector. The ions are still dissolved in a charged droplet, to remove the solvent a stream of gas is used, this helps the droplets to move away from the tube and causes them to disperse into smaller droplets. The flowing stream of gas, combined with an increased temperature induces the charged droplets to decrease in size by fragmentation and solvent evaporation. This decrease in size and solvent amount results in a higher charge density of the fine droplets, until a certain point where the ions are set free from the droplets into the gas phase. The ions are now transferred to the detector, where they are separated by a quadrupole analyzer. In a quadrupole analyzer, the ions travel through four parallel iron rods which expose them to an electric field and an alternating radio frequency. These serve as an upper and lower boundary for the m/z ratios that are allowed to pass through the quadrupole. This results in a filter allowing only a small window of ions with a certain m/z ratio to pass through, depending on the current applied to the electric and radio frequency field. After separation, the ions are registered by a detector, which measures the relative intensity of all the different m/z ratios that pass through the quadrupole. These abundances are displayed as a function of the m/z ratio on a final chart, which is the output of the ESI-MS measurement. Some care must be taken when interpreting the results since fragmentation of the ions into smaller ions and neutral species, that cannot be measured, can occur.

2.4 CHN analysis

CHN elemental analysis was used to characterize and verify the purity of all the ionic liquids. All measurements were performed on a CE-instruments EA-1110 elemental analyzer.

CHN elemental analysis is used to characterize organic samples by completely burning them and measuring the amounts of nitrogen, carbon dioxide and water released by the combustion. A small sample, around 10 mg, is loaded onto a small pan and weighed accurately. Afterwards, it is completely oxidized by increasing the temperature in the presence of oxygen, and the gasses are directed over a catalyst, which removes the excess O_2 and to converts the nitrous oxides to N_2. All the organic material is now present in the form of three gasses: N_2 (nitrogen), CO_2 (carbon dioxide) and H_2O (water). Gas chromatography is used to separate the gasses into different fractions, these are measured with the use of thermal conductivity measurements at the end of the column. The amount of each gas can be used to calculate the total contribution of carbon, hydrogen and nitrogen to the total mass of the sample. The results are given as the mass percentage of each of these three elements.

2.5 Coulometric Karl Fischer Titration

Coulometric Karl Fischer titration was used to determine the water content of all room temperature ionic liquids (RTIL). The water traces were measured with a coulometric Mettler-Toledo DL 32 titrator. This is important since the measured properties of the ionic liquids can drastically change when too much water is present. The viscosity for instance will decrease significantly when too much water is present and some solid products might never reach their solid state due to the presence of water traces e.g. 1,3-diisobutylimidazolium acetate and 1,3-dihexylimidazolium tosylate.

A Karl Fischer titrator consists of a sealed vessel containing the Karl Fischer reagent: sulfur dioxide, iodide, a base (imidazole) and methanol, which also acts as a solvent, this anolyte also contains an anode. A separate cell, the cathode, is submerged into the anolyte, both are separated by an ion-permeable membrane. The oxidation at the anode generates iodine from the iodide, this happens in the anolyte. The redox reaction is completed with the reduction of protons in the cathode compartment. The in-situ generated iodine reacts instantly with the water present in the sample according to reactions (1) and (2), which is in fact an oxidation of the sulfur dioxide by iodine. When all the water is consumed, a tiny excess of iodine is generated which can no longer react with water, this excess is detectable and the electrochemical generation of iodine is stopped. The amount of water is calculated from the total charge required to generate the iodine.

$$SO_2 + MeOH + B \longrightarrow BH^+ + SO_3Me^- \quad (1)$$

$$BH^+ + SO_3Me^- + 2\,B + H_2O + I_2 \longrightarrow BH^+ + SO_4Me^- + 2\,BH^+ + 2\,I^- \quad (2)$$

Special care must be taken when measuring organic compounds with functional groups, since Karl Fischer titrations are sensitive towards several side reactions. The most relevant ones in organic compounds are: aldehydes, ketones and acids. The carbonyl group in aldehydes and ketones reacts with two alcohol molecules present in the reagent and forms an acetal in the case of aldehydes and a ketal in the case of ketones, reaction (3). Acids can undergo esterification when exposed to the alcohols, according to reaction (4). All three reactions generate water molecules which results in incorrect measurements.

$$R_2C{=}O + 2\,MeOH \rightleftharpoons R_2C(OMe)_2 + H_2O \quad (3)$$

$$RCOOH + MeOH \rightleftharpoons RCOOMe + H_2O \quad (4)$$

Since not all of these side reactions occur to completeness, that depends on the reactivity of the molecules, it is rather complex to calculate the precise value of the deviation caused by these reactions. Also active redox reagents are not measurable with Karl Fischer titrations,

since they disrupt the redox reactions in the KF reagent. For instance nitric acid and the nitrate anion are oxidizing agents and will therefore interact with the other redox reagent comprising the sensitive Karl Fisher reagent. The water content of the nitrate ionic liquids will therefore not be measured, if the water content is really required TGA experiments are used (section 5.4.2).

2.6 Viscosimetry

The viscosity of all the room temperature ionic liquids (RTIL) was measured, this is important information since too viscous ionic liquids will have limited applicability in industrial processes. All measurements, except two, were measured on a rotating disk viscometer: Brookfield LVDVII+PRO plate-cone viscometer. Rheocalc software was used to measure the viscosity and control the temperature of the Brookfield circulating water bath. The dynamic viscosity of the ionic liquids was determined by measuring the stress of a rotating disk as a function of the rotating speed. About 0.55 mL of ionic liquid was inserted between a spindle and a fixed cup, the viscosity was measured at 25 °C and a rotation speed corresponding to a torque between 70 and 80 %.

Two measurements were performed on a rolling-ball viscometer Lovis 2000 M/ME, this rented device was only temporary at our disposal and made use of another technique to determine the viscosity. A rolling-ball viscometer measures the viscosity of a liquid by monitoring the falling speed of a ball through a small tube filled with liquid. Depending on the properties of the liquid, the right tube, with a specified length and diameter, is chosen. The liquid (1 mL) is inserted into the tube, whilst preventing the formation of any air bubbles. Afterwards, gold coated ball is placed inside the tube which is then sealed and placed in an arm capable of rotating. The tube is heated to a certain temperature and tilted several times while the dropping speed of the ball is monitored, the experiment can be repeated at other temperatures. These data are evaluated and the output is the viscosity of the liquid at one or more temperatures.

2.7 Differential Scanning Calorimetry

The melting points of all the ionic liquids solid at room temperature were determined via differential scanning calorimetry. All scans were performed on a Mettler-Toledo DSC 1 under helium atmosphere.

Differential scanning calorimetry is mostly performed to determine melting points, although it can be used to determine any chemical or physical process which is endothermic or exothermic or in which the heat capacity changes. DSC experiments measure the difference in heat flow between a reference pan and a pan filled with the sample. Both pans are slowly

heated or cooled down while their temperature is kept identical, this is monitored by a thermocouple. The sample will behave differently compared to the reference, which has a stable heat capacity over a large temperature range and shows no transitions. The sample however, is more likely to undergo phase transitions. If at some point the sample starts melting, more heat is required since the phase transition itself requires heat that is no longer being used to heat the sample. This difference in heat flow is monitored throughout the entire scan. The melting point will later be visualized by an upward peak in the scan, as is the case for all endothermic reactions. The opposite phenomena are observed when the sample is cooled down and starts solidifying, the result is a downward peak for all exothermic reactions, since during these processes less heat is needed to maintain the continuous temperature decrease. Because the first heating is rarely accurate, most samples undergo cycles of heating and cooling, in which the results stabilize with increasing number of scans. Many phenomena can be observed by DSC: melting temperatures, crystallization, glass transitions, changes in heat capacity,…

2.8 Thermogravimetric Analysis

The stability of some imidazolium ionic liquids was measured to determine their thermal stability, this information was used to dry them on the Schlenk line at elevated temperatures without destroying them. The water content of 1,3-dihexylimidazolium nitrate after homogenization with a water phase was also tested, since the water content of nitrate ionic liquids cannot be measured with Karl Fischer titrations due to the oxidative nature of nitrates. The measurements were performed on a TGA Q500 from TA instruments. While measuring, a constant stream of nitrogen gas was guided over the sample (60 mL per minute).

TGA or thermogravimetric analysis is a technique used to determine the thermal stability of compounds. Other phenomena like desorption of volatile molecules and sublimation can also be observed. The sample is weighed and prepared in an aluminum pan, which is attached to an accurate balance to constantly measure the weight. The sample can be heated under oxygen or nitrogen atmosphere while both the exact temperature and mass are being monitored. Samples can be heated at certain heating rates, kept at a certain elevated temperatures or a combination of both. When water traces are present in the sample, it is heated until 110-120 °C and then kept at that temperature for about an hour to remove all the water. This prevents possible failures of the measurement caused by the water when the temperature is increased even further. The results are interpreted as the weight percentage of the sample that remains as a function of the temperature.

3 Health, safety & environment (HSE)

All chemical operations and experiments were performed according to the standards described in the *Code of Practice for safety in the lab*.[61] The hazards of all the used products and the potential risks of the reactions and chemical operations were evaluated before any activities were performed. The necessary precautions were taken when performing the experiments and all the procedures and observations were recorded in the lab book. The standard personal protection equipment: a lab coat, safety goggles and gloves were worn at all times when performing experiments and these were conducted in the fume hood when necessary. Additional safety precautions were taken when working with exceptional compounds.

If the syntheses required overnight experiments, all information required for safely handling or terminating the experiment was provided to the central dispatch and the HSE responsible. This information was summarized on the necessary form, which was displayed on the entrance door of the lab and on the fume hood.

The risk assessments of the groupware site were consulted when working with the chemical reagents and solvents and new risk assessments were added when new products were purchased.[62] When working with diethyl ether and silica (E4), the risk assessments for working with these dangerous compounds were consulted beforehand and additional precautions were taken. When working with silica, a mask was worn to prevent inhalation of the harmful silica particles. Sodium hydride (E3) was used as well, this compound sets free hydrogen gas when exposed to air and can ignite via static electricity. When manipulations with sodium hydride were performed, a beaker with sand was placed in the vicinity to extinguish possible fires.

All the chemical reagents, solvents and mixtures were collected in the correct waste containers, all nitric acid or nitrate solutions were gathered in a specially labeled container for oxidants.

4 Synthesis of imidazolium ionic liquids

4.1 Synthetic goals

4.1.1 Introduction

An efficient synthesis of highly functionalized imidazoles and in a further extend imidazolium derivatives is targeted. This synthesis must be as versatile as possible to make it applicable to a whole range of imidazolium compounds. The synthetic strategy will ideally serve as a blueprint for future syntheses of substituted and customizable imidazolium compounds. The imidazolium ionic liquids will undergo several metathesis reactions with the goal to render ionic liquids with temperature-dependent miscibility with water. This thermomorphic behavior is advantageous in the use of ILs as extractants for rare earth elements (REEs).

4.1.2 Imidazolium synthesis

The starting point of this synthetic route will be the modified Debus-Radziszewski method for the synthesis of imidazoles from diketones, aldehydes, amines and ammonia, as described in the Arduengo patent.[2] Other synthetic routes will be investigated as well in order to obtain multiple synthetic methods for imidazoles. These imidazoles can then be quaternized using halo-alkanes or other halo-derivatives in order to create imidazolium ionic liquids.

The possibility of preparing imidazolium compounds directly from simple organic molecules will also be investigated. Such syntheses require less reaction steps and will therefore result in less synthetic effort and most probably higher yields. The absence of the quaternization step also eliminates the use of halo-derivatives, an important feature regarding the green nature of the ionic liquids. This way a *halide-free synthetic route* towards imidazolium ionic liquids can be available.

Once the imidazolium syntheses are mapped, the imidazolium compounds will be used as precursor ionic liquids for metathesis reactions.

4.1.3 Metathesis reactions

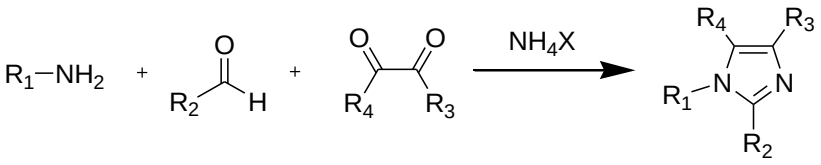
Several anion exchange metatheses will be performed on the precursor ionic liquids, with the intent of making thermomorphic ionic liquids. By changing the anions the polarity of the ionic liquids will be altered, this way the thermomorphic behavior will be targeted. The anions that will be used are the typical ionic liquids used in other research: bistriflimide, triflate, tosylate, mesylate, bis(2-ethylhexyl)phosphate (DEHP),… The use of fluorinated anions: bistriflimide,

triflate, etc. will be limited whenever possible since these do not cope with the green character of ionic liquids. The ultimate goal would be to find thermomorphic behavior with the use of non-fluorinated anions: DEHP, tosylate, etc. The thermomorphic properties of the ionic liquids throughout several series will be compared as a function of the anion and the different substituents on the imidazolium ring.

4.2 Imidazole synthesis

4.2.1 Debus-Radziszewski reaction

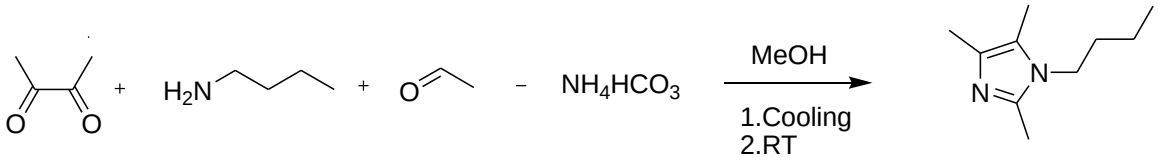
Following syntheses are based on the Debus-Radziszewski (Scheme 10) reaction and are modifications of syntheses in the Arduengo patent.[2]



Scheme 10: Debus-Radziszewski synthesis of imidazole.

Initial tests

The first reaction was the synthesis of 1-butyl-2,4,5-trimethylimidazole from 2,3-butanedione, *n*-butylamine, acetaldehyde and ammonium hydrogencarbonate in a one pot reaction (Scheme 11). Due to the reactive and light sensitive nature of the acetaldehyde some precautions were taken: the flask was sealed and wrapped in aluminum foil to block the light and the reaction mixture was cooled for the first 2 hours of the reaction.



Scheme 11: Synthesis of 1-butyl-2,4,5-trimethylimidazole

2,3-Butanedione (20 mmol, 1.76 mL), *n*-butylamine (20 mmol, 1.80 mL) and ammonium hydrogencarbonate (20 mmol, 1.92 g), these reagents were dissolved in 20 mL of methanol. The flask was sealed, wrapped in aluminum foil and placed in an ice bath, after which the acetaldehyde (20 mmol, 1.122 mL) was added, after 2 hours of stirring the ice bath was removed. After 18 hours of stirring at room temperature, a small sample was taken from the reaction, ^{1}H NMR in DMSO-d_6 confirmed the presence of 1-butyl-2,4,5-trimethylimidazole in the product. Since a lot of other impurities were present in the spectrum, an ESI-MS measurement was performed in order to identify these impurities. The results were

inconclusive: over 20 cations were found, all with higher m/z ratios than the expected 166 for 1-butyl-2,4,5-trimethylimidazole. The reaction was terminated and the methanol, water traces and possible volatile products were removed with a rotary evaporator. To remove the side products with different polarities compared to the imidazolium, column chromatography was performed, at first the eluent DCM:EtOH 9:1 was used, afterwards DCM:triethylamine 95:5. Finally, the 1-butyl-2,4,5-trimethylimidazole was eluted with DCM:MeOH:ammonia 94.5:5:0.5, this fraction was collected and all the solvents were removed with a rotary evaporator. To eliminate all side products with similar polarities the alkaline properties of imidazoles were used, the product was dissolved in 48 mL of 0.5 M HCl and the solution was washed four times with ethyl acetate after which the water was neutralized with 24 mmol (0.96 g) of NaOH. The water was removed with a rotary evaporator and a sample was taken for ^{1}H NMR in DMSO-d_6. The 1-butyl-2,4,5-trimethylimidazole remained contaminated after all the purification steps.

Autoclave synthesis

The use of an autoclave was used to synthesize imidazoles, based on the literature procedure described by Maton *et al*.[32] Steel autoclaves with Teflon reaction tubes were used. These are cylindrical steel tubes that can be sealed air tight with regular screws. A Teflon tube with a matching lid can be placed inside, this tube acts as the actual reaction vessel (Figure 14).

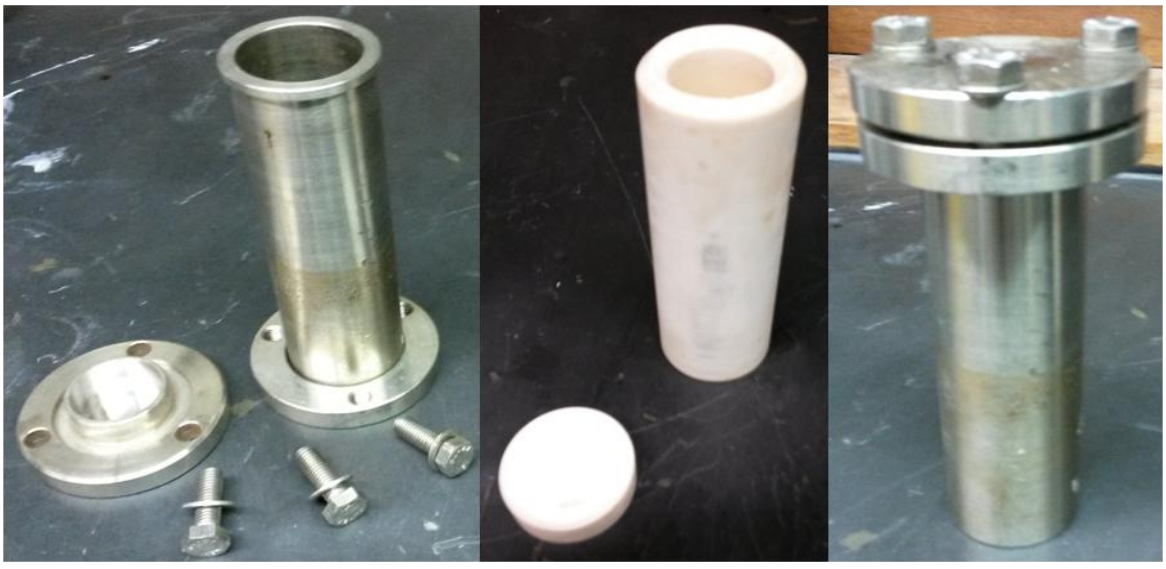
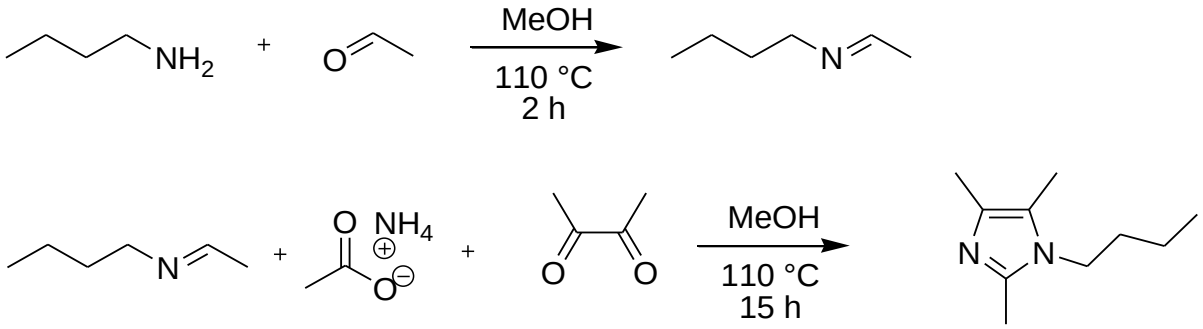


Figure 14: Steel autoclave, Teflon reaction tube and sealed setup.

Since the autoclave is a sealable cylinder in which the pressure cannot be modulated, the pressure was induced by the vapor pressure of the methanol at 110 °C, which is roughly 5 bar. To reach this temperature, the autoclave was placed in an oven at 110 °C.

Two-step synthesis:

Two-step synthesis of 1-butyl-2,4,5-trimethylimidazole from 2,3-butanedione, acetaldehyde, *n*-butylamine and ammonium acetate (Scheme 12).

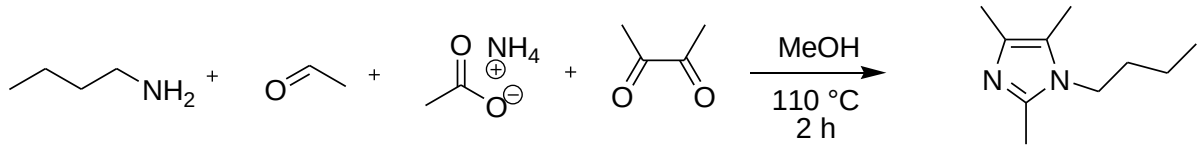


Scheme 12: Two-step synthesis of 1-butyl-2,4,5-trimethylimidazole.

n-Butylamine (20 mmol, 1.98 mL) was dissolved in 20 mL of methanol and poured into the Teflon® reaction vessel from the autoclave. Acetaldehyde (20 mmol, 1.12 mL) was added and the vessel was closed, the autoclave was sealed and placed in an oven at 110 °C for 4 h, two hours were estimated for raising and cooling the temperature. The reactor was cooled to RT and 2,3-butanedione (20 mmol, 1.81 mL) and ammonium acetate (20 mmol, 1.54 g) were added, the reactor was sealed again and placed in the oven at 110 °C overnight. The reactor was cooled and the methanol was removed with a rotary evaporator, a ^{1}H NMR of the product (a black oil) showed no indication of any imidazole formation.

One-step reaction

The synthesis of 1-butyl-2,4,5-trimethylimidazole from 2,3-butanedione, acetaldehyde, *n*-butylamine and ammonium acetate was repeated in a one-step synthesis and by adding all the products at once (Scheme 13).



Scheme 13: One-pot synthesis of 1-butyl-2,4,5-trimethylimidazole.

