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Polycondensations dans les liquides ioniques

Shaodong Zhang

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**THESE DE DOCTORAT DE
L'UNIVERSITE PIERRE ET MARIE CURIE**

Spécialité

Physique et Chimie des Matériaux
(ED 397)

Présentée par
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Pour obtenir le grade de

DOCTEUR de l'UNIVERSITÉ PIERRE ET MARIE CURIE

Sujet de la thèse :

Polycondensations dans les liquides ioniques

soutenue le 15 novembre 2012

devant le jury composé de :

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Drop the boon of the water; be to flow out spring to report mutually

—— A Chinese idiom

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General introduction

Ionic liquids (ILs) are low melting organic salts, preferably in liquid state at room temperature. They are nonvolatile under ambient conditions and used as green alternatives to organic solvents. Their structure can be easily tuned so that their properties can be adapted to some specific requirements, such as polarity, hydrophobicity/hydrophilicity, solubility and even catalytic effect. The synthesis of the commonly used ILs has been well documented during the past two decades, and their preparations are generally straightforward. A large part of them has also become commercially available. Among the yet known ILs, those containing imidazolium cation are most extensively studied and applied to academic research and industrial utilization. Their special properties and availability lead to their wide application to a large number of organic chemistry reactions, such as Diel-Alder reaction, Heck reaction, hydrogenation, olefin metathesis and Friedel-Crafts reaction.

Ionic liquids are also used as reaction media in different polymerization processes. ILs have been widely studied as solvents for radical polymerizations, including controlled radical polymerizations, and several beneficial effects have been observed. Other polymerizations such as chain polymerizations, polycondensations and ionic polymerizations, have also been studied in ionic liquids. But the major challenge is that the solubility of polymers can be limited in common ILs, and it is, sometimes, difficult to synthesize polymers of high molar mass in these reaction media.

The general goal of the research presented in the thesis is to apply specific ionic liquids to the syntheses of different polymers via polycondensation. The resulting polymers include linear and hyperbranched polyesters, linear polyethers, polypeptides and polyamides with natural amino-acid units. Efforts are made to search for proper ionic liquids to solublize monomers and/or polymers, so that polycondensation can be carried out in, if possible, homogenous reaction system and polymer of high molar mass can be obtained. Furthermore, according to the nature of certain polymerizations, ionic liquids are designed to embody catalytic functions so that the targeted reactions, polyesterification and polyetherification, for example, can be accelerated without adding any other catalyst. Finally, some polymers, which usually cannot be synthesized or whose syntheses are tedious, are obtained via straightforward polycondensation in ILs, which are thermally stable, nonvolatile and can be tuned to change their dissolving abilities.

The investigations presented in the thesis can be divided into two sections:

The first section covers Chapter 2, Chapter 3 and Chapter 4. It is about the application of Brønsted acid ionic liquids (BAILs), whose imidazolium cations are functionalized with sulfonic acid. Their dual role of solvent and catalyst is studied. The polyesterification of 12-hydroxydodecanoic acid (12-HDA) has been chosen to carry out a preliminary study for this purpose in Chapter 2, since the monomer has a very simple structure with a single hydroxyl group and a carboxylic acid group. In Chapter 3, the model reaction of 12-HDA is extended to the synthesis of linear polyesters from diols and diacids, and also to the synthesis of hyperbranched polyester from 2,2-bis(hydroxymethyl)propionic acid (BMPA). The behavior of polyesterification in two different BAILs are examined. Chapter 4 deals with poly(oxyalkylene) syntheses, inspired by a side reaction, i.e. etherification, found in the investigation described in Chapter 2. This method gives a simple way to direct polyetherification of aliphatic diols.

The following section of the thesis consists in using neutral ionic liquids as alternative polyamide solvents for poly(β -alanine), polypeptides and natural amino-acid containing copolyamides. As presented in Chapter 5, a model reaction has been first chosen, which is the direct polyamidation of β -alanine in imidazolium ionic liquids with phosphorus-containing anions. Besides, the method is applied to the synthesis of several polypeptides, directly from their corresponding α -amino acids. Further investigation, as presented in Chapter 6, is conducted on incorporating β -alanine or α -amino acids in nylon-12.

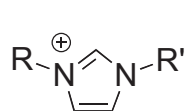
Chapter I

Theoretical concepts

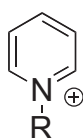
I.1 General introduction of ionic liquids

An ionic liquid (IL) is a liquid salt that is composed of an organic cation and an inorganic or organic anion. It refers to a type of salts whose melting point is below 100 °C, an arbitrary chosen temperature.¹ The most common ionic liquids for research applications are those composed of N,N'-dialkylimidazolium, N-alkylpyridinium, N-alkylpyrrolidinium and alkylphosphonium cations with various anions (Scheme 1.1). As the structures of ionic liquids can be easily tuned, it is estimated that the possible combinations of different cations and anions can result in more than different 10⁶ ILs.²

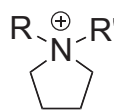
Cations:



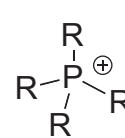
imidazolium



pyridinium

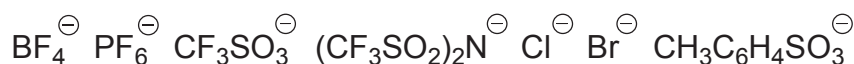


pyrrolidinium



phosphonium

Anions:



Scheme 1.1: Common cations and anions of ionic liquids.

The concept of “Ionic liquid” is not new at all, as it was first reported in 1914 when Walden succeeded in synthesizing ethylammonium nitrate, which melts at 12 °C. It is obtained by simply reacting ethylamine with concentrated nitric acid. This colorless to slightly yellowish liquid is considered as the first example of room-temperature ionic liquid.^{3,4} However, this recently extensively studied compound of great industrial potential did not attract specific attention at that time.

In the 1960s' and the following years, chloroaluminate-based ionic liquids were reported.⁵ The second half of the 1970s' is considered as the milestone of IL development, when Osteryoung et al.^{6,7} and Wilkes et al.⁸ respectively developed pyridinium and imidazolium based room-temperature molten salts. At that moment, ionic liquids were only used for electrochemical studies.

During the 1980s', several researchers, such as Hussey et al.⁹ and Seddon et al.¹⁰ used

chloroaluminate ionic liquids as solvents for transition metal complexes. They were used as reaction media for Friedel-Crafts reactions in 1986,¹¹ which was the first example of ionic liquids used as reaction medium for organic synthesis. This type of ionic liquids is however very sensitive to water and oxygen, which largely limited their application as alternative solvents.

In 1992, Wilkes et al.¹² developed the air and moisture stable imidazolium ionic liquids with anions such as BF_4^- and PF_6^- . It is considered as a remarkable breakthrough, and since then, a large number of ionic liquids have been reported and used in lots of fields. However, at that stage, almost all of the existing ionic liquids in the literature served solely as reaction media, and few works about their application as catalysts were reported.

It was not until 1999 that it was found ILs can also play a role of catalyst, when Davis and co-workers¹³ showed that a thiazolium IL could serve as both solvent and catalyst for the benzoin condensation. Afterwards, the same group introduced another type of ionic liquids, with the cations bearing an Brønsted acidic function, which led to additional application of ionic liquids for acid catalyzed reactions.¹⁴

In the recent decades, more and more ionic liquids have become available (even commercially available) and have attracted rising interest with a diversified range of applications (Figure 1.1).¹⁵ The expansion of new ionic liquid families and generations with more specific and targeted properties led to extensive studies on their physico-chemical properties and industrial applications.¹⁵

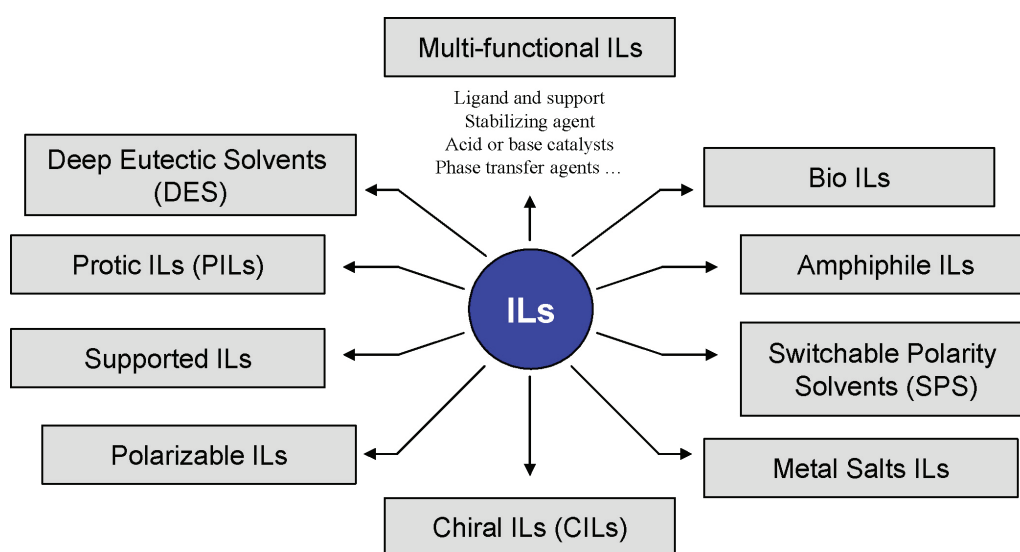


Figure 1.1: Evolution of IL generations¹⁵.

I.2 Synthesis of ionic liquids

Three basic approaches are well documented to prepare ionic liquids.^{16, 17} The metathesis of a halide salt, such as alkylammonium halides, N-alkylimidazolium halides and N-pyridinium halides, with another silver cation containing salt, is a widely used method to prepare the corresponding ILs with desired anions. The second one is to quarternerize the appropriate amines. The third approach consists in neutralization between an acid and a base.

They can also be easily synthesized in bench scale by reacting proper halogenoalkane with amines, imidazoles or pyridines.^{18, 19} Their syntheses are straightforward with the yield of almost 100%. For example, 1-butyl-3-methylimidazolium chloride ([BMIm]Cl) is prepared in conventional glassware by heating 1-butylchloride and 1-methylimidazole under reflux in an organic solvent.²⁰ However, in the case of some volatile halogenoalkanes, which have low boiling points, very careful IL preparations are required. For example, the synthesis of 1-ethyl-3-methylimidazolium chloride ([EMIm]Cl) is carried out in a sealed tube.⁸

In 1992, a new ionic liquid 1-ethyl-3-methylimidazolium tetrafluoroborate ([EMIm]BF₄) was introduced by Wilkes et al.,¹² which was prepared by metathesis of [EMIm]I with AgBF₄ in methanol. This IL with a melting point of 12 °C was then prepared much less costly by using NH₄BF₄ in acetone in 1997.²² The synthesis of 1-ethyl-3-methylimidazolium hexafluorophosphate ([EMIm]PF₆) was first reported in 1994,²³ which consists in mixing 1-ethyl-3-methylimidazolium chloride ([EMIm]Cl) with equimolar amount of HPF₆ in water, followed by simple filtration of the resulting product which precipitated as a white solid. A number of new ionic liquids were prepared by metathesis reactions afterwards, among which, thiocyanate, nonafluorobutanesulfonate, bis(trifluoromethylsulfonyl)imide, tris(trifluoromethylsulfonyl)methide, trifluoroacetate and heptafluorobutanoate ionic liquids are the commonly used ones.²⁴⁻²⁶ Tetraalkylammonium tetraalkylborides are also prepared by metathesis reaction between tetraalkylammonium bromide and lithium tetraalkylboride.²⁷ Since then, the metathesis reaction has become a popular method for ionic liquid preparation, but small amount of halide ion residue needs to be carefully eliminated to avoid contamination with solute materials.²⁸

Some examples of amine quarternerization to get the desired ionic liquids are reported.²⁹ Lithium tetraalkylboride is prepared by mixing trialkylborane with alkyllithium in dry hexane at 30-45 °C.²⁹ Methyl triflate is reacted with an equimolar amount of 1-alkylimidazolium in 1,1,1-

trichloromethane. As methyl triflate is quite sensitive to moisture, this reaction needs to be conducted carefully under anhydrous conditions.²⁶

Neutralization between amine and diluted nitric acid (20%) in aqueous solution can form the corresponding monoalkylammonium nitrate.⁴ Similarly, tetraalkylammonium sulfonates can be prepared by reacting tetraalkylammonium hydroxide with a stoichiometric amount of sulfonic acid.³⁰ The crude product must be dissolved in acetonitrile or tetrahydrofuran and treated with activated charcoal for at least 24 h to rule out the impurities, and the organic solvent was removed in vacuo.

Besides, common alkylammonium halides, N-alkylimidazolium halides and N-pyridinium halides are now commercially available from main chemical suppliers such as Sigma-Aldrich and Acros, and more often from the ionic liquid specialized companies such as Solvionic and Iolitec.

I.3 Properties of ionic liquids

As there is a wide range of ILs and applications,³¹ it is difficult to generalize their properties, but one of the most important properties which makes ionic liquids unique to traditional organic solvents is that their vapour pressure is negligible.³² It makes them advantageous in the case where reactions require high temperature, and it introduces additional possibility for removing certain products by distillation without utilization and eventual contamination of organic solvents. It can also make it possible to recycle ionic liquids which are currently quite expensive.

As more and more studies have been carried out to get a better understanding of these new media, better characterization with improved knowledge and quantification of their impurities (ion chromatography, ICP-MS) that are well known to affect the thermal properties of ILs, have been achieved in recent years.¹⁵ Some other properties described some years ago, such as electrochemical window, long-term thermal stability and polarity, become now doubtful. However, ILs still have some widely accepted unique properties. They are composed of ions (Scheme 1.1). The melting temperatures of ILs are less than 100 °C, and their ionicity is higher than 99%.³³

Some important properties of ionic liquids are summarized as following:

1. Glass transition (T_g) and melting temperature (T_m): The phase transition temperature (T_g) of an IL is governed by Van der Waals force and electrostatic interaction force,^{34, 35} and the impact of the two forces play different roles for different ILs.³³ It was found that the T_m of a quaternary ammonium based IL is governed by Van der Waals force rather than electrostatic interaction force, which means that the cation has more important influence on the phase transition temperature than an anion does. Regarding imidazolium containing ILs, when the cation structures are symmetric, e.g. 1,3-dimethylimidazolium, 1,3-diethylimidazolium, 1,2,3-trimethylimidazolium and 1,2-dimethyl-3-ethylimidazolium, the melting temperatures are often higher than those with asymmetric structures.³⁶ The length of alkyl chain can also have some impact on T_m . For example, the melting temperatures of symmetric imidazolium ILs decrease with increasing alkyl chain length. Referring to different anions, the melting temperatures generally decrease with increasing anion radius, except for PF_6^- . Generally, larger anion radius induce weaker electrostatic interactions with imidazolium cations. However, ILs with PF_6^- anion can establish strong hydrogen bonds through their F atoms and their melting temperatures are therefore comparatively higher.
2. Thermal stability: The thermal decomposition temperature (T_d) of an IL depends strongly on its structure. In opposition of organic solvents, many ILs are stable and stay in liquid state at temperature above 400 °C (with T_d ranging from 300 to 400 °C). The imidazolium cations tend to be more thermally stable than tetraalkylammonium cations. High thermal stability is also induced by some anions such as Tf_2N^- ($[(CF_3SO_2)_2N]^-$) and $BETI^-$ ($[C_2F_5SO_2)_2N]^-$). The relative anion stabilities obey the order $PF_6^- > BETI^- > Tf_2N^- > CF_3SO_3^- > BF_4^- > Me[(CF_3SO_2)_3C]^- \gg I^-, Br^-, Cl^-$.³³
3. Density and viscosity: Compared to conventional organic solvents, ionic liquids have higher densities, which are often higher than that of water. Besides, they are generally quite viscous at room temperature, which means, if required, that phase separation of an ionic liquid from an immiscible organic solvent is quicker than two solvents of similar viscosity. Some examples of density and viscosity of typical imidazolium based ionic liquids are summarized in Table 1.1.^{26,37,38} Generally, the viscosity of ionic liquids with trifluoromethylsulfonyl-based anions is relatively low. It is found that the density of an

ionic liquid decreases with the length of alkyl chain substituent on the imidazolium cation, while the viscosity increases.

4. Non flammability: ILs are often considered as “green” alternatives to conventional organic solvents, mainly because they are nonvolatile and non-flammable at ambient and higher temperatures.^{39, 40}

Table 1.1: Densities and viscosities of typical imidazolium based ionic liquids^{26, 38}.

Ionic liquid	Density at 20 °C (g/mL)	Dynamic viscosity at 20 °C (cP)
[BMIm]PF ₆	1.37 ^a	330
[BMIm]BF ₄	1.24 ^a	154
[EMIm]Tf ₂ N	1.52 ^b	34
[BMIm]Tf ₂ N	1.43	52
[EMIm]TfO ^c	1.39 ^b	45
[BMIm]TfO ^c	1.29	90

^a at 30 °C

^b at 22 °C

^c TfO⁻ = CF₃SO₃⁻

5. Conductivity and electrochemical window: Conductivity is another interesting property that distinguishes ILs from conventional organic solvents. ILs could play a role of both solvent and electrolyte in electrochemical reactions. They exhibit a wide range of conductivities from 0.1 to 20 mS/cm.¹⁵ Comparing to ammonium-based ILs, imidazolium-based ones have generally higher conductivities.⁴¹ Their conductivities depend on different parameters, such as ion size, anionic charge delocalization, aggregation, ionic motion, viscosity and density.⁴¹ For example, compared to BF₄⁻ based ionic liquids, Tf₂N⁻ based ones have lower conductivities, as their ion-pair associations and neutral ion aggregates are supposed to be stronger than the former.⁴² Another general common feature of ILs is their inherent redox-robustness, because of the robustness of the cations and anions employed for their preparation.⁴¹ Referring to their electrochemical window, it typically varies from 4.5 to 5 V, similar to or slightly wider than that found in conventional organic solvents, but larger than that of aqueous electrolytes. Generally speaking, quaternary ammonium-based ILs are more stable toward reduction than imidazolium-based ones, as the latter can lead to the formation of

N-heterocyclic carbenes.

6. Polarity: It is one of the most important properties of solvents for chemical reactions.⁴³ It is also probably the property which has involved the widest discussion in the case of ILs, since there is no single parameter or direct measurement which can characterize it. Solvatochromic dyes can be used to determine empirical polarity parameters but these parameters (Kamlet-Taft equation) are probably not truly independent on the probe molecule used.⁴⁴ Nevertheless, the Kamlet-Taft π^* value is generally used to give an order of magnitude of ILs' polarity, which is referenced to cyclohexane for a value of 0 and DMSO is given a value of 1.⁴⁵ It is found that the π^* value of ILs ranges from 0.8 to 1.2,⁴⁴ indicating that ILs can be classified as polar solvents as DMSO.

All of these properties render ionic liquids different from traditional molecular solvents and their specifically tuned structures and organizations make them applicable to specific tasks. This is the reason why ILs have attracted so much attention during the recent years.¹⁵

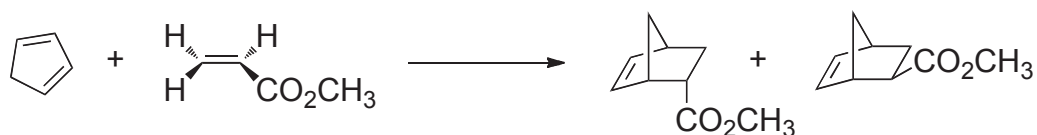
I.4 Organic reaction in ionic liquids

Ionic liquids are widely used as solvents for chemical reactions, and they are especially interesting when small molecules and/or volatile compounds are involved in the reactions. Ionic liquids can be designed to dissolve different inorganic and metalloorganic catalysts, therefore leading to convenient ways for lots of catalyst required reactions to proceed. A lot of examples of ionic liquid application to chemical reactions are summarized in some recent reviews.^{15, 16, 32, 41, 46-52} It is also reported that ionic liquids can be functionalized to fulfil specific tasks,⁴⁷ and they can even be used as both solvents and catalysts for several types of reactions.

I.4.1 Diel-Alder Reaction in ionic liquids

Ionic liquids can be used as solvents for Diel-Alder cycloaddition reactions. The reaction of cyclopentadiene and methyl acrylate was carried out in various ionic liquids ([EMIm]BF₄, [EMIm]ClO₄, [EMIm]CF₃SO₃, [EMIm]NO₃ and [EMIm]PF₆ (Scheme 1.2)).⁵³ These reactions lead to a mixture of exo and endo products, and the endo/exo selectivity as well as the reaction rate were found similar to those found in water. The advantage of ILs is that certain moisture-

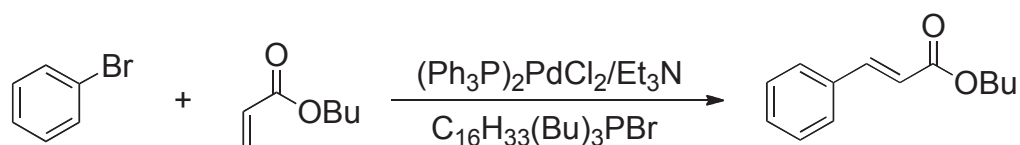
sensitive reagents can be used.¹⁶ Earle et al.⁵⁴ reported the Diels-Alder reaction of isoprene with dienophiles (ethyl acrylate, dimethyl acetylene dicarboxylate, but-2-en-3-one) in [BMIm]PF₆, [BMIm]BF₄ and [BMIm]TfO, and claimed that significant rate enhancement and high yield/selectivity were obtained.



Scheme 1.2: Diels-Alder cycloaddition of cyclopentadiene and methyl acrylate⁵³.

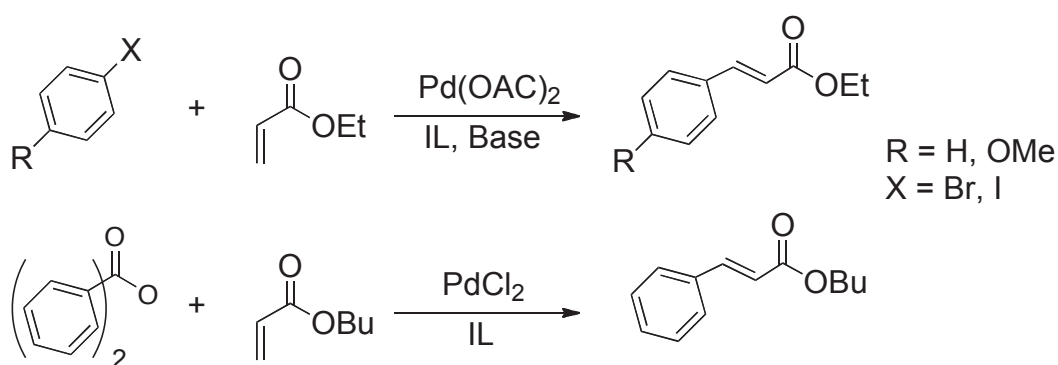
I.4.2 Heck reaction in ionic liquids

The Heck reaction is a very important reaction which is often used to prepare substituted alkenes (or aromatics) via reaction of unsaturated halides with alkenes (or aromatics). The first example of Heck reaction in ionic liquids was reported in 1996, using a phosphonium-based ionic liquid (hexadecyl tributylphosphonium bromide, C₁₆H₃₃(Bu)₃PBr).⁵⁵ The reaction of bromobenzene with butyl acrylate resulted in trans-butyl cinnamate with very high yield (Scheme 1.3). And the resulting product was obtained by a simple distillation from the ionic liquid.



Scheme 1.3: Heck reaction in ionic liquids⁵⁵.

Seddon et al.⁵⁶ carried out Heck reactions with palladium precatalysts PdCl₂ or Pd(OAc)₂ in imidazolium and pyridinium-based ionic liquids with halide, hexafluorophosphate, or tetrafluoroborate anions (Scheme 1.4). The reaction of 4-bromoanisole with ethylacrylate in phosphonium ionic liquids in the presence of triethylamine at 100 °C formed ethyl 4-methoxycinnamate in very good yield. The reaction between benzoic anhydride and butyl acrylate in ionic liquids at higher temperature (160-200 °C) also resulted in the corresponding product with high yield. Besides, it was found that [BMIm]PF₆ was an excellent medium for this reaction, as it can dissolve better the palladium catalysts than in water or alkane solvents, which also allows the ionic liquid and catalyst to be recycled.



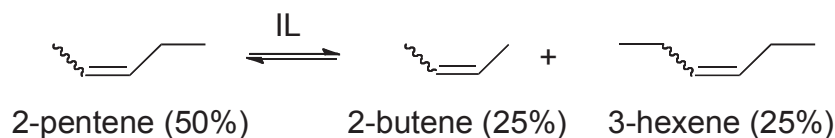
Scheme 1.4: Heck reaction in ionic liquids⁵⁶.

I.4.3 Hydrogenation reaction in ionic liquids

Vinyl group hydrogenation catalyzed by transition metal complexes is possibly one of the most widely studied reactions of homogenous catalysis, however, the product separation from the reaction media is problematic. Pioneering experiments employing $[\text{Rh}(\text{nbd})\text{PPh}_3][\text{PF}_6]$ (where nbd = norbornadiene) as catalyst for pent-1-ene hydrogenation were conducted in various ionic liquids, which can be used as potential solvents for catalyst isolation.²⁸ The hydrogenation rates were significantly improved in SbF_6^- and PF_6^- containing ILs than in acetone, probably due to the stabilization of the Rh(III) intermediate. Cyclohexane was produced from cyclohexene with a selectivity of 98% and a conversion of 96% in $[\text{EMIm}]\text{SbF}_6$. The hydrogenation of cyclohexa-1,3-diene catalyzed by $\text{RhCl}(\text{PPh})_3$ and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (where cod = cyclooctadiene) in $[\text{BMIm}]\text{BF}_4$ was also studied.⁵⁷ It was found that $\text{RhCl}(\text{PPh})_3$ led to higher turnover rates, while $[\text{Rh}(\text{cod})_2]\text{BF}_4$ gave higher overall cyclohexene conversion. Besides, it is worthwhile noting that $[\text{Rh}(\text{cod})_2]\text{BF}_4$ was much more soluble than $\text{RhCl}(\text{PPh})_3$ in the ionic liquid.

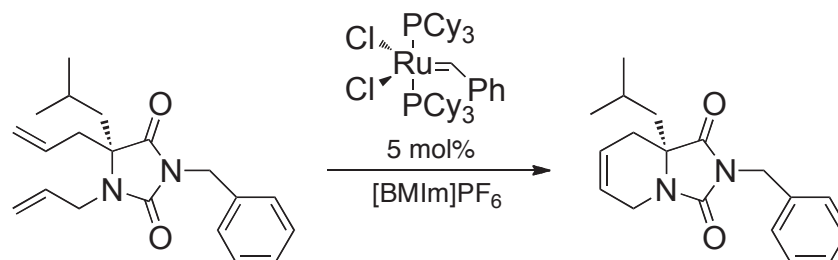
I.4.4 Olefin metathesis in ionic liquids

Olefin metathesis has provided synthetic chemists a very efficient tool to synthesize compounds, the conventional syntheses of which would consist of many tedious steps.⁵⁰ The first example of ionic liquid application to olefin metathesis reaction was reported by Chauvin in 1995 (Scheme 1.15).⁵⁸ Good results in the self-metathesis of 2-pentene were obtained when the reaction was catalysed by $\text{W}(\text{OAr})_2\text{Cl}_4$ in $[\text{BMIm}]\text{Cl}-\text{AlCl}_3-\text{EtAlCl}_2$ ionic liquid system (where $\text{ArOH} = 2,6\text{-diphenylphenol}$ or $2,4,6\text{-trimethylphenol}$). Besides, the active species was trapped in the ionic environment, which allows a facile catalyst separation and recycling by decantation of the hydrocarbon layer.



Scheme 1.5: First example of olefin metathesis in ionic liquids⁵⁸.

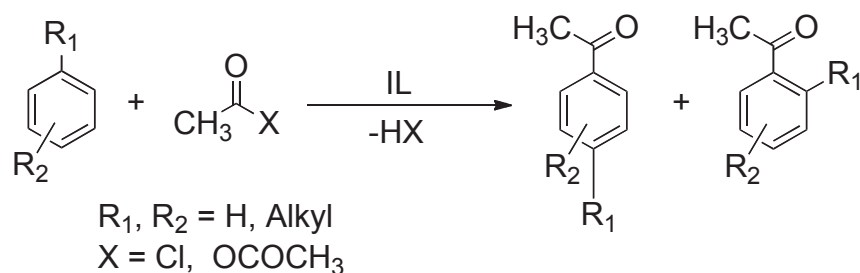
Practical synthetic applications of ionic liquids as reaction media for olefin metathesis were later systematically studied by Buijsman and co-workers.⁵⁹ In the study, [BMIm]PF₆ was proved to be an efficient medium for ring-closing metathesis (RCM) using Grubbs catalysts. High conversion and broad substrate tolerance were observed in this IL, and ruthenium catalyst and [BMIm]PF₆ were recycled by extracting the product from the organic phase.



Scheme 1.6: Ring-closing metathesis in ionic liquids⁵⁹.

I.4.5 Friedel-Crafts reaction in ionic liquids

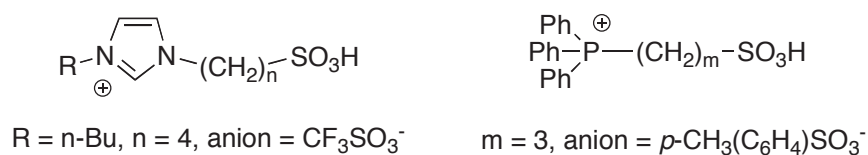
At the very beginning, room-temperature chloroaluminate (III) ionic liquids were used as both solvents and catalysts for Friedel-Crafts reactions.⁶⁰ For example, Friedel-Crafts acylations of aromatic compounds were carried out in [EMIm]Cl-AlCl₃ ionic liquid system, in which AlCl₃ was used as Lewis acid to catalyze the reactions and [EMIm]Cl served as solvent. For the reaction of acetyl chloride with benzene, it was shown that the reaction rate at which acetophenone was produced depended on the Lewis acidity of the ionic liquid, which is in turn dependant on its own composition. Isobutane alkylation was studied in ionic liquids as well, and the ionic liquids were tuned to adjust their acidity in order to improve the reaction rate.^{61,62} However, this type of ionic liquids is extremely sensitive to moisture and must be handled either in vacuo or under inert atmosphere, which unavoidably limits their applications.¹⁶ Recently, Friedel-Crafts acylation reactions were carried out by using bismuth triflate in [BMIm]PF₆, which is much more stable and therefore easier to handle.⁶³ Bismuth triflate showed excellent catalytic activity and the catalytic system was reused up to five times.



Scheme 1.7: Friedel-Crafts acylation in ionic liquids.

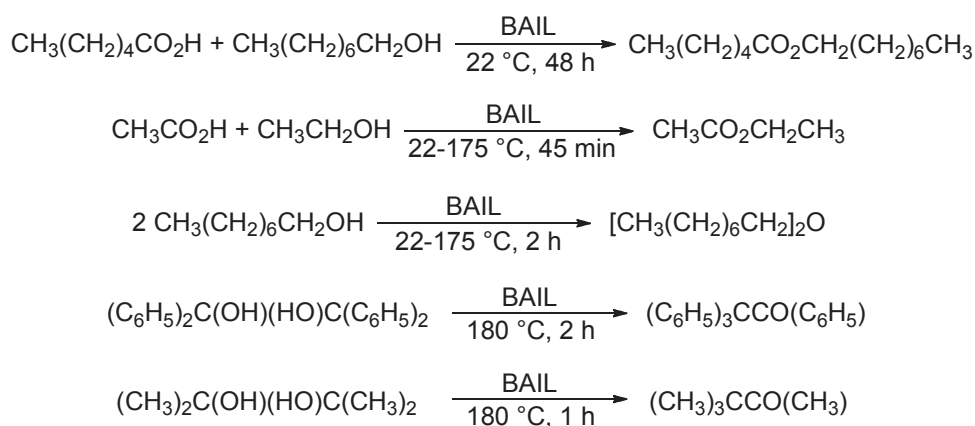
I.4.6 Brønsted acid catalyzed reaction in ionic liquids

Investigations were also reported on reactions in ILs with addition of Brønsted acids as catalysts.⁴⁷ Although the application of ionic liquids might have advantages for product separation, the added acids are vulnerable to being out-gassed from the ILs. In 2002, Cole et al.¹⁴ introduced a new type of ionic liquids in which the cations are intrinsically Brønsted acidic and nonvolatile, which are called Brønsted acid ionic liquids (BAILs).



Scheme 1.8: BAILs reported by Davis et al.⁴⁷.

Acid catalyzed reactions such as Fischer esterification, etherification of alcohols and Pinnacol rearrangement were successfully carried out in BAILs (Scheme 1.9).



Scheme 1.9: Representative reactions catalysed by BAILs reported by Davis et al.⁴⁷.

Since then, a lot of reactions have been tested in BAILs. For example, Gu et al.⁶⁴ used them to

catalyze the esterification of acetic acid by 1-heptene and several different cyclic olefins. Depending on the olefinic substrates, the yields varied from modest to excellent. Similar work was also reported with-triazolium based BAILs, which were used to catalyze Fischer esterification and hetero-Michael additions, and showed similar effect with their imidazolium analogs.⁶⁵

I.5 Polymerization in ionic liquids

During recent years, ILs were also used for polymer syntheses, mainly as reaction media in several types of polymerization processes.^{2,66,67} At the very beginning, ionic liquids with haloaluminate anions were often used as solvents for polymerization. It is well known that haloaluminates undergo hydrolysis to form HCl, which renders the reaction media acidic, and it is therefore not surprising that they were largely applied to cationic polymerization of alkenes.⁶⁶ Meanwhile, stable and chemically inert ionic liquids could be easily synthesized and even became commercially available. It stimulated an increasing interest in their application to different polymerizations, such as free radical polymerizations, ionic polymerizations and polycondensations. Some general applications of ionic liquids to various polymerization processes are summarized below with several examples.

I.5.1 Radical polymerization in ionic liquids

Carmichael et al.⁶⁸ reported Cu^I catalyzed radical polymerization of methyl methacrylate (MMA) in [BMIm]PF₆, which is considered as the first example of ionic liquid as radical polymerization medium. Although only low molar mass polymers were obtained in their study, this pioneering work inspired intensive investigation of ionic liquid utilization for radical polymerizations.⁶⁹⁻⁷⁴

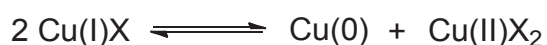
I.5.1.1 Classical radical polymerization in ionic liquids

Poly(methyl methacrylate) (PMMA) and polystyrene (PS) obtained in [BMIm]PF₆ had 10 times higher molar mass than those obtained in toluene.⁷² The resulting polymers were not soluble in this IL, which facilitated the separation by a simple extraction with a polar solvent. Haddleton et al.⁷³ found that the propagation rate constant (k_p) of MMA radical polymerization increased when [BMIm]PF₆ was added in the reaction medium. When 50 vol% of [BMIm]PF₆ was added, k_p even doubled, comparing to that of polymerization in the bulk. They further

suggested that the increase of k_p arised from a decrease in the activation energy, which would be in turn due to the increased polarity of the reaction medium, allowing an increased contribution of charge-transfer structures. They also argued that the termination rate decreased in this medium. The increase of propagation rate and decrease of termination rate contributed therefore the overall increase in the rate of polymerization.⁷⁴ Further study on MMA polymerization^{72, 75, 76} and glycidyl methacrylate (PMA)⁷⁵ in various ILs led to the same conclusions. An interesting observation was that the radical polymerization rate depended on the length of the alkyl substituent of the cation and the nature of the anion which can change the viscosity of an IL.⁷⁷ They found that the k_p increased with increasing viscosity of the IL while the average rate coefficient of termination (k_t) decreased with it.

1.5.1.2 Atom transfer radical polymerization (ATRP) in ionic liquids

It is well known that an ATRP process is an equilibrium reaction between a low concentration of active radicals ($R\bullet$) and much higher concentration of dormant species (RX).⁷⁸ This reaction involves a reversible redox reaction between a transition metal complex (M_t^n/L) and a halogen initiator (RX) or dormant species (PX), which forms a radical ($R\bullet$) and the metal halide with a higher oxidation state (XM_t^{n+1}/L) (k_a). The radical then initiates the polymerization of vinyl monomers to form propagating radical (k_p), which reacts reversibly with metal halide to reform in return the transition metal with lower oxidation state and oligomer with halogen end group (k_d). This process repeats and produces a well defined polymer. In a well-controlled ATRP reaction, the concentration of radicals is often preferentially low so that the contribution of the termination (k_t) is neglected.^{79,80} It is previously proved that the k_p/k_t ratio can be improved when controlled radical polymerization (CRP) is carried out in various ILs. Another advantage is that solubility of several transition metal complexes can be improved in ILs,⁶⁸ so that reactions can be carried out in homogenous conditions and catalysts can be easily separated from the resulting polymer at the end of the reaction.⁸¹⁻⁸³ Besides, like other polar solvents, ILs are proved to favor dismutation of $Cu(I)X$ into $Cu(0)$ and $Cu(II)X_2$ (Scheme 1.10). It is suggested that $Cu(0)$ promotes the activation of active species and $Cu(II)$ favors the reversible deactivation of radicals into alkyl halide species.²



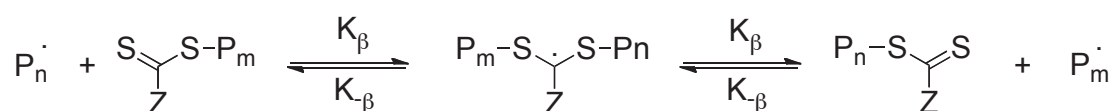
Scheme 1.10: Dismutation of $Cu(I)X$.

Percec et al.⁸⁴ reported the catalytic effect of ionic liquids when a living radical polymerization of MMA was initiated by arennesulfonyl chlorides in [BMIM]PF₆ with Cu₂O/ 2,2'-bipyridine catalyst system at temperature ranging from 22 to 80 °C, which led to a ultrafast polymerization, resulting in a nearly complete conversion of MMA with molecular weight distributions of about 1.1-1.2. They observed that the propagation rate constant (*k_p*) obeyed a relation of almost first order with respect to [BMIm]PF₆ concentration, which demonstrated a catalytic effect of the IL in the reaction system.

In some cases, ILs were used as good solvents for ATRP catalysts and the addition of organic ligands was therefore not necessary. Sarbu and Matyaszewski showed an example with the polymerization of MMA in [BMIm]Br in the presence of ferrous halides (FeBr₂ or FeCl₂), which were soluble in the medium.⁷⁰ A well controlled ATRP of acrylonitrile was also reported with the presence of FeBr₂ as catalyst in the absence of any ligand, in 1-methylimidazolium acetate, valerate and caproate.⁸⁵

1.5.1.3 Reversible addition-fragmentation chain transfer (RAFT) polymerization in ionic liquids

RAFT polymerizations are conducted in the presence of a thiocarbonylthio compound, which reacts reversibly with a propagating radical to form an intermediate radical. The latter then fragments into a new thiocarbonylthio compound and a propagating radical. Comparing to the thiocarbonylthio containing polymer chains (dormant chains), the concentration of propagating chain is low so that the termination reactions are largely unfavored (Scheme 1.11).^{86,87}



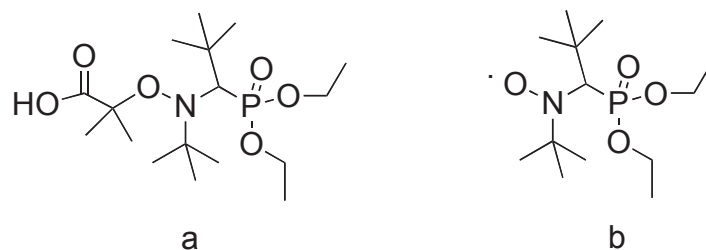
Scheme 1.11: Main equilibrium in the RAFT process.

