ionic liquids

Trabajo académicamente dirigido
Universidad de Colonia

Cristina González Hernando

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References

Introduction

Ionic liquids are a class of novel solvents with very interesting properties and without a doubt, they have captured the imagination of chemists as well as researchers in other scientific disciplines.

The principle application of ionic liquids has been as alternative solvents for synthesis and catalysis.[5]

Ionic liquids are, as their name implies, salts that are liquid at low temperature, many at room temperature or below. Composed entirely of ions they are different than molecular solvents, water and organic solvents, and chemically analogous to molten salts.

The upper temperature limit for the classification "ionic liquid" is 100 °C and higher melting ion systems are typically referred to as molten salts. These low melting points are a result of their chemical composition, which contain large asymmetric organic cations. The more asymmetry, the lower lattice energy, and therefore lowers the melting point of the resulting ionic medium. In some cases, even the anions are relatively large and play a role in lowering the melting point.[4,5]

The composition and hence associated properties of IL depend on the cation and anion combinations: there are billions of different structures that may result in an ionic liquid.

The recent interest regarding to Green Chemistry is the result of the fact that they have no measurable vapour pressure and thus can emit no volatile organic compounds (VOCs).

The missing vapour pressure has very important advantages compared to other volatile organic compounds. Therefore, ionic liquids are non flammable and non explosive and allow simple recycling and re-use. Although it is needed to find better ways to recycle ionic liquids (many processes for cleaning ionic liquids involve washing with VOCs).[5]

VOCs are used to manufacture ionic liquids, and the ionic liquids themselves are made from species that, before their combination, are VOCs.

There is currently great interest in the use of these materials as solvents for a wide range of applications, including catalysis. Many reactions show advantages when carried out in ionic liquids, either with regard to enhanced reaction rates, improved selectivity, or easier re-use of catalysts.[4,8]
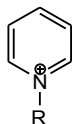
Composition

Examples of some of the different cation structures and anion pairs that may form an ionic liquid are: [2,5]
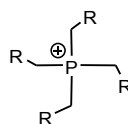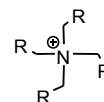
Some typical cations:
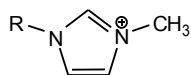
1-alkyl-3-methylimidazolium   N- alkyl-pyridinium   tetraalkyl-phosphonium   tetraalkyl-ammonium

Some typical anions:

Water immiscible: $(PF_6)^-$, $(N(SO_2CF_3)_2)^-$, $(BR_1R_2R_3R_4)^-$

Partially miscible: $(BF_4)^-$, $(CF_3SO_3)^-$

Water miscible: $(CH_3CO_2)^-$, $(NO_3)^-$, $(Cl)^-$, $(Br)^-$

Most common alkyl chains: ethyl, buthyl, hexyl, octyl, decyl.

1,3-dialkyl imidazolium salts are one of the most popular and investigated classes of room temperature ionic liquids.[2]

Actually dialkylimidazolium cations associated with relatively weak coordinating anions are compounds with unique physical-chemical properties, that can, in principle, be tuned by varying the N-alkylimidazolium substituents and/or the anion.

The introduction of different anions has become more popular since the increasing number of alternatives are being discovered that work as well as, or better than, the well-known anions, such as $AlCl_4^-$.[2,3,5]

The most commonly IL anions employed are polyatomic inorganic species:

- fluorinated-anions: $(PF_6)^-$, $(BF_4)^-$, $(CF_3SO_3)^-$, $((CF_3SO_3)_2N)^-$

- non- fluorinated anions

- non-conventional anions

fluorinated-anions

The anion chemistry has a large influence on the properties of ILs. Although little variation in properties may be expected between same cation salts of these species, the actual differences can be dramatic. For example, $[bmim]PF_6^-$ is immiscible with water, whereas $[bmim]BF_4^-$ is water-soluble.

Despite their extended use, PF_6^- and BF_4^- have been reported to sometimes decompose when heated in the presence of water, releasing HF.

This disadvantage has induced searching for alternative anions, although many of these are still fluorinated materials.

In these, the fluorine of the anion is bound to carbon, the C-F bond is inert to hydrolysis.

non- fluorinated anions

In response to safety and cost, new ILs with non- fluorinated anions have been introduced. Among the most interesting are salts in which the anions are derived from inexpensive bulk chemicals, alkylsulfate anions are likely to be reasonably non-toxic and biodegradable, for instant.

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non-conventional anions

Chemical catalogs list over one hundred commercially available salts that melt below 150°C. Many others are just above this melting point, suggesting that many new IL may be readily created by matching a desired cation from such a salt with a different anion, or vice versa.

In short, to make an ionic liquid, researchers can choose from dozens of small anions, such as hexafluorophosphate, $(PF_6)^-$ and tetrafluoroborate, $(BF_4)^-$, and hundreds of large cations, such as 1-hexyl-3-methylimidazolium or 1-butyl-3-methylimidazolium.

Ionic liquids are thus designer solvents.

Chemists are free to choose among the ions to make a liquid that suits a particular need, such as dissolving certain chemicals in a reaction or extracting specific molecules from a solution.[2,4]

Physical and Chemical properties

Melting point

It has been established that the melting point decreases when the size and asymmetry of the cation increase. Furthermore, an increase in the branching on the alkyl chain increases the melting point.[1]

Thermal stability

Most ionic liquids exhibit high thermal stability. Decomposition temperatures reported are generally above 400 ºC.

The thermal decomposition is similar for the different cations, but appears to decrease as the anion hydrophilicity increases.[1]

Viscosity

The viscosity of ionic liquids is normally higher than that of water and similar to that of oils, and decreases when increasing temperature.

Examining various anion-cation combinations, the increase in viscosity observed is attributed especially to an increase in the Van der Waals forces.[1]

Density

In general ionic liquids are denser than water.

The molar mass of the anion affects significantly the density of ionic liquids. For the same cation, density decreases with increasing the anion volume. This behaviour is attributed to the fact that a packing may become more compact while the positive and negative species become more even in size.[1]

Surface tension

Ionic liquids are widely used in catalysed reactions, and surface tension is an important property in these multiphase processes.

In general, liquid/air surface tensions for ionic liquids are higher than those for conventional solvents, although not as high as for water.

Surface tension values are affected by the alkyl chain length, while for a fixed cation, in general, the compound with the larger anion has the higher surface tension.[1]

Solubility in water

Water is often an unwanted impurity in ionic liquids and the presence of even small amounts can modify the physical properties such as viscosity, density, etc.

In general, the solubility of ionic liquids in water depends on the nature of the anion (bonded via H-bonding), the length of the alkyl chain and temperature.

Even ionic liquids which are not water soluble, tend to absorb water from the atmosphere (with a concentration in the range 0,2-1 mol.dm^{-3}).

The hydrophilic/hydrophobic behaviour is important for the solvation properties of ionic liquids as it is necessary to dissolve reactants, and also relevant for the recovery of products by solvent extraction.[1]