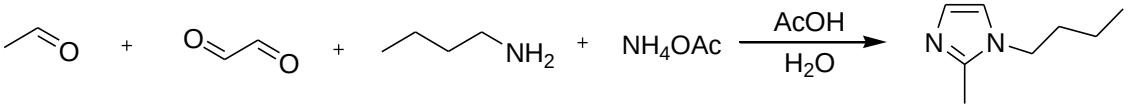
n-Butylamine (20 mmol, 1.98 mL) and ammonium acetate (20 mmol, 1.54 g) were dissolved in 20 mL of methanol and poured into the Teflon reaction vessel. Acetaldehyde (20 mmol, 1.12 mL) and 2,3-butanedione (20 mmol, 1.81 mL) were added to the mixture. The vessel was sealed within the steel tubing and placed in an oven at 110 °C. After 4 h the autoclave was cooled down to room temperature and the methanol was removed with a rotary

evaporator. A ^{1}H NMR spectrum showed no indication of any imidazole formation. A probable cause to the failure is the use of enolizable products: 2,3-butanedione and acetaldehyde.

Syntheses using glyoxal

1-Butyl-2-methylimidazole

Since the use of the enolizable compounds might be the cause of the huge amount of different side products, the 2,3-butanedione is replaced with glyoxal. Acetic acid is used as a catalyst, based on the literature procedures described by Esposito *et al*.[19] The resulting product of the synthesis is 1-butyl-2-methylimidazole (Scheme 14).



Scheme 14: Synthesis of 1-butyl-2-methylimidazole.

Acetaldehyde (20 mmol, 1.122 mL), *n*-butylamine (20 mmol, 1.977 mL), glyoxal (40 wt% in water, 20 mmol, 2.29 mL), ammonium acetate (20 mmol, 1.542 g) and acetic acid (6 eq. 120 mmol, 6.87 mL) were dissolved in 40 mL of H_2O. The reaction mixture was stirred at room temperature for 2h. The solution was washed with diethyl ether and the water was removed with a rotary evaporator. A ^{1}H NMR spectrum in DMSO-d_6 indicated that even with the use of a non-enolizable diketone (glyoxal) still a lot of undesired byproducts are formed.

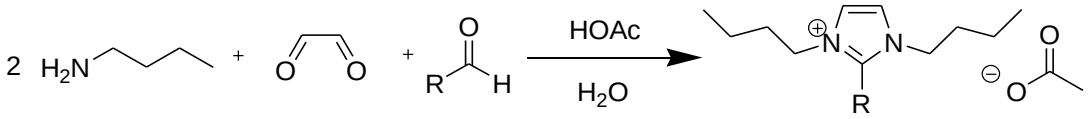
The cause of the continued presence of these side products, might be that the procedure was designed for direct imidazolium synthesis instead of imidazole. The use of the rather reactive and enolizable acetaldehyde might also be the cause.

4.3 Imidazolium synthesis

4.3.1 1,2,3-Trisubstituted imidazolium

By replacing the ammonium salt with another amine equivalent, the direct synthesis of quaternized imidazolium compounds was attempted. The straightforward advantage is that no extra synthetic step is required by means of the quaternization of the imidazole. The downside is that the control of one substituent is lost, this cannot be solved by using two different amines, since the synthesis would result in a statistical mixture of imidazolium. The syntheses were carried out based on the literature procedure described by Zimmerman *et al.*[20] The imidazolium cation will be synthesized together with an acetate anion, resulting in an actual ionic liquid. Two tests were performed: the synthesis of 1,3-dibutyl-2-

octylimidazolium acetate and 1,3-dibutyl-2-pentylimidazolium acetate. The acetaldehyde is replaced with longer aldehydes, since the failed syntheses might be attributed to the very reactive acetaldehyde. The other reagents used were: *n*-butylamine, glyoxal and acetic acid (Scheme 15).



Scheme 15: Synthesis of 2-alkyl-1,3-dibutylimidazolium acetate.

1,3-Dibutyl-2-octylimidazolium acetate

Glyoxal (50 mmol, 6.5 mL), nonanal (50 mmol, 9.05 mL), *n*-butylamine (100 mmol, 10 mL) and acetic acid (300 mmol, 17.2 mL) were dissolved in 100 mL of water and stirred at room temperature overnight. The mixture was washed with dichloromethane and the water was removed with a rotary evaporator, a brown liquid was obtained. A ^{1}H NMR spectrum indicated that many side products were present, which were inseparable via TLC.

1,3-Dibutyl-2-pentylimidazolium acetate

Glyoxal (1 mmol, 0.13 mL), hexanal (1 mmol, 0.12 mL), *n*-butylamine (2 mmol, 0.2 mL) and acetic acid (6 mmol, 0.34 mL) were dissolved in water (2 mL) and stirred at room temperature for 12h. The reaction mixture was washed with DCM and the water layer was isolated, the water was removed with a rotary evaporator, a total of 103 mg of brown imidazolium liquid was obtained. A ^{1}H NMR spectrum indicated that also in this synthesis a lot of inseparable by-products were formed.

Enolizable compounds

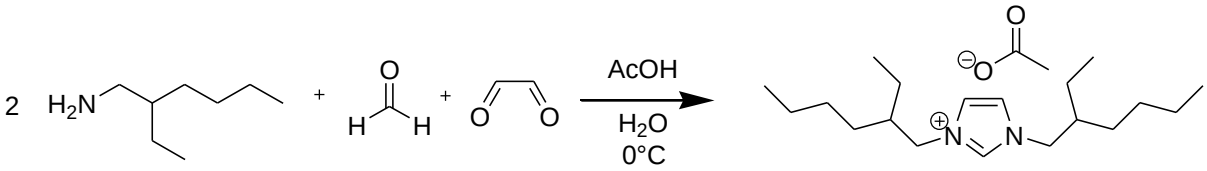
The use of less reactive aldehydes was not sufficient to eliminate the large variety of side products. The failure could still be attributed to the use of enolizable aldehydes: acetaldehyde, nonanal and hexanal.

4.3.2 1,3-Dialkylimidazolium

All enolizable compounds were abandoned from the synthesis: the 2,3-butanedione was replaced by glyoxal and the aldehydes were replaced by formaldehyde. The use of glyoxal and formaldehyde implicates the loss of three substituents and by using two amine equivalents, quaternized homo-substituted 1,3-dialkylimidazolium acetate compounds are synthesized.

1,3-Di(2-ethylhexyl)imidazolium acetate

A reaction with the non-enolizable glyoxal and formaldehyde was performed. Due to the decreased amount of substituents, a more complex and hydrophobic amine: 2-ethylhexylamine, was used to obtain a less hydrophilic imidazolium product. The resulting product is: 1,3-di(2-ethylhexyl)imidazolium acetate (Scheme 16). The synthesis was based on the literature procedure described by Zimmerman *et al*.[20]



Scheme 16: Synthesis of 1,3-di(2-ethylhexyl)imidazolium acetate.

2-Ethylhexylamine (2 eq. 50 mmol, 8.26 mL) was cooled to 0 °C in an ice bath while being stirred. Formaldehyde (38 wt% in water) (25 mmol, 1.86 mL) and acetic acid (25 mmol, 1.43 mL) were mixed in a separate flask and this mixture was added drop-wise to the cooled 2-ethylhexylamine while keeping the temperature below 10 °C. After total addition of the formaldehyde/acetic acid solution, the mixture was stirred for 30 min while kept at 0 °C. Afterwards, glyoxal (40 wt% in water) (25 mmol, 2.87 mL) was added and the reaction mixture was stirred overnight at RT. The solution was washed with diethyl ether until the organic phase became colorless and the water phase was removed using a rotary evaporator. ^{1}H NMR confirmed the purity of the product : 7.94 g (45 % yield) of a dark orange and highly viscous oil.

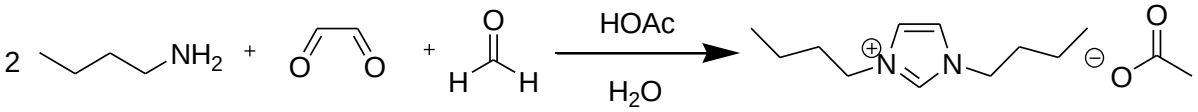
^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.84 (s, 1H, CH), 7.83 (s, 2H, 2 CH), 4.10 (m, 4H, 2 CH_2-N), 1.84 (m, 2H, 2 CH), 1.61 (s, 3H, CH_3), 1.26 (m, 16H, 8 CH_2), 0.83 (m, 12H, 4 CH_3).

Optimizing 1,3-dibutylimidazolium synthesis

After the successful synthesis of 1,3-di(2-ethylhexyl)imidazolium acetate, the procedure was repeated under different conditions in order to optimize the synthesis. The first test is to increase the yield by using a larger equivalent of acid. The reason behind this strategy is that the acid is consumed in the imidazolium synthesis and the last imidazolium formation might not be achieved due to a deficit of acetic acid. The use of other acids will also be investigated: hydrochloric acid and sulfuric acid, since they are readily used and cheap and butyric acid since it is another carboxylic acid. The tests will be performed with a cheaper and more readily accessible amine: *n*-butylamine, resulting in 1,3-dibutylimidazolium ionic liquids.

Acid equivalent

The exact procedure for 1,3-di(2-ethylhexyl)imidazolium acetate was repeated twice, but with a different amine: *n*-butylamine and with variable equivalents of acetic acid: 1.05 and 1.5. The product of this reaction is 1,3-dibutylimidazolium acetate (Scheme 17).



Scheme 17: Synthesis of 1,3-dibutylimidazolium acetate.

Used products: *n*-butylamine (2 eq. 40 mmol, 3.95 mL), formaldehyde (38wt% in water, 20 mmol, 1.43 mL), glyoxal (40 wt% in water, 20 mmol, 2.29 mL), and acetic acid (1.05 eq. 21 mmol, 1.2 mL for synthesis A and 1.5 eq. 30 mmol, 1.72 mL for synthesis B). The purity of both products was confirmed with ^{1}H NMR, meaning that working with an excess of acetic acid poses no problem since it was completely removed. The resulting product was an orange liquid, the masses and yields of both reactions are displayed below (Table 2).

Table 2: Effect of acid equivalent on the yield of the imidazolium synthesis.

Sample	Equivalent AcOH	Mass	Yield (%)
A	1.05	3.69 g	77
B	1.5	4.29 g	89

Working with a larger excess (1.5 equivalents) clearly resulted in a larger yield of the reaction (Table 2): switching from 1.05 equivalent to 1.5 equivalent of acetic acid boosts the yield from 77 % up to 89 %. An interesting discovery is that the yields of the reaction with *n*-butylamine differ a lot from those of the reaction with 2-ethylhexylamine (Table 3). This might be due to the increased steric hindrance around the amine function for long and branched alkyl groups, the results will be discussed in more detail later on in section 5.1.2.

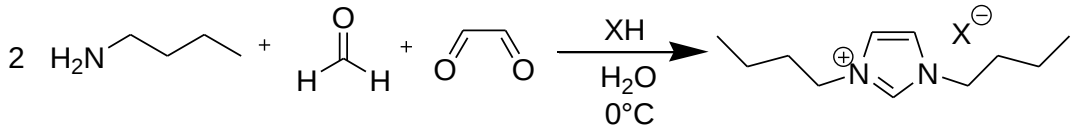
Table 3: Effect of the amine and acid equivalent.

Amine	Equivalent AcOH	Yield (%)
n-Butylamine	1.05	77
n-Butylamine	1.5	89
2-Ethylhexylamine	1	45
2-Ethylhexylamine	1.5	47

Further experiments with even greater equivalents of acetic acid were not performed, since no further increase of the yield is expected. This decision was based on the fact that some imidazolium will always be lost during the washing step with diethyl ether and therefore the maximum yield of the synthesis itself (without the extraction procedure) might already be achieved when using 1.5 equivalents.

Different acids: hydrochloric acid & sulfuric acid

Two other common and readily accessible acids were used: hydrochloric acid and sulfuric acid, both were used in one equivalent. The synthetic procedure remained identical to the previous 1,3-dibutylimidazolium syntheses (Scheme 18).



Scheme 18: Synthesis of 1,3-dibutylimidazolium using different acids.

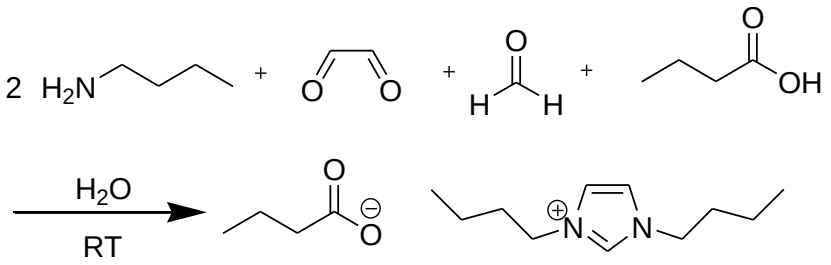
Used products: *n*-butylamine (2 eq. 40 mmol, 3.95 mL), formaldehyde (38 wt% in water, 20 mmol, 1.43 mL), glyoxal (40 wt% in water, 20 mmol, 2.29 mL), and hydrochloric acid (37 wt% in water, 20 mmol, 2.51 mL) or sulfuric acid (96 wt% in water, 20 mmol, 2.04 g).

In both cases the imidazolium products: 1,3-dibutylimidazolium chloride and 1,3-dibutylimidazolium hydrogen sulfate, were clearly formed, but a lot of side products were present, even after the washing with diethyl ether. One of these side products was identified as *n*-butylamine.

With the use of quantitative ^{1}H NMR, the yield of both reactions was determined: 61% for the synthesis with hydrochloric acid and 83% for sulfuric acid.

Similar acids: butyric acid

Another carboxylic acid was tested to investigate the use of acids resembling acetic acid (pK_a butyric acid = 4.82). Again the synthetic procedure remained identical to the previous 1,3-dibutylimidazolium syntheses (Scheme 19).



Scheme 19: Synthesis of 1,3-dibutylimidazolium butyrate.

Used products: *n*-butylamine (2 eq. 10 mmol, 3.95 mL), formaldehyde (38wt% in water, 5 mmol, 0.36 mL), glyoxal (40 wt% in water, 5 mmol, 0.57 mL), and hydrochloric acid (5 mmol, 0.47 mL).

A ^{1}H NMR spectrum indicated that no side products were present in the product, although there was an excess of butyric acid, the ratio of the product (0.731 g in total) was 1.16 mol of butyric acid for each mol of 1,3-dibutylimidazolium butyrate. The butyric acid could not be removed from the ionic liquid via attachment to the Schlenk line at 70 °C for 120 h, even though the boiling point was calculated to be 58.5 °C at reduced pressure (20 mm Hg). The yield of the imidazolium formed from the starting products was 39%.

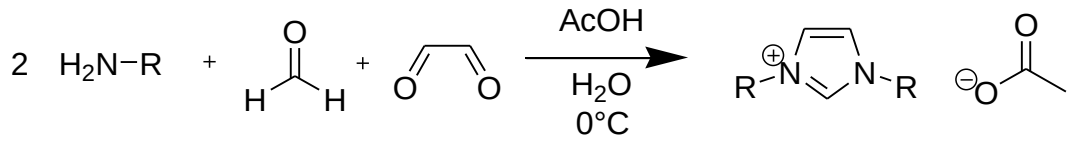
Optimized synthesis

After testing the effect of a higher equivalent of acid and the effect of using other acids, the optimal synthesis was described for future use, this will be done in more detail in the section: Results and discussion.

Of all the tested acids the acetic acid was chosen for various reasons, which are discussed in section 5.1.2, the most important reason was the capability to produce pure imidazolium compounds via extraction. Increasing the equivalent of acetic acid clearly resulted in higher yields, therefore an equivalent of 1.5 was used in future syntheses.

4.3.3 1,3-Dialkylimidazolium acetate

After the successful halogen-free and optimized synthesis of 1,3-dibutylimidazolium acetate, more 1,3-dialkylimidazolium acetate compounds were prepared using other amines: ethylamine, isobutylamine, *n*-hexylamine, *n*-octylamine, *n*-decylamine and *n*-dodecylamine. All acetate ionic liquids were synthesized according to the successful procedure for 1,3-dibutylimidazolium acetate (Scheme 20).

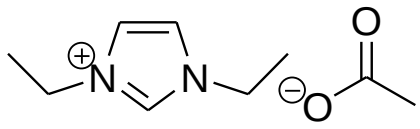


Scheme 20: Optimized synthesis of 1,3-dialkylimidazolium acetate.

Two equivalents of amine were cooled down to 0 °C in an ice bath, afterwards a mixture of formaldehyde (38 wt% in water, 1 eq.) and acetic acid (1.5 eq.) was added drop-wise while keeping the temperature under 10 °C. The mixture was stirred for 30 min at 0 °C, after which the glyoxal (40 wt% in water, 1 eq.) was added and the reaction mixture was stirred overnight at RT. The solution was washed with diethyl ether until the organic phase was colorless and the water was removed with a rotary evaporator. The product was dried on the Schlenk line at 50 °C overnight. ^{1}H NMR spectroscopy was used to confirm the purity of the formed 1,3-dialkylimidazolium acetate.

1,3-Diethylimidazolium acetate

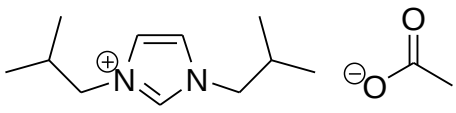
Used products: ethylamine (70 wt% in water) (2 eq. 20 mmol, 1.61 mL), formaldehyde (38 wt% in water, 10 mmol, 0.72 mL), acetic acid (15 mmol, 0.86 mL) and glyoxal (40 wt% in water, 10 mmol, 1.15 mL). Product: 1.671 g of a dark orange oil (93% yield).



^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.77 (s, 1H, CH), 7.85 (s, 2H, 2 CH), 4.22 (m, 4H, 2 CH_2-N), 1.64 (s, 3H, CH_3), 1.42 (m, 6H, 2 CH_3).

1,3-Diisobutylimidazolium acetate

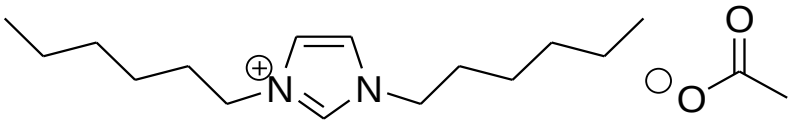
Used products: isobutylamine (2 eq. 20 mmol, 2.01 mL), formaldehyde (38wt% in water, 10 mmol, 0.72 mL), acetic acid (15 mmol, 0.86 mL) and glyoxal (40 wt% in water, 10 mmol, 1.15 mL). Product: 2.161 g of a dark orange oil (90% yield).



^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.77 (s, 1H, CH), 7.86 (s, 2H, 2 CH), 4.08 (m, 4H, 2 CH_2-N), 2.11 (m, 2H, 2 CH), 1.67 (s, 3H, CH_3), 0.87 (m, 6H, 2 CH_3).

1,3-Dihexylimidazolium acetate

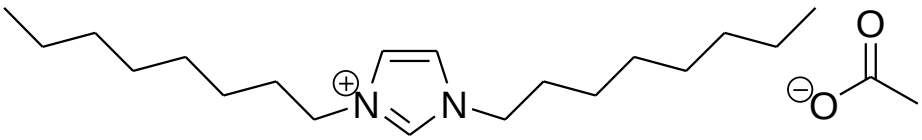
Used products: *n*-hexylamine (2 eq. 20 mmol, 2.64 mL), formaldehyde (38wt% in water, 10 mmol, 0.72 mL), acetic acid (15 mmol, 0.86 mL) and glyoxal (40 wt% in water, 10 mmol, 1.15 mL). Product: 2.846 g of a dark orange oil (96% yield).



^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.84 (s, 1H, CH), 7.86 (s, 2H, 2 CH), 4.12 (m, 4H, 2 CH_2-N), 1.79 (m, 4H, 2 CH_2), 1.62 (s, 3H, CH_3), 1.25 (m, 12H, 6 CH_2), 0.85 (m, 6H, 2 CH_3).

1,3-Dioctylimidazolium acetate

Used products: *n*-octylamine (2 eq. 20 mmol, 3.31 mL), formaldehyde (38wt% in water, 10 mmol, 0.72 mL), acetic acid (15 mmol, 0.86 mL) and glyoxal (40 wt% in water 10 mmol, 1.15 mL). Product: 2.432 g of a dark orange oil (69% yield).

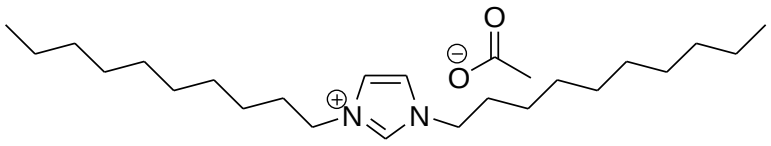


^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.92 (s, 1H, CH), 7.87 (s, 2H, 2 CH), 4.20 (m, 4H, 2 CH_2-N), 1.79 (m, 4H, 2 CH_2), 1.63 (s, 3H, CH_3), 1.25 (m, 20H, 10 CH_2), 0.85 (m, 6H, 2 CH_3).

1,3-Didecylimidazolium acetate

During this synthesis the minimal temperature of 0 °C was altered to 15 °C due to the melting point of *n*-decylamine: 13 °C. All the other synthetic steps were performed identical to the reaction in Scheme 20.

Used products: *n*-decylamine (2 eq. 10 mmol, 2.00 mL), formaldehyde (38wt% in water, 5 mmol, 0.36 mL), acetic acid (7.5 mmol, 0.43 mL) and glyoxal (40 wt% in water 5 mmol, 0.57 mL). Product: 0.795 g of a brown liquid (39% yield).



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.26 (s, 1H, CH), 7.25 (s, 2H, 2 CH), 4.29 (m, 4H, 2 CH_2-N), 1.94 (s, 3H, CH_3), 1.85(m, 4H, 2 CH_2), 1.28 (m, 28H, 14 CH_2), 0.88 (m, 6H, 2 CH_3).

1,3-Didodecylimidazolium acetate

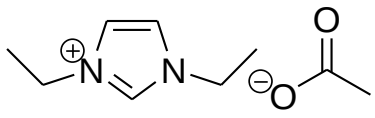
n-Dodecylamine was not soluble in water, it was therefore dissolved in ethanol before being added to the water. This ethanol needed to be evaporated before the washing step, since the mixture of products, water, ethanol and ether was a homogenous phase.