The first example of RAFT polymerization in ILs was reported in 2003 by Perrier et al..⁸⁸ The polymerizations of styrene, methyl methacrylate and methyl acrylate, mediated by 2-(2-cyanopropyl)dithiobezoate were undertaken in 1-alkyl-3-methylimidazolium hexafluorophosphate ([RMIm]PF₆). The polymerization of styrene in the ILs resulted in very low molar mass polymers, as precipitation occurred at an early stage of the reaction. In the case of methacrylate and methyl acrylate monomers, both polymers were soluble in the reaction

media, and the polymerizations reached high conversion. It was also observed that the reaction rate was higher in ionic liquids than in conventional solvents such as toluene. The MMA polymerization in the ILs led to final products with molar-mass dispersity as low as 1.11, close to the value obtained in bulk or in toluene. When RAFT-mediated polymerization of styrene was conducted in pyridium-based ILs, the reaction mixtures were homogenous, and the reaction rates were found to be slightly higher than a comparative polymerization in toluene and gave excellent control of molar mass.⁸⁹ It was also found that the RAFT polymerization depended not only on the nature of RAFT agent but also on that of IL.⁹⁰

1.5.1.4 Nitroxide mediated radical polymerization (NMP) in ionic liquids

NMP is another type of living free radical polymerization that employs an alkoxyamine initiator to prepare polymers with well controlled M_w and low molar-mass dispersity. The concentration of the reactive chain ends is reduced to extremely low level by reversible termination reaction of growing polymer chains. The low overall concentration of the propagating chain ends minimizes undesired irreversible termination reactions through combination or disproportionation. As ILs are nonvolatile compounds, they can therefore be potentially considered as suitable solvents for NMP that requires relatively high temperature. In 2004, Zhang et al.⁹¹ and Ryan et al.⁹² claimed respectively the first example of IL application to NMP. Methyl acrylate was polymerized in [HMIm]PF₆, mediated by commercially available nitroxide, 4-oxo-2,2,6,6-tetramethyl-1-piperidiny-N-oxyl (4-oxo-TEMPO) at 140 °C.⁹² However, in contrast to the polymerization in anisole, the experimental value of number-average molar mass (M_n) of the polymers obtained in the IL was considerably higher than the theoretical values. Zhang et al.⁹¹ firstly tried to polymerize styrene using benzoyl peroxide (BPO) and TEMPO system in [BMIm]PF₆ at 135 °C, resulting in low molar mass polymers, which might be due to the decomposition of TEMPO in [BMIm]PF₆ when the reaction mixture was heated to this temperature. They tried later another initiator 2,2,5-trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (TMPPAH), but they still failed to get results as good as those obtained in the bulk. In 2011, Brusseau et al.⁹³ carried out the controlled/living radical copolymerization of methyl methacrylate with a small amount of styrene in 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([BMIm]Tf₂N), in the presence of nitroxide initiators (Scheme 1.12). Like most previously mentioned applications of ILs to living radical polymerizations, the authors also observed that the copolymerization in the IL was significantly faster and reached high conversion in short time, also assigned to the increase of k_p and the decrease of k_t .



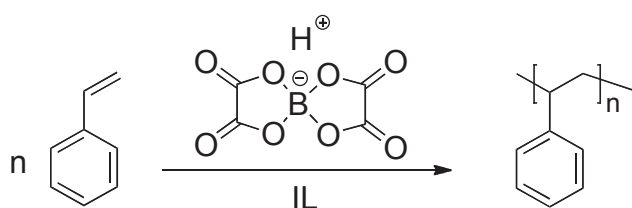
Scheme 1.12: Alkoxyamine initiator BlocBuilder (a) and SG1 (b).

1.5.2 Ionic polymerization in ionic liquids

As mentioned previously, the structures of ILs can be modified so that they can dissolve a large number of organic and inorganic compounds. ILs can be therefore used as potential solvents for ionic polymerization in which ionic polymerization initiators can be dissolved.

1.5.2.1 Cationic polymerization

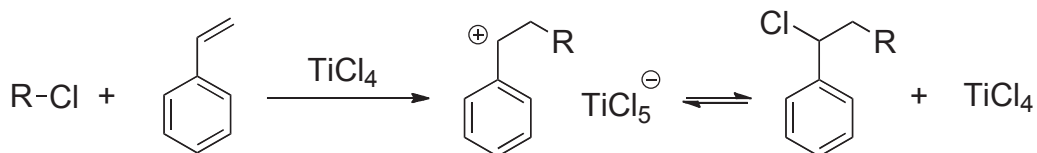
ILs have been used for some cationic polymerizations involving inorganic acids (Lewis or Brønsted acids) as initiators.⁹⁴⁻⁹⁷ For example, Vijayaraghavan et al. carried out the cationic polymerization of styrene in N,N-butylmethylpyrrolidinium bis(trifluoromethanesulfonyl)amide initiated by bis(oxalato)boric acid (HBOB) (Scheme 1.13). Comparing to the traditional cationic polymerization of styrene in dichloromethane (DCM), the yield of the reaction in ILs was much higher. This was assigned to easier deprotonation of HBOB in ILs. However, the polymerization only produced low molar mass polystyrene (M_w about 1000 g/mol).



Scheme 1.13: Cationic polymerization of styrene initiated by HBOB in ionic liquid⁹⁴.

At the early stage of IL research, it was thought that ILs were highly polar solvents, and it was expected that the polarity of ILs could favour ionization of C-Cl bond of chloroalkane initiators and promote some control on cationic polymerization (Scheme 1.14).⁹⁸ As shown with polymerization of styrene initiated by 1-phenylethyl chloride in [BMIm]PF₆ without adding any Lewis acid initiator, some macromolecules contain the head-groups resulting from initiation by proton. It was observed that the molar mass differed from calculated values and

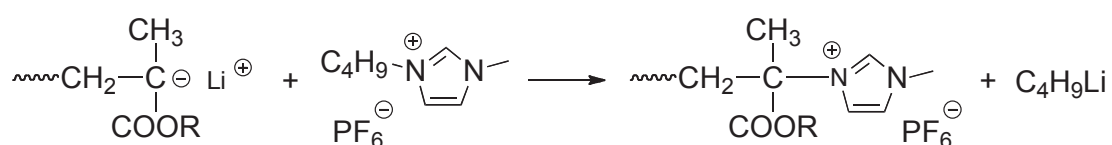
molar-mass dispersity was quite high. It indicates that polymerization cannot be fully controlled in this reaction system. Although ionization of C-Cl bond occurred in ILs in the absence of coinitiators, the solubility of styrene in [BMIm]PF₆ was limited and the polymer precipitated during the polymerization, which led to rather low molar mass.



Scheme 1.14: Schematic representation of activation-deactivation process in controlled cationic polymerization of styrene⁹⁸.

1.5.2.2 Anionic polymerization

Under basic conditions, ILs are not always stable, especially due to the presence of a proton in 2-position of the imidazolium ring.⁹⁹ Therefore, all of them can not be used as suitable solvents for anionic polymerizations. The anionic polymerization reactions of methyl methacrylate (MMA) were carried out by using alkyl lithium initiators such as n-butyl lithium and diphenylhexyl lithium in different ionic liquids.¹⁰⁰ When the reaction was carried out in the ILs with bis(trifluoromethylsulfonyl) amide anion (Tf₂N⁻), no polymerization took place, assigned to the initiator deactivation by interaction with Tf₂N⁻. Although some polymers were obtained in [BMIm]PF₆, the yields were low (5-9%) as compared with those obtained in organic solvents (15-62%). It was found that the hydrogen atom in 2-position of the imidazolium ring was withdrawn by the alkyl lithium initiators, which led to deactivation of the latter. Another side reaction was also observed in the anionic polymerization of MMA:¹⁰¹ it was found by MALDI-TOF study that chain transfer with imidazolium cation took place at the early stage of polymerization (Scheme 1.15).

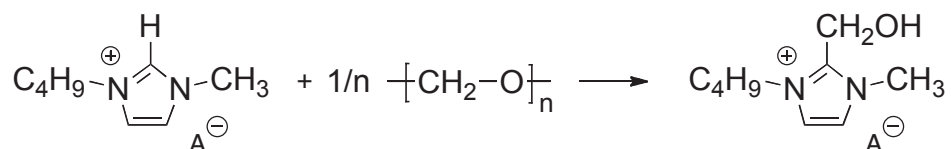


Scheme 1.15: Chain transfer to ionic liquid in anionic polymerization of methyl methacrylate¹⁰¹.

The anionic polymerization of styrene initiated by butyl lithium (BuLi) or sodium acetate (NaAc) in phosphonium-based IL ([P_{6,6,6,14}]Tf₂N) was studied.¹⁰² The reaction was not efficient, resulting only in polymers with low yield (10-20%) after 70 h. It was assigned to the

very weakly basic environment provided by TF_2N^- anion, which does not favor the initiator's dissociation. By adding imidazolium sulfonate zwitterion [BBSIm] that has a basic functionality, the ion-dissociation was enhanced so that polymer yield rised to 65-75%. Polystyrene with a molar mass (M_w) as high as 800 000 g/mol was obtained in the initiator/zwitterion/IL system, except that the polydispersity was relatively higher (1.4-2.1).

The problem arising from acidic proton can be addressed if the proton at 2-position of imidazolium ring is replaced by another group (Scheme 1.16).¹⁰³ The newly formed IL was then converted to its corresponding alkoxide by NaH and used as both solvent and initiator for the polymerization of ethylene oxide. Polymer with DP_n up to 30 was obtained without observation of side reactions.



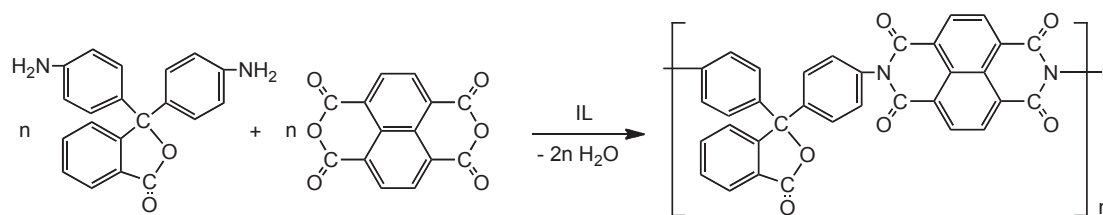
Scheme 1.16: Reaction of [BMIm]A with paraformaldehyde, $\text{A}^- = \text{BF}_4^-$ or $(\text{CF}_3\text{SO}_2)_2\text{N}^-$.¹⁰³

1.5.3 Polycondensation in ionic liquids

Polycondensations are conventionally carried out in the bulk at high temperature. The process usually requires catalysts such as metal salts, metal oxides or metal alkoxides, and high temperature (170-300 °C) as well as long reaction time (several hours). Some nonvolatile and thermally stable ionic liquids were reported as good reaction media for the synthesis of polyamides, polyimides and polyesters at lower temperature for shorter reaction time.

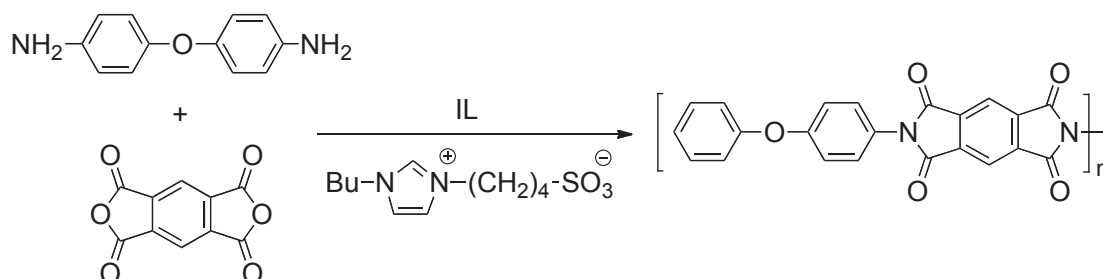
1.5.3.1 Synthesis of polyimide in ionic liquids

In 2002, Vygodskii et al.¹⁰⁴ reported the first application of ionic liquids as reaction medium for the synthesis of aromatic polyamides and polyimides. They studied the polycyclization reaction of 3,3'-bis(4'-aminophenyl)phthalide (APh) and 1,4,5,8-naphthalene tetracarboxylic acid dianhydride (DA-NTCA) in 1,3-dialkylimidazolium based ionic liquids with different anions (Scheme 1.17). Relatively high molar mass polyimides were obtained without adding any catalyst. This led them to concluding that the ILs used in their investigation served not only simply as solvents but also as catalysts.



Scheme 1.17: Synthesis of aromatic polyimides in ionic liquids¹⁰⁴.

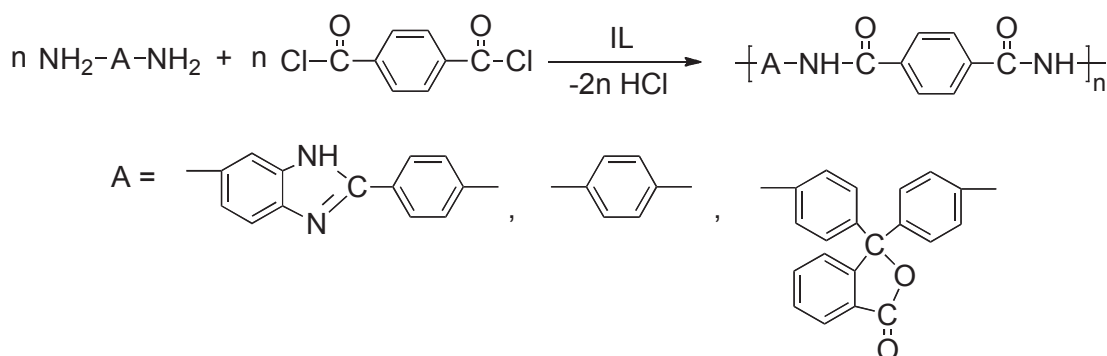
It was found that the addition of imidazolium sulfonate zwitterion [BBSIm] in ILs improved the solubility of aromatic polyimides, which were synthesized by the polycondensation of aromatic dianhydrides with aromatic diamines (Scheme 1.18), and the polyimides with higher molar mass were obtained.¹⁰⁵



Scheme 1.18: Polycondensation of aromatic dianhydride with aromatic diamine in ionic liquids¹⁰⁵.

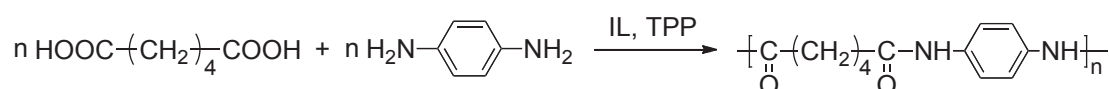
1.5.3.2 Synthesis of polyamide in ionic liquids

Vygodskii et al.¹⁰⁴ also synthesized aromatic polyamides from diamines such as 5(6)-amino-2-(4'-aminophenyl)benzimidazole and 1,4-phenylenediamine and diacid chlorides as terephthaloyl chloride in these ILs, at low temperature between 0 °C and 60 °C (Scheme 1.19). However, the instability and toxicity of acid chlorides are the main drawbacks of this method.



Scheme 1.19: Synthesis of aromatic polyamides in ionic liquids.

Due to the insolubility of some aromatic initial compounds and/or polymers in the ILs, it was necessary to perform polycondensation at higher temperature. In this case, acid chlorides can not be used to synthesize the corresponding polyamides, as high temperature resulted in side reactions of acid chlorides.¹⁰⁶ The direct polycondensation between diacids and aromatic diamines in dialkylimidazolium-based ionic liquids was therefore employed to synthesize polyamides at higher temperature (100 °C), and triphenylphosphite (TPP) was added as coupling reagent (Scheme 1.20).

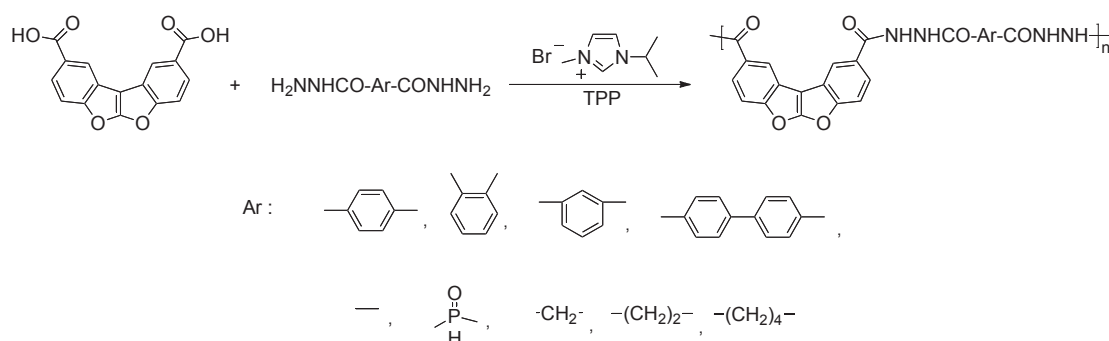


Scheme 1.20: Direct polyamidation in ionic liquids¹⁰⁶.

The molar mass of the resulting polymers was found to be dependant on the length of alkyl substituents on the imidazolium cation. Especially when the two alkyl substituents were identical, the inherent viscosity of the polymers increased with the alkyl group length.

1.5.3.3 Synthesis of polyhydrazide in ionic liquids

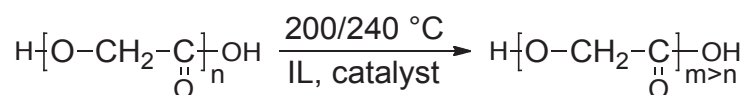
Polyhydrazides were synthesized by direct polycondensation of dicarboxylic acids and dihydrazides in ILs.¹⁰⁶⁻¹⁰⁸ The reactions were conducted in the presence of TPP in [MPlm]Br, and no extra components, such as LiCl or pyridine, were added in the reaction mixture. For example, benzofuro[2,3-b]benzofuran-2,9-dicarboxylic acid (BBDA) reacted with various dihydrazides in ILs (Scheme 1.21). Polyhydrazides were obtained with intrinsic viscosity ranging from 0.21 to 0.47 dL/g. It is worth noting that no polymer precipitation was observed during the polymerization in [MPlm]Br.



Scheme 1.21: Synthesis of polyhydrazides in ionic liquid in presence of TPP¹⁰⁷.

1.5.3.4 Synthesis of polyester in ionic liquids

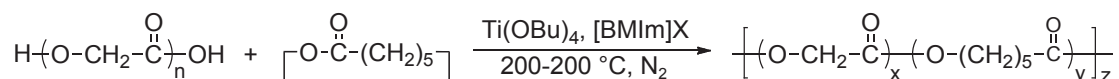
Polyesters synthesized in ionic liquids was described by Fradet et al. in 2006.¹⁰⁹ The synthesis of poly(glycolic acid) (PGA) is a good example, as this polymer exhibits a very poor solubility in organic solvents and has a low thermal stability above its melting point. PGAs of moderate molar mass were obtained from the post-polycondensation of a pre-synthesized PGA oligomer in 1-butyl-3-methylimidazolium ionic liquids with different anions (Scheme 1.22). No polymerization took place in the ionic liquid with anion Cl⁻, known for its hydrophilicity,²⁶ and is therefore a poor medium for polyesterification, as a high water content hinders polyester formation. The highest molar mass was obtained in [BMIm]Tf₂N, an IL exhibiting high hydrophobicity, which favors the elimination of byproduct water.



Scheme 1.22: Postpolycondensation of oligo-PGA in ionic liquids¹⁰⁹.

The activity of common esterification catalysts, such as Zn(OAc)₂, was low, which was assigned to preferential interactions between the catalyst and IL anions. As a common problem in other polymerizations in ILs, PGA precipitated in the reaction media, which limited therefore the formation of higher molar mass polymers.

Poly(glycolic acid) (PGA) and ε-caprolactone (CL) were used to synthesize copolymers poly(GA-co-CL). The polymerization in ILs was conducted in the presence of Ti(OBu)₄ as catalyst, and subsequent transesterification occurred, leading to random copolymers (Scheme 1.23).¹¹⁰ In this study, ILs were also used as solvents, as their nature did not have much influence on the reaction rate. Unlike the PGA homopolymer,¹⁰⁹ the copolyesters remained soluble in the ionic liquid at the copolymerization temperature.

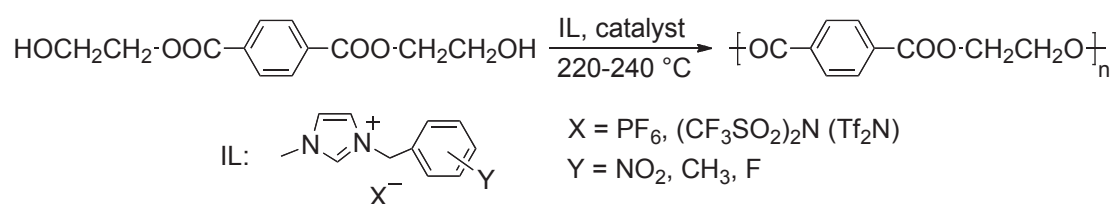


Scheme 1.23: PGA/CL copolymer synthesis in ionic liquid¹¹⁰.

Liu et al.¹¹¹ applied a two step strategy (oligomer preparation and post-polycondensation) to the polycondensation of sebacic, adipic and succinic acid with aliphatic diols in ionic liquids.

The reactions were conducted at relatively high temperature, i.e. 160 °C, with addition of SnCl₂·2H₂O as catalyst. The activity of Sn²⁺ was influenced by the anions, and was higher in Tf₂N⁻ than in PF₆⁻. It was supposed that the Sn²⁺ cation was changed into totally fluorinated complex in the PF₆⁻ ILs, which becomes therefore inactive; while Tf₂N⁻ is a stable and inert counterion. However, more investigation clearly needs to be carried out to prove this hypothesis.

The polycondensation of bis(β-hydroxyethyl)terephthalate (BHET) was performed in ILs under vacuum at 220-240 °C using a catalyst (Sb₂(OCH₂CH₂O)₃, Sb(OAc)₃ or Sb₂O₃): High molar mass poly(ethylene terephthalate) (PET, M_w up to 26000 g/mol) was obtained in benzyl substituted imidazolium ILs, synthesized in order to improve the PET solubility.¹¹² The same research group then succeeded in preparing phenylalkyl pyrrolidinium ionic liquids, in which PET was also synthesized (Scheme 1.24).¹¹³ During the reaction, however, phase separation still occurred when the molar mass of PET gradually increased.



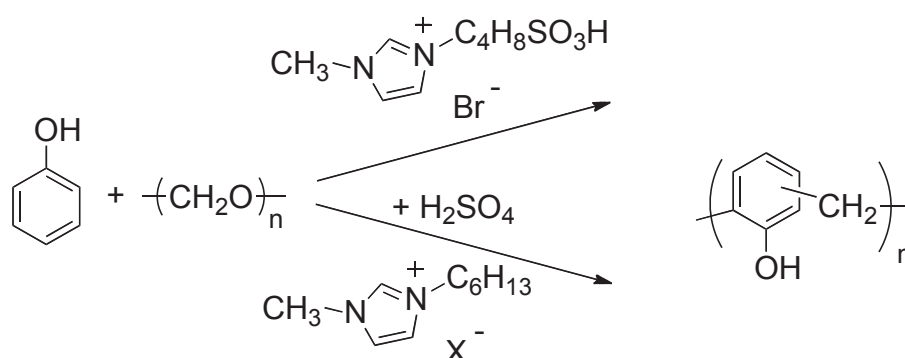
Scheme 1.24: PET synthesis in ionic liquid¹¹².

The polycondensation of L-lactic acid (LLA) was conducted in the bulk at 170-180 °C, and catalytic amount of 1,3-dialkylimidazolium ionic liquid was added to accelerate the reaction.¹¹⁴ The authors claimed to be the first for discovering the catalytic effect of neutral imidazolium salts towards melt polymerization of LLA, as high molar mass PLLA up to 20000 g/mol was obtained without additional Lewis acid. It was found that the catalytic activity of an IL depended on the anion, which increased in the order PF₆⁻ ≈ SO₄²⁻ < BF₄⁻ < NO₃⁻ < Br⁻ ≈ Cl⁻ < Ac⁻.

1.5.3.5 Phenol polymerization in ionic liquids

Polymerization of phenol with paraformaldehyde was also studied in various ionic liquids (Scheme 1.25).¹¹⁵ When this polymerization was conducted in dialkylimidazolium-based ionic liquids, sulfuric acid was added to accelerate the reaction. It was found that the molar mass of

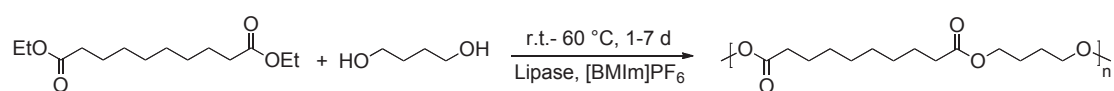
the resulting polymers depended on hydrophilicity of the ionic liquids. Only oligomers could be obtained in hydrophilic ionic liquids containing chloride or bromide, while high molar mass essentially linear polymers were obtained in those having hydrophobic anions such as tetrafluoroborate (BF_4^-) or trifluoromethanesulfonate (TfO^-). Meanwhile, they tried the same polymerization in an ionic liquid with a sulfonic acid functionalized imidazolium cation without additional catalyst, and high molar mass polymer was obtained, but the polydispersity index was extremely high, probably due to increasing chain branching.



Scheme 1.25: Polymerization of phenol in different ionic liquid systems¹¹⁵.

1.5.3.6 Enzymatic polycondensation in ionic liquids

ILs were also investigated as alternatives to organic solvents for enzymatic polycondensations, as the deactivating effect of many polar organic solvents such as methanol and DMF can be largely avoided in common ILs. Several groups tried therefore to combine enzyme-catalyst system with ILs to synthesize polyesters via polycondensation.¹¹⁶⁻¹¹⁹ For example, Nara et al.¹¹⁶ attempted enzyme-catalysed polyester synthesis of diethyl octane-1,8-dicarboxylate with 1,4-butanediol by using a lipase in [BMIm]PF₆ (Scheme 1.26). The reaction was carried out at 60 °C for 7 days, leading to polyesters of modest molar mass (5400 g/mol).



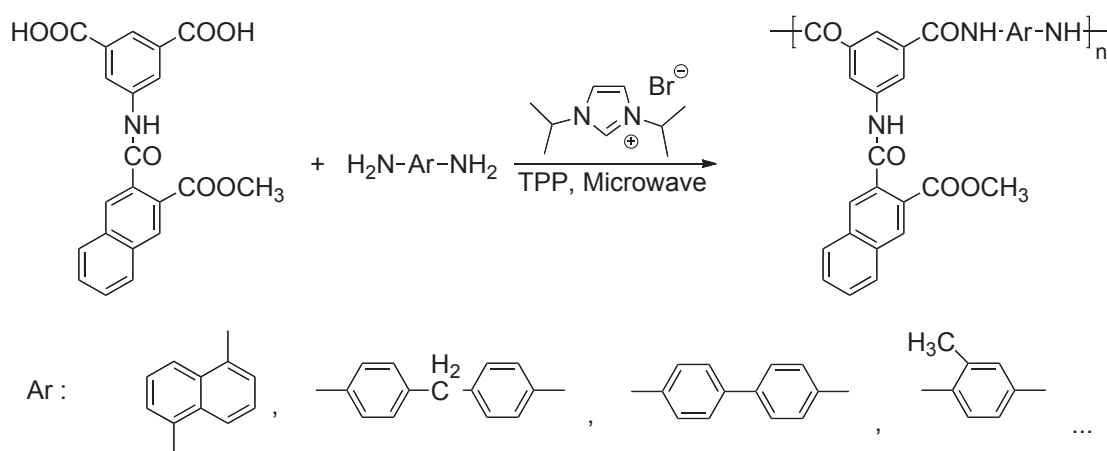
Scheme 1.26: Lipase catalyzed polyester synthesis in [BMIm]PF₆.

When the same reaction was carried out in [BMIm]Tf₂N,¹¹⁷ the reaction time was reduced to 24 h and the molar mass of the resulting polymer was slightly higher than that in Nara's study.

1.5.3.7 Microwave-aided polycondensation in ionic liquids

Some interesting properties of ionic liquids are their relatively high polarity and low heat capacity,¹²⁰ which allow the reaction media to easily absorb microwaves. The combination of ionic liquids and microwave irradiation was reported for some syntheses of different polymers.¹²¹⁻¹²⁶

Direct polycondensations in ionic liquids irradiated by microwave were intensively investigated by Mallakpour et al. for synthesis of various polyamides^{124, 125, 127} and poly(urea-urethane)s.¹²⁸ For example, direct polycondensation of 5-(3-acetoxynaphthoylamino)-isophthalic acid with several aromatic diamines was studied in 1,3-diisopropylimidazolium bromide under microwave irradiation (Scheme 1.27).¹²⁴ They carried out a comparative study on microwave-assisted reaction and conventional heating, showing that the reaction was much more efficient under microwave irradiation. It took only 90 s to obtain the polyamides with inherent viscosity in the range of 0.44-0.69 dL/g in high yield, while it required 2.5 h for conventional heating to achieve the results of the same order of magnitude.



Scheme 1.27: Polycondensation of diacid and diamine in IL under microwave irradiation¹²⁴.

Several examples of polycondensations in ILs have been described by different authors. However, the solubility of polymers in ILs still remains a major challenge, which often prevents formation of high molar mass polymer.^{110,111}

1.6 Conclusion

Since early 2000s, ILs have been used as reaction media for polymer syntheses,^{2,66,67} mainly radical polymerization processes.^{2,66} As well known, one of the major drawbacks is that the

solubility of polymers is limited in some ILs, which makes it difficult to obtain high molar mass polymers. It might also be the reason why little investigation on polycondensations in ILs can be found. Besides, in almost all the yet communicated investigations, ILs were only used as solvents, and therefore catalysts, initiators or additives are required. The separation of these additional substances were often tedious.

In the dissertation, application of ionic liquids to the synthesis of different polymers via polycondensation is described. Different type of polymers, such as linear and hyperbranched polyesters, linear polyethers, polypeptides and polyamides containing natural amino-acid units were synthesized. Specific efforts have been made to improve the solubility of monomers and/or polymers in carefully selected ILs so that the polymers of high molar mass can be obtained. Besides, the cations of the ionic liquids were functionalized with sulfonic acid so that the polyesterification and polyetherification can be catalyzed without adding any other catalyst. Some polymers, which usually cannot be synthesized or the synthesis of which is extremely complicated, have been obtained by direct polycondensation in ILs.

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Chapter II

Hydroxyacid polyesterification in Brønsted acid ionic liquids

Abstract:

Brønsted acid ionic liquids (BAILs) based on the 4-(3'-butyl-1'-imidazolio)-1-butanefulfonic acid cation were found to be very efficient polyesterification solvents and catalysts. Only 5-30 min at 90–110 °C was required to obtain high molar mass poly(12-hydroxydodecanoic acid) (M_w up to 40000 g/mol). The polyesterification was faster in BAILs with the bis(trifluoromethylsulfonyl)imidide anion (Tf_2N^-), but small amounts of ethers and double bonds arising from side reactions were detected in the final polymer. On the other hand, no side reactions took place in the BAIL with the hydrogen sulfate anion (HSO_4^-), except for the formation of a sulfonate ester intermediate that can further react with carboxylic acid groups to yield the expected ester. This intermediate, not observed in Tf_2N^- based BAILs, might be involved in the protection of hydroxy end groups from etherification side reactions in HSO_4^- based BAILs. To explain the different behaviors of these BAILs, and since the acidity of H_2SO_4 is much higher than that of Tf_2NH , it is suggested that the structure of these BAILs could be different: alkylsulfonic acid-substituted imidazolium for the former, while the latter could be just a mixture of imidazolium sulfonate zwitterion and Tf_2NH . The influence of reaction temperature, water elimination method and BAIL concentration on polyesterification are also discussed.

II.1 Introduction

The conventional way to synthesize polyester is the bulk reaction between diols and diacids or diesters.^{1,2} The process usually requires catalysts such as metal salts, metal oxides or metal alkoxides, and high temperature (170-300 °C) as well as long reaction time (several hours). Vacuum is often applied at the end of reaction to strip off the last traces of reaction water and to shift esterification equilibrium toward the formation of high molar mass polyesters. It must be underlined that metal-based catalysts cannot be removed and remain in final polymer. Alternatively, polyesters can be produced by solution reaction of diols and diacid chlorides or activated dicarboxylic acids in milder conditions and shorter reaction time.² In these processes, however, expensive and/or toxic starting monomers, activating agents and solvents are used. It is costly to remove solvents, as well as to dispose of activating agent residues.

Since the concept of green chemistry has emerged, a wide attention has been paid to organic chemistry processes involving ionic liquids (ILs) as nonvolatile, easily recyclable reaction media of highly thermal and chemical stabilities.³⁻⁹ A number of polymerization processes, either chain polymerizations or polycondensations, have also been studied in ionic liquids.¹⁰⁻¹² Most polycondensation studies were relative to the synthesis of aromatic polymers such as polyamides, polyimides, polyhydrazides or polyoxadiazoles in a range of conventional ionic liquids.¹³⁻²¹ Some syntheses of polyesters in ionic liquids have also been described: Poly(glycolic acid) and copolymers of glycolic acid and ϵ -caprolactone were obtained by high temperature post-polycondensation of oligomers,^{22,23} enzyme-catalyzed polyesterifications yielded low molar mass polyesters^{24,25} and Wang et al.²⁶ used various dialkylimidazolium salts as catalysts in the bulk synthesis of poly(lactic acid). Fu et al.²⁷ showed that high molar mass aliphatic polyesters could be obtained in dialkylimidazolium salts by post-polycondensation of oligoesters, but the two-step procedure required high temperature (160 °C), long reaction time (24 h) and the addition of a metal catalyst.

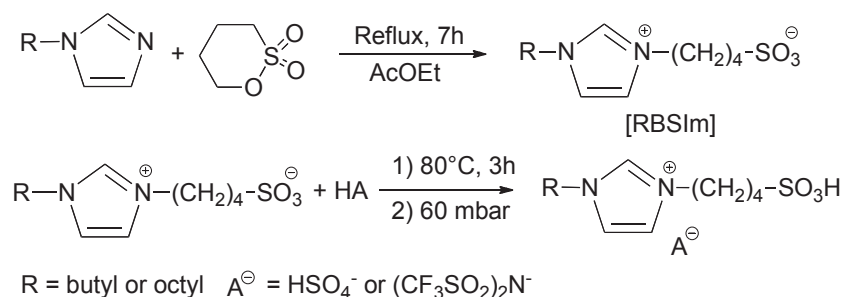
A specific category of ionic liquids, namely Brønsted acid ionic liquids (BAILs), were reported to play a double role of catalyst and solvent for various acid-catalyzed reactions and, especially, Fischer esterifications. Such reactions were carried out in BAILs with SO₃H-functionalized cations such as phosphoniums,^{28,29} ammoniums,³⁰⁻³² pyridiniums^{30,33,34} or imidazoliums,^{28,30} and/or acidic anions such as hydrogen sulfate or dihydrogen phosphate.³⁰⁻³⁷ High yields of esters, low reaction temperature and short reaction times are some of the

advantages of the method. In a recent paper,³⁸ Fradet et al. reported the synthesis of high molar mass polyesters in SO₃H-functionalized imidazoliums, at moderate temperature (90-130 °C) and for short reaction time (10-120 min).

In this chapter, the effects of imidazolium alkyl substituent, counterion, reaction time, temperature and BAIL concentration on the average molar mass of polyester were investigated, and the polyesterification of 12-hydroxydodecanoic acid (12-HDA) was taken as model reaction. The polyester solubility and side reactions were also investigated. Besides, more importantly, it was found that the polyesterification of 12-HDA behaved differently in the BAILs with different counterions. Potential reaction mechanisms are, therefore, also discussed.

II.2 Results and discussion

Three SO₃H-functionalized imidazolium-based BAILs with octyl or butyl substituents and hydrogen sulfate or bis(trifluoromethylsulfonyl) imide counterions were used as both solvents and catalysts for the polyesterification of 12-hydroxydodecanoic acid (12-HDA). These BAILs, namely 3-butyl-1-(butyl-4'-sulfonyl)imidazolium hydrogen sulfate ([BBSIm]HSO₄), 3-butyl-1-(butyl-4'-sulfonyl)imidazolium bis(trifluoromethylsulfonyl)imide ([BBSIm]Tf₂N) and 3-octyl-1-(butyl-4'-sulfonyl)imidazolium bis(trifluoromethylsulfonyl)imide ([OBSIm]Tf₂N), were synthesized in a straightforward two-step approach (Scheme 2.1):^{28,30}

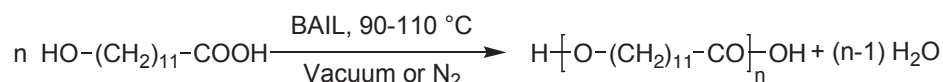


Scheme 2.1: Two-step synthesis of SO₃H-functionalized BAILs.

As generally observed, when the length of the alkyl substituents of imidazolium-based ionic liquids increases,^{39, 40} the octyl-substituted imidazolium was more viscous than its butyl homologue. The viscosities of these BAILs were also significantly modified when the counterion was replaced: at room temperature, [BBSIm]Tf₂N was much less viscous than

[BBSIm] HSO₄.

The polyesterifications of 12-hydroxydodecanoic acid (12-HDA) were carried out at 90 or 100 °C using 12-HDA/BAIL equimolar amounts. Reaction water was eliminated either by flowing nitrogen over reaction medium or by applying vacuum (10 mbar) during the reaction (Scheme 2.2).



Scheme 2.2: Polyesterification of 12-hydroxydodecanoic acid in BAIL

Table 2.1: Polycondensation of 12-HDA. Mass-average molar mass (M_w) calculated from SEC data. Number-average molar mass (M_n) obtained from SEC data and ¹H NMR.

Entry	BAIL or catalyst	T (°C)	Time (min)	M_w (g/mol)	M_n^a (g/mol)	M_n^b (g/mol)	Yield ^g %
1	Nil ^c	175	480	38700	15270	12060	95
2	<i>p</i> -TSA ^{c,d}	110	30	5950	2290	2390	95
3	[BBSIm]Tf ₂ N ^f	110	15	39010	18380	15180	96
4	[BBSIm]HSO ₄ ^e	110	30	24910	10313	10140	86
5	[BBSIm]Tf ₂ N ^f	90	30	39720	14420	12360	90
6	[OBSIm]Tf ₂ N ^e	110	30	36110	14580	15680	92

^a Values from SEC in CH₂Cl₂

^b Values from ¹H NMR (CDCl₃)

^c Reaction carried out in the bulk with 500 ml/min N₂ flow rate

^d Reaction catalyzed by 1 wt-% *p*-TSA.

^e Reaction carried out in BAILs under vacuum (10 mbar)

^f Reaction carried out in BAILs under 500 mL/min N₂ flow.

A comparison between the reactions with and without BAIL is presented in Table 2.1, demonstrating that the polyesterification of 12-HDA in the BAILs is very efficient. When no catalyst was added (entry 1, Table 2.1), the polyesterification had to be carried out in harsh conditions, namely high temperature (175 °C) and long reaction time (480 min) to obtain high molar mass polyester. In the presence of *p*-toluenesulfonic acid (*p*-TSA) catalyst, only low molar mass oligomers were obtained after 30 min reaction at 110 °C. On the other hand, when the reaction was carried out in a BAIL (entries 3-6), high molar mass polyesters were obtained in 30 min at 90-110 °C. Moreover, it is worthwhile emphasizing that the reaction was so

effective in [BBSIm]Tf₂N that polyesters of M_w up to 40000 g/mol could be obtained after only 15 min. This clearly shows, therefore, the high efficiency of BAILs for 12-HDA polyesterification.

II.2.1 Solubility of poly(12-HDA) in BAILS

The dissolving ability of an ionic liquid depends largely on the structure of both its anion and its cation,⁴¹ but little investigation has been carried out on the issue so far, especially on polymers. The polymerization of 12-HDA in each BAIL was followed under polarizing optical microscope (POM) at 110 °C. These experiments showed that the miscibility of poly(12-HDA) with the various BAILs was very different from each other. 12-HDA monomer was soluble in [BBSIm]HSO₄ and in [BBSIm]Tf₂N at 110 °C (Table 2.2). During the polyesterification, the reaction medium became viscous and heterogeneous in the former, while it was always fluid, transparent and visually homogenous in the latter. However, two phases were detected when both reaction media were examined under polarizing microscope (POM) during the polymerization, as shown in Figures 2.1a and 2.1c, where the bubble-like spots are molten poly(12-HDA) while the grey background is BAIL in each image. This could be interpreted that as polymer chain increases, poly(12-HDA) becomes more hydrophobic and less soluble in these hydrophilic ionic liquids. Upon cooling down to room temperature, poly(12-HDA) crystallized, resulting in a dispersion of solid polymer particles of 10 to 200 μm diameter in the ionic liquid (Figure 2.1b and 2.1d).

The same test was carried out in the octyl-substituted ionic liquid [OBSIm]Tf₂N. It was observed under polarizing microscope that both 12-HDA and poly(12-HDA) were soluble in this BAIL at 110 °C (Figure 2.1e). Since poly(12-HDA) was not soluble in [BBSIm]Tf₂N, the length of the alkyl substituent of the imidazolium cation seems to play an important role on solubility. The presence of the octyl substituent increases [OBSIm]Tf₂N hydrophobicity with respect to [BBSIm]Tf₂N, which could explain why poly(12-HDA) is more soluble in the former. It should also be noted that poly(12-HDA) was not soluble in any of the BAILS at room temperature (Figure 2.1b, 2.1d, 2.1f), which facilitated polymer recovery.

Table 2.2: Homogeneity of 12-HDA/BAIL reaction media at 110 °C, observed by polarizing optical microscope.

