



# Polymerization by monomer activation: application to the synthesis of polyaziridines and polyamides

Camille Bakkali-Hassani

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POUR OBTENIR LE GRADE DE  
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SPÉCIALITÉ POLYMÈRES

BAKKALI-HASSANI Camille

**Polymerization by monomer activation: application to the  
synthesis of polyaziridines and polyamides**

Polymérisation par activation du monomère : application à la synthèse de  
polyaziridines et de polyamides

Sous la direction de : Pr. Stéphane CARLOTTI

Soutenue le 11 décembre 2018

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*« Les folies sont les seules choses que l'on ne regrette jamais »*

–Oscar Wilde–

*« La lecture apporte à l'homme plénitude, le discours assurance et l'écriture exactitude »*

–Francis Bacon–



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## List of abbreviations

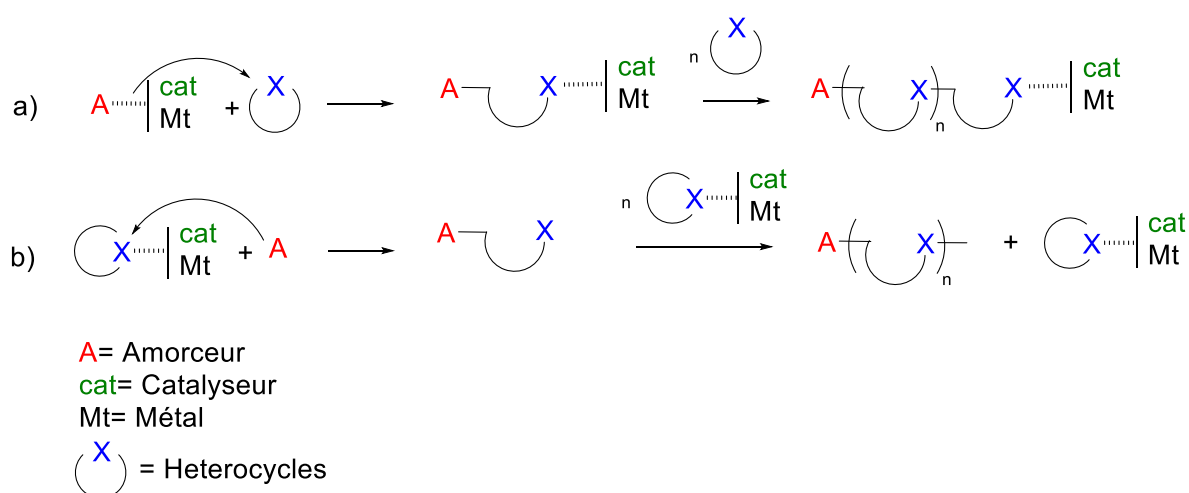
AAm: Acrylamide  
ACEM: Active chain end mechanism  
AGE: allyl glycidyl ether  
Al: Aliphatic  
AMM: Activated monomer mechanism  
Ar: Aromatic  
AROP: Anionic ring-opening polymerization  
 $\beta$ -B:  $\beta$ -butyrolactone  
BuLi: butyl lithium  
C10: sodium caprolactamate  
C20: hexamethylene-1,6-dicarbamoylcaprolactam  
CGCP: chain-growth condensation polymerization  
CROP: Cationic ring-opening polymerization  
*D*: dispersity  
 $\Delta H_m$ : melting enthalpy  
DBU: 1,8- diazabicyclo[5.4.0]undec-7-ene  
DFT: density functional theory  
DMA: dynamic mechanical analysis  
DMAP: 4-(dimethylamino)pyridine  
DMF: *N,N*-dimethylformamide  
DMSO: dimethylsulfoxide  
 $\overline{DP}_n$  : degree of polymerization  
DSC: differential scanning calorimetry  
ECH: epichlorohydrin  
EEGE: ethoxy ethyl glycidyl ether  
EO: ethylene oxide  
EtONa: sodium ethoxide  
EWG: electron withdrawing group  
FTIR : Fourier-transform infrared spectroscopy  
GTP: group transfer polymerization  
HTP: hydrogen transfer polymerization  
*i*-Bu<sub>3</sub>Al: triisobutylaluminium  
*k<sub>p</sub>*: polymerization rate  
LA : Lewis acid  
LB : Lewis Base  
LPs: Lewis pairs  
LPP: Lewis pair polymerization  
LROP: Living ring-opening polymerization  
MALDI : matrix-assisted laser desorption/ionization  
<sup>Me</sup>5-*l*pr : bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene  
MTBD: 7-Méthyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene  
M : monomer  
 $\overline{M}_n$  : number average molar mass  
NMR : nuclear magnetic resonance



NaHMDS: sodium bis(trimethylsilyl)amide  
NCA: N-carboxyanhydride  
NHCs: *N*-Heterocyclic carbenes  
NHC(IMes) : bis(2,4,6-trimethylphenyl)imidazol-2-ylidene  
NHC-OROP: *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization  
NHC-ZROP: *N*-Heterocyclic carbene zwitterionic ring-opening polymerization  
NHOs: *N*-Heterocyclic olefins  
OROP: Organocatalyzed ring-opening polymerization  
PA3 : polyamide 3  
PA6 : polyamide 6  
PA 12 : polyamide 12  
PAz : poly(aziridine)  
PECH : poly(epichlorohydrin)  
PO : propylene oxide  
PPO : poly(propylene oxide)  
ROP: Ring-opening polymerization  
T<sub>d</sub>: degradation temperature  
T<sub>g</sub>: glass transition temperature  
T<sub>m</sub>: melting point  
*t*-BuP<sub>4</sub> : tert-butylimino tris{[tris(dimethylamino)phosphoranylidene]amino}phosphorane  
ToF : time of flight  
Ts : tosyl  
TGA: thermogravimetric analysis  
THF : tetrahydrofuran  
SEC : size exclusion chromatography  
XRD : X-ray diffraction

## Résumé en Français

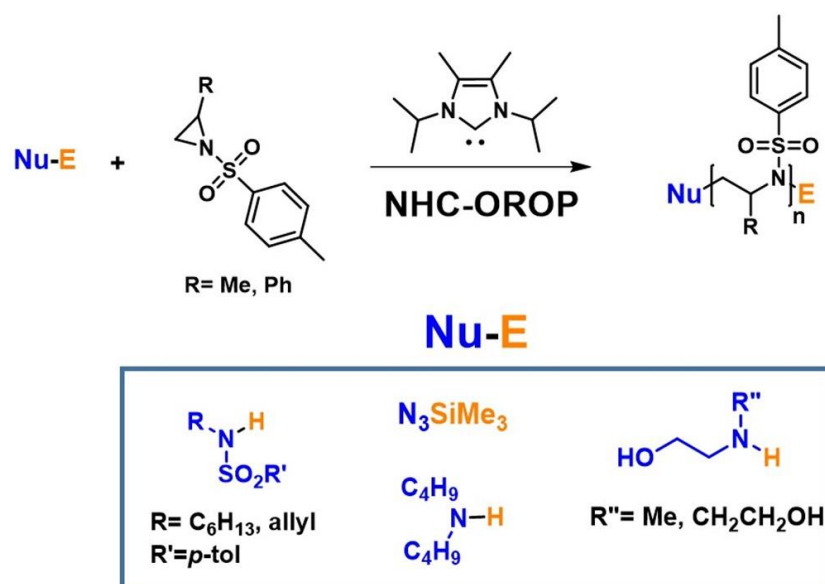
Depuis la découverte des polymérisations « vivantes/contrôlées » par les travaux pionniers de Szwarc (1956) et Flory (1940), respectivement sur la polymérisation anionique du styrène et des diènes<sup>1</sup> et la polymérisation anionique de l'oxyde d'éthylène,<sup>2</sup> de nombreuses méthodologies de synthèse sont apparues pour permettre d'obtenir des polymères aux structures variées et aux dimensions macromoléculaires parfaitement contrôlées. La polymérisation par ouverture de cycle de monomères hétérocycliques tel que les époxydes, les lactones, les lactames, les aziridines pour ne citer qu'eux, en est un des exemples les plus frappant. En effet, de par la grande variété des monomères hétérocycliques, le haut niveau de contrôle (masse molaire, bout de chaîne, dispersité ou composition chimique) ou encore la richesse architecturale accessible par cette méthode, la polymérisation par ouverture de cycle est devenue un des outils majeur de l'ingénierie macromoléculaire.<sup>3-5</sup> Par conséquent de nombreux catalyseurs, généralement inspiré de la chimie moléculaires, ont été développé pour obtenir un haut niveau de contrôle des polymérisations par ouverture de cycle, offrant ainsi une large variété de mécanisme de croissance des chaînes polymères.<sup>6</sup> Deux mécanismes majeurs de propagation sont généralement impliqués dans les réactions de polymérisation par ouverture de cycle ioniques et organocatalytiques. Le mécanisme dit du « bout de chaîne activé » où le catalyseur vient activer en premier lieu l'amorceur puis le bout de chaîne et le mécanisme dit du « monomère activé » qui implique dans ce cas l'activation du monomère par le catalyseur (Schéma 1).



**Schéma 1.** Les deux principaux mécanismes de polymérisation par ouverture de cycle a) le mécanisme du bout de chaîne activé b) le mécanisme du monomère activé

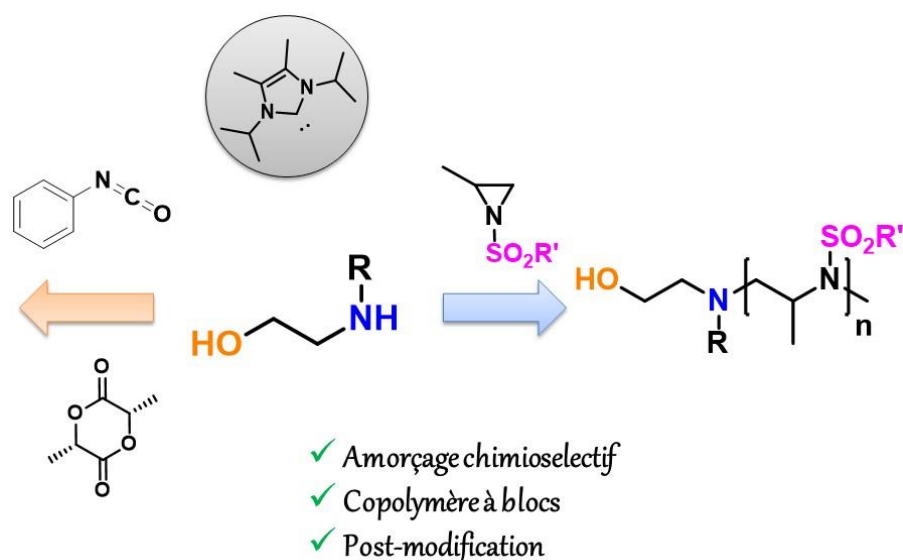
En fonction de la nature du catalyseur et donc par conséquent de la nature de l'espèce active générée, plusieurs mécanismes d'activation peuvent être distingués. Ces mécanismes sont les mécanismes d'activation nucléophiles, électrophiles, acides ou basiques. Le concept d'activation du monomère est étroitement lié à au mécanisme particulier du monomère activé. Ce dernier est un mécanisme de polymérisation qui génère de façon transitoire des espèces hautement réactives facilitant ainsi la réaction d'ouverture de cycle. Dans le cadre de ces travaux de thèses nous avons appliqué le concept de polymérisation par activation du monomère à la synthèse organocatalysée de poly(aziridine)s et à la synthèse de polyamides par voie anionique. Afin de mieux appréhender les caractéristiques essentielles du concept d'activation du monomère ainsi que les différents mécanismes associés, le premier chapitre de ce manuscrit couvrira les différentes méthodes d'activation du monomère qui ont été employées dans la littérature scientifique pour la synthèse de polyamides, de polyester, de polyéthers ou en encore de polymères moins étudiés tels que les poly(aziridine)s ou les poly(cyclopropane)s. L'accent sera mis sur les mécanismes mis en jeux lors de la polymérisation ainsi que les bénéfices apportés par l'activation du monomère par rapport aux méthodes conventionnelles.

Le chapitre 2 de ce manuscrit est consacré l'utilisation de carbènes *N*-heterocycliques (NHCs) pour la polymérisation de monomères activés de façon covalente : les *N*-sulfonyl aziridines. Basé sur les travaux de Bergmann et Toste<sup>7</sup> sur la polymérisation de ces derniers par voie anionique et en collaboration avec l'équipe du Dr. Frederik R. Wurm (Max-Planck Institute de Mayence, Allemagne), nous avons décrit pour la première fois que ces monomères pouvaient être soumis à une polymérisation vivante et contrôlée par voie organocatalytique. Des amines secondaires activées, des amines secondaires non activées, ainsi que des amorceurs fonctionnels ont été utilisés lors de cette thèse (Schéma 2). Les polymères ainsi obtenus ont été caractérisé par spectroscopie RMN, spectrométrie de masse ou encore par chromatographie d'exclusion stérique démontrant ainsi le haut niveau de contrôle de la polymérisation des aziridines *N*-activées catalysée par les NHCs. Les poly(aziridine)s possédant des fonctions réactives en position alpha (azoture ou alcène) ont également été soumis à des réactions de post-modifications par réactions « click » tels que la cyclo-addition de Huisgen ou la réaction de thiol-ène démontrant l'accessibilité de ces fonctions et la possibilité d'obtenir des PAz réactifs.



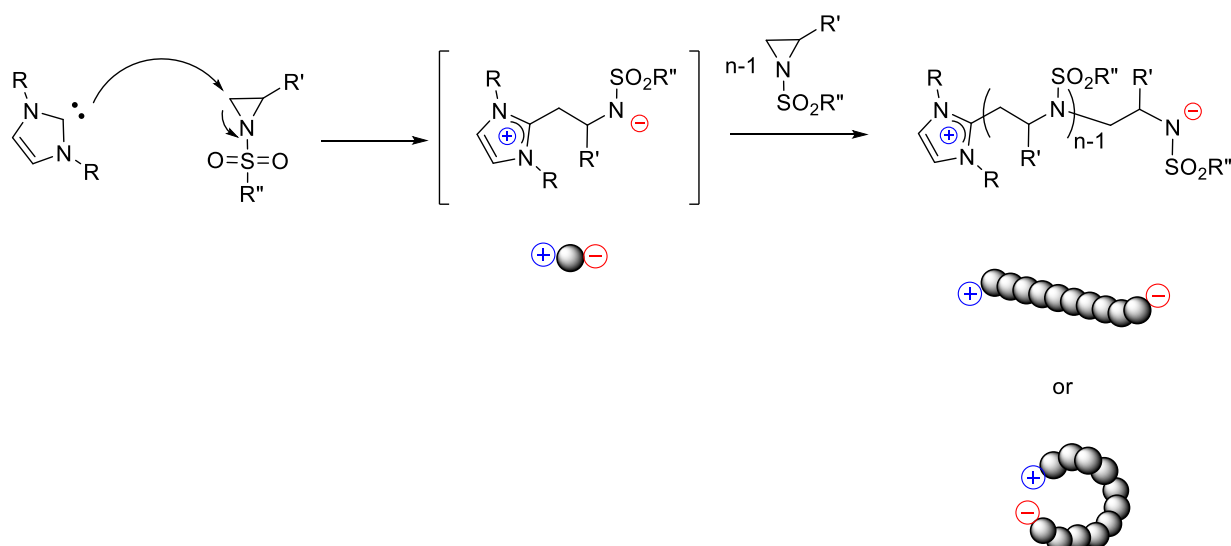
**Schéma 2.** Polymérisation des *N*-sulfonyl aziridines catalysée par les NHCs utilisant des amorceurs variés

Durant notre étude sur les potentiels amorceurs et de façon inattendue, la polymérisation organocatalysée des aziridines *N*-activées par les NHCs s'est également avérée hautement chimio-sélective. En effet, nous avons démontré que la réaction d'amorçage induite par les amino-alcools s'effectue uniquement à partir de l'amine secondaire, permettant ainsi l'obtention de PAz possédant une ou plusieurs fonctions hydroxyles en position  $\alpha$  des chaînes polymères sans aucune protection préalable de la fonction alcool. La présence de fonction(s) hydroxyle(s) en  $\alpha$  des chaînes polymères a été démontré par des réactions de post-modification puis a été judicieusement utilisée pour la synthèse contrôlée de copolymères à blocs poly(aziridine)-*b*-poly(lactide) (Figure 1).



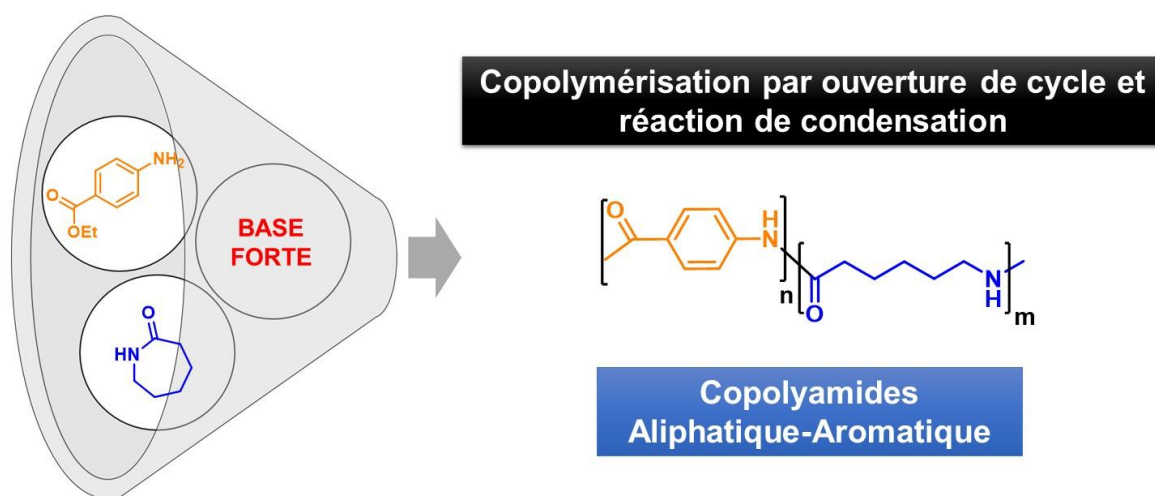
**Figure 1.** Utilisation d'amino-alcools comme amorceur chimio-sélectif pour la synthèse de poly(aziridine)s possédant des fonctions hydroxyles libres en position alpha.

Dans la dernière partie de ce second chapitre, nous avons décrit les résultats préliminaires de la polymérisation des aziridines *N*-activées directement amorcée par les NHCs. Cette polymérisation procède selon un mécanisme particulier dit de « polymérisation par ouverture de cycle zwitterionique »,<sup>8</sup> car dans ce cas, l'espèce active anionique (ici un amidure) et son contre-ion (ici un imidazolium) sont portés par la même chaîne (Schéma 3) permettant ainsi, dans certaines conditions, la synthèse de polymères cycliques. Quatre NHCs aux propriétés stéréo-électroniques différentes ont été employés pour la polymérisation zwitterionique des *N*-sulfonyl aziridines. Cette polymérisation s'est avérée extrêmement NHC-dépendante avec des résultats prometteurs démontrant ainsi le potentiel des carbènes *N*-hétérocycliques en tant qu'amorceurs pour la synthèse organocatalysée des poly(aziridine)s.



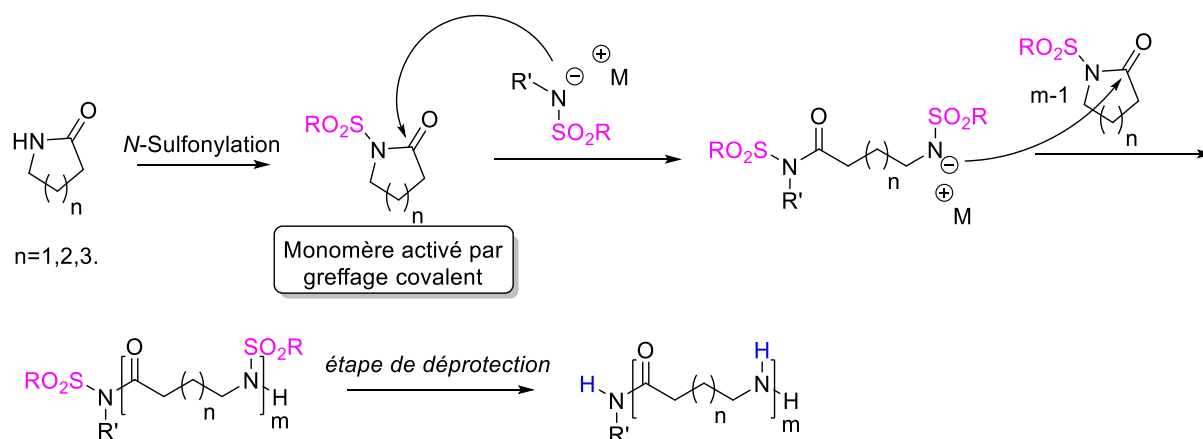
**Schéma 3.** Polymérisation par ouverture de cycle selon un mécanisme zwitterionique avec génération de poly(aziridine)s linéaires ou cycliques

Le troisième et dernier chapitre de cette thèse traite de la synthèse de polyamides par voie anionique, toujours basée sur des concepts d'activation du monomère. Nous avons décrit que la polymérisation par ouverture de cycle de l' $\epsilon$ -caprolactame, pouvait être couplée simultanément à des réactions de condensations d'amino-ester aromatique pour la synthèse de polyamides aliphatiques-aromatiques en une seule étape (Figure 2). Le but, en terme de matériaux, était d'améliorer les propriétés thermomécaniques (principalement thermique et plus particulièrement la température de transition vitreuse ( $T_g$ )) du polyamide 6 en introduisant des unités aromatiques. La possibilité de pouvoir conduire de façon simultanée les réactions d'ouverture de cycle et de condensation, tout en gardant les conditions particulières de synthèse du polyamide 6 (polymérisation en masse et à haute température), a été démontré par de nombreuses réactions modèles. Cette méthode originale de synthèse a permis la préparation de copolyamides aux propriétés thermiques améliorées (plus grande stabilité thermique, et  $T_g$  jusqu' à 79°C comparé à 55°C pour le PA6).



**Figure 2.** Synthèse de copolyamides aliphatique-aromatique par combinaison de polymérisation par ouverture de cycles et réactions de condensation

Dans le but de pouvoir contrôler la polymérisation des lactames, nous avons également appliqué la méthode d'activation par greffage covalent de groupement électroattracteurs tels que les sulfonyls (précédemment utilisé pour l'activation des aziridines) à la chimie des polyamides. En effet, les lactames polymérisent généralement selon un mécanisme dit du « monomère activé » (voir Schéma 1) mais les conditions de polymérisation (en masse, à haute température) conduisent à des réactions de transferts. Par conséquent, et hormis quelques exemples de polymérisation avec des lactames hautement réactifs<sup>9,10</sup> (cycle à quatre chaînons poly-substitués, les  $\beta$ -lactames), la polymérisation par ouverture de cycle des amides cycliques est un procédé « non-vivant ».<sup>11</sup> L'activation covalente de trois membres représentatifs des lactames que sont l' $\epsilon$ -caprolactame, le  $\delta$ -valerolactame ou encore la 2-pyrrolidone, respectivement les cycles à 7, 6 et 5 chaînons, par des groupements tosyls variés a été réalisée dans le but de changer le mécanisme de polymérisation pour obtenir de façon contrôlée des précurseurs de polyamides (Schéma 4). En revanche, les premiers résultats de polymérisations anioniques de ces derniers ont démontré une faible réactivité des lactames *N*-activés vis-à-vis de la polymérisation anionique par ouverture de cycle.

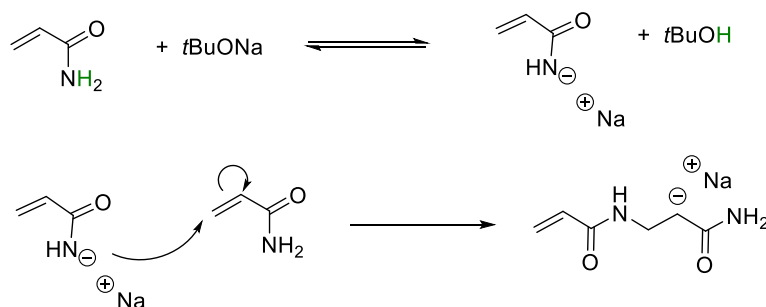


**Schéma 4.** Activation et polymérisation des lactames N-activés par sulfonation pour la synthèse contrôlée de polyamides.

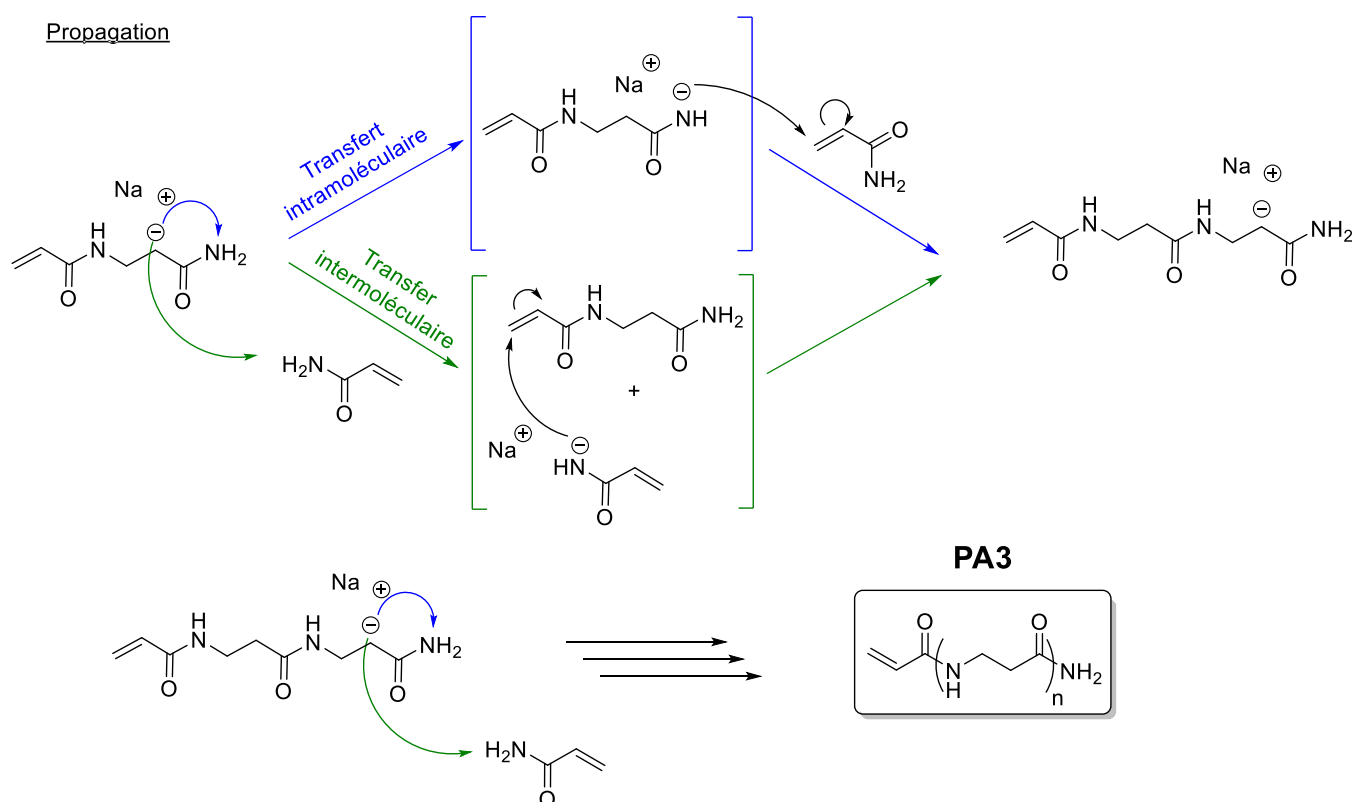
Dans une dernière partie de ce chapitre dédié aux polyamides, nous avons étudié la polymérisation en masse par transfert d'hydrogène de dérivés de l'acrylamide. Cette méthode particulière de synthèse permet l'obtention de dérivés de polyamide 3 par multiple addition de Mikael (Schéma 5). Dans le cadre de cette thèse, nous nous sommes intéressés à la copolymérisation de l'acrylamide avec des dérivés substitués par différents groupements (chaînes alkyles, aromatiques, groupements fonctionnels) soit sur l'atome d'azote, soit sur la double liaison pour étudier l'effet de la substitution sur la réactivité de ces dérivés mais également sur les propriétés des polyamides 3 obtenus.



### Amorçage

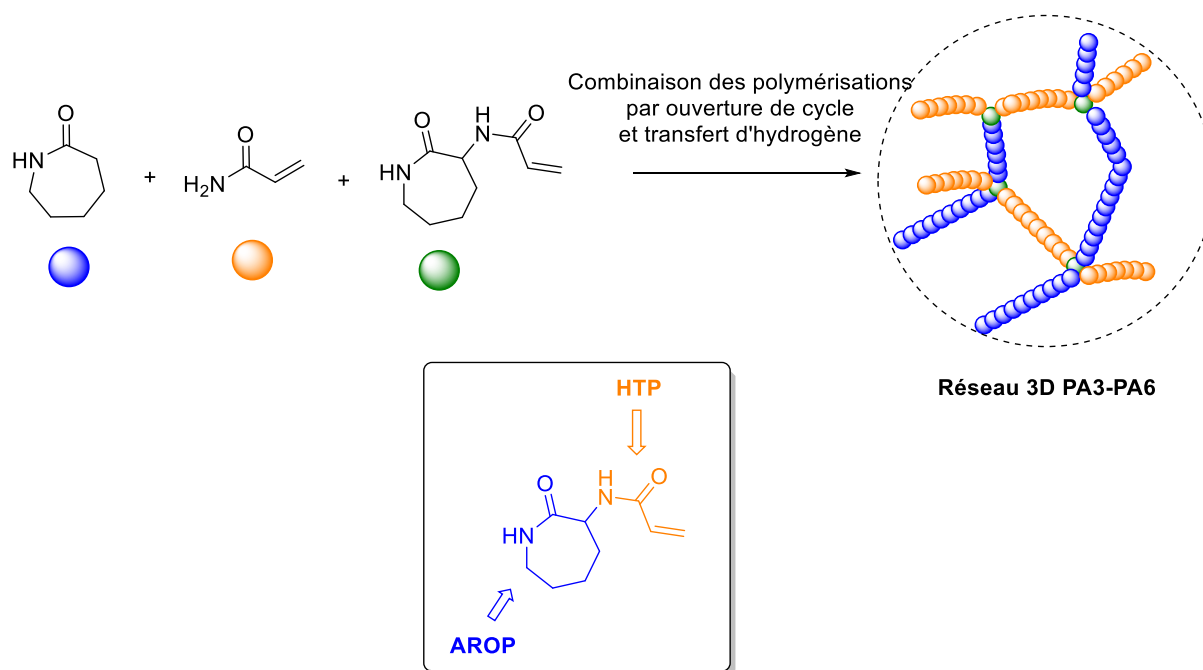


### Propagation



**Schéma 5.** Mécanisme de la polymérisation par transfert d'hydrogène de l'acrylamide pour la synthèse de polyamide 3

Durant ces travaux, la synthèse d'un monomère particulier comportant sur la même structure un motif acrylamide et un motif caprolactame, nous a permis d'envisager la synthèse d'un réseau tridimensionnel PA6-PA3 par combinaison des réactions de polymérisation par transfert d'hydrogène et d'ouverture de cycle (Schéma 6). Les travaux préliminaires réalisés sur ce monomère ont permis de démontrer sa « double » réactivité vis-à-vis des deux mécanismes de polymérisation. En revanche la présence de nombreuses réactions secondaires induite par la terpolymérisation entre l'acrylamide, l' $\epsilon$ -caprolactame et ce monomère particulier n'ont pas permis l'obtention de ce réseau tridimensionnel original.



**Schéma 6.** Stratégie de synthèse combinant la polymérisation par ouverture de cycle et transfert d'hydrogène pour la synthèse de réseaux 3D PA3-PA6.

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# General introduction

Since the discovery of living polymerizations, tremendous developments have been made in the past decades to generate various polymeric structures and architecturally well-defined macromolecules with a wide range of application such as adhesives, biomedical, personal beauty care, microelectronic device or food packaging applications. In most cases, specific applications are driving areas of research in polymer design. As an example, in the field of microelectronics, for the purpose to develop an alternative of traditional photolithography and achieve features sizes smaller than 50 nm, block copolymers with accurate control over the chain length, dispersity or functionality are required. Other diverse fields, such as drug delivery system, necessitate precisely defined macromolecules and nano-scale objects with multiple functionality for cell targeting, delivery or tracking. The ideal polymer synthesis must therefore combine the possibility to control the molar mass, the dispersity, the nature and number of polymer end-groups, the architecture or the topology of the macromolecules.

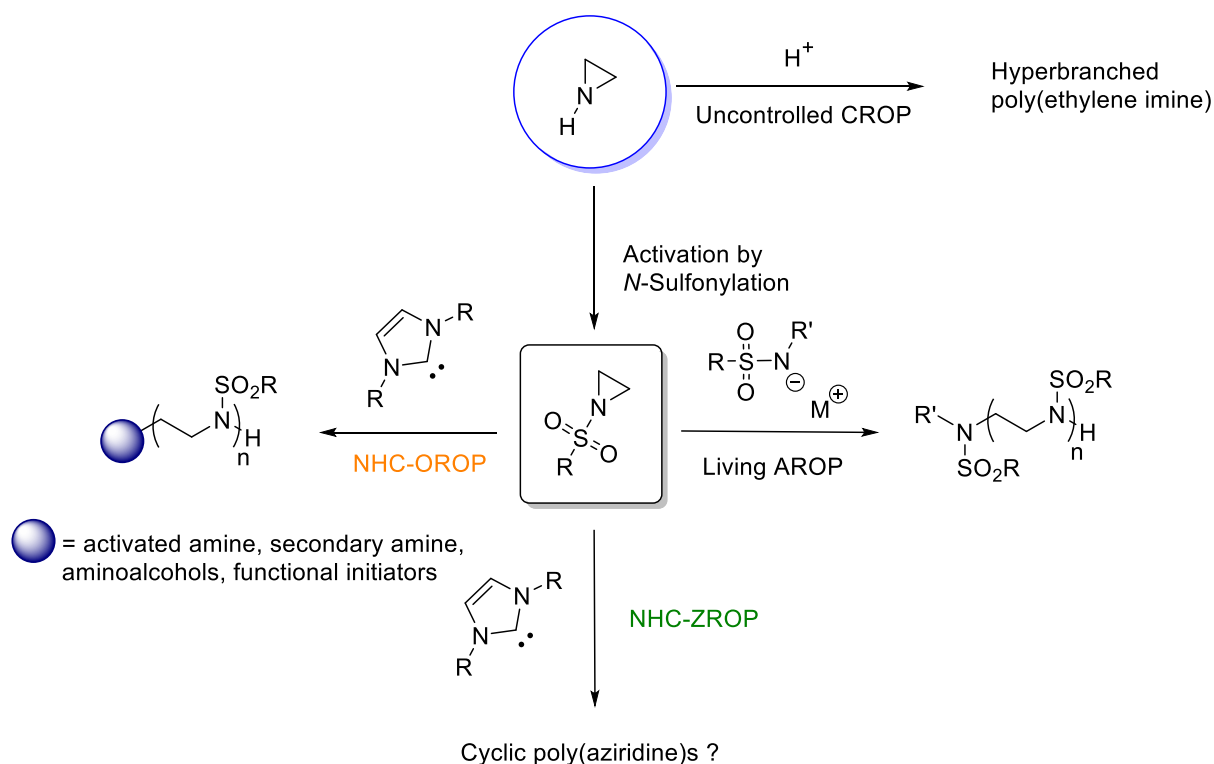
In this context, the living ring-opening polymerization (LROP) of heterocyclic monomers has been a fruitful area in synthetic polymer chemistry due to the variety of monomers that can be subjected to LROP as well as the high level of control. The ring-opening polymerization is a chain-growth process where repeated addition of the monomer to the chain-end leads to an increase of the molar mass. The kinetics and selectivity of the ring-opening process are highly influenced by the nature of the reactive chain-ends, the monomers and the catalysts. LROP proceeds by several distinctive mechanisms, like anionic, anionic, cationic, coordination (or pseudo-ionic). Majority of the monomers polymerize in the “normal way” over the so-called active chain-end mechanism (ACEM), in which the active species are located on the growing macromolecules, usually at their ends. However, there are several instances when ionic species are located not in the macromolecules but on the monomer substrate. These mechanisms of polymerization well known in cationic polymerization but also observed in the anionic polymerization of lactams and *N*-carboxyanhydrides (NCA) are known as activated monomer mechanism (AMM).

The concept of monomer activation directly originates from this particular mechanism, *i.e.* the activated monomer mechanism, and consists to generate species that are more reactive by the addition of a catalyst or by the appropriate design of the monomer substrates (covalent

activation). Over the past decades, with the achievements of molecular chemistry and the emergence of organocatalyzed polymerization,<sup>1-3</sup> numerous strategies have been applied for the activation of wide range of monomers such as lactones, cyclic ethers, lactams, cyclic carbonates etc. In order to gain a better understanding of the different mechanism of activation, the bibliographic chapter has been devoted to selected examples of monomer activation through (i) the activated anionic polymerization of lactams and epoxides, (ii) the Lewis pairs polymerization of cyclic esters and (iii) the anionic polymerization of covalently activated aziridines and carbon cycles.

During this thesis work, the concept of monomer activation has been applied for (i) the synthesis of original polyamides-based materials *via* an anionic mechanism and (ii) the organocatalyzed polymerization of less-studied monomer covalently activated: the *N*-sulfonyl aziridines.

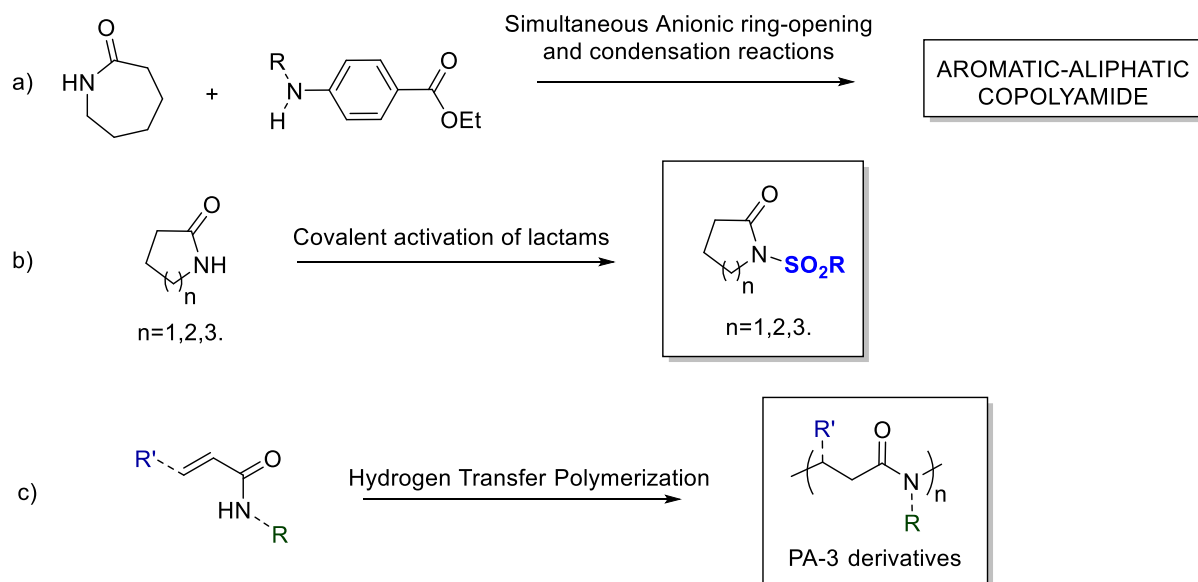
In the literature, non-activated aziridines have been primarily investigated by cationic ring-opening polymerization. The most simple aziridine monomer, namely aziridine or ethylene imine, eventually leads to a hyperbranched poly(ethylene imine) (*h*-PEI) with protonic catalyst, due to extensive chain transfer reactions both to the polymer and the monomer (Scheme 1).<sup>4</sup> In 2005, Toste, Bergmann *et al.* have discovered that *N*-activated aziridnes could be subjected to a controlled anionic polymerization process through monomer activation by *N*-sulfonylation. In the case of anionic polymerization of activated aziridines,<sup>5</sup> a stoichiometric amount of strong organometallic base is generally employed to generate the initiating species. In order to prepare poly(aziridines) free of any metallic residues, the second chapter of this manuscript will cover the organocatalyzed polymerization of *N*-tosyl aziridines mediated by *N*-heterocyclic carbenes (NHCs). This project has been conducted in collaboration with Dr. Frederik Wurm in the Max-Planck Institute of Mainz (Germany) with the aim to prepare poly(aziridines) in an organocatalytic pathway, with controlled molar masses, architecture, end groups, etc. The ability of *N*-heterocyclic carbenes to activate small organic molecules such as alcohol, amine or silylated compounds has been applied to demonstrate the variety of initiating systems allowing the control of the polymerization. Alternatively, NHCs, used directly as initiators, are also well known to generate cyclic polymers by the so-called zwitterionic ring-opening polymerization. Preliminary investigations of the zwitterionic ring-opening polymerization have been explored in order to produce cyclic poly(aziridine)s. Mechanistic investigations as well as model reactions has been performed to determine the mechanism of the NHC-OROP and ZROP of *N*-activated aziridines.