After washing the water phase with ether, no pure product of 1,3-didodecylimidazolium acetate could be isolated. The purifying steps were also extremely time consuming due to the high surfactant properties of the products.

4.3.4 Large 1,3-dialkylimidazolium acetate batches

Since a diverse series of 1,3-dialkylimidazolium acetate ionic liquids can be prepared in a halogen-free synthesis, larger batches were prepared in order to create a platform of acetate ionic liquids. From these large imidazolium acetate batches other ionic liquids could be prepared via several metathesis reactions, introducing new anions by removal of the acetate.

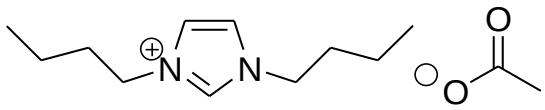
1,3-Diethylimidazolium acetate



Used products: ethylamine (70 wt% in water, 2 eq. 250 mmol, 20.13 mL), formaldehyde (38wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 21.60 g of a dark orange oil (94% yield).

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.77 (s, 1H, CH), 7.85 (s, 2H, 2 CH), 4.22 (m, 4H, 2 CH_2-N), 1.64 (s, 3H, CH_3), 1.42 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 173.04 (C=O), 136.21 (N-CH-N), 122.02 (2 CH-N), 44.02 (2 CH_2-N), 24.85 (2 CH_3), 15.08 (CH_3). CHN analysis: (calculated for $C_9H_{16}N_2O_2 \cdot 2H_2O$) (220.27 g mol^{-1}): C 48.20% (49.08%), H 8.87% (9.15%), N 12.65% (12.72%). FTIR: (v/cm^{-1}): 2960, 2934, 2874 (C-H stretch), 1577 (C=O stretch), 1381 (C-O stretch). Water content: 70326 ppm. Viscosity: Water content too high for qualitative viscosity determination.

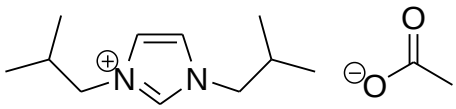
1,3-Dibutylimidazolium acetate



Used products: *n*-butylamine (2 eq. 250 mmol, 24.7 mL), formaldehyde (38wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 24.49 g of a dark orange oil (82% yield).

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.98 (s, 1H, CH), 7.88 (s, 2H, 2 CH), 4.21 (m, 4H, 2 CH_2-N), 1.78 (m, 4H, 2 CH_2), 1.63 (s, 3H, CH_3), 1.23 (m, 4H, 2 CH_2), 0.90 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 173.52 (C=O), 137.50 (N-CH-N), 122.86 (2 CH-N), 49.00 48.82(2 CH_2-N), 31.87-25.61 (4 CH_2), 19.24 (2 CH_3), 13.70 (CH_3). CHN analysis: (calculated for $C_{13}H_{24}N_2O_2 \cdot H_2O$) (258.36 g mol^{-1}): C 59.57% (60.44%), H 10.42% (10.14%), N 10.63% (10.84%). FTIR: (v/cm^{-1}): 2960, 2934, 2874 (C-H stretch), 1577 (C=O stretch), 1381 (C-O stretch). Water content: 6813 ppm. Viscosity: 516 cP (25.7 °C).

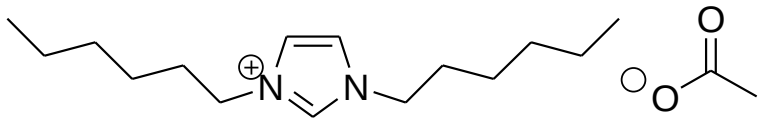
1,3-Diisobutylimidazolium acetate



Used products: Isobutylamine (2 eq. 250 mmol, 25.09 mL), formaldehyde (38 wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 26.93 of a dark orange solid (90% yield).

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.77 (s, 1H, CH), 7.86 (s, 2H, 2 CH), 4.08 (m, 4H, 2 CH_2-N), 2.11 (m, 2H, 2 CH), 1.67 (s, 3H, CH_3), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 173.47 (C=O), 137.25 (N-CH-N), 122.74 (2 CH-N), 55.33 (2 CH_2-N), 28.67 (2 CH), 24.71 (4 CH_3), 18.98 (CH_3). CHN analysis: (calculated for $C_{13}H_{24}N_2O_2 \cdot H_2O$) (258.36 g mol^{-1}): C 60.65% (60.44%), H 10.14% (10.14%), N 10.55% (10.84%). FTIR: (v/cm^{-1}): 2954, 2929, 2869 (C-H stretch), 1574 (C=O stretch), 1381 (C-O stretch). Melting point: 60 °C.

1,3-Dihexylimidazolium acetate

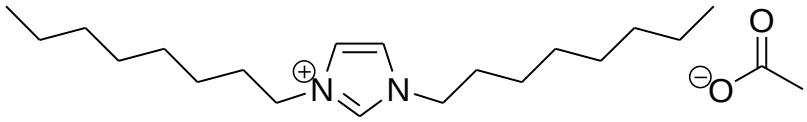


Used products: *n*-hexylamine (2 eq. 250 mmol, 33.03 mL), formaldehyde (38 wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 26.42 g of a dark orange oil (71% yield).

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.91 (s, 1H, CH), 7.87 (s, 2H, 2 CH), 4.19 (m, 4H, 2 CH_2-N), 1.79 (m, 4H, 2 CH_2), 1.62 (s, 3H, CH_3), 1.25 (m, 12H, 6 CH_2), 0.85 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 173.35 (C=O), 137.46 (N-CH-N), 122.86 123.0(2 CH-N), 49.15 (2 CH_2-N), 30.96-22.33 (8 CH_2), 25.67 (CH_3), 14.22 (2 CH_3). CHN analysis: (calculated for $C_{17}H_{32}N_2O_2 \cdot H_2O$) (314.46 g mol^{-1}): C 63.23% (64.71%), H 12.91% (10.90%),

N 8.65% (8.91%). FTIR: (v/cm^{-1}): 2956, 2928, 2859 (C-H stretch), 1579 (C=O stretch), 1381 (C-O stretch). Water content: 4049 ppm. Viscosity: 682 cP (25.7 °C).

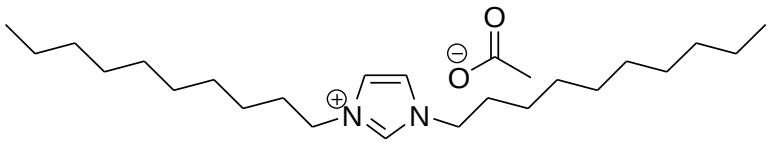
1,3-Dioctylimidazolium acetate



Used products: *n*-octylamine (2 eq. 250 mmol, 41.30 mL), formaldehyde (38wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 24.378 g of a dark orange oil (55% yield) with a melting point at 16 °C.

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.97 (s, 1H, CH), 7.89 (s, 2H, 2 CH), 4.29 (m, 4H, 2 CH_2-N), 1.79 (m, 4H, 2 CH_2), 1.63 (s, 3H, CH_3), 1.24 (m, 20H, 10 CH_2), 0.85 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 173.53 (C=O), 137.55 (N-CH-N), 122.86 123.02 (2 CH-N), 49.13 (2 CH_2-N), 31.60-22.50 (12 CH_2), 25.62 (CH_3), 14.32 (2 CH_3). CHN analysis: (calculated for $C_{21}H_{40}N_2O_2 \cdot H_2O$) (370.57 g mol^{-1}): C 68.60% (68.06%), H 13.88% (11.42%), N 7.57% (7.56%). FTIR: (v/cm^{-1}): 2956, 2924, 2856 (C-H stretch), 1576 (C=O stretch), 1385 (C-O stretch). Water content: 3727 ppm. Viscosity: 861 cP (25.7 °C).

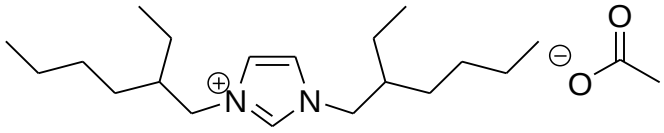
1,3-Didecylimidazolium acetate



Used products: *n*-decylamine (2 eq. 250 mmol, 49.13 mL), formaldehyde (38wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 27.07 g of a brown oil (53% yield) with a melting point of -22 °C.

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.76 (s, 1H, CH), 7.86 (s, 2H, 2 CH), 4.19 (m, 4H, 2 CH_2-N), 1.79 (m, 4H, 2 CH_2), 1.76 (s, 3H, CH_3), 1.23 (m, 28H, 14 CH_2), 0.85 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 172.98 (C=O), 137.52 (N-CH-N), 122.87 (2 CH-N), 52.02 (2 CH_2-N), 30.64-13.76 (16 CH_2), 24.67 (CH_3), 10.1 (2 CH_3). CHN analysis: (calculated for $C_{25}H_{48}N_2O_2$) (408.66 g mol^{-1}): C 74.54% (73.48%), H 14.92% (11.84%), N 6.58% (6.85%). FTIR: (v/cm^{-1}): 2958, 2926, 2853 (C-H stretch), 1578 (C=O stretch), 1385 (C-O stretch). Water content: 7103 ppm. Viscosity: 745 cP (25.0 °C).

1,3-Di(2-ethylhexyl)imidazolium acetate



Used products: 2-ethylhexylamine (2 eq. 250 mmol, 41.4 mL), formaldehyde (38 wt% in water, 125 mmol, 8.95 mL), acetic acid (180 mmol, 10.29 mL) and glyoxal (40 wt% in water, 125 mmol, 14.34 mL). Product: 27.07 g of a highly viscous, dark orange oil (47% yield).

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.83 (s, 1H, CH), 7.87 (s, 2H, 2 CH), 4.13 (d, 7.0 Hz, 4H, 2 CH_2-N), 1.84 (m, 2H, 2 CH), 1.65 (s, 3H, CH_3), 1.25 (m, 16H, 8 CH_2), 0.85 (m, 12H, 4 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 173.1 (C=O), 136.9 (N-CH-N), 122.4 (2 CH-N), 48.7 (2 CH_2-N), 31.28-22.08 (8 CH_2, 2CH), 24.38 (CH_3), 13.87 (4 CH_3). FTIR: (v/cm^{-1}): 2959, 2928, 2861 (C-H stretch), 1578 (C=O stretch) CHN analysis: (calculated for $C_{21}H_{40}N_2O_2 \cdot H_2O$) (370.57 g mol^{-1}): C 68.35% (68.06%), H 13.70% (11.42%), N 7.54% (7.56%). Water content: 3231 ppm. Viscosity: 4659 cP (25.7 °C).

Increasing the yield

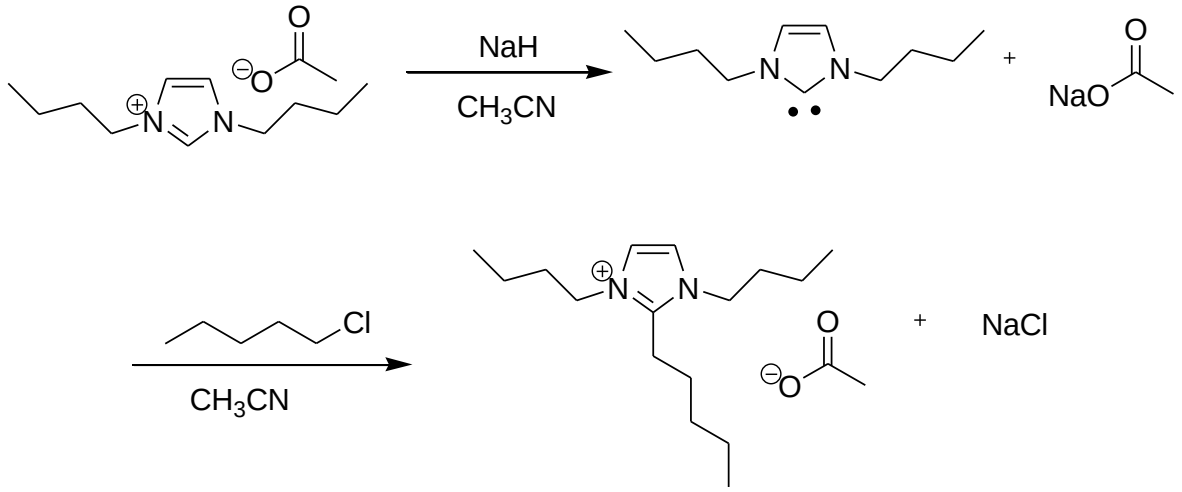
The syntheses of the more hydrophobic imidazolium acetate compounds suffered from lower yields. This effect became more prominent with increasing chain length of the amine used in the synthesis. When using the *n*-decylamine, the yield even dropped under 50%. In order to boost the yield of the reaction, an attempt was made to extract some product from the ether phases used to wash the water, this test was performed on [HHIM][AcO]. All the ether phases produced in the purification were collected, they were washed once with water and a small sample of this water was investigated via ^{1}H NMR. The extracted product from the ether phase did contain a significant amount of [HHIM][AcO], although some impurities migrated to the water phase as well. The idea to increase the yield was not investigated further due to the priority of the compounds purity over the yield of the reaction.

4.3.5 1,2,3-Trisubstituted imidazolium acetate

In order to substitute the imidazolium compounds even further, several methods were investigated to obtain 1,2,3-trisubstituted imidazolium acetate ionic liquids. A straightforward method would be to alkylate the existing 1,3-dialkylimidazolium compounds, although this results in extra synthetic steps. Another strategy might be to directly produce trisubstituted imidazolium compounds by using other aldehydes than formaldehyde, of course special care should be taken to prevent using enolizable aldehydes.

C2 alkylation of 1,3-dibutylimidazolium acetate

The alkylation of 1,3-dibutylimidazolium acetate was attempted using sodium hydride and chloropentane as described in the literature procedure of Ennis *et al*.[63] The 1,3-dibutylimidazolium acetate and sodium hydride were dissolved in acetonitrile and afterwards the chloropentane was added resulting in 1,3-dibutyl-2-pentylimidazolium acetate (Scheme 21).



Scheme 21: Synthesis of 1,3-dibutyl-2-pentylimidazolium acetate.

Sodium hydride (60% in natural oil, 6 mmol, 0.24 g) was added to dry acetonitrile under argon atmosphere. A solution of 1,3-dibutylimidazolium acetate in dry acetonitrile was added drop-wise to the sodium hydride and the solution was stirred at room temperature. After 4 h, the chloropentane was added (20 mmol, 2.13 g) and the solution was stirred overnight at room temperature. The mixture was filtered over a glass filter to remove the sodium chloride formed in the reaction, the salt was washed with acetonitrile. The acetonitrile was evaporated using a rotary evaporator and the resulting product was washed three times with diethyl ether to remove the excess of chloropentane. The remaining product was attached to the Schlenk line at 50 °C to remove any volatiles left in the product. ^{1}H NMR spectroscopy and ESI-MS were performed to detect the 1,3-dibutyl-2-pentylimidazolium acetate. These measurements indicated that the alkylation had partially succeeded but the starting product: 1,3-dibutylimidazolium acetate was still present.

The process was repeated with 0.03 g of sodium hydride (0.75 mmol) and 0.27 g of chloropentane (2.5 mmol). Again the starting product showed up in the mass spectrometry plot. In order to determine the exact molar mass and ratios of imidazolium compounds an LC-MS measurement was performed. The results indicated only a moderate fraction of 1,3-

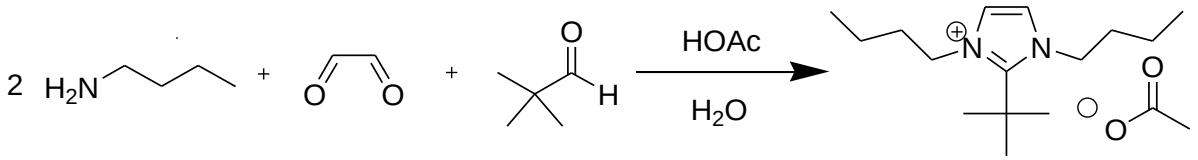
dibutyl-2-pentylimidazolium acetate, which was contaminated by the 1,3-dibutylimidazolium acetate and other contaminants that could not be identified.

Direct synthesis of 1,2,3-trisubstituted imidazolium acetate

Only formaldehyde had been used as a non-enolizable aldehyde, however other products answer these requirements, for instance: pivaldehyde and benzaldehyde. Tests were performed in which the last two replaced formaldehyde in the successful synthesis of 1,3-dialkylimidazolium acetate, all the other synthetic and extraction parameters were retained. These syntheses were also performed as a proof-of-concept for the synthesis of imidazolium compounds from non-enolizable products.

1,3-Dibutyl-2-t-butylimidazolium acetate

Used products: *n*-butylamine (2 eq. 20 mmol, 1.98 mL), pivaldehyde (10 mmol, 1.10 mL), acetic acid (1.5 eq. 15 mmol, 0.86 mL) and glyoxal (40 wt% in water, 10 mmol, 1.15 mL).

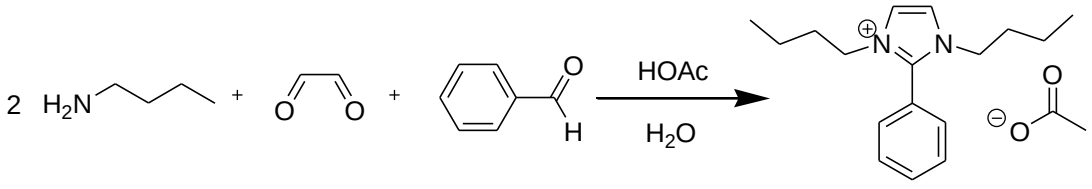


Scheme 22: Synthesis of 1,3-dibutyl-2-t-butylimidazolium acetate.

The ^{1}H NMR spectrum showed no distinctive *tert*-butyl peak and in contrast showed a proton peak of the C2 position on the imidazolium.

1,3-Dibutyl-2-phenylimidazolium acetate

Used products: *n*-butylamine (2 eq. 20 mmol, 1.98 mL), benzaldehyde (10 mmol, 0.52 mL), acetic acid (1.5 eq. 15 mmol, 0.86 mL) and glyoxal (40 wt% in water, 10 mmol, 1.15 mL).



Scheme 23:Synthesis of 1,3-dibutyl-2-phenylimidazolium acetate.

The ^{1}H NMR spectrum showed only a small portion of peaks corresponding to phenyl protons and a significant proton peak of the C2 position on the imidazolium.

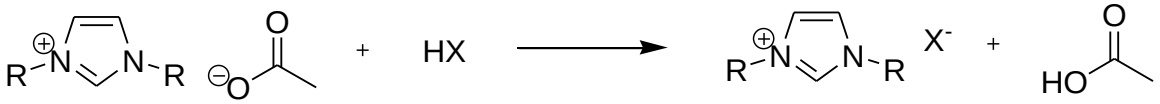
4.4 Metatheses

4.4.1 Different strategies for metathesis

Depending on the desired anion of an ionic liquid and the starting precursor, several metathesis strategies are possible. The precursors in this case were the 1,3-dialkylimidazolium acetate ionic liquids that were synthesized earlier in a halogen-free one-pot synthesis. Their applicability towards the synthesis of new ionic liquids was investigated by performing several metathesis reactions. Depending on the properties of the used reagents and the final ionic liquids, the strategies of the metatheses differed. When the acid of the new anion was much more acidic than acetic acid, it was used to protonate the acetate. When the acid had a more or less identical or a higher pK_a compared to acetic acid, a salt of the new anion was used.

Metatheses using acids

When the targeted anion for the metathesis, meaning the new anion, is a weak base, then its acid can be used in the synthesis of new ionic liquids starting from imidazolium acetate (Scheme 24).



Scheme 24: Metathesis with 1,3-dialkylimidazolium acetate using acids.

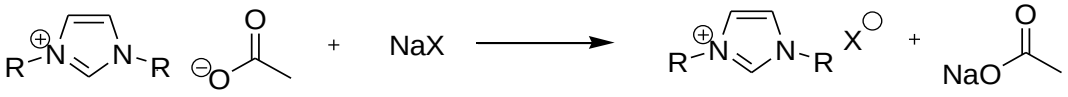
The pK_a of acetic acid is 4.76, which is moderately acidic, but many stronger acids exist. Since the pH scale is a logarithmic scale, a complete reaction is considered when the pK_a difference between the two acids covers roughly 4 pK_a units, this corresponds to 10000 molecules of acetic acid for each remaining acetate anion. This means the acids must have a pK_a of about 0.7 or lower. This seems rather low but most typical anions for ionic liquids meet this requirement, especially the fluorinated organic anions like bistriflimide and triflate. This way the protonation is complete and the acetic acid can be removed by evaporation or washing.

Metatheses using salts

If the new anion is derived of a weak acid (pK_a>0.7), it cannot be used as an acid to replace the acetate due to an incomplete protonation. In these cases a salt of the anion has to be used to replace the acetate. Special care must be taken with metatheses using salts, since not all salts can be replaced. This order is displayed in the Hofmeister series: this anion sequence shows the efficiency of anion exchange of an ionic liquid brought into contact with

a water phase containing a salt.[45,46] Fortunately, the acetate anion is placed rather low in this series so it can be exchanged with many anions, with the only exception of sulfate and halogen anions.

Since almost all anions in ionic liquids are more hydrophobic compared to acetate, the acetate can be removed by washing with a polar solvent. In order to reach the highest possible efficiency, it is beneficial to have an acetate salt that is as hydrophilic as possible. This is achieved by using sodium salts, resulting in sodium acetate (Scheme 25).



Scheme 25: Metathesis with 1,3-dialkylimidazolium acetate using salts.

If the sodium salt of the anion is not commercially available, it can be synthesized from its acid using sodium hydroxide and water as a solvent. When stoichiometry is of vital importance, the synthesis can be carried out in other solvents and the resulting salt will be a monohydrate. The use of such monohydrate salts allows for the precise addition of equimolar amounts of salt in the metathesis.

Removing the acetate

Acetic acid

The formed acetic acid can be removed in several ways, depending on the hydrophobicity of the ionic liquid. If the resulting ionic liquid is insoluble in water, the acetic acid can be removed by washing the ionic liquid with water.