BAIL	Homogeneity	
	12-HDA	poly(12-HDA)
[BBSIm]HSO ₄	Homogeneous	Heterogeneous
[BBSIm]Tf ₂ N	Homogeneous	Heterogeneous
[OBSIm]Tf ₂ N	Homogeneous	Homogeneous

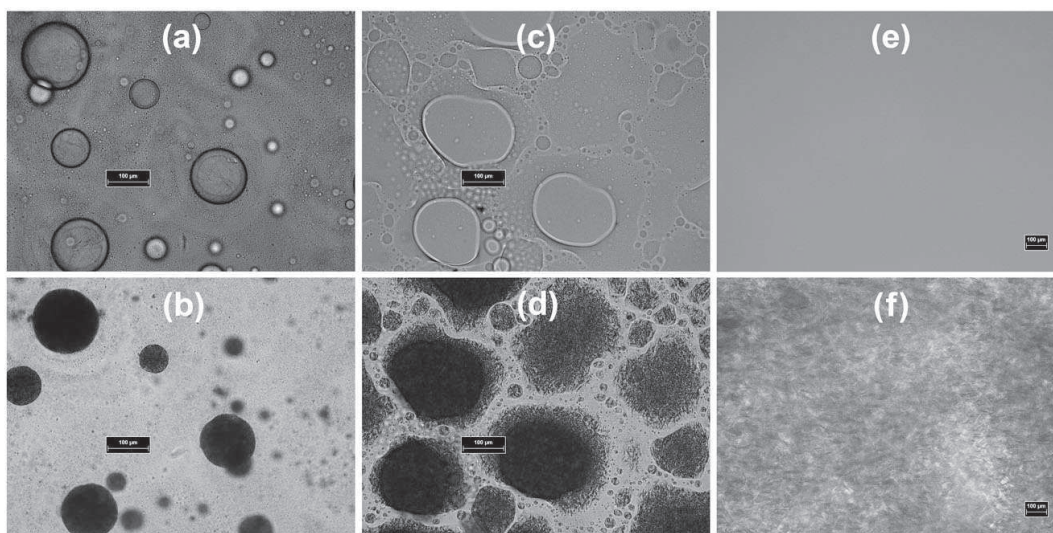


Figure 2.1: Polarizing optical microscopy images of reaction media: [BBSIm]HSO₄ at (a) 110°C and (b) room temperature, [BBSIm]Tf₂N at (c) 110 °C and (d) room temperature and [OBSIm]Tf₂N at (e) 110 °C and (f) room temperature (bar length = 100 µm).

II.2.2 Influence of temperature

Two series of experiments were carried out in [BBSIm]Tf₂N, respectively at 90 °C and 110 °C, and water was eliminated under vacuum (10 mbar) (Figure 2.2). At the beginning of the polymerization of 12-HDA, it was faster at 110 °C than at 90 °C. At 110 °C, polymer molar mass was already close to $M_w = 35000$ g/mol after only 5 min and reached a maximum of M_w close to 40000 g/mol after 15 min. As expected for a kinetically controlled polymerization, the reaction was slower at 90 °C and it took 30 min to reach its maximum of about 40000 g/mol. Therefore, compared to traditional polyesterification in the bulk, which requires high temperature (≥ 170 °C) and long reaction time, the reaction in [BBSIm]Tf₂N boasts a significant advantage in terms of time and energy effectiveness. For conventional polyesterifications, a M_w plateau is reached at long reaction time, due to several factors: diffusion control of the reaction when polymer viscosity increases, reduced mass-transfer resulting in incomplete water elimination, stoichiometric unbalance due to side reactions or the

presence of impurities. In the present case, almost the same results were found at both 110 °C and 90 °C, but instead of a plateau, a M_w decrease was observed. This point is discussed below.

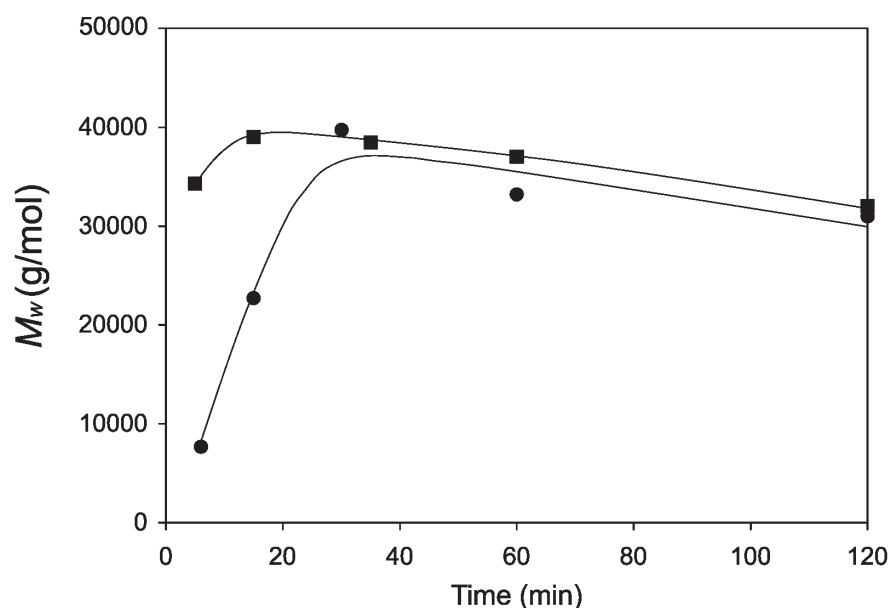


Figure 2.2: Evolution of M_w at different temperatures in [BBSIm]Tf₂N: polyesterification of 12-HDA in [BBSIm]Tf₂N (12-HDA/BAIL molar ratio =1/1) at 90 °C (●) or 110 °C (■) under vacuum (10 mbar).

II.2.3 Water elimination approaches

Due to the reversibility of polyesterification, water generated during the reaction is detrimental to molar mass growth. It is, therefore, very important to eliminate it. Moreover, according to Thomazeau et al.,⁴² the presence of water could also decrease the acidity of the proton in BAILs, meaning that it could have a negative influence on their catalytic performance. The water content of BAILs used in this study was about 0.5% by weight, which corresponds to only 1/10 of water formed during the polyesterification of 12-HDA, it might be therefore the reaction water that has more important influence on the molar mass. In order to confirm this assumption, a blank experiment was carried out without evaporating water in the reaction mixture. As shown in Table 2.3, when water remained in reaction medium (Entry 1), polymers of low molar mass were produced, whereas when water was stripped by either vacuum or N₂ flow, polyesterification was much more favored (Entries 2 and 3). The results obtained using vacuum (10 mbar) were close to those obtained with a nitrogen flow.

Table 2.3: Polyesterification of 12-HDA in [BBSIm]Tf₂N (12-HDA/BAIL molar ratio =1/1, at 110 °C, 2 h). Mass-average molar mass (M_w) calculated from SEC data, number-average molar mass (M_n) obtained from SEC data and ¹H NMR.

Entry	Water elimination	M_w (g/mo)	M_n^a (g/mol)	M_n^b (g/mol)	Yield (%)
1	Nil	13430	4180	4380	93
2	Vacuum (10 mbar)	32010	13920	13690	90
3	N ₂ (500 mL/min)	32250	15090	12670	83

^a Values from SEC in CH₂Cl₂

^b Values from ¹H NMR (CDCl₃)

II.2.4 Comparison of polyesterifications in different BAILs

The polyesterification of 12-HDA carried out in [BBSIm]HSO₄ and in [BBSIm]Tf₂N at 110 °C under nitrogen flow gave very different results. As shown in Figure 2.3, polyesterification was more efficient in [BBSIm]Tf₂N during the first 40 min, producing poly(12-HDA) of higher molar mass than that in [BBSIm]HSO₄. However, as mentioned above, the molar mass began decreasing in the former after 40 min while it kept growing before reaching a plateau at *ca.* 60 min in the latter.

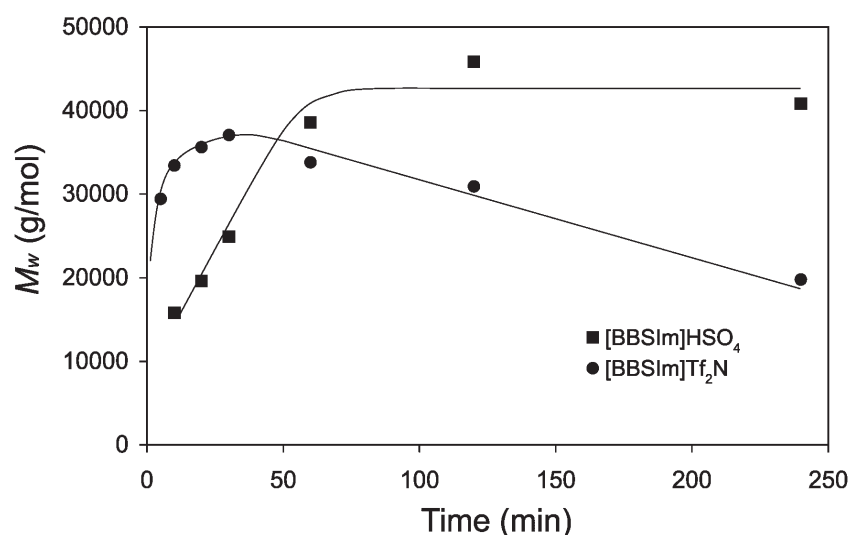
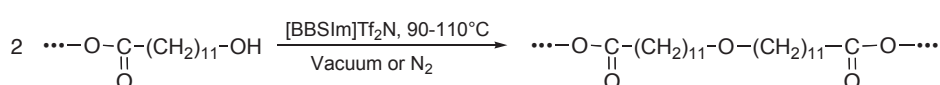


Figure 2.3: Evolution of M_w during the polycondensation of 12-HDA in [BBSIm]HSO₄ and in [BBSIm]Tf₂N (12-HDA/BAIL molar ratio =1/1, 110 °C, N₂ (500 mL/min)).

At the beginning of reaction, kinetics is the determining factor and, since acid-catalyzed polyesterifications are second-order reactions, the molar mass grows linearly with time.⁴³ As the chain length keeps increasing, the reaction medium viscosity increases and residual water

cannot be totally removed. This prevents reversible polyesterification from completion and can explain why poly(12-HDA) stopped growing after 1 h in [BBSIm]HSO₄. However, the decrease of the molar mass of the polymer formed in [BBSIm]Tf₂N seemed rather surprising and led us to further investigations. The composition of each polymer was analyzed by ¹H NMR. It was found that one single reaction, i.e. esterification, underwent in [BBSIm]HSO₄. On the other hand, a side reaction, etherification, took place in [BBSIm]Tf₂N (Scheme 2.3), as reflected by the presence of H^h resonance at 3.38 ppm in the ¹H NMR spectrum of the corresponding polyester (Figure 2.4).



Scheme 2.3: Etherification side-reaction in [BBSIm]Tf₂N.

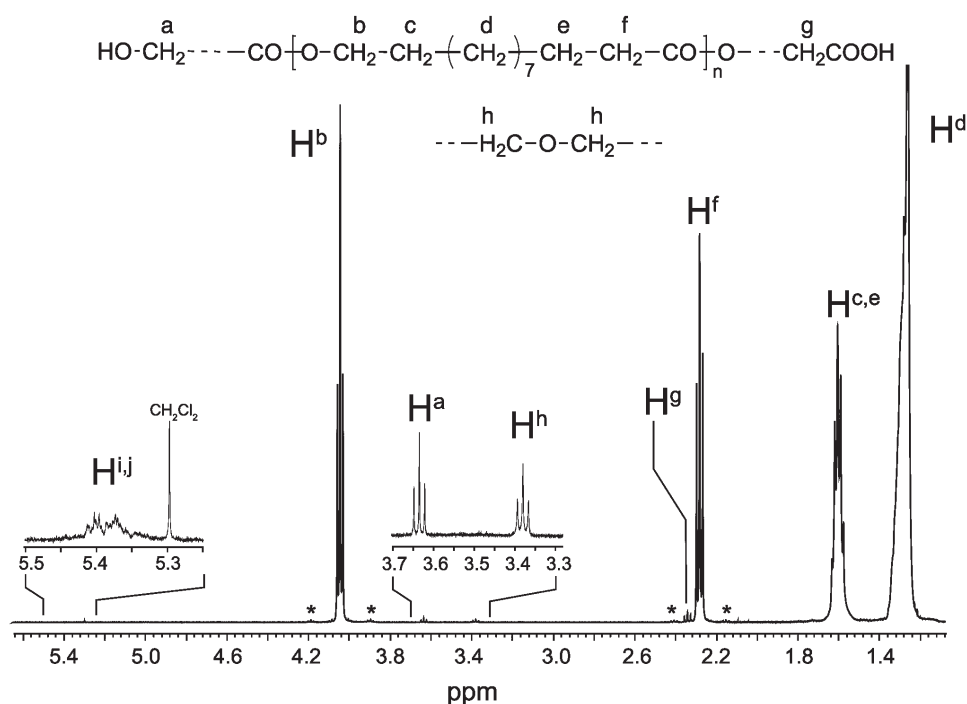


Figure 2.4: ¹H NMR spectrum (CDCl₃, 500 MHz) of poly(12-HDA) synthesized in [BBSIm]Tf₂N (110 °C, 1 h, N₂). *: ¹³C satellite peaks. H_{i,j}: See text.

Etherification is harmful to polyester growth, as it consumes –OH end-groups, making the system no longer stoichiometric for polyesterification and, therefore, limiting polyester molar mass. As can be seen in Figure 2.5, etherification took place in all the reactions conducted in [BBSIm]Tf₂N, reaching a plateau after 40 min reaction. Since 2 mol of –OH are consumed to

form 1 mol of ether, at most 0.8 % of the hydroxyl groups of starting 12-HDA was therefore consumed by etherification. Supposing the rest of –OH groups reacts totally as desired, the theoretical limit value of the number-average degree of polymerization in this IL can be calculated to be $DP_n = 249$, which corresponds to a number-average molar mass of $M_n = 49600$ g/mol and, assuming an equilibrium polycondensation, a mass-average molar mass of $M_w = 99200$ g/mol. The maximal M_w that could be obtained in our investigations was around 40000 g/mol, which means that the reaction was far from its theoretical equilibrium.

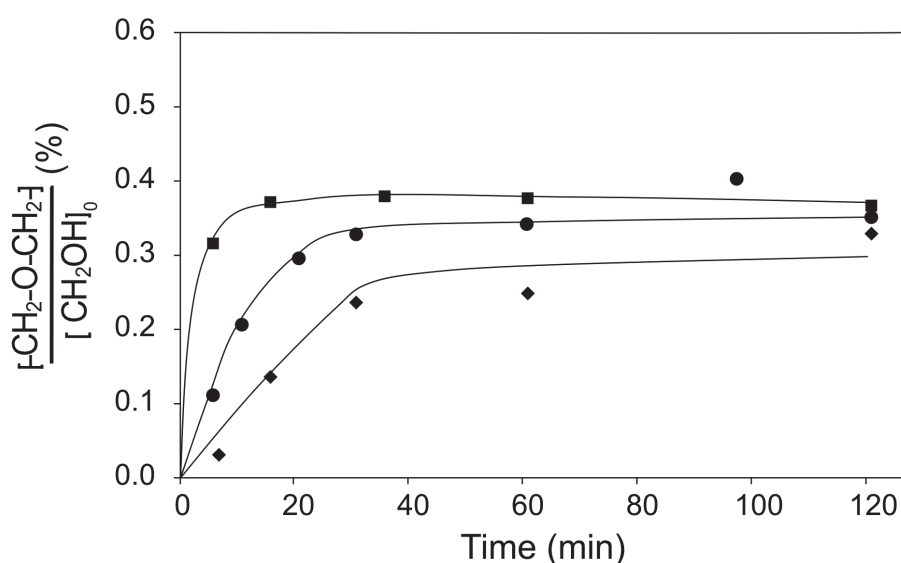
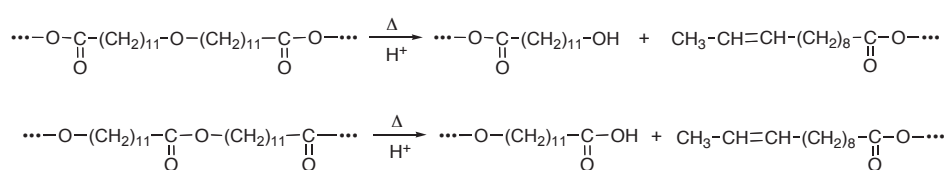


Figure 2.5: Evolution of ether group content with time during 12-HDA polyesterification in [BBSIm]Tf₂N. (●): at 110 °C under N₂ flow, (■): at 110 °C under vacuum (10 mbar), (◆) at 90 °C under vacuum (10 mbar). Ether group content, determined by ¹H NMR, is expressed in mol-% with respect to initial OH groups.

The M_w decrease observed after 40 min reaction implies the existence of side reactions other than etherification. The ¹H NMR spectra of the samples obtained in [BBSIm]Tf₂N present a resonance at 5.4 ppm (signal H^{i,j}) (Figure 2.4) that reflects the presence of CH₃-CH=CH-double bonds in the polymer. The formation of double bonds under acidic conditions is a known side-reaction during acid-catalyzed esterifications,^{44,45} or during high temperature polyesterifications such as PET synthesis.² In the present case, the double bonds may result from acid-catalyzed scission of ester bonds, from acid-catalyzed scission of ether bonds formed by etherification or from acid-catalyzed hydroxy end-group deshydration. When a poly(12-HDA) synthesized in [BBSIm]HSO₄ was heated in [BBSIm]Tf₂N for 4 h, its M_w decreased from 41500 g/mol to 26270 g/mol. Since this polymer does not contain any ether groups, it can be only attributed to ester scissions. On the other hand, when a poly(12-HDA) synthesized in

[BBSIm]Tf₂N was heated in [BBSIm]HSO₄ for 4 h, a slight *M_w* increase from 20350 g/mol to 26440 g/mol was observed. This indicates that poly(12-HDA) is stable in [BBSIm]HSO₄, while ester scission takes place in [BBSIm]Tf₂N when the reaction is prolonged (Scheme 4). It is important to note that the etherification side-reaction was always observed during polyesterifications in [BBSIm]Tf₂N. Therefore, ether scissions (Scheme 4) might also participate in the *M_w* decrease observed at long reaction times for polyesterifications in this BAIL. Neither ethers nor double bonds were found in the samples obtained by reactions in [BBSIm]HSO₄, highlighting the specific role of the Tf₂N counterion in the side reactions.



Scheme 2.4: Formation of double bonds by ether and ester scission.

In order to get more information about the different behaviors of these two BAILS as solvent/catalyst for polyesterification, model reactions with dodecanoic acid and dodecan-1-ol were carried out: dodecanoic acid was added respectively in [BBSIm]HSO₄ and [BBSIm]Tf₂N, and the mixtures were heated at 110 °C overnight. No reaction was observed in either of them. The same test was subsequently conducted between dodecan-1-ol and the two BAILS. Dodecan-1-ol reacted with [BBSIm]HSO₄, since the reaction medium became rapidly (5 min) soluble in chloroform in which [BBSIm]HSO₄ is insoluble. The ¹H NMR spectrum of the reaction product (Figure 2.6) exhibits a new resonance at 4.04 ppm that can be assigned to the -SO₃-CH₂-sulfonate ester group (H¹²).⁴⁶ This means that the dodecyl sulfonate ester of the [BBSIm] cation has been formed. The structure of this compound was confirmed by ESI Mass Spectrometry, since a cation of the expected formula (C₂₃H₄₅N₂O₃S⁺, 429.31 m/z) was detected as the main compound. On the other hand, no sulfonate dodecyl ester was detected in [BBSIm]Tf₂N.

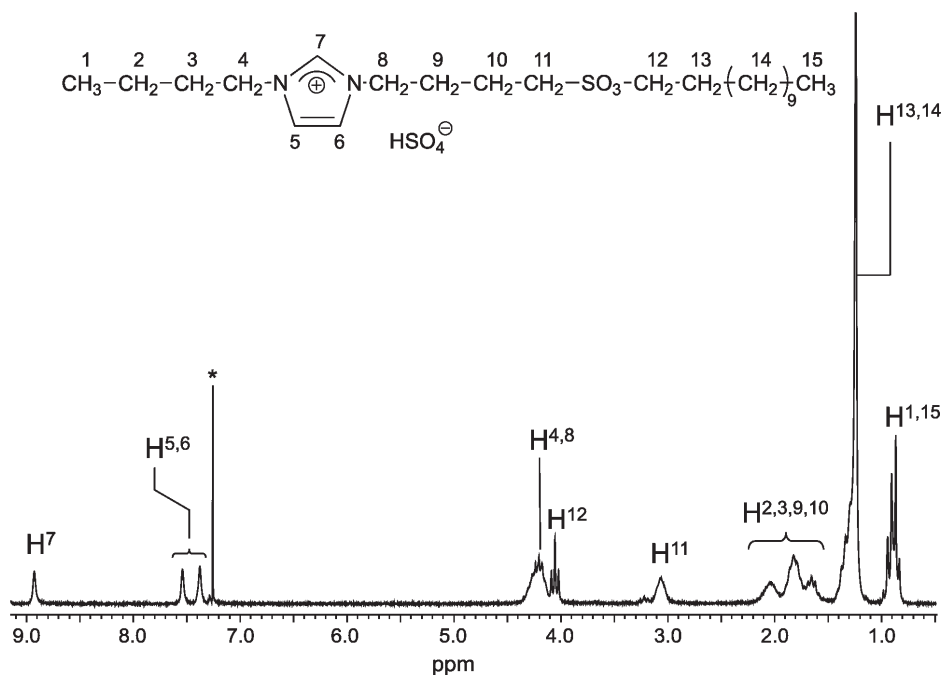


Figure 2.6: ^1H NMR spectrum (200 MHz, CDCl_3) of the product of reaction between 1-dodecanol and $[\text{BBSIm}]\text{HSO}_4$. *: signal of CHCl_3 .

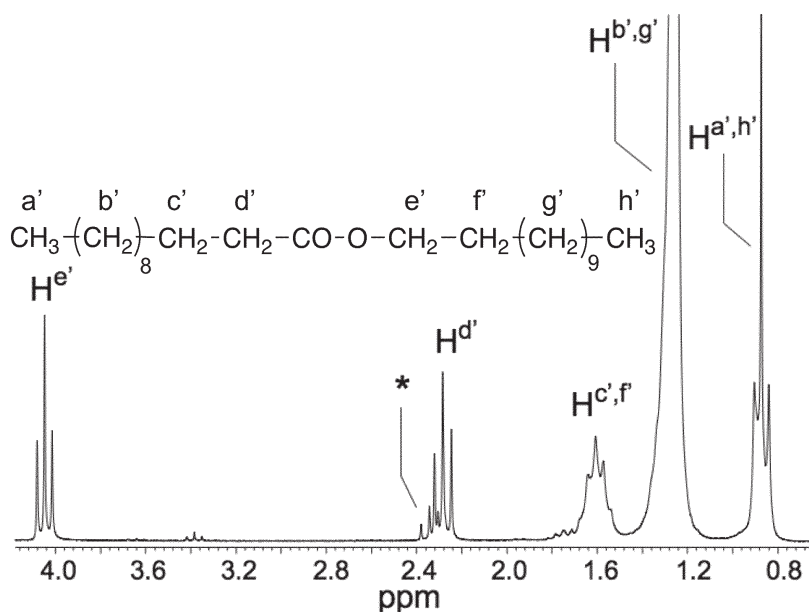
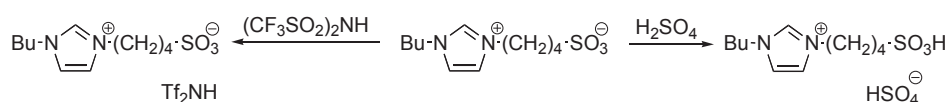


Figure 2.7: Reaction between $[\text{BBSIm}]\text{HSO}_4$ sulfonate dodecyl ester and dodecanoic acid ($110\text{ }^\circ\text{C}$): ^1H NMR spectrum (in CDCl_3) of upper phase of reaction medium. *: residual dodecanoic acid. ** traces of ether groups.

After the formation of the dodecyl sulfonate ester, dodecanoic acid was introduced in the reaction medium which was then maintained under the same conditions, and a phase separation was observed. The ^1H NMR study showed that the upper phase mainly contained dodecyl dodecanoate with traces of ether groups (Figure 2.7), while only $[\text{BBSIm}]\text{HSO}_4$ was found in

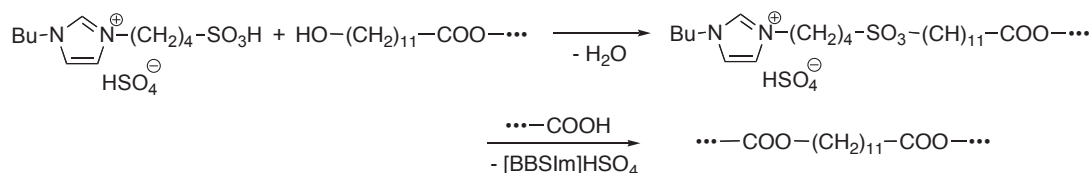
the lower phase. This shows that the dodecyl sulfonate ester reacts with carboxylic acids and can be regarded as a reaction intermediate.

It turns out that the behavior of the two BAILs is completely different, and it made us doubt if they have the same chemical structure, as assumed in Scheme 2.1. $(\text{CF}_3\text{SO}_2)_2\text{NH}$ is a moderately strong acid with a pK_a value of 1.7,⁴⁷ while H_2SO_4 and sulfonic acid are very strong acids with negative pK_a values.^{48,49} The Hammett acidity function H_0 can be used to compare their acidities.⁵⁰ The H_0 value of H_2SO_4 is -12,⁵¹ while that of sulfonic acids ranges from -5.8 to -7.9.⁵²⁻⁵⁴ This indicates that their acidities obey the order $\text{H}_2\text{SO}_4 > \text{sulfonic acid} \gg (\text{CF}_3\text{SO}_2)_2\text{NH}$. It can therefore be predicted that the acidity of the sulfonic acid group of [BBSIm] cation is higher than that of $(\text{CF}_3\text{SO}_2)_2\text{NH}$ but lower than that of H_2SO_4 . Consequently, when the [BBSIm] zwitterion is mixed with sulfuric acid, the sulfonate ion-sulfonic acid equilibrium is shifted towards sulfonic acid. On the other hand, when [BBSIm] zwitterion is mixed with Tf_2NH , sulfonic acid cannot be formed, as a stronger acid cannot be produced from a weaker one. [BBSIm] Tf_2N , should, therefore, be considered as a mixture of zwitterion and Tf_2NH , interacting through e.g. hydrogen bonds,⁵⁵ rather than an ionic liquid with separate anion and cation (Scheme 2.5).



Scheme 2.5: Reactions between [BBSIm] zwitterion and H_2SO_4 or Tf_2NH .

The sulfonate ester can be formed in [BBSIm] HSO_4 , but not in [BBSIm] Tf_2N since the anion SO_3^- cannot react with $-\text{OH}$ groups. The formation of the sulfonate ester in [BBSIm] HSO_4 competes with both the etherification side reaction and the esterification main reaction. It reduces the concentration of $-\text{OH}$ groups (etherification reactant) and that of $-\text{SO}_3\text{H}$ (etherification catalyst), and, therefore, limits the extent of the etherification reaction. At later stages of the reaction, $-\text{COOH}$ groups can react with the sulfonate ester, yielding the expected carboxylate ester. This reaction (Scheme 2.6) could explain why no etherification was observed in [BBSIm] HSO_4 .



Scheme 2.6: Polyesterification of 12-HDA in [BBSIm]HSO₄ through the sulfonate ester pathway.

II.2.5 Different concentrations of BAILs

In order to check the influence of BAIL concentration on the polyesterification, a series of experiments were carried out using 3-butyl-1-methylimidazolium hydrogen sulfate or bis(trifluoromethylsulfonyl)imidide ([BMIm]HSO₄ or [BMIm]Tf₂N, respectively), or 3-octyl-1-methylimidazolium bis(trifluoromethylsulfonyl)imidide ([OMIm]Tf₂N) as diluents (Table 2.4). The BAIL molar ratio in each BAIL/IL mixture varied from 1.0 to a low level (0.01).

Table 2.4: Polyesterification of 12-HDA carried out in BAIL/IL mixtures (at 110 °C, 30 min, under N₂ flow (500 mL/min)). Number-average and mass-average molar masses (M_n and M_w) of resulting polyesters determined by SEC and NMR.

Entry	BAIL	IL	$\frac{[\text{BA IL}]}{[\text{BAIL}] + [\text{IL}]}$	M_n (SEC)	M_w (SEC)	M_n (NMR)	ether ^a (mol-%)
1	[BBSIm]Tf ₂ N	[BmIm]Tf ₂ N	1.00	17960	37070	11780	0.33
2	[BBSIm]Tf ₂ N	[BmIm]Tf ₂ N	0.75	22840	40420	18360	0.28
3	[BBSIm]Tf ₂ N	[BmIm]Tf ₂ N	0.50	24020	44190	18970	0.29
4	[BBSIm]Tf ₂ N	[BmIm]Tf ₂ N	0.10	21240	44740	14660	0.22
5	[BBSIm]Tf ₂ N	[BmIm]Tf ₂ N	0.01	1370	3200	1530	0.00
6	[OBSIm]Tf ₂ N	[OmIm]Tf ₂ N	1.00	14580	36110	15680	0.65
7	[OBSIm]Tf ₂ N	[OmIm]Tf ₂ N	0.75	10430	32160	8200	0.60
8	[OBSIm]Tf ₂ N	[OmIm]Tf ₂ N	0.50	9830	29270	10650	0.50
9	[OBSIm]Tf ₂ N	[OmIm]Tf ₂ N	0.10	7390	26070	7880	0.30
10	[OBSIm]Tf ₂ N	[OmIm]Tf ₂ N	0.01	630	1610	1080	0.00
11	[BBSIm]HSO ₄	[BmIm]HSO ₄	1.00	10310	24910	10140	0.00
12	[BBSIm]HSO ₄	[BmIm]HSO ₄	0.50	7750	19940	5100	0.00
13	[BBSIm]HSO ₄	[BmIm]HSO ₄	0.10	950	2543	2410	0.00

^a -CH₂-O-CH₂- mol-% with respect to initial -CH₂OH groups determined by ¹H NMR.

Reactions were first conducted in [BBSIm]Tf₂N/[BMIm]Tf₂N mixtures and it turned out that diluting [BBSIm]Tf₂N in [BMIm]Tf₂N did not affect much the polymer molar mass after 30 min reaction, the maximum being obtained at 0.5 mol ratio of [BBSIm]Tf₂N. At 0.1 mol ratio, the catalysis was still effective and even better than in pure [BBSIm]Tf₂N. However, the molar

mass decreased dramatically when [BBSIm]Tf₂N mol ratio was reduced to 0.01 and the catalyst concentration was not sufficient any more to accelerate the polyesterification. The same experiments were also carried out in the mixtures of [OBSIm]Tf₂N and [OMIm]Tf₂N, but the molar masses of resulting polyesters were lower, comparing to those obtained with their butyl-substituted homologue and decreased continuously as the [OBSIm]Tf₂N concentration decreased. The same trend was observed in [BBSIm]HSO₄ as well (Table 2.4).

It is worth emphasizing that less ether was formed when the BAIL concentration decreased. This might be another reason why higher molar mass polyesters were obtained in BAIL/IL 50/50 mol mixture, since less hydroxyl groups were consumed by this side reaction.

II.3 Conclusion

The polyesterification of 12-HDA in various BAILs has been studied and found very efficient, since high molar mass polyesters (M_w of *ca.* 40000) were obtained at much lower temperature and less reaction time than conventional polyesterifications: 15-30 min at 90-110 °C versus several hours at 170-300 °C. However, there are some noticeable differences between the different BAILs studied. In [BBSIm]HSO₄ solely the desired polyesterification was observed and a M_w plateau was reached after 60 min reaction. On the other hand, the reaction was much faster in [BBSIm]Tf₂N, as a M_w close to 35000 g/mol was obtained after only 5 min reaction, but side reactions took place, i.e. etherification of -OH end groups and degradation leading to significant molar mass decrease at long reaction time. This degradation was assigned to acid-catalyzed ester scissions with formation of double bonds and carboxylic acids. However, it should be mentioned that ether scissions might also be involved in the degradation.

The different behaviors of these BAILs in polyesterification were investigated using dodecanoic acid and dodecan-1-ol as model compounds. Dodecan-1-ol was found to react with [BBSIm]HSO₄, yielding the sulfonic acid dodecyl ester of [BBSIm] cation, while it did not react with [BBSIm]Tf₂N. The sulfonate ester was found in turn to react with dodecanoic acid, leading to dodecyl dodecanoate. From these experiments, it can be inferred that, during polyesterifications in [BBSIm]HSO₄, the formation of the sulfonate ester intermediate protects -OH groups against etherification side reaction, but still allows the formation of the expected polyester by reaction with carboxylic acids. To explain the differences between these two BAILs, and considering the stronger acidity of H₂SO₄ with respect to that of Tf₂NH, we suggest that [BBSIm]HSO₄ could be composed of an imidazolium-based sulfonic acid and its

counterion HSO_4^- , while $[\text{BBSIm}]\text{Tf}_2\text{N}$ could consist of a mixture of imidazolium-based sulfonate zwitterion and proton donor Tf_2NH .

Several reaction conditions were tested. It was, of course, necessary to remove water from the reaction medium to obtain polyesters, and high molar mass polymers were obtained when the reaction was carried out either under moderate vacuum (10 mbar) or under nitrogen flow (500 mL/min), even though vacuum led to slightly higher molar masses. Increasing reaction temperature increased reaction rate, but had little influence on maximum molar masses. This work also confirms that the length of the alkyl group of the imidazolium cation and the counterion have an important impact on BAIL dissolving abilities. However, the solubility of reactants is not necessarily critical to their reactivity, since high molar mass polymers were obtained in $[\text{BBSIm}]\text{HSO}_4$ and $[\text{BBSIm}]\text{Tf}_2\text{N}$, in which large molten polymer particles (200 μm) formed during the reaction, as well as in $[\text{OBSIm}]\text{Tf}_2\text{N}$, in which polymer was soluble.

The polyesterification was also conducted in dilute BAIL/IL mixtures. Polyesters of lower molar mass were obtained after 30 min reaction when the BAIL concentration decreased, except for $[\text{BBSIm}]\text{Tf}_2\text{N}$, which was still efficient at 1/10 mol dilution in neutral $[\text{BMIm}]\text{Tf}_2\text{N}$. This may be connected to the very high reaction rate in this BAIL, where the maximum molar mass is reached after only 5 min reaction. At 1/10 dilution, 30 min reaction time appears to be enough to reach the maximum molar mass.

Even though the reaction is faster and the reaction medium is much less viscous in Tf_2N BAILS than in the HSO_4 one, the latter appears more suitable to the synthesis of well defined polyesters, as side reactions can be avoided.

II.4 Experimental

II.4.1 Chemicals

1-Butylimidazole (Aldrich, 98%), 1-octylimidazole (Iolitec, >99%), 1,4-butanediol (Aldrich, >99%), concentrated sulfuric acid (Aldrich, 96%), bis(trifluoromethylsulfonyl) imide (Iolitec, 99%, in 80% aqueous solution), dodecan-1-ol (Fluka, >99.5%), dodecanoic acid (Aldrich, >99%), 3-butyl-1-methylimidazolium hydrogen sulfate ($[\text{BMIm}]\text{HSO}_4$, Solvionic >98%), 3-butyl-1-methylimidazolium bis(trifluoromethylsulfonyl)imide ($[\text{BMIm}]\text{Tf}_2\text{N}$,

Solvionic >99.5%) and 3-octyl-1-methylimidazolium bis(trifluoromethylsulfonyl)imide ([OMIm]Tf₂N, Solvionic > 99.5%) were used as received. 12-Hydroxydodecanoic acid (Aldrich, 97%) was dried under vacuum to eliminate residual solvent prior to use.

II.4.2 Synthesis of BAILs

3-Butyl-1-(butyl-4'-sulfonic acid)imidazolium hydrogen sulfate ([BBSIm]HSO₄), 3-butyl-1-(butyl-4'-sulfonic acid)imidazolium bis(trifluoromethylsulfonyl)imide ([BBSIm]Tf₂N), and 3-octyl-1-(butyl-4'-sulfonic acid)imidazolium bis (trifluoromethylsulfonyl)imide ([OBSIm]Tf₂N) were synthesized according to known procedures,^{28,30} by reacting 1,4-butanediol with 1-alkylimidazole and converting resulting zwitterions to the corresponding BAILs by acidification with equimolar amount of sulfuric acid or bis(trifluoromethylsulfonyl)imide. The BAILs were dried under vacuum at 60 °C overnight. The water content of dried BAILs, measured by KF titration, was 0.49, 0.65 and 0.39 wt-% for [BBSIm]Tf₂N, [BBSIm]HSO₄ and [OBSIm]Tf₂N, respectively.

II.4.3 Polycondensation of 12-hydroxydodecanoic acid

In each experiment, 1 mmol (0.2630g) of 12-hydroxydodecanoic acid was mixed with 1 mmol of BAIL in a glass tube fitted with a nitrogen inlet and outlet and a magnetic stirring bar. The reaction was carried out at 90 or 110 °C for a predetermined time under nitrogen flow (500 mL/min) or under vacuum (10 mbar) to eliminate reaction water. At the end of reaction, 10 mL of isopropanol was added and the mixture heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and the precipitate was filtered, washed two times with 10 mL of isopropanol, then three times with 5 mL of diethyl ether. The polyester was then dried at 40 °C overnight under vacuum (10 mbar).

II.4.4 Reaction between dodecan-1-ol and [BBSIm]HSO₄

1 mmol (0.3581 g) of [BBSIm]HSO₄ was mixed with 1 mmol (0.1863 g) of dodecan-1-ol in a glass tube equipped with a nitrogen inlet and outlet and a magnetic stirring bar. The reaction was conducted at 110 °C for 30 minutes under nitrogen flow (500 mL/min) to strip water. The reaction product was analyzed by NMR and mass spectrometry as discussed in text.

II.4.5 Analytical Methods

NMR Spectroscopy: ^1H NMR spectra of the monomer and polymers were recorded on Bruker Avance 200 and 500 spectrometers in chloroform-*d* (ref. $\delta_{\text{H}}(\text{CHCl}_3) = 7.26$ ppm).

Steric Exclusion Chromatography (SEC): The SEC equipment consisted of a Waters 515 HPLC pump, a Waters 410 refractive index detector and a set of five Ultrastaygel columns ($50+500+10^3+10^4+10^5\text{\AA}$). CH_2Cl_2 was used as eluting solvent with a flow rate of 1 mL/min. Each sample was prepared with 8 mg of polymer, 1 mL of CH_2Cl_2 and 1 μL of toluene. For each analysis, 100 μL of sample was injected. All the analyses were carried out at room temperature. Polystyrene standards were used to calibrate the system.

Polarizing optical microscopy (POM): The polymerizations of 12-hydroxydodecanoic acid in BAILs (1/1 mol) were followed under a Leica DM2500 polarizing optical microscopy equipped with a camera. The temperature was programmed as follows: heating from 20 °C to 110 °C with a heating rate of 20 °C/min, holding for 5 min at 110 °C, then cooling down to 20 °C with a cooling rate of 20 °C/min.

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Chapter III

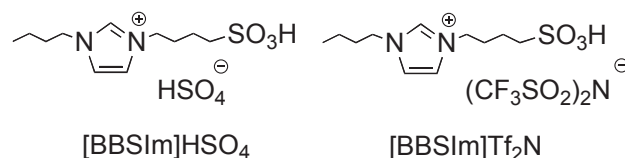
Synthesis of linear and hyperbranched polyesters in Brønsted acid ionic liquids

Abstract:

In this chapter, the polyesterification in BAILs was extended to the syntheses of linear polyesters of diols and equimolar diacids and hyperbranched polyester of 2,2-bis(hydroxymethyl)propanoic acid (BMPA). Linear polyesters of M_w up to 36000 g/mol were obtained in no more than 30 min. The polymerization was faster in [BBSIm]Tf₂N than in [BBSIm]HSO₄, but depolymerization was also observed in the former. Hyperbranched poly(BMPA)s with M_w up to 10000 g/mol were obtained in no more than 2 h in [BBSIm]HSO₄, which is higher than those reported in the literature for BMPA hyperbranched polyesterification, whereas the product obtained in [BBSIm]Tf₂N was insoluble, assigned to gelation by intermolecular ether formation. Nevertheless, it has been demonstrated that polyesterification in BAILs is a efficient method for different polyester synthesis.