In short, ionic liquids have the following profitable properties:
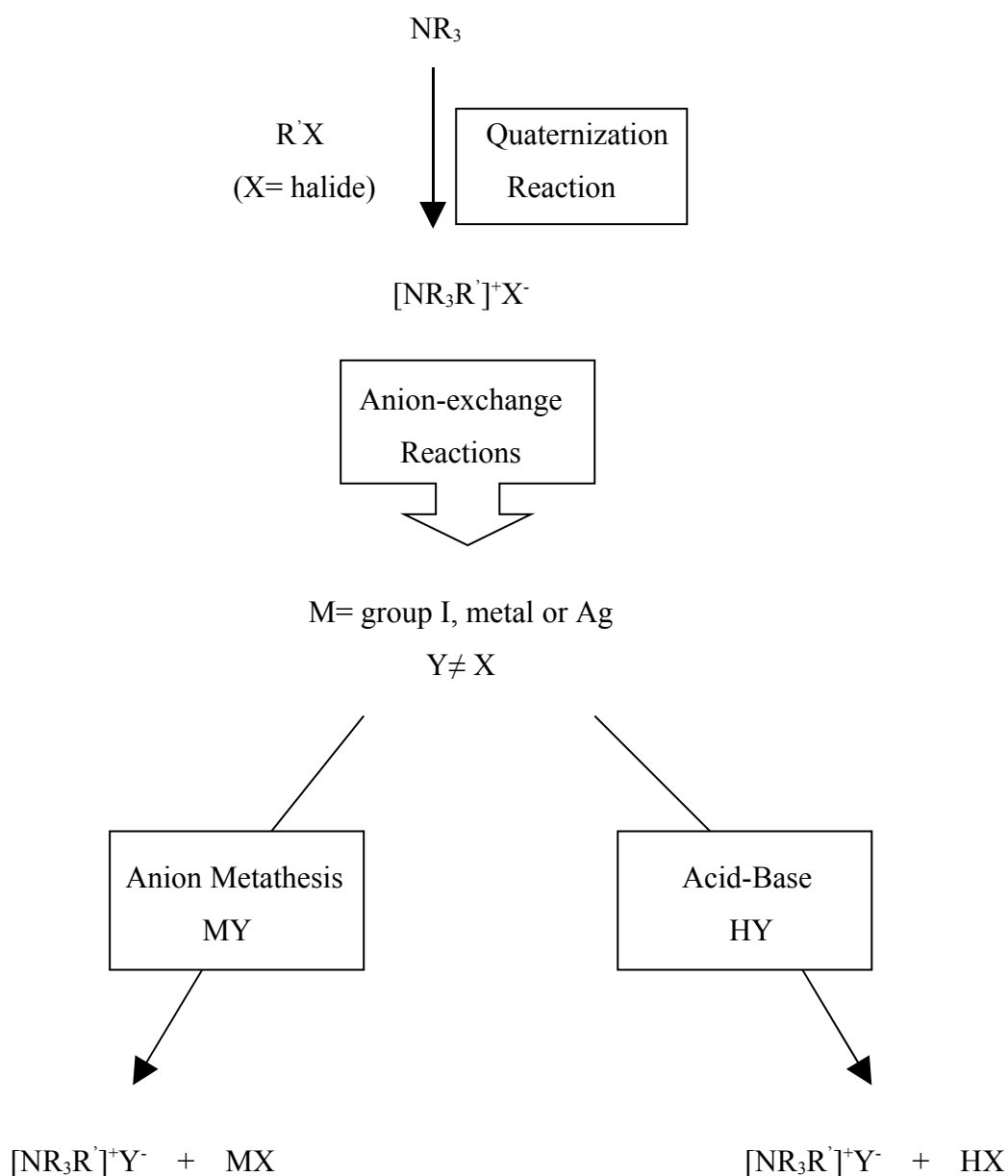
- No measurable vapor pressure
- Non-flammable below their decomposition temperature
- Tunable properties
- Excellent solvation properties for a variety of organic and inorganic compounds
- High electric conductivities
- High thermal stabilities
- Wide liquidus range

Preparation

The synthesis of ILs can be split in two sections: the formation of the desired cation and anion exchange where necessary to form the desired IL.

In many cases the desired cation is commercially available at reasonable cost, requiring thus only the anion exchange.

There are two basic methods for the preparation of ionic liquids: quaternization and anion-exchange reactions.[5]

$$NR_3$$

$$\downarrow$$

R'X
(X= halide)

Quaternization Reaction

$$[NR_3R']^+X^-$$

Anion-exchange Reactions

M= group I, metal or Ag

$$Y \neq X$$

Anion Metathesis MY

Acid-Base HY

$$[NR_3R']^+Y^- \ + \ MX \qquad\qquad [NR_3R']^+Y^- \ + \ HX$$

1. Quaternization reactions:

In the quaternization reactions the amine or phosphine is mixed with the desired haloalkane and then the mixture is stirred and heated.

The alkylation process has the advantages that a wide range of cheap haloalkanes are available and the substitution reactions generally occur at reasonable temperatures. The reaction temperature and time are very dependent on the haloalkane used and with increasing alkyl chain length, the reactivity of the haloalkane decreases.

The reaction may be carried out without the use of solvents, as the reagents are generally liquids and miscible. While the halide salt products are usually immiscible in the starting materials. Furthermore, the halide salts are generally more dense than the solvents, so removal of solvent and starting materials can be achieved by decantation.

The halide salts are generally solids at room temperature and they tend to be very hygroscopic, particularly when the alkyl chain substituents are short. 1-alkyl-3-methylimidazolium halide salts can form as extremely hard solids in round-bottomed flasks.[5]

2. Anion-exchange reactions:

The anion-exchange reactions can be divided into two categories: the formation of ionic liquids by anion metathesis and direct treatment of halide salts with Lewis acids.

2.1   Anion Metathesis reactions.

Metathesis of a halide salt with a silver, group 1 metal or ammonium salt of the desired anion. The use of silver salts permits the preparation of many salts in high yields and purities, due to the low solubility of silver salts, which allow isolation of the ILs simply by filtration. This method is the most efficient for the synthesis of water-miscible ILs although is limited by the relatively high cost of silver salts.

The most common approach for the synthesis of water-immiscible ILs is first to prepare an aqueous solution of a halide salt of the desired cation. Then the cation exchange is carried out either with the free acid of the appropriate anion, or with a metal or ammonium salt.

The use of the free acid lives only HCl, HBr or HI as the by-product, which are easy removable by washing with water (washing should continue until the aqueous residues are neutral)

Furthermore, it is recommended that these reactions be carried out with cooling in an ice bath, as the metathesis reaction is often exothermic.

When alkali metal or ammonium salts are used, presence of halide anions should be checked in the wash solutions with, for example silver nitrate.

The preparation of water-miscible ILs can be achieved with the use of silver salts, but is clearly too expensive for large-scale use. Therefore, the most common approach is to carry out the anion exchange in aqueous solution with either the free acid of the appropriate anion, the ammonium salt, or an alkali metal salt. Then the product is extracted with an organic solvent and the organic phase is washed with water.[5]

2.2 Lewis Acid-based reactions.

The most common method is simple mixing of the Lewis acid and the halide salt.

The reaction is generally quite exothermic and care should be taken when adding one reagent to the other. Although the salts are relatively thermally stable, an excess of heat can result in decomposition and discoloration of the ionic liquid.

This may be prevented by adding one component to the other in small portions or by cooling the mixing vessel.[5]

Purification

Ionic liquids can not be purified by distillation due to their lack of significant vapour pressure. The counterpoint of this is that a volatile impurity can be, in principle, separated by distillation.

However, it is better to remove as much as possible impurities from the starting materials (all solvent used in reactions may be dried and distilled before use) and where possible, use synthetic methods that generate few by-products or allow an easy separation from the ionic liquid.

These precautions should be taken if a colourless ionic liquid is required.

Most of ionic liquids should be colourless, but in practice, the amount of impurities (generally extremely small) cause coloration of the salts, which are often yellow-coloured.

The main contaminants are halide anions, organic bases (from unreacted starting material) and water.

It is certain that the impurity likely to be present in largest concentrations in most ionic liquids is water. The removal of other solvents is carried out by distillation, but water is one of the most problematic solvents to remove.[5]

Applications

Ionic liquids are used as solvents for organic synthesis, organometallic syntheses and catalysis, as electrolytes in electrochemistry, in fuel and solar cells, as lubricants, as a stationary phase for chromatography, as matrices for mass spectrometry, in biocatalysis as supports for the immobilization of enzymes, in separation technologies, as liquid crystals, nano-materials, etc.

Some applications in brief:

Homogeneous and heterogeneous catalyst

For some applications, ionic liquids offer the advantage of both homogeneous and heterogeneous catalysts. This is because selected ionic liquids can be immiscible with the reactants and products but dissolve the catalysts.

The advantage is that IL immobilize the catalyst and form a liquid phase which allows the catalyst to move freely.[8]

Ionic liquids as separating agents

If an ionic liquid can be found to preferentially dissolve certain gaseous species, then it can be used in conventional gas absorption applications.

The non-volatile nature of ionic liquids plays two important roles:

First, there will be no contamination of the gas stream by the solvent during operation. This means no solvent loss and no air pollution.