If the ionic liquid is not hydrophobic enough, causing it to dissolve, completely or partially, in water, the water washing step of the ionic liquid would result in tremendous losses. The acetic acid can then be removed by evaporation, due to its rather low boiling point: 118 °C (19.8 °C at reduced pressure: 20 mm Hg). The ionic liquids themselves show no vapor pressure so there is no risk of accidentally evaporating the products. This last procedure is only used if the washing cannot result in complete removal of the acetic acid, since the ionic liquids have some disadvantageous properties regarding the evaporation of acetic acid. They are highly viscous, resulting in difficult stirring and slow evaporation of acetic acid and show high solvating power. Attaching the ionic liquids to the Schlenk line did result in complete removal of the ionic liquid, the duration of the process depended on the ionic liquids' solvating power and viscosity.

Sodium acetate

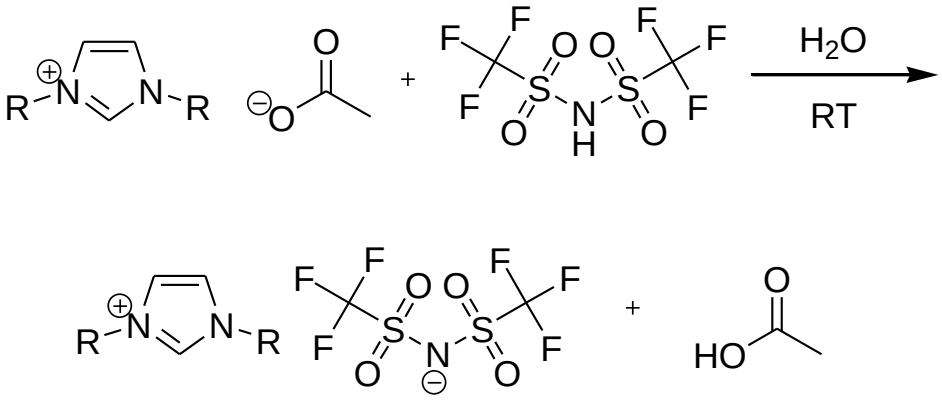
When using salts for metathesis purposes, the salts cannot be removed via evaporation and other methods must be used. The strategy depends on the hydrophilicity of the new ionic liquid. When hydrophobic ionic liquids are formed that do not dissolve in water, the sodium acetate can be washed away with water with a very limited loss of imidazolium. If however hydrophilic ionic liquids are formed which do dissolve in water this is not possible. The sodium acetate will then be removed by performing the synthesis in an apolar solvent which still dissolves the imidazolium acetate and the sodium salt. If the solvent is apolar enough, the formed sodium acetate can precipitate and therefore be removed from the mixture. To increase the effectiveness of the reaction, a minimum amount of solvent should be used, this can be done by heating it when dissolving the reagents and afterward cooling it down to decrease the solubility of the sodium acetate. Since this last technique is very sensitive towards water traces, it might not result in complete removal of the sodium acetate.

4.4.2 Bis(trifluoromethylsulfonyl)imide

The acetate ionic liquids are rather polar and therefore soluble in water, the first metathesis was performed with a popular and hydrophobic anion: bis(trifluoromethylsulfonyl)imide or bistriflimide ($[Tf_2N]^-$).

Synthesis

The acid of bistriflimide: hydrogen bistriflimide, is a superacid.[43] Therefore the acid was used in the metathesis. All seven 1,3-dialkylimidazolium acetate ionic liquids were used in the different metatheses, and for all seven the procedure was identical (Scheme 26).



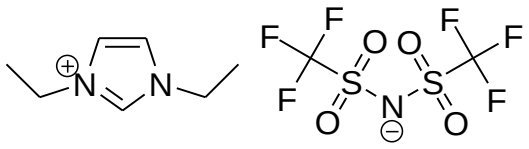
Scheme 26: Synthesis of 1,3-dialkylimidazolium bis(trifluoromethylsulfonyl)imide.

1,3-Dialkylimidazolium acetate (5 mmol) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g) were dissolved in water and stirred at room temperature for 2 h. A hydrophobic phase appeared that was not miscible with water. Dichloromethane was

added to the reaction mixture until the entire hydrophobic liquid was dissolved. The dichloromethane was separated from the water phase and washed with water. The dichloromethane was removed with a rotary evaporator and the product was dried on the Schlenk line at 50 °C.

Products + characterization

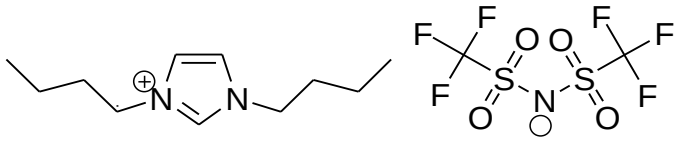
1,3-Diethylimidazolium bistriflimide



Used products: 1,3-diethylimidazolium acetate (5 mmol, 0.921 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 1.428 g of a brown oil (71% yield) with a melting point of -12 °C.

^{1}H NMR: (300 MHz, DMSO-d_6, δ/ppm): 9.18 (s, 1H, CH), 7.80 (s, 2H, 2 CH), 4.19 (m, 4H, 2 CH_2), 1.43 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, DMSO-d_6, δ/ppm): 134.40 (N-CH-N), 122.18 (2 CH-N), 117.78 (2 CF_3), 45.29 (2 CH_2-N), 14.88 (2 CH_3). CHN analysis: (calculated for $C_9H_{13}N_3O_4S_2F_6$) (405.34 g mol^{-1}): C 27.11% (26.67%), H 3.72% (3.23%), N 10.23% (10.37%). FTIR: (v/cm^{-1}): 3153, 3118, 2991 (C-H stretch), 1566 (aromatic C-N stretch), 1455 (aromatic C-C stretch), 1347, 1330, 1135 (S=O stretch), 1180 (C-F_3 stretch), 1053 (N-S stretch), 613 (SO_2 bending), 570, 513 (C-F_3 bending). Water content: 2291 ppm. Viscosity: 29 cP (25.7 °C).

1,3-Dibutylimidazolium bistriflimide

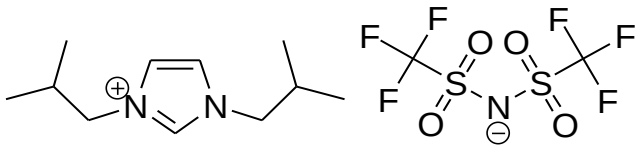


Used products: 1,3-dibutylimidazolium acetate (5 mmol, 1.20 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 2.023 g of a brown oil (88% yield).

^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 8.78 (s, 1H, CH), 7.36 (s, 2H, 2 CH), 4.18 (t, 7.5 Hz, 4H, 2 CH_2-N), 1.85 (m, 4H, 2 CH_2), 1.36 (m, 4H, 2 CH_2), 0.96 (t, 7.5 Hz, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 130.55 (N-CH-N), 117.65 (2 CH-N), 113.48 (2 CF_3), 45.16 (2 CH_2-N), 27.21 (2 CH_2), 14.54 (2 CH_2), 8.41 (2 CH_3). CHN analysis: (calculated for

$C_{13}H_{21}N_3O_4S_2F_6$) (461.44 g mol^{-1}): C 33.82% (33.84%), H 5.27% (4.59%), N 9.06% (9.11%). FTIR: (v/cm^{-1}): 2967, 2939, 2879 (C-H stretch), 1565 (aromatic C-N stretch), 1465 (aromatic C-C stretch), 1348, 1330, 1135 (S=O stretch), 1181 (C-F_3 stretch), 1054 (N-S stretch), 614 (SO_2 bending), 570, 512 (C-F_3 bending). Water content: 351 ppm. Viscosity: 66 cP (25.7 °C).

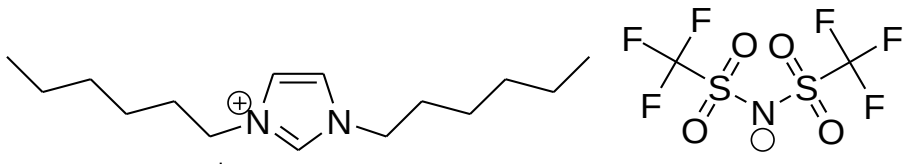
1,3-Diisobutylimidazolium bistriflimide



Used products: 1,3-diisobutylimidazolium acetate (5 mmol, 1.20 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 1.382 g of a brown oil (60% yield).

^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 8.81 (s, 1H, CH), 7.33 (s, 2H, 2 CH), 4.02 (d, 7.5 Hz, 4H, 2 CH_2-N), 2.15 (m, 2H, 2 CH), 0.95 (d, 6.5 Hz, 12H, 4 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 135.90 (N-CH-N), 122.77 (2 CH-N), 117.71 (2 CF_3), 56.92 (2 CH_2-N), 29.44 (2 CH), 19.09 (4 CH_3). CHN analysis: (calculated for $C_{13}H_{21}N_3O_4S_2F_6$) (461.44 g mol^{-1}): C 33.92% (33.84%), H 5.12% (4.59%), N 8.95% (9.11%). FTIR: (v/cm^{-1}): 2967, 2926, 2856 (C-H stretch), 1564 (aromatic C-N stretch), 1465 (aromatic C-C stretch), 1349, 1135 (S=O stretch), 1185 (C-F_3 stretch), 1056 (N-S stretch), 616 (SO_2 bending), 571, 513 (C-F_3 bending). Water content: 1953 ppm. Viscosity: 132 cP (25.7 °C).

1,3-Dihexylimidazolium bistriflimide

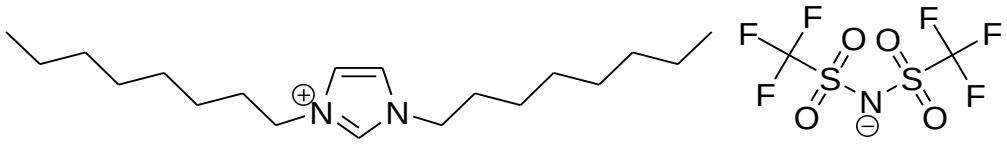


Used products: 1,3-dihexylimidazolium acetate (5 mmol, 1.48 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 2.372 g of an orange oil (92% yield).

^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 8.80 (s, 1H, CH), 7.35 (s, 2H, 2 CH), 4.18 (t, 7.5 Hz, 4H, 2 CH_2-N), 1.86 (m, 4H, 2 CH_2), 1.31 (m, 12H, 6 CH_2), 0.88 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 135.32 (N-CH-N), 122.41 (2 CH-N), 121.44 118.25 (2 CF_3), 50.16 (2 CH_2-N), 30.90 (2 CH_2), 30.04 (2 CH_2), 25.67 (2 CH_2), 22.26 (2 CH_2), 13.75 (2 CH_3). CHN analysis: (calculated for $C_{17}H_{29}N_3O_4S_2F_6$) (517.55 g mol^{-1}): C 39.29% (39.45%), H 6.34%

(5.65%), N 8.04% (8.12%). FTIR: (v/cm^{-1}): 2960, 2933, 2863 (C-H stretch), 1564 (aromatic C-N stretch), 1465 (aromatic C-C stretch), 1348, 1135 (S=O stretch), 1183 (C-F_3 stretch), 1055 (N-S stretch), 615 (SO_2 bending), 570, 513 (C-F_3 bending). Water content: 108 ppm. Viscosity: 102 cP (25.7 °C).

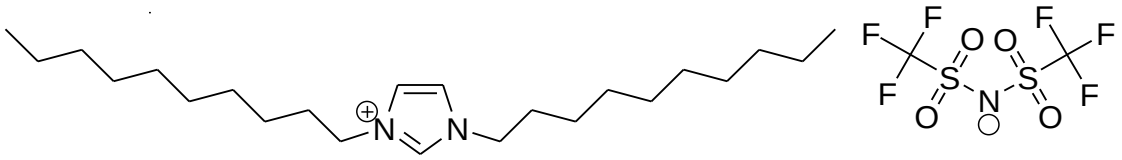
1,3-Dioctylimidazolium bistriflimide



Used products: 1,3-dioctylimidazolium acetate (5 mmol, 1.76 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 2.65 g of an orange oil (93% yield).

^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 8.80 (s, 1H, CH), 7.33 (s, 2H, 2 CH), 4.18 (t, 7.5 Hz, 4H, 2 CH_2-N), 1.86 (m, 4H, 2 CH_2), 1.29 (m, 20H, 10 CH_2), 0.89 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 135.32 (N-CH-N), 122.38 (2 CH-N), 118.75 (2 CF_3), 50.18 (2 CH_2-N), 31.58 (2 CH_2), 30.10 (2 CH_2), 28.91 (2 CH_2), 28.77 (2 CH_2), 26.04 (2 CH_2), 22.51 (2 CH_2), 13.96 (2 CH_3). CHN analysis: (calculated for $C_{21}H_{37}N_3O_4S_2F_6$) (573.66 g mol^{-1}): C 43.94% (43.97%), H 7.36% (6.50%), N 7.29% (7.32%). FTIR: (v/cm^{-1}): 2928, 2859 (C-H stretch), 1564 (aromatic C-N stretch), 1465 (aromatic C-C stretch), 1349, 1135 (S=O stretch), 1184 (C-F_3 stretch), 1055 (N-S stretch), 616 (SO_2 bending), 570, 513 (C-F_3 bending). Water content: 199 ppm. Viscosity: 147 cP (25.7 °C).

1,3-Didecylimidazolium bistriflimide

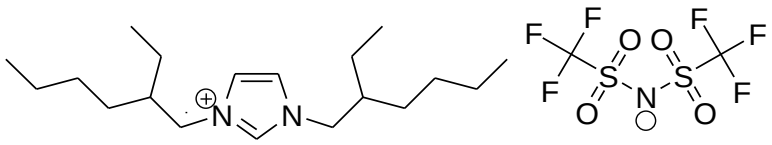


Used products: 1,3-didecylimidazolium acetate (5 mmol, 2.043 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 1.523 g of an orange oil (48% yield) with a melting point at 24 °C.

^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 8.83 (s, 1H, CH), 7.30 (s, 2H, 2 CH), 4.19 (t, 7.5 Hz, 4H, 2 CH_2-N), 1.87 (m, 4H, 2 CH_2), 1.28 (m, 28H, 14 CH_2), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 135.38 (N-CH-N), 122.36 (2 CH-N), 117.68 (2 CF_3), 50.22 (2 CH_2-N), 31.82-22.63 (16 CH_2), 14.05 (2 CH_3). CHN analysis: (calculated for $C_{25}H_{45}N_3O_4S_2F_6$) (629.76

g mol^{-1}): C 46.45% (47.68%), H 7.87% (7.20%), N 6.58% (6.67%). FTIR: (v/cm^{-1}): 3148, 2926, 2856 (C-H stretch), 1564 (aromatic C-N stretch), 1465 (aromatic C-C stretch), 1349, 1135 (S=O stretch), 1184 (C-F_3 stretch), 1055 (N-S stretch), 616 (SO_2 bending), 571, 513 (C-F_3 bending). Water content: 502 ppm. Viscosity: 131 cP (25.7 °C).

1,3-Di(2-ethylhexyl)imidazolium bistriflimide



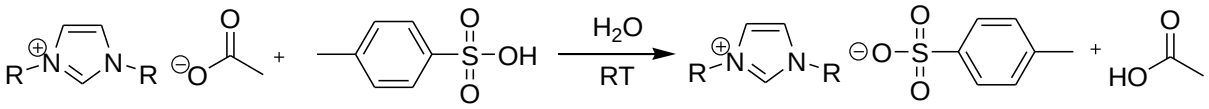
Used products: 1,3-di-(2-ethylhexyl)imidazolium acetate (5 mmol, 1.76 g) and hydrogen bis(trifluoromethylsulfonyl)imide (80 wt% in water, 5 mmol, 1.76 g). A ^{1}H NMR spectrum confirmed the purity of the product: 2.47 g of an orange oil (86% yield).

^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 8.77 (s, 1H, CH), 7.33 (s, 2H, 2 CH), 4.10 (d, 7.5 Hz, 4H, 2 CH_2-N), 1.83 (m, 2H, 2 CH), 1.23 (m, 16H, 8 CH_2), 0.90 (m, 12H, 4 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 136.13 (N-CH-N), 122.81 (2 CH-N), 118.77 (2 CF_3), 53.60 (2 CH_2-N), 40.01 (2 CH) 29.82-22.73 (8 CH_2), 13.76 (2 CH_3), 10.08 (2 CH_3). CHN analysis: (calculated for $C_{21}H_{37}N_3O_4S_2F_6$) (573.66 g mol^{-1}): C 43.11% (43.97%), H 7.35% (6.50%), N 7.25% (7.32%). FTIR: (v/cm^{-1}): 2963, 2933, 2864 (C-H stretch), 1563 (aromatic C-N stretch), 1462 (aromatic C-C stretch), 1349, 1135 (S=O stretch), 1184 (C-F_3 stretch), 1055 (N-S stretch), 615 (SO_2 bending), 570, 513 (C-F_3 bending). Water content: 1037 ppm. Viscosity: 424 cP (25.7 °C).

4.4.3 *p*-Toluenesulfonate

Synthesis

The acid of *p*-toluenesulfonate (or: tosylate): *p*-toluenesulfonic acid, is a strong acid with a pK_a of -2.8. Therefore the acid was used in the metathesis. The acetic acid could be safely removed by evaporation if necessary, due to the high T_b of the *p*-toluenesulfonic acid (140 °C). All seven 1,3-dialkylimidazolium acetate ionic liquids were used, in identical procedures (Scheme 27).



Scheme 27: Synthesis of 1,3-dialkylimidazolium *p*-toluenesulfonate.

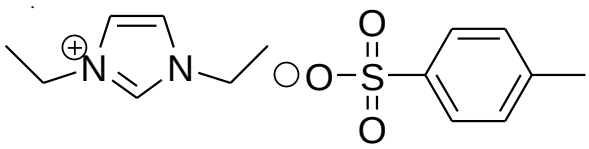
1,3-Dialkylimidazolium acetate (5 mmol) was dissolved in water and *p*-toluenesulfonic acid (monohydrate, 5 mmol, 0.952 g) was added, the reaction mixture was stirred overnight at room temperature. Depending on the hydrophobicity of the *p*-toluenesulfonate ionic liquids, different purification steps were required.

Products + characterization

1,3-Diethylimidazolium tosylate

Used products: 1,3-diethylimidazolium acetate (5 mmol, 0.921 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After the reaction, a water-soluble product was obtained, the water was removed with a rotary evaporator and the flask was attached to the Schlenk line at 70 °C to remove the acetic acid. ^{1}H NMR was used to check the removal of acetic acid until the product was pure. This resulted in 1.36 g (92 % yield) of a dark brown liquid.

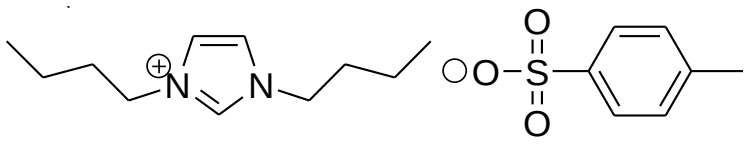


^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 9.75 (s, 1H, CH), 7.75 (s, 2H, 2 CH), 7.29 (s, 2H, 2 CH) 7.14 (s, 2H, 2 CH), 4.28 (m, 4H, 2 CH_2), 2.34 (s, 3H, CH_3), 1.50 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 142.05 (C-S), 140.19 (C-CH_3), 136.52 (CH), 128.81 (2 CH), 125.97 (2 CHN), 121.68 (2 CH), 45.07 (2 CH_2), 21.33 (1 CH_3), 15.34 (2 CH_3). CHN analysis: (calculated for $C_{14}H_{20}N_2O_3S{\cdot}H_2O$) (314.4 g mol^{-1}): C 53.50% (53.48%), H 7.88% (7.08%), N 8.07% (8.91%). FTIR: (v/cm^{-1}): 3097-2876 (C-H stretch), 1563 (N-C-N stretch), 1470 (C-C stretch), 1166, 1120 (SO_2 stretch), 1032, 1010, 816 (C-H bending), 679 (S=O stretch), 565 (C-S bending). Water content:4905 ppm. Viscosity: 1209 cP (25.0 °C).

1,3-Dibutylimidazolium tosylate

Used products: 1,3-dibutylimidazolium acetate (5 mmol, 1.202 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After the reaction, a water-soluble product was obtained, the water was removed with a rotary evaporator and the flask was attached to the Schlenk line at 70 °C to remove the acetic acid. ^{1}H NMR was used to check the removal of acetic acid until the product was pure. This resulted in 1.76 g (100 % yield) of a light brown liquid.

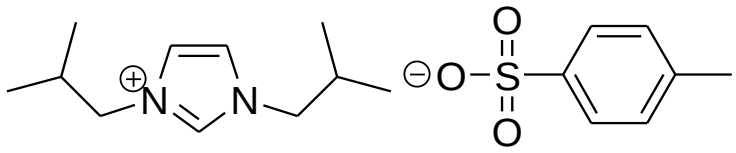


^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 9.78 (s, 1H, CH), 7.77 (s, 2H, 2 CH), 7.25 (s, 2H, 2 CH) 7.14 (s, 2H, 2 CH), 4.23 (m, 4H, 2 CH_2), 2.34 (s, 3H, CH_3), 1.81 (m, 4H, 2 CH_2), 1.30 (m, 4H, 2 CH_2), 0.91 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 142.20 (C-S), 140.04 (C-CH_3), 137.53 (CH), 128.73 (2 CH), 126.05 (2 CHN), 121.76 (2 CH), 49.76 (2 CH_2), 32.05 (2 CH_2), 21.33 (CH_3), 19.43 (2 CH_2), 13.41 (2 CH_3). CHN analysis: (calculated for $C_{18}H_{28}N_2O_3S{\cdot}H_2O$) (370.51 g mol^{-1}): C 59.73% (58.35%), H 8.70% (8.16%), N 7.47% (7.56%). FTIR: (v/cm^{-1}): 3097-2874 (C-H stretch), 1564 (N-C-N stretch), 1460 (C-C stretch), 1166, 1120 (SO_2 stretch), 1033, 1010, 816 (C-H bending), 680 (S=O stretch), 566 (C-S bending). Water content: 4174 ppm. Viscosity: 2404 cP (25.0 °C).