III.1 Introduction

In Chapter 2, the model polyesterification reaction of 12-hydroxydodecanoic acid (12-HDA) was carried out in two BAILs with different anions (Scheme 3.1). This method was very efficient, as poly(12-HDA) of high molar mass was obtained in very short time at 90-110 °C. This Chapter reports the synthesis of linear and hyperbranched polyesters in these BAILs, whose double role as solvent and catalyst has been confirmed. Different linear polyesters were synthesized by post-polycondensation of oligomers in [BBSIm]HSO₄ and [BBSIm]Tf₂N, and different polymerization behaviors were also observed in these two BAILs. Besides, hyperbranched polyester from 2,2-bis(hydroxymethyl)propanoic acid was synthesized in [BBSIm]HSO₄.

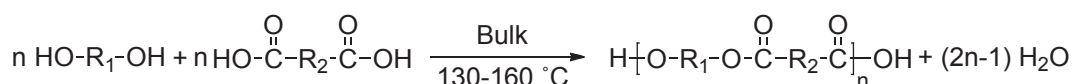


Scheme 3.1: Two BAILs used in the present study

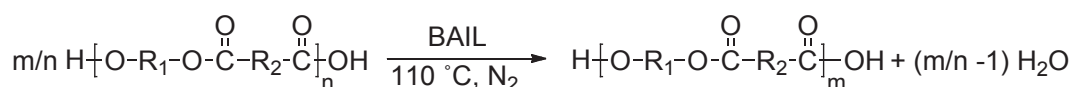
III.2 Results and discussion

III.2.1 Synthesis of linear polyester via post-polycondensation in BAILs

In order to ensure identical stoichiometry during a series of polycondensation studies, different oligomers were prepared in advance by heating the mixtures of a diol with an equimolar amount of diacid in the bulk without adding any catalyst (Scheme 3.2). Post-polycondensations of these oligomers were then studied in the BAILs at 110 °C under nitrogen flow (Scheme 3.3).



Scheme 3.2: Synthesis of oligomer in the bulk



Scheme 3.3: Post-polycondensation of oligomers in a BAIL at 110 °C under N₂ (500 mL/min)

The compositions of the oligomers and the corresponding polyesters are summarized in Table

3.1, where O_i represents an oligomer and P_i corresponds to the resulting polyester after post-polycondensation. The average molar masses and molar-mass dispersities of the starting oligomers are given in Table 3.2.

Table 3.1: Compositions of the oligoesters and corresponding copolyesters in the current study.

$$\text{H} \left[\text{O}-\text{R}_1-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}_2-\overset{\text{O}}{\parallel}{\text{C}} \right]_n \text{OH}$$

$\begin{matrix} \text{R}_1 \\ \text{R}_2 \end{matrix}$	$-(\text{CH}_2)_{12}-$	$-(\text{CH}_2)_6-$	$-(\text{CH}_2)_4-$
$-(\text{CH}_2)_2-$	O_1 / P_1	O_4 / P_4	O_7 / P_7
$-(\text{CH}_2)_4-$	O_2 / P_2	O_5 / P_5	---
$-(\text{CH}_2)_{10}-$	O_3 / P_3	O_6 / P_6	O_8 / P_8

Table 3.2: Mass-average molar mass (M_w), number-average molar mass (M_n) and molar-mass dispersity ($\mathcal{D}_M = M_w/M_n$) of oligomers, calculated from SEC data.

Oligomer	M_w (g/mol)	M_n (g/mol)	\mathcal{D}_M
O_1	4700	2290	2.1
O_2	2990	1500	2.0
O_3	4020	1850	2.2
O_4	3450	1570	2.2
O_5	2620	1500	1.7
O_6	2540	1720	1.5
O_7	1940	1340	1.5
O_8	2170	1200	1.8

At the beginning of the post-polycondensation, the oligomers were soluble in both [BBSIm]HSO₄ and [BBSIm]Tf₂N (Scheme 3.1). The reaction media quickly became viscous and heterogenous in [BBSIm]HSO₄, and it was observed that polymers precipitated in this BAIL. While it was always fluid, transparent and homogenous in [BBSIm]Tf₂N during the reaction. It is known that Tf₂N⁻ based ionic liquids are hydrophobic, and when polyester chains grow, polyesters become more hydrophobic and tend to be more soluble in [BBSIm]Tf₂N than in [BBSIm]HSO₄ which is more hydrophilic. This indicates that anions play an important role on BAILs' dissolving ability toward the polyesters. The structure of each resulting polymer was studied by NMR, which is presented here with the ¹H NMR spectrum of polyester P₁ as an example (Figure 3.1).

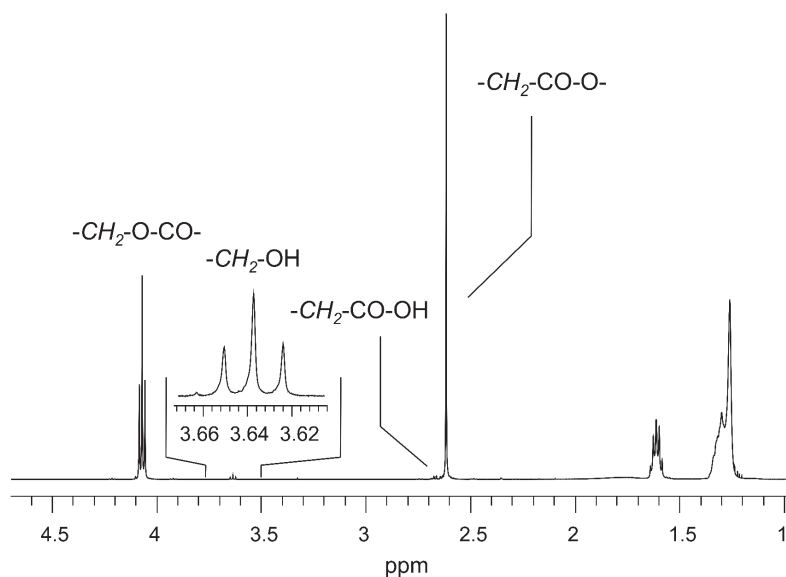


Figure 3.1: ^1H NMR Spectrum (CDCl_3 , 500 MHz) of P_1 synthesized in $[\text{BBSIm}]\text{HSO}_4$ (110 $^\circ\text{C}$, 1h, N_2).

As summarized in Table 3.3, comparing to conventional aliphatic polyester synthesis in the bulk, which requires high temperature (180-220 $^\circ\text{C}$) and long reaction time (5-7 h), the syntheses of linear polyesters were very efficient in the BAILs, except for the case of O_7 and O_8 , which will be discussed afterwards. High molar-mass polyesters were obtained in no more than 30 min in both $[\text{BBSIm}]\text{Tf}_2\text{N}$ and $[\text{BBSIm}]\text{HSO}_4$. At the early stage of reaction, the post-polycondensation was more efficient in $[\text{BBSIm}]\text{Tf}_2\text{N}$ than in $[\text{BBSIm}]\text{HSO}_4$. For example, the post-polycondensation of oligomers O_1 to O_3 yielded polyesters with molar mass higher than 20000 g/mol in 30 min in $[\text{BBSIm}]\text{HSO}_4$; while it took only 15 min to get even higher molar-mass polymers in $[\text{BBSIm}]\text{Tf}_2\text{N}$ (Table 3.3). Besides, the molar-mass dispersity ($\mathcal{D}_M = M_w/M_n$) of the polymers obtained in the two BAILs was close to 2, which is the theoretical \mathcal{D}_M value for polycondensation polymers with the most probable distribution of molar masses.

Table 3.3: Polycondensation of oligomers in BAILs (oligomer/BAIL = 1/1 mol/mol), 110 °C, nitrogen flow of 500 mL/min). Mass-average molar mass (M_w) and molar-mass dispersity ($\mathcal{D}_M = M_w/M_n$) calculated from SEC data.

Starting Oligomer	[BBSIm]Tf ₂ N						[BBSIm]HSO ₄					
	Time (min)	M_w (g/mol)	\mathcal{D}_M	Time (min)	M_w (g/mol)	\mathcal{D}_M	Time (min)	M_w (g/mol)	\mathcal{D}_M	Time (min)	M_w (g/mol)	\mathcal{D}_M
O ₁	15	24400	2.3	30	29000	2.6	15	23200	2.3	30	28000	2.1
O ₂	15	26300	1.7	30	25700	1.8	15	23300	1.8	30	26000	1.9
O ₃	15	36200	1.9	30	32600	1.7	15	16300	1.9	30	22000	2.0
O ₄	15	21000	1.9	30	12100	2.4	15	13900	1.6	30	19000	1.9
O ₅	15	21300	1.9	30	23500	2.1	15	13200	1.7	30	19200	1.9
O ₆	15	16900	1.8	30	22500	2.0	15	10300	1.7	30	16600	1.8
O ₇	5	4800	1.7	30	3400	1.8	5	9000	1.9	30	7600	2.4
O ₈	5	6400	1.6	30	4700	1.7	5	10200	1.8	30	9900	1.8

When the polycondensations of oligomers O₇ and O₈ were carried out in [BBSIm]Tf₂N and [BBSIm]HSO₄, high molar-mass polymers could not be obtained. In contrast to the polycondensation of oligomers O₁ to O₆, the reactions of O₇ and O₈ showed reverse tendency, as the molar mass of the polymers obtained in [BBSIm]Tf₂N was lower than that obtained in [BBSIm]HSO₄ during the first 5 min. As shown in the ¹H NMR spectra of oligoester O₈ and its corresponding polyester P₈ for example (Figure 3.2), equimolar amount of hydroxyl and carboxylic acid end groups are found in oligomer O₈ as starting reactant, but when the reaction was maintained in [BBSIm]Tf₂N after 5 min, the amount of hydroxyl end groups became much lower than carboxylic acid end groups. The OH/COOH ratio dropped from 1:1 to 1:6 in 5 min, which indicates that side reactions leading to the disappearance of hydroxyl groups occurred during the post-polycondensation. The existence of a side reaction was confirmed by the presence of tetrahydrofuran (THF) in the exhaust of the post-polycondensations of both O₇ and O₈, which are composed of 1,4-butanediol and a diacid (Table 3.2). As observed in the work on poly(oxyalkylene) synthesis in BAILs (Chapter IV),¹ 1,4-butanediol could hardly be polymerized but the formation of THF was preferred in [BBSIm]Tf₂N. This explains, therefore, why 4-hydroxybutyl end units disappeared during the post-condensations of oligomers O₇ and O₈. THF formation results in COOH/OH stoichiometric unbalance, and, therefore, limits to low molar mass polymers (Scheme 3.4).

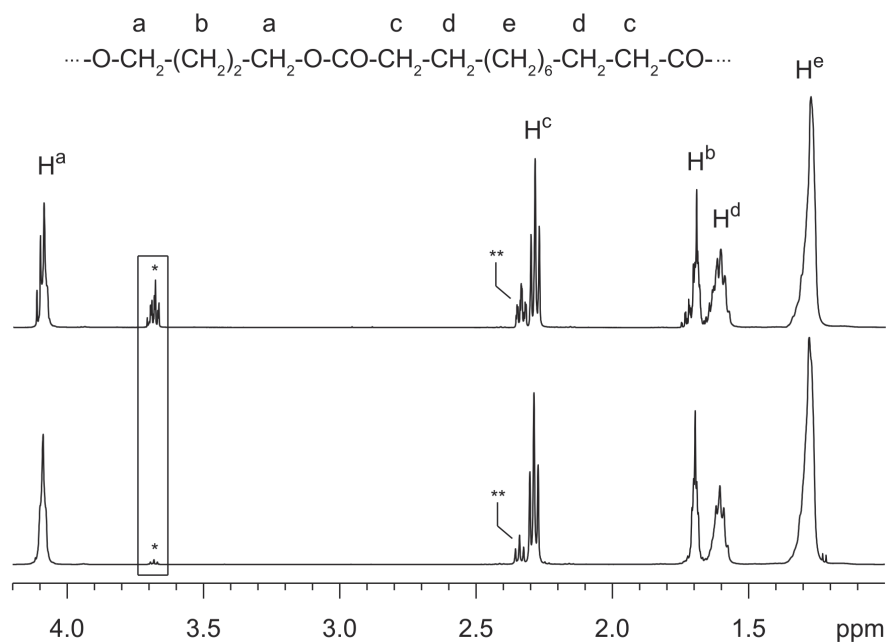
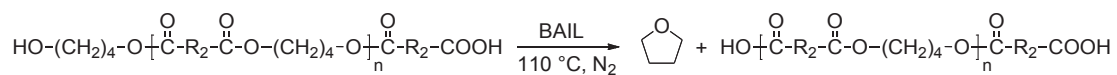


Figure 3.2: ^1H NMR Spectra (CDCl_3 , 500 MHz) of oligomer O_8 (upper trace) and P_8 (lower trace) synthesized in $[\text{BBSIm}]\text{Tf}_2\text{N}$ ($110\text{ }^\circ\text{C}$, 5 min, N_2), *: $-\text{CH}_2-\text{OH}$ end group, **: $-\text{CH}_2-\text{COOH}$ end group.



Scheme 3.4: Formation of THF in the post-polymerization of oligomers O_7 and O_8 , $\text{R}_2 = -(\text{CH}_2)_2-$ and $-(\text{CH}_2)_{10}-$.

The evolutions of the SEC chromatograms during O_1 post-condensation were followed and are presented here with an example in Figure 3.3. The mass-average molar mass M_w of oligomer O_1 was around 4700 g/mol (Table 3.2). After heating the reaction mixture at $110\text{ }^\circ\text{C}$ for 5 min, M_w increased quickly and reached about 30000 g/mol after 60 min reaction.

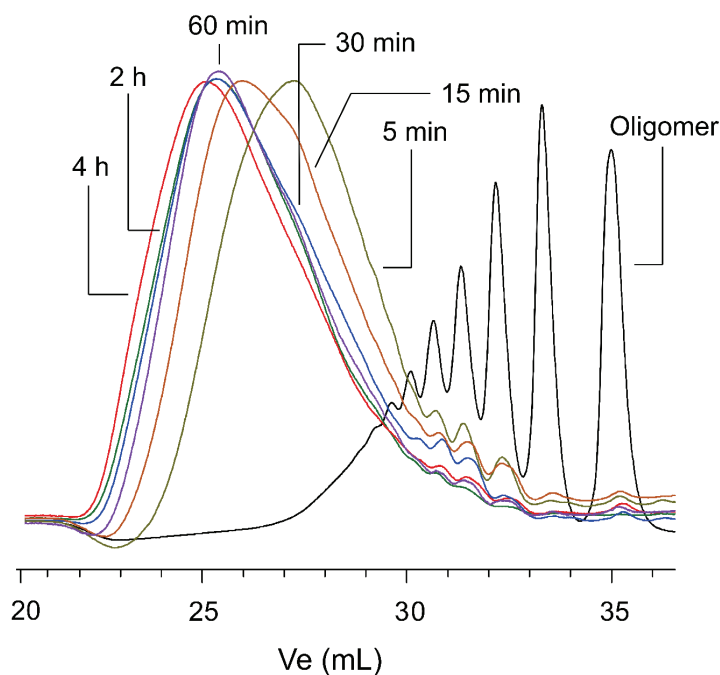


Figure 3.3: Post-polycondensation of oligomer O_1 in $[BBSIm]HSO_4$ at $110\text{ }^\circ\text{C}$ ($N_2 = 500\text{ mL/min}$): SEC chromatograms (CH_2Cl_2 , 1.0 mL/min) with different reaction times.

As described in Chapter 2, the anions of the BAILs play an important role on polyesterification behavior. The same phenomenon was also observed in the current study (Figure 3.4). At the beginning of the post-polycondensations of O_1 and O_3 , which are composed of 1,12-dodecanediol and a diacid with respectively the shortest and the longest carbon chain (Table 3.1), and it can be seen from Figure 3.4 that during the first 30 min, the molar masses of the polymers increased steadily in both $[BBSIm]HSO_4$ and in $[BBSIm]Tf_2N$. Besides, the post-polycondensation was much faster in $[BBSIm]Tf_2N$ than in $[BBSIm]HSO_4$, as only 15 min was required to get a molar mass of around 35000 g/mol in the former while it took 30 min to obtain the highest molar mass in the latter. After 30 min, the molar mass in $[BBSIm]HSO_4$ became nearly constant. It is worthwhile mentioning that the reaction medium in $[BBSIm]HSO_4$ quickly became so viscous that the stirrer stopped agitating. Consequently, residual water generated from the reaction could not be totally removed, which, therefore, prevents polyesterification from completion and could explain why the molar mass stopped growing. On the other hand, in $[BBSIm]Tf_2N$ the molar masses of the polyesters begin decreasing after more than 30 min reaction time. As described in Chapter 2, this phenomenon can be assigned to polymer scissions.

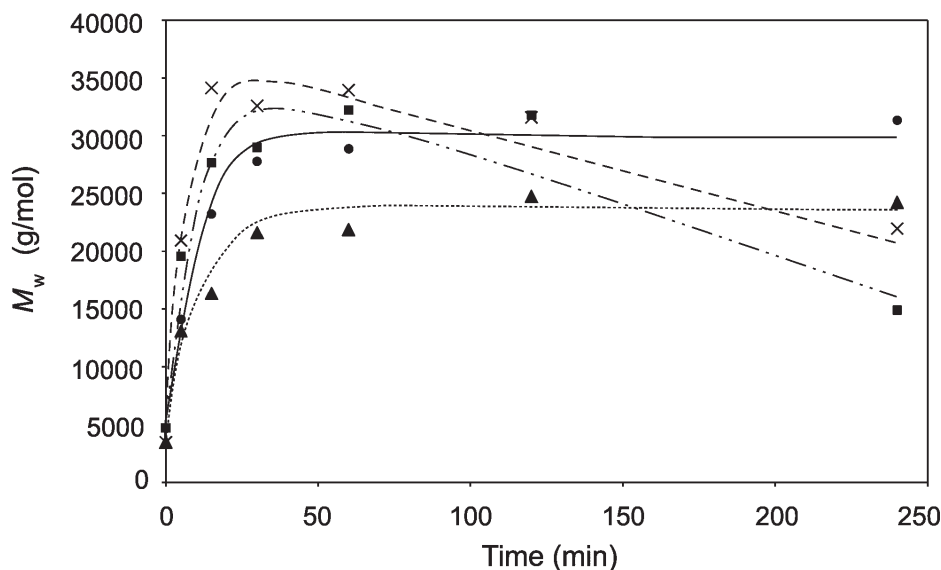


Figure 3.4: Evolution of M_w at of polyester P₁ and P₃ in [BBSIm]HSO₄ and [BBSIm]Tf₂N: post-polycondensation at 110 °C with nitrogen flow (500 ml/min), Mass-average molar mass (M_w) calculated from SEC data. O₁ in [BBSIm]Tf₂N (■), O₁ in [BBSIm]HSO₄ (▲), O₃ in [BBSIm]Tf₂N (×) and O₃ in [BBSIm]HSO₄ (●).

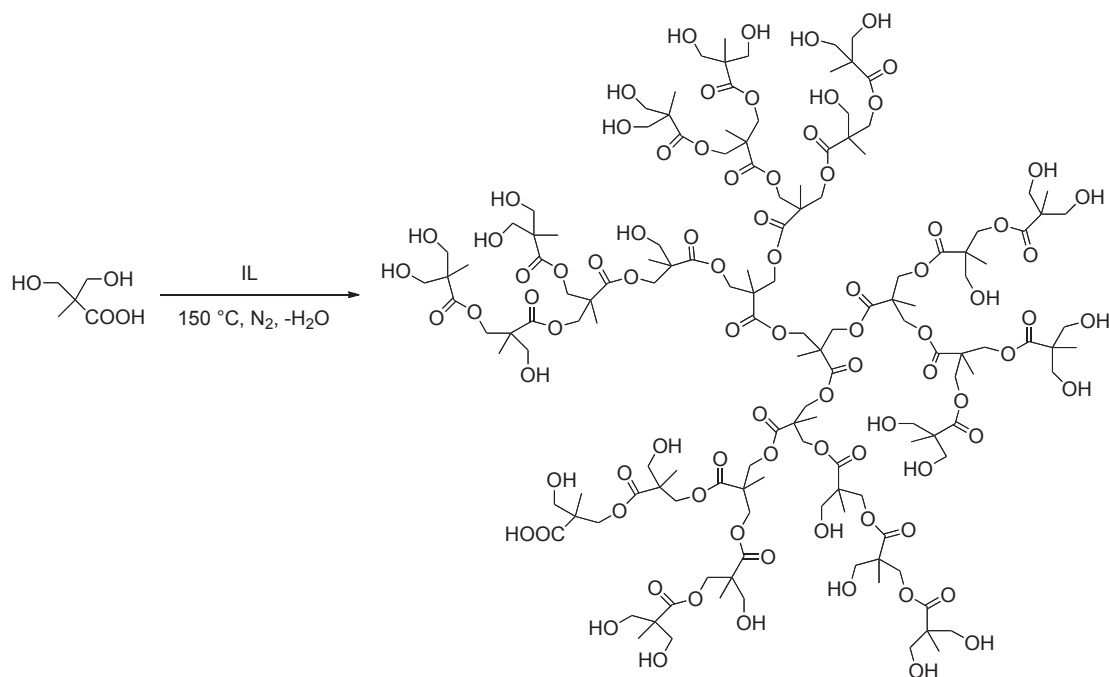
Nevertheless, high molar mass polyesters from oligomers O₁ to O₆ were obtained in both BAILs in 15-30 minutes, which tells again, that they can be used not only as solvents, but also as catalysts for acid-catalyzed polymerizations. Besides, a simple means to avoid the polymer degradation in [BBSIm]Tf₂N is to stop the reaction after 15 min, once high molar mass polymers have already been formed.

III.2.2 Polycondensation of 2,2-bis(hydroxymethyl)propanoic acid (BMPPA) in BAILs

Different from linear polymers, hyperbranched macromolecules contain a large number of branch points and functional end groups, and exhibit some properties similar to those of dendrimers.²⁻⁴ They are generally obtained by one-pot polymerization⁵⁻¹¹ One example is the hyperbranched polyester of 2,2-bis(hydroxymethyl)propanoic acid (BMPPA), which is conventionally synthesized in the bulk with addition of an inorganic acid, during long reaction time (≥ 24 h).^{12,13} In this chapter, we describe the polycondensation of BMPPA in [BBSIm]Tf₂N and [BBSIm]HSO₄.

Hyperbranched polyester poly(BMPPA) was synthesized by mixing BMPPA with an equimolar amount of BAIL at 150 °C under nitrogen flow to eliminate reaction water (Scheme 3.5). No catalyst was added in reaction medium. During the polymerization, the reaction mixture was transparent and visually homogenous in both BAILs. The viscosity increased with time, and at

the end of the reaction it became so viscous that the stirrer stopped agitating.



Scheme 3.5: Synthesis of hyperbranched polyester from BMPA in IL at 150 °C under nitrogen flow.

A preliminary study was first conducted by comparing conventional BMPA polymerization in the bulk and in two different BAILs (Table 3.4). When the polycondensation of BMPA was carried out in the bulk in the presence of a catalyst, *p*-toluenesulfonic acid (*p*-TSA), 8 h was required to obtain a polyester with a M_w of 7160 g/mol (Entry 1). When the reaction was carried out in [BBSIm]HSO₄, however, it took only 2 hours to obtain a polymer with a M_w of 9690 g/mol (Entry 3). But when the polymerization was conducted in [BBSIm]Tf₂N, the resulting product was insoluble in any solvent. It is known that intermolecular etherification takes place during BMPA polymerization (Scheme 3.6),¹² which, in some conditions, gives rise to gelation. As proved in our investigations (Chapter I and IV), ether can also be formed from hydroxyl groups in [BBSIm]Tf₂N. The etherification of some of the numerous poly(BMPA) hydroxyl end groups can explain the formation of cross-links, which leads to polymer insolubility.^{7,14}

Table 3.4: Polycondensation of BMPA at 150 °C. Mass-average molar mass (M_w) and molar mass dispersity ($\mathcal{D}_M = M_w/M_n$) calculated from SEC data, degree of branching (DB) determined by quantitative ^{13}C NMR experiment.

Entry	BAIL or catalyst	Time (h)	M_w^a (g/mol)	\mathcal{D}_M	DB ^b
1	<i>p</i> -TSA ^c	8	7160	3.3	0.40
2	[BBSIm]Tf ₂ N ^d	2	- ^e	- ^e	- ^e
3	[BBSIm]HSO ₄ ^d	2	9690	1.6	0.44

^a Values from SEC in DMF

^b Values from quantitative ^{13}C NMR (DMSO-*d*₆ with Cr(C₅H₇O₂)₃)

^c Reaction in the bulk, catalysed by 0.5 wt-% *p*-TSA

^d Reaction in IL with a nitrogen flow of 500 mL/min

^e Insoluble polymer

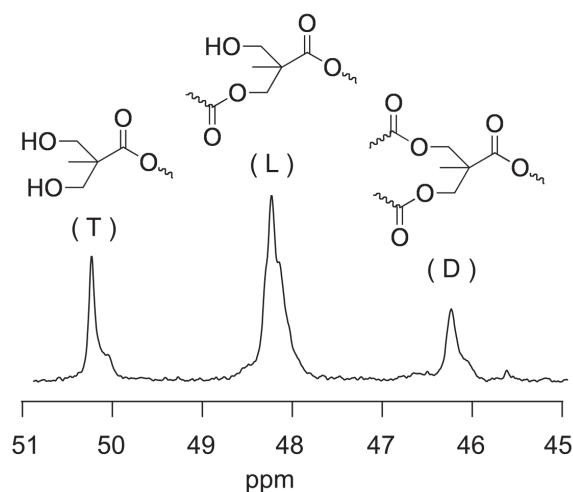
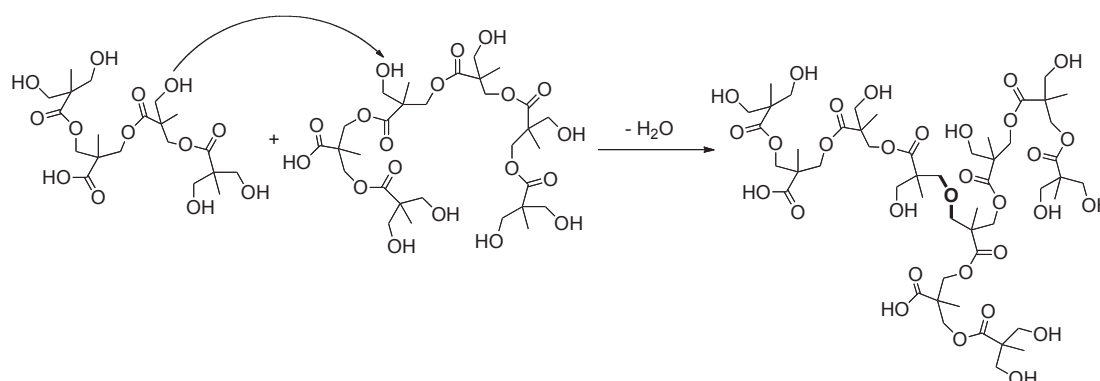


Figure 3.5: Different units in ^{13}C NMR spectrum (DMSO-*d*₆, 300 MHz) of poly(BMPA)



Scheme 3.6: Intermolecular etherification of poly(BMPA).

The degree of branching (DB) of the resulting polymer was determined by quantitative ^{13}C

NMR experiments, according to Frey's definition (Equation 1),¹⁵ where D and L correspond, respectively, to quaternary carbon integrations of dendritic and linear units of the polyester (Figure 3.5). The DB values of all the polyesters were lower than 0.5, which is the "most probable" value for a one-step hyperbranched polycondensation of AB₂-type monomers.¹⁵ These results are similar to those obtained from the bulk synthesis of poly(BMPA), and indicate a slight excess of linear units with respect to the theoretical one for a random AB₂-polymer.

$$DB = 2D/2D + L \quad \text{Equation 3.1}$$

The effect of water elimination was studied. A blank experiment was first carried out without evaporating water in the reaction mixture (Table 3.5, Entry 1), and no polymer could be obtained. On the other hand, when water was evaporated by N₂ flow (Entry 2 and 3), the polyesterification performed much better, which confirms that elimination of water is crucial to BMPA polyesterification.

Table 3.5: Polycondensation of BMPA in [BBSIm]HSO₄ (at 150 °C, 2 h, BMPA/[BBSIm]HSO₄ = 1/1 mol/mol). Mass-average molar mass (M_w) and dispersity ($D_M = M_w/M_n$) calculated from SEC data, degree of branching (DB) calculated by quantitative ¹³C NMR.

Entry	Water elimination	M_w^a (g/mol)	D_M	DB ^b
1	Nil	-	-	-
2	N ₂ (200 ml/min)	6800	1.5	0.40
3	N ₂ (500 ml/min)	9690	1.6	0.44

^a Values from SEC in DMF

^b Values from ¹³C quantitative NMR (DMSO-*d*₆ with Cr(C₅H₇O₂)₃)

The molar mass evolution of poly(BMPA) against time was studied in [BBSIm]HSO₄ under two different nitrogen flow rates (Figure 3.6, Table 3.6). When the flow rate was 200 mL/min, the molar mass increased steadily at the beginning of the reaction, arriving at $M_w = 6810$ g/mol after 2 h reaction, and then remained almost constant. When the flow rate was 500 mL/min, the molar mass increased rapidly to 9750 g/mol after only 1 h and then increased slightly to *ca.* 11000 g/mol for longer reaction time, which is a higher molar mass than those reported in the literature for BMPA hyperbranched polyesterification.¹³ Since water was stripped more efficiently from the reaction media with higher N₂ flow rate, and the reaction was shifted to

higher conversion, leading to higher molar mass polymers. Meanwhile, DB values increased from 0.36 to 0.49, i.e. to that of a completely random distribution of linear, dendritic and terminal units in polymer chains.

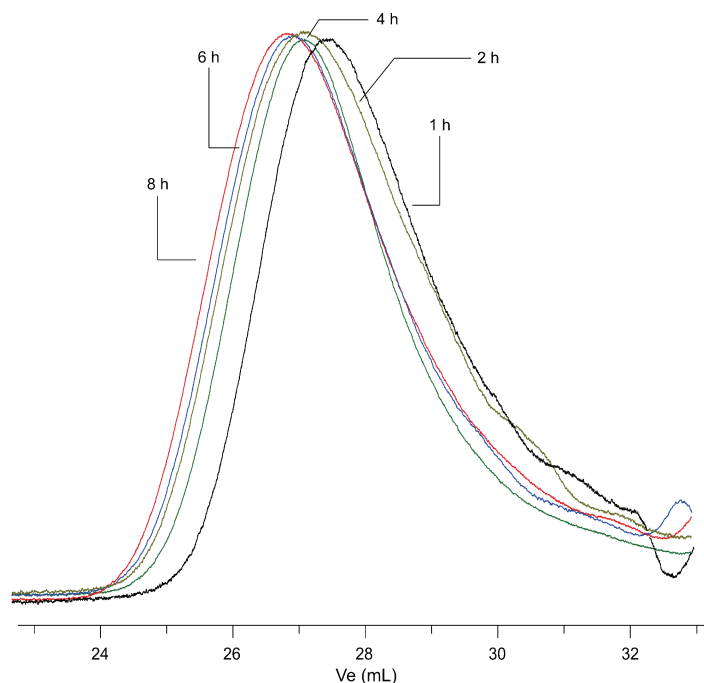


Figure 3.6: Synthesis of poly(BPMA) in [BBSIm]HSO₄ at 150 °C (N₂ = 500 ml/min): SEC chromatograms (DMF/LiBr, 0.8 ml/min) with different reaction times

Table 3.6: Influence of nitrogen flow rate on polycondensation of BPMA in [BBSIm]HSO₄ (BPMA/[BBSIm]HSO₄=1/1 mol/mol, at 150 °C). Mass-average molar mass (M_w) and dispersity ($\mathcal{D}_M = M_w/M_n$) calculated from SEC data, degree of branching (DB) calculated by quantitative ¹³C NMR experiment.

Time (h)	N ₂ flow rate = 200 mL/min			N ₂ flow rate = 500 mL/min		
	M_w (g/mol)	\mathcal{D}_M	DB	M_w (g/mol)	\mathcal{D}_M	DB
1	-	-	-	9750	1.8	0.36
2	6810	1.5	0.40	9690	1.6	0.44
6	7580	1.7	0.40	10420	1.5	0.48
8	7200	1.6	0.43	10940	1.6	0.49

III.3 Conclusion

BAILs were applied as both solvents and catalysts to linear polyester syntheses via post-polycondensation of pre-synthesized oligomers from diols and diacids. Linear polyesters with molar mass up to $M_w = 36000$ g/mol were obtained in no more than 30 min.

Hyperbranched polyester poly(BMPA) with M_w of around 10000 g/mol was also obtained in [BBSIm]HSO₄ in 2 h, which is much more efficient than the synthesis in the bulk. Besides, according to the DB values of the resulting poly(BPMA)s, at long reaction time in [BBSIm]HSO₄, the polymer architecture is more branched than that obtained in the bulk. However, the poly(BPMA) obtained in [BBSIm]Tf₂N was not soluble, probably due to intermolecular etherification, which resulted in gelation.

III.4 Experimental

III.4.1 Chemicals

1-Butylimidazole (Aldrich, 98%), 1,4-butanediol (Aldrich, >99%), concentrated sulfuric acid (Aldrich, 96%), bis(trifluoromethylsulfonyl) imide (Iolitec, 99%, in 80% aqueous solution) were used as received. 1,4-butanediol (Aldrich, 99%), 1,6-hexanediol (Aldrich, 99%), 1,12-dodecanediol (Aldrich, 99%), succinic acid (Aldrich, 99%), glutaric acid (Aldrich, 99%), dodecanedioic acid (Aldrich, 99%) were dried under vacuum to eliminate residual solvent prior to use. 2,2-bis(hydroxymethyl)propanoic acid (BMPA, Acros, >99%) was recrystallized three times in ethanol and thoroughly dried prior to use.

III.4.2 Synthesis of BAILS

3-Butyl-1-(butyl-4'-sulfonic acid)imidazolium hydrogen sulfate ([BBSIm]HSO₄), 3-butyl-1-(butyl-4'-sulfonic acid)imidazolium bis(trifluoromethylsulfonyl)imide ([BBSIm]Tf₂N) were synthesized according to known procedures,^{1,16,17} by reacting 1,4-butanediol with 1-alkylimidazole and converting resulting zwitterions to the corresponding BAILS by acidification with equimolar amount of sulfuric acid or bis(trifluoromethylsulfonyl)imide.

III.4.3 Syntheses of oligoesters

Syntheses of different oligoesters are demonstrated with an example as follows : 0.2 mol of succinic acid (23.618 g) and 0.2 mol of 1,12-dodecanediol (40.468 g) were introduced in a reactor equipped with a nitrogen inlet and outlet and an overhead stirrer. The mixture was heated at 130 °C for 1 h, 140 °C for 1 h, 150 °C for 1 h and then 160 °C for another 2 h. It was then cooled down to room temperature and 56.84 g of white to yellowish product was obtained (yield: 94%).

III.4.4 Post-polycondensation of oligomers in BAILs

The process of post-polycondensation is described with an example as follows: 285.5 mg of oligo(dodecane succinate) was mixed with either 542.2 mg (1 mmol) of [BBSIm]Tf₂N or 358.5 mg (1 mmol) of [BBSIm]HSO₄ in a glass tube equipped with a nitrogen inlet and outlet and a magnetic stirrer. The reaction was carried out at 110 °C for a predetermined time under nitrogen flow (500 mL/min) to eliminate reaction water. At the end of the reaction, 10 mL of isopropanol was added and the mixture heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and the precipitate was filtrated, washed two times with 10 mL of isopropanol, then 3 times with 5 mL of diethyl ether. The polyester was then dried at 40 °C overnight under vacuum (10 mbar).

III.4.5 Polycondensation of BMPA in BAILs

The process of BMPA polycondensation is described with an example as follows : 394.7 mg (2.942 mmol) of BMPA was mixed with 1054.5 mg (2.942 mmol) of [BBSIm]HSO₄ in a glass tube equipped with a nitrogen inlet and outlet and a magnetic stirrer. The reaction was carried out at 150 °C for a predetermined time under nitrogen flow (200-500 mL/min) to eliminate reaction water. The reaction was then quenched by cooling down to room temperature and adding 10 mL of isopropanol. The mixture was heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and separated by centrifugation. The supernatant was removed and the washing and separation procedure was then repeated twice. The white solid was finally filtered and dried at 80 °C overnight under vacuum (10 mbar).

III.4.6 Analytical Methods

NMR Spectroscopy: ¹H NMR spectra of all the linear polyesters were recorded on Bruker Avance 500 spectrometer in chloroform-*d* (ref. δ_H(CDCl₃) = 7.26 ppm). The ¹³C NMR spectra of poly(BMPA) were recorded on Bruker AC 300 spectrometer in DMSO-*d*₆ (ref. δ_C(DMSO) = 39.52 ppm). Quantitative ¹³C NMR spectra were recorded using inverse gated decoupling mode with a 2 S pulse delay and the addition of chromimun acetylacetonante (5 mg).

Steric Exclusion Chromatography (SEC):

The linear polyesters were characterized by using the SEC equipment consisted of a Waters 515 HPLC pump, a Waters 410 refractive index detector and a set of five Ultrastaygel

columns (50+500+10³+10⁴+10⁵Å). CH₂Cl₂ was used as eluting solvent with a flow rate of 1 mL/min. Each sample was prepared with 8 mg of polymer, 1 mL of CH₂Cl₂ and 1 mL of toluene. For each analysis, 100 ml of sample was injected. All the analyses were carried out at room temperature. Polystyrene standards were used to calibrate the system.

The hyperbranched polyesters poly(BPMA) were analyzed by SEC in DMF (+ LiBr, 1 g/L). The analyses were performed at 60 °C, and at a flow rate of 0.8 ml/min, at a polymer concentration of 8 mg/mL after filtration. The steric exclusion was carried out on two PSS GRAM 1000 Å columns (8 × 300 mm; separation limit: 1 to 1000 kg/mol) and one PSS GRAM 30 Å (8 × 300 mm; separation limit: 0.1 to 10 kg/mol) coupled with three detectors (Viscotek, TDA 305) : a differential refractive index (RI) detector, a viscosimeter detector and a light scattering (LS) detector (laser λ = 670 nm at 7° and 90°), PMMA standards were used to calibrate the system.

III.5 References

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Chapter IV

Poly(oxyalkylene) synthesis in Brønsted acid ionic liquids

Abstract:

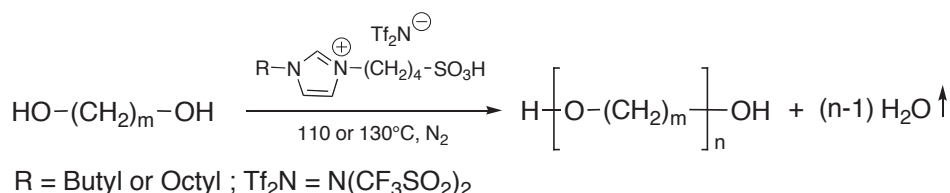
Inspired by the etherification side reaction observed when the polyesterification was carried out in [BBSIm]Tf₂N (Chapter 2), the polyetherification of diols was studied in Brønsted acid ionic liquids (BAILs) with Tf₂N⁻ anion. This method was very efficient for the synthesis of linear poly(oxyalkylene)s from diols with 7-12 methylene units, and high molar mass polyethers were obtained at relatively low temperature (130 °C). On the other hand, the reactions of 1,4-butanediol and 1,6-hexanediol in the BAILs favored cyclic ether formation, yielding THF and oxepane respectively. The NMR study showed that some double bond end groups were formed, followed by the dehydration of hydroxyl end groups, and were in turn partially hydroaminated by Tf₂NH.

IV.1 Introduction

Poly(oxyalkylene)s are generally synthesized by ring-opening polymerizations of cyclic ethers, such as poly(oxyethylene),^{1,2} poly(oxytrimethylene),³ poly(oxytetramethylene),⁴ poly(oxyhexamethylene),⁵ but polyetherification of more methylene units still remains unknown by far, probably because the cyclic ethers with more than 7 members are not commercially available. Another polyetherification process is based on Williamson reaction between activated diols and dihalides or involving monomers with both hydroxy and halide groups.⁶⁻⁸ It is a very simple and popular method, but rather ineffective when dealing with aliphatic diols.⁹ It is also reported that Williamson polyetherifications can be carried out under heterogeneous conditions with phase-transfer catalysts.¹⁰⁻¹⁴ However, polyethers precipitate during the reactions, which inevitably limits the formation of high molar mass polymers.