Second, regeneration of the solvent is easy. A simple flash distillation is all that is required to remove the gas from the solvent.[6]

Clean synthesis in ionic liquids

Ionic liquids can be used for clean synthesis in a variety of reactions. All kinds of reaction classes in neutral ionic liquids have already been investigated.

These industrially important reactions are cleaner than current processes.[6]

Ionic liquids and cross coupling reaction

Ionic liquids have the interesting to dissolve both organic and inorganic materials and thus have already found application as reaction media for all kinds of transition metal catalyzed reactions.[3]

Conclusion

One important feature of these liquids is the possibility of tuning their physical and chemical properties by varying the nature of the anion and cation. If we consider all the possible combinations, it is evident that the number of these new solvents is extremely high and in principle it should be possible to obtain the appropriate ionic liquid for any given application.

Experimental Section

Quaternization reactions of common amines used as cations in ionic liquids and anion exchange of these ionic liquids were carried out.

[bmim]Br, 1-butyl-3-methyl-imidazolium bromide.
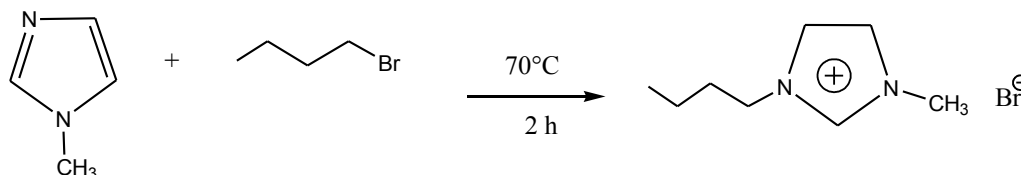
In a three-necked flask, 200 mmol (15,9 ml) 1-methylimidazole were stirred while, 200 mmol (21,6 ml) 1-bromobutane were from a dropping funnel added. Addition of the bromoalkane was dropwise, due to the exothermic reaction that takes place.

The reaction mixture was boiled to reflux for two hours to give the corresponding 1-butyl-3-methyl-imidazolium bromide.

To crystallize the ionic liquid, the crude product was spilled while stirring in an erlenmeyer flash containing ethylacetate (500 ml) in an ice-bath.

The addition of the crude product to ethylacetate was done slowly otherwise some by-products could be retained in the ionic liquid.

The product was squashed until a white powder was obtained. It was allowed to sediment and then ethylacetate was removed by transferring to another flash.

It was washed with ethylacetate (100 ml) and then transferred to a weighed round-bottomed flask, followed by evaporation of the solvent in the rotary evaporator.

Yield: 87 % (174 mmol).

Characterization [bmim]Br: NMR
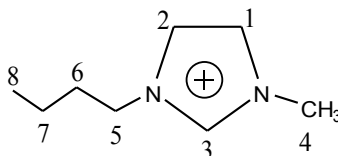
^{1}H: 300 MHz, DMSO-d$_6$, δ(ppm)

H$_1$: 7,75 (d, J= 1,73 Hz, 1H)   H$_5$: 4,15 (t, J = 7,18 Hz, 2H)

H$_2$: 7,68 (d, J = 1,71 Hz, 1H)   H$_6$: 1,75 (q, 2H)

H$_3$: 9,08 (s, 1H)   H$_7$: 1,27 (m, 2H)

H$_4$: 3,84 (s, 3H)   H$_8$: 0,89 (t, J = 7,3 Hz, 3H)

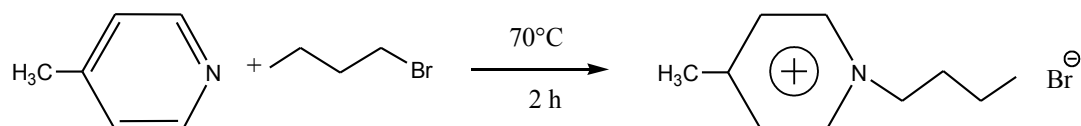^{13}C: 75 MHz, DMSO-d$_6$, δ(ppm)

C$_1$: 122,2   C$_5$: 48,5

C$_2$: 123,6   C$_6$: 31,3

C$_3$: 136,0   C$_7$: 18,7

C$_4$: 35,7   C$_8$: 13,2

[bmpy]Br, 1-butyl-4-methylpyridinium bromide.

In a three-necked flask, 200 mmol (19,6 ml) 4-picoline (methylpyridine) were stirred while, 200 mmol (21,6 ml) 1-bromobutane were from a dropping funnel added.

The reaction mixture was boiled to reflux for two hours, to give the corresponding 1-butyl-4-methylpiridinium bromide.

After that, the crude product was spilled, while stirring, into an erlenmeyer flash containing ethylacetate (500 ml) in an ice-bath in order to crystallize the ionic liquid.

Afterwards it was squashed until a powder was obtained and it was allowed to sediment.

Ethylacetate was removed by transferring to another flask.

It was a pale red powder but it should have been white, which meant that some by-products were present.

It was then washed with ethylacetate (100 ml) for five times and stand over-night with stirring in order to get rid of by-products, (although the powder thus obtained was still pale red). Finally it was transferred to a round-bottomed flask, followed by evaporation of the solvent in the rotary evaporator.

Yield: 89 % (179 mmol).

Characterization [bmpy]Br: NMR
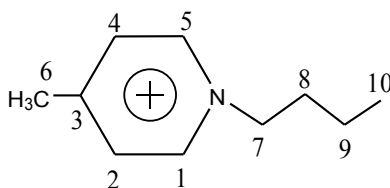
^{1}H: 300 MHz, DMSO-d_6, δ(ppm)

H_1 and H_5: 7,98 (d, J = 6,37 Hz, 2H) H_8: 1,87 (m, 2H)

H_2 and H_4: 8,90 (d, J = 6,37 Hz, 2H) H_9: 1,28 (m, 2H)

H_6: 2,60 (s, 3H) H_{10}: 0,90 (t, J = 7,29 Hz, 3H)

H_7: 4,52 (t, J = 7,38 Hz, 2H)

^{13}C: 75 MHz, DMSO-d_6, δ(ppm)

C_1 : 128,3 C_6: 21,3

C_2: 143,6 C_7: 59,7

C_3: 158,8 C_8: 32,5

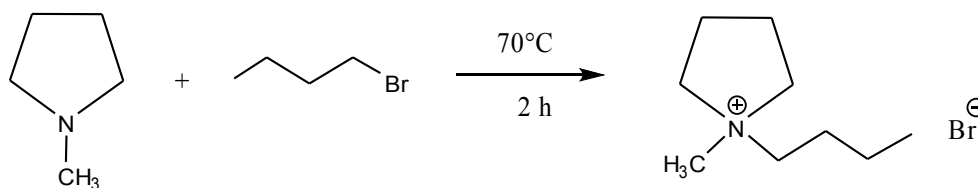C_4: 143,6 C_9: 18,7

C_5: 128,3 C_{10}: 13,2

[bmpyr]Br, 1-buthyl-1-methylpyrrolidinium bromide.

In a three-necked flask, 200 mmol (21 ml) 1-methylpyrrolidine were stirred while, 200 mmol (21,6 ml) 1-bromobutane were from a dropping funnel added.

The reaction mixture was boiled to reflux, to give the corresponding 1-buthyl-1-methyl-pyrrolidinium bromide. By the time reactants were mixed, the product was formed (a white solid), therefore it was stirred without heat.

Then the crude product was spilled into an erlenmeyer flash containing ethylacetate (500 ml) in order to wash the ionic liquid (without ice-bath because it was already crystallized). Then it was squashed until a white powder was obtained.

After that, it was afforded to sediment and ethylacetate was removed by transfer to another flask.

Finally, it was transferred to a round-bottomed flask, followed by evaporation of the solvent under vacuo.

Yield: 43,4 % (86,7 mmol).