**Scheme 1.** Activation of aziridines by *N*-sulfonylation for AROP, NHC-OROP and NHC-ZROP

In contrast to the less-studied aziridines monomers and related polymers, polyamides are widely used as engineering thermoplastics in a broad range of application areas due to their good mechanical properties. Polyamides are generally obtained by (i) step-growth polymerization starting from the corresponding diacid and diamine monomers or by (ii) anionic ring-opening polymerization (AROP).<sup>6-8</sup> The anionic polymerization of lactams proceeds through an activated monomer mechanism and is used to prepare polyamides 6 and 12 directly from the corresponding lactams. It is the fastest method due to the low activation energy needed, but the occurrence of side reactions implies that AROP of lactams is a non-living process. In a review published two decades ago, Hashimoto has described *sine qua non* conditions for the polymerization of lactams to exhibit features of a “controlled/living” process.<sup>9</sup> Thus, polymerization in solution of highly reactive lactams under mild conditions are required, but the living ring-opening polymerization of the most common lactams, such as  $\epsilon$ -caprolactam and 2-pyrrolidone, has never been reported. In this context, the third chapter has been dedicated to different approaches for the synthesis of new polyamide-based materials were investigated through (i) the simultaneous anionic ring-opening and condensation reactions for the synthesis of

aliphatic-aromatic copolyamides (ii) the covalent activation of lactams by electron withdrawing groups and (iii) the synthesis polyamide 3-based materials by hydrogen transfer polymerization of acrylamide derivatives.



**Scheme 2.** Anionic strategies employed in this thesis work for the synthesis of new polyamide-based materials

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**Chapter 1.**  
**Bibliographic Chapter: Concept of**  
**Monomer Activation in Anionic and**  
**Organocatalytic Ring Opening**  
**Polymerization**

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## 1. Introduction

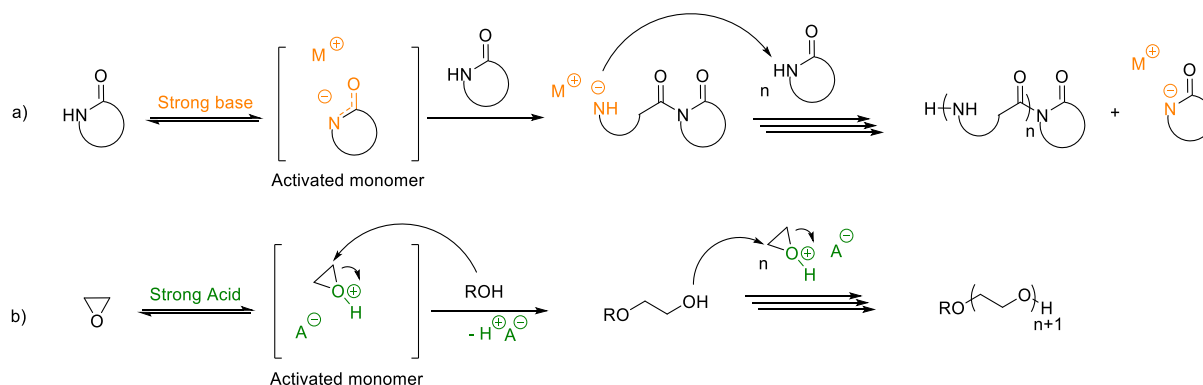
The publication by Paul Flory about anionic ring-opening polymerization (AROP) of ethylene oxide, in 1940, is considered as being the first example of living ring-opening polymerization (LROP).<sup>1</sup> Despite a subtle comparison between molar mass distribution obtained by living polymerization (Poisson distribution) and polycondensation, Flory did not qualify the reaction as “living”, a term which was later introduced by Szwarc in his pioneering works about living polymerization of styrene and dienes.<sup>2,3</sup> LROP of heterocyclic compounds has been widely used to synthesize polymeric materials for a use in numerous applications. Due to the variety of heterocycles that can be subjected to LROP, the high level of control (chain end, molar mass, dispersity or chemical compositions), as well as the broad range of macromolecular architectures accessible, this polymerization method has become a powerful tool in macromolecular engineering.<sup>4</sup>

Several recent conceptual advances in polymer chemistry take advantage of the design criteria and practical techniques of molecular-level control in organic chemistry, in order to access well-defined polymers and nanostructured materials.<sup>5</sup> For instance, countless catalysts have been developed for ROP of heterocycles, with a source of inspiration arising from molecular chemistry, and offering a large diversity of mechanistic pathways to control the polymerization. Depending on the nature of the catalyst, hence on the type of active center generated, different activation modes and related mechanisms can be distinguished, including nucleophilic, electrophilic, acidic and basic. Polymerization proceeding by activation of the initiator/polymer chain ends corresponds to the active chain-end mechanism (ACEM), whereas polymerization by monomer activation involves the so-called activated monomer mechanism (AMM). In both cases, the activation can follow either a nucleophilic or an electrophilic pathway. Concomitant activation of initiator first-then of the polymer chain-ends- and of the monomer substrate in a cooperative fashion refers to as a dual activation.

The concept of monomer activation originates from a particular mechanism, *i.e.* the activated monomer mechanism (AMM), occurring in ionic polymerization where the chain-growth does not involve an ionically activated end-group. The anionic ring-opening polymerization (AROP) of lactams or the cationic ring-opening polymerization (CROP) of epoxides are typical examples of the so-called activated monomer mechanism (Scheme 1.a and b). In both case the

## Chapter 1. Bibliographic chapter: Concept of monomer activation in anionic and organocatalytic ring-opening polymerization

activated monomer is generated by an acid-base reaction yielding the activated monomer and the propagation occurs by attack on/by the neutral chain-end by/on the activated monomer.



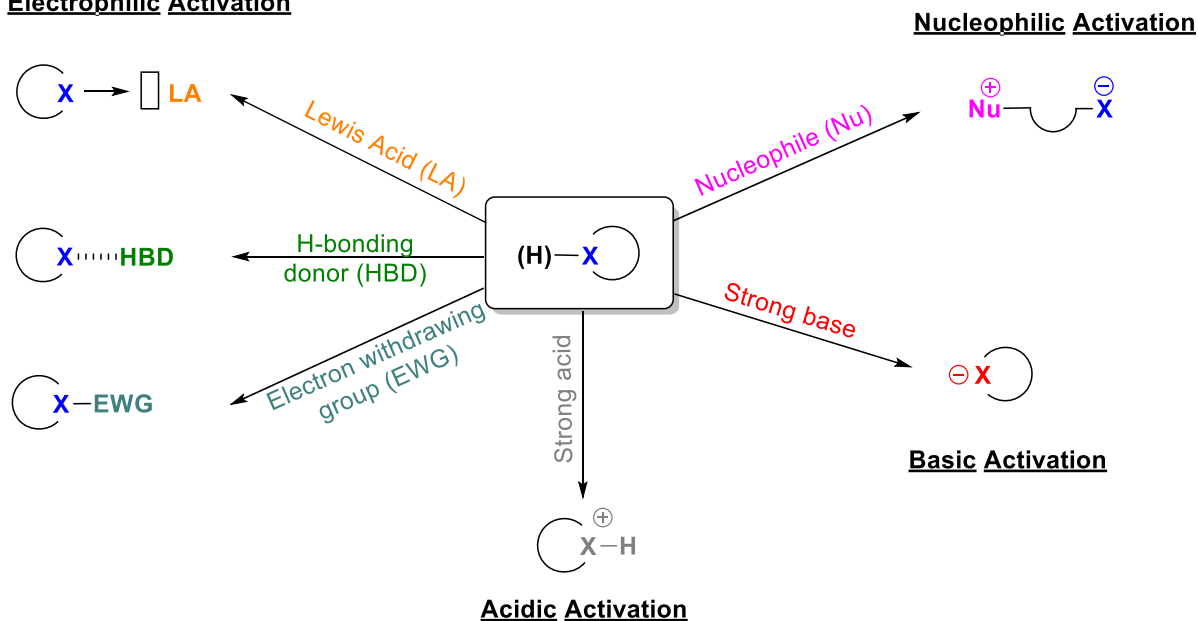
**Scheme 1.** Activated monomer mechanism in a) AROP of lactams and b) CROP of epoxides

Inspired by the activated monomer mechanism observed in the CROP of cyclic ethers or the AROP of lactams (described in Scheme 1) as well as the achievements of molecular chemistry, numerous methodologies have been applied for the monomer activation over the last three decades and are listed in Figure 1. Basically, the electrophilic monomer activation consists to reduce the electron density of the heterocycle and has been initially triggered by interaction between Lewis acids or Brønsted acids and the heteroatom of the cyclic monomer. During the last two decades, with the rapid development of organocatalysis, the electrophilic activation by H-bonding interactions of mainly carbonyl-containing monomers (lactide, lactones, cyclic carbonates, etc.) has emerged as a powerful and selective methodology of activation. Alternatively, electrophilic monomer activation can be achieved through covalent grafting of an activating substituent enhancing the reactivity of the monomer, and which can be removed in the final polymer (see further, the section about ROP of aziridine *vs* *N*-activated aziridines).

In opposite, the nucleophilic activation consists to increase the electron density of the heterocycles *via* the generation of anionically activated monomer, *e.g.* the AROP of lactams. With the rapid development of organocatalyzed polymerization, new mechanism has emerged for the nucleophilic activation through the direct attack of the cyclic monomer by a neutral nucleophilic catalyst, thus generating the activated monomer in the form of a highly reactive zwitterion.

## Chapter 1. Bibliographic chapter: Concept of monomer activation in anionic and organocatalytic ring-opening polymerization

### Electrophilic Activation

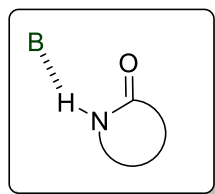


$(H)-X$  = Epoxides, aziridines, carbon cycles, lactones, lactams, cyclic carbonates, *N*-carboxy-anhydrides, O-carboxyanhydrides, cyclic phosphoesters, cyclic carbosiloxanes, etc.

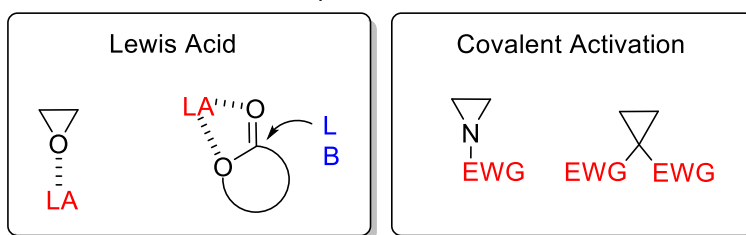
**Figure 1.** General mechanism for monomer activation

Considering the large number of activation mechanisms as well as the variety of heterocyclic monomers which can be subjected to ring-opening polymerization *via* a monomer activation methodology, we decided to restrict our literature review to various examples directly related to this thesis work. After an overview of the different mechanisms of polymerization abovementioned (ACEM, AMM and dual activation), this bibliographic chapter discusses selected examples found in the context of i) anionic ROP of lactams and epoxides, ii) ROP of cyclic esters utilizing Lewis pairs, and iii) anionic ROP of activated aziridines and carbon cycles (Figure 2).

### Nucleophilic Activation



### Electrophilic Activation

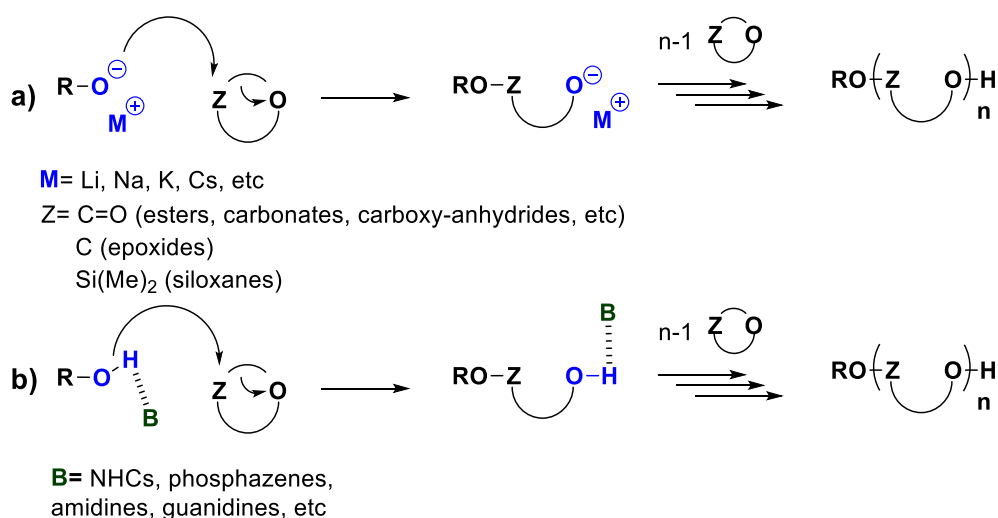


**Figure 2.** Overview of the monomer activation strategy discussed in this bibliographic chapter

## 2. General polymerization mechanisms

### 2.1. Active chain-end mechanism (ACEM)

ACEM eventually operates in many ROP methods, including in cationic, anionic, ionic coordinated (or pseudo-ionic) and organocatalytic ROP, and ACEM applies to miscellaneous heterocycles, such as oxiranes, lactones, cyclic phosphoesters, carbonates, etc. In the specific context employing organometallic-based catalysts, propagation occurs by direct attack of the active chain-end, e.g. an alkoxide, a carboxylate, or an amidate, onto the cyclic monomer (Scheme 2.a). With metal-free organocatalytic systems, the chain-end is either activated by hydrogen bonding or can undergo complete deprotonation depending on the pKa difference between the initiator/chain-ends and the catalyst (Brønsted base, Scheme 2.b). Organic (super)bases, such as *N*-heterocyclic carbenes (NHCs), phosphazenes, guanidines and amidines, have been extensively used to control the organocatalytic ROP (OROP) of heterocycles. Several reviews on organocatalytic molecular transformations and organocatalytic polymerization have been published in the last decades.<sup>6–11</sup>



**Scheme 2.** ACEM in a) AROP and b) Organocatalyzed-ROP initiated by alkoxides.

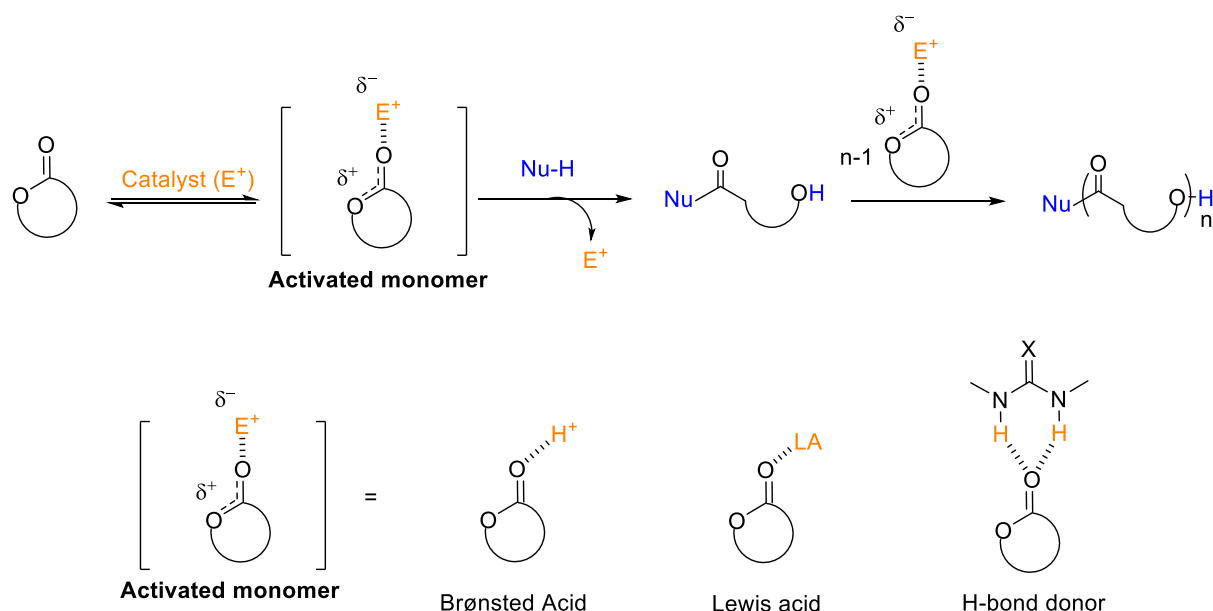
### 2.2. Activated Monomer Mechanism (AMM)

#### 2.2.1. Electrophilic activated monomer mechanism

AMM has been pioneered by the Penczek group in the context of the cationic ROP (CROP) of epoxides first, then of cyclic esters.<sup>12–15</sup> In the electrophilic AMM, a Lewis acid or a Brønsted

## Chapter 1. Bibliographic chapter: Concept of monomer activation in anionic and organocatalytic ring-opening polymerization

acid activates the heterocycle through coordination/protonation of the heteroatom: the oxygen atom for cyclic ethers or the carbonyl groups for cyclic esters. The resulting activated monomer undergoes ring-opening by nucleophilic attack of the initiating/propagating species (generally an alcohol), thus regenerating the acidic catalyst (Scheme 3).



**Scheme 3.** Activated monomer mechanism via electrophilic activation exemplified for the ROP of cyclic esters.

### 2.2.2. Nucleophilic activated monomer mechanism

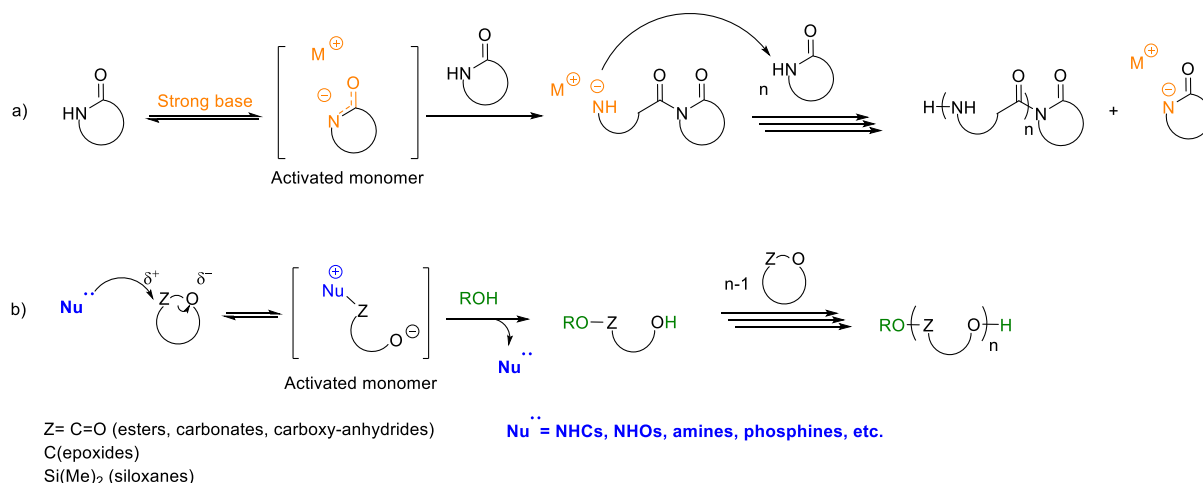
AMM proceeding *via* nucleophilic activation has been suggested in the early 1970's in a few polymerization reactions initiated by organometallic species. The anionic ROP of lactams is the representative example of such a nucleophilic AMM, as illustrated in Scheme 4.a. In that case, AMM consists in the deprotonation of the lactam monomer, yielding an activated lactamate anion able to attack the neutral *N*-acyllactam chain-end through ring-opening. More details on this topic are given in section 2.

With the rapid development of organocatalyzed polymerization, many examples based on a nucleophilic AMM have been reported. In this case, AMM proceeds through direct attack of the cyclic monomer by a nucleophilic catalyst (Scheme 4.b),<sup>7-9,16-20</sup> ring-opening generating a zwitterionic intermediate species. The latter can eventually be viewed as case of an activated monomer. For instance, many reports have suggested the existence of pyrimidium or imidazolium alkoxides, that are, zwitterions featuring a bulky and soft counter-cation in OROP



## Chapter 1. Bibliographic chapter: Concept of monomer activation in anionic and organocatalytic ring-opening polymerization

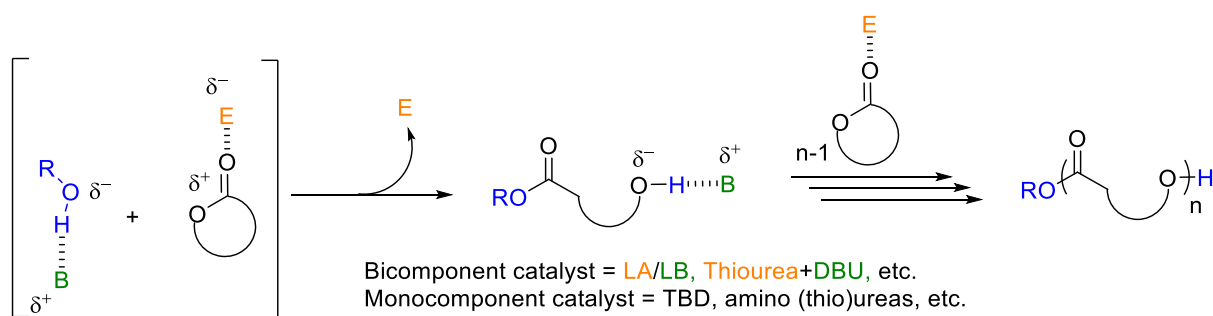
reactions.<sup>6-9,18</sup> Subsequent protonation of this zwitterionic activated monomer species yields a ring-opened mono-adduct regenerating the catalyst for a further monomer activation cycle. A wide range of cyclic monomers, such as epoxides, lactones, lactide, cyclic carbonates, cyclic siloxanes or *N*- or *O*-carboxy-anhydrides etc. have been proposed to undergo polymerization by such a nucleophilic AMM.



**Scheme 4.** a) Nucleophilic AMM in the ROP of lactams and b) AMM via nucleophilic monomer activation.

### 2.3. Dual activation

Concomitant activation of both the monomer and the initiator/chain-end refers to as a cooperative dual activation. This can be achieved using specific catalysts consisting of mono- or bi-component systems, e.g. urea and thiourea-amino derivatives and their related anions, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), and Lewis pairs.<sup>7,17,21-26</sup> Dual activation generally involves electrophilic activation by a proton or a Lewis acid of the heteroatom of the cyclic monomer, while the initiating/propagating species activated by a basic entity, typically a Lewis (Scheme 5).



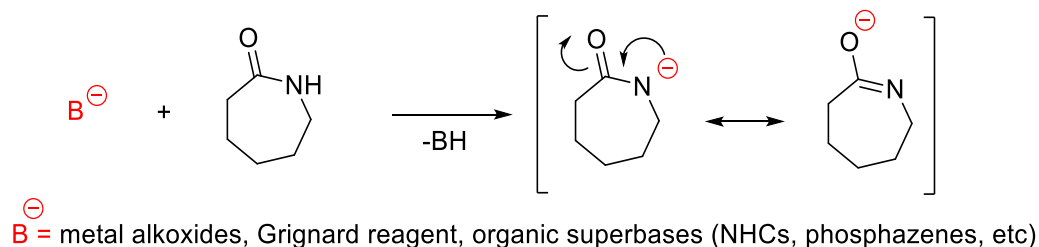
**Scheme 5.** Dual cooperative activation of both monomer (by an electrophile) and the alcohol initiator (by a nucleophile) exemplified for the ROP of cyclic esters.

### 3. Nucleophilic Activation: Polymerization of lactams

As mentioned, a typical example of nucleophilic AMM is the AROP of lactams, which greatly differs from the mechanism characterizing AROP of many unsaturated and heterocyclic monomers. In AMM, indeed, chain growth does not involve an anionically activated end-group, but an *N*-acylated species in its neutral form. AROP of lactams is thus initiated through the formation of a lactamate anion arising from the deprotonation of the lactam monomer by a strong base. Several reviews on this topic, for instance, reported by Reimschuessel,<sup>27</sup> Sebenda,<sup>28</sup> Hashimoto,<sup>29</sup> Roda<sup>30</sup> and Russo<sup>31,32</sup> can be found elsewhere.

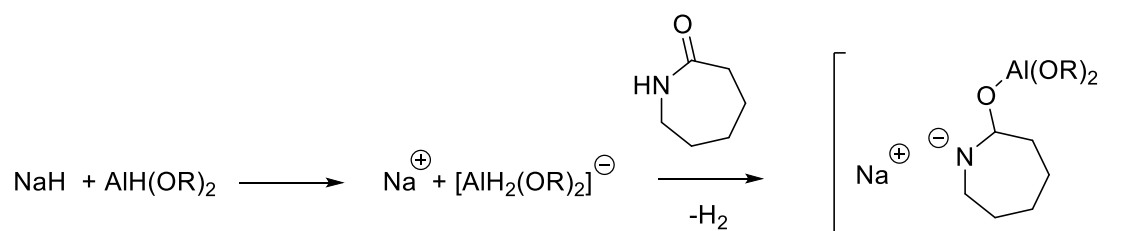
#### 3.1. Initiating and activating systems

The lactamate anion, that is, a very strong nucleophile thus corresponds to the activated monomer during AROP of lactams. The negative charge is actually delocalized on the amide group by conjugation with the carbonyl group (Scheme 6). The probability for the direct nucleophilic attack of the lactamate anion onto the carbonyl of the lactam is actually low, as this is a slow process because the as-formed exocyclic amidate is not stabilized by resonance. Instead, it rapidly deprotonates another lactam molecule, yielding an imide dimer by regenerating an activated monomer. The initiation rate depends on several factors, including the nature of the counter-ion, the polarity of reaction medium (bulk or solution), the lactam ring-size, and the presence of substituent.<sup>33</sup> If not proceeding through this AMM, polymerization of lactams would require very high temperatures ( $T \geq 250\text{ }^{\circ}\text{C}$ ), and only the more reactive lactams, such as  $\epsilon$ -caprolactam or  $\beta$ -propiolactam, can undergo such AROP via a non-activated pathway.



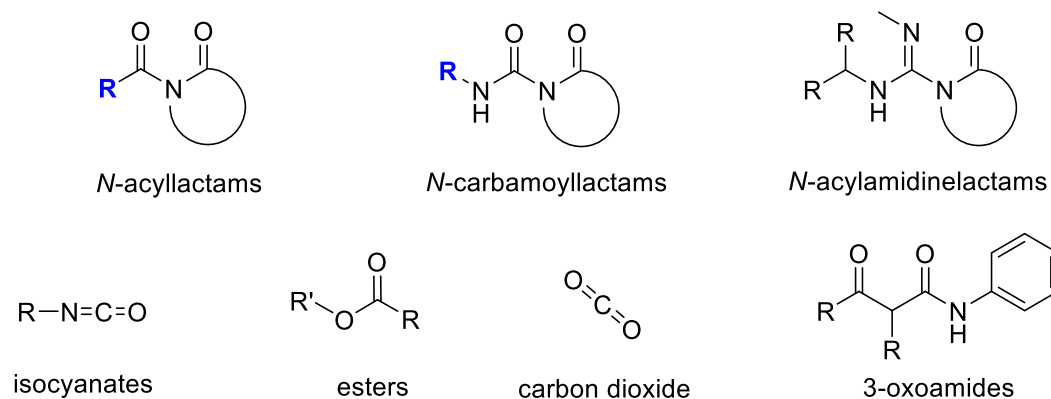
**Scheme 6.** Structures of anionically activated monomer exemplified for  $\epsilon$ -caprolactamate.

The activated monomer can be generated by reaction of a lactam with an organometallic base such as a metal alkoxide or halide, an alkali metal or a Grignard reagent).<sup>34</sup> Recent studies have shown that organic superbases, such as pentamethylene guanidine, phosphazenes,<sup>35</sup> protophosphatranes<sup>36–38</sup> or *N*-heterocyclic carbenes can also be employed to this end.<sup>39,40</sup> Alternatively, combination of a strong base (NaH, LiH or BuLi) with a reducing agent, such as metal dialkyl or dialkoxy aluminium hydrides, can be used to form lactamates.<sup>41,42</sup> In the latter case, the activated monomer exists in the form of 2-(dialkylaluminoxy)-1-azacycloheptane metal salt (Scheme 7).



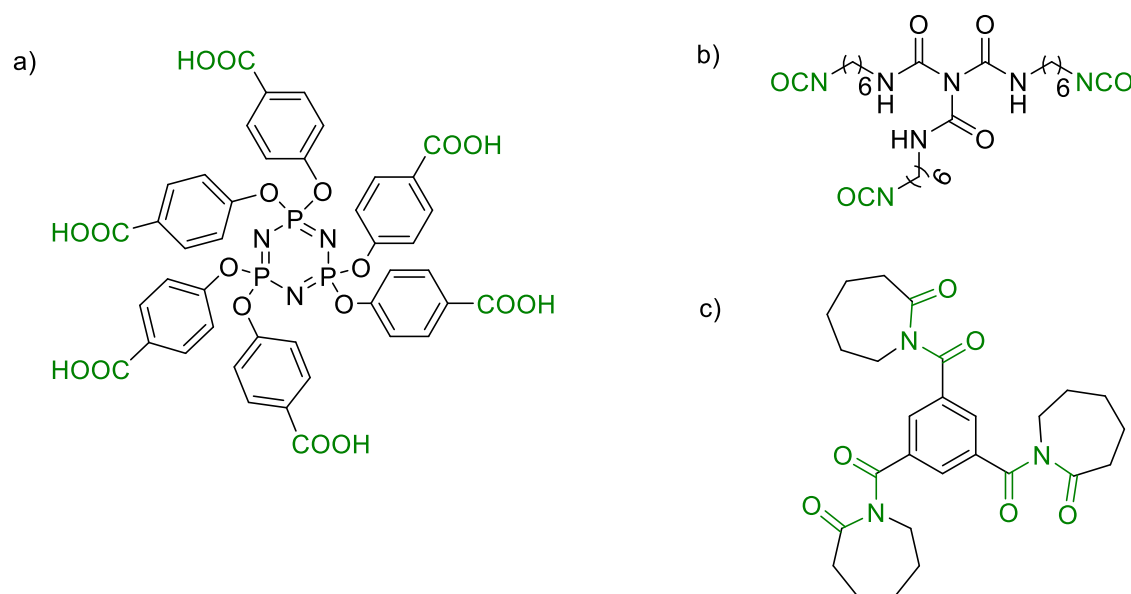
**Scheme 7.** Generation of 2-(dialkylaluminoxy)-1-azacycloheptane sodium salt

In contrast to the non-activated AROP of lactams, where induction period and slow kinetics are observed,<sup>43</sup> rapid polymerization in a range of temperatures 130–180 °C is observed in presence of an activator.<sup>44</sup> Main activators are shown in Figure 3, and include *N*-substituted lactams (*N*-acyllactams or *N*-carbamoyllactam) with an acylating ability, the latter of which can be modulated by introducing electronegative substituent (**R**).<sup>44</sup> Compounds capable of producing *N*-substituted lactams under the conditions of anionic polymerization, e.g. isocyanates, acid halides, esters, carbon dioxide, or more complex derivatives (oxoamides, *N*-acylamidine, etc), can also serve as activators. By the AMM can poorly reactive lactams, such as 2-pyrrolidone<sup>45,46</sup> and 2-piperidone,<sup>47</sup> and the 5- and 6-membered cyclic amide monomers thus be polymerized in presence of the acylating activator.



**Figure 3.** Main activators in anionic lactam ring-opening polymerization.

In order to achieve “complex” polyamide-based architectures, efforts have been put to design multifunctional (macro)initiators.<sup>48</sup> For instance, tri-isocyanates,<sup>49</sup> triacyllactams<sup>50,51</sup> or cyclotriphosphazenes<sup>52</sup> have been designed for AROP of  $\epsilon$ -caprolactam to prepare star-shaped (co)polymers based on polyamide-6 (Figure 4).



**Figure 4.** Multifunctional initiator based on a) cyclotriphosphazene, b) triisocyanate and c) triacyllactam for the AROP of  $\epsilon$ -caprolactam.

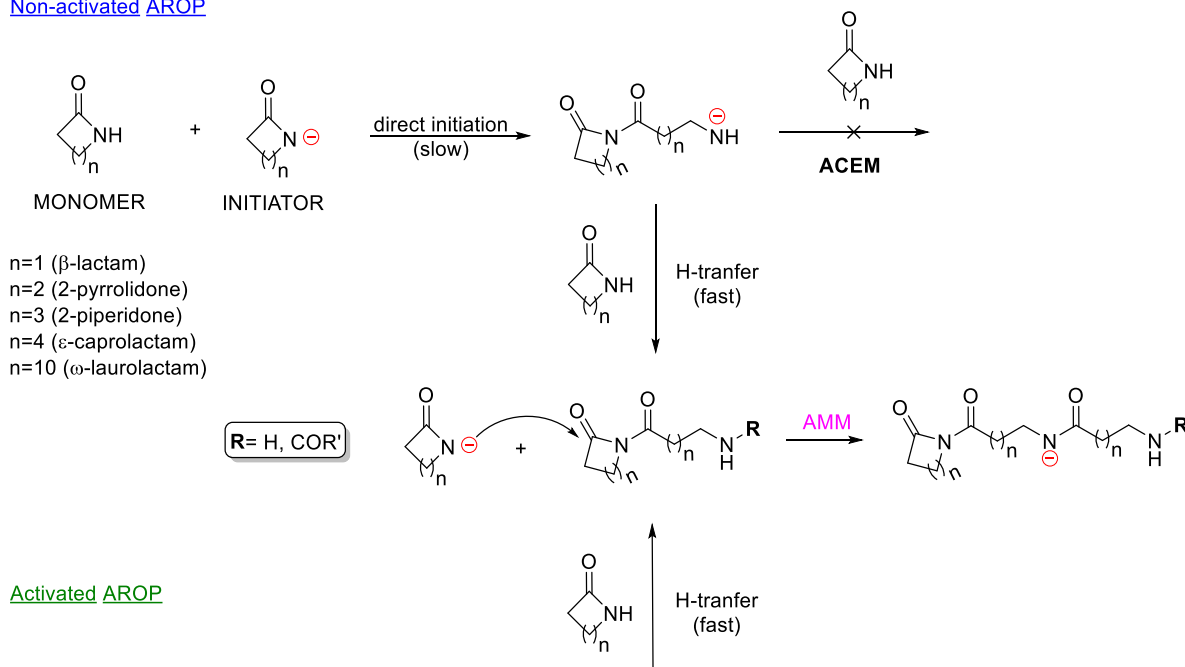
### 3.2. Polymerization mechanism: Activated vs. non-Activated

In the non-activated mechanism, slow formation of the *N*-acyllactam by reaction between the monomer and the lactamate anion ( $k_i = 10^{-7} \text{ L.mol}^{-1}.\text{s}^{-1}$  for sodium caprolactamate at 160-190 °C) is followed by fast proton transfer ( $k_H = 10^2\text{-}10^5 \text{ L.mol}^{-1}.\text{s}^{-1}$  depending on the lactam structure and the reaction conditions), regenerating the activated monomer. Fast proton exchange

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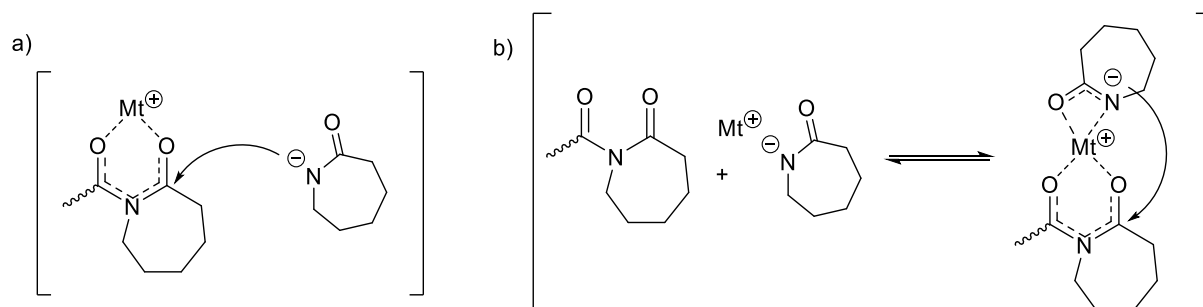
eventually prevents the process of ring-opening from occurring by the ACEM. Propagation takes place by the AMM instead, through nucleophilic attack to the acyllactam chain-end and subsequent proton transfer from the amidate to the lactam monomer (Scheme 8).

### Non-activated AROP



**Scheme 8.** Formation of active species in anionic ring-opening polymerization of lactams: activated monomer mechanism vs. active chain-end mechanism.

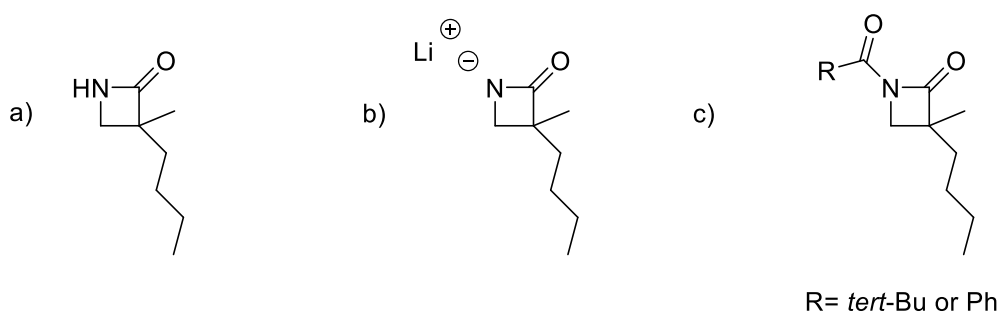
Sekiguchi *et al.* have reported a “lactamolytic AMM”,<sup>53</sup> involving transfer and coordination of an alkali metal from the activated monomer to the imide group of the neutral chain-end (Scheme 9.a). Alternatively, Frunze *et al.* have postulated that ions pairs of lactam salts could participate to the propagation step, thus suggesting an ion-coordinative mechanism (Scheme 9.b).<sup>54</sup> Again, both mechanisms depend on the polarity of the medium and the temperature.



**Scheme 9.** a) Lactamolytic and b) ion-coordinative mechanism.

In polymerizations proceeding through AMM, the number average molar mass is determined by the concentration of the activator relatively to that of the monomer. However, occurrence of side reactions, such as the Claisen condensation or formation of cyclic oligomers, implies that AROP of lactams is a non-living process.<sup>55,56</sup> The structure of the activators, in particular the nature of the exocyclic acyl in *N*-acyl lactam-based activator, plays a crucial role on the quality of the polymerization control and kinetic. Efficient activators, like *N*-carbamoyl lactams, allowed for rapid synthesis of high molar mass polyamides at 140°C, *i.e.* from a few seconds to a few minutes, with limited side reactions.

In his review, Hashimoto has described *sine qua non* conditions for the polymerization of lactams to exhibit features of a “controlled/living” process.<sup>29</sup> Thus, polymerization in solution of highly reactive lactams under mild conditions are required, but the LROP of the most common lactams, such as  $\epsilon$ -caprolactam and 2-pyrrolidone, has never been reported. Sebenda *et al.* have prepared structurally well-defined polyamides from substituted  $\beta$ -lactams bearing bulky substituents in  $\alpha$ -position. For example, 3-butyl-3-methyl-2-azetidinone was polymerized in a living manner operating by AMM in THF at 27 °C.<sup>57,58</sup> Use of such mild conditions and, obviously, substitution of the hydrogen in  $\alpha$ -position by bulky methyl and butyl groups enables to totally suppress side reactions (Scheme 10).



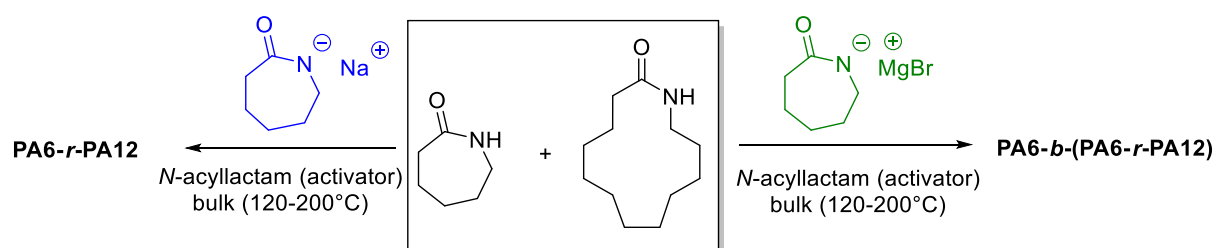
**Scheme 10.** Structure of the a) monomer, b) initiator and c) activators for the LROP of 3-butyl-3-methyl-2-azetidinone

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The case of synthesis of polyamide-6 (PA6) by AROP of  $\epsilon$ -caprolactam will be present in the third part of this manuscript. Despite the non-living character of the AROP of lactams, synthesis of polyamide-based copolymers remains possible, as discussed hereafter.<sup>59–64</sup>

### 3.3. Copolymerization of $\epsilon$ -caprolactam and $\omega$ -laurolactam

The anionic ring-opening copolymerization (AROCp) of  $\epsilon$ -caprolactam and  $\omega$ -laurolactam, that, 7 and 13-membered cyclic amide, respectively, has been developed to expand the properties of PA-6, in particular by increasing the notched Izod impact or decreasing the water absorption.<sup>65</sup> Roda et al. have described the effect of the initiating system (sodium caprolactamate vs. magnesium halide caprolactamate and *N*-benzoyl- $\epsilon$ -caprolactam as activator) on the copolymer composition and thermal properties.<sup>59,60</sup> Copolymerization initiated by sodium caprolactamate exhibits higher reactivity, especially with high content in the  $\omega$ -laurolactam comonomer, yielding a copolyamide with one melting endotherm and one single crystalline form. In contrast, two melting endotherms (at 140 °C and 210 °C) and two distinct crystalline forms ( $\alpha$  and  $\gamma$ ) have been determined for compounds synthesized by AROCp initiated with magnesium halide caprolactamate. This is due to the higher reactivity of  $\epsilon$ -CL over  $\omega$ -laurolactam giving rise to a blocky-like structure based on PA-6 PA-11. Using sodium caprolactamate that is a stronger nucleophile than magnesium derivatives, occurrence of transamidation reactions leads to full randomization (Scheme 11).