In the early 1950s', Rhoad and Flory¹⁵ reported the self-condensation of 1,10-decanediol and of benzylic diols. In their pioneering work, the polyethers were synthesized in the presence of sulfamic or sulfuric acids at elevated temperature (200-300 °C). Later on, Kobayashi et al.¹⁶ also conducted the synthesis of linear polyoxyalkylenes with the same method in the presence of H₂SO₄ and (C₂H₅)₂O·BF₃, but the polymer molar mass was not reported. These results encouraged us to try direct polyetherification of different dialcohols carried out in Brønsted acid ionic liquids (BAILs), as to the latter a burgeoning attention has been paid in recent years. BAILs are nonvolatile, easily recyclable reaction media of highly thermal and chemical stabilities,¹⁷⁻²⁰ which can be used as both alternatives of organic solvent and catalysts for acid-catalyzed reactions.²¹⁻²⁴

In this chapter, we report, to our best knowledge, the first direct polyetherification of different aliphatic diols in BAILs, namely 4-(3'-butyl-1'-imidazolio)-1-butanefluoroborate ([BBSIm]Tf₂N) and 4-(3'-octyl-1'-imidazolio)-1-butanefluoroborate ([OBSIm]Tf₂N). High molar mass polyethers were produced in these two BAILs (Scheme 4.1), which served as both reaction media and catalysts.



Scheme 4.1: Synthesis of linear polyethers in 3-alkyl-1-(butyl-4-sulfonic acid)imidazolium bis(trifluoromethylsulfonyl)imide ([RBSIm]Tf₂N), m>6.

IV.2 Results and discussion

A preliminary study on the direct polyetherification of 1,12-dodecanediol was conducted in the two BAILs, under various experimental conditions (Table 4.1). The influence of temperature was first studied, and as expected for a kinetically controlled polymerization, the reaction was slower at lower temperature, as the molar masses of the resulting products were only about 7000-8000 g/mol at 110 °C (Entries 1 and 2). However, when the reaction was carried out at 130 °C, high molar mass polyethers were produced, as the molar mass increased to *ca.* 23000 g/mol (Entries 3 and 4). It seems that the length of the alkyl substituent of imidazolium-based ionic liquids does not necessarily have an impact on 1,12-dodecanediol polyetherification. For example, when the polyetherification was carried out in the two BAILs at 110 °C, no significant difference was observed between the molar masses or polydispersities of the corresponding polyethers (Entries 1 and 2). The same tendency was observed at 130 °C (Entries 3 and 4).

Table 4.1: Polyetherification of 1,12-dodecanediol in BAILs under N₂ flow (200 mL/min). Mass-average molar mass (M_w) and dispersity ($\mathcal{D}_M = M_w/M_n$) calculated from SEC data and melting temperature (T_m) measured by DSC.

Entry	BAIL	T (°C)	Monomer/ BAIL ^a (mol/mol)	Time (h)	Yield ^b (%)	M_w (g/mol)	\mathcal{D}_M
1	[OBSIm]Tf ₂ N	110	2/1	63	73.2	8000	1.9
2	[BBSIm]Tf ₂ N	110	2/1	63	72.0	7300	1.9
3	[BBSIm]Tf ₂ N	130	2/1	63	85.7	22000	2.2
4	[OBSIm]Tf ₂ N	130	2/1	63	71.2	23000	2.4
5	[OBSIm]Tf ₂ N	130	3/1	65	72.6	21000	3.8
6	[OBSIm]Tf ₂ N	130	1/1	96	69.0	12000	4.4
7	[BBSIm]Tf ₂ N	130	1/1	70	63.8	14000	3.7

^a Starting monomer ratio between monomer and BAIL

^b Isolated yield

The influence of diol concentration on the polyetherification was also examined. No significant molar mass variation was observed when the monomer/BAIL molar ratio increased from 2:1 to 3:1 (Entries 4 and 5), though it was found that the viscosity of the reaction medium increased. On the other hand, when the molar ratio decreased to 1:1 (Entries 6 and 7), even though the reactions were maintained for a longer time (70 to 96 h), the molar masses of the resulting poly(oxydodecamethylene)s were only 12000 and 14000 g/mol, which shows that the reaction is less effective in a diluted medium. It is also worthwhile mentioning that the dispersity (D_M) of the polyether was close to the theoretical value of 2 when the molar ratio was 2 :1. As around 20% of 1,12-dodecanediol was evaporated with the N₂ flow, the recovered yield of each reaction was about or less than 80%. Whatever the experimental conditions were, the molar mass was limited to 23000 g/mol, which may be due to diffusion control of the kinetics when the viscosity of the reaction medium increases with chain growth or the existence of side reactions during the polymerization.

The influence of reaction time on 1,12-dodecanediol polyetherification in [BBSIm]Tf₂N was also studied (Figure 4.1). It was found that the molar mass increased almost proportionally with time between 10 h to 40 h ($M_w = 6000-20000$ g/mol). After that, the molar mass grew slowly until $M_w = 23000$ g/mol after 63 h reaction.

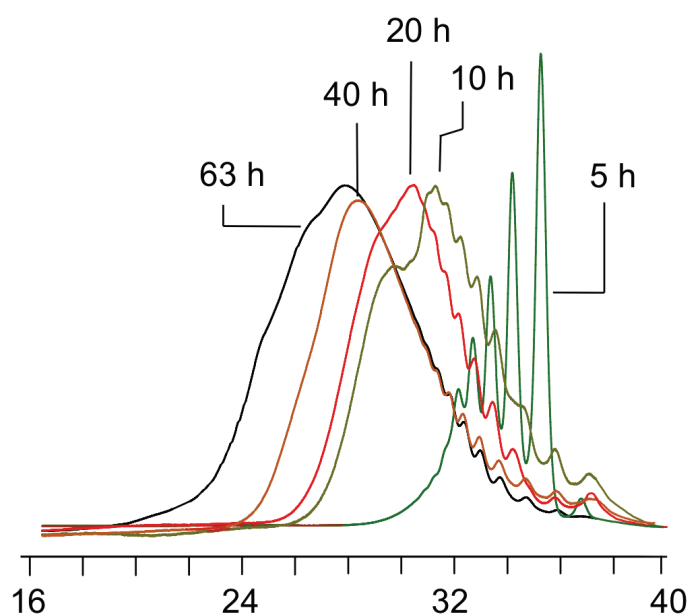
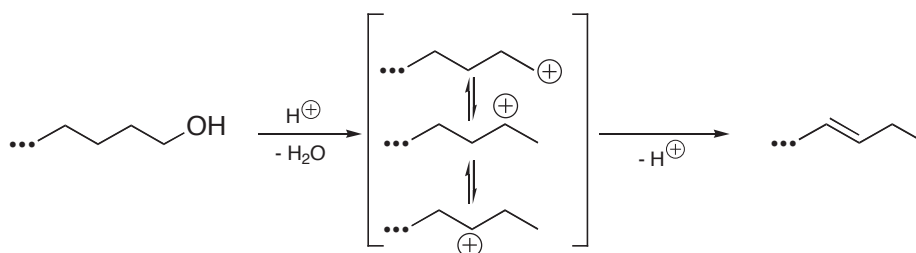


Figure 4.1: Polyetherification of 1,12-dodecanediol in [BBSIm]Tf₂N at 130 °C under N₂ flow (200 mL/min), diol/BAIL= 2/1 : SEC chromatograms (CH₂Cl₂, 1.0 mL/min)

The ^1H NMR spectra of the resulting poly(oxydodecamethylene)s present the expected main peaks of the repeating units but no OH end-group resonance ($\text{CH}_2\text{-OH}$ at 3.6 ppm). However, they present a peak of very low intensity at 5.4 ppm, together with other resonances ($\text{H}^{1,2,5,1'',5'',3''',5'''}$, Fig. 2), which are assigned to unsaturations by 2D ^1H - ^1H NMR (Figure 4.A1). It appears that H^+ -catalyzed hydroxyl end group dehydration side reaction took place, followed by carbocation migration, leading to the formation of a double bond in α , β and γ position to the original -OH group (Scheme 2).



Scheme 4.2: Dehydration of alcohol in BAILs

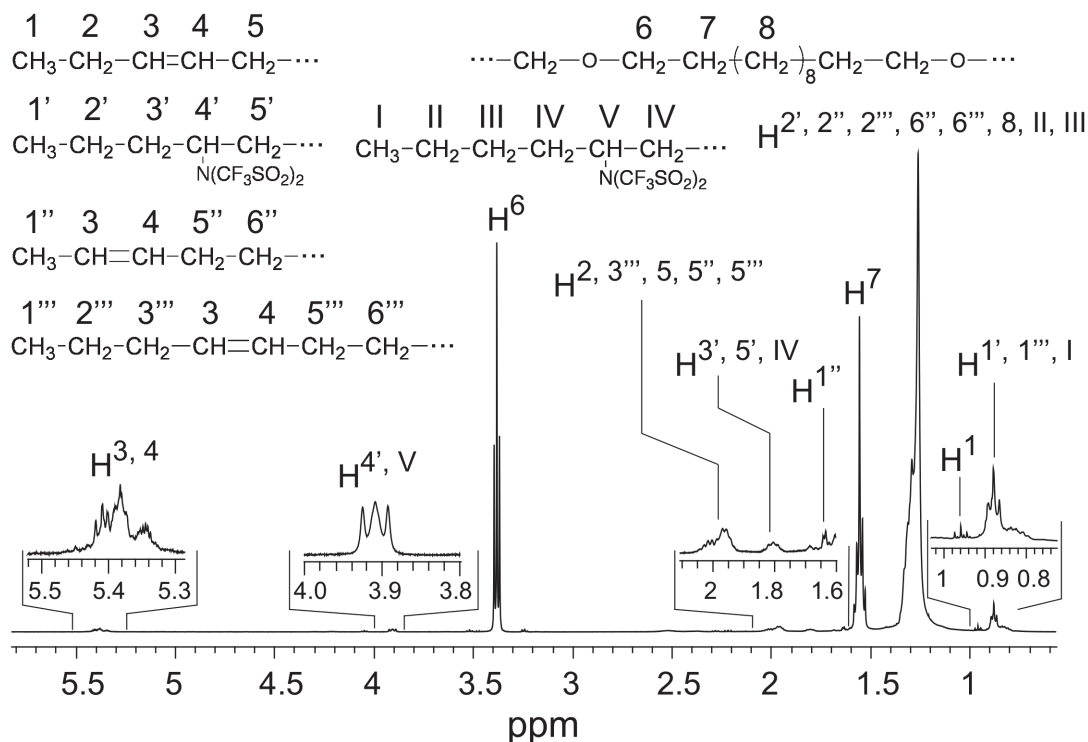
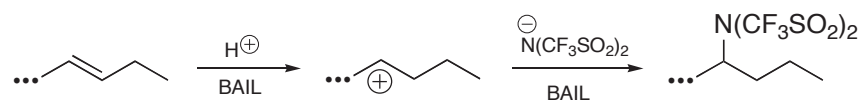


Figure 4.2: ^1H NMR spectrum (500 MHz, CDCl_3) of resulting poly(oxydodecamethylene), reaction undertaken at $130\text{ }^\circ\text{C}$, diol/BAIL= 2/1, 63 h in $[\text{OBSIm}]\text{Tf}_2\text{N}$ under N_2 flow (200 mL/min).

The ^1H NMR spectra also present small resonances at 3.9 and 1.8 ppm ($\text{H}^{3',4',5',\text{IV},\text{V}}$, Figure 4.2), which are assigned to the product of double bond hydroamination (Scheme 4.3). According to

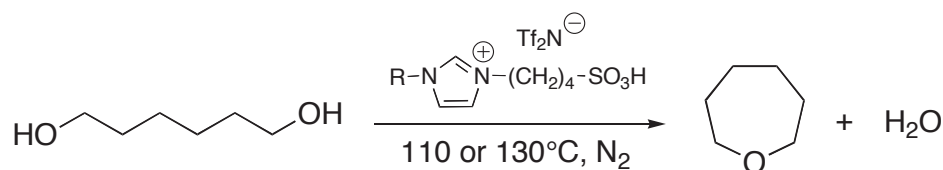
Kuhnert et al.²⁵, double bonds can be hydroaminated by Tf₂NH under acidic conditions. The ¹⁹F NMR spectrum of this product presents a new resonance at -75.2 ppm (Figure 4.A2), different from that of the Tf₂N⁻ counterion in the BAIL at -80.0 ppm, which is a further indication of the hydroamination. These two side reactions could also explain why the polymer chain was limited at the late stages of the reaction.



Scheme 4.3: Hydroamination of double bonds by Tf₂N⁻ in BAILs.

Nevertheless, it was found that the high molar mass polyether could be obtained in either [BBSIm]Tf₂N or [OBSIm]Tf₂N with a molar ratio of 2:1 (monomer:IL) at 130 °C. The same conditions were therefore used to study the polyetherification of other aliphatic diols in these two BAILs.

Table 4.2 shows that high molar mass polyethers could also be synthesized from the diols with 7 to 10 methylene units. Polyethers could not be produced from 1,6-hexanediol or 1,4-butanediol in these two BAILs, but oxepane and THF were detected respectively. It appears that the formation of cyclic ethers of 1,4-butanediol and 1,6-hexanediol rather than polyetherification was favored under the same conditions in the BAILs, as volatile products were distilled from the reaction media, which were respectively THF and oxepane (Scheme 4.4).



Scheme 4.4: Formation of oxepane in [RBSIm]Tf₂N, R= Octyl or Butyl.

Table 4.2: Polyetherification of different aliphatic diols in BAILs with diol/BAIL (mol/mol) = 2/1 at 130 °C under N₂ flow (200 mL/min). Mass-average molar mass (M_w) and molar mass dispersity ($\mathcal{D}_M = M_w/M_n$) calculated from SEC data, melting temperature (T_m) measured by DSC.

Entry	BAIL	Monomer	Time (h)	Yield ^a (%)	M_w (g/mol)	\mathcal{D}_M	T_m (°C)
8	[OBSIm]Tf ₂ N	1,10-decanediol	50	65.0	25500	2.3	73.8
9	[OBSIm]Tf ₂ N	1,9-nonanediol	60	61.1	23900	2.3	69.5
10	[OBSIm]Tf ₂ N	1,8-octanediol	50	73.2	26700	2.6	73.0
11	[BBSIm]Tf ₂ N	1,8-octanediol	50	77.3	42000	2.2	68.4
12	[BBSIm]Tf ₂ N	1,7-heptanediol	60	56.2	20400	2.0	50.6
13 ^b	[RBSIm]Tf ₂ N	1,6-hexanediol	60	-	-	-	-
14 ^b	[RBSIm]Tf ₂ N	1,4-butanediol	60	-	-	-	-

^a Isolated yield

^b No polyether was formed in either [BBSIm]Tf₂N or [OBSIm]Tf₂N

IV.3 Conclusion

As a conclusion, we have demonstrated for the first time that, in [BBSIm]Tf₂N or [OBSIm]Tf₂N, high molar mass linear polyethers can be synthesized by a simple direct polyetherification of diols with 7 to 12 methylene units. On the other hand, cyclic ethers of 1,6-hexanediol and 1,4-butanediol rather than polyethers were formed in the same conditions, which could be another method of cyclic ether synthesis.

IV.4 Experimental

IV.4.1 Chemicals

1-Butylimidazolium (Aldrich, 98%), 1-octylimidazolium (Iolitec, >99%), 1,4-butanediol (Aldrich, >99%), bis-(trifluoromethylsulfonyl)imide (Iolitec, 99%, in 80% aqueous solution), 1,12-dodecanediol (99%, Sigma-Aldrich), 1,10-decanediol (98%, Sigma-Aldrich), 1,9-nonanediol (99%, Sigma-Aldrich), 1,8-octanediol (98%, ABCR), 1,7-heptanediol (98%, ABCR), 1,6-hexanediol (99% Sigma-Aldrich), 1,4-butanediol (99%, Alfa Aesar) were also used without any further purification.

IV.4.2 Synthesis of BAILs

Brønsted acid ionic liquids (BAILs) used in the investigation were synthesized according to a

two-step approach:

The zwitterions were synthesized by mixing 1-alkylimidazolium with 1 mole equivalent of 1,4-butanediol, under reflux in ethyl acetate. 4-(3'-butyl-1'-imidazolium)-1-butanesulfonate ([BBSIm]), precipitated in the reaction medium. It was then washed with ethyl acetate and diethyl ether, while 4-(3'-octyl-1'-imidazolium)-1-butanesulfonate ([OBSIm]), was recrystallized in acetone/hexanol (0.86/0.14 vol/vol) mixture. The zwitterions were obtained in 95-98% yields as white solids.

The second step is demonstrated as follows: in a round flask, 4-(3'-alkyl-1'-imidazolium)-1-butanesulfonate was mixed with 1 mol equivalent of bis-(trifluoromethylsulfonyl)imide ($(\text{CF}_3\text{SO}_2)_2\text{NH}$). The flask was first heated in a water bath at 80 °C; once the mixture melted, residual water in the reaction medium was eliminated under vacuum (60 mbar). The two 4-(3'-alkyl-1'-imidazolium)-1-butanesulfonic acid bis(trifluoromethylsulfonyl)imides were obtained in quantitative yields.

IV.4.3 Polyetherification of diols (m>6)

The polyetherification of 1,12-dodecanediol in 4-(3'-butyl-1'-imidazolium)-1-butanesulfonic acid bis(trifluoromethylsulfonyl)imide ([BBSIm]Tf₂N) is given as an example: 1 mmol of [BBSIm]Tf₂N (0.5415 g) was blended with 2 mmol of 1,12-dodecane diol (0.4047 g) in a glass tube with a magnetic headcross stirrer. The mixture was maintained at 130 °C under nitrogen flow (200 mL/min) for a predetermined time (50 to 96 h). The reaction medium was then cooled down to room temperature, and 10 mL of methanol was added to solubilize the BAIL with the help of an ultrasonic bath. The insoluble polyether was filtrated, washed with 2x10 mL of methanol and dried at 40 °C under vacuum overnight. As around 20% of 1,12-dodecanediol was evaporated with the N₂ flow, the recovered yield of each reaction was about or less than 80%. The loss of 1,12-dodecanediol was calculated from the mass difference of the reaction medium before and after the reaction, and the percentage of lost mass was calculated accordingly.

IV.4.4 Reaction of 1,6-hexane diol and 1,4-butane diol

The reactions of these two diols in 4-(3'-butyl-1'-imidazolium)-1-butanesulfonic acid bis-(trifluoromethylsulfonyl)imide ([BBSIm]Tf₂N) are demonstrated with that of 1,6-hexanediol

as an example: 1 mmol of [BBSIm]Tf₂N (0.5415 g) was blended with 2 mmol of 1,6-hexane diol (0.2364 g) in a glass tube with a magnetic headcross stirrer. The mixture was maintained at 130 °C under nitrogen flow (200 mL/min) for a predetermined time (50 to 60 h). The volatile composition was distilled and collected in a trap equipped with liquid nitrogen. The reaction medium was then cooled down to room temperature and 10 mL of methanol added to solubilize the BAIL with the help of an ultrasonic bath. No polymer was obtained.

IV.4.5 Analytical Methods

NMR Spectroscopy: The ¹H NMR spectra and 2D ¹H-¹H COSY-45 NMR spectra of monomers and polymers were recorded on Bruker Avance 500 spectrometers in chloroform-*d* (ref. δ (CHCl₃) = 7.26 ppm), while the spectra of 4-(3'-alkyl-1'-imidazolio)-1-butanesulfonic acid bis-(trifluoromethylsulfonyl)imidide ([RBSIm]Tf₂N) were recorded in D₂O/TSP-*d*₄ (ref. δ(TSP-*d*₄) = 0 ppm). ¹⁹F NMR spectra were recorded on a Bruker Avance 300 spectrometer in chloroform-*d* (ref. δ(C₆F₆) = -164.9 ppm).

Size Exclusion Chromatography (SEC): SEC was used to determine the number-average and mass-average molar masses of polymers, *M_n* and *M_w*, respectively. The SEC equipment consisted of a Waters 515 HPLC pump, a Waters 410 RI detector and a set of five Ultrastaygel columns (50+500+10³+10⁴+10⁵ Å). CH₂Cl₂ was used as eluting solvent with a flow rate of 1 mL/min at room temperature. Each sample was prepared with 8 mg of polymer, 1 mL of CH₂Cl₂ and 1 μL of toluene. 100 μL of sample solution was injected for each analysis. The system was calibrated with polystyrene standards.

Differential Scanning Calorimetry (DSC) was performed on a TA Instruments 9900 apparatus equipped with a DSC910 module using the following heating/cooling cycles: (1) heating from -85 °C to 210 °C at 20 °C/min, (2) cooling to -85 °C at 20 °C/min. (3) heating from -85 °C to 210 °C at 10 °C/min. Experiments were run under nitrogen atmosphere at low temperature by means of a liquid nitrogen cooling accessory LNCA-II. Melting temperatures (*T_m*) were taken at the minima of the melting endotherms of the second run.

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IV.6 Appendix

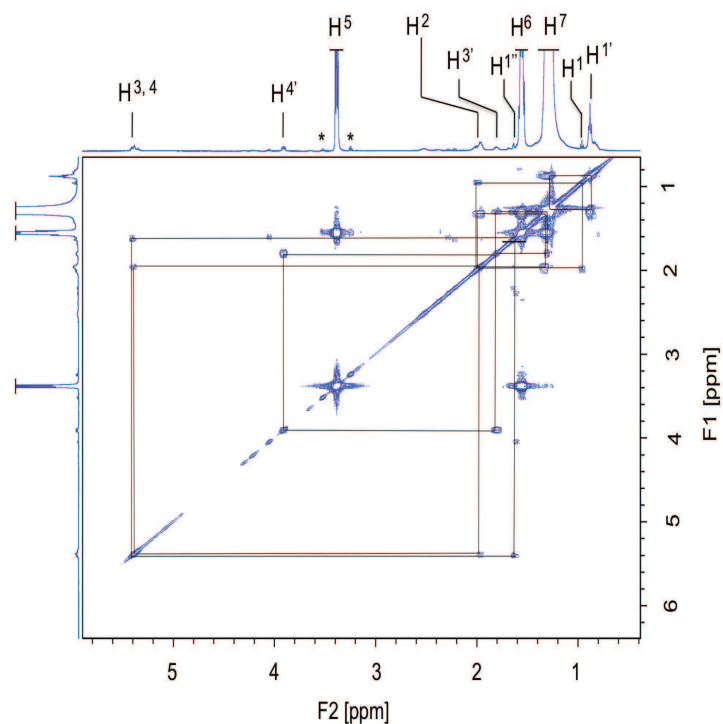


Figure 4.A1: 2D ^1H - ^1H COSY-45 NMR spectrum (500 MHz, CDCl_3) of purified poly(oxydodecamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 63 h in $[\text{OBSIm}]\text{Tf}_2\text{N}$ under N_2 flow (200 mL/min), * : ^{13}C satellites.

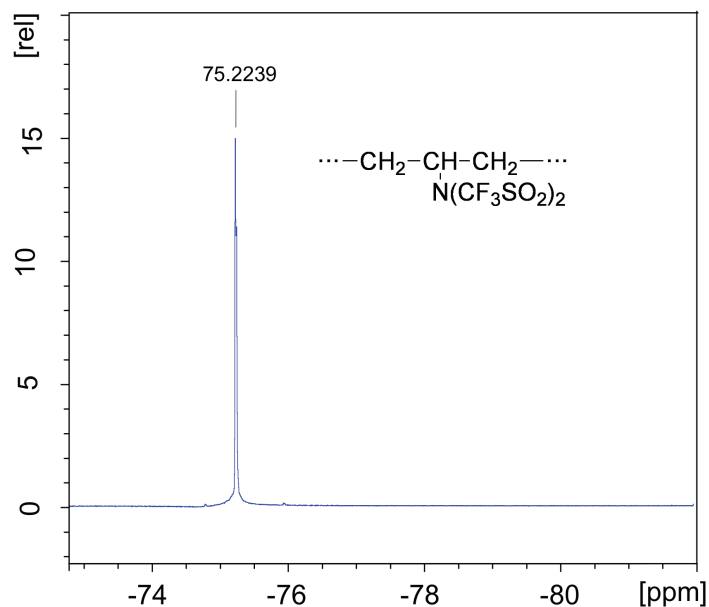


Figure 4.A2: ^{19}F NMR spectrum (300 MHz, CDCl_3) of purified poly(oxydodecamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 63 h in $[\text{OBSIm}]\text{Tf}_2\text{N}$ under N_2 flow (200 mL/min).

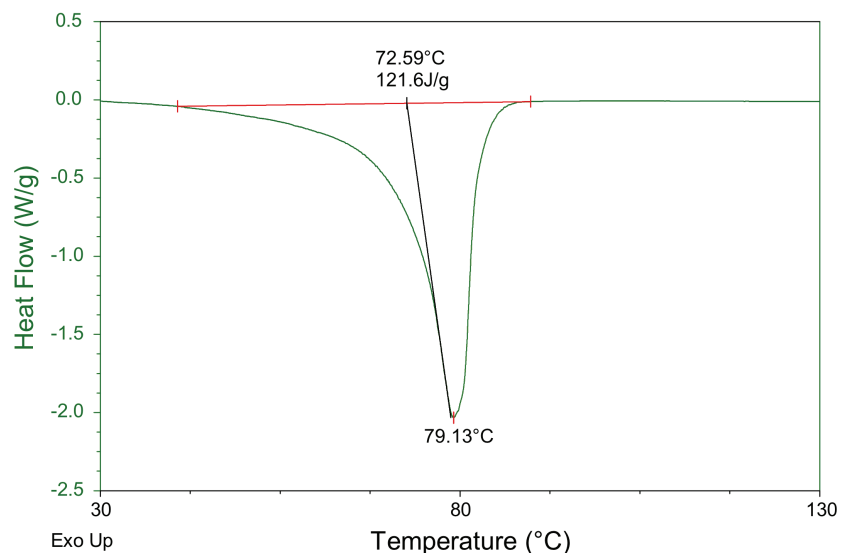


Figure 4.A3: DSC thermogram of purified poly(oxydodecamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 63 h in [OBSIm]Tf₂N under N₂ flow (200 mL/min).

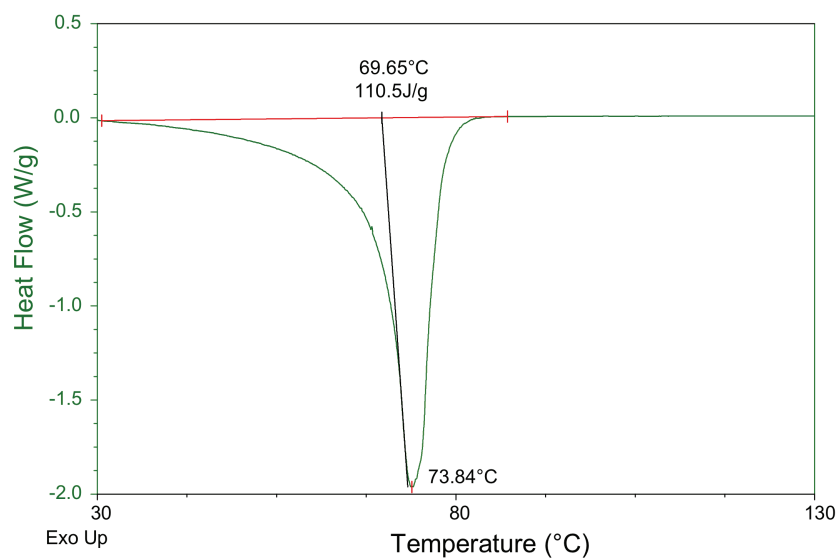


Figure 4.A4: DSC thermogram of purified poly(oxydecamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 50 h in [OBSIm]Tf₂N under N₂ flow (200 mL/min).

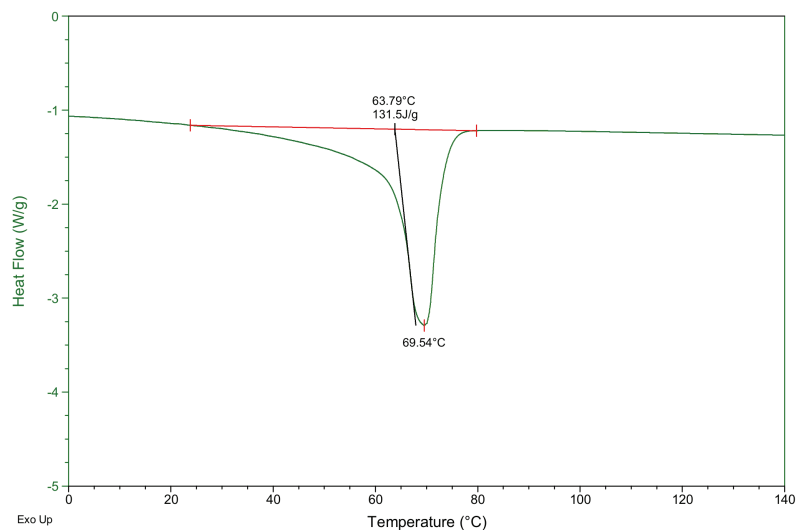


Figure 4.A5: DSC thermogram of purified poly(oxyonamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 50 h in [OBSIm]Tf₂N under N₂ flow (200 mL/min).

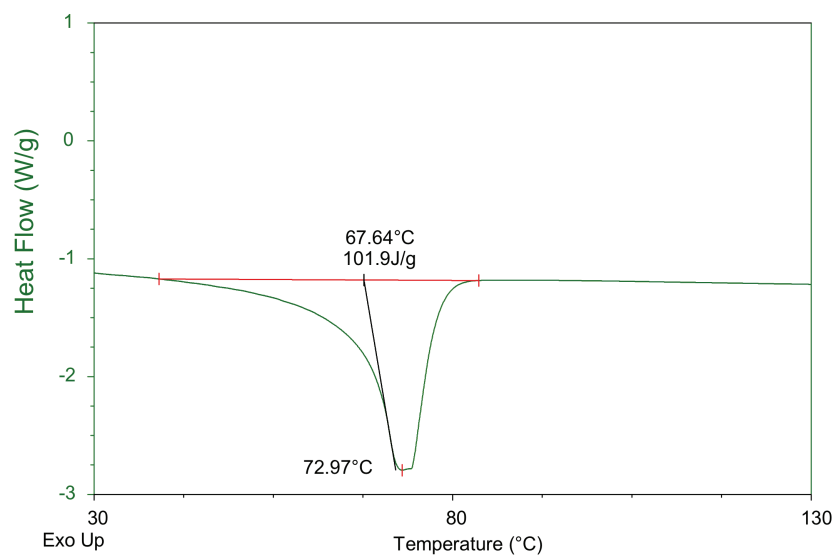


Figure 4.A6: DSC thermogram of purified poly(oxyoctamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 50 h in [OBSIm]Tf₂N under N₂ flow (200 mL/min).

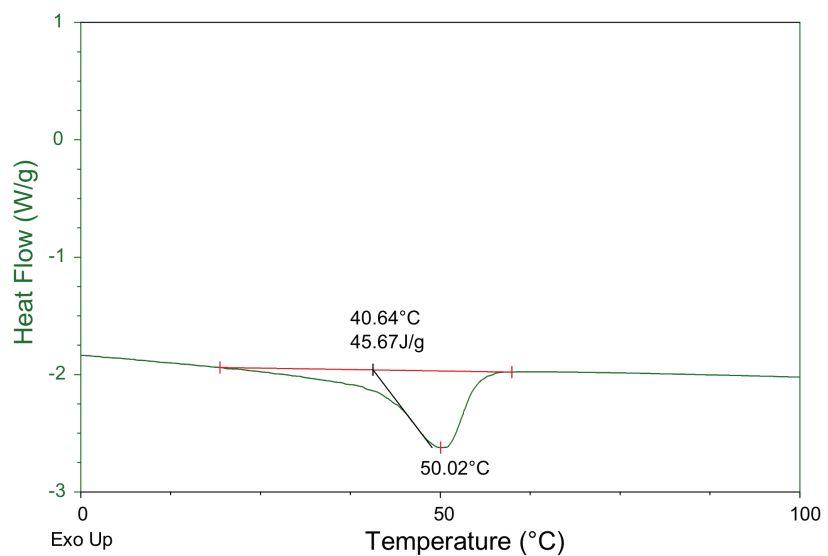


Figure 4.A7: DSC thermogram of purified poly(oxyheptamethylene), reaction undertaken at 130 °C, diol/BAIL= 2/1, 60 h in [OBSIm]Tf₂N under N₂ flow (200 mL/min).

Chapter V

Direct poly(β -alanine) synthesis via polycondensation in ionic liquid

Abstract:

In this chapter, ionic liquids were utilized as alternative polyamide solvents, and stoichiometric amount of condensing agent (TPP) was added. Poly(β -alanine) has been successfully synthesized by direct polyamidation of β -alanine. 1,3-Dimethylimidazolium dimethylphosphate was the most suitable reaction medium, in which poly(β -alanine) with a number-average degree (DP_n) of polymerization up to 49.5 has been obtained. Thanks to NMR and MALDI-TOF experiments, different species were identified in the resulting poly(β -alanine), such as the target macromolecules with amine/carboxylic acid end groups, macrocyclic polymer and polymer with phenyl ester end group. It was also proved that the method was applicable to the direct synthesis of polypeptides, such as poly(L-valine) and poly(L-isoleucine).

V.1 Introduction

β -Alanine is a naturally occurring β -amino acid, found as component of vitamin B5 and several proteins.¹⁻³ The oligomers and polymers of β -alanine derivatives are inherently protein mimetic⁴ and can adopt secondary structures.⁵ They have been attracting a lot of attention as biomimetic materials with potential biomedical applications.⁵⁻⁷

Poly(β -amino acid)s can be prepared by ring-opening polymerization (ROP) of β -propiolactam and its derivatives in the presence of strong bases.⁸⁻¹¹ However, due to the acidity of active hydrogens, side reactions take place during the polymerization of the unsubstituted β -propiolactam, leading to chain branching. This method has therefore been mainly applied to substituted derivatives, with the recent exceptions of phosphazene-catalyzed¹² and of enzyme-catalyzed^{13,14} polymerizations.

The synthesis of poly(β -alanine) by base-catalyzed Michael polyaddition of acrylamide has been extensively investigated. It is usually carried out at 80-120°C in aprotic solvents, like DMF, in the presence of a strong base catalyst, such as sodium tert-butoxide.¹⁵⁻¹⁸ The reaction proceeds mainly by the addition of primary amide anion to acrylamide double bond, but also involves secondary amide anion addition, resulting in formation of branched polymers.¹⁹

The polycondensation of β -alanine could be a straightforward method of poly(β -alanine) synthesis. However, this polymer is insoluble in most organic solvents and undergoes degradation reactions before melting, and, therefore, cannot be prepared by conventional polycondensation. During recent years, ionic liquids (ILs) have drawn wide attention, as they are nonvolatile, easily recyclable reaction media and have high thermal and chemical stabilities.²⁰⁻²² Some chain polymerizations and polycondensations have been investigated in ILs.²³⁻³² Aromatic polyamides were synthesized in ILs from diamines and diacid chlorides at low temperature (0-60 °C)²⁷ or from diamines and diacids with addition of triphenyl phosphite (TPP) at higher temperature.³³⁻³⁶

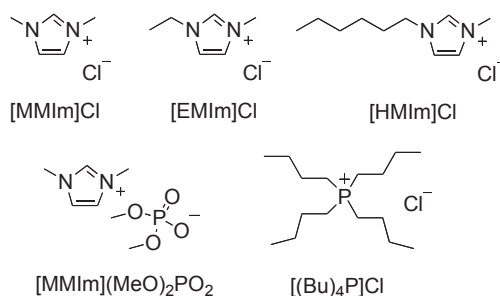
On the basis of these investigations, we studied the synthesis of poly(β -alanine) via direct polycondensation of β -alanine in various ionic liquids, which to our best knowledge, is the first example of direct poly(β -alanine) synthesis in solution. In order to get insight into the polymer

structure, the resulting polymers were carefully examined by NMR spectroscopy and MALDI-TOF mass spectrometry. Besides, the straightforward approach was also applied to synthesis of several polypeptides, such as poly(L-valine) and poly(L-isoleucine).

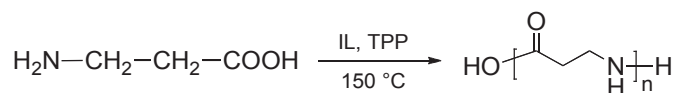
V.2 Results and discussion

V.2.1 Synthesis of poly(β -alanine)

The reaction was carried out in various ILs (Scheme 5.1) in the presence of stoichiometric amount of condensing agent, triphenyl phosphite (TPP) (Scheme 5.2).



Scheme 5.1: Ionic liquids used in the current study.



Scheme 5.2: Synthesis of poly(β -alanine) in ionic liquid in the presence of TPP.

As expected for polyamides, the resulting poly(β -alanine)s were insoluble in common organic solvents. They were not soluble in polyamide solvents either, such as chloroform trifluoroacetic anhydride mixtures, but soluble in pure formic acid.

The FTIR spectra of the resulting products reflect the formation of a polyamide (Figure 5.1), as two intense bands at 3291 cm^{-1} (s) and 1629 cm^{-1} (s) can be observed, which correspond to typical N-H and C=O amide stretching vibrations.

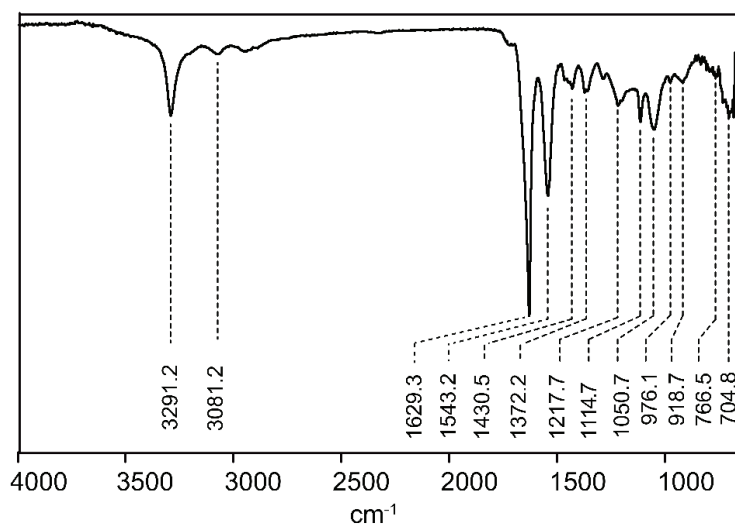


Figure 5.1: Polymerization of β -alanine in [HMIM]Cl at 150 °C for 18 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol): FTIR spectrum of the poly(β -alanine).

The MALDI-TOF mass spectra (Figure 5.2) of the products show a distribution of peaks with a mass increment of m/z 71.07, which corresponds exactly to one monomer unit. Taking the peak at m/z 1674.70 for instance, it corresponds to $\text{H}[\text{NH}-\text{CH}_2-\text{CH}_2-\text{CO}]_{23}-\text{OH}, \text{Na}^+$, which is the macromolecule with 23 β -alanine repeating units cationized by Na^+ . It proves that poly(β -alanine) was produced by direct polymerization in ILs.

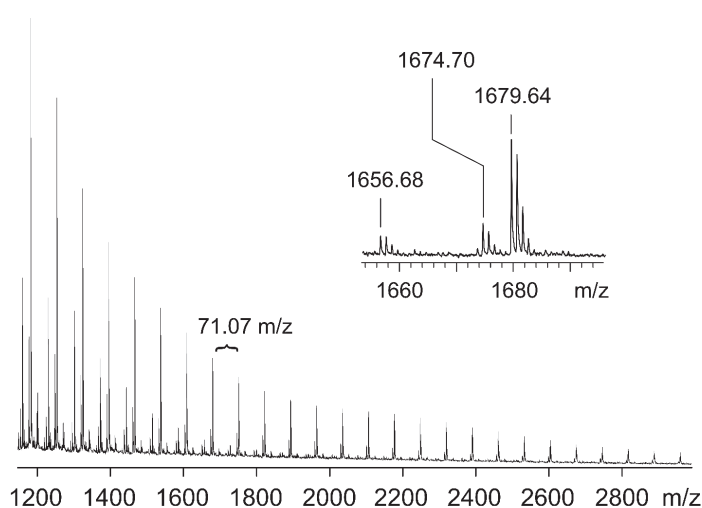
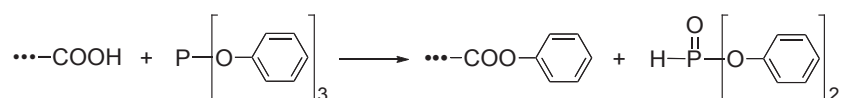


Figure 5.2: Polymerization of β -alanine in [HMIm]Cl at 150 °C for 18 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol): MALDI-TOF mass spectrum of the poly(β -alanine).