Characterization [bmpyr]Br: NMR
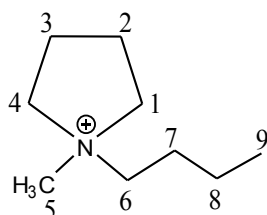
^{1}H: 300 MHz, DMSO-d_6, δ(ppm)

H_1 and H_4: 3,44 (m, 4H) H_7: 1,67 (m, 2H)

H_2 and H_3: 2,07 (m, 4 H) H_8: 1,32 (m, 2H)

H_5: 2,98 (s, 3H) H_9: 0,95 (t, J = 7,38 Hz, 3H)

H_6: 3,30 (t, J = unable to measure, 2H)

^{13}C: 75 MHz, DMSO-d_6, δ(ppm)

C_1: 63,8 C_6: 63,3

C_2: 25,4 C_7: 21,5

C_3: 25,4 C_8: 19,8

C_4: 63,8 C_9: 14,0

C_5: 47,9

Anion-exchange reactions

[bmim]NTf$_2$, 1-butyl-3-methyl-imidazolium bis-(trifluoromethanesulfon)imide.

$$\text{[bmim]}^+ \, Br^{\ominus} \quad + \quad F_3C-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}-N^{\ominus}-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}-CF_3 \quad Li^{\oplus} \xrightarrow[\text{12 h}]{70°C}$$

$$\text{[bmim]}^+ \quad \overset{CF_3}{\underset{CF_3}{\overset{|}{O=S=O} \atop \underset{O=S=O}{\overset{|}{N^{\ominus}}}|}} \quad + \quad LiBr$$
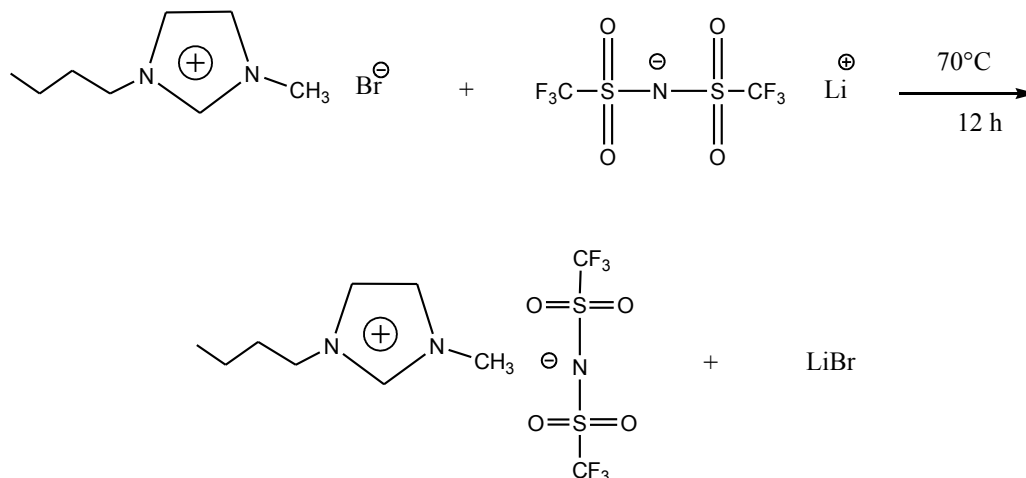
In a three-necked-flask, 90 mmol (20 g) [bmim]Br were dissolved in water (90 ml) and stirred while 90 mmol (25,83 g) LiNTf$_2$ dissolved in water (180 ml) were added and boiled to reflux for twelve hours at 70 °C.

By the time reactants were mixed, the product was formed. Therefore it was stirred overnight without heat.

After, the crude product was transferred to a separation funnel and same volume of water was added of ethylacetate, in order to extract [bmim]NTf$_2$ which was insoluble in water, whereas by-products ([bmim]Br that did not react, LiBr and NTf$_2$) were soluble in water.

Then the aqueous phase was removed and the organic phase washed with portions of water (30 ml for five times (10% v/v)), in order to get rid of the water-soluble by-products.

To verify there was no bromide in the organic phase, in a pipe of test, drops of the final portion of cleaning-water were checked with silver nitrate.

If there was bromide, silver bromide would have formed. In case of a positive test, additional wash is needed.

Finally ethylacetate was evaporated, first in the rotary evaporator and then under vacuum. A pale yellow liquid was thus obtained.

Yield: 96 %, (86,4 mmol).

Characterization [bmim]NTf$_2$: NMR
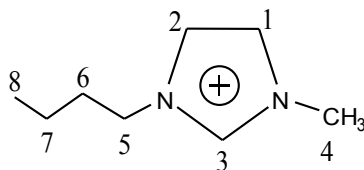
^{1}H: 300 MHz, DMSO-d$_6$, δ(ppm)

H$_1$: 7,84 (d, J = 1,57 Hz, 1H)   H$_5$: 4,19 (t, J = 7,13 Hz, 2H)

H$_2$: 7,76 (d, J = 1,52 Hz, 1H)   H$_6$: 1,75 (q, 2H)

H$_3$: 9,32 (s, 1H)   H$_7$: 1,25 (m, 2H)

H$_4$: 3,86 (s, 3H)   H$_8$: 0,87 (t, J = 7,34 Hz, 3H)

^{13}C: 75 MHz, DMSO-d$_6$, δ(ppm)

C$_1$: 122,2   C$_5$: 48,3

C$_2$: 123,5   C$_6$: 31,3

C$_3$: missing   C$_7$: 18,7

C$_4$: 35,7   C$_8$: 13,2

[bmpy]NTf$_2$, 1-butyl-4-methylpyridinium bis-(trifluoromethanesulfon)imide.
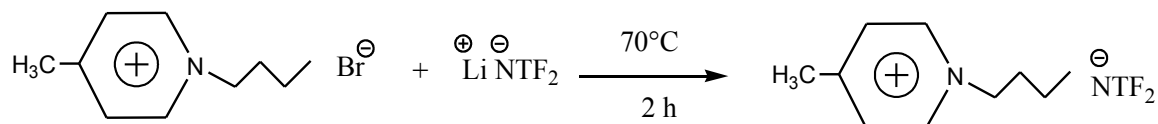
In a three-necked-flask provided with stirrer, 90 mmol (20,7 g) [bmpy]Br were dissolved in water (90 ml) while 90 mmol (25,83 g) LiNTf$_2$ dissolved in water (180 ml) were added and boiled to reflux for twelve hours at 70 °C.

The crude product was transferred to a separation funnel and same volume of water was added of ethylacetate.
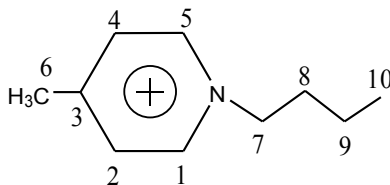
Then the aqueous phase was removed and the organic phase washed with 30 ml. of water for five times (10% v/v).

Silver nitrate was used to verify there was no bromide.

Afterwards ethylacetate was evaporated under vacuum and an orange ionic liquid was obtained.

Yield: 95% (86,4 mmol).

Characterization [bmpy]NTf$_2$: NMR

^{1}H: 300 MHz, DMSO-d$_6$, δ(ppm)

H$_1$ and H$_5$: 8,91 (d, J = 6,42 Hz, 2H)   H$_8$: 1,86 (m, 2H)

H$_2$ and H$_4$: 7,97 (d, J = 6,23 Hz, 2H)   H$_9$: 1,28 (m, 2H)

H$_6$: 2,60 (s, 3H)   H$_{10}$:0,90 (t, J = 7,37 Hz, 3H)

H$_7$: 4,51 (t, J = 7,28 Hz, 2H)

^{13}C: 75 MHz, DMSO-d$_6$, δ(ppm)

C$_1$: 143,6   C$_6$: 21,3

C$_2$: 117,3   C$_7$: 59,7

C$_3$: 158,7   C$_8$: 32,5

C$_4$: 121,6   C$_9$: 18,7

C$_5$: 128,3   C$_{10}$: 13,2

[bmpyr] NTf$_2$, 1-buthyl-1-methylpyrrolidinium bis-(trifluoromethanesulfon)imide.
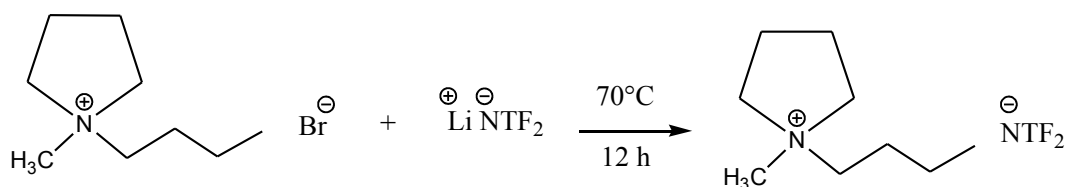
In a three-necked-flask, 73 mmol (16,39 g) [bmpyr]Br were dissolved in water (73 ml) while, 73 mmol (20,95 g) LiNTf$_2$ dissolved in water (146 ml) were added, stirred and boiled to reflux for twelve hours at 70 °C.