1,3-Diisobutylimidazolium tosylate

Used products: 1,3-diisobutylimidazolium acetate (5 mmol, 1.202 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After the reaction, a water-soluble product was obtained, the water was removed with a rotary evaporator and the flask was attached to the Schlenk line at 70 °C to remove the acetic acid. ^{1}H NMR was used to check the removal of acetic acid until the product was pure. This resulted in 1.64 g (93 % yield) of a light brown liquid. Upon measuring the viscosity (at 25.0 °C) the product solidified, indicating that it had been super cooled at room temperature. Exposing it to the metal plate of the viscometer caused the product to crystallize, resulting in a light brown powder with a melting point of 95 °C.

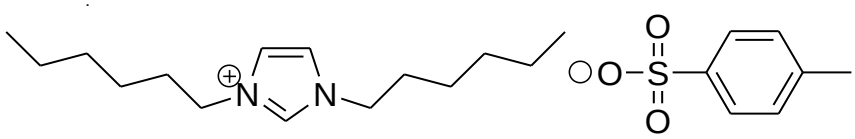


^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 9.78 (s, 1H, CH), 7.76 (s, 2H, 2 CH), 7.23 (s, 2H, 2 CH) 7.15 (s, 2H, 2 CH), 4.10 (m, 4H, 2 CH_2), 2.35 (s, 3H, CH_3), 2.13 (m, 2H, 2 CH), 0.91 (m, 12H, 4 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 141.85 (C-S), 140.22 (C-CH_3), 137.97 (CH), 128.77 (2 CH), 126.11 (2 CHN), 122.17 (2 CH), 56.79 (2 CH_2), 29.40(2 CH), 21.34 (CH_3), 19.33 (4 CH_3).CHN analysis: (calculated for $C_{18}H_{28}N_2O_3S{\cdot}H_2O$) (370.51 g mol^{-1}): C 58.64% (58.35%), H 8.87% (8.16%), N 7.27% (7.56%). FTIR: (v/cm^{-1}): 3141-2982 (C-H stretch), 1565 (N-C-N stretch), 1450 (C-C stretch), 1165, 1119 (SO_2 stretch), 1032, 1009, 817 (C-H bending), 680 (S=O stretch), 565 (C-S bending). Melting point: 95 °C.

1,3-Dihexylimidazolium tosylate

Used products: 1,3-dihexylimidazolium acetate (5 mmol, 1.202 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After reaction, a water-insoluble product was formed, the water was separated and ^{1}H NMR indicated that there remained some 1,3-dihexylimidazolium acetate in the product. The product was added to water to dissolve the imidazolium acetate and an excess of *p*-toluenesulfonic acid was added. The remaining *p*-toluenesulfonic acid and acetic acid were washed away with water and the product was dried on the Schlenk line. Upon total removal of water, the product solidified. This resulted in 1.357 g (66% yield) of a light brown powder with a melting temperature of 67 °C.

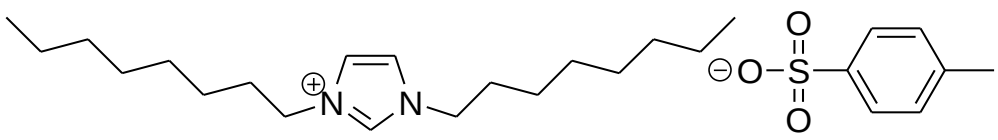


^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.22 (s, 1H, CH), 7.81 (s, 2H, 2 CH), 7.17 (s, 2H, 2 CH) 7.12 (s, 2H, 2 CH), 4.29 (m, 4H, 2 CH_2), 2.36 (s, 3H, CH_3), 1.86 (m, 4H, 2 CH_2), 1.29 (m, 12H, 6 CH_2), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 143.79 (C-S), 139.13 (C-CH_3), 138.44 (CH), 128.55 (2 CH), 125.96 (2 CHN), 121.35 (2 CH), 50.10 (CH_3), 31.08 (2 CH_2), 30.18 (2 CH_2), 25.88 (2 CH_2), 22.39 (2 CH_2), 21.30 (2 CH_2), 13.91 (2 CH_3). FTIR: (v/cm^{-1}): 3086-2870 (C-H stretch), 1565 (N-C-N stretch), 1466 (C-C stretch), 1194, 1121 (SO_2 stretch), 1035, 1012, 814 (C-H bending), 679 (S=O stretch), 561 (C-S bending). Melting point: 67 °C.

1,3-Dioctylimidazolium tosylate

Used products: 1,3-dioctylimidazolium acetate (5 mmol, 1.763 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After reaction a suspension was formed, the product was separated using a glass filter and washed with water. ^{1}H NMR confirmed the purity of the product which was pulverized and dried in the vacuum oven. This resulted in 1.98 g (85% yield) of a fine, white powder with a melting point of 97 °C.

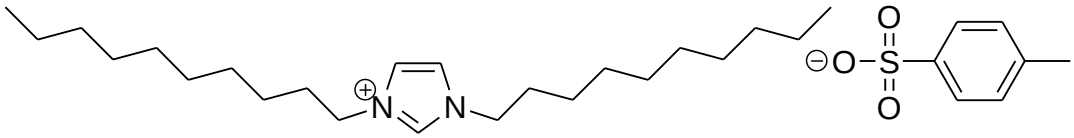


^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.24 (s, 1H, CH), 7.82 (s, 2H, 2 CH), 7.15 (s, 2H, 2 CH) 7.13 (s, 2H, 2 CH), 4.29 (m, 4H, 2 CH_2), 2.34 (s, 3H, CH_3), 1.87 (m, 4H, 2 CH_2), 1.27 (m, 20H, 10 CH_2), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 143.83 (C-S), 139.10 (C-CH_3), 138.40 (CH), 128.55 (2 CH), 125.96 (2 CHN), 121.38 (2 CH), 50.10 (2 CH_2), 31.69 (2 CH_2), 30.24 (2 CH_2), 29.05 (2 CH_2), 28.95 (2 CH_2), 26.23 (2 CH_2), 22.59 (2 CH_2), 21.37 (CH_3), 13.91 (2 CH_3). FTIR: (v/cm^{-1}): 3060-2854 (C-H stretch), 1561 (N-C-N stretch), 1467 (C-C stretch), 1195, 1120 (SO_2 stretch), 1033, 1011, 814 (C-H bending), 678 (S=O stretch), 564 (C-S bending). Melting point: 97 °C.

1,3-Didecylimidazolium tosylate

Used products: 1,3-didecylimidazolium acetate (5 mmol, 2.043 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After reaction, a suspension was formed, the product was separated using a glass filter and washed with water. ^{1}H NMR confirmed the purity of the product which was pulverized and dried in the vacuum oven. This resulted in 2.197 g (84% yield) of a light brown powder with a melting point of 76 °C.



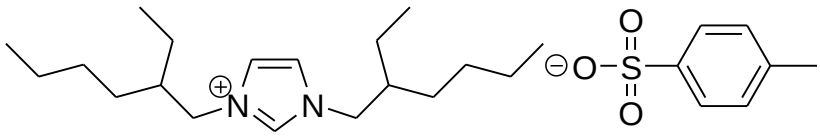
^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.13 (s, 1H, CH), 7.81 (s, 2H, 2 CH), 7.20 (s, 2H, 2 CH) 7.15 (s, 2H, 2 CH), 4.27 (m, 4H, 2 CH_2), 2.34 (s, 3H, CH_3),1.85 (m, 4H, 2 CH_2), 1.24 (m, 28H, 14 CH_2), 0.88 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 143.73 (C-S), 139.16 (C-CH_3), 138.25 (CH), 128.58 (2 CH), 125.95 (2 CHN), 121.43121.38 (2 CH), 50.09 (CH_3), 31.86 (2 CH_2), 30.24 (2 CH_2), 29.47 (2 CH_2), 29.40 (2 CH_2), 29.27 (2 CH_2), 29.00 (2 CH_2), 26.24 (2 CH_2), 22.67 (2 CH_2), 21.30 (2 CH_2), 14.11 (2 CH_3). FTIR: (v/cm^{-1}): 3096-2852 (C-H stretch), 1564 (N-C-N stretch), 1467 (C-C stretch), 1194, 1121 (SO_2 stretch), 1034, 1012, 814 (C-H bending), 679 (S=O stretch), 563 (C-S bending). Melting point: 76 °C.

1,3-Di(2-ethylhexyl)imidazolium tosylate

Used products: 1,3-di(2-ethylhexyl)imidazolium acetate (5 mmol, 1.763 g) and *p*-toluenesulfonic acid (5 mmol, 0.975 g).

After reaction, a water-insoluble product was formed, the water was separated and ^{1}H NMR indicated that there remained some 1,3-di(2-ethylhexyl)imidazolium acetate in the product. The product was added to water to dissolve the imidazolium acetate and an excess of *p*-toluenesulfonic acid was added. The remaining *p*-toluenesulfonic acid and acetic acid were

washed away with water and the product was dried on the Schlenk line, resulting in 1.795 g (77% yield) of a yellow solid with a melting point of 56 °C.



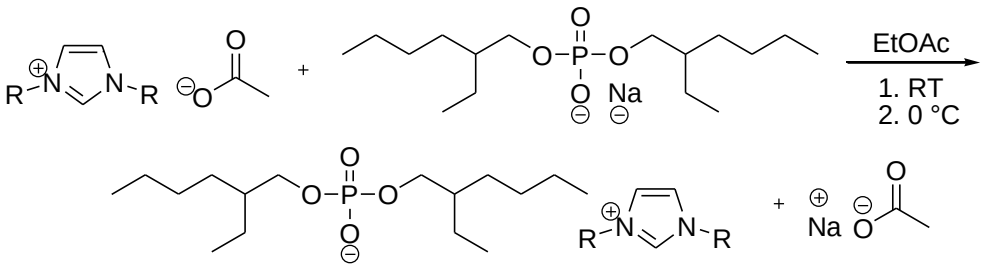
^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.05 (s, 1H, CH), 7.80(s, 2H, 2 CH), 7.16 (s, 2H, 2 CH) 7.12 (s, 2H, 2 CH), 4.19 (m, 4H, 2 CH_2), 2.34 (s, 3H, CH_3),1.78 (m, 2H, 2 CH), 1.24 (m, 16H, 8 CH_2), 0.88 (m, 12H, 4 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 143.91 (C-S), 139.21 (C-CH_3), 139.02(CH), 128.49 (2 CH), 126.01 (2 CHN), 121.77 (2 CH), 53.40 (CH_3), 40.07 (2 CH), 29.95 (2 CH_2), 28.30 (2 CH_2), 23.29 (2 CH_2), 22.83 (2 CH_2), 21.29 (2 CH_2), 13.93 (2 CH_3), 10.34 (2 CH_3). FTIR: (v/cm^{-1}): 3087-2861 (C-H stretch), 1564 (N-C-N stretch), 1460 (C-C stretch), 1192, 1120 (SO_2 stretch), 1033, 1011, 815 (C-H bending), 679 (S=O stretch), 563 (C-S bending). Melting point: 56 °C.

4.4.4 Bis(2-ethylhexyl)phosphate

Synthesis

The pK_a of di(2-ethylhexyl)phosphoric acid (pK_a= 1.47) is not sufficiently low to guarantee a full conversion of the acetate to the acetic acid (pK_a < 0.7). The sodium salt will therefore be used: sodium bis(2-ethylhexyl)phosphate (or: sodium DEHP), which was prepared from di(2-ethylhexyl)phosphoric acid and sodium hydroxide. When the metathesis reactions are performed with sodium salts, the crucial step is the removal of the sodium acetate. To decrease its solubility the synthesis was carried out in ethyl acetate and under argon atmosphere.

The 1,3-dialkylimidazolium acetate (5 mmol) and sodium bis(2-ethylhexyl)phosphate (5 mmol, 1.812 g) were dissolved in ethyl acetate under argon atmosphere (Scheme 28).



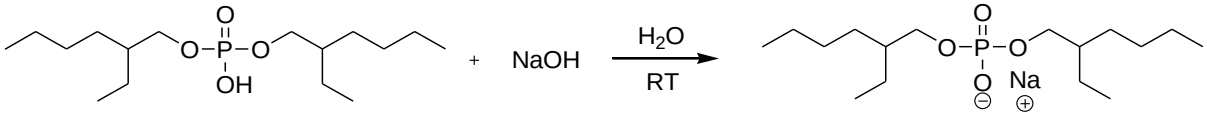
Scheme 28: Synthesis of 1,3-dialkylimidazolium bis(2-ethylhexyl)phosphate.

A minimum amount of solvent was used, therefore heating was required to dissolve the products. The solution was stirred overnight and cooled down to 0 °C in order to decrease the solubility of sodium acetate, which was separated by filtration with a glass filter. The ethyl acetate was removed with a rotary evaporator. ^{1}H NMR indicated that there was still acetate present in all of the imidazolium DEHP products, which were dissolved in dichloromethane and washed twice with ice water. In the case of the more hydrophilic imidazolium cations, centrifugation was needed to separate the two phases completely. This technique resulted in pure 1,3-dialkylimidazolium DEHP for the following cations: $[OOIM]^+$, $[DDIM]^+$ and $[EhEhIM]^+$. The other products contained an excess of sodium DEHP, since some imidazolium acetate also migrated to the water phase, leaving the sodium DEHP behind. To tackle this problem, the product was redissolved in dichloromethane and an excess (2 mmol) of the corresponding imidazolium acetate was added, the phase was carefully washed with small amounts of ice water. This way the sodium acetate was removed and by using ^{1}H NMR to check the product between the washing steps the only imidazolium acetate that was removed was the excess added before. With this procedure also the [HHIM][DEHP] could be purified. The other 3 more hydrophilic ILs: [EEIM][DEHP], [BBIM][DEHP] and [iBiBIM][DEHP] again contained an excess of sodium DEHP in spite of the careful and limited washing.

Products + characterization

Sodium DEHP

Since sodium DEHP is not commercially available, it was prepared from di(2-ethylhexyl)phosphoric acid and sodium hydroxide (Scheme 29).

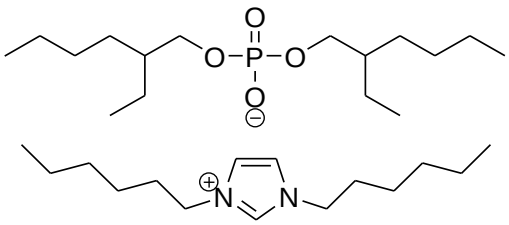


Scheme 29: Synthesis of sodium bis(2-ethylhexyl)phosphate.

Di(2-ethylhexyl)phosphoric acid (50 mmol, 16.71 mL) was dissolved in water and a sodium hydroxide solution in water was added while the pH was observed with an electrode, until neutral pH was reached. Next, the water was evaporated, the product was dried on the Schlenk line and in the vacuum oven and stored for further use.

1,3-Dihexylimidazolium DEHP

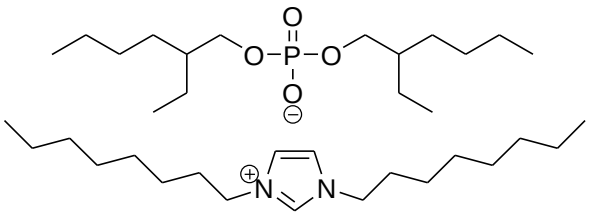
Used products: 1,3-dihexylimidazolium acetate (5 mmol + 2 mmol, 2.076 g) and sodium bis(2-ethylhexyl) phosphate (5 mmol, 1.812 g). The final product was 2.198 g (79 % yield) of a highly viscous and honey resembling liquid.



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 11.04 (s, 1H, CH), 7.09 (s, 2H, 2 CH), 4.35 (m, 4H, 2 CH_2), 3.76 (m, 4H, 2 CH_2), 1.88 (m, 4H, 2 CH_2), 1.31 (m, 30H, 2 CH + 14 CH_2), 0.87 (m, 18H, 6 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 140.48 (N-CH-N), 120.73 (2 CH-N), 67.70 (2 CH_2-O), 50.01 (2 CH_2-N), 40.47 (2 CH), 31.21-22.42 (16 CH_2), 14.15 (2 CH_3), 13.93 (2 CH_3), 11.01 (2 CH_3). FTIR: (v/cm^{-1}): 2957-2873 (C-H stretch), 1564 (N-C-N stretch), 1461 (C-C stretch), 1239 (P=O stretch), 1038 (P-O-C stretch), 852 815 (C-H bending), 555 (C-S bending). Water content: 7593 ppm. Viscosity: 7928 cP (25.0 °C).

1,3-Dioctylimidazolium DEHP

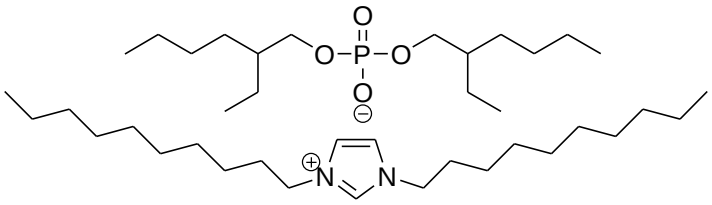
Used products: 1,3-dioctylimidazolium acetate (5 mmol, 1.763 g) and sodium bis(2-ethylhexyl) phosphate (5 mmol, 1.812 g). The final product was 1.037 g (34 % yield) of a highly viscous and honey resembling liquid.



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 11.01 (s, 1H, CH), 7.10 (s, 2H, 2 CH), 4.35 (m, 4H, 2 CH_2), 3.76 (m, 4H, 2 CH_2), 1.89 (m, 4H, 2 CH_2), 1.26 (m, 38H, 2 CH + 18 CH_2), 0.87 (m, 18H, 6 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 140.50 (N-CH-N), 120.70 (2 CH-N), 67.55 (2 CH_2-O), 50.01 (2 CH_2-N), 40.50 (2 CH), 31.70-22.59 (20 CH_2), 14.15 (2 CH_3), 14.04 (2 CH_3), 11.02 (2 CH_3). FTIR: (v/cm^{-1}): 2957-2873 (C-H stretch), 1563 (N-C-N stretch), 1461 (C-C stretch), 1239 (P=O stretch), 1039 (P-O-C stretch), 851 815 (C-H bending), 556 (C-S bending). Water content: 8507 ppm. Viscosity: 11402 cP (25.0 °C).

1,3-Didecylimidazolium DEHP

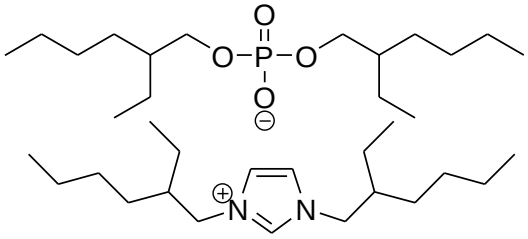
Used products: 1,3-didecylimidazolium acetate (5 mmol, 2.043 g) and sodium bis(2-ethylhexyl) phosphate (5 mmol, 1.812 g). The final product was 2.905 g (87 % yield) of a highly viscous and honey resembling liquid.



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 11.01 (s, 1H, CH), 7.10 (s, 2H, 2 CH), 4.35 (m, 4H, 2 CH_2), 3.76 (m, 4H, 2 CH_2), 1.89 (m, 4H, 2 CH_2), 1.26 (m, 46H, 2 CH + 22 CH_2), 0.87 (m, 18H, 6 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 140.43 (N-CH-N), 120.72 (2 CH-N), 67.61 (2 CH_2-O), 50.02 (2 CH_2-N), 40.48 (2 CH), 31.86-22.67 (24 CH_2), 14.16 (2 CH_3), 14.10 (2 CH_3), 11.03 (2 CH_3). FTIR: (v/cm^{-1}): 2957-2873 (C-H stretch), 1564 (N-C-N stretch), 1463 (C-C stretch), 1236 (P=O stretch), 1039 (P-O-C stretch), 852 815 (C-H bending), 555 (C-S bending). Water content: 5191 ppm. Viscosity: 12337 cP (25.0 °C).

1,3-Di(2-ethylhexyl)imidazolium DEHP

Used products: 1,3-di(2-ethylhexyl)imidazolium acetate (5 mmol, 2.043 g) and sodium bis(2-ethylhexyl) phosphate (5 mmol, 1.812 g). The final product was 2.647 g (86 % yield) of an extremely viscous and honey resembling liquid.



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.91 (s, 1H, CH), 7.07 (s, 2H, 2 CH), 4.28 (m, 4H, 2 CH_2), 3.71 (m, 4H, 2 CH_2), 1.82 (m, 2H, 2 CH), 1.26 (m, 34H, 2 CH + 16 CH_2), 0.86 (m, 24H, 8 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 141.24 (N-CH-N), 121.11 (2 CH-N), 67.76 (2 CH_2-O), 53.29 (2 CH_2-N), 40.45 (2 CH), 40.17 (2 CH), 30.15-22.84 (16 CH_2), 14.02 (4 CH_3), 10.74 (4 CH_3). FTIR: (v/cm^{-1}): 2958-2873 (C-H stretch), 1563 (N-C-N stretch), 1461 (C-C stretch), 1240 (P=O stretch), 1038 (P-O-C stretch), 852 816 (C-H bending), 555 (C-S bending). Water content: 4401 ppm. Viscosity: 23508 cP (25.0 °C).

4.4.5 Nitrate

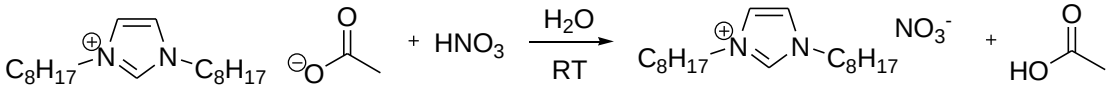
Synthesis

The pK_a of nitric acid is low enough (pK_a = -1.4) to use the acid during the metathesis toward nitrate imidazolium ionic liquids. The removal of the resulting acetic acid is a bigger concern, since nitric acid has a lower boiling point (T_b = 83 °C) than water (T_b = 100 °C) and acetic acid

(T_b = 118 °C). Even though the nitric acid is a strong acid, there will still be some minor traces of nitric acid present in the solution that might evaporate before water and acetic acid. According to the principles of Le Chatelier, these trace amounts will be regenerated and eventually this might result in a significant amount of evaporated nitric acid, leaving acetate anions behind. This will result in contamination by the starting products and impure imidazolium nitrate. Because of this reason great care must be taken with the water-soluble imidazolium nitrates. When the resulting ionic liquid is not soluble in water, the acetic acid and excess nitric acid can easily be removed by washing with water.