Carboxylic acids react with TPP during the formation of polyamides, forming phenyl ester and diphenyl phosphite (DPP) (Scheme 5.3).³⁷ Phenyl ester was formed in the current study as well, since a series of peaks corresponding to $\text{H}[\text{NH}-\text{CH}_2-\text{CH}_2-\text{CO}]_n-\text{OC}_6\text{H}_5, \text{Na}^+$ is detected in the MALDI-TOF mass spectra, with an example at 1679.64 m/z ($n=22$) (Figure 5.2). As

expected for a polycondensation process, macrocyclic poly(β -alanine) species were also formed during the polymerization. For example, the peak at 1656.68 m/z corresponds to the cyclic poly(β -alanine) molecule with 23 repeating units. Therefore, the MALDI-TOF MS study confirms that poly(β -alanine) was synthesized in the ILs, and shows that both carboxylic acid- and phenyl ester-terminated polymers were formed during the reaction, together with cyclic species.



Scheme 5.3: Formation of phenyl ester and DPP during β -alanine polymerization.

In order to get more information of the present species in the resulting products, NMR experiments were carefully carried out. The assignments of all the resonances are summarized in the ^1H NMR spectrum of the resulting polymer (Figure 5.3). It presents classical polyamide patterns with broad peaks at 2.31 and 3.25 ppm, assigned to the methylene groups of the repeating units (H^2 and H^3 , respectively). The end groups can be detected as well: There is a resonance at 3.31 ppm, coupled with another resonance at 2.28 ppm that overlaps with H^2 in the zone of $-\text{CH}_2\text{-CO-NH-}$ resonances and can be assigned to the methylene H^{14} in β position to the amine end groups (Figure 5.4, 2D ^1H - ^1H COSY-45 NMR spectrum). The peak at 3.31 ppm corresponds, therefore, to the methylene H^{15} in α position to the amine end groups. Two triplets of low intensity are present at 2.52 ppm and 2.61 ppm, which can be assigned to the methylenes connected to either the carboxylic acid or the phenyl ester chain ends detected in the MALDI-TOF mass spectrum. The resonance at 2.52 ppm is assigned to the $-\text{CH}_2\text{-COOH}$ methylene (H^6), with the help of the ^1H NMR spectrum of $\text{N,N}'\text{-(Z-octadec-9-endioyl)bis}(\beta\text{-alanine})$ (**1**), a model compound which presents a $-\text{CONH-CH}_2\text{-CH}_2\text{-COOH}$ methylene resonance at 2.53 ppm in formic acid solution. The quadruplet at 3.19 ppm, coupled with H^6 in the 2D ^1H - ^1H COSY-45 NMR spectrum, is then easily assigned to the methylene (H^7) in β position to the carboxylic acid end groups. The remaining triplet at 2.61 ppm is consequently assigned to the methylene H^{10} of phenyl ester chain ends. The three peaks present in the aromatic zone between 6.7 and 7.1 ppm (H^{17} (6.76 ppm), H^{19} (6.93 ppm) and H^{18} (7.06 ppm)) reflect the presence of the corresponding phenyl groups. It is worth mentioning that their integrations correspond exactly to the required values for phenyl ester end-groups, as expected from H^{10} integration. The quadruplet at 3.37 ppm, coupled with H^{10} is finally assigned to H^{11} .

These assignments were confirmed by the 2D HSQC and HMBC NMR spectra (Figure 5.5 and 5.6). The NMR study demonstrates, therefore, that poly(β -alanine) with the expected structure was obtained and that the carboxylic acid end groups were partially modified to the corresponding phenyl ester.

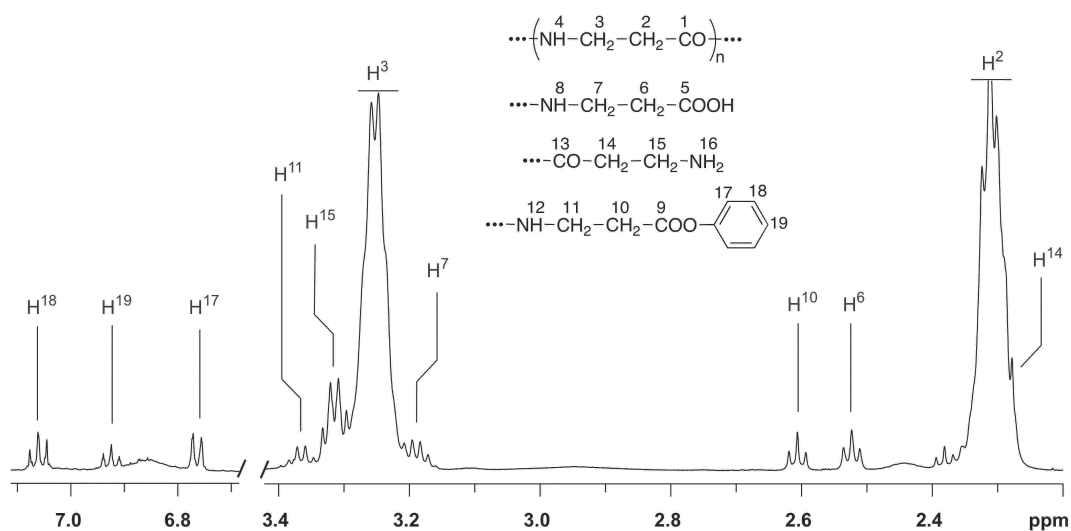


Figure 5.3: Polymerization of β -alanine in [(Bu)₄P]Cl at 150 °C for 2 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol): ¹H NMR spectrum of resulting poly(β -alanine) (500 MHz, formic acid with external acetone-*d*₆, ref. δ (acetone-*d*₆) ¹H = 2.05 ppm).

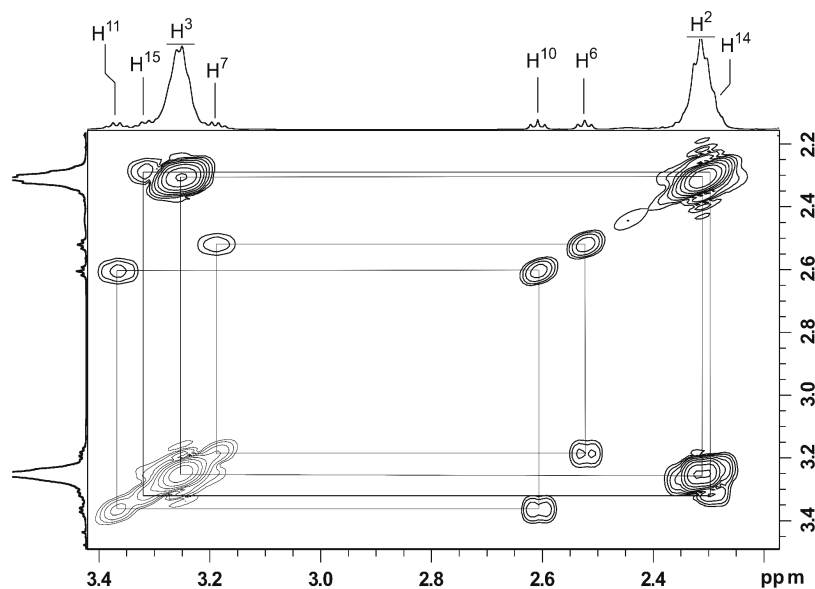


Figure 5.4: Polymerization of β -alanine in [HMIM]Cl at 150 °C for 18 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol): 2D ¹H-¹H COSY-45 NMR spectrum of resulting poly(β -alanine) (500MHz, formic acid with external acetone-*d*₆, ref. δ (acetone-*d*₆) ¹H = 2.05 ppm).

With the help of the 2D ¹³C-¹H correlation HSQC and 2D ¹³C-¹H long-distance correlation

HMBC spectra, the assignments of all the resonances are further confirmed as follows:

- (i) The presence of amide structure is confirmed by the correlations in the aliphatic region (H^2-C^2 at 2.31/36.43 ppm and H^3-C^3 at 3.25/38.01 ppm) in HSQC spectrum (Figure 5.5); it is also confirmed by the long-distance correlations of H^2-C^3 (2.31/38.01 ppm) and H^3-C^2 (3.25/36.43 ppm) in HMBC spectrum (Figure 5.6);
- (ii) End groups with low intensity correlations are observed in the HSQC spectrum (Figure 5.5): H^6-C^6 at 2.52/33.03 ppm and H^7-C^7 at 3.20/38.68 ppm, reflecting to $-NH-CH_2-CH_2-COOH$. $H^{15}-C^{15}$ at 3.32/38.10 ppm and $H^{14}-C^{14}$ at 2.28/36.99 ppm, corresponding to $-CO-CH_2-CH_2-NH_2$. These assignments are further confirmed by the long-distance correlations H^6-C^7 (2.52/38.68 ppm), H^7-C^6 (3.20/33.03 ppm), $H^{14}-C^{15}$ (2.28/38.10 ppm) and $H^{15}-C^{14}$ (3.32/36.99 ppm) in HMBC spectrum (Figure 5.6).

Besides, correlations $H^{10}-C^{10}$ at 2.61/34.94 ppm and $H^{11}-C^{11}$ at 3.37/37.35 ppm are also detected in the HSQC spectrum (Figure 5.5) and $H^{11}-C^{10}$ and $H^{10}-C^{11}$ in the HMBC spectrum (Figure 5.6). This further demonstrates that C^{10} and C^{11} are connected with each other.

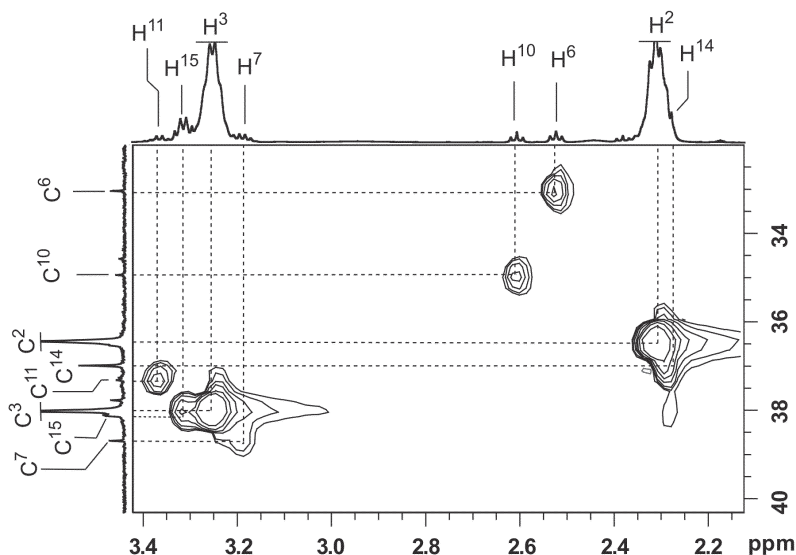


Figure 5.5: Polymerization of β -alanine in $[(Bu)_4P]Cl$ at 150 °C for 2 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol): 2D 1H - ^{13}C HSQC NMR spectrum of resulting poly(β -alanine) (500MHz, formic acid with external acetone- d_6 , ref. δ (acetone- d_6) $^1H/^{13}C$ = 2.05/29.84 ppm).

4 different carbonyl resonances are observed in the HMBC spectrum (Figure 5.6):

- (i) The carbonyl C^1 is connected to C^2 , since H^2-C^1 (2.31/176.46 ppm) correlation is

present. Furthermore, a long-distance correlation between H³ and C¹ is seen at 3.25/176.46 ppm.

- (ii) The carbonyl C⁵ of the carboxylic acid end group is recognized by the correlations H⁶-C⁵ (2.52/174.19 ppm) and H⁷-C⁵ (3.20/174.19 ppm).
- (iii) The carbonyl C¹³ of the amine end group is also confirmed by the correlations H¹⁴-C¹³ (2.28/176.18 ppm) and H¹⁵-C¹³ (3.32/176.18 ppm).
- (iv) The last carbonyl, C⁹, which refers to a phenyl ester, is connected to C¹⁰, as there is a correlation H¹⁰-C⁹ at 2.61/173.16 ppm and another correlation H¹¹-C⁹ at 3.37/173.16 ppm.

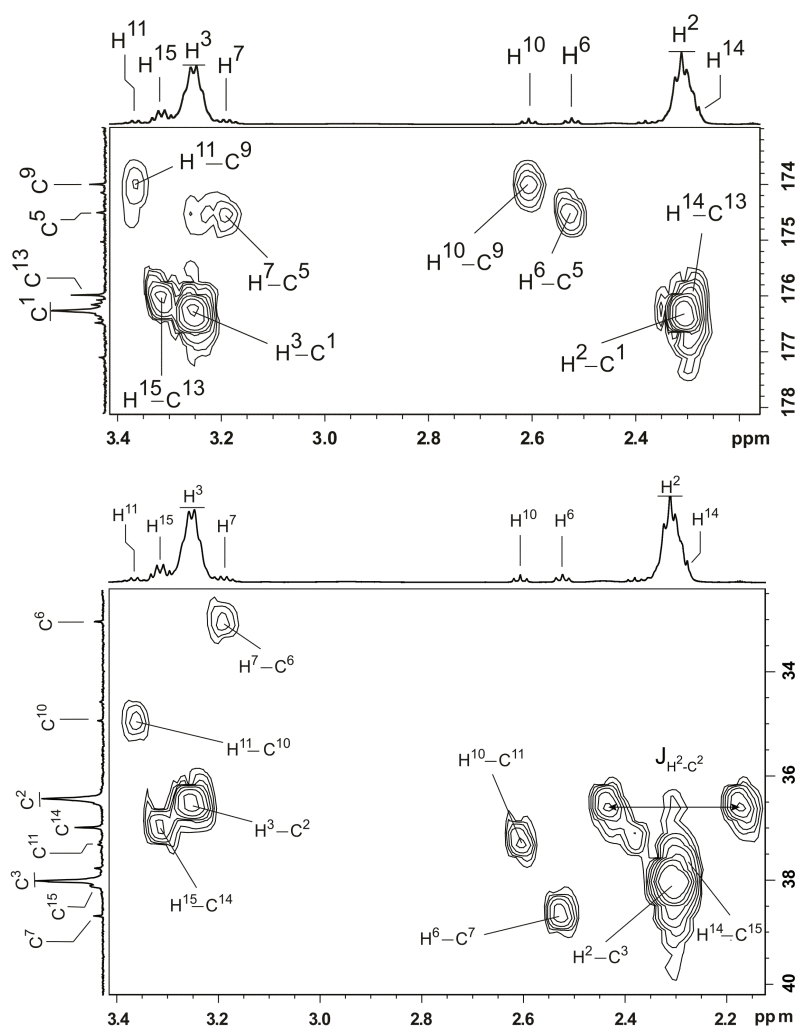


Figure 5.6: Polymerization of β -alanine in [(Bu)₄P]Cl at 150 °C for 2 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol): 2D ¹H-¹³C HMBC NMR spectrum of resulting poly(β -alanine) (500MHz, formic acid with external acetone-d₆, ref. δ (acetone-d₆) ¹H/¹³C = 2.05/29.84 ppm).

The solubility of β -alanine in different ILs was tested at 150 °C. The monomer showed limited

solubility in the ILs with Cl⁻ anion ([MMIm]Cl, [EMIm]Cl and [HMIm]Cl), but was soluble in [MMIm](MeO)₂PO₂, showing that its solubility strongly depends on IL anion structure. The results of β-alanine polymerization in different ILs are presented in Table 5.1.

Table 5.1: Polymerization of β-alanine (150 °C, β-alanine/IL (wt/wt) = 1/2, β-alanine /TPP (mol/mol) = 1/1). Number-average degree of polymerization (DP_n) obtained by ¹H NMR.

Entry	Ionic liquid	Time (h)	DP _n	Yield ^b (%)
1 ^a	[HMIm]Cl	18	-	-
2 ^a	[MMIm](MeO) ₂ PO ₂	18	-	-
3	[MMIm]Cl	2	28.4	67
4	[MMIm]Cl	8	29.5	87
5	[MMIm]Cl	18	27.8	94
6	[EMIm]Cl	2	12.2	68
7	[EMIm]Cl	18	31.3	82
8	[HMIm]Cl	2	13.5	65
9	[HMIm]Cl	18	20.0	77
10	[(Bu) ₄ P]Cl	2	17.2	65
11	[(Bu) ₄ P]Cl	8	19.2	67
12	[(Bu) ₄ P]Cl	18	19.9	71
13	[MMIm](MeO) ₂ PO ₂	2	24.5	66
14	[MMIm](MeO) ₂ PO ₂	8	35.5	75
15	[MMIm](MeO) ₂ PO ₂	18	49.5	83

^a Reaction carried out without TPP. No polymer was formed.

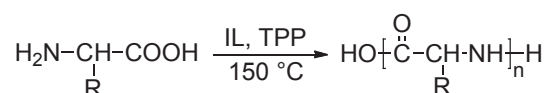
^b Yield of resulting product after purification

The number-average degree of polymerization (DP_n) was determined from the ratio of the integrations of repeating units and end-group resonances. When the reaction was conducted without TPP, no polymer was formed (Table 5.2, Entries 1 and 2), while in the presence of TPP, poly(β-alanine) was obtained in all the ionic liquids. When the reaction was carried out during 2 h, no obvious difference was observed between [EMIm]Cl and [HMIm]Cl, as the DP_n of poly(β-alanine) was respectively 12.2 (Entry 6) and 13.5 (Entry 8). On the other hand, when the reaction time was prolonged to 18 h, DP_n increased to 31.3 in [EMIm]Cl (Entry 7) but remained around 20 in [HMIm]Cl (Entry 9). The polymerization in [MMIm]Cl was more efficient at the beginning of the reaction than those in both [EMIm]Cl and [HMIm]Cl, as the DP_n was around 28 after 2 h (Entry 3), but remained almost constant when it was heated for a longer time (Entries 4 and 5). Increasing the alkyl chain length of imidazolium ILs with Cl⁻ counterion does not favor the polymerization. Poly(β-alanine) was obtained in [(Bu)₄P]Cl as

well, and the DP_n remained around 20 after 8 and 18 h (Entries 11 and 12). Comparing to other ILs, the polymerization was much more efficient in $[\text{MMIm}](\text{MeO})_2\text{PO}_2$, as a DP_n of 24.5 was obtained after 2 h (Entry 13) and went up to 49.5 when the reaction was carried out for 18 h (Entry 15).

V.2.2 Application of polymerization of α -amino acids

This direct synthesis approach in ionic liquids was also employed to prepare several polypeptides from their corresponding α -amino acids. For example, poly(L-isoleucine) and poly(L-valine) were successfully obtained from L-isoleucine and L-valine (Scheme 5.4), when the reactions were carried out in a very common ionic liquid $[\text{EMIm}]\text{Cl}$. Both of them were confirmed by MALDI-TOF MS study.



Scheme 5.4: Synthesis of polypeptide from L-isoleucine ($\text{R} = \text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)-$) or L-valine ($\text{R} = (\text{CH}_3)_2\text{CH}-$) in ionic liquid in the presence of TPP.

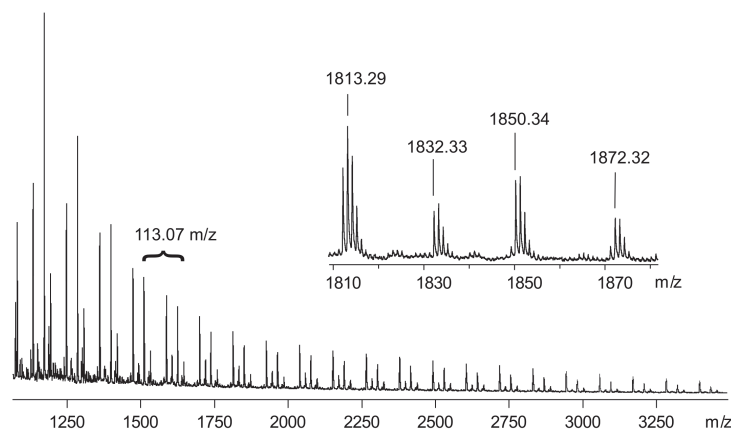


Figure 5.7: Polymerization of L-isoleucine in $[\text{EMIm}]\text{Cl}$ at $150\text{ }^\circ\text{C}$ for 18 h (L-isoleucine/IL = 1/2 wt/wt, L-isoleucine/TPP = 1/1 mol/mol): MALDI-TOF mass spectrum of resulting poly(L-isoleucine).

The MALDI-TOF MS study confirms that poly(L-isoleucine) was obtained in the IL, as the mass spectrum of the resulting product (Figure 5.7) shows a distribution of peaks with a mass increment of m/z 113.07, which corresponds exactly to one L-isoleucine monomer unit. Macromolecules with various end groups are present. Taking the peak at m/z 1850.34 for example, it corresponds to $\text{H}-[\text{NH}-\text{CH}(\textit{iso}-\text{C}_4\text{H}_9)-\text{CO}]_{16}-\text{OH}, \text{Na}^+$, i.e. the macromolecule with 16 L-isoleucine repeating units cationized by Na^+ . Another species $\text{H}-[\text{NH}-\text{CH}(\textit{iso}-$

C_4H_9)-CO] $_{16}$ -ONa,Na $^+$, corresponds to the peak at m/z 1872.32. Macrocyclic poly(L-isoleucine) species were also formed during the polymerization. For example, the peak at 1832.33 m/z corresponds to the cyclic poly(L-isoleucine) molecule with 16 repeating units. Furthermore, phenyl ester was formed as well, as a series of peaks corresponding to H-[NH-CH(*iso*-C $_4$ H $_9$)-CO] $_n$ -OC $_6$ H $_5$,Na $^+$ is detected, with an example at 1813.29 m/z ($n=15$). In a word, as previously mentioned in the study of poly(β -alanine), carboxylic acid- and phenyl ester-terminated polymers, as well as cyclic species, were formed during the polymerization of L-isoleucine.

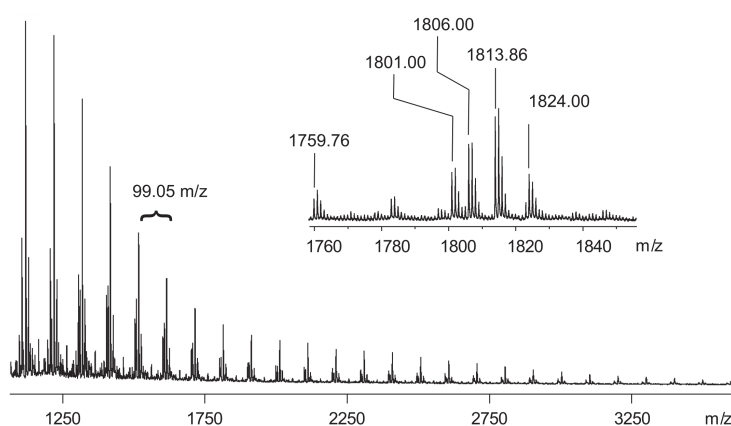


Figure 5.8: Polymerization of L-valine in [EMIm]Cl at 150 °C for 18 h (L-valine/IL = 1/2 wt/wt, L-valine/TPP = 1/1 mol/mol): MALDI-TOF mass spectrum of resulting poly(L-valine).

The formation of poly(L-valine) was also confirmed by the MALDI-TOF mass spectrum of the yielded product (Figure 5.8). It shows a distribution of peaks with a mass increment of m/z 99.05, which corresponds exactly to one L-valine monomer unit. Taking the peak at m/z 1824.00 for instance, it corresponds to H-[NH-CH(C $_3$ H $_7$)-CO] $_{18}$ -OH,Na $^+$, i.e. the macromolecule with 18 L-valine repeating units cationized by Na $^+$. Macrocyclic poly(L-valine) species were also formed during the reaction. For instance, the peak at 1806.00 m/z corresponds to the cyclic poly(L-valine) molecule with 18 repeating units. Besides, phenyl ester was formed as well, since a series of peaks corresponding to H-[NH-CH(C $_3$ H $_7$)-CO] $_n$ -OC $_6$ H $_5$,Na $^+$ is present, with an example at 1801.00 m/z ($n=17$). Furthermore, it is worth mentioning that some intermediate species were also observed in the in the MALDI-TOF mass spectrum. For example, a peak at 1759.76 m/z is present, which corresponds to the polymer with the structure PH(OC $_6$ H $_5$) $_3$ -[NH-CH(C $_3$ H $_7$)-CO] $_{14}$ -ONa,Na $^+$; and another peak at 1813.86 m/z is present, which reflects the polymer with the structure PH(OC $_6$ H $_5$) $_3$ -[NH-CH(C $_3$ H $_7$)-CO] $_{14}$ -OC $_6$ H $_5$,Na $^+$. In a word, the MALDI-TOF MS study confirms, therefore, that poly(L-valine) was synthesized in the IL. As previously described,

carboxylic acid- and phenyl ester-terminated polymers, as well as cyclic species, were formed during the reaction.

V.3 Conclusion

In conclusion, linear unsubstituted poly(β -alanine) was synthesized for the first time, via a straightforward polymerization of β -alanine in ILs in the presence of TPP. Polymers with a number-average degree of polymerization up to 49.5 were obtained. As generally observed in conventional polyamidation, small amount of macrocyclic species was also formed in the ILs. Besides, it was found that part of the carboxylic acid end groups was modified to its corresponding phenyl ester, which might be involved in the reaction mechanism. This method can be also applied to the synthesis of polypeptides from natural α -amino acids, such as L-isoleucine and L-valine. More study needs to be carried out on the direct polyamidation of other natural α -amino acids.

V.4 Experimental

V.4.1 Chemicals

β -Alanine (Aldrich, 99%), 1,3-dimethylimidazolium chloride ([MMIm]Cl, TCI, >98%), 1-ethyl-3-methylimidazolium chloride ([EMIm]Cl, Aldrich, 98%), 1-hexyl-3-methylimidazolium chloride ([HMIm]Cl, Aldrich, \geq 97%), tetrabutylphosphonium chloride ($[(\text{Bu})_4\text{P}]\text{Cl}$, Aldrich, \geq 97%), 1,3-dimethylimidazolium dimethyl phosphate ([MMIm](MeO)₂PO₂, Iolitec, \geq 98%) were used as received. Triphenyl phosphite (Aldrich, 97%) was dried by P₂O₅ at 60 °C under vacuum overnight prior to use. N,N'-(Z-octadec-9-endioyl)bis(β -alanine) (model compound (**1**)) was synthesized by enzymatic amidation between dimethyl Z-octadec-9-endioate and β -alanine.

V.4.2 Polymerization of β -Alanine

In each experiment, 0.200 g of β -alanine (2.27 mmol), 0.400 g of ionic liquid and 0.704 g of triphenyl phosphite (2.27 mmol) were introduced in a glass tube fitted with a nitrogen inlet and outlet and a magnetic stirring bar. The glass tube was immersed into an oil bath at 150 °C for a predetermined time under nitrogen flow (200 mL/min). The reaction was then quenched by cooling down to room temperature and adding 10 mL of methanol. The mixture was heated

under reflux for 10 min. The resulting suspension was cooled down to room temperature and separated by centrifugation. The supernatant was removed and the washing and separation procedure was then repeated twice. The white solid was finally filtered and dried at 80 °C overnight under vacuum (10 mbar) (yield \geq 65%).

V.4.3 Polymerization of L-Isoleucine

In each experiment, 0.400 g of L-isoleucine (3.05 mmol), 0.800 g of ionic liquid [EMIm]Cl and 0.946 g of triphenyl phosphite (3.05 mmol) were introduced in a glass tube fitted with a nitrogen inlet and outlet and a magnetic stirring bar. The glass tube was immersed into an oil bath at 150 °C for 18 h under nitrogen flow (200 mL/min). The reaction was then quenched by cooling down to room temperature and adding 10 mL of methanol. The mixture was heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and separated by centrifugation. The supernatant was removed and the washing and separation procedure was then repeated twice. 0.233 g of white solid was finally filtered and dried at 80 °C overnight under vacuum (10 mbar) (yield = 59 %).

V.4.4 Polymerization of L-Valine

In each experiment, 0.400 g of L-valine (3.41 mmol), 0.800 g of ionic liquid [EMIm]Cl and 1.059 g of triphenyl phosphite (3.41 mmol) were introduced in a glass tube fitted with a nitrogen inlet and outlet and a magnetic stirring bar. The glass tube was immersed into an oil bath at 150 °C for 18 h under nitrogen flow (200 mL/min). The reaction was then quenched by cooling down to room temperature and adding 10 mL of methanol. The mixture was heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and separated by centrifugation. The supernatant was removed and the washing and separation procedure was then repeated twice. 0.305 g of white solid was finally filtered and dried at 80 °C overnight under vacuum (10 mbar) (yield = 76%).

V.4.5 Synthesis of N,N'-(Z-octadec-9-endioyl)bis(β -alanine) (1)

Z-Octadec-9-enedioic acid was kindly supplied by Institut Français du Pétrole (IFP, France) and was purified by recrystallization in petroleum ether before use (T_m = 66 °C). Chirazyme L2 c.-f. was obtained from Boehringer, Germany. Z-octadec-9-enedioic acid (13,6 g, 43.6 mmol) was heated in 12% BF₃ solution in MeOH (100 mL) at 60 °C for 3 h. The mixture was poured

in 100 mL water, neutralized to pH = 7-8 with 4 M aqueous NaOH and extracted with CH₂Cl₂ (4x80 mL). Organic phases were combined, washed with brine, dried over MgSO₄ and evaporated under reduced pressure. The residue was dissolved in 20 mL CH₂Cl₂ and filtered on 100 g silica gel. After CH₂Cl₂ evaporation, dimethyl Z-octadec-9-endioate was obtained as colorless oil (13.9 g, 94%). 3.4 g (10 mmol) of the diester, β-alanine methyl ester hydrochloride (3.4 g, 22 mmol) and 2-methylbutan-2-ol (60 mL) were heated at 60 °C until a clear solution was obtained. Potassium carbonate (3.35 g, 24 mmol) and Chirazyme L2 (1 g) were added to the solution and the mixture was heated at 60 °C for 12 h. After cooling, the mixture was diluted with methanol (50 mL), the enzyme was removed by filtration and washed with warm methanol (3x50 mL). The filtrate was then evaporated under reduced pressure and the residue was hydrolyzed with 2 M aqueous NaOH (20 mL) overnight at room temperature. The mixture was diluted with water (20 mL) and acidified to pH = 2 with 2 M aqueous HCl. The resulting suspension was filtered, washed with water and oven dried. The crude product, a mixture of oligomers, was heated in acetone/methanol (100:5 v/v) at 65 °C for 15 min. Hot filtration and crystallization at room temperature afforded a off-white solid mainly composed of **1** (1.30 g). **1** was further purified by chromatography on silica gel (ethyl acetate/formic acid, 100:2 v/v). T_m = 139 °C; ¹H NMR (500 MHz, formic acid, ref. δ (external acetone-*d*₆ = 2.05 ppm) δ = 5.09 (t, 2H), 3.41 (q, 4H), 2.53 (t, 4H), 2.18 (t, 4H), 1.75 (q, 4H), 1.39 (m, 4H), 1.04 (broad, 16H); FTMS (ESI) *m/z*: [M + Na⁺] calcd for C₂₄H₄₂N₂O₆Na: 477.2935; found: 477.2931.

V.4.6 Analytical Methods

Fourier Transform Infrared (FTIR) spectra were recorded on a Nicolet iS10 FTIR spectrometer in the range of 4000-400 cm⁻¹ using KBr pellets containing 1% finely ground samples.

The MALDI-TOF MS analyses were performed on a Bruker Autoflex III smartbeam time-of-flight mass spectrometer equipped with a nitrogen laser (λ = 337 nm). Spectra were recorded in reflector delayed extraction mode at an acceleration voltage of 20 kV. 0.2 mL of polymer solution in formic acid (1 g/L) was mixed with 0.8 mL of the matrix solution (20 g/L of 2,5-dihydroxybenzoic acid in methanol/dichloromethane (1:1 v:v)) and 0.2 mL of NaI solution (10 g/L in methanol/dichloromethane (1:1 v:v)). 3 μL of this solution was deposited onto the stainless steel sample slide and dried. The spectra represent averages of 5000 consecutive laser shots. The MALDI-TOF mass spectrometer was calibrated with a monomethyl ether

poly(ethylene glycol) standard ($M_n = 1000$ g/mol).

The NMR spectra were recorded on a Bruker Avance 500 spectrometer at 500 MHz (^1H NMR and 2D ^1H - ^1H COSY-45 NMR) and 125 MHz (^{13}C NMR) using a 5 mm inverse probe. 2D ^{13}C - ^1H correlation spectra were recorded through a phase sensitive gradient enhanced 2D HSQC using echo-antiecho experiment (HSQCETGP sequence). 2D ^{13}C - ^1H long-distance correlation HMBC spectra were recorded via heteronuclear zero and double quantum coherence (HMBCGPLNDQF sequence). The product was dissolved in formic acid ($\geq 98\%$) in a NMR tube equipped with a capillary containing acetone- d_6 as deuterium lock compound and reference (2.05 ppm for ^1H NMR and 29.84 ppm for ^{13}C NMR).

V.5 References

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Chapter VI

Synthesis of copolyamides containing natural amino acids in ionic liquids

Abstract:

In this chapter, the simple direct polyamidation described in Chapter 5 is extended to the synthesis of copolyamides from 12-amino dodecanoic acid (ADA) and natural α - or β -amino acids. Copolyamidation of ADA and β -alanine (β -Ala) was studied as model reaction, and the structure of the resulting polymer was examined by NMR spectroscopy. 4 different polymer connections were identified. High molar mass copolyamides with inherent viscosity up to 1.36 dL/g were obtained in imidazolium ILs with phosphate and phosphonate-based anions, while ILs with chloride anion were not efficient reaction media for this type of reaction.

VI.1 Introduction

Synthetic aliphatic polyamides, usually known as Nylon, are materials with very good properties such as excellent strength and durability. They are largely produced by plastic industry and commonly used in automotives, textiles, and household consumptions. Almost all the commercially available polyamides are prepared from fossil-based compounds and the very stable amide linkages make them hardly biodegradable. On the other hand, some biobased and biodegradable polyamides, such as wool and silk, also have high strength but are biodegradable. In order to produce polymers with similar properties, it is necessary to develop simple synthetic routes for biobased and biodegradable polyamides or for incorporating naturally occurring materials into the synthetic polyamides.

Polyamides are usually synthesized by polycondensation of dicarboxylic acids and diamines in the bulk at high temperature (200-280 °C). This high temperature reaction is not suitable to synthesize polyamides that contain natural amino acid units, as they suffer significant thermal degradation above 200 °C.^{1,2}

N-Carboxyanhydride (NCA) polymerization is the method of choice to prepare polyamides containing natural amino acid.³⁻⁹ The polymerization is commonly initiated by amines⁴⁻⁶ or strong bases such as sodium methoxide.⁷ These conventional initiators can result in chain-breaking transfer and termination reactions.^{7,10,11} Intensive studies were carried out to understand reaction mechanism and eliminate the problematic side reactions.^{6,8,12} The method is widely used for the preparation of polypeptide analogs. However, it requires the synthesis of starting NCA from commercially available amino acids, and anionic polymerization in carefully controlled experimental conditions, which makes it limited to small scale specific syntheses.

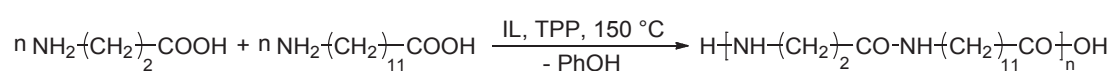
Polyamides which contain natural amino acid can also be synthesized by the polycondensation of activated diamines and activated diacids. For example, Katsarava et al.¹³ and Munoz-Guerra et al.¹⁴ synthesized polyamides from N,N'-bis(trimethylsilyl)L-lysine alkyl esters and dicarboxylic derivatives. Similarly, Sekiguchi et al.¹⁵ prepared low molar mass non-peptidic polyamides from protected L-lysine and L-aspartic acid by activation polyamidation.

During recent years, ionic liquids (ILs) have drawn wide attention, as they are nonvolatile,

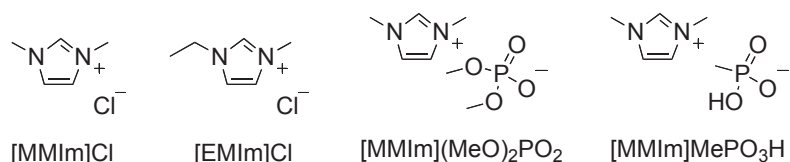
easily recyclable reaction media and have high thermal and chemical stabilities.^{9,16,17} Several polymerization processes, such as chain polymerizations and polycondensations, have been investigated in ILs.¹⁸⁻²⁶ In Chapter V, we have reported the synthesis of homopolymers from natural occurring amino acids such as β -alanine, L-isoleucine and L-valine in various ILs, in the presence of triphenyl phosphite (TPP) as condensing agent. The present chapter reports the copolymerization between 12-amino dodecanoic acid (ADA) and various natural amino acids.

VI.2 Results and Discussion

Various copolyamides were synthesized via direct polycondensation by simply mixing 12-aminododecanoic acid (ADA) with a natural amino acid, such as β -alanine or α -amino acid, leading to the incorporation of natural amino acid units in polyamide-12. The reactions were carried out in different ionic liquids (ILs), in the presence of triphenyl phosphite (TPP) used as condensing agent (Scheme 6.1). In order to find the most suitable reaction conditions, a preliminary study of copolymerization was first conducted on the reaction between β -alanine (β -Ala) and equimolar amount of ADA. Four different ILs were used for the synthesis of copolyamides (Scheme 6.2). All of them were found to be good solvents for these copolyamides, as the reaction media were homogenous and no precipitation was observed during the reaction. The resulting copolymer is named as poly(β -Ala-*co*-ADA) in the following discussion.



Scheme 6.1: Synthesis of poly(β -Ala-*co*-ADA) in ionic liquid in the presence of TPP.



Scheme 6.2: Ionic liquids used in the current study.

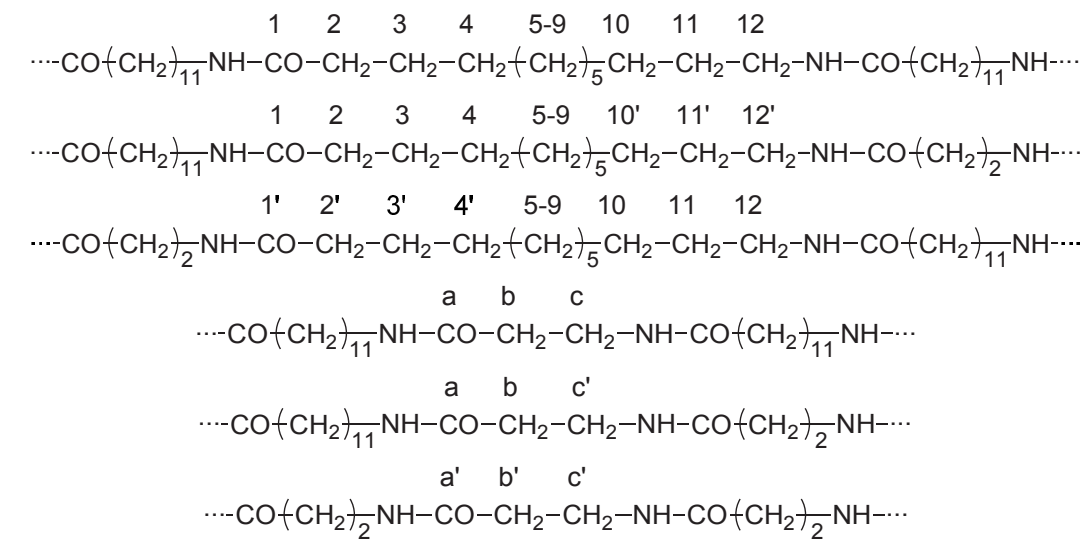
VI.2.1 Poly(β -Ala-*co*-ADA) characterization

As poly(β -Ala-*co*-ADA) is synthesized for the first time, 2D ¹³C-¹H correlation NMR experiments (HSQC and HMBC) of the resulting product were therefore carefully conducted to

get an insight into its structure:

Different peaks are observed at around 2.0 ppm in the ^1H axis of 2D ^1H - ^{13}C NMR correlation spectrum (HMBC and HSQC, Figure 6.1 and 6.2), which correspond to $-\text{NH}-\text{CO}-\text{CH}_2-$ signals. According to the ^1H NMR spectrum of poly(β -alanine) in the previous chapter, the broad peak at 2.30 ppm can be assigned to the methylene group of β -alanine monomer units. According to the assignments of poly(12-amino dodecanoic acid) synthesized in the same conditions (Figure 6.3), two other resonances with higher chemical shift at 2.12 and 2.04 ppm are assigned to the methylene group at the α -position to carbonyl group of ADA monomer units: the peak at 2.12 ppm is assigned to H^2 of the ADA block, and the peak at 2.04 ppm is consequently assigned to $\text{H}^{2'}$. According to the previous investigation, the broad peak at 3.27 ppm corresponds to another methylene group of β -alanine monomer units, and the two higher chemical shift resonances at 3.01 and 2.94 reflect the methylene groups H^{12} and $\text{H}^{12'}$. More precisely, the peak at 3.01 ppm corresponds to H^{12} and another peak at 2.94 ppm refers therefore to $\text{H}^{12'}$ (Figure 6.3).