The crude product was transferred to a separation funnel and same volume of water was added of ethylacetate in order to extract the ionic liquid.
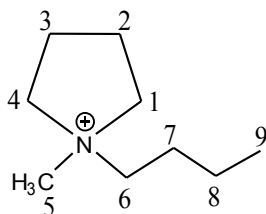
Followed by remove the aqueous phase. The organic phase was washed with 30 ml. of water for five times (10% v/v).

Silver nitrate was used for checking bromide.

Finally, ethylacetate was evaporated under vacuum, giving place an orange ionic liquid.

Yield: 78% (57 mmol).

Characterization [bmpyr] NTf$_2$: NMR

^{1}H: 300 MHz, DMSO-d$_6$, δ(ppm)

H$_1$ and H$_4$: 3,44 (m, 4H)

H$_2$ and H$_3$: 2,07 (m, 4 H)

H$_5$: 2,97 (s, 3H)

H$_6$: 3,28 (t, J = 8,14 Hz 2H)

H$_7$: 1,67 (m, 2H)

H$_8$: 1,33 (m, 2H)

H$_9$: 0,93 (t, J = 7,41 Hz, 3H)

^{13}C: 75 MHz, DMSO-d$_6$, δ(ppm)

C$_1$: 121,6

C$_2$: 63,4

C$_3$: 62,9

C$_4$: 117,3

C$_5$: 47,5

C$_6$: 24,9

C$_7$: 21,1

C$_8$: 19,3

C$_9$: 13,4

[bmim]BF$_4$, 1-butyl-3-methyl-imidazolium tetrafluoroborate.
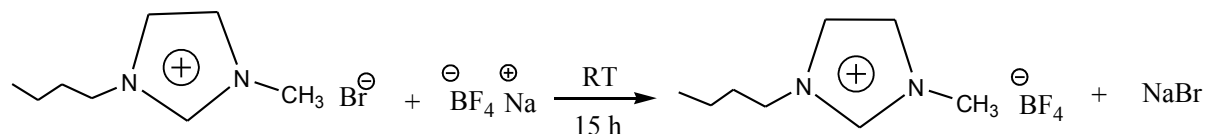
In a round-bottomed flask 60 mmol (13,13 g) [bmim]Br were dissolved in acetone (two ml of acetone per mmol of ionic liquid), while 60 mmol (2,7 ml) sodium tetrafluoroborate were added with continuous stirring and a drying tube, at room temperature during fifteen hours. Both reactants were insoluble in acetone, whereas the product did.

When the reaction was finished, the by-product (sodium bromide) which was insoluble in acetone, had to be filtered.

Then, the crude product was charged in an alumina column, in order to remove completely sodium bromide, which was retained in the column, whereas the ionic liquid was eluted.

Finally, solvent was removed in vacuo and a yellow ionic liquid is obtained.

Yield: 95 % (57 mmol).

Characterization [bmim]BF$_4$: NMR
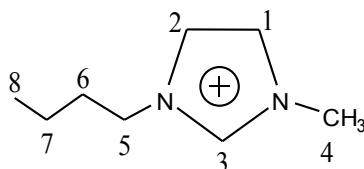
^{1}H: 300 MHz, DMSO-d$_6$, δ(ppm)

H$_1$: 7,75 (d, 1H)	H$_5$: 4,15 (t, J = 7,13 Hz, 2H)
H$_2$: 7,68 (d, 1H)	H$_6$: 1,73 (m, 2H)
H$_3$: 9,08 (s, 1H)	H$_7$: 1,27 (m, 2H)
H$_4$: 3,84 (s, 3H)	H$_8$:0,89 (t, J = 7,36 Hz, 3H)

^{13}C: 75 MHz, DMSO-d$_6$, δ(ppm)

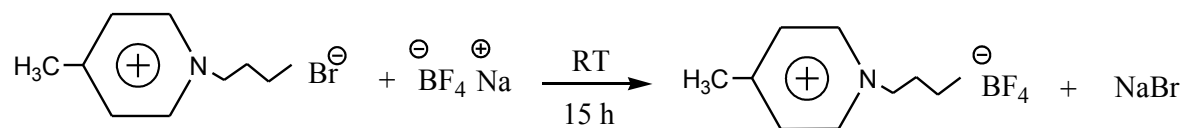|	
C$_1$: 123,6	C$_5$: 48,5
C$_2$: 122,2	C$_6$: 31,3
C$_3$: 136,5	C$_7$: 18,7
C$_4$: 35,7	C$_8$: 13,2

[bmpy]BF₄, 1-butyl-4-methylpyridinium tetrafluoroborate.

In a round-bottomed flask 60 mmol (13,801 g) [bmpy]Br were dissolved in acetone (120 ml) while 60 mmol (2,7 ml) sodium tetrafluoroborate were added with continuous stirring and a drying tube, at room temperature during fifteen hours.
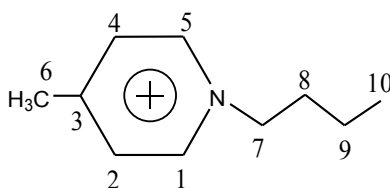
When the reaction was finished, sodium bromide was filtered.

Then, the crude product was charged in an alumina column in order to remove sodium bromide.

Afterwards, solvent was removed in vacuo to give place an orange-yellow ionic liquid.

Yield: 86 % (51,6 mmol).

Characterization [bmpy]BF₄: NMR

^{1}H: 300 MHz, DMSO-d$_6$, δ(ppm)

H_1 and H_5: 7,98 (d, J = 6,39 Hz, 2H) H_8: 1,86 (m, 2H)

H_2 and H_4: 8,23 (d, J = 6,39 Hz, 2H) H_9: 1,28 (m, 2H)

H_6: 2,60 (s, 3H) H_{10} :0,90 (t, J = 7,32 Hz, 3H)

H_7: 4,48 (t, J = 7,25 Hz, 2H)

^{13}C: 75 MHz, DMSO-d$_6$, δ(ppm)

C_1: 143,6 C_6: 21,6

C_2: 117,3 C_7: 59,7

C_3: 158,8 C_8: 32,5

C_4: 121,3 C_9: 19,0

C_5: 128,3 C_{10}: 13,2

Conclusions

The synthesis of these ionic liquids presented not much difficulty and was carried out without significant problems. Good yields were also obtained (except for [bmim]NTf$_2$).

Purification of chemical reactions performed in Ionic Liquids.

Introduction

As in the most of chemical reactions, the product of interest has to be isolated or purified from the reaction mixture, which may contain remaining starting material, by-products as well as impurities.

A classical method of purification is the chromatography column.

The technique is based on passing a mixture dissolved in a "mobile phase" through a "stationary phase", which separates the analyte to be measured from other molecules in the mixture and allows it to be isolated.

Some substances can not be purified through a common column (alumina or silica), due to their sensitivity towards these materials. Thus, cellulose columns are tested in order to see if they represent a proper medium in which reach the aim.

Experimental section

The aim of this work was that the ionic liquid did not eluate from the column. Therefore, to achieve the target less than one per cent of IL should elute.

The ionic liquid [bmim]NTf$_2$ was used to carry out all experiments, especially due its liquid state at room temperature.

Regarding the mixture of solvents used as eluent, two considerations had to be in mind: in one hand, a polar solvent could dissolve cellulose. In the other hand, an unpolar solvent could not eluate the ionic liquid.