1,3-Dioctylimidazolium nitrate

A first synthesis was performed with 1,3-dioctylimidazolium acetate to serve as a proof-of-concept for the other syntheses. [OOIM][AcO] (5 mmol, 1.763 g) was dissolved in water and nitric acid (65 wt% in water, 2 eq. 10 mmol, 0.697 mL) was added (Scheme 30).

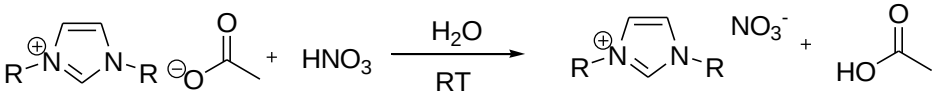


Scheme 30: Synthesis of 1,3-dioctylimidazolium nitrate ([OOIM][NO_3]).

After addition of the nitric acid, a water-insoluble phase appeared: [OOIM][NO_3]. It was extracted with dichloromethane and washed with water, the organic phase was removed with a rotary evaporator and ^{1}H NMR indicated the presence of 0.04 equivalents of acetate for each 1,3-dioctylimidazolium cation. The product was dissolved in dichloromethane and washed with water containing nitric acid. The dichloromethane was removed with a rotary evaporator and the product was dried on the Schlenk line, this resulted in 1.088 g (74 % yield) of a brown liquid.

General synthesis

After the successful synthesis of 1,3-dioctylimidazolium nitrate, the other six imidazolium nitrate ionic liquids were prepared. The 1,3-dialkylimidazolium acetate (5 mmol) was dissolved in water and nitric acid (65 wt% in water, 2 eq. 10 mmol, 0.697 mL) was added to the solution (Scheme 31).



Scheme 31: Synthesis of 1,3-dialkylimidazolium nitrate.

Products + characterization

As mentioned earlier (section 2.5) the water content of nitrate ionic liquids cannot be measured with a Karl Fischer titrator due to the oxidative nature of the nitrate anion.

1,3-Diethylimidazolium nitrate

After the addition of the nitric acid, no separate hydrophobic phase was formed. Dichloromethane was added to the reaction mixture but according to the color of the two phases, no imidazolium compound was present in the organic phase. Due to limited time, the uncertainty on the possible removal of acetic acid and the (most likely) not thermomorphic IL, this project was abandoned.

1,3-Dibutylimidazolium nitrate

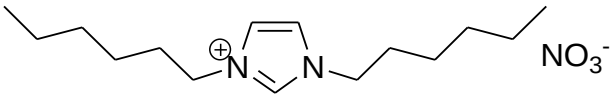
After the addition of the nitric acid, no separate hydrophobic phase was formed. Dichloromethane was added to the reaction mixture but according to the color of the two phases, only a limited fraction of imidazolium compound was present in the organic phase. Since washing the organic phase would result in an even greater loss, the yield would be negligible if the purification would have been carried out as is described for the 1,3-dioctylimidazolium nitrate. Due to limited time, the uncertainty on the possible removal of acetic acid and the (most likely) not thermomorphic IL, this project was abandoned.

1,3-Diisobutylimidazolium nitrate

After the addition of the nitric acid, no separate hydrophobic phase was formed. Dichloromethane was added to the reaction mixture but according to the color of the two phases, only a limited fraction of imidazolium compound was present in the organic phase. Since washing the organic phase would result in an even greater loss, the yield would be negligible if the purification would have been carried out as is described for the 1,3-dioctylimidazolium nitrate. Due to limited time, the uncertainty on the possible removal of acetic acid and the (most likely) not thermomorphic IL, this project was abandoned.

1,3-Dihexylimidazolium nitrate.

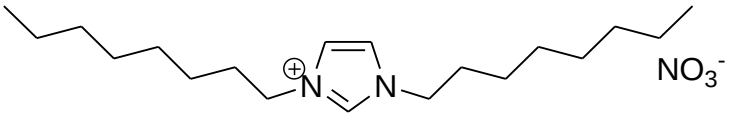
After addition of the nitric acid, the transparent solution turned into an emulsion. After two hours, dichloromethane was added to the reaction mixture and according to the color, almost all imidazolium compounds were present in the organic phase. The two phases were separated, the organic phase was washed two times with water and the dichloromethane was removed with a rotary evaporator. ^{1}H NMR confirmed the purity of the 1,3-dihexylimidazolium nitrate, the last traces of DCM were removed on the Schlenk line. This resulted in 1.052 g of a dark yellow and viscous liquid (4.43 mmol, 89% yield).



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.09 (s, 1H, CH), 7.39 (s, 2H, 2 CH), 4.26 (m, 4H, 2 CH_2), 1.89 (m, 4H, 2 CH_2), 1.30 (m, 12H, 6 CH_2), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 137.81 (N-CH-N), 122.00 (2 CH-N), 50.14 (2 CH_2-N), 31.03 (2 CH_2), 30.19 (2 CH_2), 25.85 (2 CH_2), 22.38 (2 CH_2), 13.90 (2 CH_3). FTIR: (v/cm^{-1}): 2956-2859 (C-H stretch), 1564 (N-C-N stretch), 1461 (C-C stretch), 1334 (N-O symmetric stretch), 830 (C-H bending). Viscosity: 1520 cP (25.0 °C).

1,3-Dioctylimidazolium nitrate

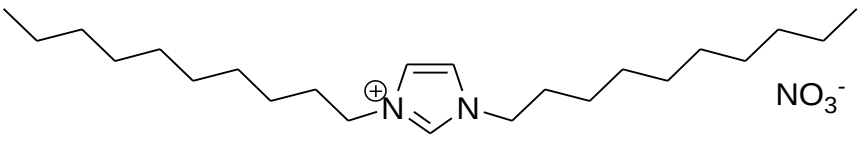
Synthesis described above.



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.05 (s, 1H, CH), 7.40 (s, 2H, 2 CH), 4.26 (m, 4H, 2 CH_2), 1.89 (m, 4H, 2 CH_2), 1.27 (m, 20H, 10 CH_2), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 137.71 (N-CH-N), 122.05 (2 CH-N), 50.14 (2 CH_2-N), 31.66 (2 CH_2), 30.24 (2 CH_2), 29.01 (2 CH_2), 28.90 (2 CH_2), 26.23 (2 CH_2), 22.56 (2 CH_2), 14.02 (2 CH_3). FTIR: (v/cm^{-1}): 2956-2856 (C-H stretch), 1564 (N-C-N stretch), 1464 (C-C stretch), 1335 (N-O symmetric stretch), 829 (C-H bending). Viscosity: 1944 cP (25.0 °C).

1,3-Didecylimidazolium nitrate

After addition of the nitric acid, a water-insoluble precipitate was formed . After 2 hours, dichloromethane was added to the reaction mixture until all the solid particles were dissolved and the 2 phases were separated, the organic phase was washed 2 times with water and the dichloromethane was removed with a rotary evaporator. ^{1}H NMR confirmed the purity of the 1,3-didecylimidazolium nitrate, the last traces of DCM were removed on the Schlenk line. This resulted in 1.705 g of a brown and viscous liquid (4.88 mmol, 98% yield).

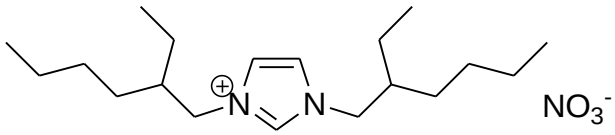


^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.03 (s, 1H, CH), 7.40 (s, 2H, 2 CH), 4.25 (m, 4H, 2 CH_2), 1.89 (m, 4H, 2 CH_2), 1.27 (m, 28H, 14 CH_2), 0.87 (m, 6H, 2 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 137.81 (N-CH-N), 121.93 (2 CH-N), 50.15 (2 CH_2-N), 31.84 (2 CH_2), 30.25 (2

CH_2), 29.45 (2 CH_2), 29.38 (2 CH_2), 29.24 (2 CH_2), 28.96 (2 CH_2), 26.24 (2 CH_2), 22.65 (2 CH_2), 14.09 (2 CH_3). FTIR: (v/cm^{-1}): 2956-2854 (C-H stretch), 1564 (N-C-N stretch), 1465 (C-C stretch), 1336 (N-O symmetric stretch), 829 (C-H bending). Viscosity: 3341 cP (25.0 °C).

1,3-Di(2-ethylhexyl)imidazolium nitrate

After addition of the nitric acid, a water-insoluble product appeared. After two hours, dichloromethane was added to the reaction mixture and the two phases were separated, the organic phase was washed two times with water and the dichloromethane was removed with a rotary evaporator. ^{1}H NMR confirmed the purity of the 1,3-di(2-ethylhexyl)imidazolium nitrate, the last traces of DCM were removed on the Schlenk line. This resulted in 1.431 g of a dark yellow and viscous liquid (4.88 mmol, 98% yield).



^{1}H NMR: (300 MHz, CCl_3D, δ/ppm): 10.25 (s, 1H, CH), 7.29 (s, 2H, 2 CH), 4.18(m, 4H, 2 CH_2), 1.85 (s, 2H, 2 CH), 1.28 (m, 16H, 8 CH_2), 0.88 (m, 12H, 4 CH_3). ^{13}C NMR: (75 MHz, CCl_3D, δ/ppm): 139.11 (N-CH-N), 122.13 (2 CH-N), 53.49 (2 CH_2-N), 40.15 (2 CH), 30.00 (2 CH_2), 28.28 (2 CH_2), 23.34 (2 CH_2), 22.84 (2 CH_2), 13.92 (2 CH_3), 10.29 (2 CH_3). FTIR: (/cm^{-1}): 2959-2862 (C-H stretch), 1564 (N-C-N stretch), 1461 (C-C stretch), 1335 (N-O symmetric stretch), 829 (C-H bending). Viscosity: 12245 cP (25.0 °C).

5 Results and discussion

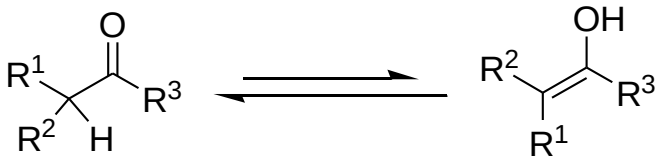
5.1 Imidazolium synthesis

5.1.1 Enolizable products

After multiple attempts to synthesize highly substituted imidazole and imidazolium compounds, it turned out that the use of enolizable aldehydes and ketones was not feasible with the reactions.

Keto-enol equilibrium

Most ketones and aldehydes are susceptible towards the keto-enol equilibrium, this is the conversion of carbonyl groups towards their respective enol tautomer (Scheme 32).



Scheme 32: Equilibrium between a ketone and enol.

This conversion is possible due to the presence of a β-hydrogen atom next to the carbonyl function, which can be eliminated by an oxygen atom, resulting in the enol compound. The more acidic this β-proton is, the easier the conversion becomes. At neutral pH, the rate of the conversions is negligible, but working under acidic or basic conditions establishes a fast keto-enol equilibrium. Energetically the aldehydes and ketones are favored over the enol form, but the carbon-carbon double bond in the enol form is much more reactive since it is activated by the oxygen atom. This reactive double bond, however small the presence of the enol form, can react with numerous carbonyl electrophiles resulting in a large variety of aldol-type products. These side products can result in a difficult or even impossible purification of the desired product. Preventing the keto-enol equilibrium is therefore preferred since products cannot be purified easily.

Arduengo patent

The Arduengo patent describes the imidazole synthesis for several substituents on the aldehyde and diketone: “any hydrogen, hydrocarbyl or substituted hydrocarbyl”.[2] The research in this thesis was started from these claims, as described in the experimental section. After several reactions, it became clear that the use of enolizable compounds resulted in various side products not all of which could be removed with the means at our

disposal. Since the claims and results in the patent could not be reproduced in our experiments, the claims and delivered proof thereof were investigated more thoroughly.

The patent claims to be valid for highly substituted carbonyl functions (aldehyde and diketone) bearing any hydrocarbyl group. However, the inventors never succeeded in preparing pure substituted imidazole compounds from enolizable products. Instead, they prepared imidazolium compounds bearing a very low number of substituents, most of which placed on a nitrogen atom (therefore originating from the amines used). The substituents on the carbon atoms (2, 4 and 5 position) of purified imidazoles were: trifluoromethyl, phenyl and mesityl (Figure 15).[2]

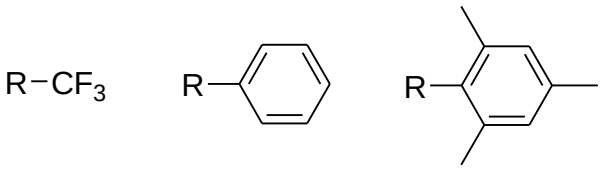


Figure 15: Several imidazole substituents in the Arduengo patent: trifluoromethyl, phenyl and mesityl.[2]

The sole exception to this rule is the successful synthesis of pure 1,2-dimethylmidazole, which was prepared with a lot of side products and could be purified via fractional distillation. The successful purification probably results from the use of low molecular mass compounds, resulting in the formation of volatile products that can be removed via distillation.

Current research

Selecting carbonyl substituents

After closer investigation of the Arduengo patent, it turned out that the use of enolizable products could not result in pure and highly substituted imidazoles. This significantly reduces the amount of products that can be used in the synthesis of imidazoles and imidazolium compounds. The most straightforward choices of substituents that are not enolizable are: hydrogen, trifluoromethyl, trisubstituted carbon atoms and phenyl substituents (Figure 16). Other substituents surely exist but were not considered.

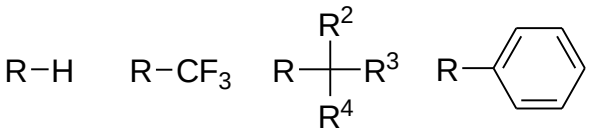


Figure 16: Possible carbonyl substituents, not susceptible to keto-enol conversion.

Keeping in mind that the goal is to make imidazolium ionic liquids, several substituents are not compatible with certain principles of ionic liquids. First of all, the IL should have a low melting point, therefore the use of phenyl groups should be limited. Substituting imidazoles with phenyl groups results in high melting temperatures due to increased intermolecular forces caused by the π-stacking between the aromatic structures. Regarding the green character and reduced toxicity of ionic liquids and their potential use in industrial processes, the use of fluorinated acetyl groups is also not justified. This leaves the trisubstituted carbon atoms and hydrogen atoms as potential substituents.

Diketone compounds

The trisubstituted carbon atom is not compatible as a substituent for the diketone compound: when 2 of these groups would be implemented on neighboring carbonyl groups, the steric hindrance would be too high to allow the carbonyl groups to be positioned parallel to each other. Since this conformation is required for the formation of imidazole, it is not possible to use such sterically hindered molecules. Equipping the diketone compound with one of these groups and one hydrogen atom is in theory possible, although this would results is statistical mixtures of 4- and 5-substituted imidazoles. The only relevant substituent left to use is the hydrogen atom, the corresponding diketone compound is glyoxal. Therefore glyoxal was used in the further syntheses of both imidazoles and imidazolium compounds. The obvious consequence is that the 4,5-positions remain unsubstituted.

Aldehyde compounds

The choice for the substituent on the aldehyde is not limited by steric hindrance, but the use of phenyl groups and fluorinated compounds is still not favored due to the reasons explained above. However, also for the aldehyde the hydrogen substituent was chosen, for the following reasons. First, the commercial availability of formaldehyde is an important advantage, both for this as for future research. The use of formaldehyde also leaves the option of further alkylation open, this is not the case when other aldehydes would be used.

Imidazolium synthesis using formaldehyde and glyoxal

The use of formaldehyde and glyoxal resulted in a very efficient synthesis of 1,3-dialkylimidazolium acetate compounds. The synthesis yielded high amounts of product whilst suffering from a negligible amount of side products. This small amount of side products could be removed easily by washing the water mixture with diethyl ether resulting in pure imidazolium acetate. The washing step did suffer from higher losses of product when longer alkyl groups are used on the imidazolium ring. However, this is not a real problem since the synthetic method itself proved to be incompatible with long amines before the extraction

resulted in extremely low yields e.g. the *n*-dodecylamine was no longer compatible with the imidazolium synthesis while the overall yield of the synthesis using *n*-decylamine was still around 50%.

Proof-of-concept

Later in the research, some tests with phenyl and *tert*-butyl substituents on aldehydes were performed, as described section 4.3.5. This was done as a proof-of-concept for the fact that using non-enolizable carbonyl functions would result in a significant decrease of side reactions. These reactions are discussed below.

Pivaldehyde:

The use of pivaldehyde as a replacement of formaldehyde as described in the experimental section, does result in imidazolium acetate formation. However, some important remarks have to be made. First of all, the reactivity of the pivaldehyde is rather low: the reaction was stirred overnight, which is more than sufficient for reactions with formaldehyde. The product of the reaction: 1,3-dibutyl-2-*tert*-butylimidazolium acetate was indeed formed but there were still a considerable amount of starting reagents, indicating that the steric hindrance has an effect on the reactivity. At the same time, the imidazolium formed was very susceptible towards fragmentation, this was observed via the C2 proton peak on NMR spectra where the *tert*-butyl group should have been and the complete lack of any *tert*-butyl peak in the spectrum.

Benzaldehyde

Like the pivaldehyde, the benzaldehyde was used as a proof-of-concept, the same reaction procedure was carried out as before but with benzaldehyde, the expected product was 1,3-dibutyl-2-phenylimidazolium acetate. This product was indeed formed but again the C2 proton peak emerged on the ^{1}H NMR spectrum, together with a deficient signal for aromatic protons. This indicates that the 1,3-dibutyl-2-phenylimidazolium acetate is indeed formed but somehow the 1,3-dibutylimidazolium acetate is formed as well.

General conclusion

It can be concluded that the pivaldehyde suffered from low reactivity and the formed product was susceptible to fragmentation of the *tert*-butyl group, which was probably washed away with the diethyl ether. The benzaldehyde was sufficiently reactive but the product was obtained in a mixture with 1,3-dibutylimidazolium acetate. The formaldehyde on the other hand showed excellent reactivity and resulted in stable imidazolium products, as already discussed in detail.

The use of aldehydes that cannot be enolized, does meet the expectation of not having a broad variety of side products. However, not all of them (with the obvious exception of formaldehyde) meet the requirements of efficient imidazolium formation, since additional complications might occur, like insufficient reactivity and fragmentation of stable cations from the C2 position. This last phenomenon is not surprising, since the C2 position has shown to be rather unstable. It is for instance used as a carbene in certain metal complexes and 2-methylimidazole has been described to show a strongly polarized carbon-carbon double bond that has been used to capture CO_2 as a C1 building block.[64,65] Another explanation might be that the glyoxal is incorporated in the ring instead of the formaldehyde. This effect can be investigated more thoroughly in future research.

5.1.2 Halogen-free synthesis of 1,3-dialkylimidazolium

As described earlier, the synthesis using glyoxal, formaldehyde and two amine equivalents resulted in the formation of stable imidazolium salts. This procedure was derived from the literature procedure described by Zimmerman *et al*.[20] With the successful synthesis of 1,3-di(2-ethylhexyl)imidazolium acetate from 2-ethylhexylamine, glyoxal, formaldehyde and acetic acid, finally a pure imidazole derivative could be prepared from standard building blocks. This synthesis was then optimized by using other acids and acid equivalents.

Different acids

The halogen-free synthesis towards 1,3-dialkylimidazolium ionic liquids was tested and optimized for 1,3-dibutylimidazolium, using the cheaper *n*-butylamine. The effect and applicability of different acids on the synthesis was tested: acetic acid, hydrochloric acid, sulfuric acid and butyric acid. The hydrochloric acid and sulfuric acid were chosen for their low cost and high availability, the butyric acid was chosen for its similar acidic properties and more hydrophobic character compared to acetic acid. The properties of the acids and the results of the syntheses are listed below (Table 4).

Table 4: Acid properties and synthetic results.

Acid	pK_a	T_B (°C)	T_B at 20 mm Hg (°C)	Yield (%)	Pure product by extraction?
Acetic acid	4.8	118	19.8	77	Yes
HCl	-7.0	<100	<4.6	61	No
H_2SO_4	-3.0	>250	>130.9	83	No
Butyric acid	4.8	164	58.5	39	No

Boiling point

The boiling point of the acids, however trivial it may seem, is in fact an important parameter. If any excess of acid might be present in the ionic liquids, it can be removed via evaporation when the boiling point is low enough. If this is not the case, some other and more complex, purification step is required resulting in more synthetic effort and cost and almost always product is lost. The hydrochloric acid and acetic acid have low boiling points, and under vacuum they can be removed at low temperatures. The boiling point of the sulfuric acid is too high, even under vacuum, since heating the imidazolium compounds to such high temperatures results in degradation. The butyric acid can be assumed to be an intermediate case, a boiling point of 58.5 °C at reduced pressure seems reasonable, however the experiments showed that removing an excess of butyric acid from the ILs is not possible. The acetic acid and hydrochloric acid have this advantage over the other two acids.

Reaction yield

The overall yield of the reaction clearly differs from acid to acid, although it is not solely determined in the synthetic step. The extraction with diethyl ether also results in losses, which can be dependent on the anion of the ionic liquid and thus the acid used. When more hydrophilic acids are used, this results in more hydrophilic anions, and therefore a lower loss of product during the extraction. This will be discussed in detail below.

Product purity

The most important criterion however, is the purity of the resulting 1,3-dibutylimidazolium salt after the extraction step. The only acid that resulted in pure imidazolium salts was the acetic acid. The hydrochloric acid and sulfuric acid showed several side products formed during the reaction that were not removed in the extraction step. The butyric acid did not result in any side product formation, but the acid itself was present in excess and could not be removed by evaporation or washing. This indicates that the reaction is dependent on the strength of the acid used: the strong acids (hydrochloric and sulfuric) caused several side reactions, while the weak acids (acetic and butyric) did not give such problems.

As already mentioned, the purity of the products is of higher importance than the yield of the reaction, especially when working with ionic liquids, which do not always demonstrate efficient purification. Therefore, acetic acid was favored for future syntheses.