**Scheme 11.** AROCp of  $\epsilon$ -caprolactam and  $\omega$ -laurolactam initiated by sodium caprolactamate and magnesium halide lactamate.

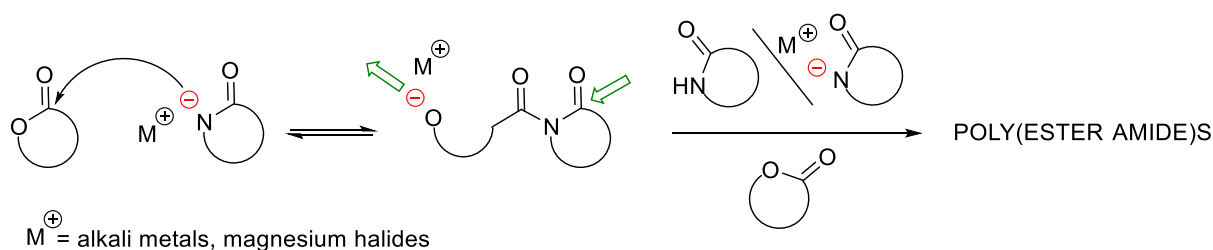
Recently, Naumann, Buchmeiser *et al.* have designed protected NHC-CO<sub>2</sub> adducts as thermally latent initiators for ARO(c)P of  $\epsilon$ -caprolactam and  $\omega$ -laurolactam in bulk at 180 °C, enabling to achieve full conversion after 45min.<sup>39,40,66,67</sup> Free NHCs are *in situ* generated by thermal deprotection and act as deprotonating agent, triggering the direct ARO(c)P of lactams by a non-activated mechanism in absence of activator. As also observed in a previous work by Roda *et al.* a gradient copolymer is obtained, with a preferential insertion of  $\epsilon$ -CL at the onset of the

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polymerization, using 1,3-di(cyclohexyl)-tetrahydropyrimidinium-2-carboxylate as the most active NHC-CO<sub>2</sub> adduct.

### 3.4. Poly(ester amide)s

Poly(ester amide)s combine thermal and mechanical properties of polyamides with the biocompatibility and biodegradability of polyesters.<sup>68,69</sup> Degradable polyamides can thus be achieved through AROcP of lactams and lactones despite very distinct mechanisms characterize homopolymerization of the two monomers, *i.e.* AMM with lactams and ACEM with lactones. Early studies have described AROcP of  $\epsilon$ -caprolactam, 2-pyrrolidone and 2-piperidone with  $\epsilon$ -caprolactone or  $\delta$ -valerolactone, in presence of alkali metal salts or Grignard reagents as deprotonating agents.<sup>68,70</sup> The initiation step consists of an acylation reaction between a lactamate anion and the reactive lactone, which plays the role of the activator. The propagation mechanism involves simultaneous addition of the lactamate anion at the acyllactam neutral chain-end, and addition of the lactone at the other chain-end by the oxyanion formed during initiation. This results in the formation of polyamide segments (Scheme 12).



**Scheme 12.** Parallel initiation of lactams and lactones in the presence of lactamate anion.

Variation of both the  $\epsilon$ -caprolactam/ $\epsilon$ -caprolactone ratio and experimental conditions (extrusion, temperature, sequential addition, etc.) enables the synthesis of random and multiblock copolymers. Recently, Basterretxea *et al.* have reported the bulk AROcP of  $\epsilon$ -caprolactam and L-lactide using a phosphazene base organocatalyst at 180 °C. Difference in reactivity of the monomers has also allowed achieving blocky-like structures and formation of semi-crystalline copolymers.<sup>71</sup>



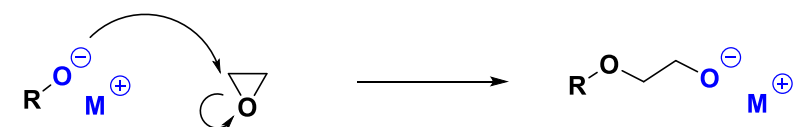
## 4. Activation by Lewis complexes for the synthesis of polyesters and polyethers

This part is devoted to both the anionic polymerization of epoxides proceeding by a monomer activation strategy and the polymerization of cyclic esters triggered by Lewis pairs.

### 4.1. Activated monomer strategy for the ring-opening polymerization of cyclic ethers

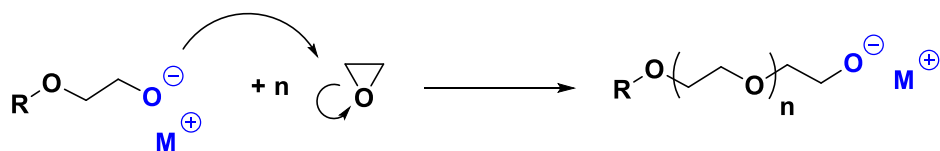
AROP of epoxides is a well-established method to produce polyethers at the industrial scale. Despite limited molar masses are achieved, due the occurrence of side reactions, AROP has been the synthetic method of choice to poly(propylene oxide) (PPO) and poly(ethylene oxide) (PEO) since the 1930's. Polymerization is typically initiated by alkali metal derivatives (Na, K, Cs) and is carried out in coordinative solvent such as DMSO or DMF; it requires relatively high temperature ( $T \geq 80^{\circ}\text{C}$ ) and long reaction time ( $t \geq 24\text{h}$ ). AROP of epoxides operates via a mechanism shown in Scheme 12. Initiation consists of a nucleophilic substitution of  $\text{S}_{\text{N}}2$  type involving the alkoxide initiator, forming a new alkoxide and so forth. Termination usually occurs after addition of acidic water or alcohols quenching propagating alkoxides. Note that the conventional AROP of PO initiated by alkali metal alkoxide restricts the molar mass<sup>72</sup> of the obtained PPO to  $15\,000\text{ g}\cdot\text{mol}^{-1}$  even with the use of soft counter-ion (cesium) or by addition of crown ethers.<sup>73–75</sup>

Initiation

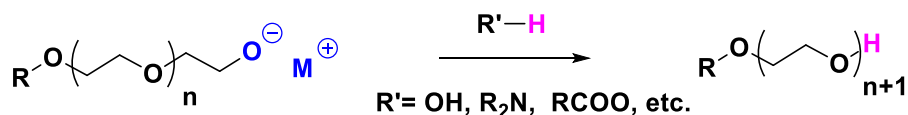


R= H, alkyl, polymer, etc.  
M= Na, K, Cs

Propagation

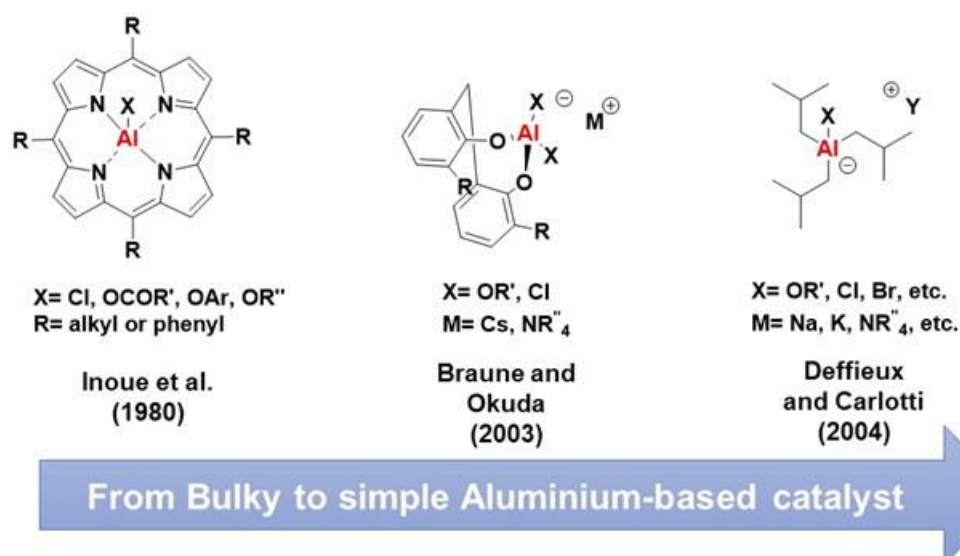


Termination



**Scheme 13.** Anionic ring-opening polymerization of ethylene oxide initiated by alkali metal alkoxide.

The concept of monomer activation in the context of anionic or anionic coordinative polymerization of epoxides has been first investigated in the 1980's by the Inoue group who have employed peculiar alumino-porphyrin-based Lewis acids for this purpose (Figure 5).<sup>76–78</sup> Later on, Braune, Okuda *et al.*<sup>79</sup> have used phenolate aluminium complexes in combination with a bulky Lewis acid (Figure 5). Ethylene oxide (EO), propylene oxide (PO), butene oxide and epichlorohydrin (ECH) have thus been polymerized and also copolymerized with lactones.<sup>78</sup> Inspired by these pioneering works, Carlotti, Deffieux *et al.* have proposed to use simple aluminium activators, e.g. triisobutylaluminium (*i*-Bu<sub>3</sub>Al), for the AMM-induced AROP of miscellaneous epoxides.<sup>80</sup>

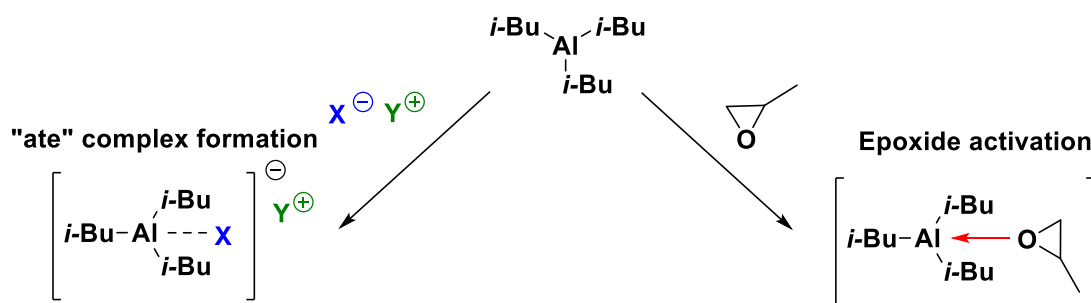


**Figure 5.** Aluminium-based catalysts for the AMM-mediated AROP of cyclic ethers.

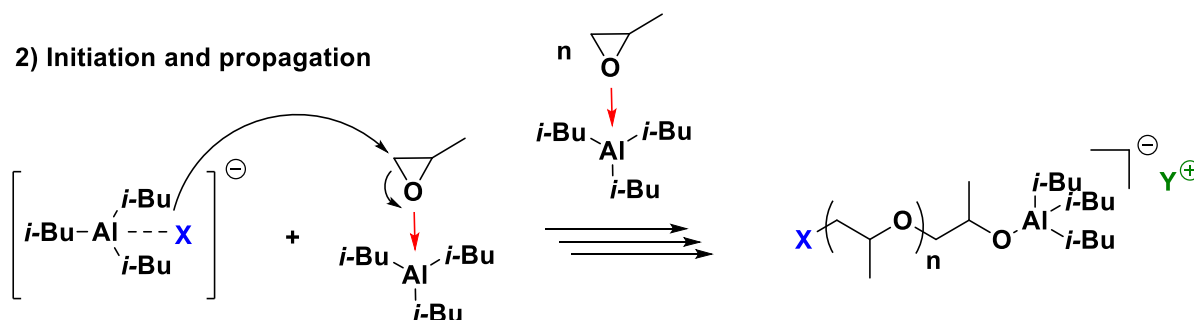
#### 4.1.1 General features and initiating complex.

In 2004, Carlotti, Deffieux et al. have reported the high speed AROP of EO and PO through monomer activation.<sup>80</sup> In their approach, epoxides are polymerized in a controlled fashion thanks to the combination of a simple Lewis acid -typically *i*-Bu<sub>3</sub>Al and a alkali metal alkoxide or an onium salt at room temperature or below.<sup>81,82</sup> Electrophilic monomer activation is based on the reduction of the electron density of the cyclic ether, a result of the interaction of the Lewis acid and the lone pair of electron on oxygen of the epoxide, facilitating its ring-opening. Formation of an « ate complex » between the Lewis acid and the initiator has been evidenced, as described in Scheme 13. Excess of the Lewis acid relatively to the initiator is required for efficient AROP reactions. This AMM strategy has key benefits compared to the more conventional AROP process, including (i) higher polymerization rates making possible the synthesis of polyether derivatives under mild conditions (hydrocarbon solvents, temperature around 20 °C or lower, shorter reaction times), (ii) well-controlled and high molar mass polyethers owing to the limited basicity of propagating “ate” species, which enables to minimize transfer reactions to the monomer.

1) "Ate" complex formation and epoxide activation



2) Initiation and propagation



3) Termination



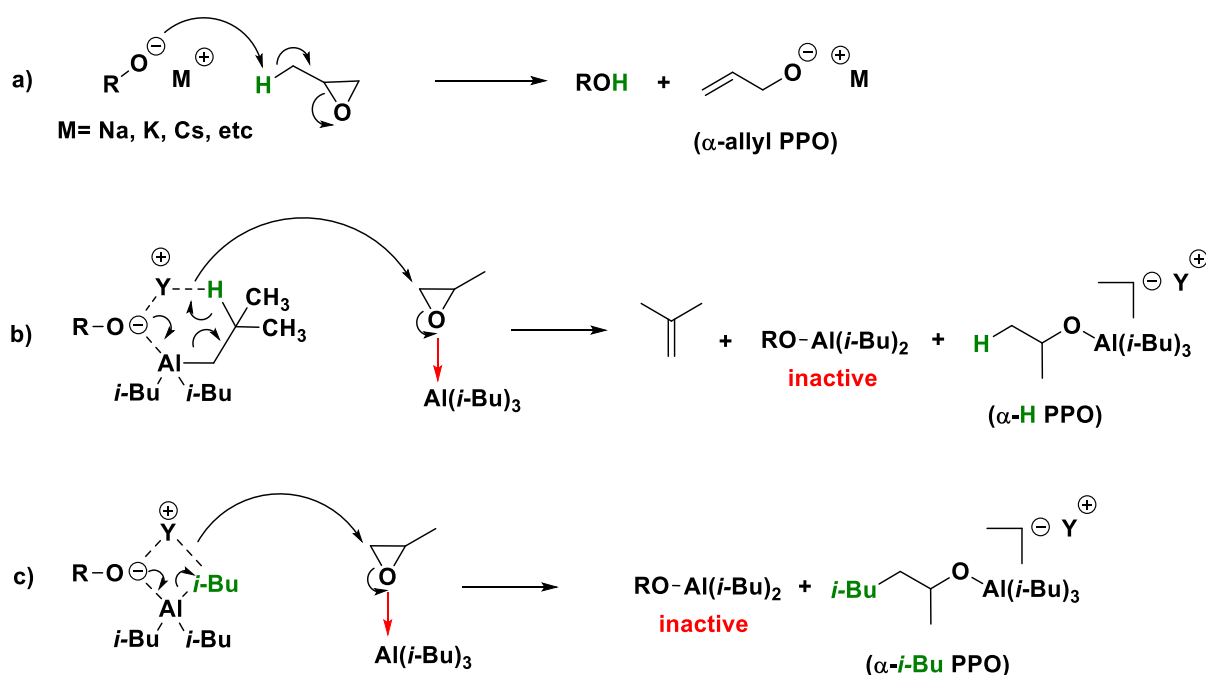
**Scheme 13.** AROP of propylene oxide in presence of  $i\text{-Bu}_3\text{Al}$  as activator proceeding by AMM.

Alkali metal alkoxides of sodium and potassium have first been employed as initiators, yielding poly(propylene oxide)s up to  $20\,000\text{ g}\cdot\text{mol}^{-1}$  within a few hours.<sup>80</sup> Nevertheless, some transfer reactions to the monomer (forming allyloxy group in alpha position of PPO chains) and to the catalyst have been still noted under these conditions (Scheme 14.a, b and c). In addition, side initiation by hydride and isobutyl groups can occur (Scheme 14.b and c), which is specific to this AMM-induced AROP of epoxides.

It is worth reminding that, due to strong aggregation of lithium species, lithium alkoxides do not enable to trigger AROP of epoxides. Use of an excess of  $i\text{-Bu}_3\text{Al}$  induces the disaggregation of lithium species through the formation of lithium/aluminate complexes, enabling the AROP process to take place by AMM. PEO's with molar masses up to  $10\,000\text{ g}\cdot\text{mol}^{-1}$  can be prepared in this way. However, ligand exchanges in the lithium aluminate complex causes slow

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deactivation of active species. Despite these shortcomings, this strategy combining lithium alkoxides and aluminium derivatives as activators allows synthesizing PS-*b*-PEO and PI-*b*-PEO block copolymers one-pot.<sup>83</sup> Use of tetraalkyl ammonium or phosphonium salts as non-coordinating and bulky counter ions enable to totally suppresses transfer reactions to the monomer. This is explained by a decrease in basicity of the active bi-component system, affording well-defined PPO's with high molar mass up to 170 000 g.mol<sup>-1</sup> ( $\bar{D} = 1.34$ ) at low temperature -30 °C, within less than 2 h.<sup>84</sup>

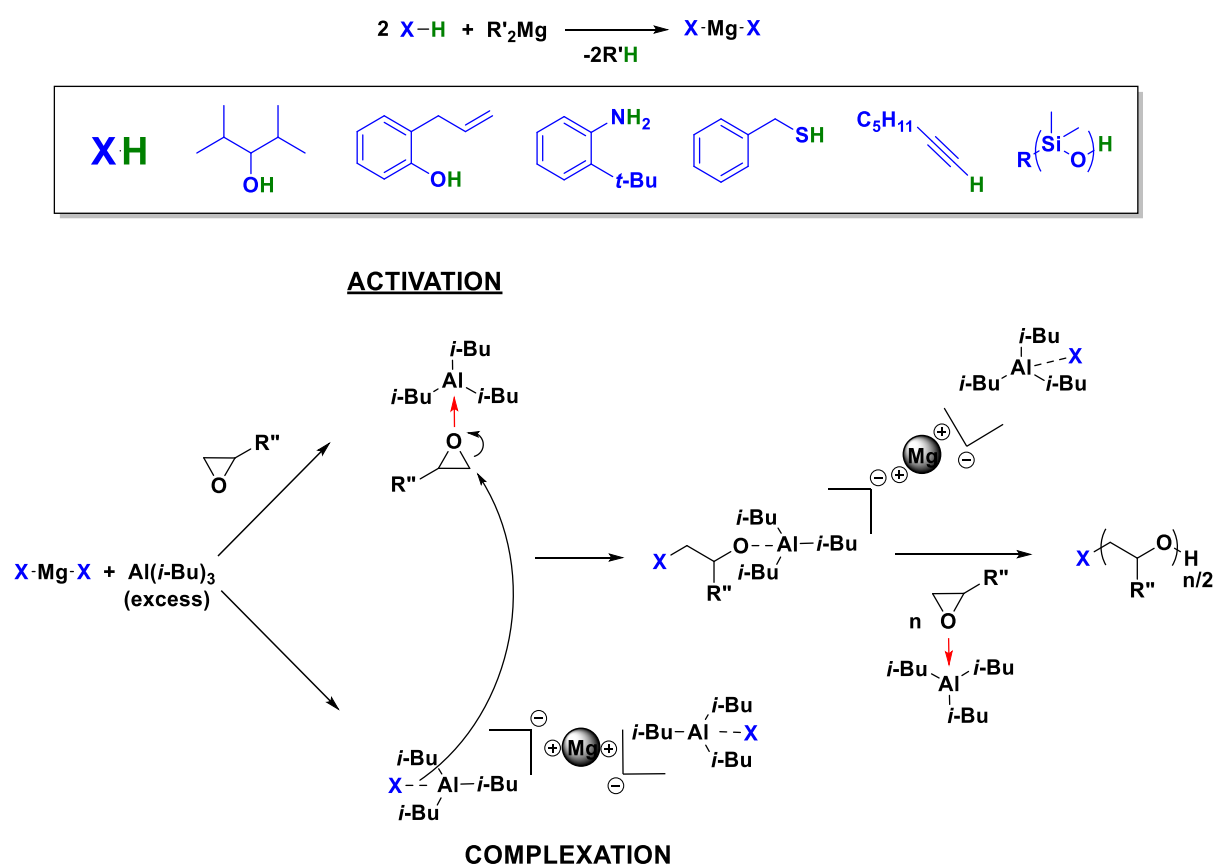


**Scheme 14.** Transfer reactions: a) to the monomer in conventional AROP of PO; b) and c) to the catalyst in the *i*-Bu<sub>3</sub>Al-AMM-mediated AROP method.

Recently, Carlotti *et al.* have resorted to either Grignard reagents<sup>85</sup> (R-MgX) or to di-alkyl-magnesium<sup>86</sup> (R<sub>2</sub>Mg) as deprotonating agents, in combination with triisobutylaluminium, for the AMM-mediated AROP of PO. PPO's with molar masses from 2 500 g.mol<sup>-1</sup> to 10 000 g.mol<sup>-1</sup> and a disparity,  $1.2 \leq \bar{D} \leq 1.37$ , have thus been prepared. Chain-end analysis by MALDI ToF mass spectrometry and by <sup>1</sup>H NMR spectroscopy has evidenced the occurrence of several modes of initiation, namely, by (i) the expected magnesium alkoxide halide, (ii) the hydride emanating from the aluminium derivative, and (iii) the halide from the magnesium alkoxide complex. Dialkylmagnesium (R<sub>2</sub>Mg) compounds have also been investigated as deprotonating agents of alcohols, thiols, amine, or alkynes, but also of macroinitiators such as mono-hydroxyl terminated polydimethylsyloxane (Scheme 15). Such reactive complexes have been further

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investigated for the AROP of ethylene oxide, propylene oxide, butylene oxide, and methyl glycidyl ether, in presence of  $i\text{-Bu}_3\text{Al}$ . Higher polymerization rates (hours) and good control over molar masses ( $\overline{M}_n$  up to 10 000  $\text{g mol}^{-1}$  and  $\overline{D} \leq 1.30$ ) have been achieved from magnesium-aluminium initiating complexes. MALDI ToF mass spectrometry has revealed that expected initiation takes place to an extent of 70 and 80 % with alcohols or primary amines as initiators. In contrast, side initiation and transfer to the monomer are more pronounced when polymerization is initiated by a thiol or by an alkyne-containing magnesium complex.

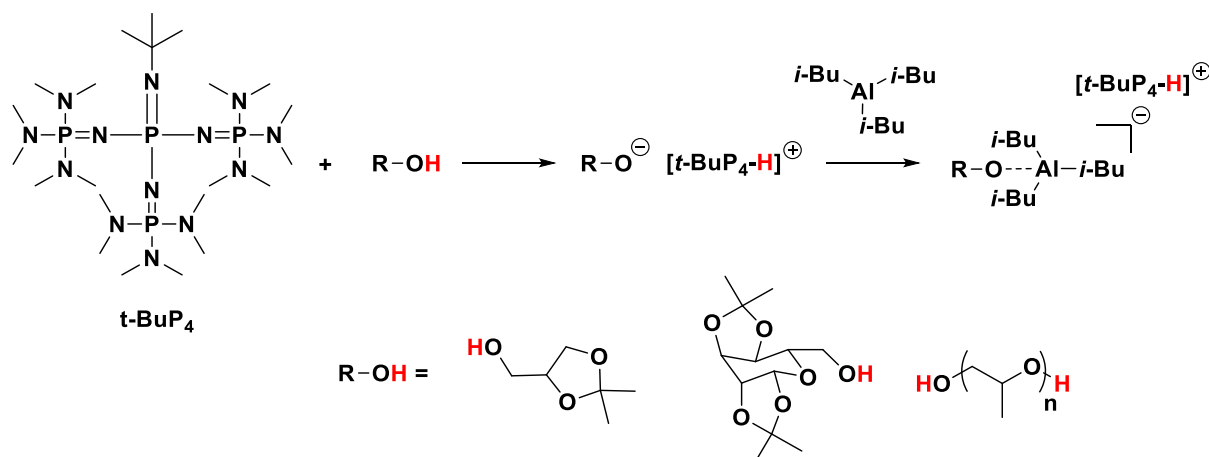


**Scheme 15.** Proposed mechanism for the activated anionic ring-opening polymerization of epoxide initiated by the system  $\text{XH}/\text{MgR}'_2/\text{Al}(i\text{-Bu})_3$ .

In parallel to the « activated monomer strategy », numerous organocatalysts such as NHCs,<sup>87,88</sup> NHOs<sup>16</sup> or phosphazene superbases<sup>89–91</sup> have been used to polymerize EO or PO derivatives. A recent review by Zhao et al. has highlighted synthetic developments to polyethers by an organocatalyzed pathway.<sup>92</sup> Phosphazene Brønsted “super” bases have been widely employed as deprotonating agents in the context of “controlled/living” AROP.<sup>89</sup> Phosphazene bases can also be combined with aluminum derivatives to trigger AROP by AMM. PEO’s and PPO’s with molar masses up to 80 000  $\text{g.mol}^{-1}$  ( $\overline{D} = 1.11\text{-}1.46$ ) have thus been synthesized at room

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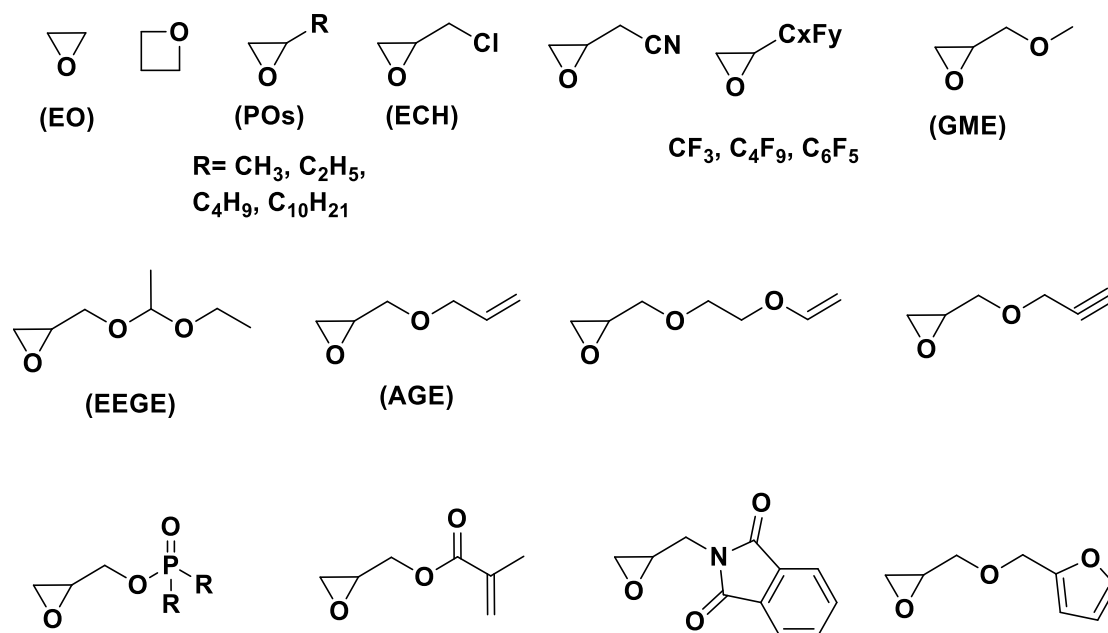
temperature,<sup>93</sup> using alcohols as initiators, *t*-BuP<sub>4</sub> as organic base and Al(*i*-Bu)<sub>3</sub> as activator. The as-formed phosphazanium alkoxide/aluminium complex (Scheme 16) thus enables the quantitative and controlled synthesis of  $\alpha$ -(multi)hydroxy- $\omega$ -hydroxy PPO's. Following a similar AMM strategy Illy, Guegan *et al.* have reported the controlled AROP of 1,2 epoxybutene through the combination of carbamate-containing initiators, *t*-BuP<sub>4</sub> and aluminium-based activator control.<sup>94</sup>



**Scheme 16.** Formation of the « ate » complex between phosphazanium alkoxide and tri-*iso*-butylaluminium.

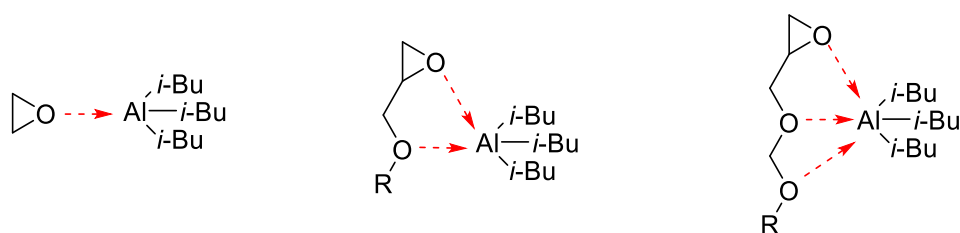
### 4.1.2 Epoxide monomers bearing side chain functional group

The possibility to drastically activate the epoxide ring through the use of electrophilic additives, such aluminium compounds, enables to polymerize a wide range of less reactive epoxides, for instance, those substituted by alkyl side chains<sup>95</sup> or even carrying functional group such as epichlorohydrin (ECH),<sup>96–98</sup> epicyanohydrin,<sup>99,100</sup> allyl glycidyl ether (AGE),<sup>99</sup> propargyl glycidyl ether,<sup>101</sup> glycidyl methacrylate,<sup>102</sup> glycidylphthalimide<sup>103</sup> or fluorinated epoxides (Figure 6).



**Figure 6.** Scope of oxirane monomers that can be subjected to AMM-mediated AROP.

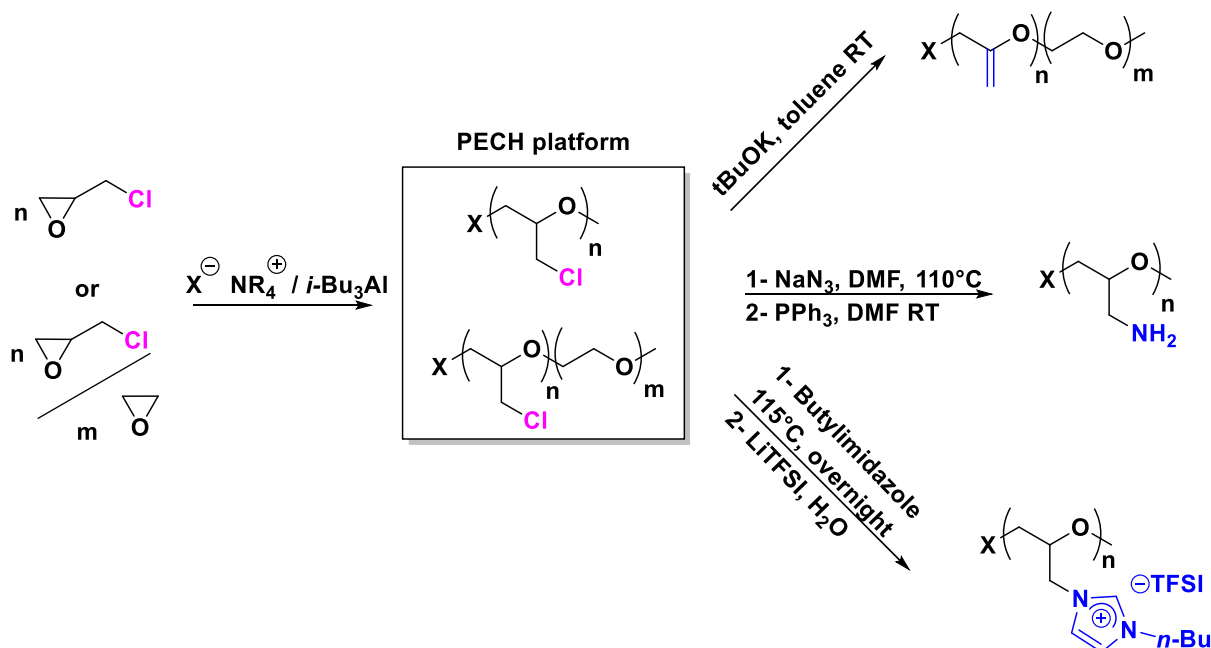
AROP of monomers featuring strongly coordinating substituents, *e.g.* ethoxy ethyl glycidyl ether (EEGE) or glycidyl methyl ether (GME)<sup>104–106</sup> requires special care, in particular, through a proper selection of the  $[\text{Al}]/[\text{Initiator}]$  ratio, (generally  $\geq 2$ ; Figure 7). Poly(glycidyl methyl ether)s, linear poly(2-ethoxyethyl glycidyl ether)s, and related copolymers with EO, showing low dispersities and controlled molar masses have thus been reported.



**Figure 7.** Interaction of triisobutylaluminum with ethylene oxide, glycidyl methyl ether and ethoxy glycidyl methyl ether.

The high tolerance towards functional groups during AROP proceeding by AMM has also enabled the synthesis of high molar mass PECH (up to  $80\,000\text{ g}\cdot\text{mol}^{-1}$ ), and of PEO-*r*-PECH copolymers without the occurrence of side reaction involving the chloromethyl group. This strategy has given access to a wide range of original (co)polymers derived from PECH by post-modification, for instance as hydrolytically degradable PEG derivatives,<sup>107</sup> poly(ionic liquid)s for battery applications,<sup>108</sup> or poly(glycidyl amine)<sup>109</sup> (Scheme 17).





**Scheme 17.** Controlled synthesis of PECH and post-modification reactions.

Apart from a few reports regarding anionic coordinative polymerization,<sup>110</sup> 4-membered cyclic ethers, referred to as oxetanes (Ox), are polymerized *via* a cationic route.<sup>111</sup> Recently, the aforementioned activated monomer methodology in AROP developed for epoxides has been successfully applied to the synthesis of polyoxetanes with molar masses up to  $10\,000\text{ g}\cdot\text{mol}^{-1}$  ( $D \leq 1.20$ ).<sup>112</sup> AROP of oxetane has been found to be initiated by tetraoctylammonium bromide salts, at  $[Al]/[NOct_4]$  ratio = 5 achieving high conversion  $\geq 90\%$ , while maintaining good control over molar masses. The reactivity difference between EO and Ox has then been effectively exploited to prepare PEO-*b*-POx and PEO-*b*-POx-*b*-PEO block copolymers one-pot, *i.e.* from a mixture of both monomers in batch.

In summary, the activated monomer strategy has emerged as a very efficient polymerization method to achieve well-defined and high molar mass (co)polyethers, expanding the scope of monomer substrate significantly, as not only common epoxides but also monomers featuring long alkyl chains or functional side groups can undergo controlled/living ARO(c)P via AMM.

## 4.2. Lewis pairs for ring-opening polymerization of cyclic esters

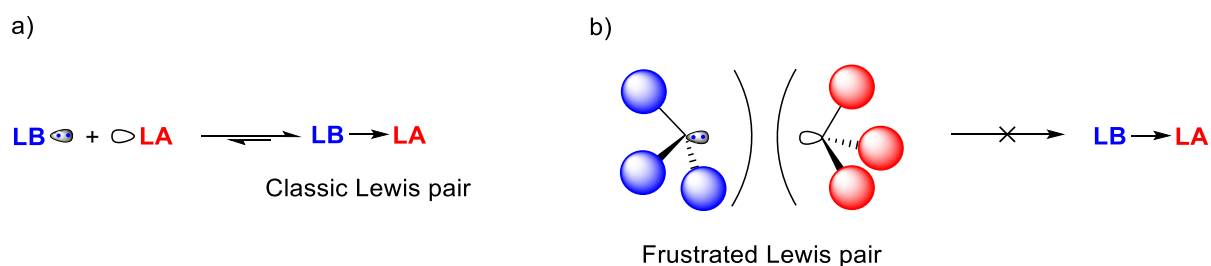
The combination of two distinct catalysts in a bicomponent system, in which both catalysts activate the reaction partners in a dual/cooperative manner, appears as a powerful methodology to allow the synthesis of complex molecules which are not readily accessible using a single

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catalyst.<sup>113–116</sup> Most of the examples are based on the association of a metallic complex (Lewis acid) and an organic catalyst (Lewis base). In the context of polymer chemistry, early studies reported that the combination of aluminium-based catalyst and organic Lewis base such as pyridine or phosphines enhanced the polymerization rate and decrease the occurrence of side transesterification reactions for the ROP of lactones. Recent examples of dual activation using organic/organometallic polymerization catalyst, in a mono- or bicomponent system, mainly concern the ROP of rac-lactide, trimethylene carbonate or lactones.

This concept of dual activation is actually connected to the concept of frustrated Lewis pairs (FLPs) regarding the activation of poorly reactive substrates such as  $H_2$ ,  $CO_2$ ,  $S_2O$ ,  $NO$  or  $NO_2$ . Classically, the combination of electron acceptors (Lewis acid) and electron donors (Lewis Base) has been known to give Lewis acid-base adduct through a dative bonding. In FLPs chemistry, the introduction of steric demands or a dissociative equilibrium provides access to free donors and acceptors, allowing them to interact with a third molecule. The concept of FLPs has been applied to metal-free reductions, asymmetric hydrogenation, C-C bond formation or C-H bond functionalization.

Over the past few years, classical and frustrated Lewis pairs (LPs) have demonstrated an excellent activity in the so-called Lewis pair polymerization (LPP) mainly of conjugated polar alkenes,<sup>117–121</sup> lactides,<sup>122,123</sup> lactones,<sup>23</sup> *N*-carboxy anhydride,<sup>117,124</sup> carbonates.<sup>125</sup> Generally, in order to be active, the Lewis base and the Lewis acid have to be separated by a steric hindrance (frustrated LP) or a dissociative equilibrium (Scheme 18).

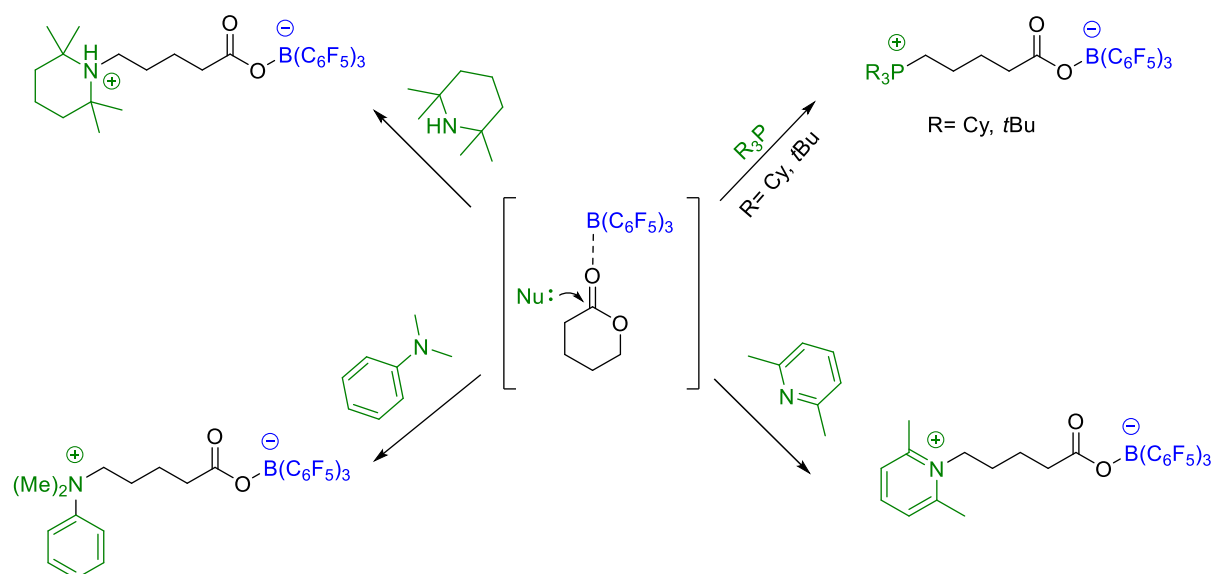


**Scheme 18.** Equilibrium in a) classic Lewis pair and b) frustrated Lewis pair

In molecular chemistry, both the Stephan and the Eckert groups have pioneered the use of FLP's that combine a bulky Lewis acid, e.g.  $B(C_6F_5)_3$  and a Lewis bases, e.g. amines, phosphines or NHCs for the molecular ring-opening of  $\delta$ -valerolactone.<sup>126</sup> The electrophilic activation of the carbonyl function by Lewis acid and subsequent nucleophilic attack of the Lewis base afford a zwitterionic adduct as described in Scheme 19. The zwitterionic ammonium/phosphonium

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borate alkoxides were found to be inactive toward the polymerization of lactones and only ring contraction was observed for lactide.



**Scheme 19.** Ring-opening reaction of activated  $\delta$ -valerolactone with amine and phosphine nucleophiles.

Such a combination prevents quenching between the acid and the Lewis base owing to steric hindrance. In the context of polymer synthesis, LP's enables activation of both the monomer and the initiating/propagating species. Typical LP's utilizes a Lewis acid- type complex combined with a nucleophile (alcohols, amines). The Lewis base can also play the role of initiator and directly attack the activated monomer usually yielding both linear and cyclic structures. In this part, the Lewis pair polymerization of lactide and lactones will be discussed and a focus on the mechanism of activation and polymerization will be given.