Dichloromethane which is in the middle of the polarity index, was thus used first. But results were not in agreement with the fixed aim, due to the whole ionic liquid loaded in the column was eluted in the first eluting fraction. Dichloromethane is quite polar and ionic liquids are super-polar.

Other solvents in the middle of the polarity index are quite toxic, not environmentally healthy or they have a low vapour pressure and in consequence, distill them will be a tedious work.

Therefore, a mixture of ethylacetat-cyclohexane was used.

The experiments were consisting in loading all columns with the same amount of cellulose (1 g) and ionic liquid (0,5 g), whereas the mixture of solvents and their ratio had to be optimized.

The ionic liquid was loaded into the column previously mixed with cellulose (0,5 g) and dissolved in dichloromethane (10 ml). Finally removed the solvent in the rotary evaporator.

Alicuots of eluate (5 ml) were taken, transferred to a weighed rounded-bottom flask, then evaporated the solvent in the rotary evaporator and finally weighted. This methodology was done until a constant weight was obtained. In the evaporation of the solvent, all samples had to stand the same time in the rotatory evaporator (half-one hour) in order to maintain repetibility.

Experiments carried out are summarized in the following table:

Solvent	Gram of IL in the column	Gram of cellulose in the column	% IL eluted
CH$_2$Cl$_2$	0,52	1,12	100
EE:cyclohexane 1:1	0,56	1,17	100
EE:cyclohexane 1:5	0,55	1,02	2,7
EE:cyclohexane 1:10	0,55	1,13	6
EE:cyclohexane 1:20	1,03	1,02	2,7
EE:cyclohexane 1:20	1,0	1,03	0,07

Dichloromethane and ethylacetat-cyclohexane in a ratio 1:1 were too much polar solvents, therefore EE:cyclohexane 1:20 achieved the best results. The less polar the mixture of solvents was, the less ionic liquid was eluted.

Furthermore, when the amount of the ionic liquid loaded in the column was doubled, practically the mayority of the ionic liquid was retained in the column.

The fact that the amount of ionic liquid could be doubled in the column was a very satisfying result.

There were some misunderstood results concerning to experiments three (EE:cyclohexane 1:5) and four (EE:cyclohexane 1:10). The explanation to this could be, in one hand, that in the experiment four, evaporation of the solvent was not sufficient. In the other hand, some mistakes concerning to weigth could have been done.

Conclusions

Results obtained were in agree with the aim of the work.

In addition, more experiments should be developed in order to optimize the amount of ionic liquid that could be loaded in the cellulose column.

Besides, more experiments should be performed with different ionic liquids to support the results mentioned above.

Synthesis of 2-mercapto-5-imidazolecarboxylate.

The target molecule was 4(5)-Fluoro imidazolium, a compound which will be used for NMR experiments (H,F-HOESY). But the synthesis of this molecule from the starting materials implied many steps and there was not enough time to carry out the synthesis of this compound, hence the final step was the synthesis of 2-mercapto-5-imidazolecarboxylate .

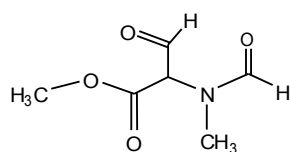Four principal steps were done:
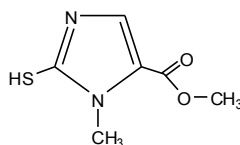
- Synthesis of N-methylglycine methyl ester hydrochloride
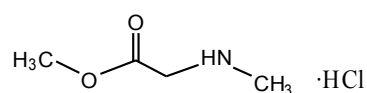
- Synthesis of N-formyl-N-methylglycine methyl ester

- Condensation of N-formyl-N-methylglycine methyl ester with ethyl formate

- Synthesis of 2-mercapto-5-imidazolecarboxylate

Synthesis of N-methylglycine methyl ester hydrochloride.

$$H_3C-NH_2 \xrightarrow{\text{HCOH}} H_3C-N=CH_2 \xrightarrow{\text{KCN}} H_3C-NH-CH_2-CN$$

$$\xrightarrow[\text{MeOH}]{\text{HCl}} H_3C-NH-CH_2-C(=O)-O-CH_3 \cdot HCl$$
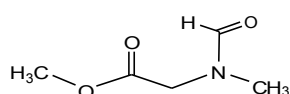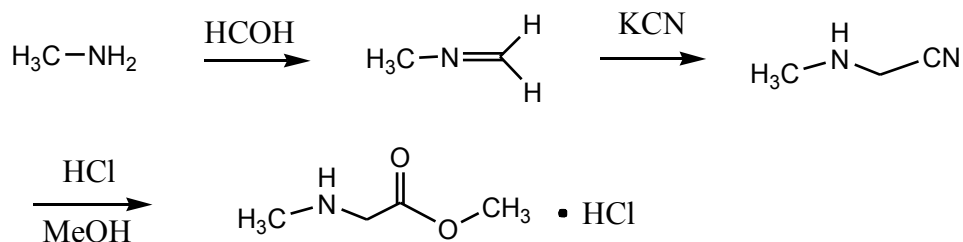
In a three-necked-flask, provided with a stirrer and a thermometer, a mixture of methyl-amine (100 mmol, 8,63 ml), water (5 ml) and formalin (40%, 12,5 ml) was cooled in an ice bath while stirring.

The reaction was quite exothermic, hence cooling with an ice bath was necessary.

Then, a solution of potassium cyanide saturated in cold, was added dropwise during a period of time of two hours.

From time to time, dry ice was added to maintain the temperature below 10 °C in order to avoid secondary reactions, due to the exothermic reaction between the imine and the cyanide.

The staff contaminated with cyanide was cleaned first with a solution of sodium hydroxide, pH above 12 (to avoid HCN gas releasing) and then with a sodium perchlorate solution.

As soon as the cyanide was added, the mixture was stirred for an additional hour and then extracted with ether (two portions of 25 ml).

After drying the solution over magnesium sulphate, ether was removed in the rotary evaporator and finally under vacuum.

Thus, a crude product of 2-(methylamino)acetonitrile was obtained (a yellow liquid which was stored in the fridge until the next step was performed).

It was then dissolved in dry methanol (125 ml) which has been previously saturated in the cold with hydrogen chloride. In the presence of water, acidic hydrolysis of nitrile moiety affords the formation of the acid whereas in a free-water medium the product obtained is the methyl ester moiety.

This solution was stirred and allowed to stay all over night at room temperature and finally heated to reflux (70 ° C) for four hours.

The ammonium chloride which had separated was removed by filtration. Followed by evaporation of filtrate on the rotary evaporator, to a volume of 40 ml and again filtered.

To end, evaporation of methanol left a residue of 3,47 g of N-methylglycine methyl ester hydrochloride.

Yield: 24,9 % (2,5 mmol).

Literature yield based on cyclohexilamine hydrochloride was 80,6 %.