Table 6.1: Chemical structures and atom numbering.



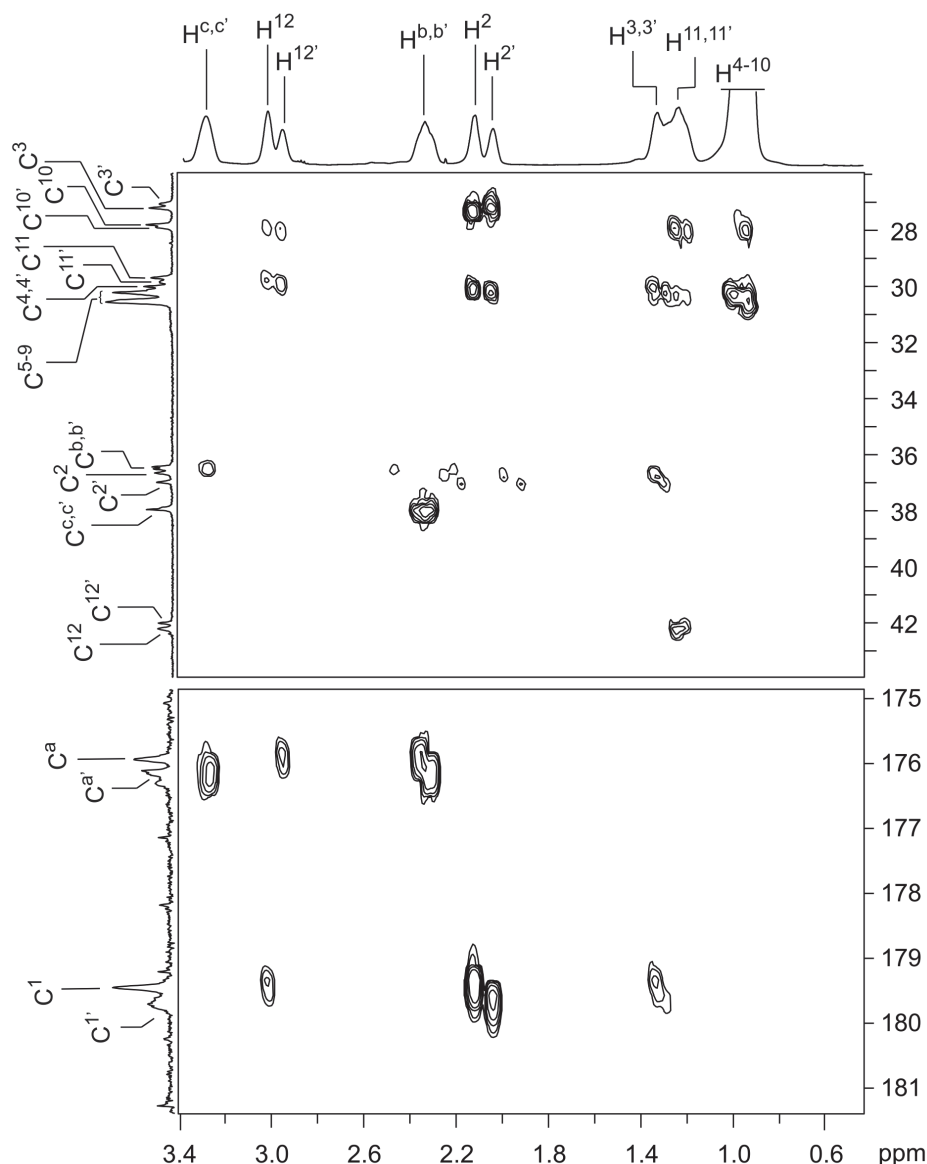


Figure 6.1: Copolymerization of β -alanine and ADA in $[\text{MMIm}]\text{CH}_3\text{PO}_3\text{H}$ at $150\text{ }^\circ\text{C}$ for 16 h (N_2 , β -alanine/ADA (mol/mol) = 1/1, monomers /IL (g/g) = 1/1): 2D ^1H - ^{13}C HMBC NMR spectrum of resulting poly(β -Ala-co-ADA) (500MHz, formic acid with external benzene- d_6 , ref. δ (benzene- d_6) $^1\text{H}/^{13}\text{C} = 7.16/128.06$ ppm).

As can be seen in the carbonyl zone (175-181 ppm) of the ^1H - ^{13}C long-distance correlation HMBC spectrum (Figure 6.1), two series of resonances are present. Based on the previously acquired knowledge in Chapter V, the two peaks at around 176 ppm in the ^{13}C axis are assigned to the carbonyl of β -alanine monomer units, and the lower chemical shift signals at *ca.* 179 ppm correspond therefore to carbonyl group of ADA units. More details are given as the following: H^2 - C^1 coupling is observed at 2.12/179.45 ppm, and a long-distance coupling between H^{12} and C^1 can be also detected at 3.01/179.45 ppm, which confirms that the peaks H^2 and H^{12} belong to the methylenes groups of ADA monomer units; a coupling between $\text{H}^{2'}$ and ^{13}C resonance of a carbonyl group at 179.70 ppm is present, which can reflect the coupling of

$H^{2'}-C^{1'}$. It is observed that the broad peak at 2.30 ppm is coupled with two different carbonyl ^{13}C resonances at around 176 ppm, indicating that it consists of two overlapping resonances belonging to β -alanine monomer units, and the corresponding 1H resonances reflect H^b and $H^{b'}$ which overlap and can be hardly distinguished. With the help of poly(β -alanine) assignments in Chapter V, the carbonyl group at 176.15 ppm corresponds to $C^{a'}$, and another peak at 175.93 can be assigned to C^a , since it is coupled with $H^{12'}$. Besides, two overlapping couplings are observed at 1.34/179.45 ppm and 1.32/179.70 ppm in the HMBC spectrum, suggesting that C^1 and $C^{1'}$ are coupled respectively with the methylene protons H^3 (1.34 ppm) and $H^{3'}$ (1.32 ppm) at β position to carbonyl group of ADA monomer units.

In the zone of methylene groups (Figure 6.1), other resonances can be recognized: H^2 is coupled with the carbon atoms of its adjoining methylenes, which are assigned respectively to C^3 (27.20 ppm) and C^4 (30.00 ppm), for a coupling at 2.12/27.20 ppm (H^2-C^3) and another coupling at 2.12/30.00 ppm (H^2-C^4) are present. Two spots at 2.04/27.06 ppm and 2.04/30.22 ppm present respectively $H^{2'}-C^{3'}$ and $H^{2'}-C^{4'}$ couplings, and two other spots at 1.34/30.00 ppm and 1.32/30.14 ppm reflect respectively H^3-C^4 and $H^{3'}-C^{4'}$. C^{12} and $C^{12'}$ are coupled with their adjacent methylene protons because their two overlapping spots at 1.24/42.24 ppm and 1.20/42.00 ppm are present in the spectra, corresponding respectively to $H^{11}-C^{12}$ and $H^{11'}-C^{12'}$.

In the HSQC spectrum (Figure 6.2), couplings at 3.27/37.95 ppm and 2.33/36.51 ppm are present, which correspond respectively to the coupling H^c-C^c (overlying with $H^{c'}-C^{c'}$) and H^b-C^b (overlying with $H^{b'}-C^{b'}$). With the resonance assignments mentioned above and their corresponding $^1H-^{13}C$ couplings, C^2 (36.66 ppm), $C^{2'}$ (36.98 ppm), C^3 (27.20 ppm), $C^{3'}$ (27.06 ppm), C^4 (30.00 ppm), $C^{4'}$ (30.22 ppm), C^{11} (29.70 ppm), $C^{11'}$ (29.85 ppm), C^{12} (42,21 ppm) and $C^{12'}$ (42,01 ppm) are recognized in the ^{13}C axis accordingly.

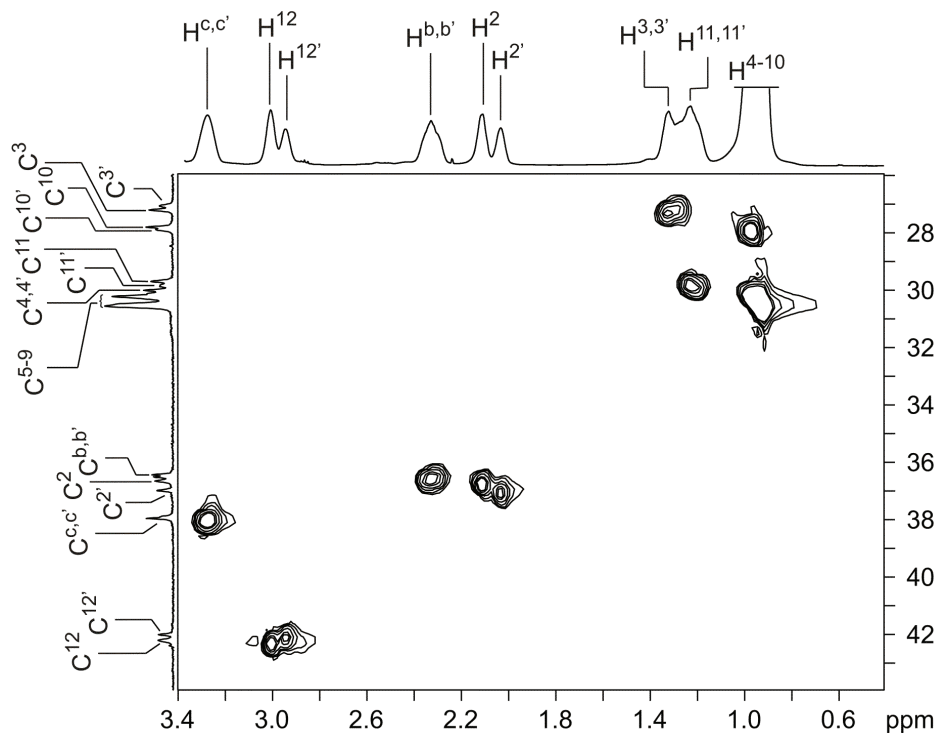


Figure 6.2: Copolymerization of β -alanine and ADA in $[\text{MMIm}]\text{CH}_3\text{PO}_3\text{H}$ at 150°C for 16 h (N_2 , β -alanine/ADA (mol/mol) = 1/1, monomers /IL (g/g) = 1/1): 2D ^1H - ^{13}C HSQC NMR spectrum of resulting poly(β -Ala-co-ADA) (500MHz, formic acid with external benzene- d_6 , ref. δ (benzene- d_6) $^1\text{H}/^{13}\text{C}$ = 7.16/128.06 ppm).

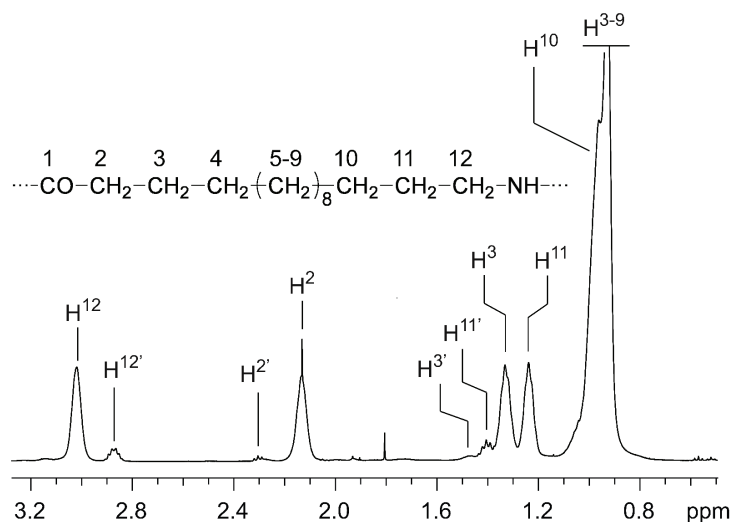


Figure 6.3: Polymerization of ADA in $[\text{MMIm}]\text{CH}_3\text{PO}_3\text{H}$ at 150°C for 16 h (N_2 , ADA/IL (g/g) = 1/1): ^1H NMR spectrum of resulting poly(ADA) (500MHz, formic acid with external benzene- d_6 , ref. δ (benzene- d_6) ^1H = 7.16 ppm).

It can be observed, again in the HMBC spectrum (Figure 6.1), that H^{12} (3.01 ppm) is coupled with C^{11} (29.70 ppm) and another resonance at 27.80 ppm. The latter is, therefore, assigned to C^{10} (27.80 ppm). $\text{H}^{12'}$ (2.94 ppm) is coupled with $\text{C}^{11'}$ (29.85 ppm) and another resonance at

27.89 ppm that is assigned to C^{10'}. The Assignments of C¹⁰ and C^{10'} are further confirmed by the couplings H¹¹-C¹⁰ (1.24/27.80 ppm) and C^{11'}-C^{10'} (1.20/27.89 ppm).

The assignments of all the resonances are summarized as the following:

Four different methylene groups at the α -position to the carbonyl groups are observed in ¹H and ¹³C NMR spectra (H²/C², H^{2'}/C^{2'}, H^b/C^b and H^{b'}/C^{b'} signals in Figure 6.1 and 6.4), and it indicates that four different connections are present in the resulting copolyamide (Table 6.1), which are ADA-ADA (H², C²), β -Ala-ADA (H^{2'}, C^{2'}), ADA- β -Ala (H^b, C^b) and β -Ala- β -Ala (H^{b'}, C^{b'}). The fact that four different amide connections are present can be further confirmed by the existence of four different methylenes at the α -position to the amino groups (H¹², H^{12'}, H^c and H^{c'} at 2.8-3.4 ppm, Figure 6.1) and of four different resonances in the carbonyl zone (170-180 ppm) of the ¹³C spectrum (Figure 6.4).

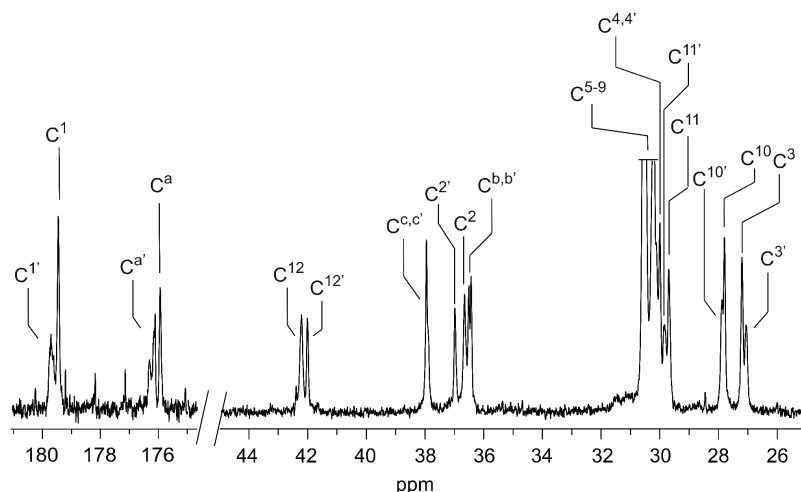


Figure 6.4: Copolymerization of β -alanine and ADA in [MMIm]CH₃PO₃H at 150 °C for 16 h (N₂, β -alanine/ADA (mol/mol) = 1/1, monomers /IL (g/g) = 1/1): ¹³C NMR spectrum of resulting poly(β -Ala-co-ADA) (500MHz, formic acid with external benzene-d₆, ref. δ (benzene-d₆) ¹³C = 128.06 ppm).

VI.2.2 Influence of different parameters on poly(β -Ala-co-ADA) synthesis

As a comparison between classical polyamide synthesis in organic solvents and in ILs, the polymerization reaction was first carried out in a conventional polyamide solvent, N-methyl-2-pyrrolidone (NMP) in the presence of TPP. It can be seen in Table 6.2 that the inherent viscosity (η_{inh}) of the resulting polymer was limited to 0.25 dL/g when the reaction was maintained during 16 h (Entries 1 and 2), while when the polymerization was conducted in [MMIm]Cl and [EMIM]Cl (Entries 3-6), only traces of product could be obtained after

purification. The NMR study of the reaction media shows that only oligomers were formed in these two ILs. It is well known that phosphonate compounds²⁷ and phosphate^{28,29} are commonly used as condensing agent for peptide synthesis and polyamides. Polymerization were then carried out in the ILs containing phosphonate and phosphate anions. Poly(β -Ala-*co*-ADA) were formed with quantitative yield in [MMIm]CH₃PO₃H and [MMIm](CH₃O)₂PO₂, and the inherent viscosity of the resulting copolyamide was the same as, or even higher than that obtained in NMP (Entries 7-14). It is proved therefore [MMIm]CH₃PO₃H and [MMIm](CH₃O)₂PO₂ can be used as suitable alternative solvents for polyamide synthesis.

Table 6.2: Polymerization between β -alanine (β -Ala) and 12-amino dodecanoic acid (ADA) at 150 °C, β -alanine/ADA (mol/mol) = 1/1, monomers/TPP (mol/mol) = 1/1.

Entry	Reaction medium	Monomers/IL (g/g)	Time (h)	η_{inh} (dL/g)
1	NMP	1/1	16	0.24
2	NMP	1/2	16	0.25
3	[MMIm]Cl	1/1	16	- ^a
4	[MMIm]Cl	1/2	16	- ^a
5	[EMIm]Cl	1/1	16	- ^a
6	[EMIm]Cl	1/2	16	- ^a
7	[MMIm]CH ₃ PO ₃ H	1/1	7	0.25
8	[MMIm]CH ₃ PO ₃ H	1/1	16	0.23
9	[MMIm]CH ₃ PO ₃ H	1/2	7	0.32
10	[MMIm]CH ₃ PO ₃ H	1/2	16	0.52
11	[MMIm](CH ₃ O) ₂ PO ₂	1/1	7	0.56
12	[MMIm](CH ₃ O) ₂ PO ₂	1/1	16	0.59
13	[MMIm](CH ₃ O) ₂ PO ₂	1/2	7	0.29
14	[MMIm](CH ₃ O) ₂ PO ₂	1/2	16	0.30

^a Polymer obtained with very low yield

The concentration of monomer mixture was studied for reactions in [MMIm]CH₃PO₃H and [MMIm](CH₃O)₂PO₂. When carried out in [MMIm]CH₃PO₃H, the polymerization was favored in the diluted reaction media. Only low molar mass polymers with inherent viscosity (η_{inh}) around 0.25 dL/g were obtained when the mass ratio of monomer mixture and IL was 1:1 (monomers/IL = 1/1 g/g, Entries 7 and 8), while polymer with η_{inh} up to 0.52 dL/g was formed in the diluted medium with monomers/IL = 1/2 g/g (Entry 10). Surprisingly, when conducted in [MMIm](CH₃O)₂PO₂, the reaction was, however, more efficient in the concentrated media.

Polymers with η_{inh} up to 0.59 dL/g were obtained in monomers/IL (g/g) = 1/1 mixture (Entries 11 and 12), whereas it was limited to 0.30 dL/g in monomers/IL (g/g) = 1/1 media (Entries 13 and 14). The reason why the influence of monomers/IL ratio on polymer size is different in these two ILs still remains unknown.

The reaction time was also investigated. It was found that the polymerization did not complete when the reaction mixture was heated for 2-4 h (results not shown), but reached the plateau at the end of 7 h, as the viscosity of resulting polymers remained almost constant even though the reaction time was prolonged to 16 h. There is, however, one exception when the reaction was conducted in [MMIm]CH₃PO₃H with monomers/IL (g/g) = 1/2, as the viscosity increased from 0.32 dL/g at 7 h to 0.52 dL/g at 16 h.

VI.2.3 Poly(β -Ala-co-ADA) composition and mass evolution

Poly(β -Ala-co-ADA) composition and viscosity evolution against time were studied for the reaction in [MMIm](CH₃O)₂PO₂ with monomers/IL = 1/1 g/g at 150 °C, i.e. the best experimental conditions found above. The initial composition of β -alanine (β -Ala_{ini}, mol%) in monomer mixture was varied from 30% to 70% (Table 6.3). It was observed that the inherent viscosity (η_{inh}) increased with decreasing β -Ala_{ini} (or increasing ADA initial percentage). Taking the polymerizations during 7 h for instance, η_{inh} of the resulting polymer was 0.50 dL/g when the β -Ala_{ini} was 70%, and it progressively increased to 0.67 dL/g when the β -Ala_{ini} was decreased to 30%. But when β -Ala_{ini} was less than 30% (results not shown), the resulting polymer became insoluble in formic acid that was used as polyamide solvent to measure the viscosity. The reaction time was prolonged to 16 h, and no significant viscosity evolution was observed when β -Ala_{ini} varied from 70% to 50%, but it increased slightly from 0.62 dL/g to 0.75 dL/g for β -Ala_{ini} = 40% and from 0.67 dL/g to 0.80 dL/g for β -Ala_{ini} = 30%. It must, however, be underlined that care must be taken to extrapolate these results to M_v variations, due to the parallel variation of copolyamide compositions.

Table 6.3: Composition and viscosity evolutions of poly(β -Ala-co-ADA) obtained by reaction between β -alanine (β -Ala) and 12-aminododecanoic acid (ADA) in [MMIm](CH₃O)₂PO₂ (150 °C, monomers /TPP (mol/mol) = 1/1 and monomers/IL = 1/1 g/g). Compositions of resulting polymers obtained by ¹H NMR.

Time = 7 h			Time = 16 h		
β -Ala _{ini} ^a (mol%)	β -Ala _{fin} (mol%)	η_{inh} ^b (dL/g)	β -Ala _{ini} ^a (mol%)	β -Ala _{fin} (mol%)	η_{inh} ^b (dL/g)
30	25	0.67	30	25	0.80
40	32	0.62	40	31	0.75
50	40	0.56	50	35	0.59
60	63	0.51	60	67	0.52
70	83	0.50	70	85	0.51

^a β -Ala_{ini} = molar percentage of β -alanine in initial monomer mixture

^b η_{inh} = inherent viscosity measured in HCOOH (2.5 g/L)

The compositions of resulting poly(β -Ala-co-ADA)s were followed by ¹H NMR studies. The final composition of β -alanine (β -Ala_{fin}) was calculated according to Equation 6.1:

$$\gamma = \frac{I_b + I_{b'}}{I_b + I_{b'} + I_2 + I_{2'}} \quad \text{Equation 6.1}$$

Where γ represents the percentage of β -alanine in the copolyamide, and I represents the resonance intensity of methylene group b, b', 2 and 2' (Table 6.1).

Table 6.3 shows that the composition of resulting poly(β -Ala-co-ADA) differs from the initial one. When β -Ala_{ini} \geq 60%, the resulting polymers were enriched in β -alanine. Taking β -Ala_{ini} = 60% for example, the β -alanine monomer unit content in the copolymer was 63% after 7 h reaction, and 67% after 16 h. On the other hand, it was ADA monomer unit content that was enriched in the resulting copolyamide when the initial β -alanine \leq 50%. The corresponding final composition variation vs. initial one is a S-shape curve (Figure 6.5). Similar curves are commonly observed in chain copolymerizations but the growth of the polymer chains in our system, i.e. polycondensatin, is completely different and composition equations cannot easily be established. The reason of this phenomenon, e.g. reactivity or solubility differences, remains therefore an open question.

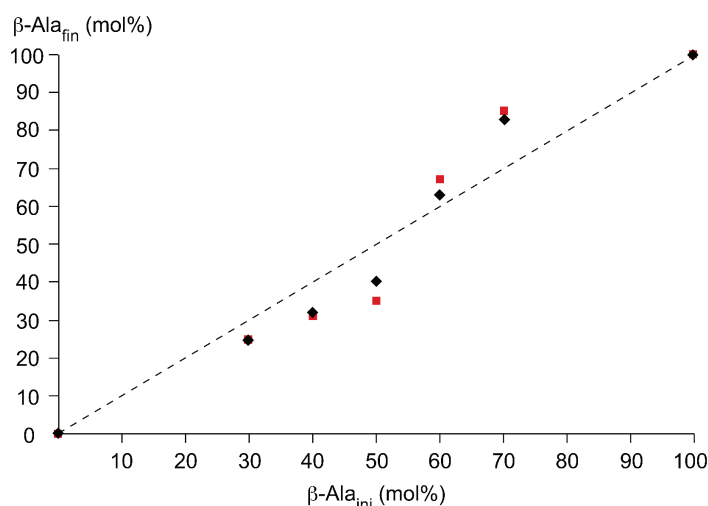
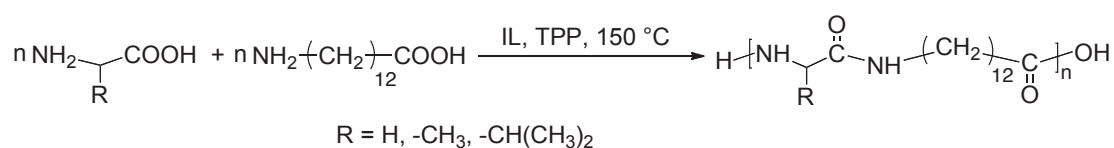


Figure 6.4: Evolution of β -alanine percentage in resulting poly(β -Ala-*co*-ADA), polymerization of β -alanine and ADA in [MMIm](CH₃O)₂PO₂ at 150 °C for 7 h (◆) and for 16 h (■).

VI.2.4 Copolymers from ADA and other natural amino acids

The method was applied to the synthesis of copolyamides from ADA and α -amino acids in [MMIm](CH₃O)₂PO₂ at 150 °C (Scheme 6.3, Table 6.4).



Scheme 6.3: Synthesis of copolyamide in [MMIm](CH₃O)₂PO₂ in the presence of TPP.

The polymerization between glycine (Gly) and ADA yielded the expected poly(Gly-*co*-ADA) copolymer in [MMIm](CH₃O)₂PO₂. When the reaction was conducted with monomers/IL = 1/2 g/g, poly(Gly-*co*-ADA) with high viscosity (0.93 dL/g, Entry 1) was produced after 7h reaction and the polymer continued growing with time, as its viscosity increased to 1.36 dL/g after 16 h reaction (Entry 2). On the other hand, the poly(Gly-*co*-ADA) synthesized in the concentrated media (monomers/IL = 1/1 g/g) were not soluble in formic acid (results not shown), which might indicate that their molar mass is very high.

The influence of monomer mixture concentration on the polymerization between valine (Val) and ADA was also examined: the reaction is favored in the concentrated media, in which poly(Val-*co*-ADA) with an inherent viscosity (η_{inh}) up to 1.02 dL/g was obtained (Entry 4). While η_{inh} was limited to 0.32 dL/g in the media with monomers/IL = 1/2 g/g.

In contrast to poly(Val-*co*-ADA) synthesis, The influence of monomer mixture concentration upon polymerization between leucine (Leu) and ADA was different: only traces of the corresponding polymer poly(Leu-*co*-ADA) were obtained in the medium of monomers/IL = 1/1 g/g for 7 h (Entry 7), and only low molar mass polymer was yielded when the reaction was prolonged to 16 h (Entry 8). On the other hand, in the diluted media (Entries 9 and 10), high molar mass polymers were yielded.

Copolymers could be formed from isoleucine (Ile) and ADA in [MMIm](CH₃O)₂PO₂, and poly(Ile-*co*-ADA) with medium inherent viscosity were obtained (Entry 11-14).

Table 6.4: Polymerization between 12-amino dodecanoic acid (ADA) different natural amino acids (AA) at 150 °C, AA/ADA (mol/mol) = 1/1, monomers /TPP (mol/mol) = 1/1.

Entry	Natural amino acid	Monomers/IL (g/g)	Time (h)	η_{inh}^a (dL/g)
1	Glycine	1/2	7	0.93
2	Glycine	1/2	16	1.36
3	Valine	1/1	7	0.76
4	Valine	1/1	16	1.02
5	Valine	1/2	7	0.24
6	Valine	1/2	16	0.32
7	Leucine	1/1	7	- ^b
8	Leucine	1/1	16	0.34
9	Leucine	1/2	7	0.64
10	Leucine	1/2	16	0.72
11	Isoleucine	1/1	7	0.51
12	Isoleucine	1/1	16	Insoluble
13	Isoleucine	1/2	7	0.32
14	Isoleucine	1/2	16	0.44

^a η_{inh} = inherent viscosity measured in HCOOH (2.5 g/L)

^b Polymer was obtained with very low yield

VI.3 Conclusion

High molar mass copolyamides were synthesized by a simple direct polycondensation of amino acids in imidazolium ILs containing phosphate and phosphonate-based anions. On the other hand, ILs with chloride anions were not efficient reaction media for this type of reactions.

More investigation is clearly required to understand how phosphate and phosphonate interact in this polymerization, so that the variations of copolyamide composition and different concentration influence on copolymer size can be explained.

VI.4 Experimental

VI.4.1 Chemicals

β -Alanine (Aldrich, 99%), glycine (Aldrich, 98%), L-isoleucine (Aldrich, 99%), L-valine (Aldrich, 99%), L-leucine (Aldrich, $\geq 99.5\%$), 12-aminododecanoic acid (Fluka, 97%), 1,3-dimethylimidazolium chloride ([MMIm]Cl, TCI, $>98\%$), 1-ethyl-3-methylimidazolium chloride ([EMIm]Cl, Aldrich, 98%), 1,3-dimethylimidazolium dimethylphosphate ([MMIm](MeO)₂PO₂, Aldrich, $\geq 98\%$), 1,3-dimethylimidazolium methylphosphonate ([MMIm]CH₃PO₃H, Solvionic, $>98\%$) were used as received. Triphenyl phosphite (Aldrich, 97%) was dried by P₂O₅ at 60 °C under vacuum overnight prior to use.

VI.4.2 General procedure of copolymerization

The copolymerization process is described with an example as follows: a mixture of 0.1015 g (1.15 mmol) of β -alanine and 0.2481 g (1.15 mmol) of 12-aminododecanoic acid was introduced in a glass tube fitted with a nitrogen inlet and outlet and a magnetic stirring bar, and 0.6992 g of ionic liquid (IL, monomers/IL = 1/2 wt/wt) and 0.7159 g of dry triphenyl phosphite (TPP, monomers/TPP = 1/1 mol/mol) were added to start the reaction. The polymerization was carried out at 150 °C for a predetermined time under nitrogen flow (100 mL/min). The reaction was then quenched by cooling down to room temperature and adding 10 mL of methanol. The mixture was heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and separated by centrifugation. The supernatant was removed and the washing and separation procedure was then repeated twice. The white to yellowish solid was finally filtered and dried at 80 °C overnight under vacuum (10 mbar).

VI.4.3 Polymerization of 12-aminododecanoic acid

0.2481 g (1.15 mmol) of 12-aminododecanoic acid (ADA) was introduced in a glass tube fitted with a nitrogen inlet and outlet and a magnetic stirring bar, and 0.4962 g of ionic liquid (IL, ADA/IL = 1/2 wt/wt) and 0.3568 g of dry triphenyl phosphite (TPP, ADA/TPP = 1/1 mol/mol)

were added to start the reaction. The polymerization was carried out at 150 °C for 16 h under nitrogen flow (100 mL/min). The reaction was then quenched by cooling down to room temperature and adding 10 mL of methanol. The mixture was heated under reflux for 10 min. The resulting suspension was cooled down to room temperature and separated by centrifugation. The supernatant was removed and the washing and separation procedure was then repeated twice. The white solid was finally filtered and dried at 80 °C overnight under vacuum (10 mbar).

VI.4.4 Analytical Methods

The NMR spectra were recorded on a Bruker Avance 500 spectrometer at 500 MHz (^1H NMR and 2D ^1H - ^1H COSY-45 NMR) and 125 MHz (^{13}C NMR) using a 5 mm inverse probe. 2D ^1H - ^{13}C correlation spectra were recorded through a phase sensitive gradient enhanced 2D HSQC using echo-antiecho experiment (HSQCETGP sequence). 2D ^1H - ^{13}C long-distance correlation HMBC spectra were recorded via heteronuclear zero and double quantum coherence (HMBCGPLNDQF sequence). The product was dissolved in formic acid ($\geq 98\%$) in a NMR tube equipped with a capillary containing Benzene- d_6 (7.16 ppm for ^1H NMR and 128.06 ppm for ^{13}C NMR) as reference.

Viscosimetry: Inherent viscosities (η_{inh}) were measured using Ubbelohde type viscometer (0.05 g of polymer in 20.0 ml of formic acid at 30 °C).

Differential Scanning Calorimetry (DSC) was performed on a TA Instruments 9900 apparatus equipped with a DSC910 module using the following heating/cooling cycles: (1) heating from -80 °C to 250 °C at 20 °C/min, (2) cooling to -80 °C at 20 °C/min. (3) heating from -80 °C to 250 °C at 10 °C/min. Experiments were run under nitrogen atmosphere at low temperature by means of a liquid nitrogen cooling accessory LNCA-II. Melting temperatures (T_m) were taken at the minima of the melting endotherms of the second run.

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General conclusion

In this dissertation, we successfully used ionic liquids in various polycondensation processes. Different polymers, such as linear and hyperbranched polyesters, linear polyethers, poly(β -alanine), polypeptides and copolyamides with natural amino acid units, have been obtained from specifically adapted IL systems.

First of all, we synthesized different Brønsted acid ionic liquids (BAILs), [RBIIm]HSO₄ and [RBIIm]Tf₂N, with the cations functionalized with sulfonic acid.

These BAILs served as both reaction media and catalysts for the polyesterifications of 12-hydroxydodecanoic acid (12-HDA), 2,2-bis(hydroxymethyl)propanoic acid (BMPA) and pre-synthesized oligoesters from diacid/diol equimolar mixtures. The polyesterifications in the BAILs were much more efficient than conventional methods such as those in the bulk. Linear polyesters with a M_w of about 40000 g/mol were obtained after only 5-30 min reaction time at 90-110 °C in the BAILs, while when the reaction is carried out in the bulk, it takes several hours at high temperature (170-300 °C) under high vacuum. Similarly, hyperbranched poly(BMPA) of $M_w = 10000$ g/mol was obtained in 1 h at 150 °C in the BAILs, whereas it takes at least 8 h in the bulk.

We have found that the BAILs' structure played a very important role on 12-HDA polycondensation behavior, as only polyesterification took place in [BBSIm]HSO₄, while apart from polyesterification, ether formation and chain scissions were observed in [BBSIm]Tf₂N. This could be explained by their different structure: [BBSIm]HSO₄ is composed of sulfonic acid containing imidazolium cation and HSO₄⁻ anion, while [BBSIm]Tf₂N is a simple mixture of [BBSIm] zwitterion with Tf₂NH. By employing a model reaction, we have found that the sulfonic acid of [BBSIm]HSO₄ reacts with hydroxyl groups, resulting in formation of the corresponding sulfonic esters, which consumes, therefore, hydroxyl groups. This sulfonic ester reacts in turn with carboxylic acid, forming carboxylic ester and liberating the sulfonic acid. In such a way, the hydroxyl groups are protected against ether formation which takes place at the beginning of polyesterification. On the other hand, no esterification between alcohol and [BBSIm]Tf₂N but etherification of hydroxyl groups takes place.

Investigations were carried out to understand the influence of BAILs concentration on 12-HDA

polyesterification in [BBSIm]Tf₂N/[BMIm]Tf₂N and [BBSIm]HSO₄/[BMIm]HSO₄ mixtures. We showed that 10 mol% of [BBSIm]Tf₂N was enough to get polyesters of high molar mass, while at least 50% of [BBSIm]HSO₄ was required.

The work was extended to the polyesterification of diacids and diols. The polymerisations were also very efficient, as polyesters with M_w of 25000 to 35000 g/mol were obtained in only 15-30 min. As previously observed in 12-HDA polyesterification, the polymerization was also faster in [BBSIm]Tf₂N than in [BBSIm]HSO₄, while the molar mass decreased in [BBSIm]Tf₂N for longer reaction time, which is due to polymer scissions.

The synthesis of hyperbranched polyester of 2,2-bis(hydroxymethyl)propanoic acid (BMPA) was also studied in BAILs. When the polymerization of BMPA was carried out in [BBSIm]Tf₂N, the resulting product was insoluble in solvents. This was assigned to gelation arising from intermolecular etherification. On the other hand, soluble hyperbranched poly(BMPA) was obtained in [BBSIm]HSO₄. The degree of branching (DB) of the resulting polyesters were close to that obtained in the bulk, which tells that the polyester architecture was not influenced by the presence of [BBSIm]HSO₄.

Linear polyethers of long chain aliphatic diols, which are very difficult to synthesize by traditional methods, were obtained by direct polyetherification in [RBSIm]Tf₂N. The polyetherification of 1,12-dodecanediol at 130 °C resulted in the corresponding polyether with M_w up to 23000 g/mol after 60 h reaction time. The polymer structure was carefully examined and it was found that hydroxy end groups were modified to double bonds by dehydration, followed by partial Tf₂NH addition. This method was also applied to linear polyether of other diols with different chain length, and polyethers of molar mass up to 42000 g/mol were obtained.

We also carried out syntheses of polyamides that are difficult or impossible to synthesize by direct polyamidation. We succeeded in obtaining homopolyamides of β -alanine, L-valine and L-isoleucine and copolyamides of 12-aminododecanoic acid and natural α and β -amino acids in phosphorus-containing ILs, in the presence of triphenylphosphite as condensing agent. These polyamides are insoluble in organic solvents and their synthesis in the bulk is impossible due to thermal degradation at high temperature (e.g. melting temperature). Poly(β -alanine) with DP_n up to 49.5 was obtained. Apart from the normal product with carboxylic acid and amine

end groups, small amount of macrocyclic species was formed in the ILs, and part of the carboxylic acid end groups was modified to its corresponding phenyl ester. Copolyamides with inherent viscosity as high as 1.36 dL/g was produced.

During the studies, we have made some efforts to improve the solubility of certain polymers in ILs by modifying IL structure and choosing specific polymer/IL system. But fundamental knowledge on the relationships between IL structure and polymer solubility still needs to be gained, so that a specific IL can be chosen as reaction medium to adapt to a particular polymer solubility requirement.

BAILs were found to present efficient catalyst properties for polyesterification and polyetherification. The way how phosphonate and phosphate anions interact in polyamidation, however, needs to be understood.

The direct polyamidation of amino acids in IL should clearly be extended to establish a library of polymerizable α -amino acids in IL system, so that more polypeptides can be easily obtained. Besides, the structure and chirality of the resulting polypeptides needs to be examined, in relation to IL nature as well as reaction conditions.

Finally, in the polymerization processes presented in this dissertation, no IL recycling has been described, to which, however, more effort should be devoted, so that these processes can be made more industrially interesting.

Résumé en français

The work of the revolution is not yet done, and comrades still need to work hard

——— Dr. Sun Yat-sen, father of modern China

Dans ce travail, nous avons étudié l'application des liquides ioniques en synthèse de polymères par polycondensation. Nous avons synthétisé des polyesters linéaires et hyperramifiés, des polyéthers linéaires et des polyamides et copolyamides linéaires contenant des unités provenant d'acides aminés naturels (β -alanine et acides α -aminés).

1 Synthèse de polyesters et de polyéthers dans des liquides ioniques acides

Dans un premier temps, nous avons synthétisé des liquides ioniques ayant une fonction acide de Brønsted (BAILs) selon un protocole déjà établi.¹ la synthèse comprend deux étapes (Schéma 1). Deux anions différents (HSO_4^- et Tf_2N^-) ont été introduits par simple mélange du zwitterion [RBSIm] avec les acides forts correspondants (H_2SO_4 et Tf_2NH).

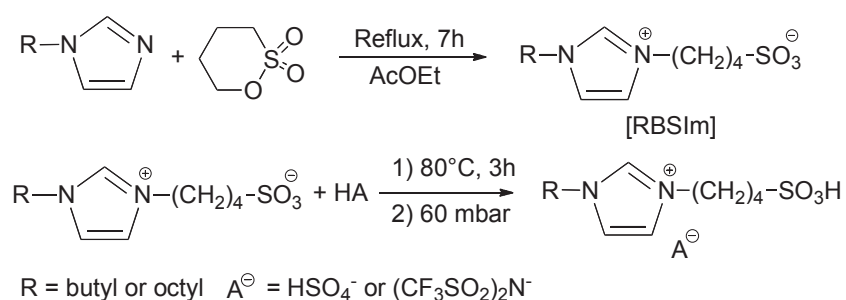


Schéma 1 : Synthèse de BAILs en deux étapes.

1.1 Polyestérification de l'acide 12-hydroxydodécanoïque dans des liquides ioniques acides

Nous avons étudié une réaction modèle, la polyestérification de l'acide 12-hydroxydodécanoïque (12-HDA) dans différents BAILs (Schéma 2).¹

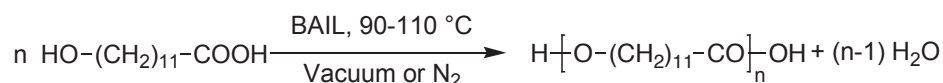


Schéma 2 : Polyestérification du 12-HDA dans BAIL.