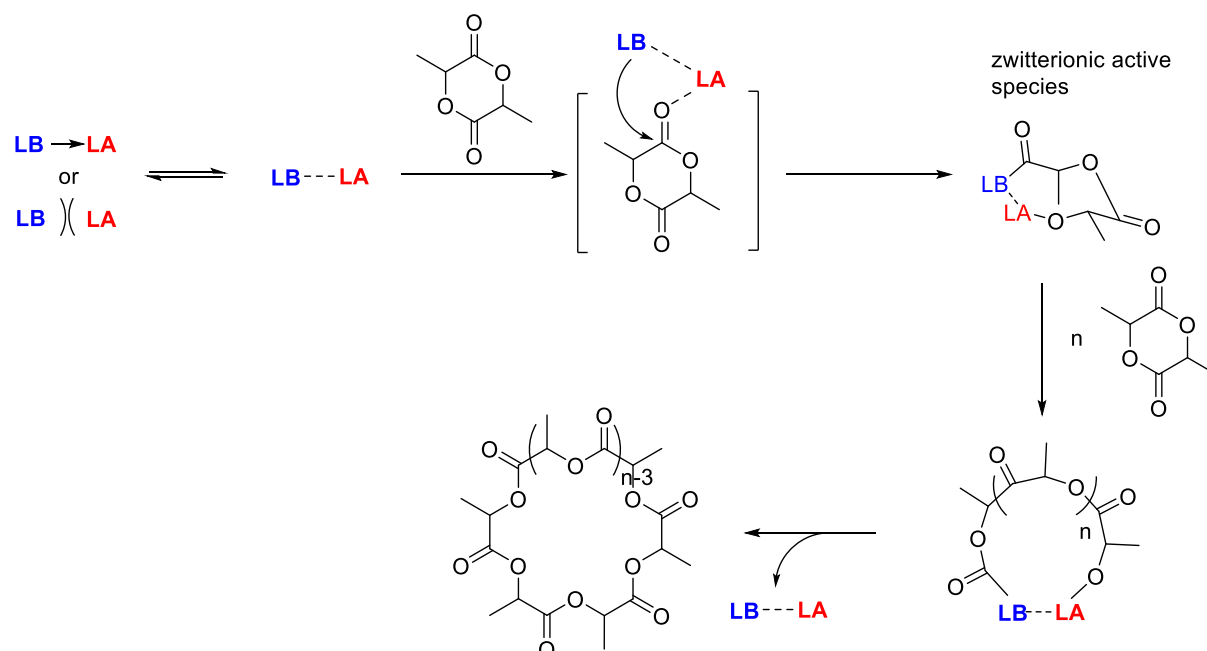
### 4.2.1. Lewis base as initiator

Interestingly, the combination of a Zn-based Lewis acid, *i.e.*  $\text{Zn}(\text{C}_6\text{F}_5)_2$ , and organic bases (amines or phosphines) can promote the controlled ring-opening polymerization of *rac*-lactide and  $\epsilon$ -caprolactone affording only cyclic structures.<sup>22</sup> High conversions (up to 95 %) within a few hours at 80 °C were obtained by mixing different organic bases such as 1,2,2,6,6-pentamethylpiperidine (PMP), *N,N*-dimethylaminopyridine (DMAP), triphenylphosphine or tri-*n*-butylphosphine, with an equimolar amount of  $\text{Zn}(\text{C}_6\text{F}_5)_2$  in MeTHF or toluene (non

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coordinative solvent). Cyclic homopolymers and PLA-*b*-PCL block copolymers were accessed by efficient chain extension as assigned by combining viscosimetric analysis and MALDI ToF mass spectrometry.

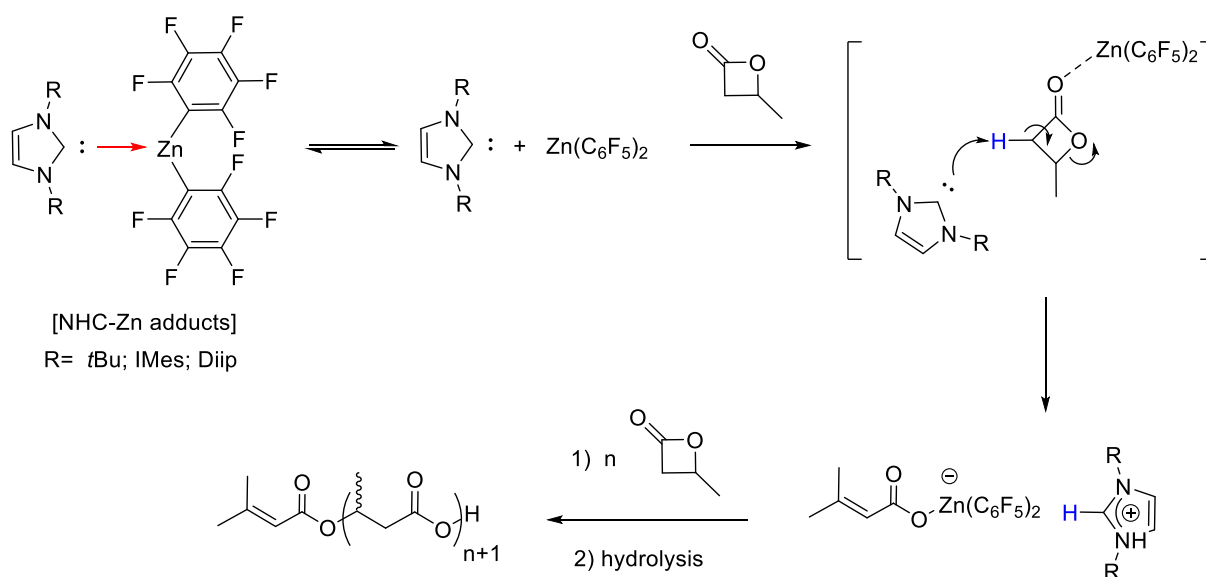
The mechanism and the interaction modes of different Lewis pair (frustrated or not) was further investigated by Li and co-workers for the polymerization of *rac*-lactide.<sup>122</sup> Different sterically hindered organic bases such as DMAP, 1,3-bis(trimethylphenyl)imidazole-2-ylidene (<sup>IMes</sup>NHC), DBU or MTBD were used in combination with Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>. The less bulky DMAP forms a classical Lewis neutral adduct [Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>·2DMAP] but can initiate the polymerization of *rac*-lactide at high temperature (80 °C) due to a partial dissociation of the Lewis complex. In contrast, the more frustrated Lewis pair Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>/MTBD exhibited higher reactivity even at room temperature because of the weaker interaction between the LA and LB. Less frustrated Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>/DBU or Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>/NHC Lewis pairs exhibited moderate reactivity. Based on these results, the authors proposed a bifunctional activation for the ROP of *rac*-lactide involving zwitterionic species. The lactide is activated by coordination with the Lewis acid followed by the addition of Lewis base, thus generating the zwitterionic active species, in which each chain bears one amine and one Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> alkoxide moiety. Both chain-ends work in a cooperative manner to activate the lactide monomer during the propagation, and the termination is obtained by intramolecular cyclization releasing the Lewis pair (Scheme 20).



**Scheme 20.** Proposed mechanism for the ring-opening polymerization of *rac*-lactide initiated by Lewis Pair

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Despite their relative stability, NHC-metal adduct compounds may dissociate in the presence of polar substrate, such as lactones, which makes them interesting in Lewis pair polymerization. A variety of *N*-heterocyclic carbene (NHC) zinc(II) adducts were reported by Dagorne *et al.* for the ring-opening of  $\beta$ -butyrolactone ( $\beta$ -BL) (Scheme 21).<sup>127</sup> Low molar mass poly( $\beta$ -butyrolactone) ( $\overline{M}_n = 810\text{--}1670\text{ g.mol}^{-1}$ ;  $\overline{D} \leq 1.22$ ) were synthesized in toluene at 90 °C by using NHC-Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> adducts. The presence at the  $\alpha$ -position of the chain of crotonate moiety, determined by MALDI ToF mass spectrometry and <sup>1</sup>H NMR end-group analysis, indicates that NHCs act probably as a base and deprotonate  $\beta$ -BL. The zinc crotonate intermediate further initiates the ROP of  $\beta$ -BL and propagation occurs via an anionic mechanism, the resulting imidazolium playing the role of counter cation. The role of the Lewis acid activator cannot be overlooked. Indeed, polymerizations initiated by the free NHC homologs exhibit longer reaction times and poorer control ( $\overline{D} \geq 1.36$ ) than those obtained by the adduct under the same conditions.



**Scheme 21.** Proposed anionic mechanism for the ROP of  $\beta$ -BL initiated by NHC-Zn(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub> adducts

The same group has resorted to NHC-group 13 metal Lewis pair adducts as efficient to promote the controlled ROP of *rac*-lactide.<sup>128</sup> Different sterically hindered NHC associated with tri-*alkyl* aluminium, gallium and indium (NHC-MR<sub>3</sub>) Lewis acids were synthesized allowing access to either linear or cyclic PLA depending on the nature of the initiator and the reaction conditions. In these systems, the activation of lactide is achieved by coordination between the carbonyl and

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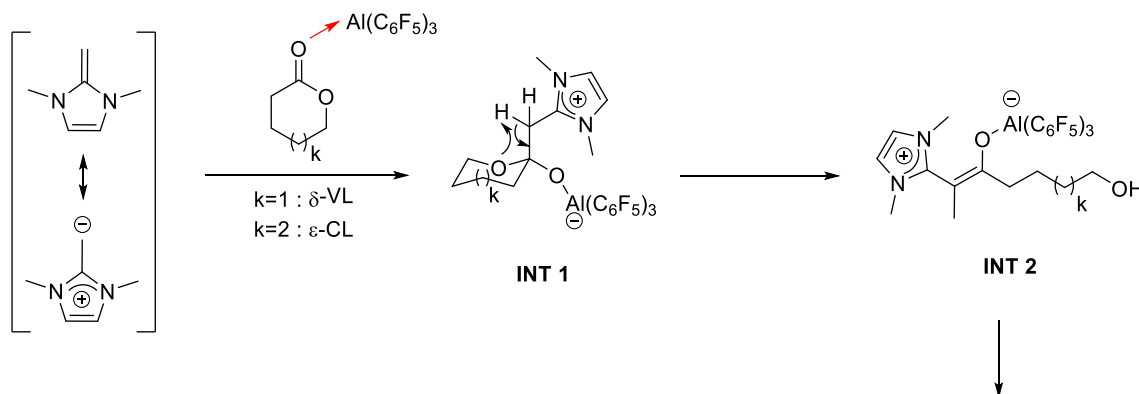
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the  $\text{MR}_3$  fragment. Subsequently, the NHC ring-opens the activated monomer forming the zwitterionic active species and chain-growth occurs from the alkoxide metal center.

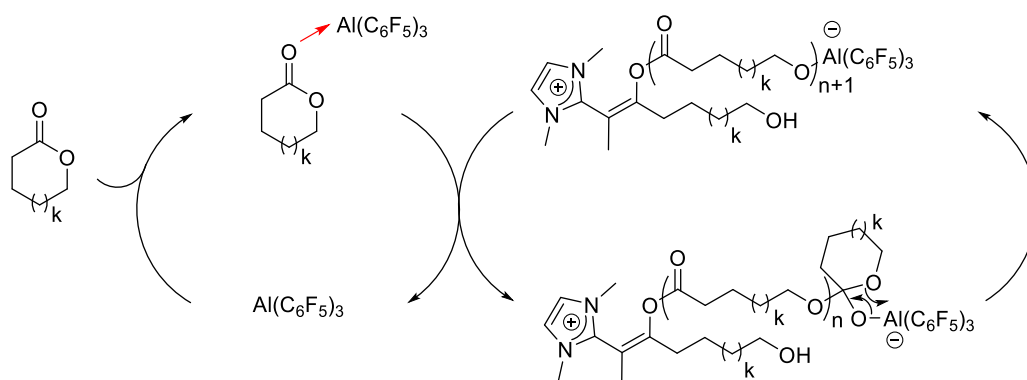
In 2012, Chen et al. have shown that the  $\text{Al}(\text{C}_6\text{F}_5)_3\text{-P}(\text{tBu})_3$  Lewis pair can polymerize  $\epsilon$ -caprolactone at room temperature (58% after 24h), but in a non-controlled manner ( $\bar{D} \geq 1.56$ ).<sup>117</sup> In contrast to NHCs, *N*-heterocyclic olefins (NHOs) used alone have proven less efficient in controlling the ROP of  $\delta$ -VL or  $\epsilon$ -CL. However, when employed in conjunction with  $\text{Al}(\text{C}_6\text{F}_5)_3$ , some NHOs have been demonstrated to effectively control the LP-RO(c)P of  $\delta$ -VL and  $\epsilon$ -CL. Various copolyesters with molar mass up to 855 000  $\text{g.mol}^{-1}$  and low dispersities ( $\bar{D} = 1.02\text{-}1.63$ ) could be obtained in this way. Polymerizations have been carried out in toluene at 25 °C with 2 equiv. of the Lewis acid relatively to NHO, so that each propagation step involves the monomer in its activated form (i.e. the polymerization proceeds via AMM). The living character of the ROP process has been supported through successful chain extension experiments, and formation of well-defined di- and triblock copolymers with no side transesterification noted ( $\bar{D} \leq 1.15$ ).<sup>129</sup> Successful isolation and characterization (XRD and NMR spectroscopy) of several key intermediates, including the activated monomer ( $\text{Al}(\text{C}_6\text{F}_5)_3\text{-}\epsilon\text{-CL}$ ) and the zwitterionic tetrahedral intermediate (INT 1 in Scheme 22), has been correlated with polymerization kinetics to elucidate the ROP mechanism. As illustrated in Scheme 22, this mechanism involves the nucleophilic attack of the activated monomer by the NHO, forming the zwitterionic tetrahedral intermediate (INT 1) and generating the ring-opened zwitterionic enolaluminate active species (INT 2). The latter species further attacks the activated lactone leading to a newly formed tetrahedral intermediate, which is followed by ring-opening and regeneration of the zwitterionic active species.

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### Initiation



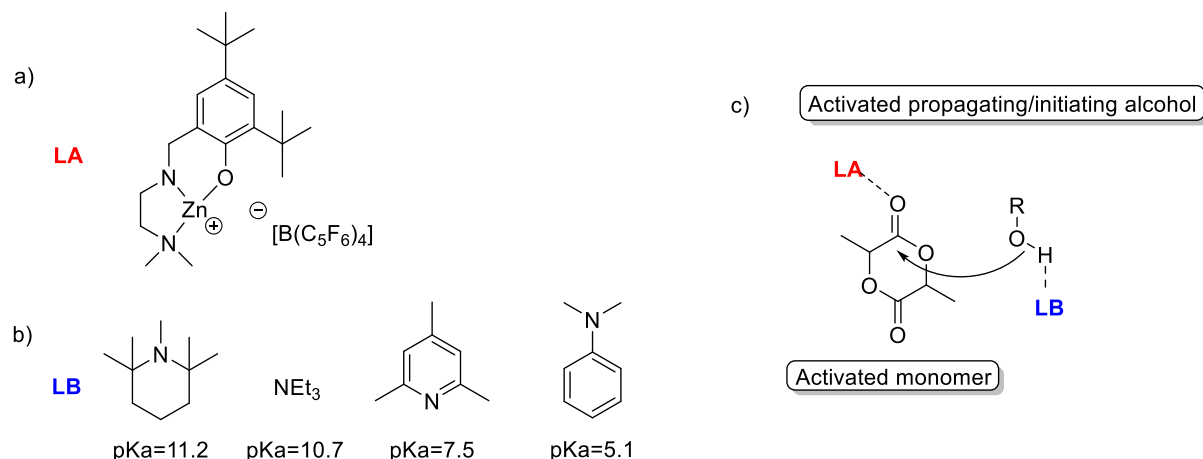
### Propagation



**Scheme 22.** Proposed mechanism for the LP-ROP of  $\delta$ -VL and  $\epsilon$ -CL by  $\text{NHO-Al}(\text{C}_6\text{F}_5)_3$ .

#### 4.1.2. Lewis pairs as true ROP catalysts

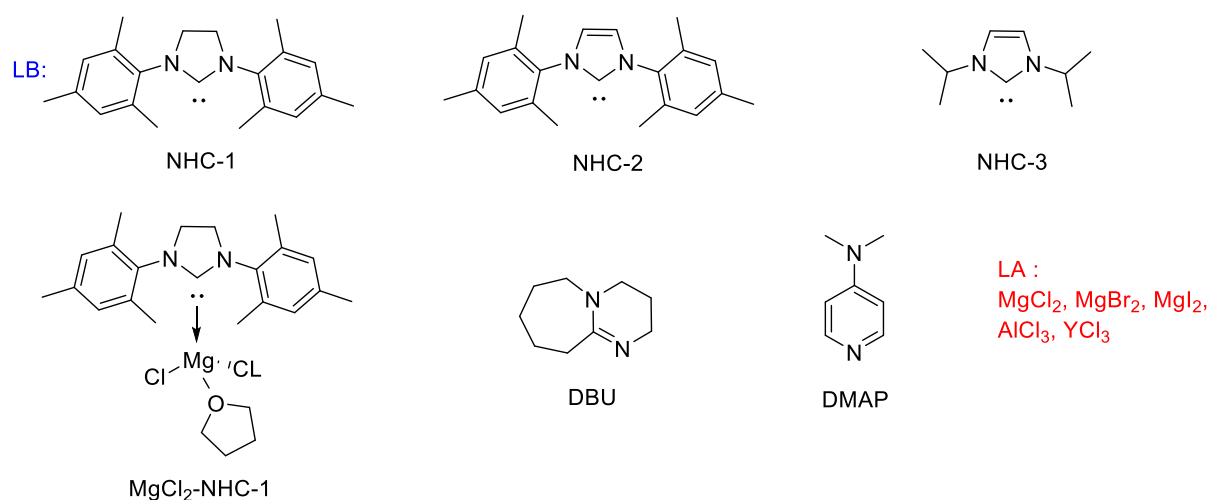
In 2011, Bourissou et al. have reported that ROP of *rac*-lactide initiated can be controlled in presence of a discrete cationic complex, namely,  $[\{\text{NNO}\}\text{Zn}]^+[\text{B}(\text{C}_6\text{F}_5)_4]^-$  for monomer activation and combined with a tertiary amine activating the initiating/propagating alcohol.<sup>130</sup> Well-defined PLA with molar mass up to 14 500  $\text{g}\cdot\text{mol}^{-1}$  and low dispersities ( $D \leq 1.34$ ) have thus been synthesized at  $T = 25^\circ\text{C}$  within a few hours using neo-pentanol as initiator and toluene or dichloromethane as solvent. In this system, the cooperative action mode of both the Lewis acid and the Lewis base is essential to ensure high activity and rapid polymerization (Scheme 23). Indeed, no polymerization has been observed by using neo-pentanol with either the discrete cationic Lewis acid or the tertiary amine alone. Reactivity has been found to depend on the basicity of the tertiary amine. As an example, complete conversion of 100 equiv. of lactide has been achieved within 3 h, in presence of pentamethylpiperidine, but hardly any polymerization occurs with  $\text{PhNMe}_2$ . Activation of the initiating/propagating alcohol has been suggested to occur by hydrogen bonding.



**Scheme 23.** a) Discrete cationic zinc complex  $[\{NNO\}Zn]^+[B(C_6F_5)_4]^-$ ; b) Scope of tertiary amine; c) Bifunctional activation by the Lewis acid (monomer) and the propagating/initiating chain-end (by tertiary amine) for the ROP of *rac*-lactide.

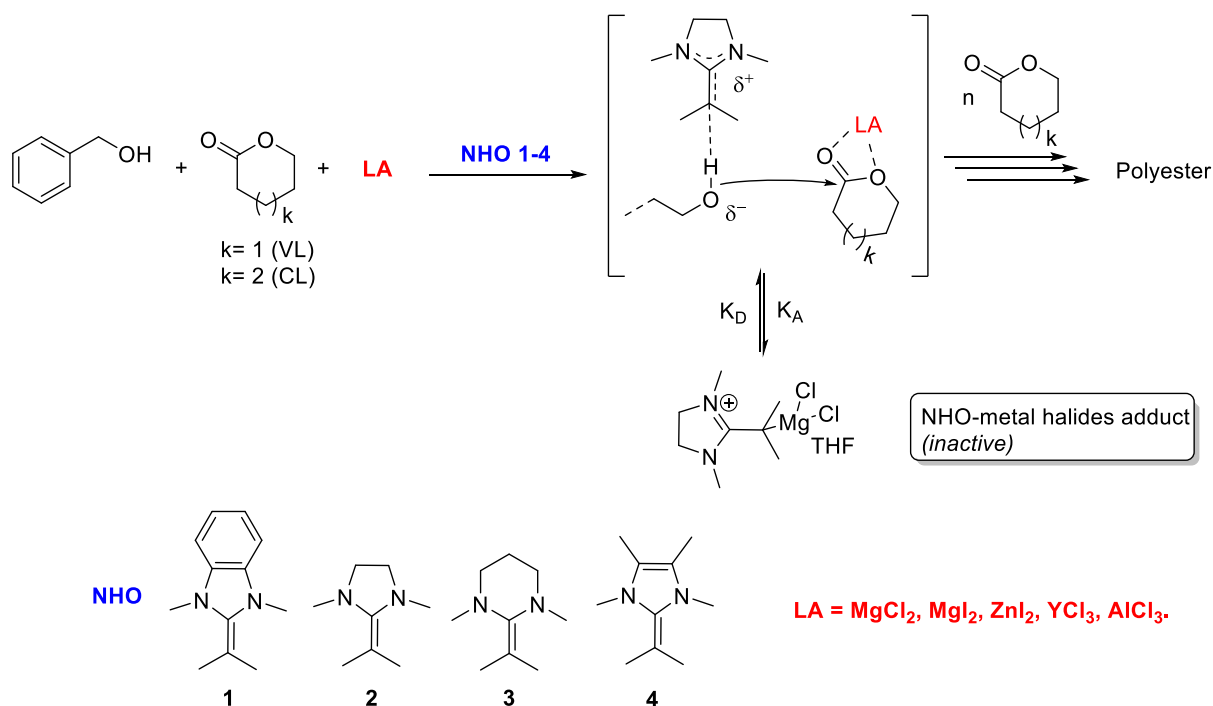
Based on previous works by Buchmeiser *et al.* regarding use of NHC-Lewis acid adducts ( $SnCl_2$ ,  $AlCl_3$  or  $MgCl_2$ ) as thermal latent catalysts for the ROP of CL or for the synthesis of polyurethanes,<sup>131,132</sup> Naumann *et al.* have recently shown NHCs, DBU and DMAP combined with simple Lewis acids, e.g.  $MgX_2$ ,  $AlCl_3$ ,  $YCl_3$ , can efficiently and rapidly promote the ROP of pentadecalactone (Scheme 24).<sup>133</sup> The authors have suggested that a fast and complete dissociation of the adduct  $MgCl_2$ -NHC-1 is obtained at 110 °C. Excess of the Lewis acid (5 equiv. as rel. to the initiator) has to be employed to achieve high conversion  $\geq 80\%$  in toluene after 2 h, using benzyl alcohol as initiator. Interestingly, only a few variations in the activity has been observed by changing the Lewis base, allowing the use of simple organic bases such as DMAP. Nevertheless, the nature of the Lewis acid significantly influences the reactivity in the following order:  $MgX_2 \geq YCl_3 \geq AlCl_3$  and  $MgI_2 \geq MgBr_2 \geq MgCl_2$ , confirming that Lewis acid-monomer interaction is the determining factor in this type of dual activation. This study has been extended to the RO(c)P of other cyclic esters, such as  $\beta$ -BL,  $\delta$ -VL,  $\epsilon$ -CL, lactide, and pentadecalactone. Selection of the Lewis acid thus enables to control the copolymer composition by simple catalyst combinations. As an example, from the same equimolar mixtures, very different copolyester can be generated. Copolymerizations of CL and VL (1:1) were undertaken using  $MgI_2$ ,  $MgCl_2$ ,  $YCl_3$  and  $ZnCl_2$  as cocatalysts with DMAP. While only  $MgI_2$  and  $YCl_3$  cocatalysts resulted in isolated polymer, the  $MgI_2$ -DMAP system showed an overall conversion of 52% after 2 h and displayed a slightly preferred incorporation of VL. Contrasting this, application of  $YCl_3$  entailed a conversion of 58% after only 10 min but displayed an inverted and somewhat stronger preference for CL incorporation.<sup>134</sup>





**Scheme 24.** Lewis bases, Lewis acids and structure of the pre-catalyst  $\text{MgCl}_2\text{-NHC-1}$  for the (co)polymerization  $\beta\text{-BL}$ ,  $\delta\text{-VL}$ ,  $\epsilon\text{-CL}$ , lactide, and pentadecalactone.

The same group has later reported that NHOs and a range of metal halides as Lewis acid cocatalysts ( $\text{MgCl}_2$ ,  $\text{MgI}_2$ ,  $\text{ZnCl}_2$ ,  $\text{AlCl}_3$ ,  $\text{YCl}_3$  and  $\text{BiCl}_3$ ) can be employed in cooperative manner for the RO(c)P of  $\delta\text{-VL}$  and  $\epsilon\text{-CL}$ , while each of the single component is inactive on its own.<sup>133</sup> Poly( $\epsilon$ -caprolactone) and poly( $\delta$ -valerolactone) with predictable molar mass (up to  $23\,500\text{ g}\cdot\text{mol}^{-1}$ ), defined end-groups and low dispersities ( $D = 1.05\text{-}1.15$ ) can thus be obtained at room-temperature in THF, using catalyst loading of 0.25-0.50 mol%, benzyl alcohol as initiator, and various combinations of NHOs and Lewis acids. Again, polymerization rates are strongly dependent on the nature of the Lewis acid (5 equiv. relative to the initiator) in the order  $\text{MgI}_2 \geq \text{YCl}_3 \geq \text{AlCl}_3 \geq \text{MgCl}_2$ . In the proposed mechanism (Scheme 25), formation of  $[\text{NHO-MgCl}_2]$  adducts keeps the concentration of free NHO low, enabling to minimize the occurrence of side transesterifications often encountered in the organopolymerization of  $\delta\text{-VL}$  or  $\epsilon\text{-CL}$ .



**Scheme 25.** Schematic representation of the proposed mechanism for the ROP of CL and VL, including possible adduct formation

Naumann *et al.* have further applied Lewis pairs based on NHOs and metal halides to less reactive lactones, such as  $\omega$ -pentadecalactone (PDL, 16-membered cycle) or  $\gamma$ -butyrolactone ( $\gamma$ -BL).<sup>135</sup> The cooperative interaction of NHO 2-4 (Scheme 25) with MgCl<sub>2</sub>, LiCl or YCl<sub>3</sub> promotes the rapid ROP reaction of  $\omega$ -pentadecalactone in toluene at 110°C without excessive side transesterifications ( $D = 1.45$ -1.79). PDL has then been copolymerized with  $\omega$ -CL,  $\delta$ -VL and  $\gamma$ -BL. As an example, fully poly(PDL-*r*- $\epsilon$ -CL) or poly(PDL-*r*- $\delta$ -VL) random copolymers have prepared combining NHO-3 and MgI<sub>2</sub> or NHO-3 and YCl<sub>3</sub>, whereas almost pure P $\delta$ -VL is achieved in presence of NHO-2 and MgI<sub>2</sub> as Lewis pair.

Even more recently,  $\gamma$ -butyrolactone ( $\gamma$ -BL), *i.e.* a usually poorly reactive five-membered cyclic ester, has been shown to homopolymerize via dual catalysis employing Lewis pairs. Based on seminal works by Chen *et al.*,<sup>136</sup> NHOs in conjunction with LiCl have allowed polymerizing  $\gamma$ -GBL at -40 °C at rather high monomer concentration ( $[\gamma\text{-BL}]_0 = 10 \text{ mol.L}^{-1}$ ) or even in bulk.<sup>137</sup> Same reaction conditions used for the ROP of other lactones, *i.e.* NHO/BnOH/metal halides (1 : 2 : 5), has been found to convert the monomer after 96h at -36 °C for MgI<sub>2</sub>, ZnI<sub>2</sub> or YCl<sub>3</sub>. This result has strongly suggested that the NHO-metal complex cannot be dissociated at low temperature, preventing the generation of free-NHO.

Over the past few years, Lewis pair polymerization has appeared as a powerful method to enable ROP under industrial conditions (high temperature, bulk) due to the higher thermal stability of the Lewis pair. The versatility of Lewis pairs accessible, as well as the control over the reactivity by the dual activation, offer an interesting alternative to classic organometallic or organocatalytic polymerization. Some challenges remain such as the improvement of the polymerization control or the accessibility of high molar mass polyesters.

## **5. Covalent activation of cyclic monomers for anionic ring-opening polymerization**

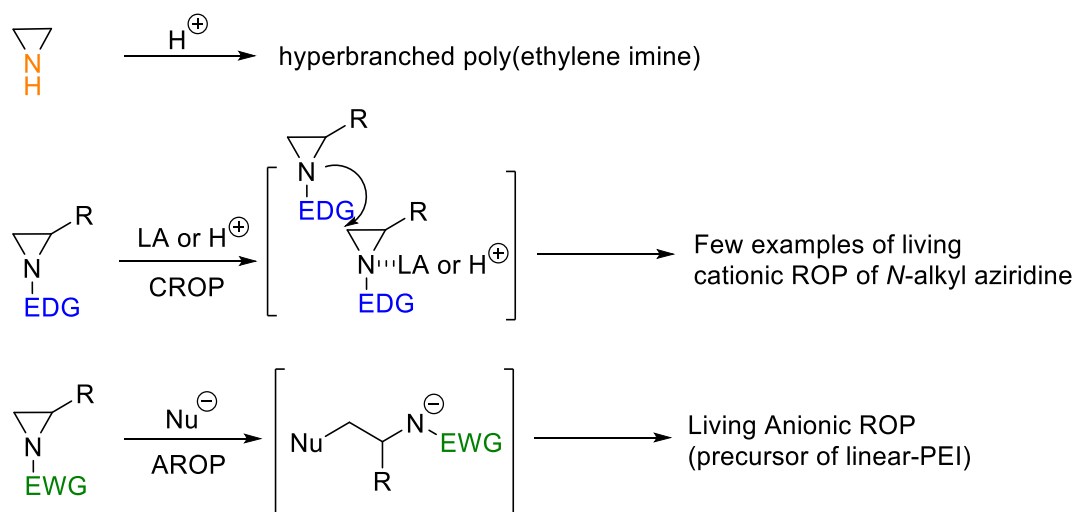
Covalent activation concerns here a special class of monomers featuring an electron withdrawing group (EWG) that is covalently grafted in their cyclic structure, which facilitates their AROP. The covalent activation differs from other methodologies of activation discussed above. Basically, the monomer activation requires the use of a (organo)catalyst which create transitionally a more reactive species, *i.e.* the activated monomer. In the case of covalent activation, the latter is achieved by grafting covalently an appropriate EWG on the cyclic structure, thus enhancing their reactivity for anionic ring-opening. This will be illustrated in this section with a focus on AROP of *N*-activated aziridines and activated cyclopropanes as specific will be given.

### **5.1. *N*-Activated aziridines vs. non activated aziridines**

While epoxide activation has been extensively studied for polyether synthesis,<sup>81,82,138</sup> only a few reports deal with the ROP of aziridines, that are, the nitrogenous analogues of epoxides. In molecular chemistry, aziridines, also known as *ethyleneimine* or *azaethylene*, have been widely used to synthesize miscellaneous building blocks, which enables the further construction of a variety of biologically and pharmaceutically important drugs.<sup>139–142</sup> The trivalent geometry of the nitrogen atom in the aziridine ring enables to tune its reactivity toward nucleophilic ring-opening reaction of these *N*-heterocycles, by introducing substituents with different electronic properties on the nitrogen center.

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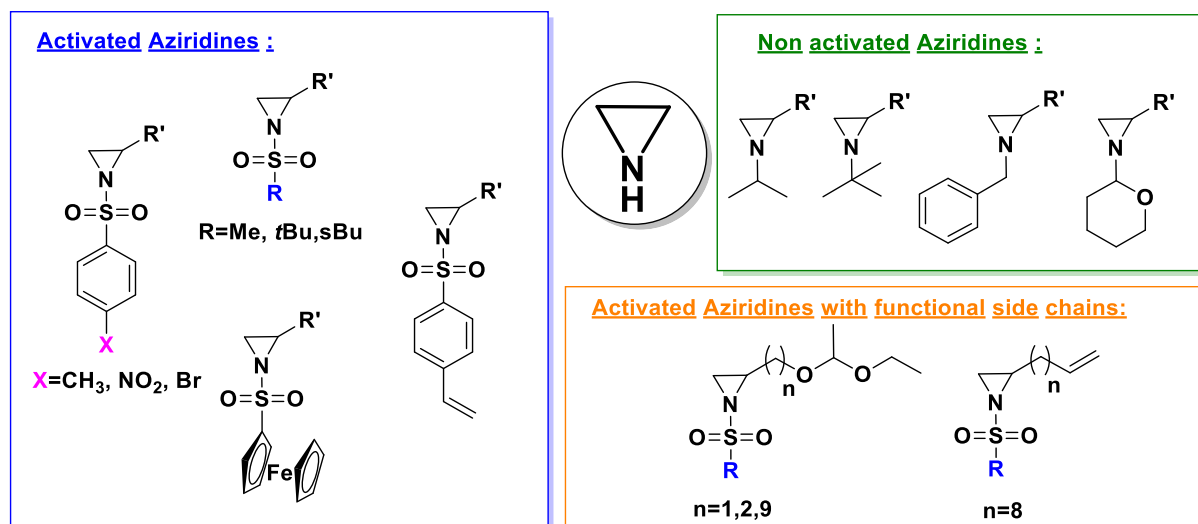
Aziridines containing a hydrogen or electron donating group (EDG) are « non-activated aziridines» and can be activated in an electrophilic manner through interaction of the nitrogen atom with a Lewis or Brønsted acid. On the other hand, covalent substitution on the nitrogen atom with electron withdrawing groups leads to (i) reduction of the electron density of the aziridine ring and (ii) stabilization of the negative charge resulting from the ring-opening reaction (Scheme 26).



**Scheme 26.** Difference of reactivity of *N*-H, *N*-alkyl and *N*-activated aziridines.

In polymer chemistry, non-activated aziridines have been primarily investigated by CROP. The most simple aziridine monomer, namely aziridine or ethylene imine, eventually leads to a commercially available hyperbranched poly(ethylene imine) (*h*-PEI) with protonic catalyst, due to extensive chain transfer reactions both to the polymer and the monomer.<sup>143</sup> Commercial *h*-PEI is thus produced since the early 1940's (Scheme 26) is a potentially charged water-soluble polymer. Despite its toxicity, *h*-PEI is often used as a DNA complexation agent for transfection applications in gene therapy.<sup>144,145</sup>

Non activated aziridines monomers, *i.e.* containing a *N*-alkyl substituent (ethyl, isopropyl, *tert*-butyl, benzyl or tetrahydropyranyl; Figure 8) can be initiated by Lewis or Brønsted acids, alkyl halides, carboxylic acids, etc.<sup>146–148</sup> 1-Substituted ethyleneimine monomers can undergo CROP in a « living » manner. As an example, the CROP of 1-butylethylenimine initiated by oxonium salts ( $Et_3OBF_4$ ) in dichloromethane at 0 °C leads to the formation of a linear polymer, due to the bulkyness of the *tert*-butyl group, by minimizing chain transfer and back biting reactions.



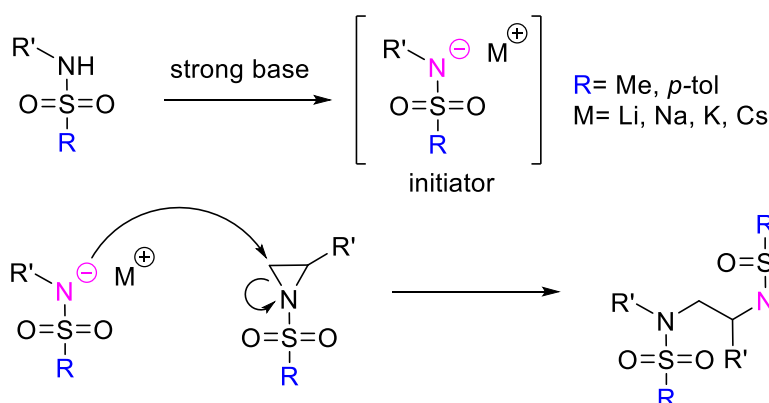
**Figure 8.** Scope of the *N*-activated aziridines and non activated aziridines

#### 5.1.1. General features of AROP of 2-*n*-alkyl-*N*-sulfonylaziridines

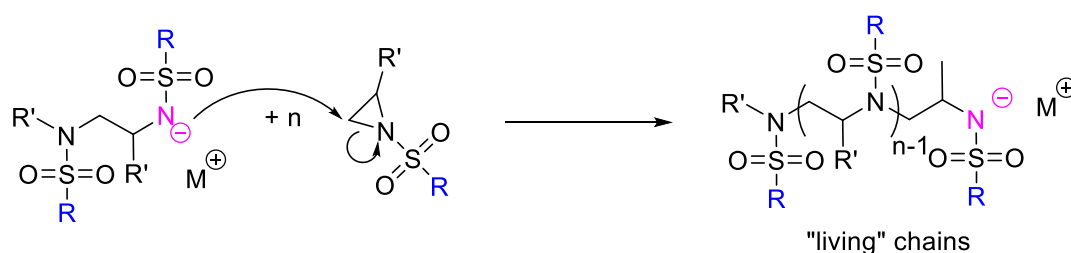
Ring-opening reaction of *N*-sulfonyl aziridines has been intensively investigated in molecular chemistry.<sup>139,141,149–155</sup> In 2005, Toste, Bergmann *et al.* have discovered that 2-*n*-alkyl-*N*-sulfonylaziridines could be subjected to a controlled AROP process through monomer activation by *N*-sulfonylation.<sup>156</sup> Racemic 2-decyl and 2-methyl aziridines containing a mesyl or a tosyl as EWG, have thus been polymerized in a living manner in DMF at 50 °C, in presence of *N*-benzylmethanesulfonamide salts as initiators. Well-defined polysulfonamides with molar masses from 2 800 to 22 000 g.mol<sup>-1</sup> and low dispersities ( $D \leq 1.10$ ) have been achieved under these rather mild conditions. The as-obtained polysulfonamides have further serve as precursors of linear PEI derivatives, using strong reducing agents (e.g. naphtalenide lithium). Inspired by these seminal works, several other groups have resorted to this “covalent activation strategy” to access well-defined polyaziridines. AROP of the *N*-sulfonyl aziridines is usually initiated by deprotonated secondary sulphonamides. The latter are *in situ* generated using a stoichiometric amount of a strong organometallic base (see Scheme 27). The initiator then attacks the monomer at its less substituted position, forming an « aza-anion » propagating species. Propagation occurs by nucleophilic attack of the sulfonamide chain-end onto the aziridine monomer. The “controlled/living” character of this AROP process has been evidenced; quenching of living chain-ends is typically achieved by adding an electrophile, or protic moieties, *e.g.* generally alcohols (MeOH, EtOH, etc.) or propargyl bromide.

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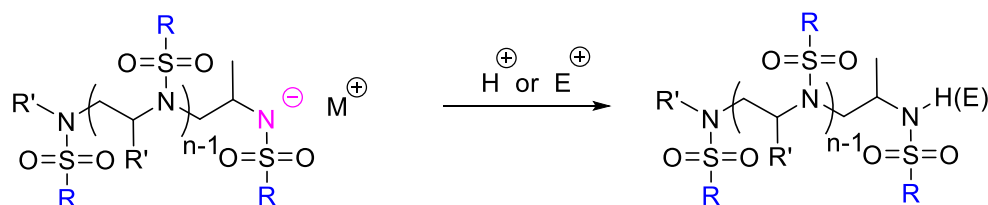
### Initiation



### Propagation



### Termination



**Scheme 27.** AROP of *N*-sulfonyl aziridines.

Reaction kinetics have been studied by real-time  $^1\text{H}$  NMR spectroscopy, as reported by Wurm *et al.* for the aza-AROP of 2-methyl aziridine with a mesyl or a tosyl activating group.<sup>157</sup> Highly polar aprotic solvents, such as DMSO or DMF, have proven suitable. As an example, propagation rates in DMSO and DMF, are equal to:  $k_p = 13.17 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$  and  $k_p = 12.53 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$ , respectively, while polymerization carried out in THF or benzene show lower values,  $k_p = 0.56\text{-}0.76 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$ . In constrast to AROP of epoxides, only slight variations have been noted upon changing the counter-cation (Cs, Li, Na or K).