Mechanism reaction:
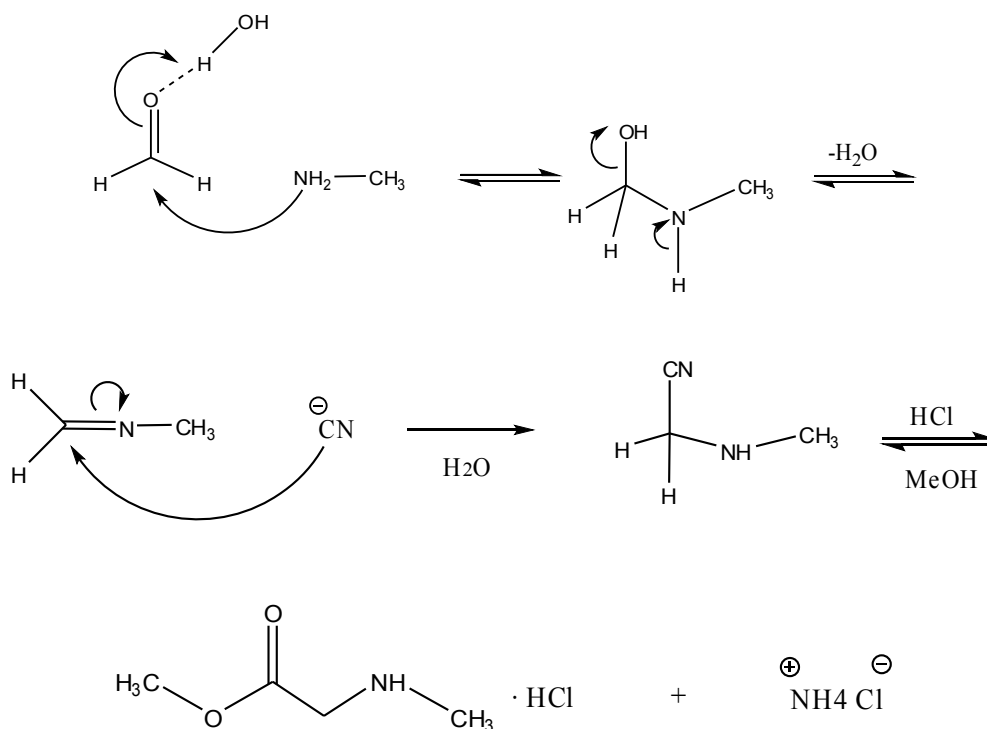
Condensation of the amine with the carbonyl group to form hydroxylamine intermediate, which is spontaneously rearrange in the corresponding imine derivative through the loss of water.

With the addition of potassium cyanide the following N-methylenemethanamine gives 2-(methylamino)acetonitrile which, after acidic hydrolysis in the presence of methanol, affords the desired methyl 2-(methylamino)acetate hydrochloride.

Synthesis of N-formyl-N-methylglycine methyl ester.
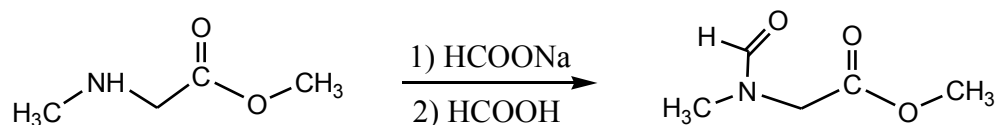
The crude ester hydrochloride was dissolved by warming in 2,5 ml of 98 % formic acid. To this solution, a hot solution of sodium formate (1,53 g) in 2,1 ml of 98 % formic acid was added.

After the mixture had stood for one hour (without heat), the precipitated sodium chloride was removed by filtration.

Acetic anhydride (4,6 ml) was added in portions and the mixture was stirred to reflux (90 °C) for one-half hour as soon as the addition of acetic anhydride was completed.

Acetic and formic acids were removed under vacuum.

Then the residual liquid was dissolved in acetone (10 ml) and filtered the sodium chloride formed. Follow by removing of acetone under vacuum. Finally the material was purified by distillation under vacuum to give a pure liquid N-formylglycine methyl ester.
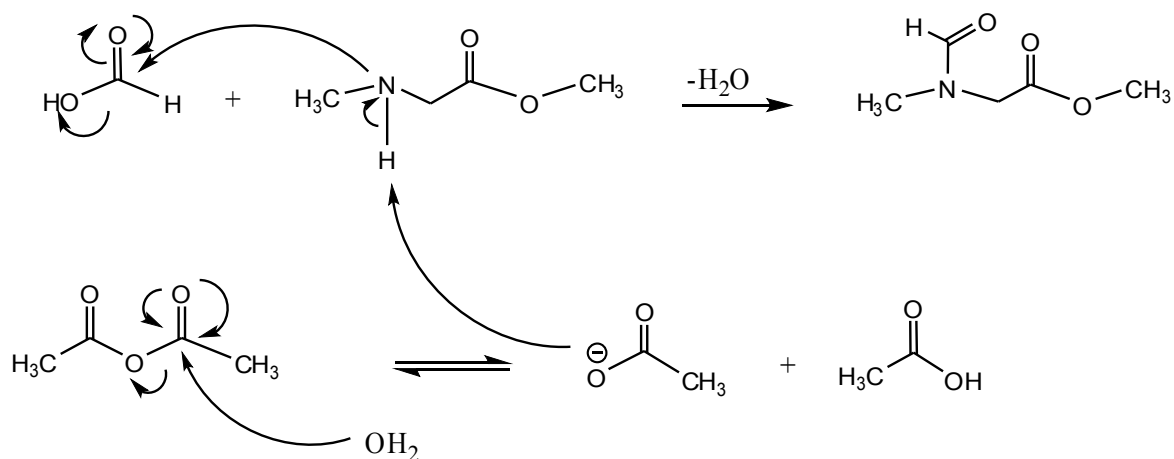
According to literature, the desired compound was a colourless liquid. After distillation the one obtained was a pale-yellow liquid.

N-formyl-N-methylglycine methyl ester yield was 72,6 % (18 mmol)

Literature yield based on N-formyl-N-cyclohexylglycine methyl ester was 76 %.

Mechanism reaction:
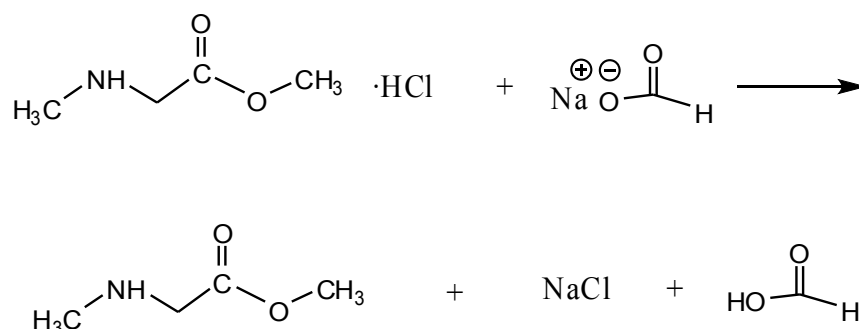
Hydrochloride salt was released by using sodium formate. N-formylglycine methyl ester was obtained thanks to condensation of the substrate with formic acid, with the loss of water.

Acetic anhydride decomposes in the presence of water to give acetic acid which affords the loss of water.

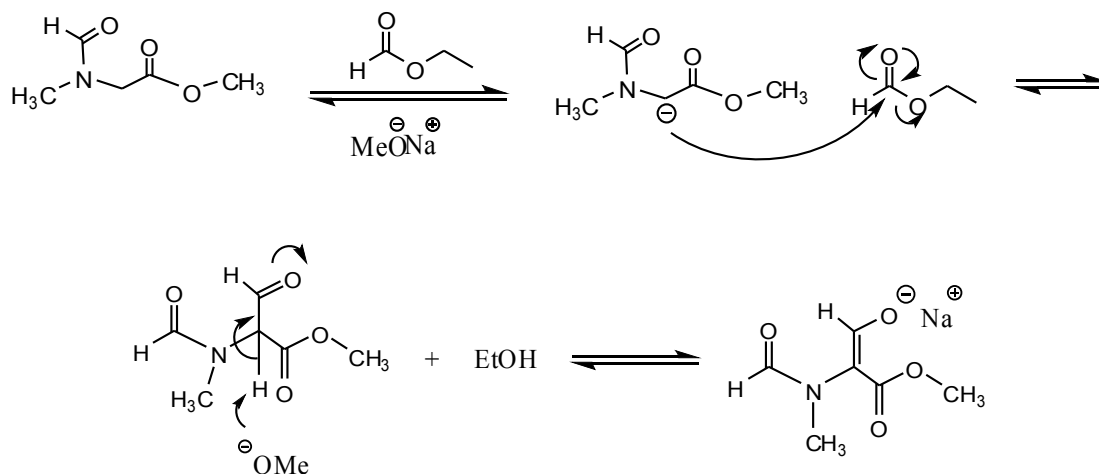**Condensation of N-formyl-N-methylglycine methyl ester with ethyl formate.**
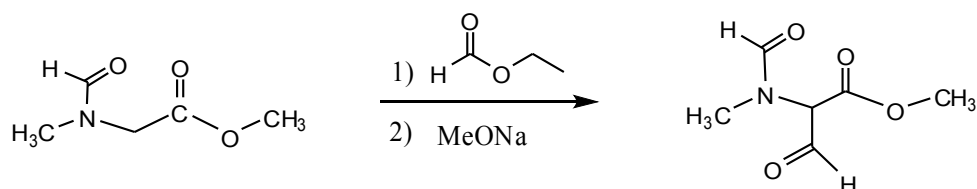
In a three-necked flask provided with stirrer and thermometer was placed in an ice-bath, N-formyl-N-methylglycine methyl ester, (18 mmol, 2,38 g) and ethyl formate (53,7 mmol, 3,97 g) with continuous stirring, then a suspension of sodium methoxide (19 mmol, 1,25 g) in dry toluene (4 ml) was added in five portions during a period of one hour.