La polyestérification est considérablement plus efficace dans les BAILs que lorsqu'elle est

menée en masse : le polyester présente une masse molaire moyenne en masse (M_w) d'environ 40000 g/mol après seulement 5 à 30 minutes de réaction à 90-110 °C dans les BAILs, au lieu de plusieurs heures à environ 200 °C sous vide en masse.

Lorsque la polyestérification du 12-HDA est menée à 110 °C, le milieu réactionnel devient visqueux et hétérogène dans [BBSIm]HSO₄ alors qu'il reste fluide et transparent dans [BBSIm]Tf₂N et [OBSIm]Tf₂N. Cependant, sous microscope optique en lumière polarisée (POM), une séparation de phases est observée dans [BBSIm]HSO₄ et [BBSIm]Tf₂N alors que le milieu est homogène dans [OBSIm]Tf₂N. Cela montre que la solubilité du poly(12-HDA) est améliorée lorsque la longueur de chaîne du substituant alkyle du cation imidazolium augmente. Cela indique également qu'une séparation de phases n'est pas un frein à l'obtention de poly(12-HDA)s de forte masse.

La polymérisation se comporte différemment dans [BBSIm]HSO₄ et dans [BBSIm]Tf₂N (Figure 1) : La polyestérification se produit sans réaction secondaire dans [BBSIm]HSO₄ alors que des réactions d'éthérification des alcools (Schéma 3) et de coupure des groupes ester sont observées dans [BBSIm]Tf₂N (Schéma 4).

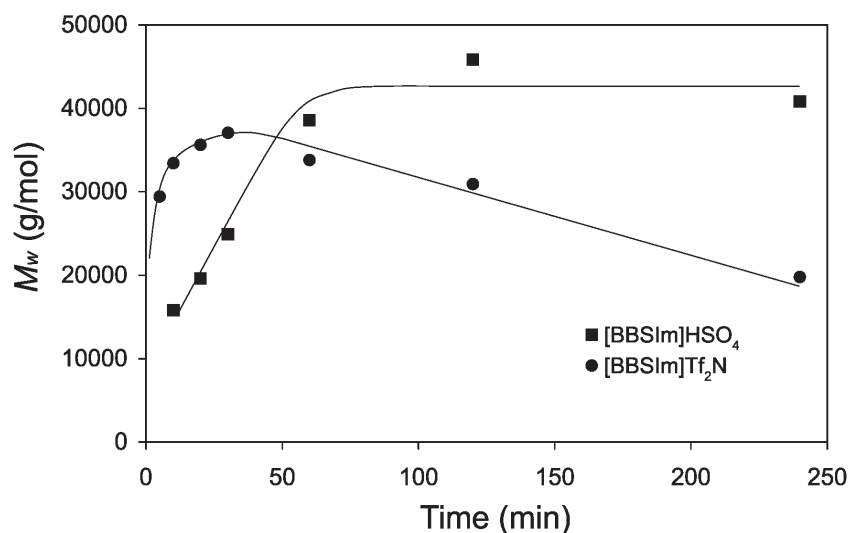


Figure 1: Evolution de M_w (SEC) pour les poly(12-HDA)s synthétisés par polycondensation sous N₂ (500 mL/min) dans [BBSIm]HSO₄ et dans [BBSIm]Tf₂N.

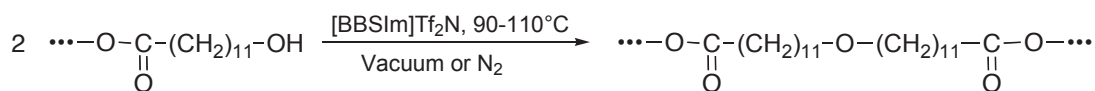


Schéma 3 : Ethérification dans [BBSIm]Tf₂N.

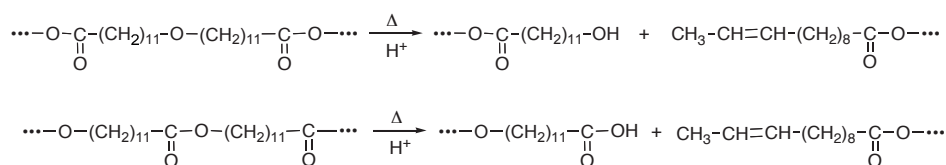


Schéma 4 : Formation de doubles liaisons par coupure des liaisons d'ester.

Pour comprendre cette différence, nous avons étudié les mécanismes de réaction dans les deux BAILs. Lorsque le dodécane-1-ol seul est chauffé à 110 °C dans [BBSIm]HSO₄, il se forme un ester sulfonique. Cet ester sulfonique réagit lorsque de l'acide dodécanoïque est introduit dans le milieu pour donner le dodécanoate de dodécanyle et libérer l'acide sulfonique (Schéma 5). Aucune réaction entre le dodécane-1-ol et [BBSIm]Tf₂N n'a été observée dans les mêmes conditions. Cela pourrait indiquer que la polymérisation de 12-HDA procède via la formation d'un ester sulfonique intermédiaire, qui peut ensuite réagir sur les acides carboxyliques pour conduire au poly(12-HDA). La formation de cet intermédiaire consomme les groupes hydroxyles et les protège des réactions secondaires d'éthérisation, et limite donc la formation d'éther. (schéma 5).

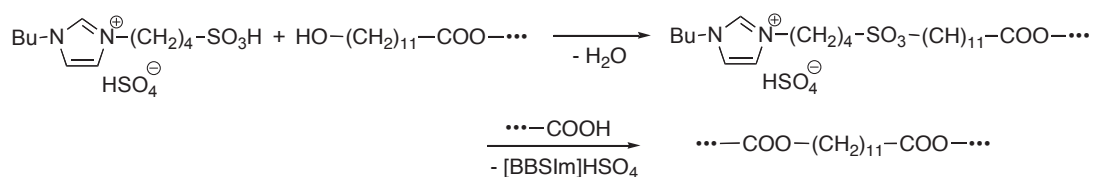


Schéma 5 : Polyestérisation du 12-HDA dans [BBSIm]HSO₄ via la formation de l'ester sulfonique intermédiaire.

Nous avons ensuite étudié l'influence de la concentration en BAIL sur la polyestérisation de 12-HDA. Les BAILs ont été mélangés en différentes proportions avec des liquides ioniques neutres, par exemple [BBSIm]Tf₂N avec [BMIm]Tf₂N, et [BBSIm]HSO₄ avec [BMIm]HSO₄. Nous avons montré que 10 mol% de [BBSIm]Tf₂N est une proportion suffisante pour obtenir un polymère de masse molaire élevée. Cependant, il est nécessaire d'utiliser au moins 50 mol% de [BBSIm]HSO₄ pour obtenir des résultats du même ordre de grandeur dans le système [BBSIm]HSO₄/[BMIm]HSO₄.

1.2 Polyestérification de diacides et de diols dans les BAILS²

Tableau 1 : Post-polycondensation des oligomères dans des BAILS à 110 °C sous N₂ (500 mL/min).

$$\text{H} \left[\text{O}-\text{R}_1-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}_2-\overset{\text{O}}{\parallel}{\text{C}} \right]_n \text{OH} \xrightarrow[110^\circ\text{C}, \text{N}_2]{\text{BAIL}} \text{H} \left[\text{O}-\text{R}_1-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}_2-\overset{\text{O}}{\parallel}{\text{C}} \right]_m \text{OH} - (m-n) \text{H}_2\text{O}$$

		R ₁		
		—(CH ₂) ₁₂ —	—(CH ₂) ₆ —	—(CH ₂) ₄ —
R ₂	—(CH ₂) ₂ —	O ₁ / P ₁	O ₄ / P ₄	O ₇ / P ₇
	—(CH ₂) ₄ —	O ₂ / P ₂	O ₅ / P ₅	---
	—(CH ₂) ₁₀ —	O ₃ / P ₃	O ₆ / P ₆	O ₈ / P ₈

Nous avons étendu notre travail à la polyestérification de diacides et de diols en milieu liquide ionique acide. Pour des raisons d'ajustement stoechiométrique, nous avons préalablement préparé des oligoesters de différents types (Tableau 1), puis étudié leur post-polycondensation dans les BAILS.

Tous les oligomères sont solubles dans [BBSIm]HSO₄ et dans [BMIm]Tf₂N. Cependant, le milieu réactionnel devient rapidement visqueux et hétérogène dans [BBSIm]HSO₄, alors qu'il reste toujours fluide et homogène dans [BMIm]Tf₂N.

Les polymérisations se sont avérées très efficaces dans les deux BAILS. Des polyesters ayant des masses molaires de 25000 à 35000 g/mol sont obtenus après seulement 15 à 30 min de réaction. En début de réaction, les polymérisations sont plus rapides dans [BMIm]Tf₂N que dans [BBSIm]HSO₄. Cependant, comme observé précédemment, les masses molaires décroissent dans [BMIm]Tf₂N lorsque le temps de polymérisation augmente à cause de coupures des groupes esters avec formation de doubles liaisons et d'acides.

Les polymérisations conduites sur des oligomères comportant des unités 1,4-butanediol (O₇ et O₈) n'ont pas permis d'obtenir de polymères de forte masse molaire. La Figure 2 présente une comparaison des spectres RMN ¹H de l'oligomère O₈ et du polymère correspondant, P₈. Elle montre une diminution drastique du rapport stoechiométrique OH/COOH après seulement 5 min de réaction à 110 °C, et, par conséquent, qu'une partie des unités 1,4-butanediol situées en extrémité ont disparu.

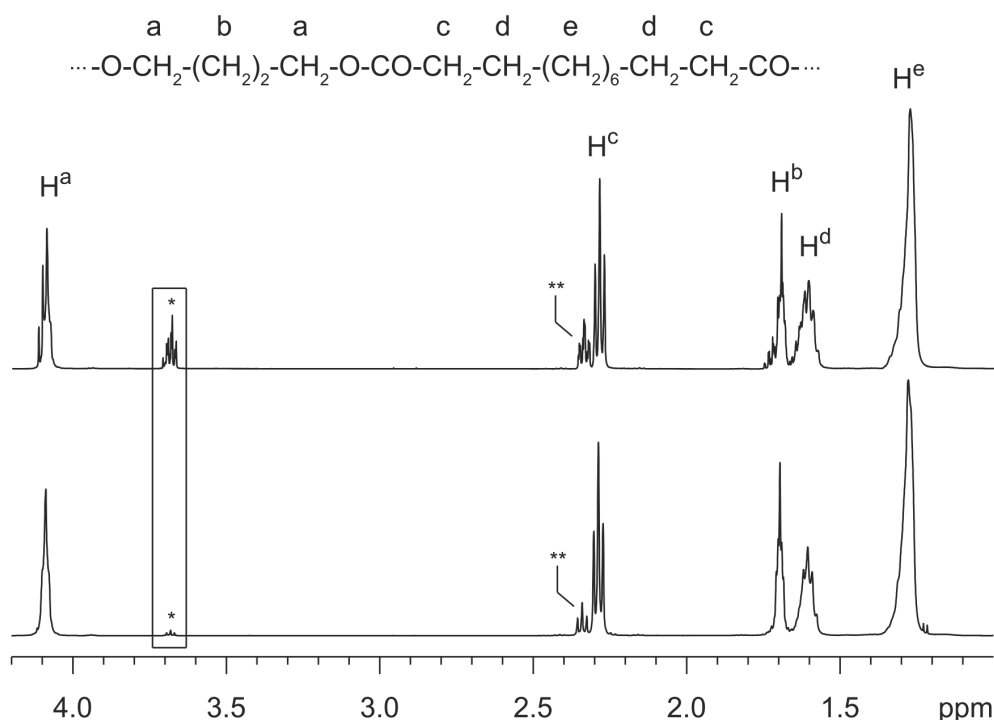


Figure 2 : Spectre RMN ^1H (CDCl_3 , 500 MHz) de l'oligomère O_8 (spectre du haut) et du polymère P_8 synthétisé dans $[\text{BBSIm}]\text{Tf}_2\text{N}$ ($110\text{ }^\circ\text{C}$, 5 min, N_2) (spectre du bas). *: Extrémités $-\text{CH}_2-\text{OH}$, **: Extrémités $-\text{CH}_2-\text{COOH}$.

Du tétrahydrofurane (THF) a été identifié dans le piège connecté au réacteur. Une cyclisation des extrémités 4-hydroxybutyl de O_7 et O_8 en milieu acide permet donc d'expliquer la disparition des extrémités OH pendant la post-polymérisation dans les BAILS (Schéma 6).

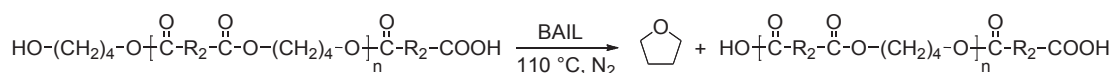


Schéma 6 : Formation de THF pendant la post-polymérisation des oligomères O_7 et O_8 , $\text{R}_2 = -(\text{CH}_2)_2-$ et $-(\text{CH}_2)_{10}-$.

1.3 Synthèse de poly(acide 2,2-bis(hydroxyméthyl)propanoïque) dans les BAILS²

La synthèse d'un polyester hyperramifié par polyestérification de l'acide 2,2-bis(hydroxyméthyl)propanoïque (BMPA) a ensuite été étudiée dans les BAILS (Schéma 7). La synthèse dans $[\text{BBSIm}]\text{HSO}_4$ est beaucoup plus rapide que la méthode habituelle utilisant une polyestérification en masse en présence d'acide paratoluènesulfonique (p -TSA) : 2 h de réaction permettent d'obtenir un poly(BMPA) de $M_w = 9690\text{ g/mol}$ contre 7160 g/mol après 8 h de réaction en masse, valeur qu'il est très difficile de dépasser. Cependant, les produits synthétisés dans $[\text{BBSIm}]\text{Tf}_2\text{N}$, dans lequel les polyestérifications sont plus rapides, ne sont pas solubles dans les solvants organiques usuels, probablement parce que les réactions

d'étherifications observées précédemment dans ce BAIL conduit à des réticulations (Schéma 8).

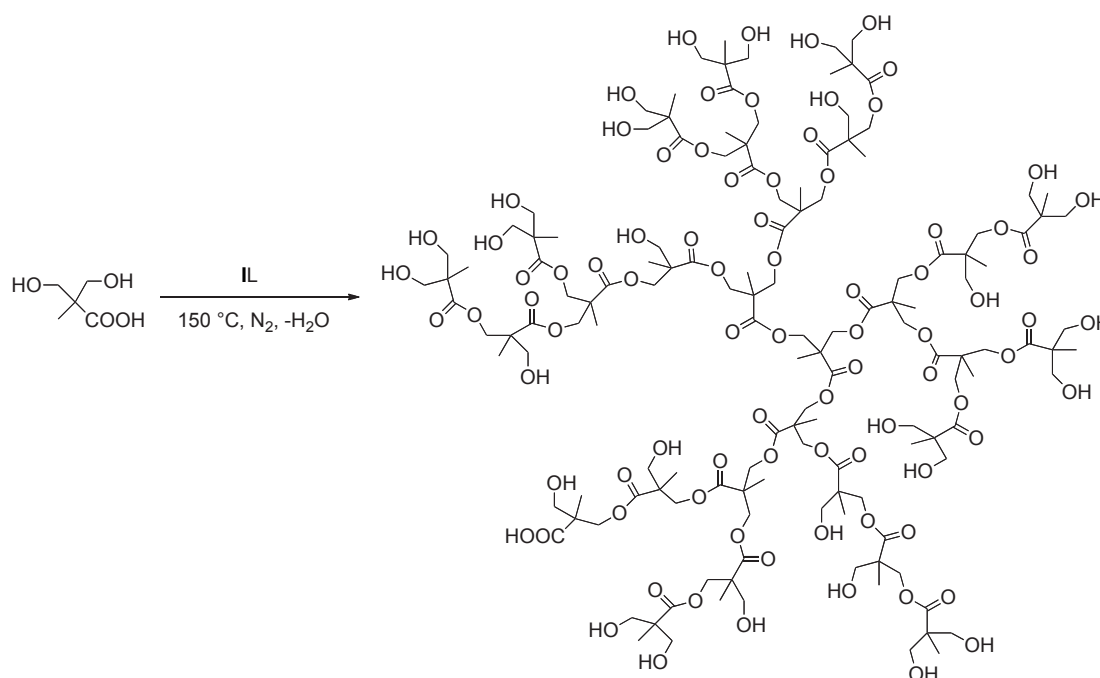


Schéma 7 : Synthèse de poly(BMPA) dans les BAILS.

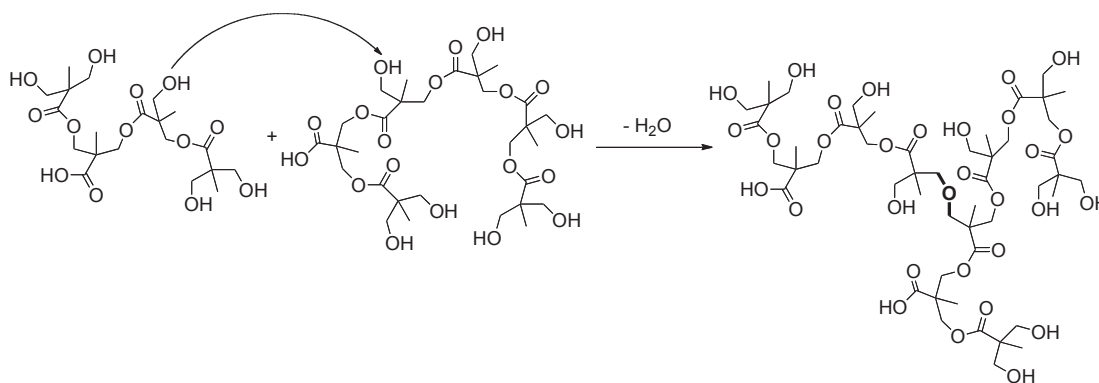


Schéma 8 : Étherification intermoléculaire lors de la synthèse du poly(BPMA).

L'influence du débit d'azote a été examinée. Ce débit a joué un rôle non-négligeable sur l'avancement de la polymérisation. Quand le débit d'azote augmente de 200 à 500 mL/min, les masses molaires des poly(BPMA)s obtenus augmentent sensiblement, en passant, par exemple, de 6810 g/mol à 9690 g/mol après 2 h de réaction.

Les valeurs du degré de branchement (DB) sont légèrement inférieures à 0,5 ce qui montre que l'architecture du poly(BMPA) est proche de celles obtenues en masse, avec une proportion

légèrement supérieure d'unités linéaires par rapport à un polymère "statistique".

1.4 Polyéthérification de diols dans les BAILS

L'observation de réactions secondaires d'éthérification des groupes hydroxyle dans [BBSIm]Tf₂N nous ont conduit à essayer de les appliquer à la synthèse de polyéthers à partir de diols aliphatiques.³

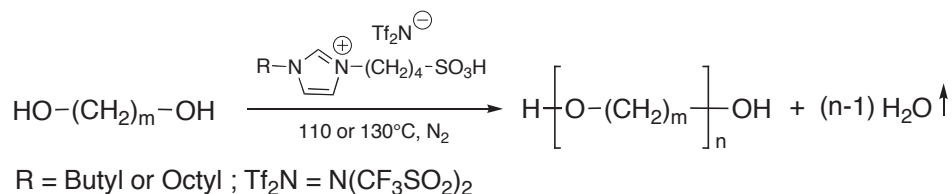


Schéma 9 : Polyéthérification de diols dans [RBSIm]Tf₂N, m > 6.

L'optimisation de la réaction a été effectuée en utilisant la polyéthérification du 1,12-dodécanediol comme réaction modèle. La polymérisation est beaucoup plus efficace à 130 °C qu'à 110 °C : La masse molaire du polyéther obtenu à 130 °C après 63 h de réaction est d'environ 23000 g/mol, alors qu'elle est seulement d'environ 7000 g/mol à 110 °C. Aucune influence significative de la longueur de la chaîne aliphatique du substituant du cation imidazolium n'a été observée, la masse molaire et l'indice de polymolécularité du polyéther obtenu dans [BBSIm]Tf₂N et dans [OBSIm]Tf₂N étant quasiment identiques. La concentration en monomère a également été étudiée. Lorsque le rapport molaire diol/BAIL varie de 2/1 à 3/1, la viscosité du milieu réactionnel augmente, mais la masse molaire du polyéther ne varie pas significativement. Cependant dans un milieu plus dilué en diol, soit diol/BAIL = 1/1, la masse molaire obtenue est beaucoup plus faible, probablement pour des raisons cinétiques, une diminution de la concentration diminuant la vitesse de réaction et augmentant parallèlement le temps de réaction nécessaire pour atteindre des masses molaires élevées.

L'évolution de la masse molaire du poly(oxydodécaméthylène) en fonction du temps de réaction a été suivie par SEC (Figure 3). M_w augmente de 6000 à 20000 g/mol entre 10 h et 40 h de réaction pour atteindre une valeur de 22000 g/mol au bout de 63 h.

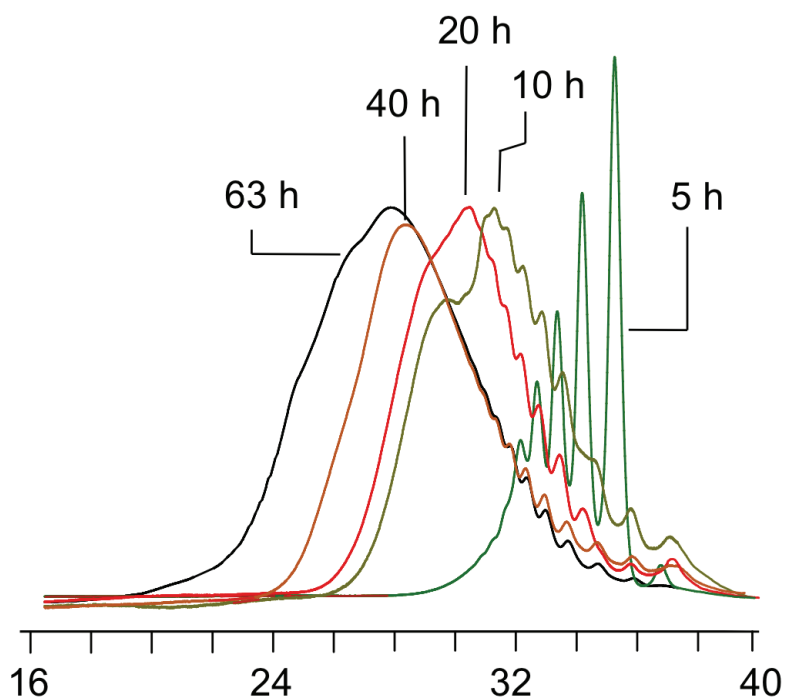


Figure 3 : Polyéthérification du 1,12-dodecanediol dans [BBSIm]Tf₂N à 130 °C sous N₂ (200 mL/min), diol/BAIL= 2/1 : SEC chromatogrammes (CH₂Cl₂, 1.0 mL/min).

La structure du poly(oxydodécaméthylène) obtenu a été examinée par RMN ¹H. Il n'est pas possible de détecter les extrémités hydroxyle, mais la présence de signaux provenant de doubles liaisons α, β et γ des extrémités est observée. Les extrémités hydroxyle subissent donc des réactions secondaires de déshydratation, suivies par une migration du carbocation intermédiaire, formant des doubles liaisons dans les positions α, β et γ du groupe hydroxyle original.

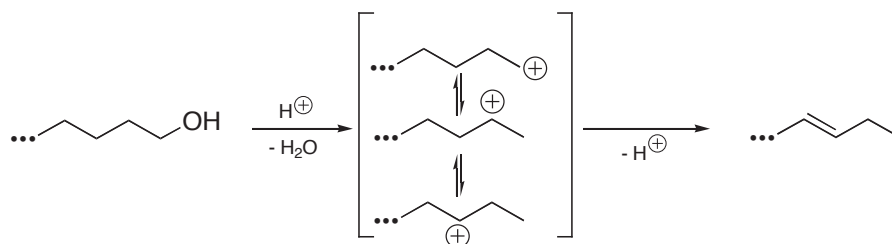


Schéma 10 : Déshydratation des extrémités hydroxyles dans [RBSIm]Tf₂N.

L'étude RMN indique également qu'une partie des doubles liaisons formées est ensuite hydroaminée par Tf₂NH, en conduisant à la formation du produit illustré dans le Schéma 11. La déshydratation et l'hydroamination expliquent pourquoi la masse molaire du polymère peut difficilement croître au-delà de 30000 g/mol dans ces milieux.

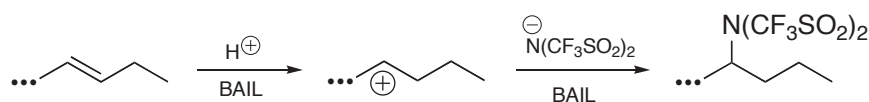


Schéma 11 : Hydroamination des doubles liaisons par Tf_2N^- dans $[\text{RBSIm}]\text{Tf}_2\text{N}$

La méthode a été appliquée à la synthèse d'autres polyéthers linéaires (Tableau 2). Des polyéthers de forte masse molaire ont été obtenus à partir de diols ayant de 7 à 10 unités méthylène. Les réactions du 1,6-hexanediol et du 1,4-butanediol ne conduisent qu'à la formation de THF et d'oxépane, car les réactions intramoléculaires sont favorisées pour ces diols (Schéma 12).

Tableau 2 : Polyétherification de différents diols aliphatiques dans des BAILs (diol/BAIL (mol/mol) = 2/1 à 130 °C sous N_2 (200 mL/min). M_w et \mathcal{D}_M mesurés par SEC et point de fusion (T_m) mesuré par DSC.

Essai	BAIL	Monomère	Temps (h)	Rdt ^a (%)	M_w (g/mol)	\mathcal{D}_M	T_m (°C)
1	$[\text{OBSIm}]\text{Tf}_2\text{N}$	1,10-decanediol	50	65.0	25500	2.3	73.8
2	$[\text{OBSIm}]\text{Tf}_2\text{N}$	1,9-nonanediol	60	61.1	23900	2.3	69.5
3	$[\text{OBSIm}]\text{Tf}_2\text{N}$	1,8-octanediol	50	73.2	26700	2.6	73.0
4	$[\text{BBSIm}]\text{Tf}_2\text{N}$	1,8-octanediol	50	77.3	42000	2.2	68.4
5	$[\text{BBSIm}]\text{Tf}_2\text{N}$	1,7-heptanediol	60	56.2	20400	2.0	50.6
6 ^b	$[\text{RBSIm}]\text{Tf}_2\text{N}$	1,6-hexanediol	60	-	-	-	-
7 ^b	$[\text{RBSIm}]\text{Tf}_2\text{N}$	1,4-butanediol	60	-	-	-	-

^a Rendement après purification.

^b Aucun polyéther formé ni dans $[\text{BBSIm}]\text{Tf}_2\text{N}$ ni dans $[\text{OBSIm}]\text{Tf}_2\text{N}$

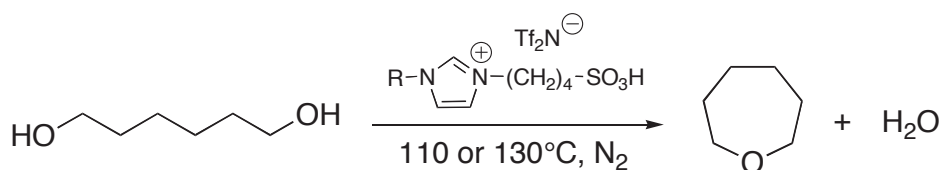


Schéma 12 : Formation d'oxépane par étherification intramoléculaire du 1,6-hexanediol dans $[\text{RBSIm}]\text{Tf}_2\text{N}$, R = octyle or butyle.

2 Synthèse de polyamides à partir d'acides aminés naturels dans des liquides ioniques

Nous avons choisi d'étudier des synthèses de polyamides difficiles ou impossibles à obtenir par polyamidification directe : des polyamides de la β -alanine, L-valine et L-isoleucine et des copolyamides de l'acide 12-aminododecanoïque et d'acides α - et β - aminés. Ces polyamides ne

sont pas solubles dans les solvants organiques et leur synthèse en masse est impossible à cause de réactions de dégradation des unités aminoacide à température élevée (dégradation à la fusion). Nous avons utilisé des liquides ioniques neutres (Schéma 13), les acides forts n'étant pas des catalyseurs de cette réaction.^{4,5}

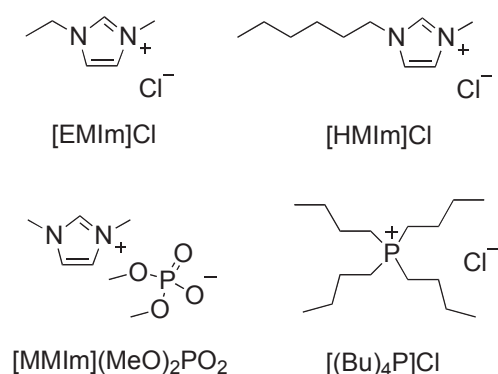


Schéma 13 : Liquides ioniques neutres utilisés pour la synthèse des polyamides.

La synthèse directe de la poly(β -alanine) a été réalisée à 150 °C en présence de triphénylphosphine (TPP), qui joue le rôle d'agent d'activation (Schéma 14). La poly(β -alanine) de degré de polymérisation le plus élevé ($DP_n = 49,5$) a été obtenue dans [MMIm](MeO)₂PO₂ qui solubilise la β -alanine de départ, au contraire des liquides ioniques à anion chlorure.

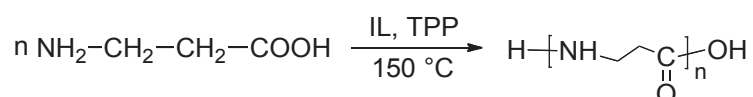


Schéma 14 : Synthèse de poly(β -alanine) dans un liquide ionique en présence du TPP.

La structure de la poly(β -alanine) a été examinée par MALDI-TOF MS. En dehors de l'espèce linéaire attendue à extrémités amine et carboxyle, nous avons identifié des espèces macrocycliques et des espèces ayant une extrémité ester de phényle provenant de l'intermédiaire de réaction. La présence d'esters de phényle a été confirmée par RMN (Figure 4).

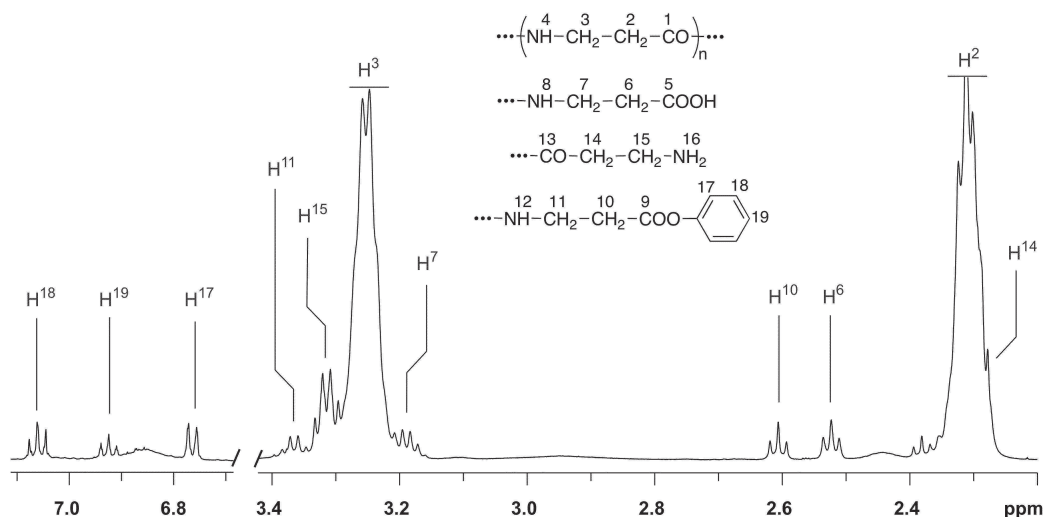


Figure 4 : Polymérisation du β -alanine dans $[(\text{Bu})_4\text{P}]\text{Cl}$ à $150\text{ }^\circ\text{C}$ pendant 2 h (β -alanine/IL = 1/2 wt/wt, β -alanine/TPP = 1/1 mol/mol). ^1H NMR spectre du poly(β -alanine) (500 MHz, l'acide formique avec l'acétone- d_6 externe, ref. δ (acétone- d_6) = 2.05 ppm).

Des polypeptides comme la poly(L-isoleucine) et la poly(L-valine) ont été préparés de la même façon. Comme pour la poly(β -alanine), les spectres MALDI-TOF MS montrent la présence de trois espèces : la macromolécule avec les extrémités attendues, le polymère macrocyclique ainsi que celui terminé par l'ester de phényle.

Cette méthode a ensuite été étendue à la synthèse de copolyamides de l'acide 12-aminododécanoïque (ADA) et d'acides aminés naturels. Les conditions opératoires ont tout d'abord été optimisées à l'aide de la copolyamidation ADA- β -alanine (β -Ala), le produit obtenu est nommé poly(β -Ala-*co*-ADA) (Schéma 15).⁴

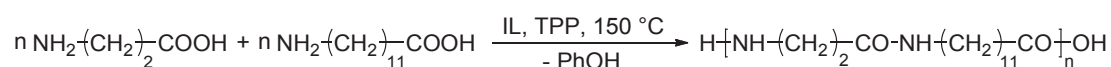


Schéma 15 : Synthèse de poly(β -Ala-*co*-ADA) dans un LI en présence du TPP.

Parmi les LIs étudiés (Schéma 16), nous avons trouvé que $[\text{MMIm}]\text{CH}_3\text{PO}_3\text{H}$ et $[\text{MMIm}](\text{CH}_3\text{O})_2\text{PO}_2$ étaient les plus appropriés, conduisant aux poly(β -Ala-*co*-ADA)s de viscosités les plus importantes. La viscosité inhérente du polymère augmente progressivement jusqu'à un plateau au bout de 7 h de réaction.

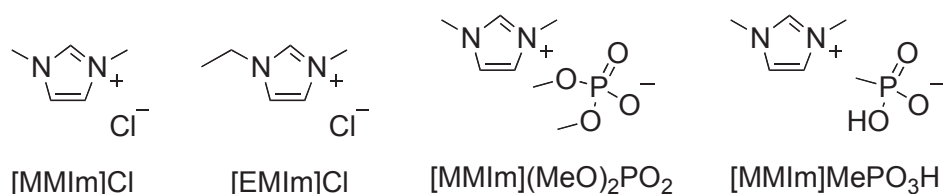


Schéma 16 : LIs utilisés pour la synthèse de poly(β -Ala-co-ADA).

Les autres copolyamides tels que les poly(Gly-co-ADA), poly(Val-co-ADA), poly(Leu-co-ADA) et poly(Ile-co-ADA) ont été synthétisés à partir d'ADA et de respectivement la glycine (Gly), la valine (Val), la leucine (Leu) et l'isoleucine (Ile) (Schéma 17).

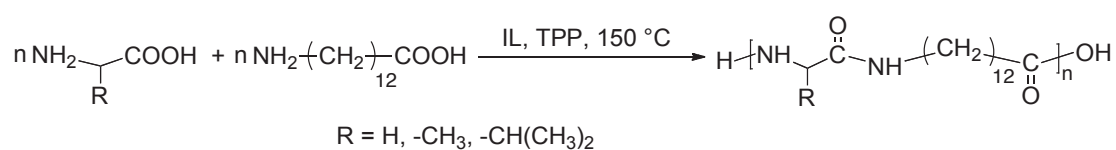


Schéma 17 : Synthèse des copolyamides dans [MMIm](CH₃O)₂PO₂ en présence du TPP.

Tableau 3 : Synthèse de copolyamides à partir d'acide 12-aminododecanoïque (ADA) et de différents acides aminés naturels (AA) à 150 °C, AA/ADA (mol/mol) = 1/1, monomères /TPP (mol/mol) = 1/1.

No. d'essai	AA	Monomères/IL (g/g)	Temps (h)	η_{inh} (dL/g)
1	Glycine	1/2	7	0.93
2	Glycine	1/2	16	1.36
3	Valine	1/1	7	0.76
4	Valine	1/1	16	1.02
5	Valine	1/2	7	0.24
6	Valine	1/2	16	0.32
7	Leucine	1/1	7	- ^a
8	Leucine	1/1	16	0.34
9	Leucine	1/2	7	0.64
10	Leucine	1/2	16	0.72
11	Isoleucine	1/1	7	0.51
12	Isoleucine	1/1	16	Insoluble
13	Isoleucine	1/2	7	0.32
14	Isoleucine	1/2	16	0.44

^a Rendement du polymère obtenu négligeable

Les poly(Gly-*co*-ADA) et poly(Val-*co*-ADA) présentent des viscosités inhérentes élevées (> 1 dL/g) et donc des masses molaires élevées. En revanche, les poly(Leu-*co*-ADA) et poly(Ile-*co*-ADA) présentent des viscosités plus faibles. (Tableau 3).

Conclusion

Les liquides ioniques acides fonctionnalisés avec des groupes sulfoniques sont des milieux qui permettent d'obtenir des polyesters beaucoup plus rapidement et à température beaucoup plus basse (15 min à 110 °C) que par les polyestérifications en masse classiques (quelques heures à 200 °C). Cette méthode permet d'obtenir des polyesters linéaires ou hyperramifiés de forte masse molaire.

Les liquides ioniques permettent d'un autre côté d'effectuer des polymérisations difficiles ou impossibles en utilisant les méthodes classiques. Nous avons ainsi pu obtenir des polyéthers linéaires par polyétherification directe de diols aliphatiques et des polyamides et copolyamides par (co)polyamidification directe d'acides aminés naturels : poly(β -alanine), poly(L-valine), poly(L-isoleucine), poly[acide 12-aminodo-décanoïque-*co*-(acides α - et β -aminés naturels)].

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Polycondensations dans les liquides ioniques

Résumé

Dans ce travail, nous montrons que les liquides ioniques (ILs) sont des milieux réactionnels efficaces pour des polycondensations difficiles ou impossibles à mener dans les milieux classiques.

Des liquides ioniques acides de Brønsted (BAILS) ont été utilisés à la fois comme milieux réactionnels et comme catalyseurs pour la polyestérification de l'acide 12-hydroxy-dodécanoïque (12-HDA), pour celle d'oligoesters préformés à partir de mélanges diol/diacide équimolaires et pour celles de l'acide 2,2-bis(hydroxyméthyl)propanoïque. Les polyestérifications dans les BAILS sont beaucoup plus rapides que les polyestérifications traditionnelles en masse. Des polyesters linéaires de M_w environ 40000 g/mol ont été obtenus après seulement 5-30 min de réaction à 110°C au lieu de plusieurs heures à 200 °C en masse. De la même manière, des polyesters hyperramifiés de $M_w=10000$ g/mol ont été obtenus après 1 h de réaction à 150°C dans les BAILS au lieu de plus de 8 h en masse.

Des polyéthers linéaires de diols à longues chaînes aliphatiques, difficiles à synthétiser par les méthodes traditionnelles ont été obtenus très simplement par polyétherification directe dans des BAILS.

Nous avons également mené des synthèses de polyamides difficiles ou impossibles à obtenir par polyamidification directe. Nous avons ainsi pu préparer des homopolyamides de la β -alanine, de la L-valine et de la L-isoleucine et des copolyamides de l'acide 12-amino-dodécanoïque et d'acides α - et β -aminés naturels dans des ILs à anion phosphoré en présence de triphénylphosphite comme agent de condensation.

Mots clés : liquide ionique, polycondensation, polyester, polyéther, polyamide

Abstract

Ionic liquids (ILs) were proved to be efficient reaction media for polycondensations that are difficult or impossible to carry out in conventional media.

Brønsted acid ionic liquids (BAILS) were used as both reaction media and catalysts for the polyesterification of 12-hydroxydodecanoic acid, of pre-synthesized oligoesters from diacid/diol equimolar mixtures and of 2,2-bis(hydroxymethyl)propanoic acid. The polyesterifications in the BAILS were much more efficient than conventional methods such as those in the bulk. Linear polyesters with a M_w of about 40000 g/mol were obtained after only 5-30 min reaction time at 90-110 °C in the BAILS, instead of several hours at 200 °C in the bulk. Similarly, hyperbranched polyesters of $M_w=10000$ g/mol were obtained in 1 h at 150 °C in the BAILS, whereas it takes at least 8 h in the bulk.

Linear polyethers of long chain aliphatic diols, which are very difficult to synthesize by traditional methods, were obtained by direct polyetherification in BAILS.

We also carried out syntheses of polyamides that are difficult or impossible to synthesize by direct polyamidation. We succeeded in obtaining homopolyamides of β -alanine, L-valine and L-isoleucine and copolyamides of 12-aminododecanoic acid and natural α - and β -amino acids in phosphorus-containing ILs, in the presence of triphenylphosphite as condensing agent.

Keywords: ionic liquid, polycondensation, polyester, polyether, polyamide