Acid equivalent

When the formation of 1,3-dibutylimidazolium salts proceeds, the acid is consumed since its conjugate base serves as the anion of the ionic liquid. This might result in a deficit of acid

towards the end of the synthesis. To investigate the proportion of this phenomenon, the synthesis was carried out with different equivalents of acetic acid (1.05 and 1.5), the results are presented below (Table 5).

Table 5: Effect of acid equivalent on reaction yield.

Equivalent AcOH	Mass	Yield (%)
1.05	3.69 g	77
1.5	4.29 g	89

From the results in Table 5 it can be concluded that the yield does increase when using higher acid equivalents, however other parameters, like the acid and amine used, might have a larger impact, as can be seen in Table 4 and Table 6.

Table 6: Effect of acid equivalent and amine on the reaction yield.

Amine	Equivalent AcOH	Yield (%)
n-Butylamine	1.05	77
n-Butylamine	1.5	89
2-Ethylhexylamine	1	45
2-Ethylhexylamine	1.5	47

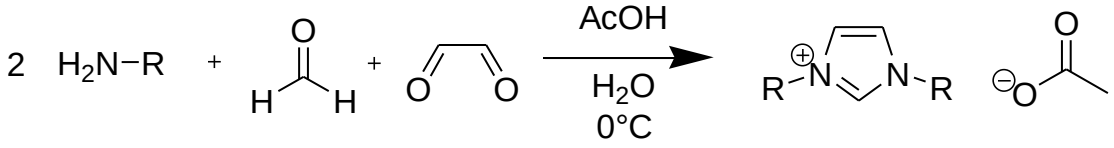
Although the acetic acid equivalents are not exactly identical (1 and 1.05) it is clear that the yields are much higher for *n*-butylamine. The explanation behind this large difference in yield might be twofold. First, the 2-ethylhexylamine is much more sterically hindered due to the ethyl group close to the amine functionality, this might result in a lower reactivity causing the reaction to be terminated at an incomplete stage. Nevertheless, this effect seems a bit too weak to result in such a large difference, since both amines are primary amines so their reactivity should not differ hugely. The lower yield is also explained by the hydrophilicity of the products: the longer side chains of the [EhEhIM][AcO] result in a higher hydrophobicity of the cation, causing more product to be lost during the washing step. This is confirmed by the rather similar yield with different amounts of acetic acid, indicating that the overall yield is not significantly influenced during the synthetic step but elsewhere.

Using an acid equivalent of 1.5 clearly results in better yields, but due to the reasons explained above, no further research using higher equivalents was performed.

Optimized synthetic procedure

The optimized synthetic procedure is described below (Scheme 33):

Two equivalents of amine were cooled down to 0 °C in an ice bath, afterwards a mixture of formaldehyde (38 wt% in water, 1 eq.) and acetic acid (1.5 eq.) was added drop-wise while keeping the temperature under 10 °C. The mixture was stirred for 30 min at 0 °C, after which the glyoxal (40 wt% in water, 1 eq.) was added and the reaction mixture was stirred overnight at RT. The solution was washed with diethyl ether until the organic phase was colorless and the water was removed with a rotary evaporator. The product was dried on the Schlenk line at 50 °C.



Scheme 33: Optimized synthesis of 1,3-dialkylimidazolium acetate.

Dependency of yield on anion and cation hydrophilicity

A correlation between the yield of the imidazolium formation and the hydrophilicity of the anion (used acid) was observed (Figure 17). Also the alkyl chains on the imidazolium cation had an influence on the reaction yield (Figure 18).

In the Hofmeister series, anions and cations are listed on their capability to exclude or induce the dissolution of certain compounds in a water phase.[47,66] Since this property is directly linked to their charge density, it is a good indication of their relative hydrophilicity. The acetate, chloride and sulfate anion are listed in this Hofmeister series, the butyrate anion is not.[46,47] When the anions are listed with decreasing hydrophilicity according to the Hofmeister series, and the butyrate is assumed to be the most hydrophobic of the four anions, the following sequence is obtained: SO_4^-, AcO^-, Cl^- and butyrate.[45,46] When the acids are ranked with decreasing yield the same sequence is observed, indicating a correlation between the hydrophilicity of the anion and the reaction yield (Figure 17).

This decrease can be explained by the increased affinity for the apolar diethyl ether phase during the extraction. The less hydrophilic the ionic liquid, the more it is absorbed in the organic phase and the lower the reaction yield.

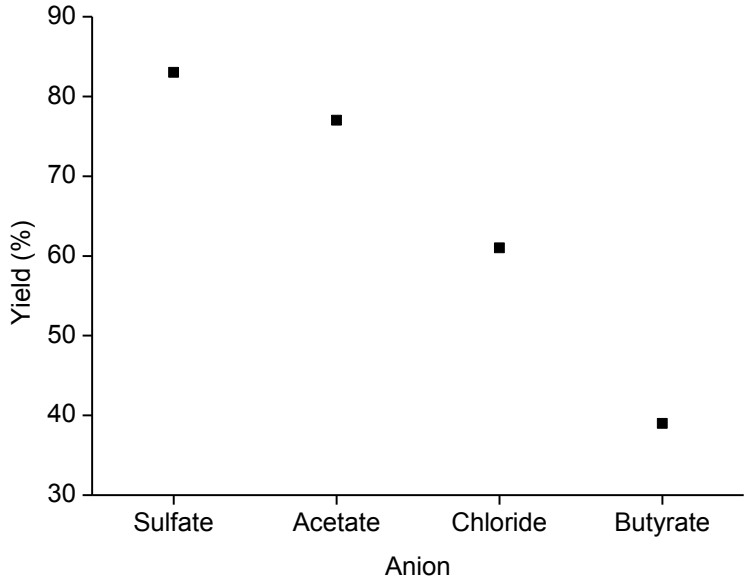


Figure 17: Reaction yield as a function of anion hydrophobicity.

The same trend can be observed with the 1,3-dialkylimidazolium cations. When they are listed with increasing number of carbon atoms in the substituents, the reaction yield decreases (Figure 18). The branched substituents (isobutyl and 2-ethylhexyl) are indicated separately since the lower yield might be partially explained by their increased steric hindrance, as was already mentioned for 2-ethylhexylamine in section 4.3.2.

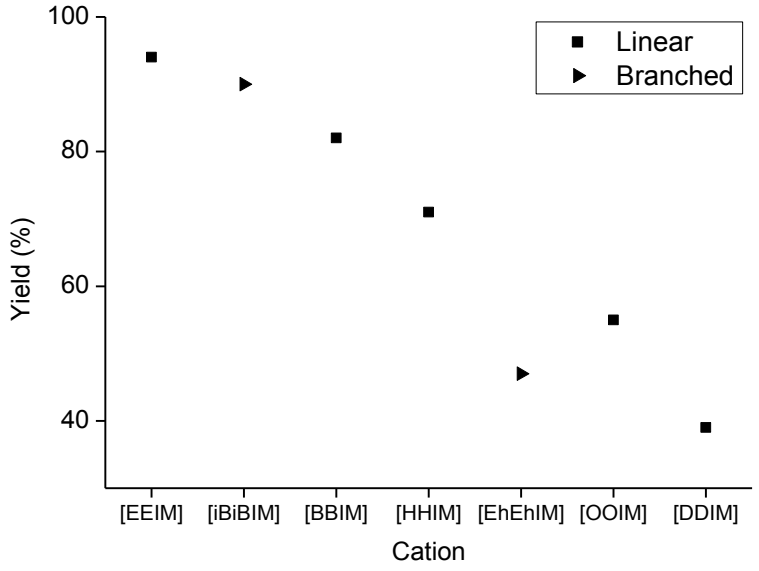


Figure 18: Reaction yield as a function of imidazolium cation.

5.2 Metatheses

Several possible strategies for metathesis reactions starting from acetate ionic liquids were confirmed, not all of which were equally efficient or time consuming. Different procedures were required depending on following factors: acidity of the anions' conjugate acid, the volatility of this acid and the hydrophilicity of the resulting ionic liquid and used reagents.

5.2.1 Decisive parameters

Acidity

When the conjugate acid of the anion is acidic enough compared to acetic acid, its use in the metathesis hold many benefits over the use of a salt. First of all, most acids are commercially available, in contrast to many salts, which require an extra synthetic step. Thereafter, the acid will ensure a complete protonation of the acetate towards acetic acid, which can be removed by evaporation, an advantage acetate salts do not hold. Therefore using the acid is always beneficial provided that it is strong enough ($pK_a \leq 0.7$).

Volatility

The boiling point of the new anions' conjugate acid is ideally much higher than the boiling point of acetic acid (118 °C), allowing the removal of acetic acid via evaporation. This technique was successfully applied with certain tosylate ionic liquids. Evaporating the acetic acid from ionic liquids synthesized using acids with a boiling point below 118 °C might be troublesome. The extend of this problem was not investigated since the only used acid with a low boiling point was nitric acid, which has the additional problem of being potentially dangerous when exposing it to high temperature when under vacuum.[67]

Hydrophilicity

When the difference in hydrophilicity between the new anion and the acetate (salt or acetic acid) is large, they can be separated via extraction, as was done for all the ionic liquids insoluble in water (e.g. bistriflimide ionic liquids). If the difference in hydrophilicity is too small, for example: [BBIM][TsO], other methods must be applied to purify the ionic liquid, for instance the evaporation of acetic acid.

5.2.2 Successful conditions for metatheses

Depending on the properties of the used reagents and the ionic liquid created in the metathesis, different synthetic parameters are required. Most of them result easily in pure ionic liquids, others require intensive purification steps and some could not be synthesized. A schematic overview is given in Table 7.

Table 7: Schematic overview of the different metathesis strategies resulting in imidazolium ionic liquids, starting from 1,3-dialkylimidazolium acetate.

Resulting IL	Using acids ($pK_a \leq 0.7$)	Using salts ($pK_a \leq 0.7$)
Hydrophobic	Washing IL with water	Washing IL with water
Hydrophilic	Evaporating AcOH under vacuum (not confirmed for volatile acids: T_b < 118 °C, e.g. HNO_3)	Variable, no guaranteed procedure for pure ionic liquids

5.3 Properties of ionic liquids

5.3.1 Color

All the ILs had a brown, yellow or orange color, this is often observed with ILs.[66] Ideally, ILs should be colorless, the fact that they are not is the result of very minor impurities, probably at ppb level.[68] These are not detectable using standard techniques like NMR, FTIR and ESI-MS. The color can be removed with the use of activated charcoal.[66] However, this step was not performed since a lot of product can be lost during these purification steps and because the impurity is so small that it does not affect the properties of the IL significantly.

5.3.2 Water content

The water content of all ionic liquids with a melting point lower than room temperature was measured. This was done after drying them on the Schlenk line at 70 °C. Measuring the water content gives an indication of the hygroscopic properties of the ionic liquid. The water content is also needed to check the purity of the ionic liquid: if they contain too much water, viscosity measurements might be underestimated. TGA and DSC samples need special handling when being measured. The Karl Fischer titrator and reagent are sensitive towards several contaminants and might therefore be temporary disrupted, this can result in deviations that cannot always be foreseen. Since the water content of the ionic liquids was not measured at the same time, this can result in some deviating values or incoherent trends throughout anion or cation series.

The water content of all the synthesized imidazolium ionic liquids (besides nitrate ILs) liquid at room temperature is displayed in Figure 19. The value of 1,3-diethylimidazolium acetate ([EEIM][AcO]) is not displayed, due to its unusually high water content: 0.73 wt%. (section 4.3.4).

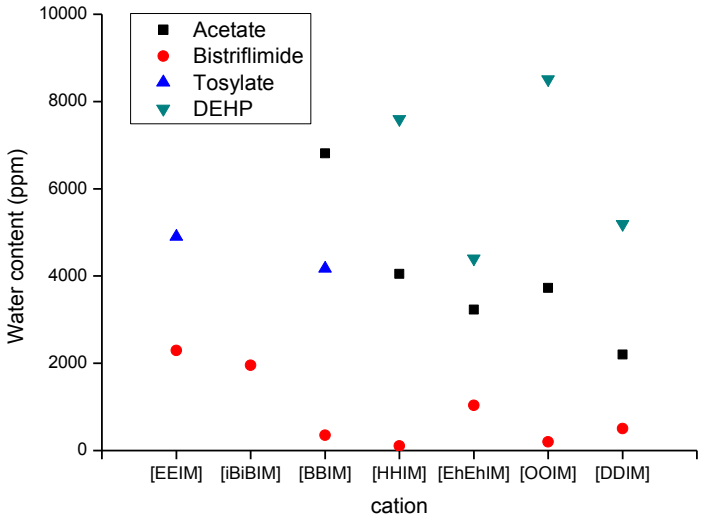


Figure 19: Water content of all the liquid imidazolium ionic liquids, with the exception of [EEIM][AcO] and the nitrate ILs. The imidazolium cations are listed according to increasing alkyl chain length.

As expected, the water content drops with increasing alkyl chain length on the imidazolium cation, this is the result of the decreasing hydrophilicity of the cations.

The hydrophobic characteristics of the bistriflimide anion are reflected in the water content, which is low for all the bistriflimide ionic liquids. The hydrophilicity of the tosylate anion, which is intermediate between acetate and bistriflimide, is also reflected in the water content. The only surprising observation is that the water content for all the DEHP ionic liquids is higher compared to their acetate precursors. The opposite is observed with the solubility of the ionic liquids: all acetate ionic liquids were completely water-soluble, while the DEHP ionic liquids were insoluble in water, as can be seen in section 5.4.1. This strange behavior might be explained by the high viscosity of the DEHP ionic liquids (Figure 20), causing a much more difficult and incomplete removal of the water molecules on the Schlenk line.

5.3.3 Viscosity

Rotating disk viscometer

The viscosities of all the liquid ionic which were liquid at room temperature were determined using a rotating disk viscometer, the viscosities are listed in Table 8. Since the viscosities are very sensitive towards the contamination of the ionic liquid by water traces, as already mentioned in section 5.3.2, the viscosity of [EEIM][AcO] was not measured due to its extremely high water content: 0.73 wt%.

Table 8: Viscosities of all liquid imidazolium ionic liquids, the viscosity of [EEIM][AcO] was not determined due to the extremely high water content present in the ionic liquid: 0.73 wt%.

Imidazolium ionic liquid	Viscosity (cP) at 25.0 °C	Imidazolium ionic liquid	Viscosity (cP) at 25.7 °C
[EEIM][TsO]	1209	[EEIM][AcO]	Water contaminated
[BBIM][TsO]	2404	[BBIM][AcO]	516
[HHIM][DEHP]	7928	[HHIM][AcO]	682
[OOIM][DEHP]	11402	[OOIM][AcO]	861
[DDIM][DEHP]	12337	[DDIM][AcO]	475
[EhEhIM][DEHP]	23508	[EhEhIM][AcO]	4659
[HHIM][NO_3]	1520	[EEIM][Tf_2N]	29
[OOIM][NO_3]	1944	[BBIM][Tf_2N]	66
[DDIM][NO_3]	3341	[iBiBIM][Tf_2N]	131
[EhEhIM][NO_3]	12245	[HHIM][Tf_2N]	102
		[OOIM][Tf_2N]	147
		[DDIM][Tf_2N]	131
		[EhEhIM][Tf_2N]	424

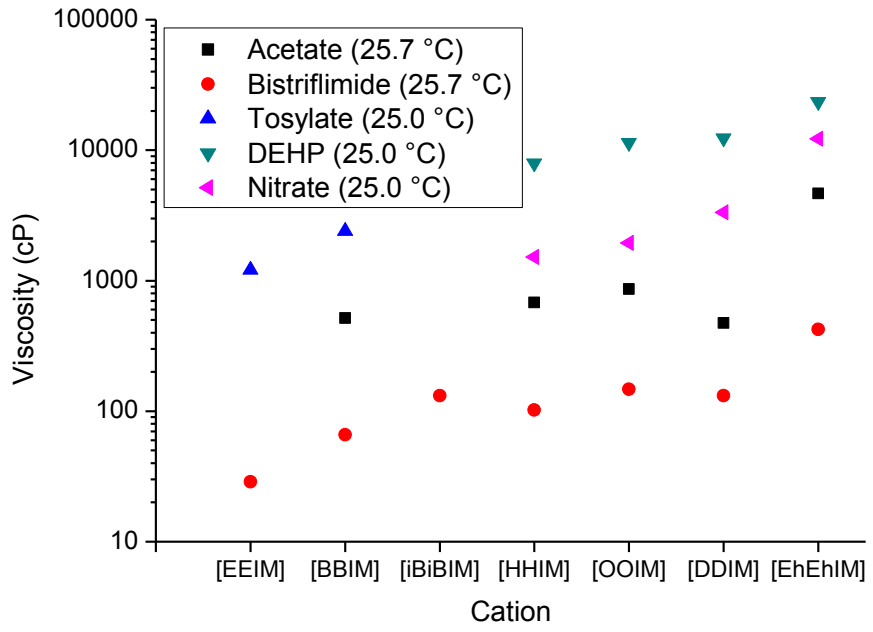


Figure 20: Viscosities of all liquid imidazolium ionic liquids. The cations are listed with increasing alkyl chain length and increasing degree of branching.

Figure 20 clearly illustrates the influence of the different anions and imidazolium cations on the viscosities of the imidazolium ionic liquids.

The following observation is made for the imidazolium cations: the longer the alkyl substituents and their degree of branching, the higher the viscosity. These results are perfectly in line with the observed trends found in literature as described in section 1.5.3. Which also stated that the viscosity increases with increasing alkyl chain length and higher degree of branching.[35,40,50] This is clearly observed when looking at the bistriflimide series: the viscosity increases from 29 cP ([EEIM][Tf_2N]) up to 424 cP ([EhEhIM][Tf_2N]).

The anions have an even greater effect on the viscosity: the following order is observed: Tf_2N^- < AcO^- < TsO^- / NO_3^- < $DEHP^-$. These results might seem surprising since the two largest anions: bistriflimide and DEHP, result in the highest and lowest viscosities respectively. However, as mentioned in section 1.5.3, not only the bulkiness but also the charge delocalization of the anion contributes to the viscosity of the IL.[35,50] The effect of increasing viscosity with more voluptuous substituents is not only clear for the imidazolium cations, but also for the anions. Tosylate and DEHP anions have a comparable charged entity (sulfate and phosphate), however the DEHP has more, longer and branched substituents. This is translated in a much higher viscosity, even up to 23508 cP for [EhEhIM][DEHP]. As expected, the bistriflimide series shows low viscosities due to a good charge distribution over the entire anion structure. The acetate and nitrate anions also show the expected properties: the acetate is rather small and has a good charge delocalization therefore having intermediate viscosities. The nitrate anion is even more capable of delocalizing a negative charge but it contains two negatively charged oxygen atoms. This increased charge density is translated into higher viscosities.

Rolling-ball viscometer

The influence of the temperature on the viscosity was determined using a more accurate and user friendly viscometer. This rolling-ball viscometer was capable of automatically heating the sample to various temperatures whilst measuring the viscosity. The temperature dependence of the viscosity was measured on the [BBIM][AcO], the viscosity was measured at 25, 35, 45 and 55 °C. These data were compared with the previously measured viscosity with the rotating disk viscometer at 25.7 °C: 516 cP. The results are displayed in Figure 21.

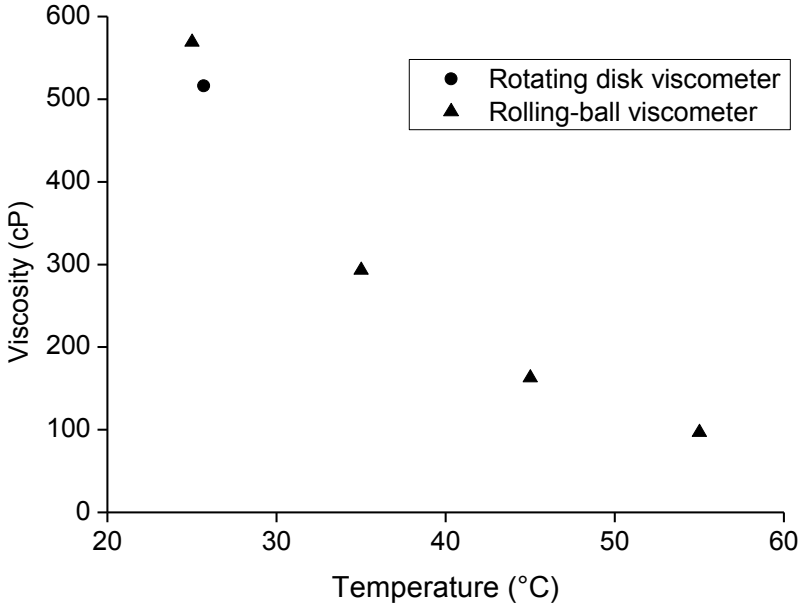


Figure 21: Temperature dependence of the viscosity for [BBIM][AcO].

The first observation is that the viscosity measured with the rotating disk viscometer copes very well with the viscosity trend measured with the rolling-ball viscometer. The fact that two different devices using two different techniques produce comparable results indicates that the measured viscosities of the ionic liquids are reliable.

In order to numerically determine the viscosity as a function of the temperature, the viscosities were fitted to an exponential decay. This was done using the origin 8 software, resulting in an exponential decay function of the following form: $y = A * e^{-x/t} + y_0$.

The results are displayed in Table 9, resulting in the following formula (5) for the viscosity of [BBIM][AcO]:

$$Viscosity\ (cP) = 3200 * e^{-Temperature\ (°C)/13.99} + 33.0 \qquad (5)$$

Table 9: Exponential fit parameters for the temperature dependence of the [BBIM][AcO] viscosity.

Symbol	Value	Standard error
A	3200	99
t	13.99	0.27
Y_0	33.0	3.,6
R^2	0.99986	

5.3.4 Melting point

The exact melting temperature of all the ionic liquids with melting points above room temperature are listed in Table 10. These include most of the tosylate ionic liquids and one acetate ionic liquid: 1,3-diisobutylimidazolium acetate.

Table 10: Melting temperatures of the solid imidazolium ionic liquids.