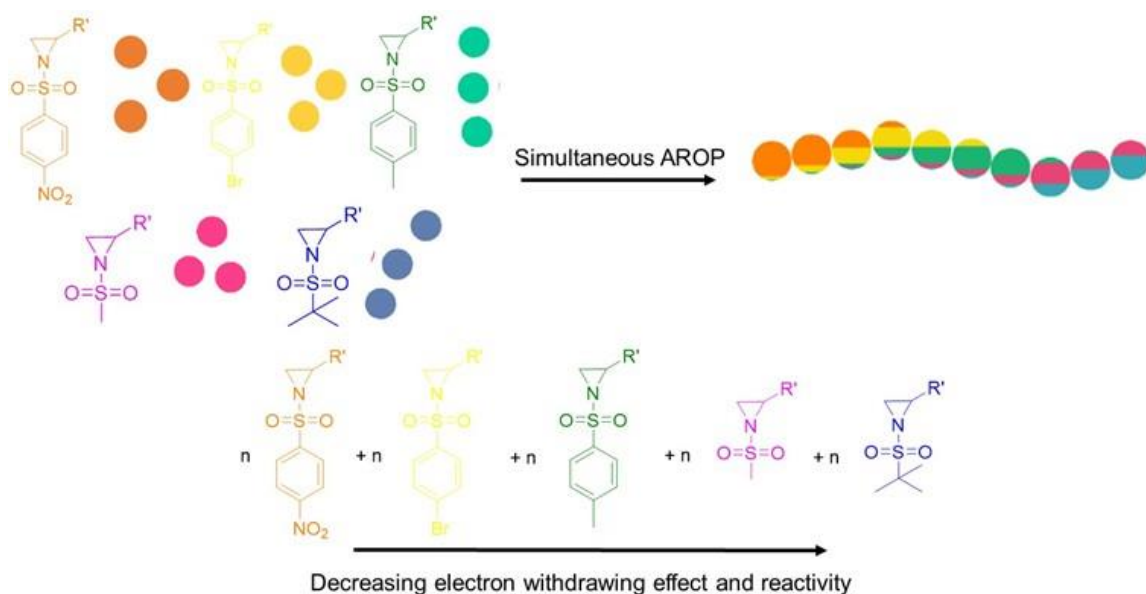
Organic superbases such as the *t*-BuP<sub>4</sub> phosphazene, Verkade's bases, DBU, MTBD, and *N,N,N',N'*-tetramethylguanidine (TMG) can also play the role of deprotonating agents for the AROP of *N*-activated aziridines (tosyl and mesyl) in catalytic or stoichiometric amount as compared to the initiator.<sup>158</sup> During this thesis, we have focused our interest on the NHC-organocatalyzed ring-opening polymerization (NHC-OROP) of *N*-tosyl aziridines using

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various initiators and NHC catalysis as initiating system. The NHC-OROP of *N*-tosyl aziridine will be further described in the second chapter of this manuscript.

### 5.1.2. Copolymerization of 2-*n*-alkyl-*N*-sulfonylaziridines and functional monomers

The group of Wurm has reported the synthesis of activated aziridines bearing different EWG's with the aim at tuning their polymerizability. Functional side chains have also been introduced for further post-modification reactions<sup>159–163</sup> (click reaction, deprotection). Di, tri or multi-gradient block polymers have thus been prepared by simultaneous « aza-anionic » AROcP, under the same conditions used for AROP, *i.e.* use of sulfonamide salt as initiator, DMF as solvent at 50 °C.<sup>160</sup> A correlation has been evidenced between homopolymerization rates of monomers and to the EWG, in the following order: nosyl > brosyl > tosyl > mesyl > busyl (Figure 9).



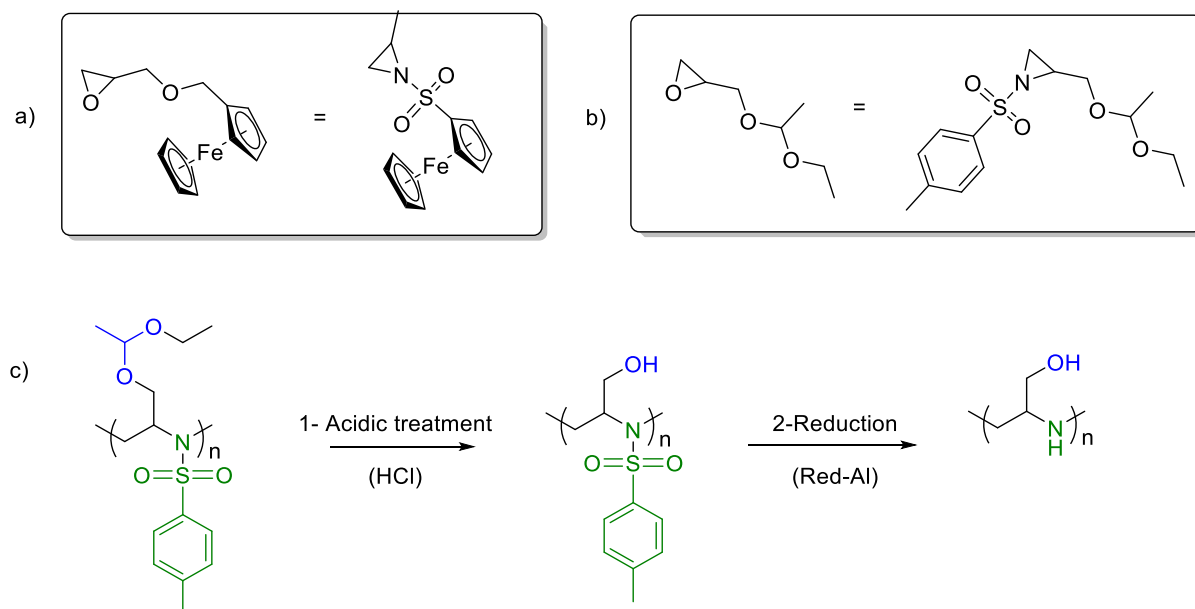
**Figure 9.** Gradient multi-block copolymers by AROP of *N*-sulfonyl aziridines.

In contrast, *n*-alkyl substituents at the aziridine ring only slightly influence the kinetic of the AROP, and random copolymers are eventually achieved from such aziridines. Interestingly, Wurm et al. have reported the preparation of gradient copolymers by compartmentalization of two monomers bearing different side chains (methyl or *n*-decyl) in an emulsion polymerization process.<sup>164</sup> Physical separation between the two monomers can be implemented by a surfactant-free DMSO in cyclohexane emulsion, owing to the difference in solubility of the monomers. The aziridine with the methyl substituent shows a “DMSO-philic” character, while the long-

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alkyl chain monomer has a preference for cyclohexane. The gradient microstructure of the resulting copolymers thus only depends on the ratio methylAz/*n*-decylAz inside the DMSO droplets.

By analogy with AROP of ethoxy ethyl glycidyl ether (EEGE) and ferrocenyl epoxide monomers, aziridines containing acetal-protected<sup>163</sup> side chains or ferrocenylsulfonyl activating group<sup>165</sup> have also been subjected to AROP affording well-defined functional polyaziridines (Scheme 28.a and b). Acetal-protected *N*-sulfonyl aziridines lead to doubly protected polymers the selective modification of which can release pendant hydroxyl groups and/or amine groups along the backbone. The sulfonyl moiety can be removed partially under reductive conditions (Red-Al), while treatment with hydrochloric acid enables to release pendant hydroxyl groups (Scheme 28.c).



**Scheme 28.** a) Ferrocenyl epoxides and *N*-activated aziridines; b) acetal protected epoxides and *N*-activated aziridines; c) selective deprotection of *N*-activated aziridines bearing acetal protected side chains.

### 5.1.3. Anionic ring-opening polymerization of ethylene imine precursors and polymers deprotection reaction.

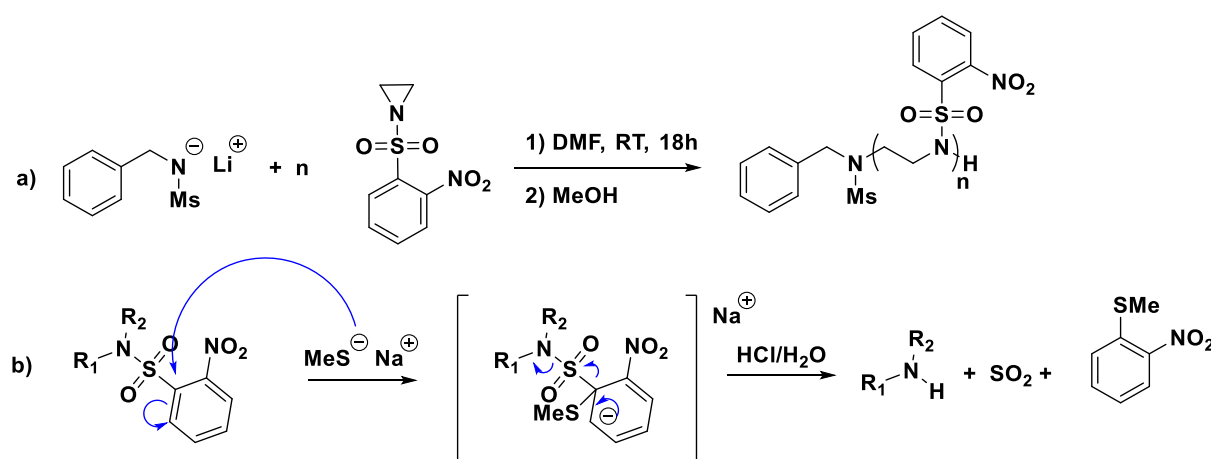
Early precipitation is observed during AROP of both 1-tosylaziridines and 1-mesylaziridines for degrees of polymerization  $\leq 10$ , explaining why reports mentioned above only concern 2-alkylated *N*-sulfonyl aziridines. In order to directly achieve polysulfonylaziridines free of alkyl



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chains in 2-position, Reisman *et al.* have described the random copolymerization of aziridines bearing different alkyl sulfonyl activating groups, namely, sec-butyl (<sup>s</sup>BsAz) and a methyl group (MsAz).<sup>166</sup> A molar ratio of 1:1 between the two monomers has been selected giving well-defined P(MsAz-*r*-<sup>s</sup>BsAz) copolymers soluble in DMF, DMSO and HMPA, with molar masses up to 20 000 g.mol<sup>-1</sup> ( $\bar{D} \leq 1.10$ ). Linear PEI derivatives have been obtained by removing the sulfonyl moiety under reductive conditions (Li, *t*BuOH, DMF, -5 °C). Despite being constituted of different sterically hindered sulfonyl groups, comonomers have been found to exhibit nearly the same reactivity, as demonstrated by <sup>1</sup>H NMR spectroscopy at low conversion and thermal analysis (DSC) of the copolymers.

As mentioned, reducing agents such as lithium naphthalenide, Red-Al, elemental lithium or strong acidic conditions are needed to remove sulfonyl moieties and give polyimines.<sup>156,166,167</sup> Only a papers have reported such a deprotection of PAz under reductive or acidic conditions, and only partial deprotectios has been observed (70-80%). Recently, however, Rupar *et al.* have proposed the AROP of 1-((*o*-nitrophenyl)sulfonyl)aziridine (oNsAz), known to be easily deprotected using sodium thiomethoxide (NaSMe) under mild conditions (Scheme 29.a).<sup>168</sup> The mechanism of deprotection involves nucleophilic aromatic substitution with elimination of SO<sub>2</sub>, yielding the corresponding deprotected amine (Scheme 29.b). However, removing the *o*-nitrosulfonyl appears difficult and side rearrangements prevents accurate identification of the polymer composition.

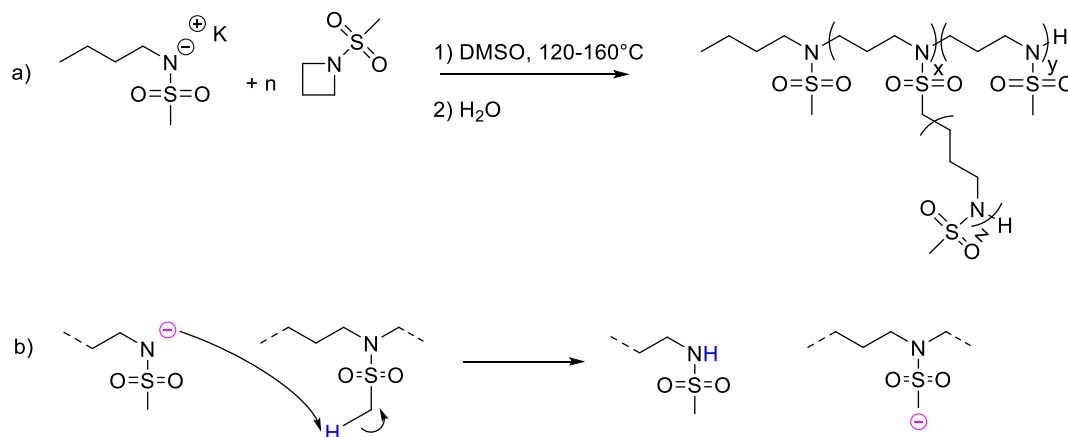


**Scheme 29.** a) AROP of 1-((*o*-nitrophenyl)sulfonyl)aziridine; b) deprotection of *o*-nitrophenylsulfonylamine by sodium thiolmethoxide.

Azetidines, that are four-membered cyclic amines, behave similarly to aziridines in AROP processes. They also lead a hyperbranched poly(trimethyleneimine) by non-controlled

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CROP. Recently, Reisman *et al.* have reported AROP of *N*-sulfonylazetidine from the same initiating system used for *N*-activated aziridines, namely, the secondary sulfonamide salt generated *in situ*.<sup>169</sup> AROP of *N*-mesylazetidine has been shown effective in DMSO at temperature  $\geq 100^\circ\text{C}$  (vs.  $50^\circ\text{C}$  for AROP of aziridines, but transfer reactions to both the polymer and the solvent (DMSO) have been evidenced (Scheme 30).



**Scheme 30.** a) AROP of *N*-mesyl azetidine and b) transfer reaction to the monomer. .

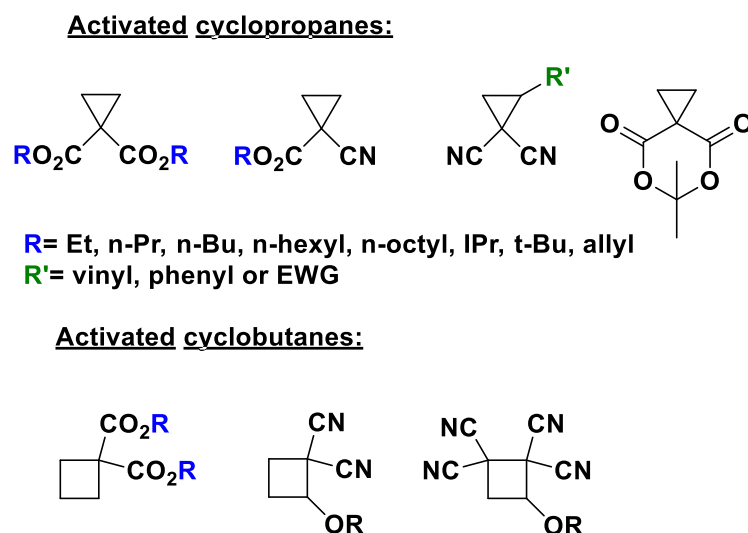
In conclusion, AROP of *N*-activated aziridines is a relevant example of covalent activation through grafting of electron withdrawing sulfonamide group on the nitrogen atom. Not only strong metal bases, but also organic superbases (NHCs, phosphazenes or amidines) afford high control over molar masses, low dispersities and high chain-end fidelity. A variety of macromolecular structures are accessible by this method, from diverse monomers, including functional ones.

### 5.2. Cyclopropane and cyclobutane derivatives

Activation of 3- and 4-membered ring cycloaliphatic monomers, through covalent attachment of specific activating groups has also been considered, and appears as an elegant way to produce C-C bonds by ROP. Despite the high ring strain of cyclopropanes, which makes their ring-opening thermodynamically favorable, drastic conditions only allow their oligomerization to occur. This is due to the kinetically unfavoured propagation step.<sup>170</sup> In order to enhance kinetics of propagation, and similarly to *N*-activated aziridines discussed above, polymerizability of carbon-based cycles can be significantly enhanced in AROP by covalently grafting two EWG's

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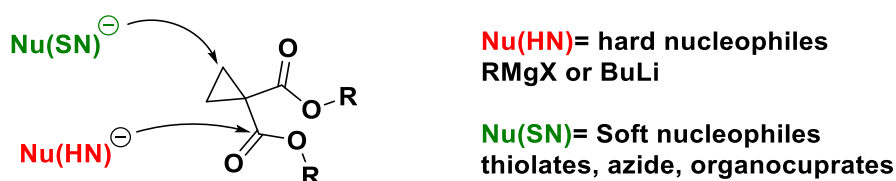
in geminal position. This indeed causes polarization of the C-C bond, while also stabilizing the carbanionic propagating species after ring-opening. The different monomer structures and related activating groups are displayed in Figure 10. Cyclopropanes can be geminally substituted by two esters, two nitriles or a combination of a nitrile and an ester (Figure 9).



**R**= Et, n-Pr, n-Bu, n-hexyl, n-octyl, iPr, t-Bu, allyl  
**R'**= vinyl, phenyl or EWG

**Figure 10.** Scope of activated cyclopropanes and cyclobutanes polymerized by AROP.

Cho *et al.* have first reported the AROP of 1,1 disubstituted cyclopropanes containing two cyano activating groups and a third substituent (vinyl, phenyl, or another EWG) on one of the adjacent carbon atom.<sup>171,172</sup> Polymerization has been initiated by soft nucleophiles, such as sodium cyanide, thiolates, or organocuprates to avoid side reactions on the carbonyl activating groups, as eventually observed with strong nucleophiles like BuLi or RMgX (Scheme 31).



**Scheme 31.** Difference of reactivity between hard and soft nucleophiles towards the AROP of 1,1 dialkyl cyclopropane carboxylates.

Penelle *et al.* have also resorted to this strategy by reporting the AROP of 1,1 dialkyl cyclopropane carboxylates in high solvents such as DMSO or DMF and at temperature  $\geq 140$  °C.<sup>173–177</sup> The process shows features of a controlled/living polymerization, enabling to achieve

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full conversion, narrow molar mass distributions and high chain-end fidelity. Dicyano activating groups have been shown to provide monomers with the higher reactivity and polymerized rapidly, full conversion being reached within a few minutes at 60 °C using sodium phenylthiolate as initiator. As its vinylic homolog, namely, poly(vinylidene cyanide), poly(trimethylene cyanide) is insoluble in common organic solvents.

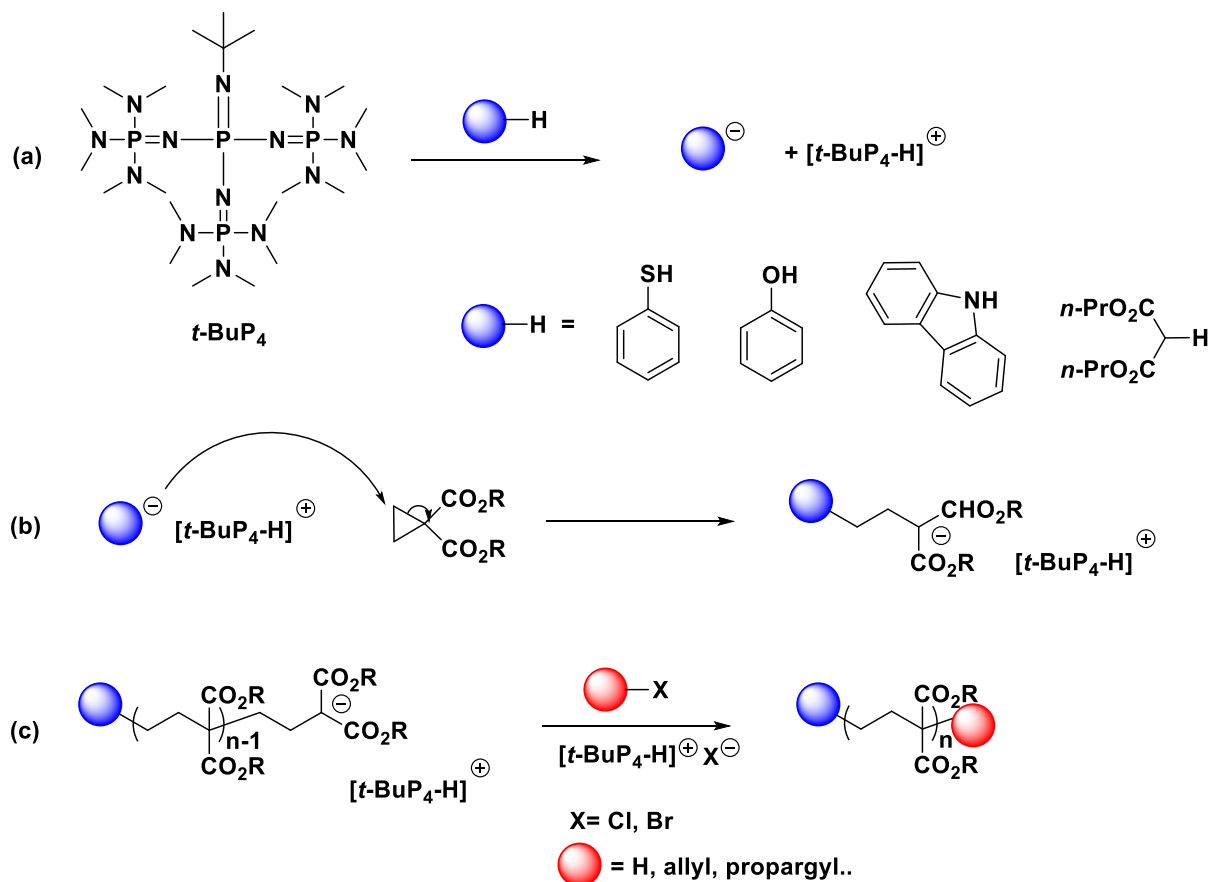
In contrast, cyclopropanes bearing di-alkylcarboxylates groups only react at high temperature, but introduction of alkyl side chain increases solubility and also introduces functionality for post-modification chemistry. Logically, alkyl 1-cyanocyclopropane carboxylates exhibit intermediate reactivity and polymerize twice slower than dicyano cyclopropanes at 60 °C.<sup>174</sup> In contrast, diethyl cyclobutane-1,1-dicarboxylate or 1,1 dicyanocyclobutane do not polymerize under the same conditions used for activated cyclopropanes, due to side initiation.<sup>178–180</sup> Only activated cyclobutanes containing an additional ether group on the vicinal position have been found to be reactive by AROP.<sup>181</sup>

Thiophenolates salts are commonly used as initiators for AROP of activated carbon cycles, as they provide quantitative and rapid initiation. Lithium, sodium or potassium thiophenolates salts have been investigated first as organometallic initiators. As expected, the nature of the counter-cation of the dimethyl ethylmaleonate carbanion strongly affects the rate and the selectivity of the polymerization. As an example, substituting the sodium cation by potassium roughly doubles the propagation rate of the polymerization of 1,1 dialkyl cyclopropanes carboxylate at 140 °C. Kinetic experiments have demonstrated that the reactive species under these conditions, is the free ion and strong ion-pairing are formed by lithium and sodium, thus transforming the majority of the active species into dormant ones.

Organocatalyst superbases, including phosphazenes, amidines have been recently investigated as deprotonating agents for the AROP of activated cyclopropanes.<sup>182–184</sup> For instance, the *t*-BuP<sub>4</sub> phosphazene base in combination with different thiols has proven an excellent initiating system showing higher reactivity than organometallic systems. The soft and bulky counter-cation formed by deprotonation of the thiol enables a fast ring-opening of 1,1-di-*n*-propyl cyclopropane carboxylates under mild conditions. For this metal-free initiating system, the polymerization occurs at 60 °C in THF or toluene (vs. 140 °C in DMSO for organometallic-based initiators) providing well-defined poly(1,1-di-*n*-propyl cyclopropane carboxylate)s with molar masses up to 30 000 g.mol<sup>-1</sup> ( $\bar{D} \leq 1.15$ ). Other organic bases such as 1,1,3,3-tetramethylguanidine (TMG), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5-

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diazabicyclo[4.3.0]non-5-ene (DBN), Verkade base or *t*-BuP<sub>2</sub> have not enabled to initiate the polymerization of cyclopropanes under the same conditions used with *t*-BuP<sub>4</sub>.<sup>182</sup>



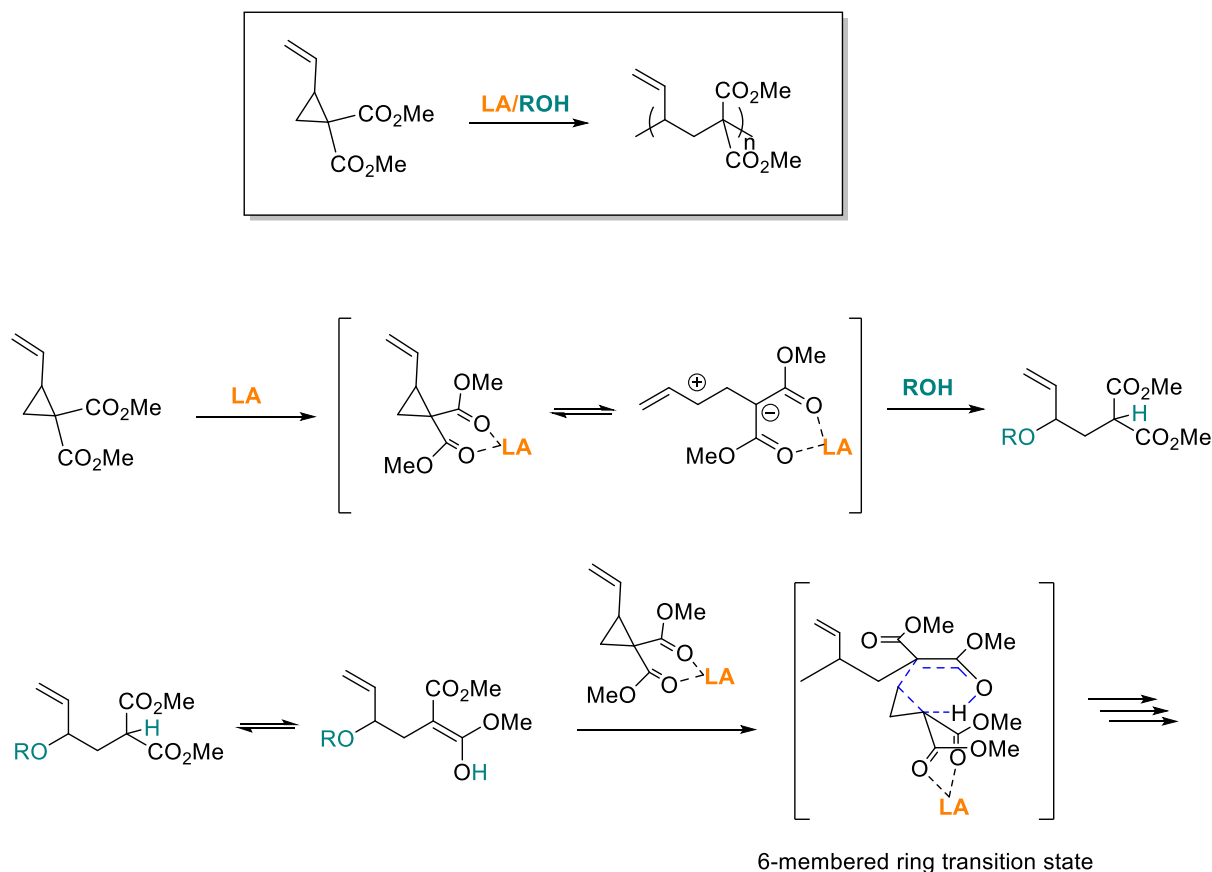
**Scheme 32.** Mechanism of: (a) activation; (b) initiation; (c) end capping reaction in the AROP of cyclopropane-1,1-dicarboxylates using *t*BuP<sub>4</sub> phosphazene base as deprotonating agent.

The combination of *t*-BuP<sub>4</sub> phosphazene base with a thiol, or an alcohol or a carbarzole or a malonate has been further investigated as a means to introduce specific end groups in poly(cyclopropane-1,1-dicarboxylate)s. Heterotelechelic polymers with low dispersities, controlled molar masses and high chain-end fidelity have thus been obtained by end-capping reaction between the propagating malonate carbanion and an alkylating agent, e.g. allyl or propargyl halides (Scheme 32).

Recently, Hayakawa *et al.* have proposed the ROP of activated donor-acceptor cyclopropanes initiated by an alcohol and catalyzed by a Lewis acid, such as  $\text{Al}(\text{OTf})_3$ ,  $\text{GaCl}_3$  or  $\text{SnCl}_4$  at room temperature<sup>185</sup>. The polymerization of di-alkyl-2-vinylcyclopropane-1,1-dicarboxylates selectively affords 1,5 addition and molar mass up to 12 600  $\text{g}\cdot\text{mol}^{-1}$  can be reached in high yield and mild conditions. In this case, and in contrast to the AROP of activated cyclopropanes,

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the Lewis-acid catalysed ROP proceeds via an activated monomer mechanism. The proposed mechanism involves the initial coordination of the Lewis acid by the two carbonyl groups at the geminal position (activated monomer) and subsequent ring-opening by the alcohol initiator (Scheme 33). The enol intermediate further reacts *via* a six-membered ring transition leading to the 1,5 addition.



**Scheme 35.** Proposed mechanism for the ROP of activated cyclopropanes catalyzed by a Lewis acid.

To summarize, the location of two geminal ester substituents on every three carbons along a carbon-chain polymer provides (i) the activation toward AROP and (ii) an elegant synthetic pathway to prepare novel polymers by introducing side functional groups during the monomer synthesis or by post-modification reactions. Alkali poly(trimethylene carboxylate) polyelectrolytes of lithium, sodium or potassium, containing two carboxylate anions on the same carbon can be easily obtained by hydrolysis.<sup>186</sup> Polymer displaying densely packed arrays of crown-ethers lateral substituent,<sup>186</sup> clickable side chains<sup>184</sup> as well as amphiphilic liquid crystal polymers<sup>187</sup> were obtained by AROP of activated cyclopropanes.

## 6. Conclusion and Aims of this thesis work

Since the discovery of living anionic polymerization of vinyl compounds by Michael Szwarc, tremendous efforts have been made to find conditions in order to attempt “livingness” in other areas of polymerization such as ring-opening polymerization.

In this context and due to the variety of heterocycles that can be subjected to ROP, numerous catalysts and organocatalysts, and consequently numerous mechanistic pathways have been investigated to achieve LROP. In this bibliographic chapter, we have focused our interest on the different mechanisms of activation through the activated anionic polymerization of challenging monomers like lactams and aliphatic epoxides, the Lewis pair polymerization of lactones and the covalent activation of less-studied monomers, *i.e.* *N*-activated aziridines and activated carbon cycles. The activation provides, in all cases abovementioned, an increase of reactivity, a better control over molar mass, end-groups and molar mass distributions and also allows the preparation of new polymers which were not accessible by conventional ring-opening polymerization.

In this context, we decided to focus this Ph.D. thesis works on the synthesis of new polyamides-based materials following an activated monomer mechanism thought i) the simultaneous combination of AROP and condensation reactions for the synthesis of aliphatic-aromatic copolyamides ii) the covalent activation of lactams by sulfonylation and iii) the hydrogen transfer polymerization (HTP) of acrylamide derivatives for the synthesis of polyamide 3-based materials.

In parallel with the synthesis of original (co)polyamides, we have also investigated in collaboration with Dr. F. R. Wurm (Max-Planck Institute of Mainz, Germany) the organocatalytic ring-opening polymerization (OROP) of the *N*-activated aziridines, *i.e.* the *N*-sulfonyl aziridines, discussed above by *N*-heterocyclic carbenes.

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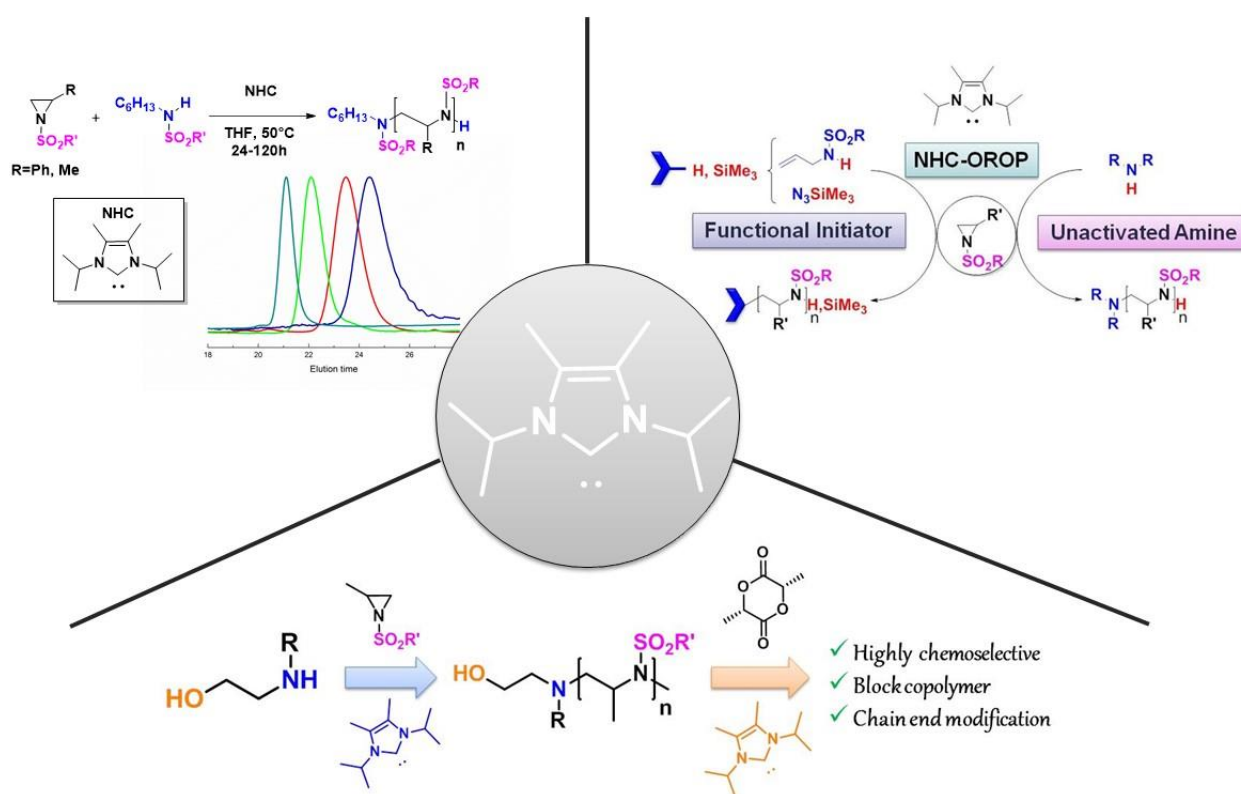


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## Chapter 2. *N*-Heterocyclic Carbene-Organocatalyzed Ring-Opening Polymerization of *N*-Tosyl Aziridines



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## Introduction

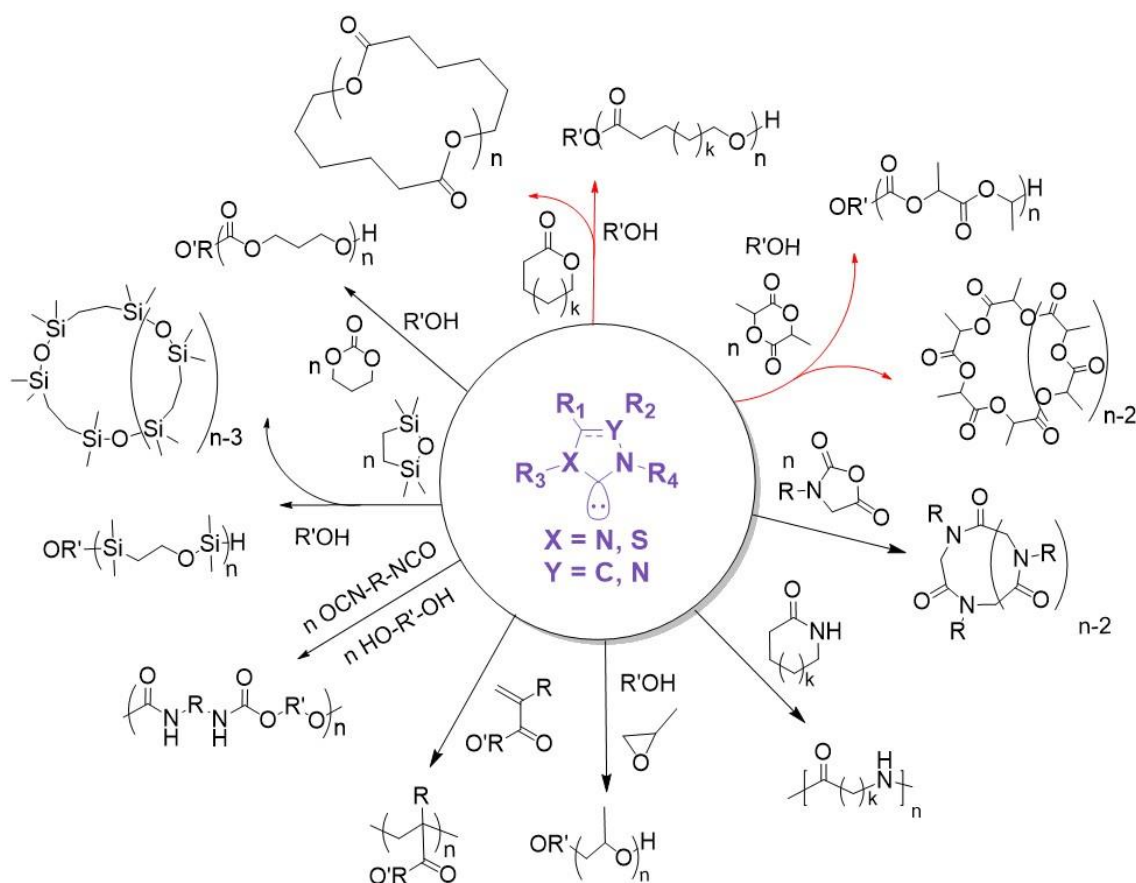
Tremendous developments have been made in the past three decades to employ organocatalysts in a variety of transformations. Mainly focused on asymmetric reactions, small organic catalysts operate under mild reaction conditions, without some of the shortcomings of biocatalysts, such as a complex structure/conformation/function relationship, or lack of robustness.<sup>1-6</sup> Organocatalysts have also been introduced in polymer synthesis.<sup>7-15</sup> Their often lower toxicity in comparison to many metal-based catalysts is driving their development in, for instance, biomedical, personal beauty care, microelectronic device and food packaging applications.<sup>1,7</sup> Several classes of organic activators, including Brønsted/Lewis acids or bases, and mono- or bicomponent bifunctional catalytic systems have been utilized, both for step-growth and chain-growth polymerizations, and for depolymerization reactions as well. Several general reviews or highlights on organo-catalyzed polymerizations are available,<sup>7-15</sup> while other reviews have dealt with more specific aspects, e.g. the ring-opening polymerization (ROP),<sup>12-14</sup> the group-transfer polymerization (GTP) of acrylics and methacrylics,<sup>15,16</sup> the zwitterionic polymerization,<sup>17</sup> or organo-catalyzed polymerizations induced by H-bond components.<sup>18-20</sup>

In this context, *N*-heterocyclic carbenes (NHCs) have been among the first organocatalysts employed for polymer synthesis, providing a straightforward synthetic strategy to a wide range of polymers.<sup>10,11,17,21-23</sup> This is obviously related to the near unlimited structural diversity of NHCs, which allows finely tuning their steric and electronic properties and using them either as Brønsted and/or Lewis bases.<sup>24-27</sup> Cyclic esters (e.g. lactide and lactones) have been by far the most investigated monomer substrates in NHC-organocatalyzed ROP (NHC-OROP).<sup>21,28-30</sup> Yet, the range of monomers amenable to polymerization by a NHC catalysis has largely been expanded to the ROP of other heterocycles, including five-membered *O*-carboxyanhydrides,<sup>31</sup> *N*-substituted carboxyanhydrides,<sup>32-34</sup> phosphoesters,<sup>35</sup> carbonates,<sup>36,37</sup> siloxanes and carbosiloxanes,<sup>38</sup> lactams,<sup>39,40</sup> epoxides<sup>41,42</sup> and *N*-activated aziridines,<sup>43,44</sup> also to the polymerization of alkyl (meth)acrylates,<sup>45-48</sup> and finally to some polymerizations proceeding by a step-growth process, such as polyurethane (Figure 1).<sup>49</sup>

Besides their role as true catalysts, *i.e.* in organo-catalyzed polymerizations, some NHCs can operate as direct nucleophilic initiators in absence of an initiator, *i.e.* in organo-initiated polymerization, for instance, through ring-opening of heterocyclic monomers<sup>7-11,17,21,41</sup> or through 1,4-conjugate addition of some (meth)acrylic substrates.<sup>50-52</sup> In many cases, NHCs

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provide high polymerization rates, excellent chain-end fidelity, control over molar masses of resulting polymers, and also allow achieving cyclic polymer structures.<sup>5-6,17</sup>



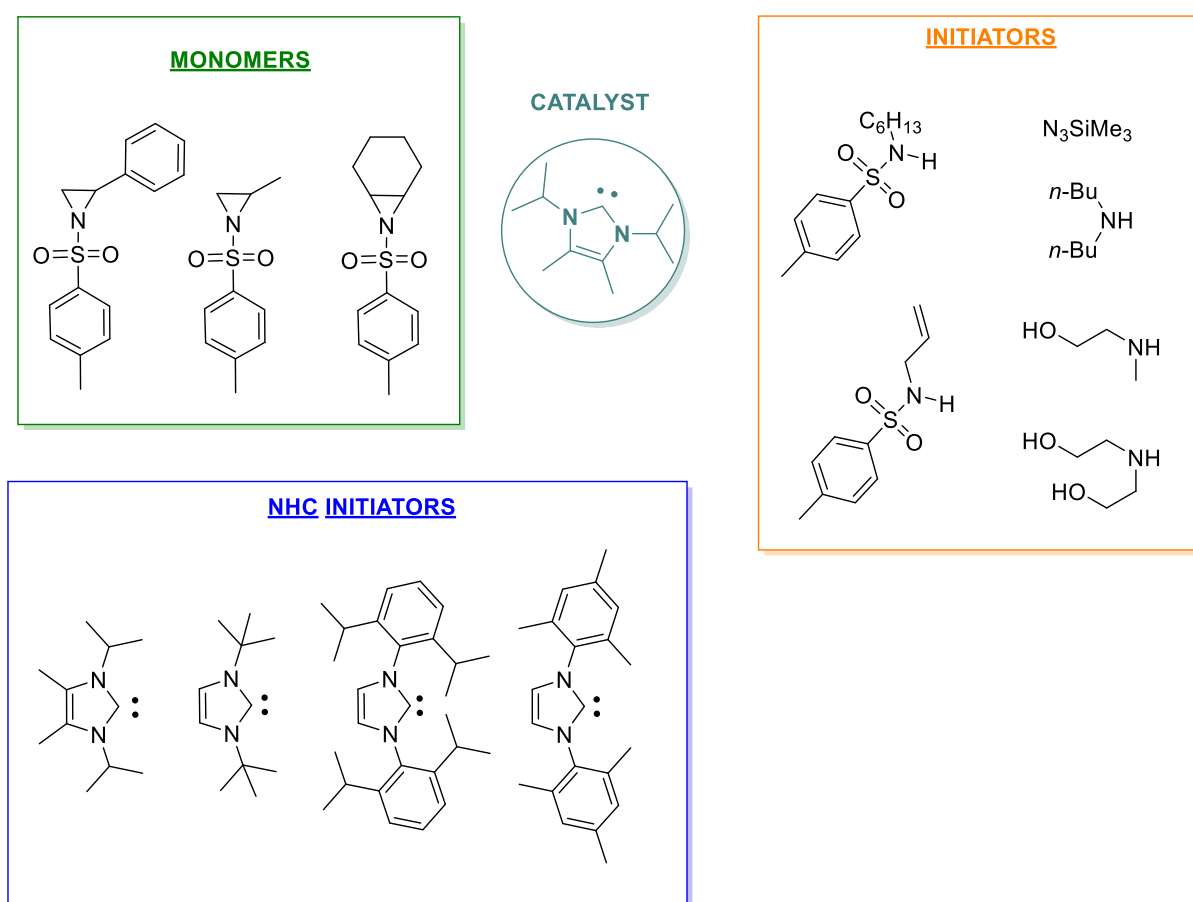
**Figure 1.** Overview of polymers obtained from *N*-heterocyclic carbenes as catalysts (or initiator)

As previously mentioned in the bibliographic chapter, while aziridines and oxiranes are isoelectronic, the two types of monomers behave very differently in ROP. For instance, the simplest representative of each family, *i.e.* ethylene oxide and aziridine (often called *ethylene imine*) is polymerized by an anionic mechanism and a cationic mechanism, respectively. While poly(ethylene oxide) can be prepared by anionic means in a controlled fashion, the cationic ROP of aziridine is accompanied by chain transfer reactions to the polymer, forming hyperbranched poly(ethylene imine) (*h*-PEI) with broad dispersity.