Temperature was maintained below 15 °C, and stirring was continued for one additional hour after sodium methoxide was added.

The mixture was then placed in the refrigerator and allowed to stand for twenty four hours.

Mechanism reaction:

α-desprotonation of N-formyl-N-methylglycine methyl ester with sodium methoxide generate "in situ" the corresponding anion which, attacks the carbonyl of ethyl formate to give in a basic medium sodium methyl 2-(N-methylformamido)-3-oxopropanoate enolate.

**Synthesis of 2-mercapto-5-imidazolecarboxylate.**
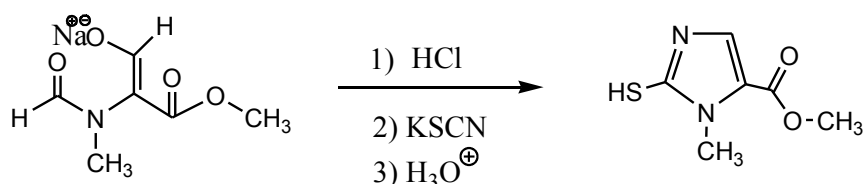
The reaction mixture was shaken with water (6 ml) in a separation funnel. When all solid had dissolved, the aqueous solution was separated and cooled in an ice-bath.

While stirring, a solution of hydrochloric acid 12 N (1,4 ml) was added slowly.

To the resulting solution, potassium cyanide (21 mmol, 2 g) was added. Then the reaction mixture was heated for two hours (70 °C) and finally allowed to stay all over night with stirring.

The crystalline 2-mercapto-5-imidazolecarboxylate was obtained by cooling in an ice-bath and collected on a filter. Follow by washing with water and air dried.

Mechanism reaction:
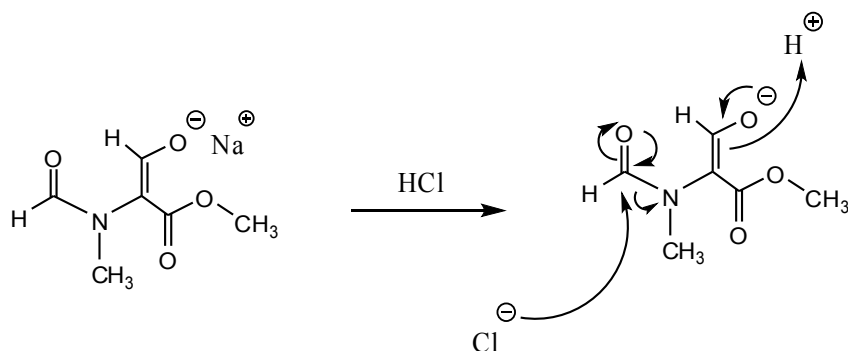
Sodium salt is neutralised and deformilation occurs with the nucleophilic attack of the chloride anion to the formyl substituent of the amide.
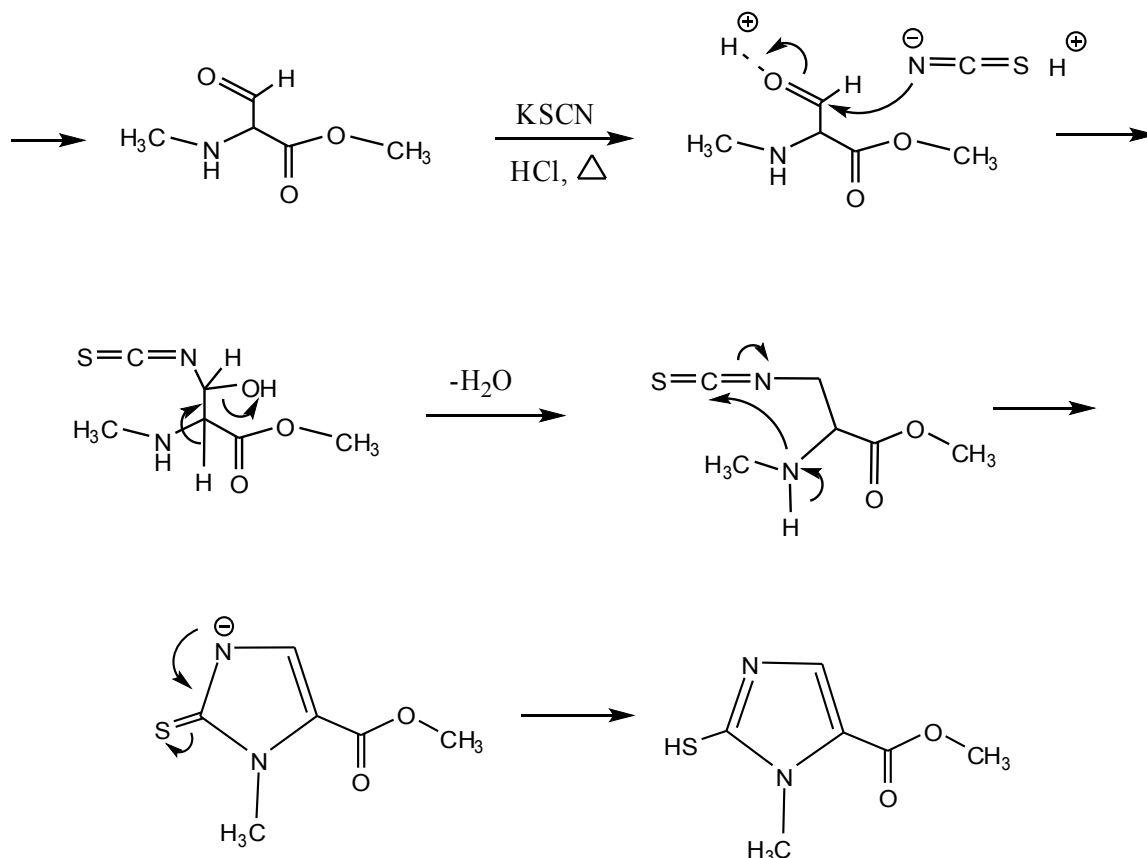
By adding potassium thiocyanate, thiocyanic acid is generated "in situ". Nitrogen atom first condenses with the aldehyde moiety. The resulting intermediate undergoes dehydratation and spontaneously cyclises through the attack of the amine on the carbon of the thiocyanate moiety.

The cyclised intermediate finally rearranges to give the imidazole derivative.

Yield of 2-mercapto-5-imidazolecarboxylate based on N-formyl-N-methylglycine methyl ester was 2 % (0,29 mmol).

According to literature a yield of 43 %was obtained.

It might be expected that purification of N-formyl-N-methylglycine methyl ester did not succeed.

In addition, NMR measurements were not the expected ones. Therefore re-crystallization was carried out.

The imidazolium derivative was dissolved in water and allowed to stand in the fridge over night. Then filtered, washed with cold water and finally dried under vacuum.

NMR spectra showed that the desired compound was not isolated successfully.

To evidence the presence of other substances Thin Layer Chromatography was taken into account.

In organic solvents such as dichloromethane, methanol or tetrahydrofurane the mixture of substances was not dissolved. Hence it was dissolved in water.

As for the solvent mixture used as eluent, dichloromethane:methanol (10:1) fitted the best and three compounds were found.

Conclusions

The first step of the synthesis did not afford the expected quantities which would have allowed performing the following reaction sequence. In addition, NMR measurements were not in agreement with the published results. This suggests that the reaction did not proceed successfully.

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