Ionic liquid	Melting point (°C)
[iBiBIM][AcO]	60
[iBiBIM][TsO]	95
[HHIM][TsO]	67
[OOIM][TsO]	97
[DDIM][TsO]	76
[EhEhIM][TsO]	56

A general rule is that the more symmetrical the compound, the higher its melting point.[49,50] This is clearly observed for the acetate series: the most symmetric ionic liquid, [iBiBIM][AcO] is the only one with a melting point above RT: 60 °C. It must be noted that this ionic liquid is only solid when completely dry and liquefies when it is contacted to a moist atmosphere for a long time (section 4.3.4).

5.4 Thermomorphic behavior

5.4.1 Solubility of imidazolium ionic liquids

The water solubility of the synthesized 1,3-dialkylimidazolium ILs was investigated at several temperatures in order to detect any temperature-dependent miscibility. All ionic liquids were tested according to the same procedure, as described below.

A sample, 200 mg, of purified ionic liquid was added to a small cylindrical vial, an equal amount of distilled water was added and the vial was sealed (Figure 22).

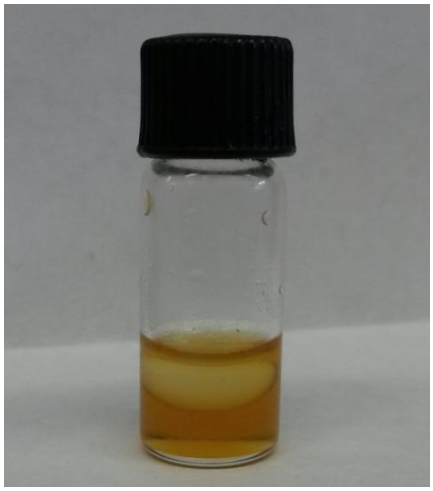


Figure 22: Testing vial filled with 200 mg of IL and 200 mg of distilled water.

The miscibility of the IL-water mixtures was determined visually: if a clear, translucent mixture was obtained, the mixture was considered homogeneous and the IL and water were completely soluble. When two immiscible phases are observed or when the mixture is clouded or blurred, the IL-water mixtures were considered immiscible. These observations were rather easy and reliable since all the ionic liquids were colored. The samples were heated and cooled between the relevant temperature window: the freezing and boiling point of water. They were heated to 100 °C with a heat gun and cooled towards 0 °C in an ice bath while any changes in their solubility were determined. This heating and cooling cycle was performed twice in order to eliminate any coincidental human errors, when the results were unclear, the second opinion of a coworker was consulted.

Imidazolium acetate

Since the acetate ionic liquids are very soluble in water, (their purification even relied on their affinity for the water phase) no temperature-dependent miscibility with water is expected for the acetate series. These expectations were confirmed in the experiments: all acetate ILs were completely soluble between 0 °C and 100°C. The only noteworthy observation is the liquefying of the [iBiBIM][AcO] when it was water saturated, as already discussed above.

Imidazolium bistriflimide

The bistriflimide anion was used to render hydrophobic ILs, immiscible with water. This behavior was indeed observed (see section 4.3.3), also the low water content of the bistriflimide ILs copes with the very hydrophobic nature of the anion. The possibility of discovering an IL with temperature-dependent miscibility with water was not excluded since some bistriflimide ILs have been reported to show UCST behavior with water.[56]

However, no temperature-dependent miscibility of the bistriflimide ILs and water was observed, all were completely insoluble between 0 °C and 100 °C. The bistriflimide anion proved to be too hydrophobic, causing a too large difference in polarity between the ionic liquids and the water phase to render miscible conditions for the mixture.

Imidazolium tosylate

A less hydrophobic anion compared to the bistriflimide was investigated: tosylate. Many of the 1,3-dialkylimidazolium tosylate ionic liquids were solid at room temperature with various melting temperatures, as can be seen in Table 10. The solid particles absorbed a lot of water, resulting in a wet powder instead of two phases when an equal amount of water and ionic liquid was mixed. The miscibility of the tosylate ionic liquids with water was therefore tested with a larger equivalent of water: IL:water 1:2, as shown in Table 11.

Table 11: Temperature dependence of the miscibility of imidazolium tosylate ionic liquids with water. 1: Homogeneous system 2: Biphasic system, IL phase=liquid 3: Biphasic system, IL phase=solid.

Composition	**Pure IL**	**IL:Water 1:2**		
Temperature	RT	RT	100 °C	0 °C
[EEIM][TsO]	Liquid	1	1	1
[BBIM][TsO]	Liquid	1	1	1
[iBiBIM][TsO]	Solid	1	1	1
[HHIM][TsO]	Solid	3	2	3
[OOIM][TsO]	Solid	3	2	3
[DDIM][TsO]	Solid	3	2	3
[EhEhIM][TsO]	Solid	3	2	3

As indicated in Table 11, the solid imidazolium tosylate ionic liquids melted when heating them and solidified again when cooling them down, this was accompanied without any difference in solubility. The changing water solubility throughout the tosylate series indicates that some of the tosylate ionic liquids are barely or barely not soluble in water, especially the [BBIM][TsO], [iBiBIM][TsO] and [HHIM][TsO]. Nevertheless, this property did not result in any thermomorphic behavior of the ionic liquids with water.

Imidazolium DEHP

The DEHP ILs did not show any temperature-dependent miscibility with water. All of the 1,3-dialkylimidazolium ILs were too hydrophobic to be miscible with water at any temperature between 0 °C and 100 °C.

Imidazolium nitrate

The imidazolium nitrate ionic liquids were heated with special safety precautions due to their potentially explosive and dangerous nature.[67] The samples were heated behind the protective screen of the fume hood and were clamped using tweezers, so that in the event of an explosion, no glass fragments could cause serious injury.

Table 12: Temperature dependence of the miscibility of imidazolium nitrate ionic liquids with water. 1: Homogeneous system 2: Biphasic system, IL phase=liquid.

Composition	Pure IL	IL:Water 1:1		
Temperature	RT	RT	100 °C	0 °C
[HHIM][NO_3]	Liquid	2	1	2
[OOIM][NO_3]	Liquid	2	2	2
[DDIM][NO_3]	Liquid	2	2	2
[EhEhIM][NO_3]	Liquid	2	2	2

Besides the [HHIM][NO_3], all imidazolium nitrate ionic liquids were immiscible with water at any temperature. In contrast: the [HHIM][NO_3] showed thermomorphic behavior: heating the biphasic mixture resulted in a clear and transparent solution at nearly 90 °C (Figure 23). This UCST behavior is investigated more thoroughly in section 5.4.2.

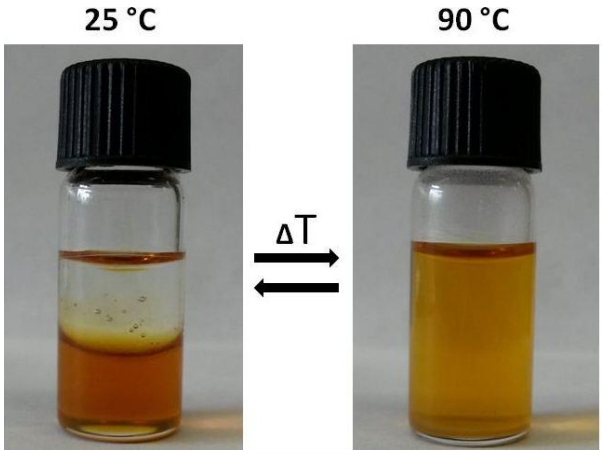


Figure 23: Temperature dependent miscibility of the [HHIM][NO_3] with water.

The fact that a nitrate ionic liquid with a temperature-dependent miscibility has been found is quite remarkable, to our knowledge, no nitrate ionic liquid was ever reported to show thermomorphic behavior. A study performed by Kohno *et al*. listed all published ionic liquids showing temperature-dependent miscibility with solvents, both water and organic solvents.[56] The paper did not mention any nitrates, meaning that they as well could not find any thermomorphic nitrate ionic liquid. Therefore, the discovery of a nitrate IL: [HHIM][NO_3], is

extremely interesting, even more so since it was prepared in a halogen-free synthesis in two easy synthetic and extraction steps.

5.4.2 1,3-Dihexylimidazolium nitrate

After the discovery of thermomorphic behavior for a mixture of [HHIM][NO_3] and water, a second test under identical conditions but with a new sample was performed, which confirmed the outcome of the first experiment. After this conformation, a larger batch of [HHIM][NO_3] (6.87 g, 23 mmol) was prepared from the [HHIM][AcO] precursor, identical to the synthesis described in section 4.4.5. This large amount was used for further experiments on the thermomorphic behavior.

Cloud point determination

Setup

The cloud point temperatures were determined visually by increasing the temperature while distinguishing between a cloudy, biphasic system and a clear, homogeneous mixture, this was done using the setup shown in Figure 24.

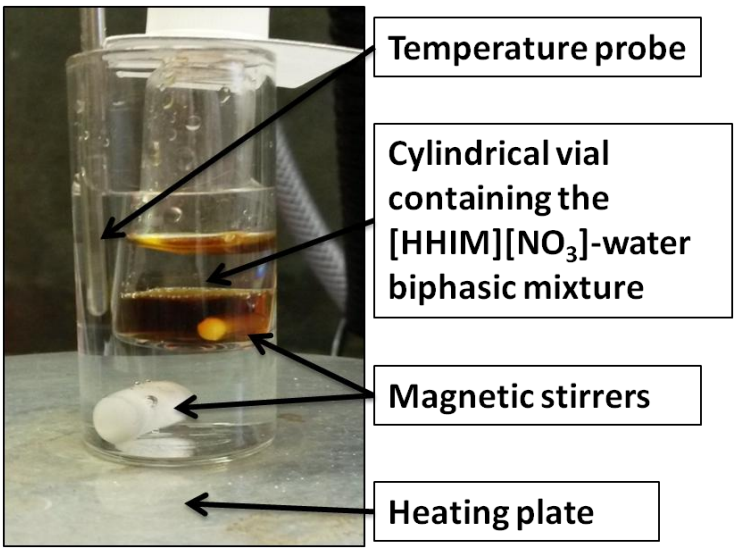


Figure 24: Cloud point determination setup.

A cylindrical vial was filled with the appropriate [HHIM][NO_3]-water mixture and a small magnetic stirrer. The vial was submerged in a water bath, also containing a magnetic stirrer. A temperature probe was submerged in the water at the same height as the vial, in order to the temperature of the IL-water mixture as accurately as possible. The setup was placed on a heating plate and the temperature was slowly increased while stirring both the water bath

and the IL-water mixture. The temperature at which the biphasic and cloudy mixture turned transparent (the cloud point temperature) was measured and reported.

Results

The exact temperature at which the [HHIM][NO_3]:water 1:1 mixture shows a transition between a cloudy, biphasic system and a clear, homogeneous solution was determined more exactly: 84.1 °C. This cloud point temperature was also measured for many different ratios between the [HHIM][NO_3] and water, ranging from 6 up to 71 wt%. These cloud points form the liquid-liquid equilibrium phase diagram of the [HHIM][NO_3]-water mixtures, this curve is displayed in Figure 25.

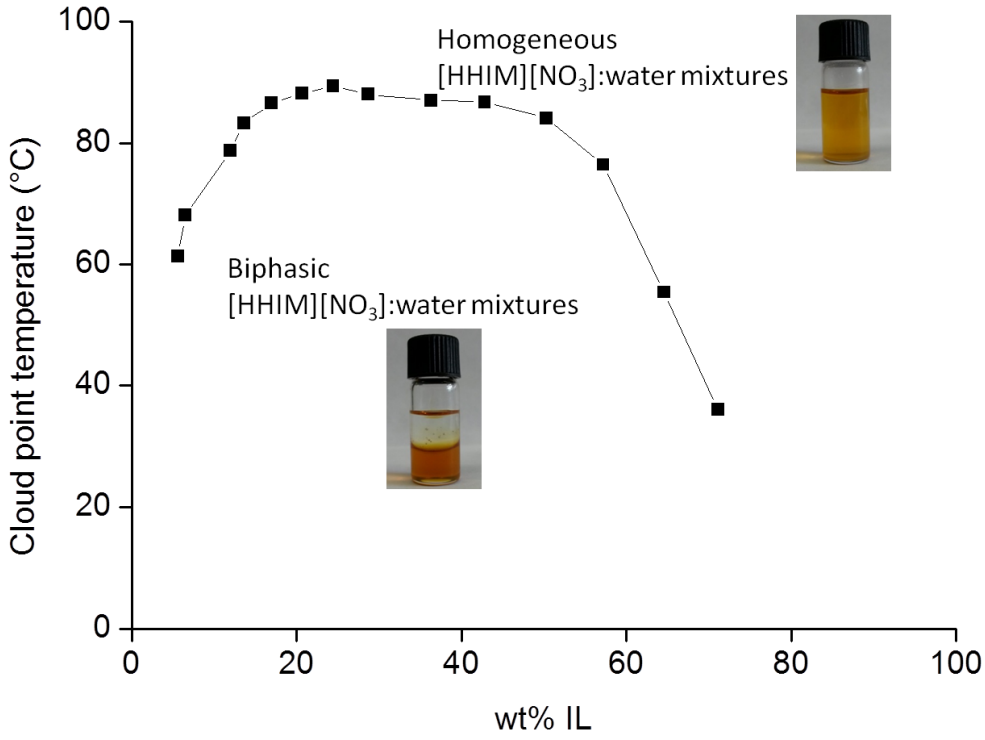


Figure 25: Liquid-liquid equilibrium phase diagram of the [HHIM][NO_3]-H_2O binary mixtures.

Mutual solubility of the IL and water phase

The solubility of the [HHIM][NO_3] in the water phase and vice versa, was determined in order to calculate the losses of IL and water to the aqueous phase and IL phase respectively. This is useful information to quantify the loss of both phases in extractions. A vial was filled with 500 mg of IL and 500 mg of distilled water, heated above the cloud point and allowed to cool

down. The two phases that separated upon cooling were used to determine the mutual solubility.

Under normal circumstances, the amount of water lost to the ionic liquid phase is measured via Coulometric Karl Fischer titrations. In the case of nitrate ionic liquids, this is not possible since nitrates disrupt the redox reactions in the KF reagent. Instead, the amount of water was determined using thermogravimetric analysis (TGA). The amount of IL dissolved in the water phase was determined using quantitative NMR spectroscopy with a 1,4-dioxane standard.

Water dissolved in IL

A small sample of [HHIM][NO_3] (13.8 mg) was measured with TGA. The sample was heated at 5 °C/min until 120 °C, it was kept at 120 °C for 60 minutes to evaporate all the water. Afterwards, it was heated until 500 °C at 5 °C/min to completely burn the sample. The mass of the water saturated [HHIM][NO_3] phase as a function of the temperature is displayed below in Figure 26.

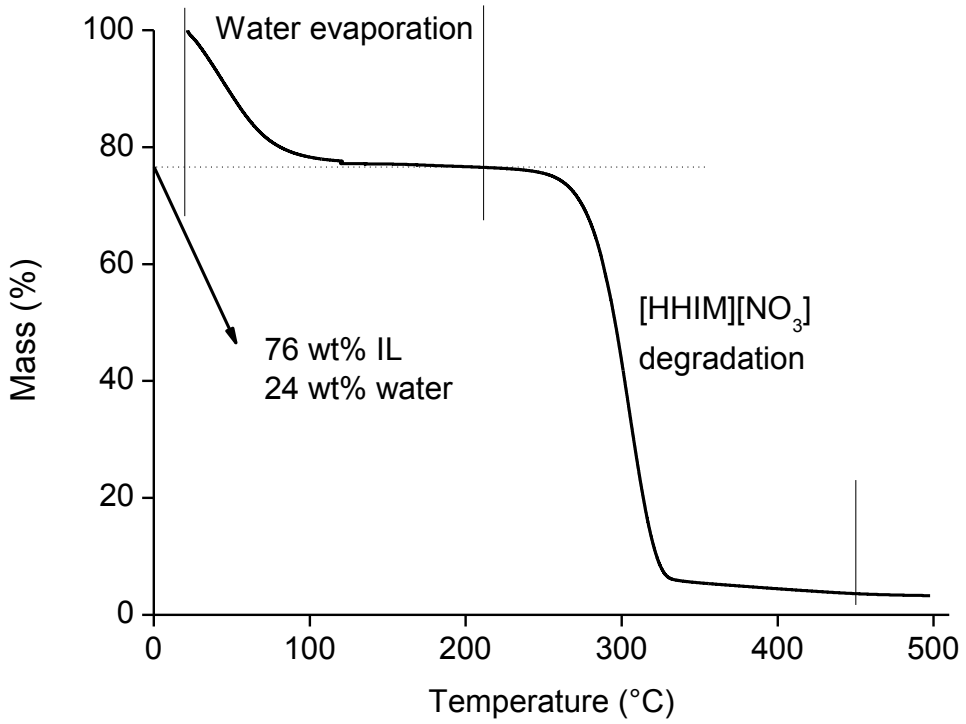


Figure 26: Mass of the water saturated [HHIM][NO_3] as a function of the temperature.

As can be seen in Figure 26, the water started evaporating from the sample until roughly 200 °C, after which all the water had been removed. When heating to higher temperatures, the [HHIM][NO_3] started to degrade starting at roughly 225 °C. At a temperature between 200

and 225 °C, when all the water is removed but the IL has not start degrading yet, the weight percentage was determined, this corresponds to the amount of water dissolved in the IL phase. The total amount of water dissolved in the [HHIM][NO_3] phase was: 24 wt%.

IL dissolved in water

The amount of IL dissolved in the water phase was determined with quantitative NMR using a standard of 1,4-dioxane. A tiny amount of standard (±5 mg) was added to a fraction of the water phase (±100 mg), this mixture was diluted with D_2O to obtain the required volume for ^1H NMR spectroscopy. From the response signals in the NMR spectrum and the amounts of standard and sample, the amount of IL dissolved in the water phase was calculated to be 5 wt% of the total water fraction.

Both these values are also encountered in the cloud point curve of [HHIM][NO_3] and water (Figure 25). The cloud point temperature drops significantly when the weight fraction of IL reaches 5 and 76 wt%, indicating complete miscibility of these specific mixtures. Concurrently, any mixture containing less than 5 wt% or more than 76 wt% [HHIM][NO_3] in water is also completely miscible at any given temperature.

6 Conclusions and Outlook

In this master thesis, a synthetic route towards substituted imidazolium ILs from standard molecules was targeted. The synthesis of 1,3-dibutylimidazolium ILs was investigated and improved, testing different acids and acid equivalents. The optimized synthesis prepared 1,3-dialkylimidazolium acetate from glyoxal, formaldehyde, a primary amine (2 eq.) and an excess of acetic acid (1.5 eq.). These acetate ILs could be purified by a simple extraction with diethyl ether with excellent yields, depending on the ILs hydrophilicity (94% for [EEIM][AcO] to 47 % for [DDIM][AcO]). This way 1,3-dialkylimidazolium ILs could be prepared in an easy, halogen-free one-pot and two-step synthesis and purified in good yields by a simple extraction step. Starting from this 1,3-dialkylimidazolium acetate platform, several other 1,3-dialkylimidazolium ILs were prepared via metathesis reactions. If anions had sufficiently strong acids (pK_a<0.7), the acid was used. The strong acid ensured a complete protonation of the acetate, resulting in the acetic acid that could be removed via evaporation. If the acids were not sufficiently strong, sodium salts of the new anion were employed. The completeness of the metathesis reactions in water was influenced by the position of both anions in the Hofmeister series. A general rule for these metatheses is: exchange towards higher placed anions exceeds more efficiently. When the metatheses resulted in hydrophobic ILs, the acetate (salt or acid) was removed by washing with water. The acetic acid could also be completely removed via evaporation, but this step is more time consuming compared to washing the ionic liquid. The evaporation of acetic acid was used to purify water soluble ILs, since they cannot be purified by washing. Sodium salts were eliminated by precipitation in an apolar solvent. This last approach was not 100% effective due to the high solvating power of the ILs. Depending on the solubility of all the products involved, an additional washing step was required. All the ionic liquids were fully characterized using ^{1}H NMR, ^{13}C NMR, FTIR and sometimes ESI-MS. The water content of RTILs was determined using Karl Fischer titrations and the viscosity was determined using a rotating disk viscometer. The temperature dependence of the viscosity was determined for [BBIM][AcO] with a rolling-ball viscometer. The melting point of the ILs solid at room temperature were determined using DSC measurements, all of the melting temperatures were lower than 100 °C. The solubility of all the ILs with water at different temperatures was investigated to detect any thermomorphic behavior. IL:water 1:1 mixtures (1:2 for tosylate ILs) were heated up to 100 °C and cooled down to 0 °C while their miscibility was observed. All acetate ILs were completely soluble and the Tf_2N^- and DEHP ILs were insoluble at any given temperature. The three short chain tosylate ILs were water soluble, the four long chain ILs were not. Besides the [HHIM][NO_3], all nitrate ILs were immiscible with water between

100 °C and 0 °C. The [HHIM][NO_3]:water 1:1 mixture showed UCST behavior with a cloud point at 84.1 °C and the full cloud point curve was determined. The mutual solubility of the [HHIM][NO_3] and water was determined, the IL phase contained 24 wt% water and the water phase contained 5 wt% IL. These values are also encountered in the cloud point curve, where the cloud point temperature drops when the weight fraction of IL approaches 5 and 76 wt% of IL. The discovery of the thermomorphic 1,3-dihexylimidazolium nitrate is remarkable, since, to our knowledge, no other nitrate IL was ever reported to show thermomorphic properties. Even more so, this IL could be synthesized with an efficient metathesis reaction from an imidazolium acetate platform. On top of that, both the metathesis reaction as well as the synthesis of the acetate precursor were performed halogen-free.

A lot of potential research is still available for the future. The halogen-free synthesis of 1,3-dialkylimidazolium can still be investigated further: more acids can be tested, techniques for increasing the yield of more hydrophobic ILs can be investigated and attempts can be made to introduce functional groups on the imidazolium rings. The metathesis strategies can be perfected and applied to many other anions. The most straightforward choice however, would be to further investigate the thermomorphic properties of [HHIM][NO_3] and its performance in extractions of REEs. Adding salts might help to reduce the cloud point temperature. More research can also be conducted to recover IL from the water phase after phase separation, which is beneficial for its use in large scale extractions.

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