Interestingly, seminal works by Toste, Bergman *et al.*,<sup>53</sup> have reported in 2005 that 2-alkyl-*N*-sulfonylaziridines can be subjected to a controlled anionic ROP through monomer activation by *N*-sulfonylation. Typically, the ROP of the *N*-sulfonylaziridine is performed at 50°C in DMF, in the presence of a 1:1 molar ratio of *N*-alkyl-methanesulfonamide : KHMDS as an initiating system which affords substituted polyaziridines of narrow molar mass distribution.

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Later on, and in fact in the course of this PhD thesis, the group of Wurm has reported the synthesis and the anionic ring-opening polymerization of activated aziridines bearing different EWG's with the aim at tuning their polymerizability.<sup>57</sup> Functional side chains have also been introduced for further post-modification reactions (click reaction, deprotection).<sup>54-56, 58-61</sup> Even more recently, Rupar *et al.* described the synthesis and the anionic (co)polymerization of non-alkylated activated aziridines<sup>62,63</sup> and azetidines<sup>64</sup> (the four membered cyclic amine). In the context of this thesis, we decided to investigate the *N*-heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-activated aziridines. The monomer candidates, the initiators and the catalyst are presented in Figure 2.



**Figure 2.** Scope of the monomers, initiators and catalyst employed for the NHC-OROP of *N*-activated aziridines

The first part of this chapter will show that those 3-membered ring heterocycles can be subjected to a controlled NHC-OROP providing well-defined and metal-free PAz. Specifically, NHC-OROP of 2-methyl and 2-phenyl *N*-*p*-toluene-sulfonyl aziridine carried out in presence of various initiators, including secondary activated amines, trimethylsilyl azide or simple secondary amines, will be discussed. The second part will be devoted to the selective initiation



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from unprotected amino alcohols for the synthesis of aziridine-based telechelic and block copolymers. In a last part, we will present the preliminary results of the polymerization of *N*-activated aziridines in total absence of initiator (also referred as the zwitterionic ring-opening polymerization).

Note that, also in the course of this PhD thesis, Guo *et al.* have reported that OROP of *N*-sulfonyl aziridines using various “super organic” bases (See Bibliographic chapter).<sup>65</sup> Organic superbases such as the *t*-BuP<sub>4</sub> phosphazene, Verkade’s bases, DBU, MTBD, and *N,N,N',N'*-tetramethylguanidine (TMG) have been used as deprotonating agents for the AROP of *N*-activated aziridines (tosyl and mesyl) in catalytic or stoichiometric amount as compared to the initiator.

## **PART 2.A: NHC-Organocatalyzed Ring-opening Polymerization of *N*-Tosyl Aziridines from Amino- and Azido-containing Initiators**

This part 2.A deals with the organocatalyzed ring-opening polymerization (OROP) of 2-methyl- and 2-phenyl-*N*-*p*-toluenesulfonyl aziridines triggered by a peculiar NHC, namely 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene. For this purpose and based on the initiating system generally used in AROP of *N*-tosyl aziridine, we have firstly employed activated secondary amines as initiators. The potential of NHCs to activate a large variety of small organic molecules (mainly by hydrogen-bonding) has been judiciously applied to extend the scope of initiators suitable for the NHC-OROP of *N*-activated aziridines. Functional and non-activated amine initiators were then employed in order to introduce functionality at the  $\alpha$ -position of polymer chains. Poly(aziridine)s (PAz) thus obtained by NHC-OROP have been thoroughly characterized by NMR spectroscopy, size exclusion chromatography (SEC) and mass spectrometry in order to determine the mechanism of polymerization. The post-modification by click reaction of  $\alpha$ -functionalized PAz obtained by NHC-OROP will be also investigated to highlight the accessibility of those functional groups.

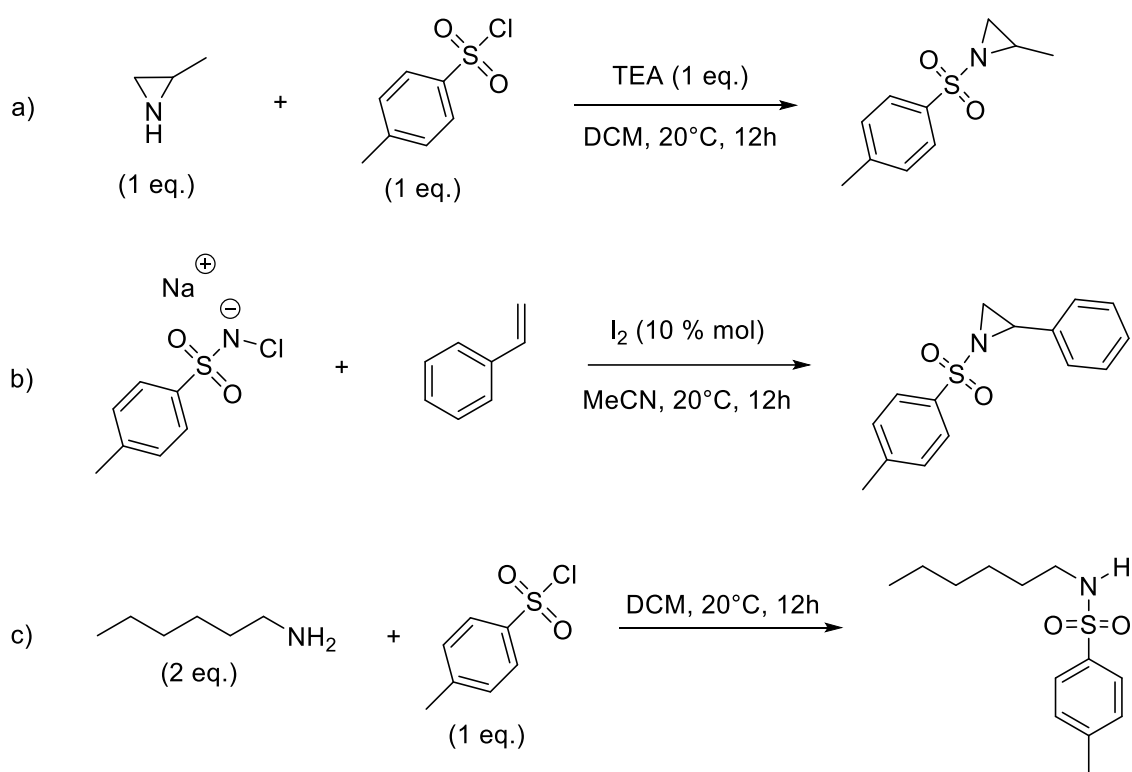
### **2.A.1. Monomer and initiator synthesis.**

Both the racemic 2-methyl-*N*-*p*-toluenesulfonyl aziridine and the *N*-hexyl-*p*-toluenesulfonylamine initiator were synthesized in good yields (51-98%) by simple tosylation of the corresponding 2-methyl-aziridine and *N*-hexylamine, respectively, using *p*-toluenesulfonyl chloride as tosylated agent (Scheme 1.a and 1.c). The synthesis of racemic 2-phenyl-*N*-*p*-toluenesulfonyl aziridine was performed by reacting styrene, *N*-chloro-*N*-sodio-*p*-toluenesulfonamide (Chloramine T) and a catalytic amount of iodide (I<sub>2</sub>) following an already reported procedure (91%, Scheme 1.b).<sup>66</sup> Figure 3 shows <sup>1</sup>H NMR spectra of each compound. All expected peaks were observed, in particular the signals corresponding to the aromatic group between 7.25-7.90 ppm (CH aromatic) and methyl group at 2.40 ppm of the activating tosyl group, confirming the high chemical purity of both reagents.

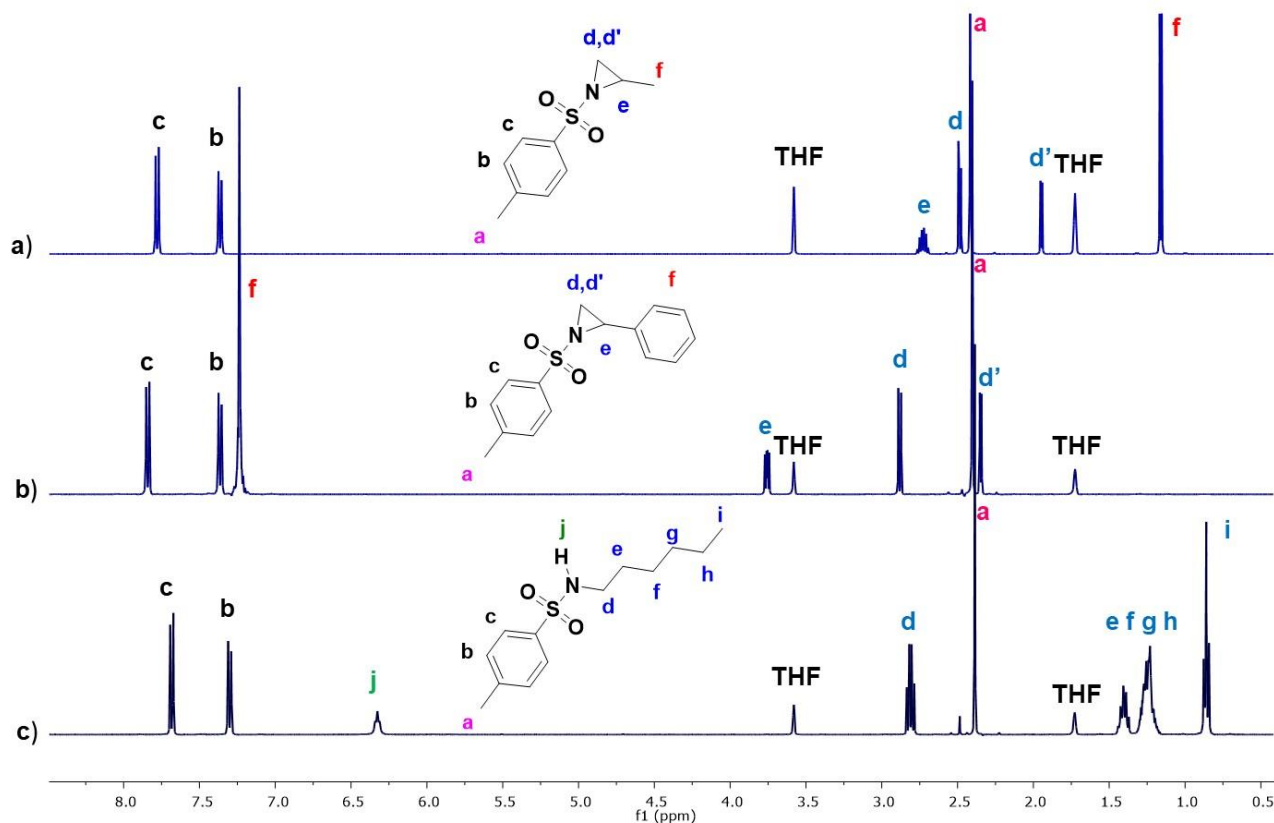
In the proposed mechanism forming aziridine (Scheme 2), chloramine-T reacts with iodine to form iodine-chloramine-T. The latter complex then reacts with the double bond of styrene,

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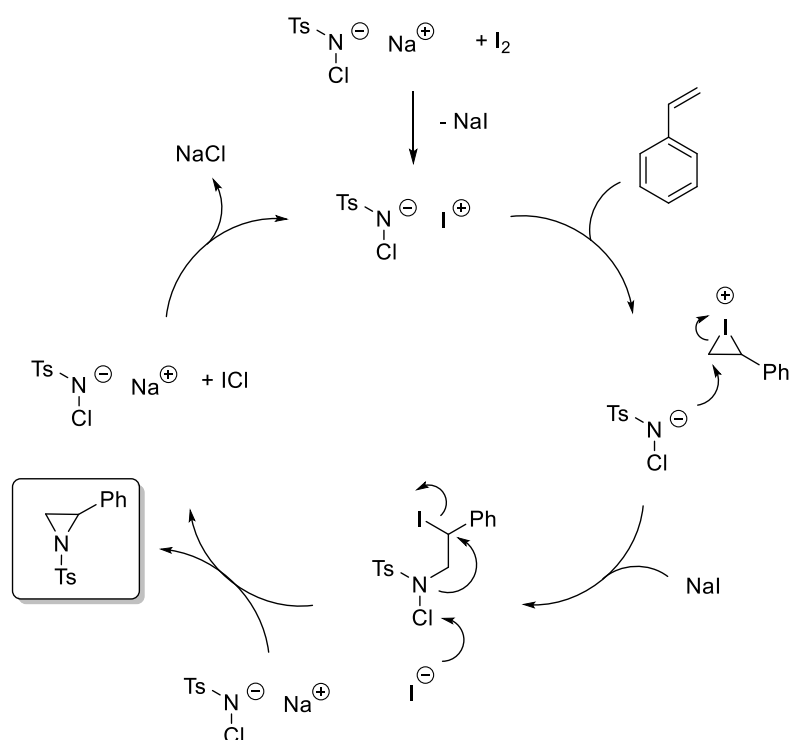
yielding an iodonium cation intermediate species. The iodoaminated compound is formed by attack of the nitrogen of Chloramine-T onto the iodonium cation, which is followed by intramolecular cyclization of the iodoaminated intermediate, leading to the aziridine and regenerating iodine-chloramine-T.



**Scheme 1.** Synthesis of a) 2-methyl-*N*-p-toluenesulfonyl aziridine, b) 2-phenyl-*N*-p-toluenesulfonyl aziridine and c) *N*-hexyl-p-toluenesulfonylamine.



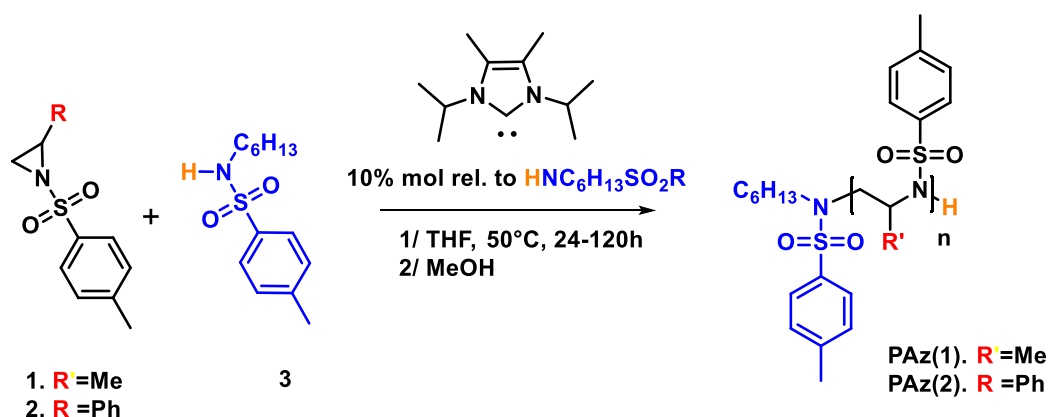
**Figure 3.** Overlay of  $^1\text{H}$  NMR spectra (THF-*d*8) of a) racemic 2-methyl-*N*-p-toluenesulfonyl aziridine b) 2-phenyl-*N*-p-toluenesulfonyl aziridine and c) *N*-hexyl-p-toluenesulfonylamine.



**Scheme 2.** Proposed mechanism for the synthesis of the 2-phenyl-*N*-p-toluenesulfonyl aziridine<sup>66</sup>

### 2.A.2. Polymerization initiated by *N*-activated secondary amine

Both 2-methyl-*N*-p-toluenesulfonyl aziridine (**1**) and 2-phenyl-*N*-p-toluenesulfonyl aziridine (**2**) were investigated as monomer substrates for the 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene organocatalyzed ring-opening polymerization (<sup>Me</sup>5-IPr-OROP). Polymerization of (**1**) was first carried out at 50 °C in THF instead of DMF used in previous works,<sup>53-64</sup> in the presence of *N*-hexyl-*p*-toluenesulfonylamine (**3**) as initiator and 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene (<sup>Me</sup>5-IPr) as a catalyst (Scheme 3).



**Scheme 3.** Organocatalytic ring-opening polymerization induced by <sup>Me</sup>5-IPr

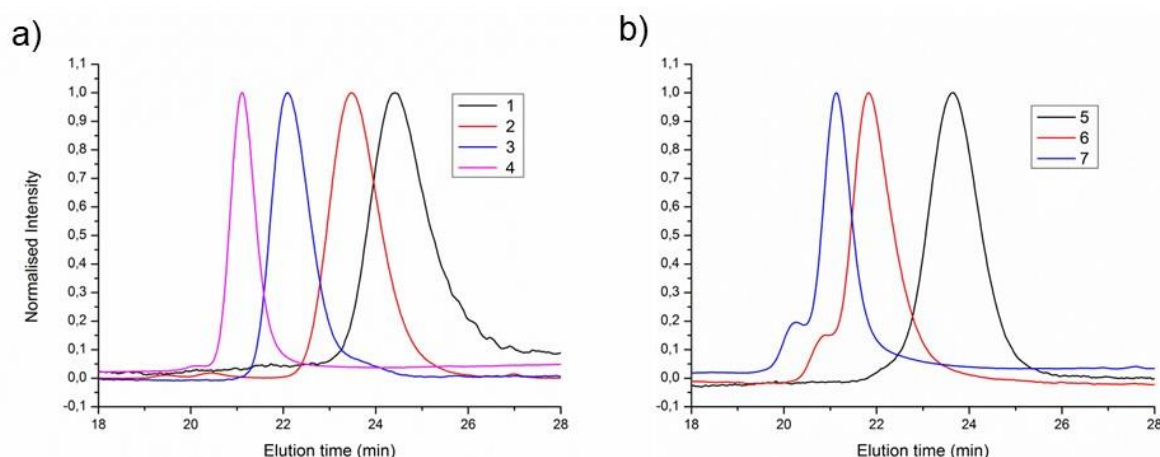
Under these conditions, well-defined PAz(**1**) with excellent control over molar masses (up to 20 000 g.mol<sup>-1</sup>) and low dispersities ( $\mathcal{D} \leq 1.10$ ) were obtained (run 1–4, Table 1, Figure 4.a). While 100 eq. of **1** could be quantitatively converted within 24 h, 5 days were needed to reach completion of the OROP of **2**, due to the effect of steric hindrance of the 2-substituent on the aziridine ring on monomer reactivity. Yet, PAz(**2**) exhibiting molar masses increasing with the initial  $[\mathbf{2}]_0/[\mathbf{3}]_0$  molar ratio (run 5–7, Table 1, Figure 4.b) were also achieved in this case. In contrast to PAz(**1**), however, a small shoulder progressively appeared in the high molar mass region of SEC traces of PAz(**2**) (Figure 4.b), as the initial  $[\mathbf{2}]_0/[\mathbf{3}]_0$  was increased, *i.e.* for higher molar masses targeted.

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**Table 1.** NHC-OROP of 2-alkyl-*N*-*p*-toluenesulfonyl aziridines initiated by *N*-hexyl-toluenesulfonyl amine (THF, 50 °C, 24h-120h).

Run	R	[Az]/[3]/[NHC]	Time(h)	Conv(%) <sup>a</sup>	$\overline{M}_{n\text{calcd}}^c$ (g/mol)	$\overline{M}_{n\text{exp}}^b$ (g/mol)	$\overline{D}^b$
1	Me	10/1/0.1	24	100	2 100	1 880	1.10
2	Me	20/1/0.1	24	100	4 200	2 500	1.06
3	Me	50/1/0.1	24	100	10 600	6 000	1.06
4	Me	100/1/0.1	24	100	21 100	11 700	1.04
5	Ph	20/1/0.1	120	≥ 95	5 300	2 600	1.06
6	Ph	50/1/0.1	120	≥ 95	13 400	6 250	1.12
7	Ph	100/1/0.1	120	≥ 95	27 000	10 800	1.15

<sup>a</sup> Determined by NMR <sup>1</sup>H, <sup>b</sup> determined by SEC in THF (PS calibration), <sup>c</sup>  $\overline{M}_{n\text{calcd}} = ([\text{Az}]/[\mathbf{3}]) \times M_{\text{Az}} \times \text{conv.}$

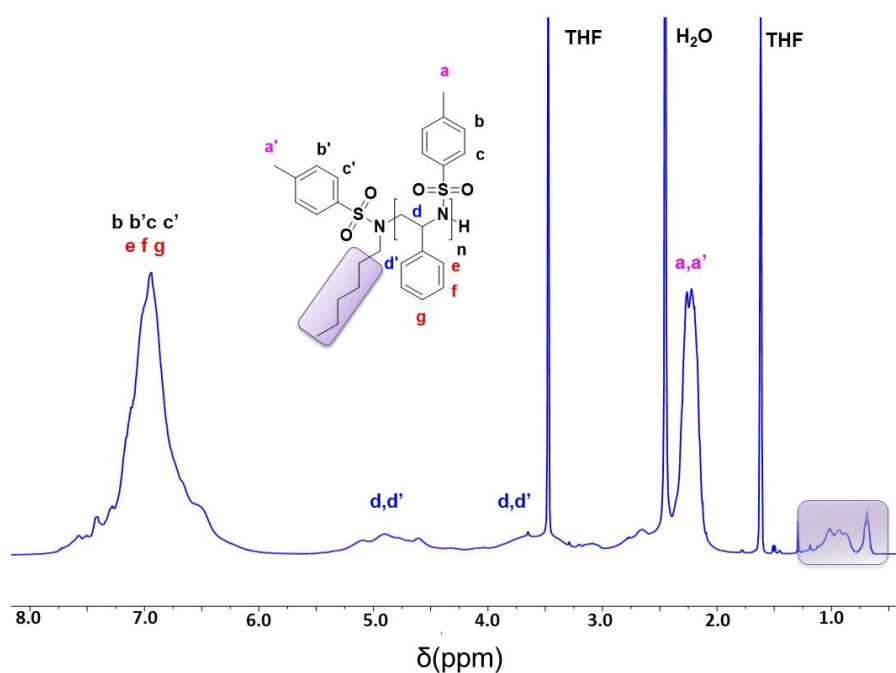


**Figure 4.** SEC Traces of a) poly(2-methyl *N*-*p*-toluene sulfonyl aziridines) (run 1-4, Table 1) and b) SEC Traces of poly(2-phenyl *N*-*p*-toluene sulfonyl aziridines) (run 5-7, Table 1)

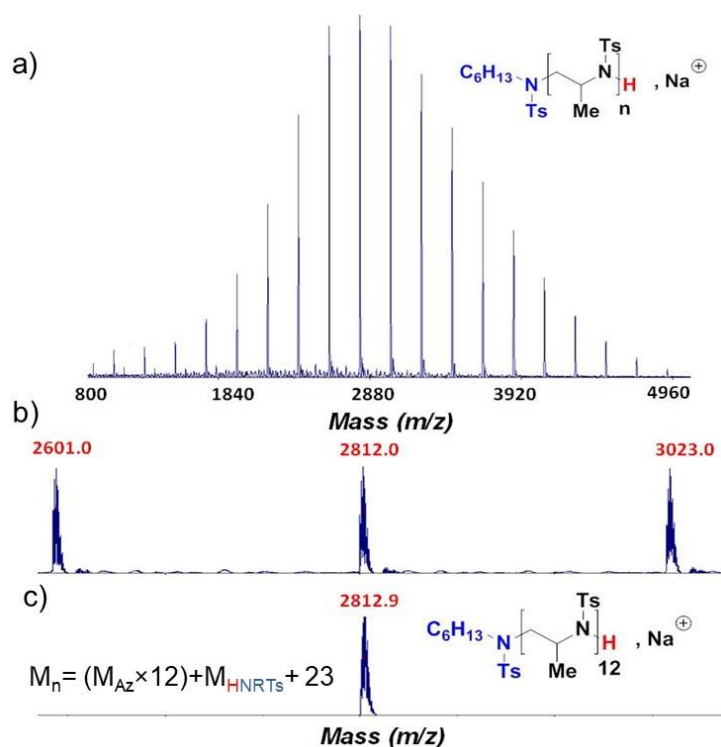
The discrepancy noted between experimental and theoretical molar masses (Table 1) was attributed to the calibration of SEC with PS standards. Molar masses of PAz(**2**), as determined using <sup>1</sup>H NMR spectroscopy (5 200 and 27 000 g.mol<sup>-1</sup>, run 5 and 7, Table 1, respectively) indeed closely matched theoretical values. Figure 5 shows a typical <sup>1</sup>H NMR of a purified PAz(**2**) (run 5), with the presence, in particular, of the characteristic signals of the hexyl group from the amine initiator at 0.7–1.3 ppm. The relative integration of these signals with those corresponding to the main chain protons (d) of PAz(**2**) allowed estimation of the PAz(**2**) molar mass (Table 1). The agreement between experimental and theoretical molar masses attested to the complete initiation of polymer chains by secondary amine **3**. In the case of PAz(**1**), overlapping of both signals due to aliphatic protons and to the pendant methyl group in the

## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

backbone precluded an accurate determination of the molar masses of these compounds (Figure S1). The presence of the *N*-hexyl-*p*-toluenesulfonylamino group from **3** in the  $\alpha$ -position could yet be evidenced by MALDI-ToF MS analysis of low molar mass PAz(**1**) (run 1, Table 1). As shown in Figure 6, a single population, corresponding to cationized PAz(**1**), with a peak-to-peak mass increment of  $211.3 \text{ g.mol}^{-1}$  corresponding to the molar mass of one monomer unit derived from **1**, was indeed unambiguously observed.

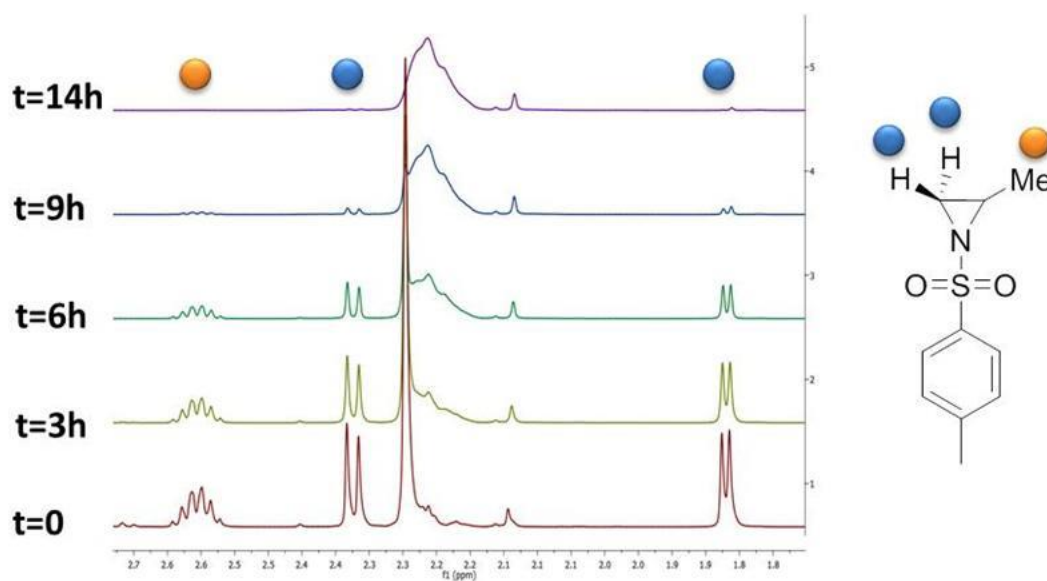


**Figure 5.**  $^1\text{H}$  NMR spectrum of purified PAz(**2**) (entry 5, Table 1)



**Figure 6.** Experimental (a and b) and computed (c) MALDI ToF MS of PAz(**1**) (run 1, Table 1)

In addition, kinetics of the reaction was studied by real-time  $^1H$  NMR spectroscopy, by directly performing the reaction in a NMR Young tube. The conversion was easily monitoring by the disappearance of the aziridine ring proton at 1.83 ppm, 2.24 ppm ( $CH_2$  in blue) and 2.60 ppm ( $CH$  in orange), as shown in Figure 7.

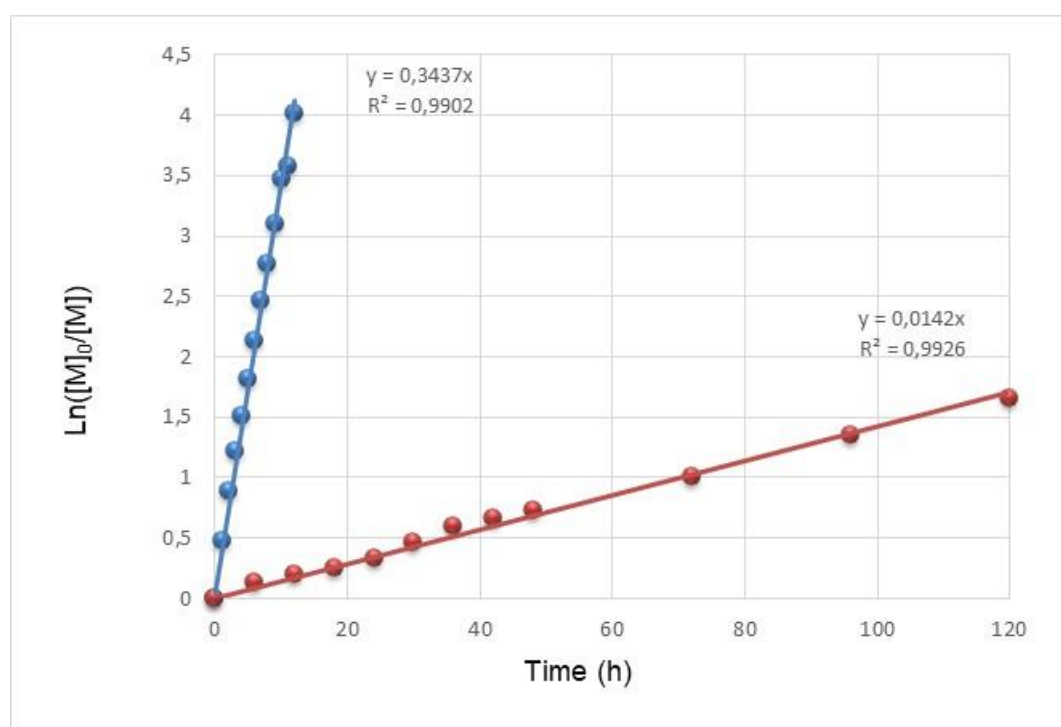


**Figure 7.**  $^1H$  NMR spectra (zoom 1.8-2.7 ppm) at different polymerization times for NHC-OROP of the 2-methyl- *N*-p-toluenesulfonyl aziridine



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The linear evolution of  $\ln([M]_0/[M])$  vs. time for the <sup>Me</sup>5-Ipr-OROP of the two aziridine monomers using real-time <sup>1</sup>H NMR spectroscopy were consistent with a “controlled/living” NHC-OROP process (Figure 8). The apparent propagation rates determined from linear plots of  $\ln([M]_0/[M])$  vs. time were found equal to  $k_p$  (**1**) =  $6.36 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$  and  $k_p$  (**2**) =  $2.62 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$ , respectively for the aziridine bearing a methyl (**1**) or a phenyl side chain (**2**). These values proved ten times higher than those found for the AROP of (**1**) carried out in THF or benzene ( $k_p = 0.56\text{--}0.76 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$ ), but were close to the values for AROP carried out in polar aprotic solvents, such as DMSO or DMF ( $10.53\text{--}12.46 \times 10^{-3} \text{ L.mol}^{-1}.\text{s}^{-1}$ ).<sup>53</sup>



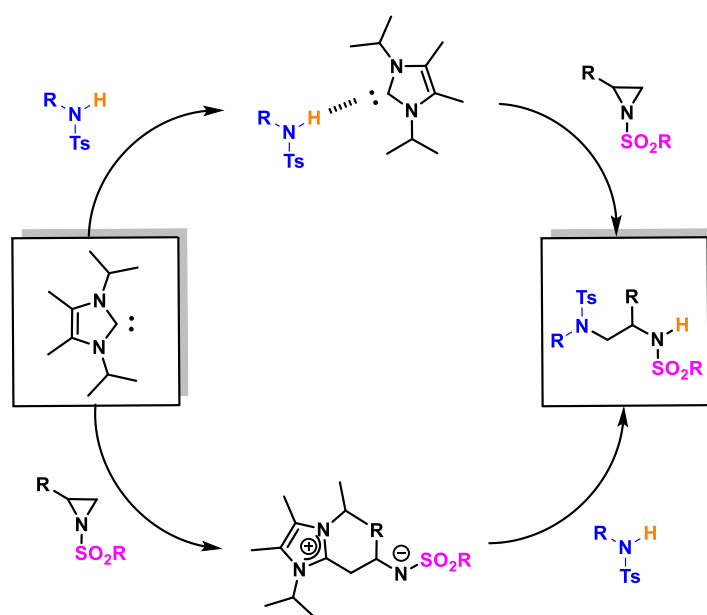
**Figure 8.** Evolution of  $\ln([M]_0/[M])$  in function of time ( $[Az]=0.285\text{M}$ ,  $[3]=0.015\text{M}$ ,  $[NHC]=0.0015\text{M}$ ) for 2-methyl- *N*-p-toluenesulfonyl aziridine (in blue) and 2-phenyl-*N*-p-toluenesulfonyl aziridine (in red).

Based on the background literature regarding other examples of NHC-mediated OROP,<sup>10-13</sup> either a nucleophilic or a basic mechanism, *i.e.* through the aziridine or the amine activation by the <sup>Me</sup>5-Ipr NHC, respectively (vide infra) could be operative (Scheme 4). The former mechanism would involve ring-opening of the aziridine by direct attack by <sup>Me</sup>5-Ipr, forming an imidazolium amide zwitterionic intermediate that would be further displaced by the secondary amine (**3**). However, given the high basicity of <sup>Me</sup>5-Ipr ( $pK_a = 24$  in DMSO<sup>67</sup>), in particular compared to that of the sulfonylamine group. Model reactions as well as DFT calculations will

## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

have to be performed to determine which mechanism is predominant under the polymerization conditions.

In order to verify that a majority of <sup>Me</sup>5-Ipr OROP-derived PAz chains could be reactivated, chain extension experiments were performed as follows (see also Figure S2). Polymerization in THF at 50°C of 20 eq. of **1**, using 10 mol% of <sup>Me</sup>5-Ipr, afforded a PAz(**1**) precursor ( $\overline{M}_n = 2500 \text{ g.mol}^{-1}$ ;  $\mathcal{D} = 1.06$ ). Addition of 30 eq. of **1** increased the molar mass to  $\overline{M}_n = 6000 \text{ g.mol}^{-1}$  while maintaining a low dispersity ( $\mathcal{D} = 1.06$ ) after 24 h of the reaction at 50°C (Figure S2), confirming quantitative reinitiation of the OROP from the PAz(**1**) precursor.

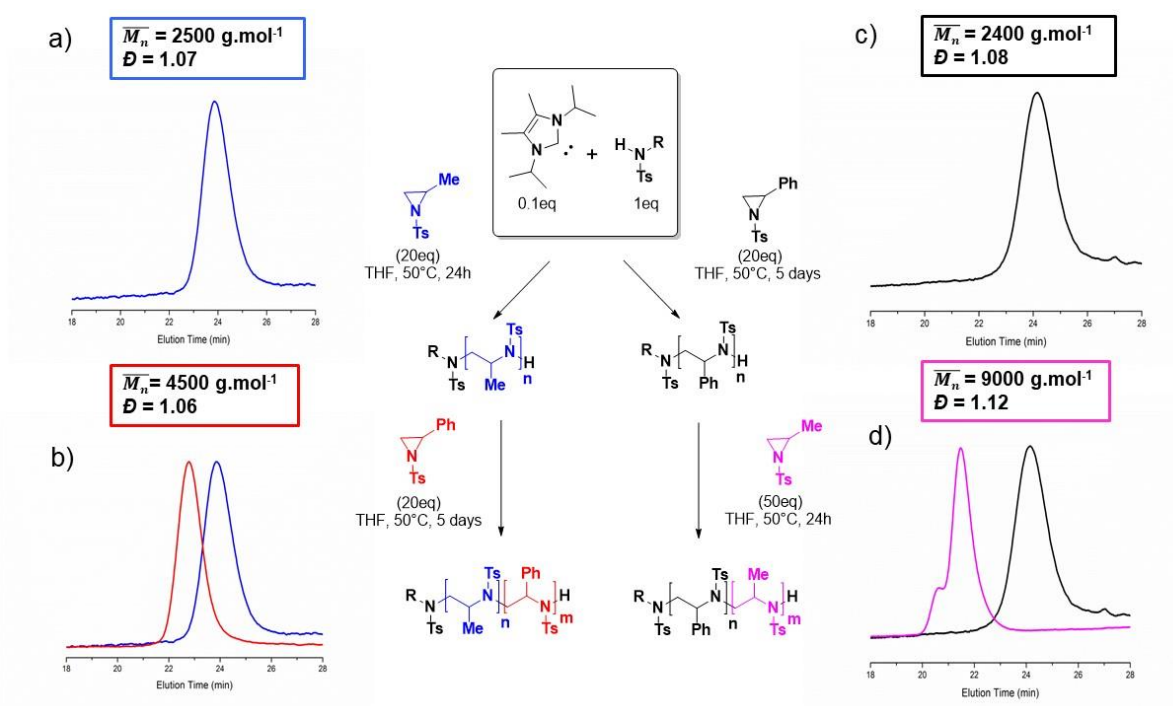


**Scheme 4.** Proposed mechanism of NHC-organocatalyzed polymerization of *N*-tosyl aziridines initiated by secondary *N*-activated amine.

These results prompted us to further investigate the synthesis of PAz-based block copolymers, *via* sequential NHC-OROP of **1** and (**2**) (Figure 9). Both monomers were added either in this order (**1** then **2**) or in the other (**2** then **1**). Synthesis of a well-defined PAz(**1**)-*b*-PAz(**2**) block copolymer was first achieved, *i.e.* using the more reactive aziridine (**1**) first (20 eq.), giving a PAz(**1**) precursor ( $\overline{M}_n = 2500 \text{ g.mol}^{-1}$ ;  $\mathcal{D} = 1.07$ ; Figure 9.a and b) after 1 day, followed by addition of 20 eq. of the less reactive aziridine (**2**). Block copolymerization proved effective, as illustrated by the SEC trace of final compound collected after 5 days of reaction at 50 °C in THF. One can indeed note a clear shift to the higher molar masses ( $\overline{M}_n = 4500 \text{ g.mol}^{-1}$ ;  $\mathcal{D} = 1.06$ ), compared to the SEC trace of the PAz(**1**) macroinitiator (Figure 9.a and b), thus attesting to an effective crossover reaction. Interestingly, a PAz(**1**)-*b*-PAz(**2**) block copolymer (Figure

## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

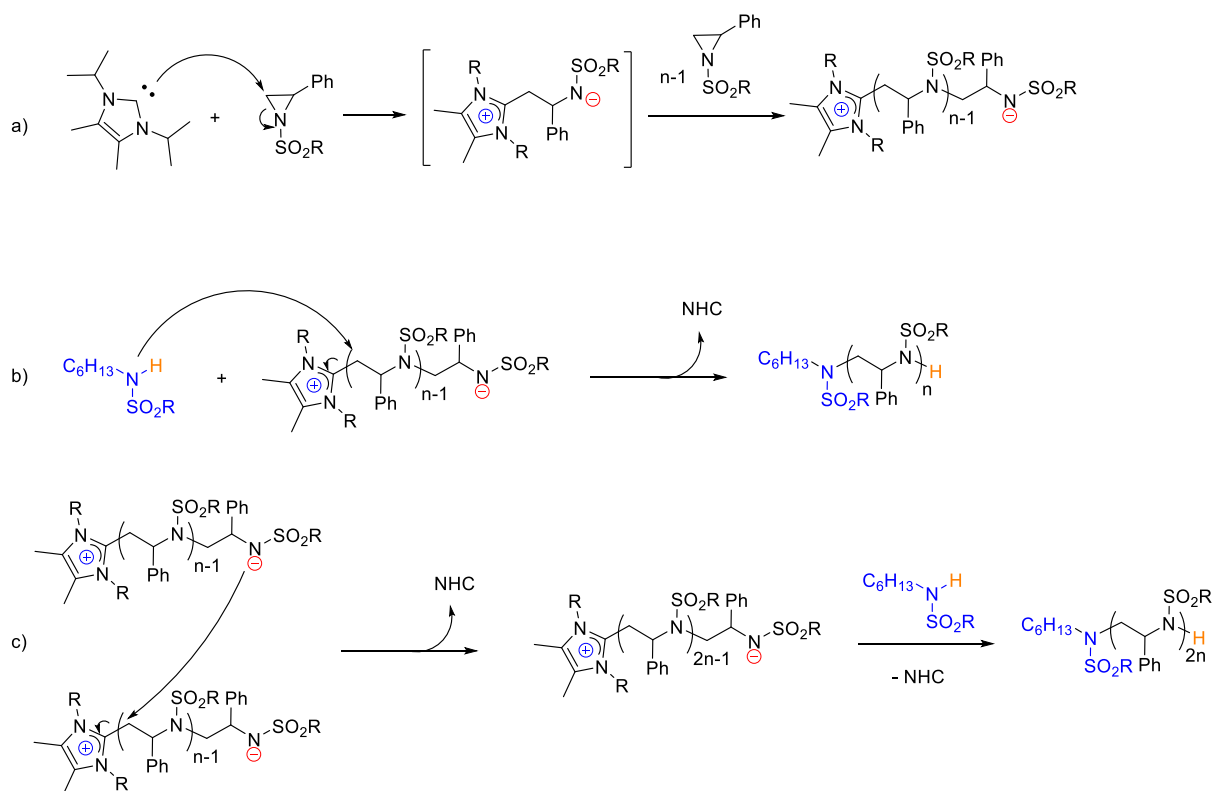
8.c and d) could also be obtained by reversing the order of addition of the two monomers (**2** then **1**; Figure 9). A shoulder in the high molar mass region was observed though, presumably to some coupling reactions at high monomer conversions when the amount of initiator is low. In the expected mechanism (Scheme 4), two possible mechanisms have been proposed for enchainment: a chain-end activating mechanism where the carbene activates the initiator/chain-end by H-bonding, and a nucleophilic mechanism involving zwitterionic intermediates. Both mechanisms depending on the nature of the monomer substrate, NHC, solvent as well as the ratio monomer to initiator.



**Figure 9.** Block Copolymer synthesis by sequential NHC-OROP

In the case of NHC-OROP of 2-phenyl-*N*-*p*-toluenesulfonyl aziridine, at high ratio monomer to initiator ( $[Az]_0/[I]_0=50$ ), a second population, which corresponds to twice the mass predicted by the initial feed ratio, appears in the high molar mass region. These results suggested that the propagation occurred *via* a zwitterionic mechanism by a direct nucleophilic attack of the NHC (Scheme 5.a), the second population resulting probably from the coupling of two zwitterionic growing chains at high monomer conversion (Scheme 5.c).

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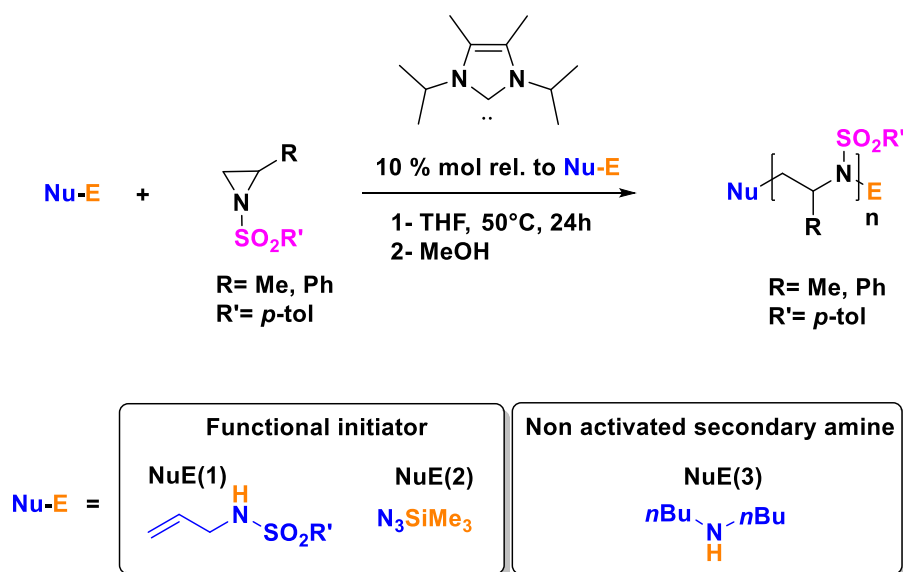


**Scheme 5.** a), b) Zwitterionic mechanism for the polymerization of 2-phenyl-*N*-*p*-toluenesulfonyl aziridine and c) reaction of coupling between two zwitterions

In summary, the “controlled/ living” organocatalyzed ring-opening polymerization (OROP) of *N*-activated aziridines by an *N*-heterocyclic carbene (NHC), namely, 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene has been established. Reactions can be conducted in THF at 50 °C in the presence of an *N*-activated secondary amine as an initiator to mimic the growing chains. This provides a straightforward access to structurally well-defined and metal-free polyaziridines (PAz) that can serve as precursors of linear 2-*n*-alkyl-substituted poly(ethylene imine)s after removal of the *N*-tosyl groups.<sup>48,51</sup> This method can also be applied to achieve well-defined all PAz-based block copolymers by sequential OROP employing a carbene catalysis. Overall, this work further expands the monomer substrate diversity in NHC-mediated polymerization reactions. Extensive mechanistic investigation as well as DFT calculations should be performed in order to determine which mechanism, *i.e* AMM or ACEM, is involved during NHC-OROP of *N*-tosyl aziridines.

### 2.A.3. Polymerization initiated by functional and non-activated initiators

In this part, we expand the scope of this NHC-OROP of *N*-tosyl aziridines, by resorting to novel types of amine initiators. These include an allyl functionalized *N*-activated amine and a representative non-activated secondary amine, namely, di-*n*-butylamine that is commercially available. We show that trimethylsilyl azide ( $\text{N}_3\text{SiMe}_3$ ), another commercial compound, can also readily initiate the NHC-OROP of *N*-tosyl aziridines, affording well-defined  $\alpha$ -azido functionalized PAz chains. OROP of 2-methyl-*N*-*p*-toluenesulfonyl aziridine ( $\text{R} = \text{Me}$ ) was performed at 50 °C in THF, using three representative initiators, NuE(**1-3**), where Nu and E represent nucleophilic and electrophilic moieties, respectively (Scheme 6), in presence of a catalytic amount (10 mol.% relative to the NuE initiator) of 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene ( $^{\text{Me}_5}\text{IPr}$ ). However, despite its low reactivity and “poorer” control towards NHC-OROP under the condition described above, 2-phenyl-*N*-*p*-toluenesulfonyl aziridine ( $\text{R} = \text{Ph}$ ) was also investigated as monomer substrate.



**Scheme 6.** NHC-OROP of 2-alkyl *N*-*p*-toluenesulfonyl aziridines initiated by a functional initiator, NuE(**1**) or NuE(**2**), and by an non-activated secondary amine NuE(**3**).

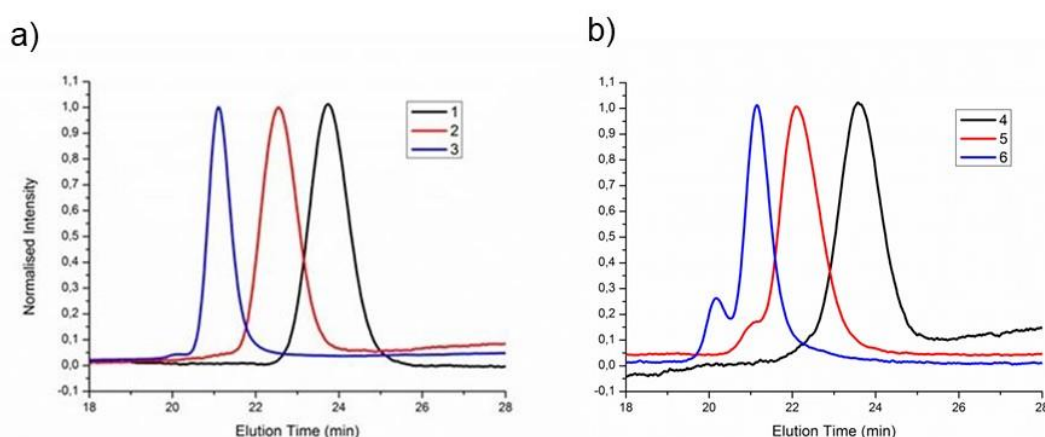
### 2.A.3.1 Polymerization initiated by *N*-allyl-sulfonyl amine

Under such conditions, the *N*-allyl-sulfonyl amine initiator NuE(**1**) was found to efficiently control the NHC-OROP of 2-methyl-*N*-*p*-toluenesulfonyl aziridine, providing a direct access to metal-free,  $\alpha$ -allyl functionalized PAz (Runs 1-3, Table 2). Figure 1 shows that as-derived PAz exhibit symmetrical and monomodal size exclusion chromatography (SEC) traces, with a narrow molar mass distribution (dispersity,  $\bar{D}$ , lower than 1.05). As expected for a “controlled/living » polymerization process, SEC molar masses increased with the monomer to the initiator ratio (Figure 10.a).

**Table 2.** NHC-OROP of 2-alkyl-*N*-*p*-toluenesulfonyl aziridine initiated by *N*-allyl-sulfonyl amine (THF, 50 °C, 24h-120h).

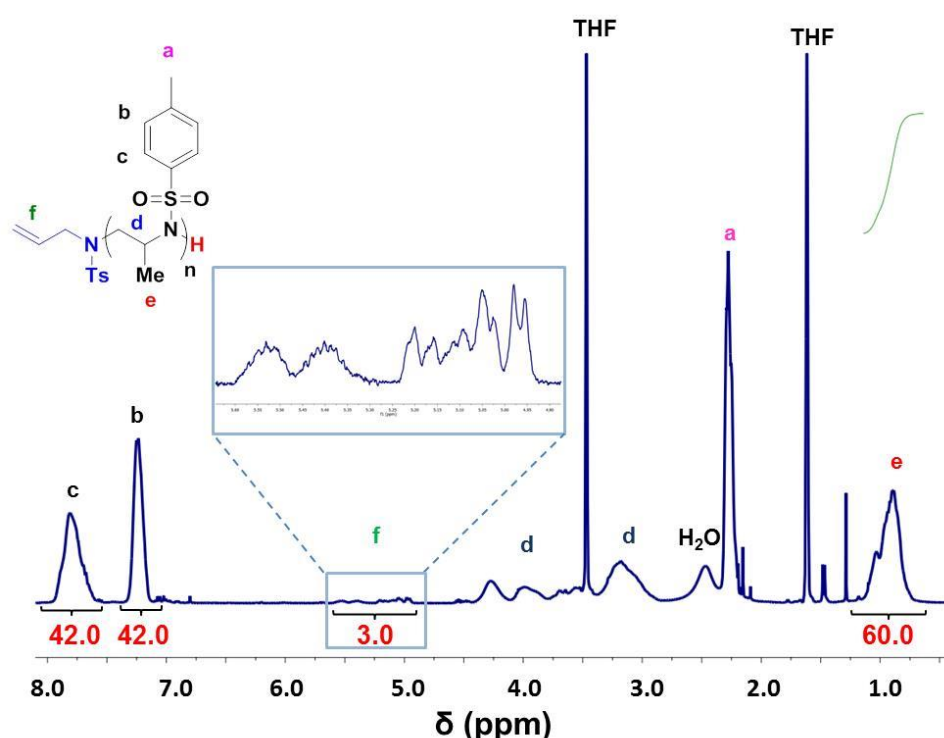
Run	Initiator	R	[Az]/[NuE]/[NHC]	Conv <sup>(a)</sup> (%)	$\bar{M}_n$ THEO <sup>(b)</sup>	$\bar{M}_n$ SEC <sup>(c)</sup>	$\bar{D}$ <sup>(c)</sup>
1 <sup>(d)</sup>	(allyl)NHTs	Me	20/1/0.1	100	4 200	2 800	1.04
2	(allyl)NHTs	Me	50/1/0.1	100	10 600	5 700	1.05
3 <sup>(d)</sup>	(allyl)NHTs	Me	100/1/0.1	100	21 100	11 700	1.04
4	(allyl)NHTs	Ph	20/1/0.1	≥ 95 <sup>e</sup>	5 400	2 850	1.05
5	(allyl)NHTs	Ph	50/1/0.1	≥ 95 <sup>e</sup>	13 400	6 000	1.09
6	(allyl)NHTs	Ph	100/1/0.1	≥ 95 <sup>e</sup>	26 500	10 800	1.15

<sup>a</sup> Conversion was calculated by <sup>1</sup>H NMR; <sup>b</sup>  $\bar{M}_n$  THEO = ([Az]/[NuE]) ×  $M_{Az}$  × conv. (in g.mol<sup>-1</sup>); <sup>c</sup> Number-average molar mass (in g.mol<sup>-1</sup>) and dispersity determined by size exclusion chromatography in THF (PS calibration); <sup>d</sup> Molar mass determined by <sup>1</sup>H NMR  $\bar{M}_n$  (Run 1) = 4 200 g.mol<sup>-1</sup> and  $\bar{M}_n$  (Run3) = 21 000 g.mol<sup>-1</sup>; <sup>e</sup> Conversion was calculated by <sup>1</sup>H NMR after 120h at 50 °C.



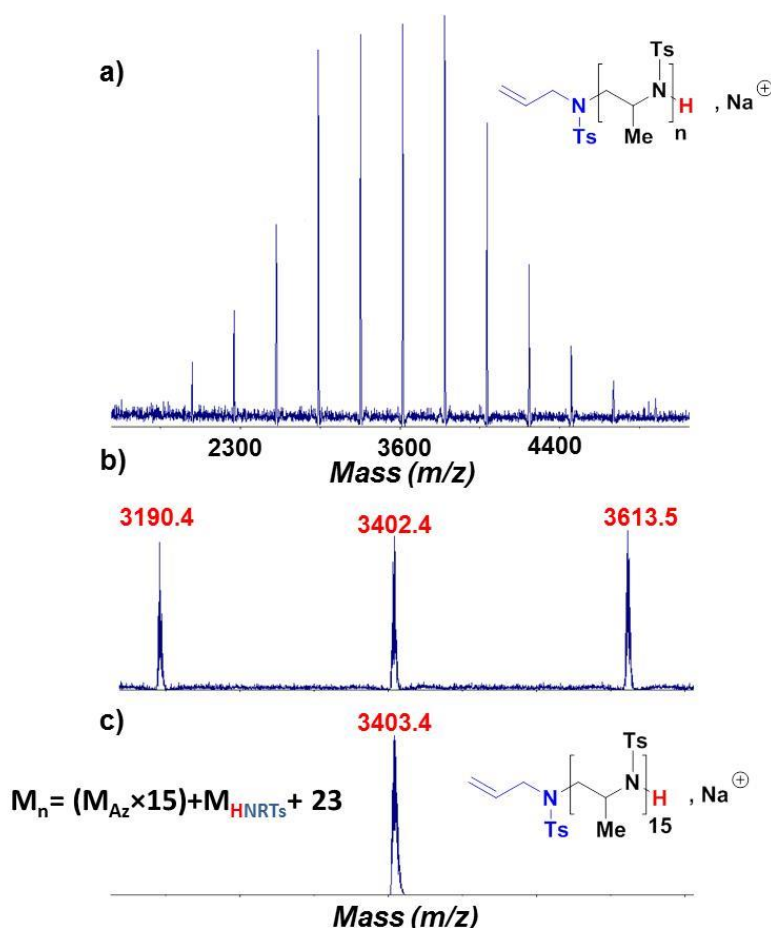
**Figure 10.** SEC Traces (RI detection) of a) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) and b) poly(2-phenyl *N*-*p*-toluenesulfonyl aziridine) initiated by *N*-allyl *N*-*p*-toluenesulfonylamine (Runs 1-3, Table 2).

As previously observed for the NHC-OROP of 2-phenyl-*N*-*p*-toluenesulfonyl aziridine, a small shoulder progressively appeared in the high molar mass region of SEC traces of poly(2-phenyl-*N*-*p*-toluenesulfonyl aziridine) (Figure 10.b). The presence of the allyl group was evidenced by  $^1\text{H}$  NMR spectroscopy with the appearance of diagnostic signals between 4.90-5.60 ppm, allowing the molar mass of those polymers to be determined (Figure 11). While these molar masses closely matched theoretical values, those determined by SEC using PS standards were roughly twice lower:  $\overline{Mn}_{\text{SEC}} = 2800 \text{ g.mol}^{-1}$  vs.  $\overline{Mn}_{\text{NMR}} = 4200 \text{ g.mol}^{-1}$  and  $\overline{Mn}_{\text{SEC}} = 11700 \text{ g.mol}^{-1}$  vs.  $\overline{Mn}_{\text{NMR}} = 21000 \text{ g.mol}^{-1}$  for Runs 1 and 3, Table 2, respectively.



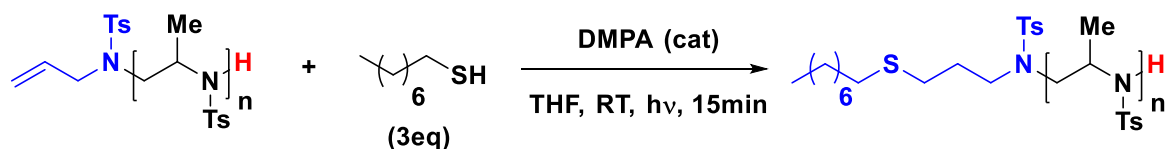
**Figure 11.**  $^1\text{H}$  NMR spectrum of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by *N*-allyl *N*-*p*-toluenesulfonylamine (Run 1, Table 2).

Analysis by MALDI ToF mass spectrometry of a purified allyl-functionalized PAz revealed an experimental isotopic distribution that perfectly agreed with the expected structure, as illustrated in Figure 12.



**Figure 12.** a) and b) experimental and c) computed MALDI ToF MS of a poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by *N*-allyl *N*-*p*-toluenesulfonylamine (Table 2, Run 1).

Further derivatization of a low molar mass allyl-containing PAz (Run 1, Table 2) was then evidenced through a thiol-ene reaction (Scheme 7). This “click” reaction was achieved using octanethiol under UV irradiation, in presence of a catalytic amount of 2,2-dimethoxy-2-phenylacetophenone (DMPA). Quantitative modification of the allyl chain end was confirmed by the complete disappearance of corresponding signals at 4.90-5.60 ppm in the  $^1\text{H}$  NMR spectrum, after 15 minutes of irradiation (see Figure S3 and S4 for SEC traces before and after chemical modification by thiol-ene chemistry).



**Scheme 7.** Thiol-ene reaction of  $\alpha$ -allyl-PAz (Run 1, Table 1) with octanethiol



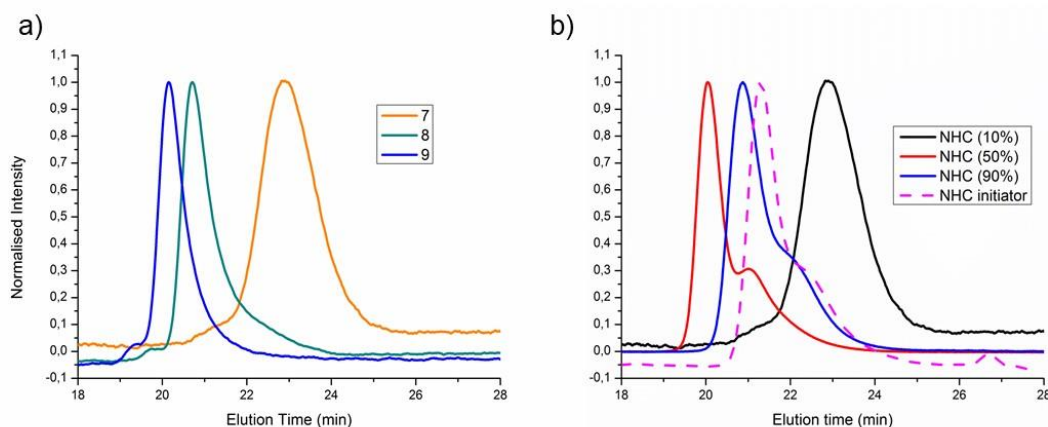
### 2.A.3.2. Polymerization initiated by di-*n*-butylamine

We next resorted to a commercially available non-activated secondary amine, namely, di-*n*-butylamine as initiator ( $n\text{Bu}_2\text{NH} = \text{NuE}(\mathbf{3})$  in Scheme 6). Remarkably, this simple amine led to a well-defined PAz, demonstrating that activation of the amino-containing initiator is eventually not required for the controlled NHC-OROP to proceed. However,  $n\text{Bu}_2\text{NH}$ -initiated PAz (Runs 7-9, Table 3, Figure 13.a) exhibited a slightly higher molar mass than that predicted by the initial  $[\text{Az}]_0/[\text{NuE}(\mathbf{3})]_0$  ratio, though still with a low dispersity ( $\bar{D} < 1.20$ ). This might be explained by an incomplete initiation of the reaction by  $n\text{Bu}_2\text{NH}$ . However, increasing the NHC amount to 0.5 and 0.9 equivalent as compared to the initiator has not afforded an increase of the initiation efficiency and the resulting PAz exhibited higher molar mass and bimodal distribution probably induced by NHC side initiation (Figure 13.b). In this case, the polymerization proceeds via the so-called zwitterionic ring-opening mechanism where one chain-end is the propagating amidate anion and at the other chain-end an imidazolium moiety generated by the direct nucleophilic attack of the NHC.

**Table 3.** NHC-OROP of 2-alkyl-*N*-*p*-toluenesulfonyl aziridine initiated by *N*-allyl-sulfonyl amine (THF, 50 °C, 24h-120h).

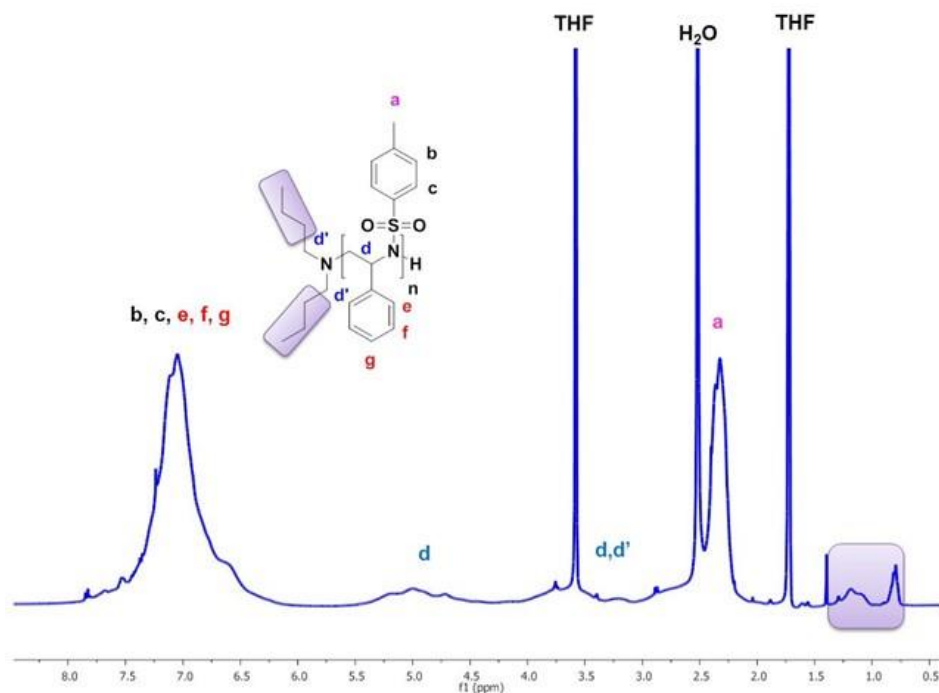
Run	Initiator	R	[Az]/[NuE]/[NHC]	Conv <sup>(a)</sup> (%)	$\overline{M}_n$ THEO <sup>(b)</sup>	$\overline{M}_n$ SEC <sup>(c)</sup>	$\bar{D}$ <sup>(c)</sup>
7	( <i>n</i> Bu) <sub>2</sub> NH	Me	20/1/0.1	100	4 200	4 500	1.13
8	( <i>n</i> Bu) <sub>2</sub> NH	Me	50/1/0.1	100	10 600	10 600	1.16
9	( <i>n</i> Bu) <sub>2</sub> NH	Me	100/1/0.1	100	21 100	18 000	1.11
10	( <i>n</i> Bu) <sub>2</sub> NH	Ph <sup>e</sup>	10/1/0.1	≥ 95 <sup>d</sup>	2 700	2 100	1.08
11	( <i>n</i> Bu) <sub>2</sub> NH	Ph <sup>e</sup>	50/1/0.1	88 <sup>d</sup>	13 400	5 000	1.12
12	( <i>n</i> Bu) <sub>2</sub> NH	Ph <sup>e</sup>	100/1/0.1	93 <sup>d</sup>	26 500	7 200 (14 500)	1.17
13	( <i>n</i> Bu) <sub>2</sub> NH	Ph <sup>e</sup>	200/1/0.1	79 <sup>d</sup>	43 000	11 000 (22 500)	1.20

<sup>a</sup> Conversion was calculated by <sup>1</sup>H NMR; <sup>b</sup>  $\overline{M}_n^{\text{THEO}} = ([\text{Az}]/[\text{NuE}]) \times M_{\text{Az}} \times \text{conv.}$  (in g.mol<sup>-1</sup>); <sup>c</sup> Number-average molecular weight (in g.mol<sup>-1</sup>) and dispersity determined by size exclusion chromatography in THF (PS calibration); <sup>d</sup> Conversion was calculated by <sup>1</sup>H NMR after 120h at 50 °C. <sup>e</sup> See Fig. S5 (SEC traces).



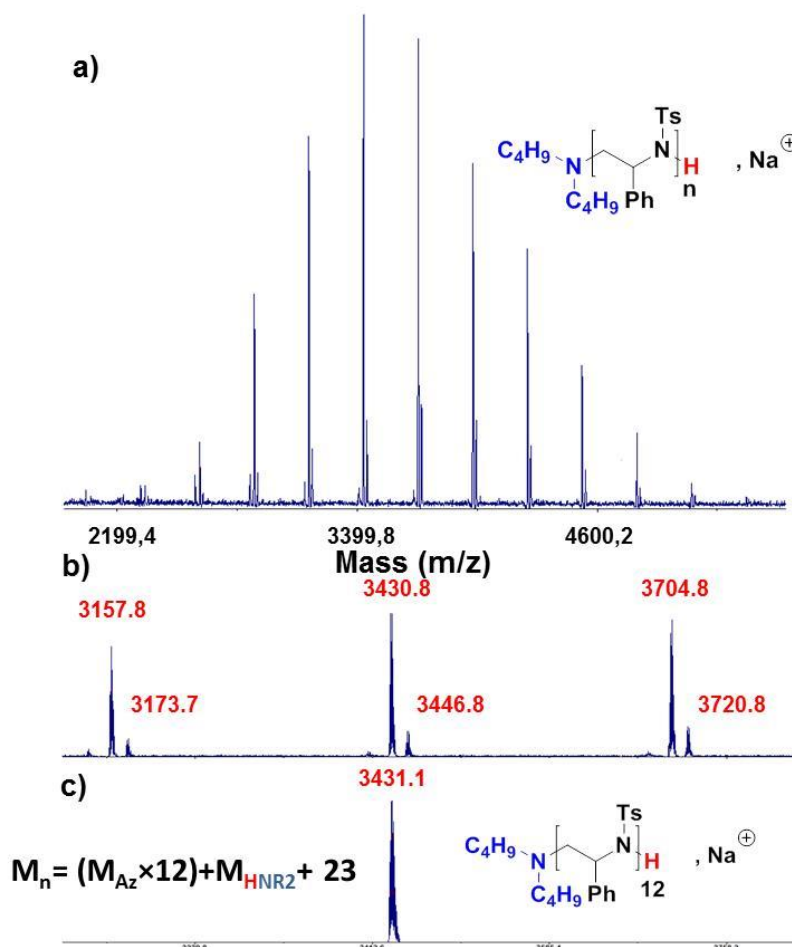
**Figure 13.** SEC traces of (a) poly(2-methyl-*N*-tosyl aziridine) initiated by di-*n*-butylamine and b) poly(2-methyl-*N*-tosyl aziridine) initiated by di-*n*-butylamine and various ratio  $[R_2NH]/[NHC]$ .

MALDI ToF MS analysis (Figure S6) and overlapping between signals due to the di-*n*-butyl protons of the initiator and those of the pendant methyl group of monomer units, as observed by NMR spectroscopy, did not allow for a quantitative analysis of *n*Bu<sub>2</sub>NH-derived PAz chain ends (Figure S7). Nonetheless, the presence of the secondary amino group in  $\alpha$ -position could be evidenced on another PAz obtained in this case by the NHC-OROP of 2-phenyl *N*-tosyl aziridine, *i.e.* consisting of a phenyl substituent instead of the methyl group at the 2-position of the aziridine ring. Representative reactions are described in Runs 10-13, Table 3.



**Figure 14.** <sup>1</sup>H NMR spectrum of poly(2-phenyl *N*-*p*-toluenesulfonyl aziridine) initiated by di-*n*-butylamine (Run 10, Table 3).

In the latter case, distinctive signals of the di-*n*-butyl group from the initiator could be clearly observed, between 0.75-1.40 ppm in the  $^1\text{H}$  NMR spectrum (Figure 14). In addition, MALDI ToF MS analysis of a low molar mass poly(2-phenyl-*N*-tosyl aziridine) (Run 10, Table 1) revealed a single population with a peak-to-peak mass increment of  $273.0\text{ g.mol}^{-1}$  corresponding to the molar mass of the monomer unit. This result further attested to the presence of the secondary amine in the  $\alpha$ -position of PAz chains (Figure 15).



**Figure 15.** a), b) Experimental and c) computed MALDI ToF MS of poly(2-phenyl *N*-*p*-toluene sulfonyl aziridine)s (Table 1, Run 10).\* The second population ( $\Delta m=16$ ) corresponds to potassium ionization.

### 2.A.3.3. Polymerization initiated by trimethylsilyl azide

Finally, trimethylsilyl azide,  $\text{N}_3\text{SiMe}_3 = \text{NuE(2)}$  was investigated as initiator with the aim at directly preparing PAz chains with an azido function in  $\alpha$ -position. Control of this  $\text{N}_3\text{SiMe}_3$ -initiated, NHC-OROP was established, in particular by SEC, showing a shift to the higher molar mass region, as the monomer to initiator ratio increased (Figure 16.a; see also

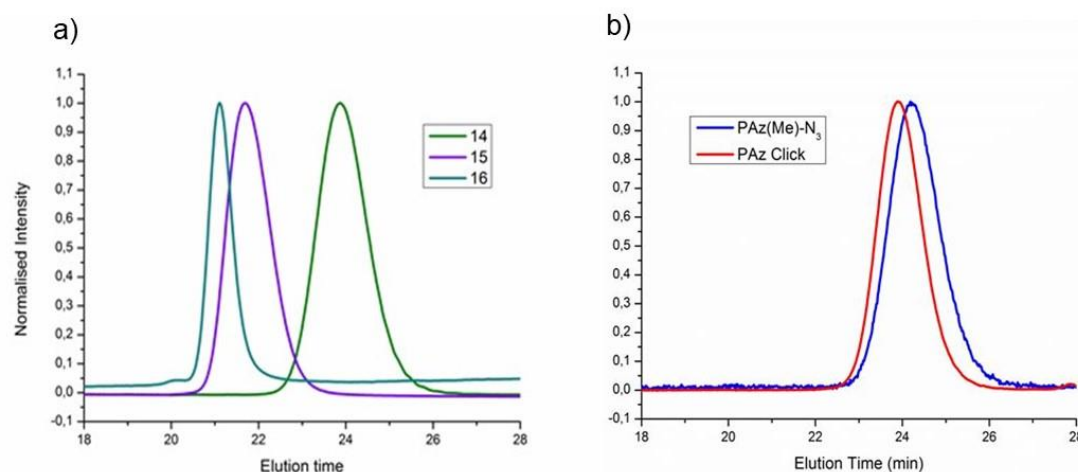
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

Runs 14-16 in Table 4). Characterization by MALDI ToF MS (Figure 17) of the as-synthesized  $\alpha$ -azido PAz gave, in this case, two distinct populations: one corresponded to the targeted  $\alpha$ -azido PAz structure, while the other resulted from the loss of dinitrogen of azido moiety during the ionization process, as already observed for other azido-functionalized polymers<sup>36-37</sup>. Of particular interest, formation of well-defined PAz chains from  $N_3SiMe_3$  revealed that chain growth might occur *via* a trimethylsilyl amide, *i.e.* a proton is here substituted by a  $SiMe_3$  in comparison to the two former initiators NuE(1) and NuE(2) (see proposed mechanism in Scheme 9). However, trimethylsilyl amide end groups could not be detected in the final PAz, very likely because they were readily hydrolyzed during workup.

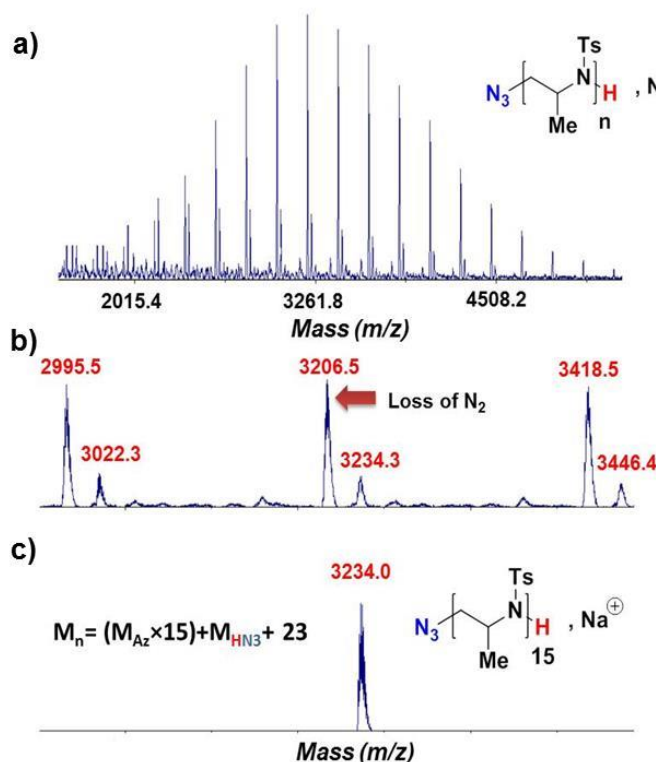
**Table 4.** NHC-OROP of 2-methyl-*N*-*p*-toluenesulfonyl aziridine initiated by trimethylsilyl azide (THF, 50 °C, 24h).

Run	Initiator	R	[Az]/[NuE]/[NHC]	Conv <sup>(a)</sup> (%)	$\overline{Mn}_{THEO}^{(b)}$	$\overline{Mn}_{SEC}^{(c)}$	$\mathcal{D}^{(c)}$
14	$N_3SiMe_3$	Me	20/1/0.1	100	4 200	2 600	1.05
15	$N_3SiMe_3$	Me	50/1/0.1	100	10 600	6 900	1.07
16	$N_3SiMe_3$	Me	100/1/0.1	100	21 100	11 800	1.04

<sup>a</sup> Conversion was calculated by  $^1H$  NMR; <sup>b</sup>  $\overline{Mn}_{THEO} = ([Az]/[NuE]) \times M_{Az} \times \text{conv.}$  (in  $g \cdot mol^{-1}$ ); <sup>c</sup> Number-average molar mass (in  $g \cdot mol^{-1}$ ) and dispersity determined by size exclusion chromatography in THF (PS calibration).

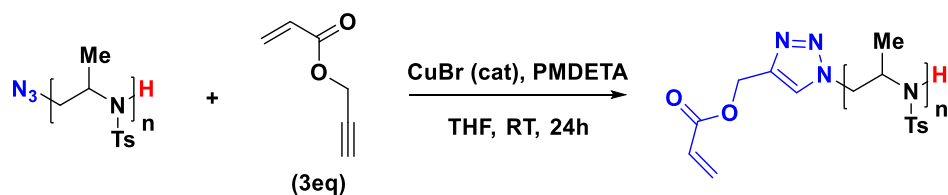


**Figure 16.** SEC traces (RI detection) of a) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by trimethylsilyl azide (Runs 14-16, Table 4) and b) before (in blue) and after (in red) CuAAC click reaction.

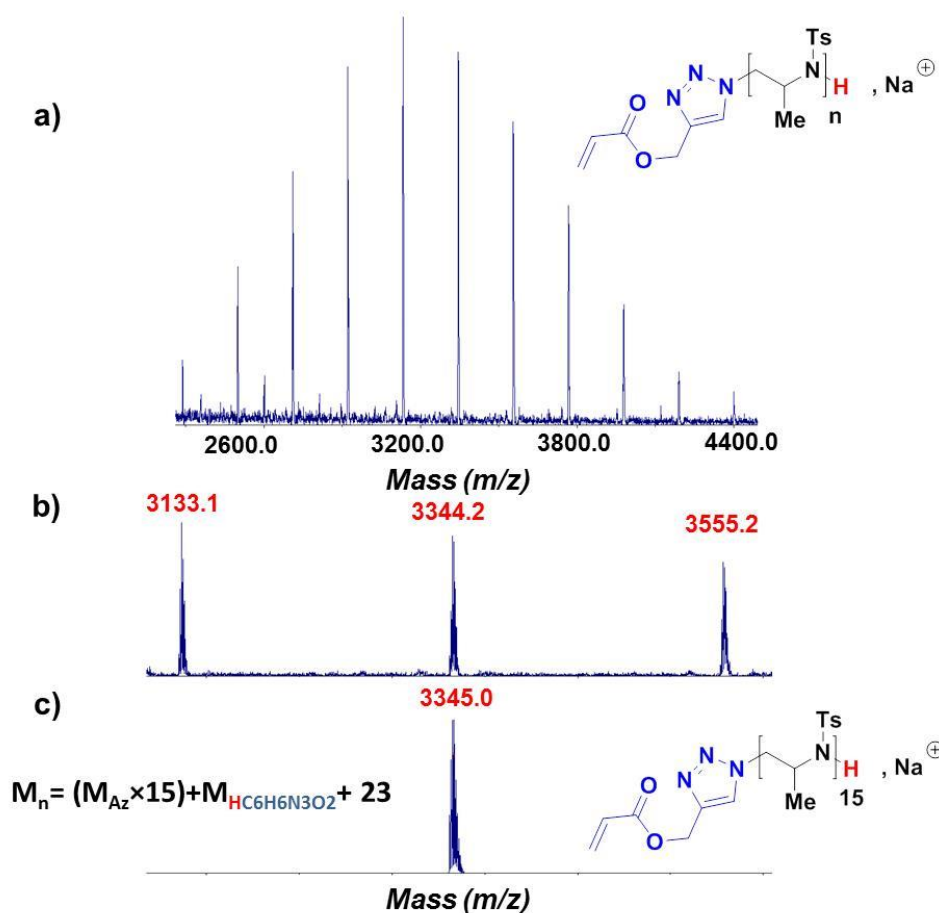


**Figure 17.** a), b) Experimental and c) computed MALDI ToF MS of an  $\alpha$ -azido poly(2-methyl *N*-*p*-toluene sulfonyl aziridine) (Table 4, Run 14).

To illustrate the reactivity of the azido chain end, the  $\alpha$ - $N_3$  PAz was further reacted with an alkyne-containing acrylate under click-chemistry conditions, *i.e.* using copper bromide (CuBr) and *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA) as catalyst, yielding the corresponding PAz-based acrylate-containing macromonomer (Scheme 8). Monitoring of this click reaction by IR spectroscopy showed that the peak at  $2100\text{ cm}^{-1}$  due to the azido functionality totally vanished after 24h of reaction at RT, while the peak of the carbonyl group from the acrylate moiety appeared at  $1710\text{ cm}^{-1}$  (Figure S8). The presence of the acrylate moiety in the  $\alpha$ -position of the PAz chain was also attested by the appearance of characteristic signals in the  $^1\text{H}$  NMR spectrum (peaks at 5.20 ppm and between 5.70-6.40 ppm in Figure S9). Furthermore, a single population was observed in the corresponding MALDI ToF mass spectrum, in perfect agreement with the expected structure of a PAz-based acrylate-containing macromonomer (Figure 18). In Figure 16.b) are also provided the SEC traces before and after reaction, showing the slight increase after the copper-alkyne-azide cycloaddition click reaction, and the retention of low dispersity.



**Scheme 8.** Copper-mediated alkyne-azide coupling reaction of  $\alpha$ -N<sub>3</sub>-PAz (Run 14, Table 4) with propargyl acrylate.

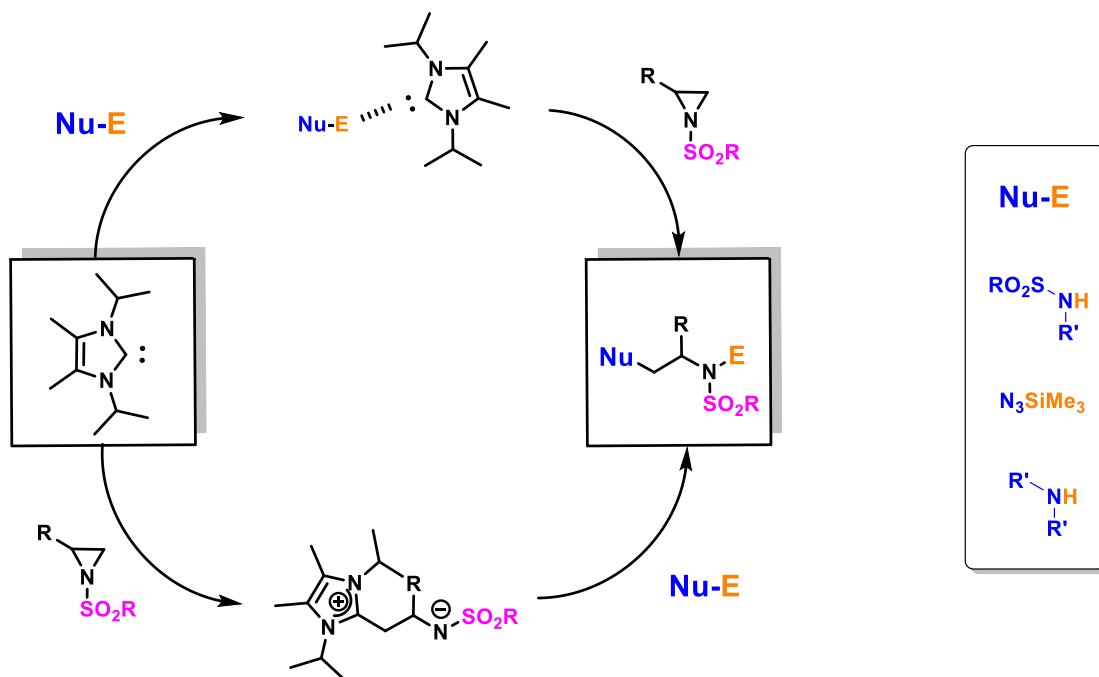


**Figure 18.** a), b) Experimental and c) computed MALDI ToF MS of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) derivatized by copper-mediated click reaction.

Based on background literature<sup>5-8</sup>, either a nucleophilic or a basic mechanism might be operative during the NHC-OROP of 2-alkyl *N*-*p*-toluenesulfonyl aziridines. These two mechanisms, also referred as the activated and the active chain end mechanisms (AMM vs. ACEM), respectively, are displayed in Scheme 9. In the AMM, the direct nucleophilic attack of the cyclic monomer by <sup>Me</sup>5-Ipr results in the formation of an imidazolium amidate zwitterionic intermediate. This active species can be further displaced by the initiator, NuE(1-3), via concomitant protonation (or silylation) of the amidate and substitution of the imidazolium moiety by Nu. In the meantime, the <sup>Me</sup>5-Ipr organocatalyst is released and can

## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

activate another aziridine monomer substrate. However, a basic ACEM, where the initiator first, then PAz chain ends, would be deprotonated/activated by <sup>Me</sup>5-Ipr thus aiding the attack of Nu onto the activated aziridine is also plausible (see Scheme 9).



**Scheme 9.** Possible mechanisms for the NHC-OROP of 2-alkyl *N*-*p*-toluenesulfonyl aziridines initiated by *N*-allyl *N*-*p*-toluenesulfonyl amine, di-*n*-butylamine and trimethylsilyl azide.

In summary, the facile and direct synthesis of metal-free  $\alpha$ -functionalized poly(*N*-tosylaziridine)s by an *N*-heterocyclic carbene catalysis has been achieved. Alkyl or allyl-functionalized *N*-sulfonyl amine and trimethylsilyl azide prove potent initiators for the NHC-OROP of 2-alkyl *N*-*p*-toluenesulfonyl aziridines, providing  $\alpha$ -functionalized PAz. Characterizations by NMR spectroscopy, size exclusion chromatography and MALDI ToF mass spectrometry provide evidence that the NHC-OROP is tolerant to both types of initiators. The accessibility of the allyl and the azido functions in  $\alpha$ -position was also established, through quantitative derivatization of related PAz chains by appropriate click reactions. In addition, a representative non-activated and commercially available secondary amine, namely, di-*n*-butylamine, can serve to initiate the NHC-OROP of *N*-tosylaziridines. Many commercial secondary amines being available, this provides a novel option for engineering polyaziridines in a simple way. Overall, this NHC-OROP methodology warrants high chain end fidelity, good control over molar masses and dispersities, while providing a straightforward synthetic access to metal-free and potentially functionalized polyaziridines.

## **PART 2.B: Selective Initiation From Unprotected Aminoalcohols for the *N*-Heterocyclic Carbene-Organocatalyzed Ring-opening Polymerization of 2-Methyl-*N*-Tosyl Aziridine: Telechelic and Block Copolymer Synthesis**

During the course of our investigation of suitable initiators for the NHC-OROP of *N*-activated aziridines, we observed that alcohols could not initiate the polymerization. Interestingly, in this particular case, the polymerization occurred by the direct attack of the NHC (<sup>Me</sup>5-Ipr) on the aziridine monomer following a zwitterionic mechanism without any incorporation of the alcohol moiety. Moreover, we demonstrated in the previous part 2.A that non-activated secondary amine could serve as an initiator for the NHC-OROP yielding well-defined PAz. Based on these results, commercial aminoalcohols, namely, 2-(methyl amino)ethanol (**1**) and amino-diethanol (**2**), were investigated as direct initiators, *i.e.* with no need of protection of the hydroxyl groups, for the *N*-heterocyclic carbene organocatalyzed ring-opening polymerization (NHC-OROP) of 2-methyl-*N*-*p*-toluenesulfonyl aziridine. NHC-OROP's were performed at 50 °C in tetrahydrofuran, in the presence of 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene (<sup>Me</sup>5-IPr) as organocatalyst. The preparation of poly(*N*-tosyl aziridine)-*b*-poly(L-lactide) block copolymers by sequential and selective NHC-OROP using the same NHC organocatalyst was also investigated.

### **2.B.1. Alcohol initiation**

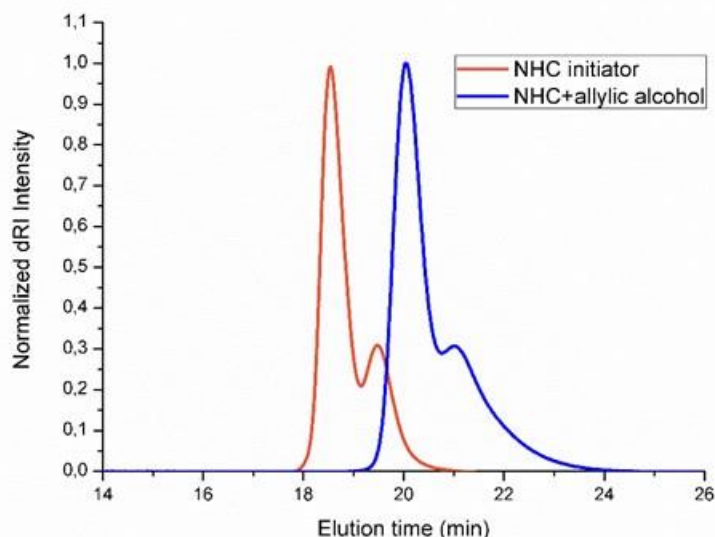
#### **2.B.1.1. NHC-OROP *N*-Tosyl aziridine in presence of allyl alcohol as initiator**

Initially, primary alcohol was investigated as initiator for the <sup>Me</sup>5-Ipr-OROP of 2-methyl-*N*-*p*-toluenesulfonyl aziridine (MeAz). The reaction was performed under the same conditions above-mentioned in the presence of allyl alcohol as an initiator, in order to figure out whether this simple primary alcohol could somehow affect the polymerization outcome. Although polymerization did take place (entry 5, Table 5), forming a PAz with a higher molar mass than



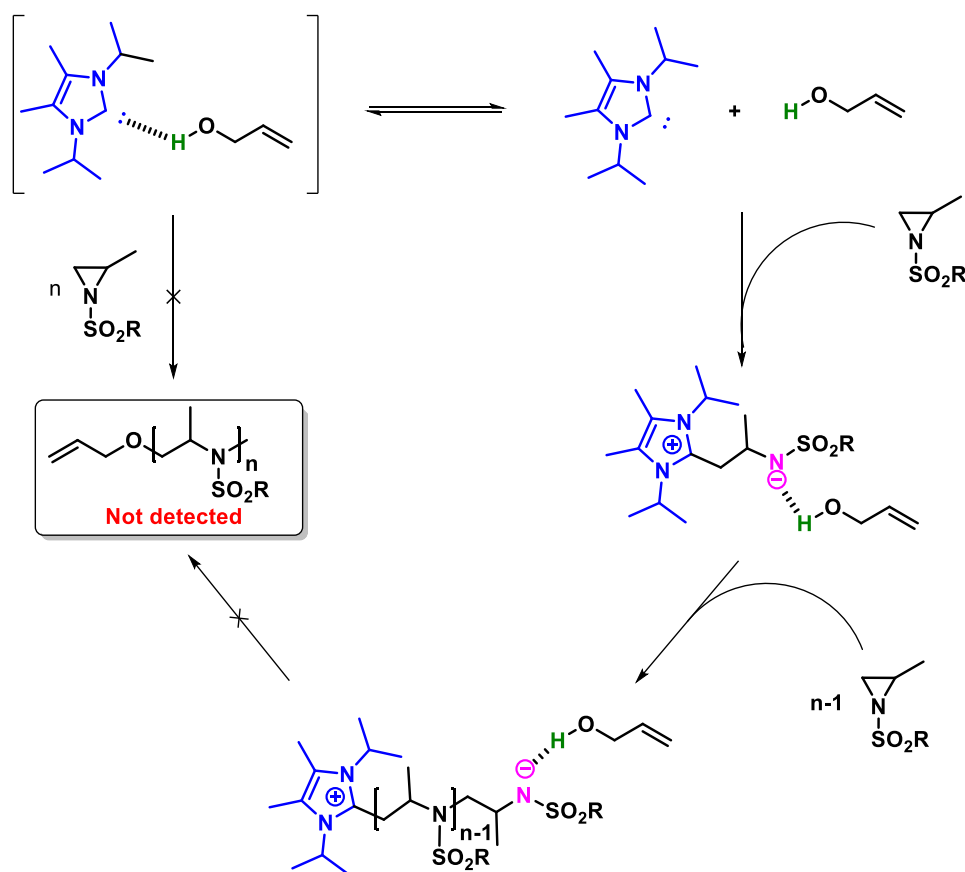
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

expected,  $\overline{M}_n = 17\,000\text{ g.mol}^{-1}$  and  $\overline{D} = 1.23$ ,  $^1\text{H}$  NMR analysis of this polymer did not show any evidence of the incorporation of allyl alcohol; no diagnostic signal due to the allylic protons was detected. A control experiment directly utilizing  $\text{Me}_5\text{-IPr}$  and the monomer, *i.e.* in absence of any other reagent, also formed a PAz derivative with in this case a  $\overline{M}_n$  value of  $60\,000\text{ g.mol}^{-1}$  and  $\overline{D} = 1.25$  (Figure 19), very likely *via* the so-called zwitterionic ring-opening polymerization (ZROP) mechanism.



**Figure 19.** SEC traces of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by allylic alcohol and 10 % mol. of  $\text{Me}_5\text{-IPr}$  and (in blue) and  $\text{Me}_5\text{-IPr}$  (in red).

In other words, due to its nucleophilic character,  $\text{Me}_5\text{-IPr}$  was able to directly initiate the ROP 2-methyl *N*-tosylaziridine. Yet, the presence of allyl alcohol somehow affected the ROP kinetics: longer reaction times were indeed needed to reach complete conversion in this case, compared to a direct ZROP experiment (see the proposed mechanism in Scheme 10). While complete conversion was reached in less than 14h for the ZROP experiment, 48h were necessary to reach a quantitative conversion in the case of NHC-OROP initiated by allylic alcohol. This decrease of the polymerization kinetic might be ascribed to the existence of hydrogen bonding between allylic alcohol and propagating chain-ends, which could reduce nucleophilicity of the latter. Different solvents (DMSO and DMF), higher temperature (50–80°C) and low amount of NHC (1–10 mol. %) were also used to performed the NHC-OROP of MeAz initiated by allyl alcohol but the same behavior was observed, *i.e.* side initiation by direct nucleophilic attack of the NHC and propagation *via* a zwitterionic mechanism.



**Scheme 10.** Proposed mechanism for NHC-OROP (ZROP) of 2-methyl *N*-*p*-toluenesulfonyl aziridine initiated by allylic alcohol.

These preliminary results prompted us to investigate the NHC-OROP of *N*-activated aziridines using amino-alcohols as chemo-selective initiators without any protection of the hydroxyl function. Information gained in the previous section 2.A indeed showed us that non-activated amines were able to directly initiate OROP of *N*-activated aziridines. Through the use of amino-alcohols, it was expected that the initiation occurs selectively from the amine function yielding  $\alpha$ -hydroxyl PAz derivatives.

#### 2.B.1.2. Anionic ring-opening polymerization of *N*-sulfonyl aziridines in presence of alcohol and water impurities

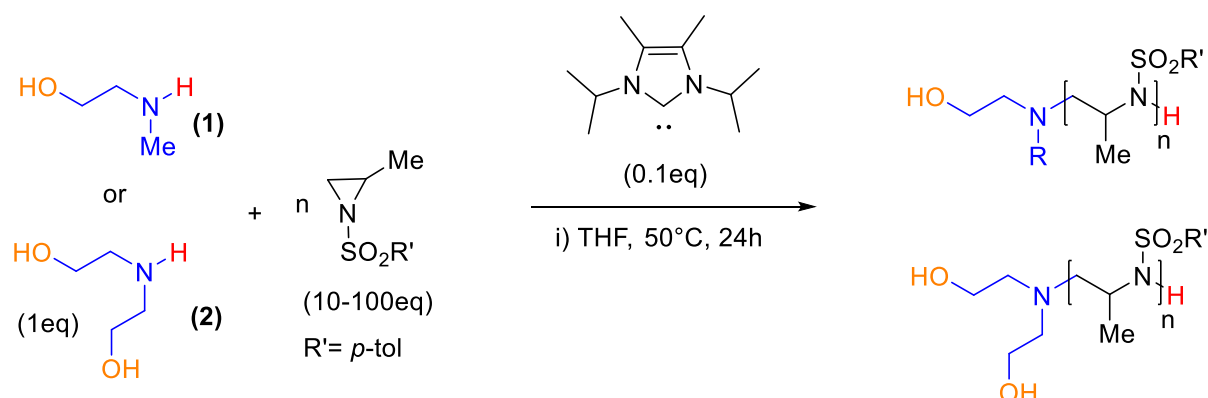
Concomitantly, a recent paper in *Macromolecules* published by the group of F. R. Wurm (Max-Planck Institute of Mainz), in collaboration with our group, demonstrated that the AROP of activated aziridines bearing a mesyl or a tosyl activating group is “alcohol and water tolerant”.<sup>64</sup>

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The AROP initiated by activated secondary amine salts (DMF, 50 °C, Bibliographic chapter) was found to be insensible to the presence of large amount of protic impurities such as methanol, ethanol, isopropanol and even water (up to 1000 eq. as compared to the initiator/active species), keeping its living character. These works clearly demonstrate the high tolerance to protic species of the propagating aza-anion, *i.e.* the active species in the AROP of *N*-tosyl aziridines, which is unprecedented in the context of anionic polymerization.

### 2.B.2. Initiation from commercially available amino alcohols

As mentioned in section 3.2. (PART 2.A), a simple non-activated secondary amine (di-*n*-butylamine) can directly initiate the <sup>Me</sup>5-IPr-OROP of 2-methyl or phenyl-*N*-*p*-toluenesulfonyl aziridine. Here, two different commercially available hydroxyl-containing non-activated amines were examined as novel initiators to directly prepare  $\alpha$ -hydroxy- $\omega$ -aminotelechelic poly(*N*-tosyl aziridine)s, as depicted in Scheme 11. Reactions were carried out at 50 °C in THF, with 10 mol.% of 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene (<sup>Me</sup>5-IPr) relative to the initiator. Table 5 summarizes the different polymerization experiments. Indeed, well-defined polyazirines (PAz) were obtained using 2-(methyl amino)ethanol (**1**) under those conditions (entries 1-4, Table 5), good control over molar masses (up to 16 600 g.mol<sup>-1</sup>) and low dispersities ( $\bar{D} < 1.20$ , see Figure 20.a) being achieved, with symmetrical and monomodal size exclusion chromatography (SEC) traces. In addition, apparent molar masses, as determined by SEC, increased when increasing the initial monomer to the initiator molar ratio (Figure 20.a; run1-4 Table 5).



**Scheme 11.** NHC-OROP of 2-methyl *N*-*p*-toluenesulfonyl aziridine initiated by aminoalcohols

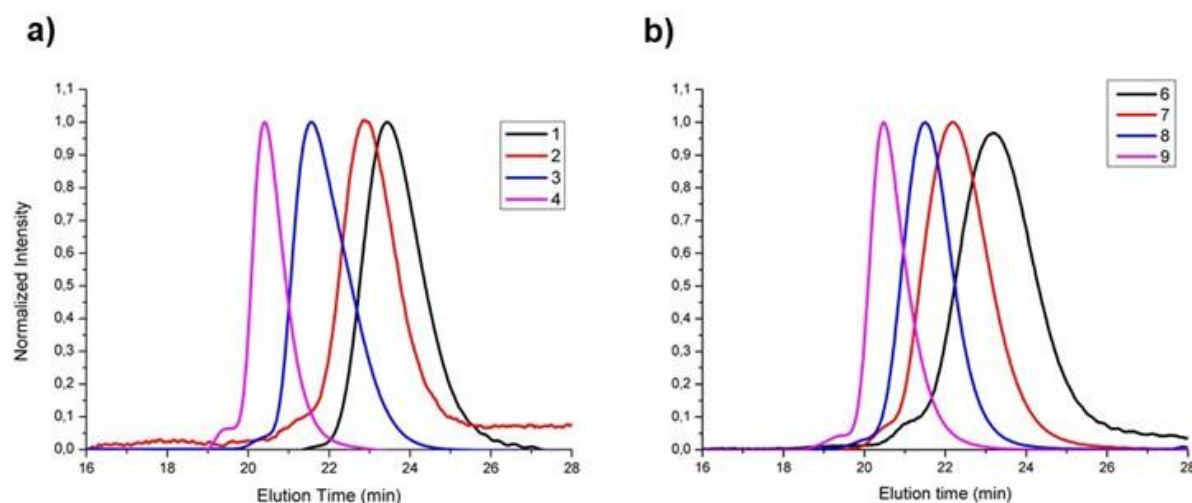
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

**Table 5.** NHC-OROP of 2-methyl-*N*-*p*-toluenesulfonyl aziridine using allyl alcohol and aminoalcohol **1** or **2** as initiator (THF, 50 °C, 24h)

Run	Initiator	[Az]/[Initiator]/[NHC]	Conv. <sup>(a)</sup> (%)	$\overline{Mn}_{THEO}^{(b)}$	$\overline{Mn}_{SEC}^{(c)}$	$\overline{D}^{(c)}$
1		10/1/0.1	100	2 100	2 650	1.10
2		20/1/0.1	100	4 200	3 750	1.08
3		50/1/0.1	100	10 600	7 800	1.15
4		100/1/0.1	100	21 100	16 600	1.09
5		20/1/0.1	100	4 200	17 000	1.23
6		10/1/0.1	100	2 100	2 400	1.18
7		20/1/0.1	100	4 200	3 800	1.18
8		50/1/0.1	100	10 600	6 500	1.10
9		100/1/0.1	100	21 100	13 200	1.11

<sup>a</sup>Conversion was calculated by <sup>1</sup>H NMR; <sup>b</sup> $\overline{Mn}_{THEO} = ([Az]/[Initiator]) \times M_{Az} \times \text{conv. (in g.mol}^{-1}\text{)}$ ;

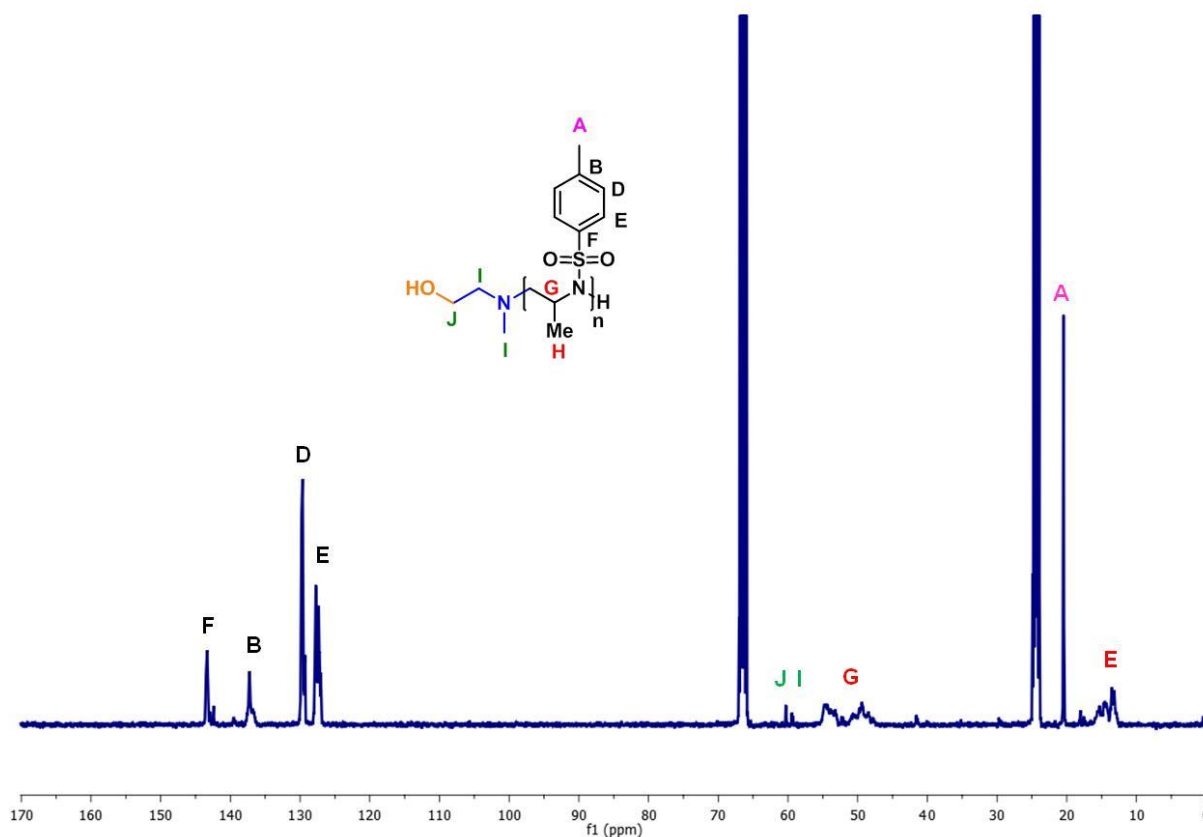
<sup>c</sup>Number-average molar mass (in g.mol<sup>-1</sup>) and dispersity determined by size exclusion chromatography in THF (PS calibration)



**Figure 20.** SEC traces (RI detection) of a) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine)s initiated by 2-methyl aminoethanol (Runs 1-4, Table 1) and b) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine)s initiated by diethanolamine (Runs 6-9, Table 1)

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The  $^1\text{H}$  NMR spectrum of a typical PAz initiated from **1** showed all signals due to the resonance of the protons of the repeating unit (Figure 21.a.). However, the presence of the hydroxyl group in  $\alpha$ -position of PAz chains could not be directly detected but small signals in  $^{13}\text{C}$  NMR spectra around 60 ppm (J and I) can be attributed to the amino alcohol chain-ends (Figure 21).

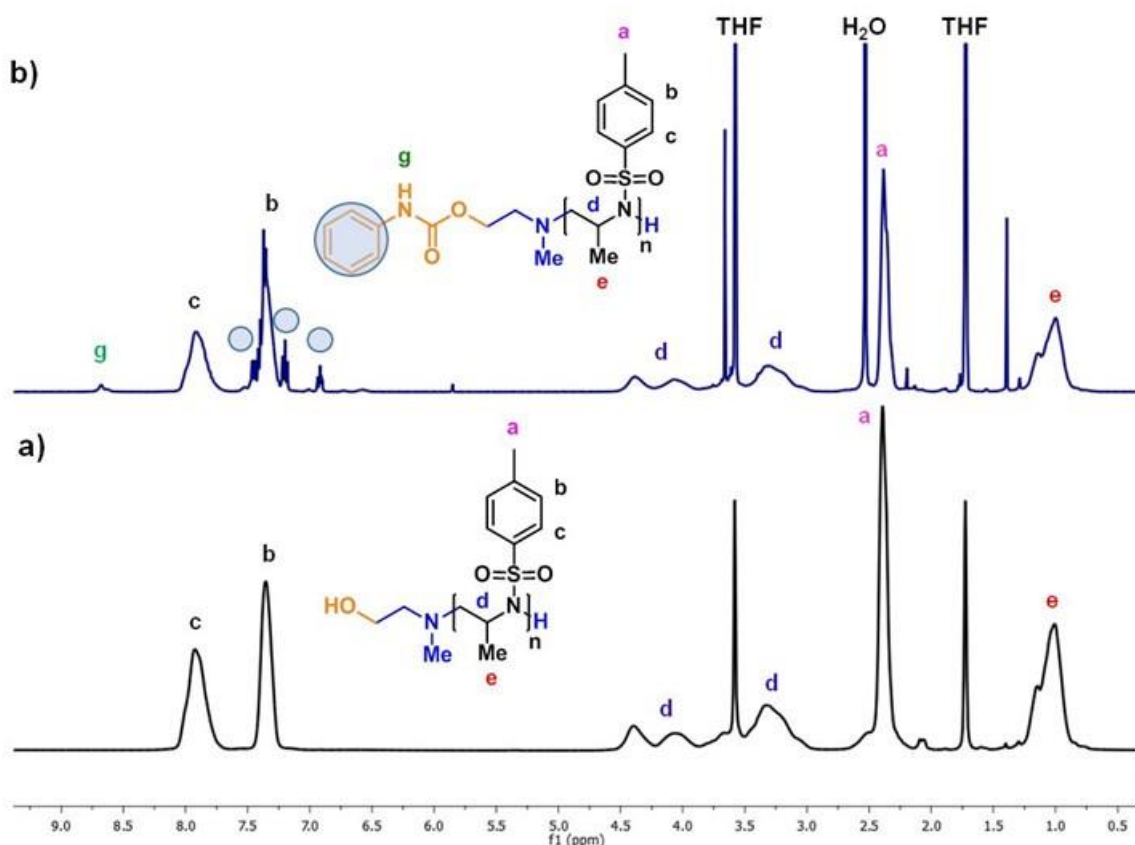


**Figure 21.**  $^{13}\text{C}$  NMR (THF- $d_8$ ) spectrum of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by 2-(methyl amino)ethanol (Run 1, Table 1)

Thus, further derivatization of this PAz precursor using an excess of phenyl isocyanate (20 eq.) led to an  $\alpha$ -urethane PAz, the characterization of which by SEC showed a slight shift toward the higher molar masses due to the introduction of the carbamate moiety in PAz chain-ends (Figure 23.d), with retention of a low dispersity. Characteristic signals in the aromatic region at 6.90-7.50 ppm and around 8.60 ppm, assigned to the phenyl ring and to the *NH* of the carbamate moiety, respectively, were unambiguously detected by  $^1\text{H}$  NMR after this post-chemical modification step (Figure 22.b). This attested to the presence of the hydroxyl group in the parent PAz derived from **1**, also confirming that PAz chains were grown from the secondary  $\omega$ -NH(Ts) amino functionality in a controlled manner, with no interference of the hydroxyl group. In addition, PAz molar mass could be precisely estimated by comparing the relative intensity of the urethane signals with those corresponding to the main chain protons, assuming that the

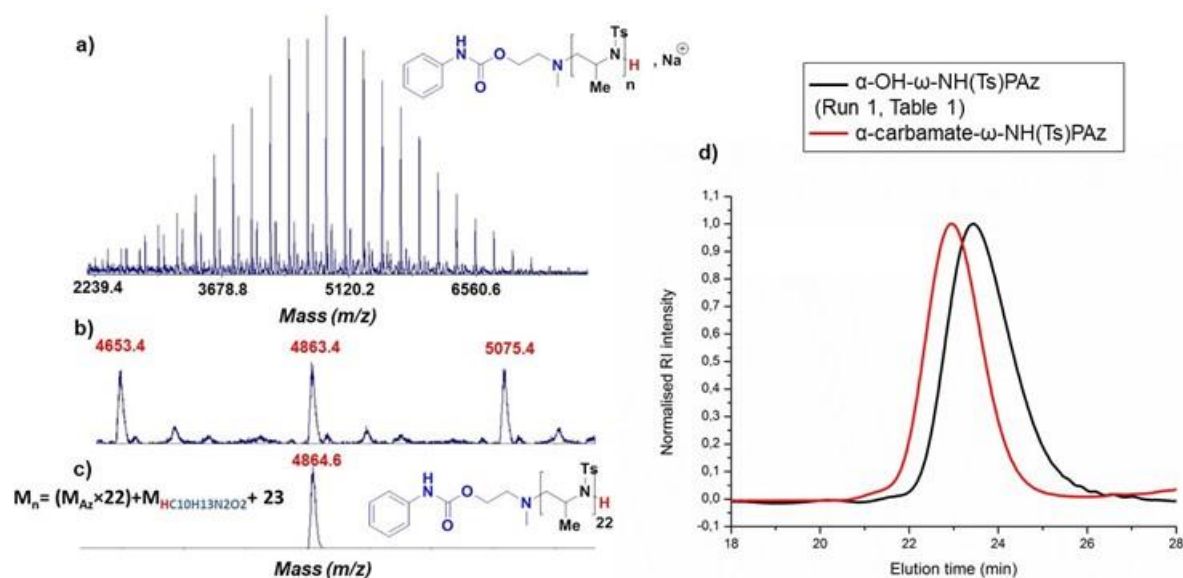
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

modification reaction was quantitative. Agreement between experimental molar masses and theoretical values (Table 5) supported that both the initiation of NHC-OROP and the derivatization of -OH end-groups into -O(C=O)N(H)Ph were highly efficient. As already noted in paragraph 1.2 (PART 2A), apparent molar masses as determined by SEC using PS standards were lower than those predicted.



**Figure 22.**  $^1\text{H}$  NMR spectrum of an  $\alpha$ -hydroxy,  $\omega$ -NH(tosyl) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by 2-methyl aminoethanol (a) (Run 1, Table 5) and its  $\alpha$ -carbamate derivative obtained after post-functionalization (b)

In Figure 23 is displayed the MALDI ToF mass spectrum of the carbamate-functionalized PAz. The isotopic distribution perfectly matched the expected structure, supporting the accessibility of the hydroxy function in  $\alpha$ -position through quantitative derivatization of the  $\alpha$ -OH PAz precursor. All these results thus demonstrated that 2-methyl aminoethanol **1** initiated the NHC-OROP of 2-methyl *N*-tosylaziridine in THF at 50 °C from the secondary amino group in a highly chemoselective manner, the unprotected primary OH group remaining inactive.



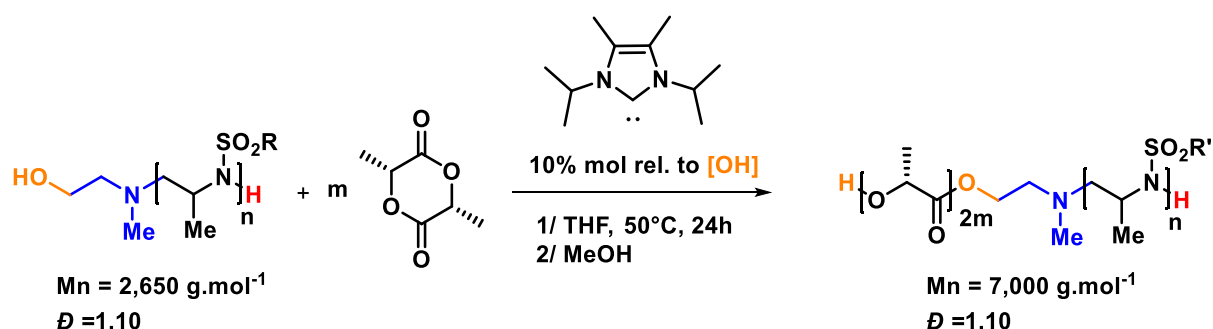
**Figure 23.** Experimental (a and b) and computed (c) MALDI ToF mass spectra of a  $\alpha$ -carbamate- $\omega$ -NH(Tosyl) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) obtained by post-functionalization and d) SEC traces of  $\alpha$ -hydroxy-poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) before (in black) and after (in red) derivatization by phenylisocyanate

The synthesis of well-defined  $\alpha$ -functionalized PAz by NHC-OROP, and evidence of the easy accessibility of the OH group through quantitative derivatization, prompted us to derive a novel family of block copolymers using this precursor as a macroinitiator. Synthetic strategies to block copolymers generally include i) sequential polymerization, *i.e.* consecutive addition of at least two monomers, ii) coupling of preformed homopolymers with antagonist end-groups, iii) switch from one to another polymerization mechanism, and iv) use of a “double-headed” initiator.<sup>65-68</sup> In PART 2.A, all PAz-based block copolymers have been successfully obtained by sequential NHC-OROP, using an *N*-activated amine initiator. Here, we envisioned that 2-(methyl amino)ethanol could serve as a double-headed initiator to grow two types of polymer chains, namely, a PAz chain and a poly(L-lactide) (PLLA) from the secondary amino and the hydroxyl group, respectively. Thus, we took advantage of the presence of the OH group in  $\alpha$ -position of the  $\alpha$ -hydroxy- $\omega$ -aminotelechelic PAz precursor to grow a PLLA block in presence of the same <sup>Me</sup>5-IPr organocatalyst. As a proof of concept, L-lactide (L-LA) was added onto a THF solution of the preformed  $\alpha$ -hydroxy PAz initiated by **1** and catalyzed by <sup>Me</sup>5-IPr, playing here the role of a macroinitiator. It was thus expected that initiation of the NHC-OROP of LA selectively took place from the primary hydroxyl, in this case with no interference by secondary  $\omega$ -NH(Ts) amino-end group of the PAz precursor (Scheme 12). After stirring the solution overnight at 50 °C, the SEC trace of the resulting compound clearly shifted to the higher molar



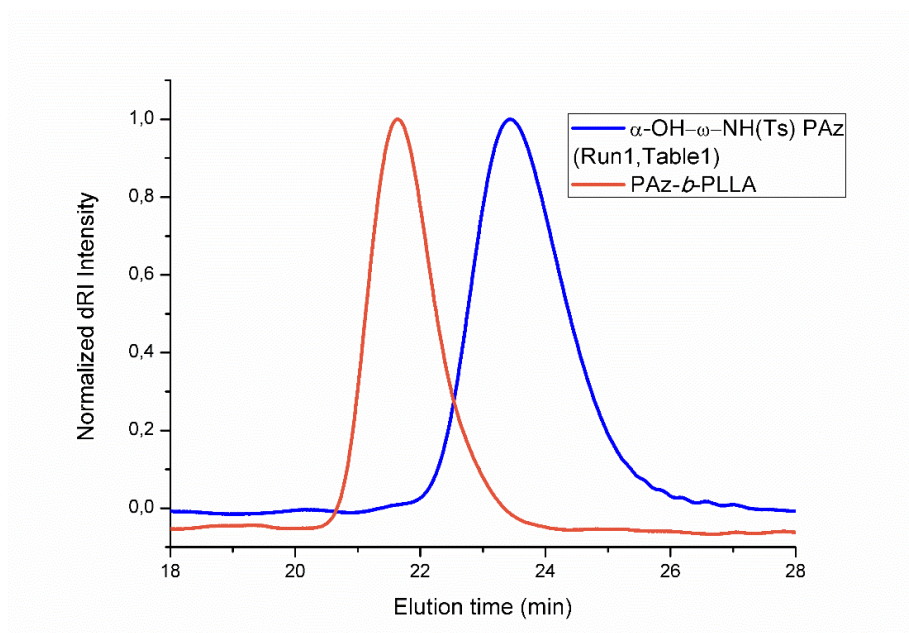
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

masses, while the dispersity remained very low, attesting to a highly effective crossover reaction from PAz to PLLA (Figure 24). Analysis by  $^1\text{H}$  NMR confirmed the presence of both PAz and PLLA blocks. The overall composition of the PAz-*b*-PLLA block copolymer could be estimated, knowing the molar mass of the  $\alpha$ -OH PAz precursor, from the relative integrations of characteristic signals of both blocks at 7.70-8.10 ppm (*Ar*) and at 5.16 ppm (*Me*), for PAz and PLLA blocks, respectively. A value of 8600 g.mol $^{-1}$ , vs. 7000 g.mol $^{-1}$  by SEC analysis, was thus calculated for a total molar mass of 4300 and 4300 g.mol $^{-1}$  for the PAz and the PLA blocks, respectively (Figure 25). The latter value agreed with the expected molar mass based on a quantitative initiation from the  $\alpha$ -OH PAz precursor. Thus, block copolymer synthesis could be readily achieved by sequential NHC-OROP of aziridine and L-lactide, using 2-methyl aminoethanol as a double-headed initiator. Intriguingly, the sequential growth by NHC-OROP occurs with a high selectivity, PAz and PLA blocks being grown from the secondary  $\omega$ -NH(Ts) amino- and the primary hydroxy- function, respectively. This fully metal-free synthetic strategy enables to synthesize well-defined and unprecedented PAz-*b*-PLLA diblock copolymers from the same NHC organocatalyst.

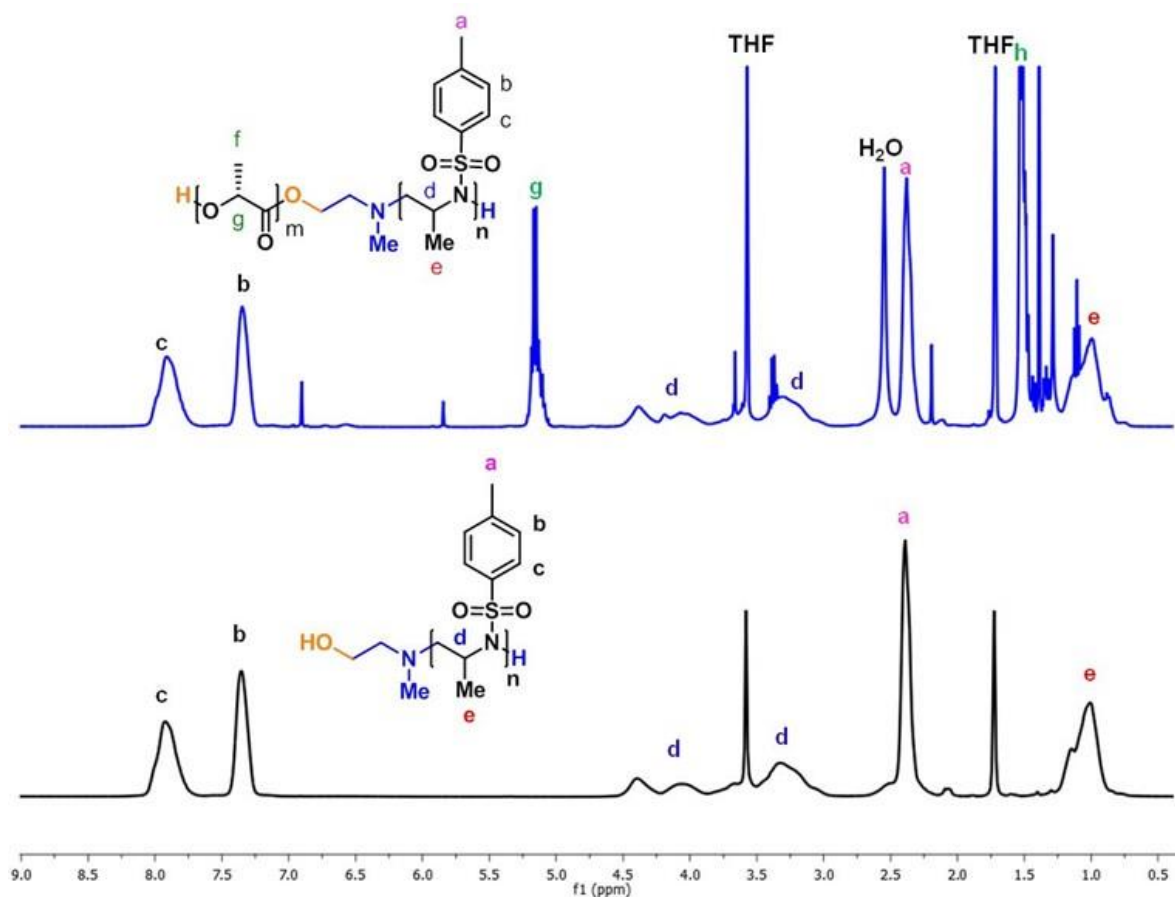


**Scheme 12.** Synthesis of poly(2-methyl *N*-*p*-toluene sulfonyl aziridine)-*b*-poly(L-lactide) block copolymer by sequential NHC-OROP using 2-(methyl amino)ethanol as double-headed initiator and  $^{\text{Me}}5\text{-IPr}$  as the same organocatalyst





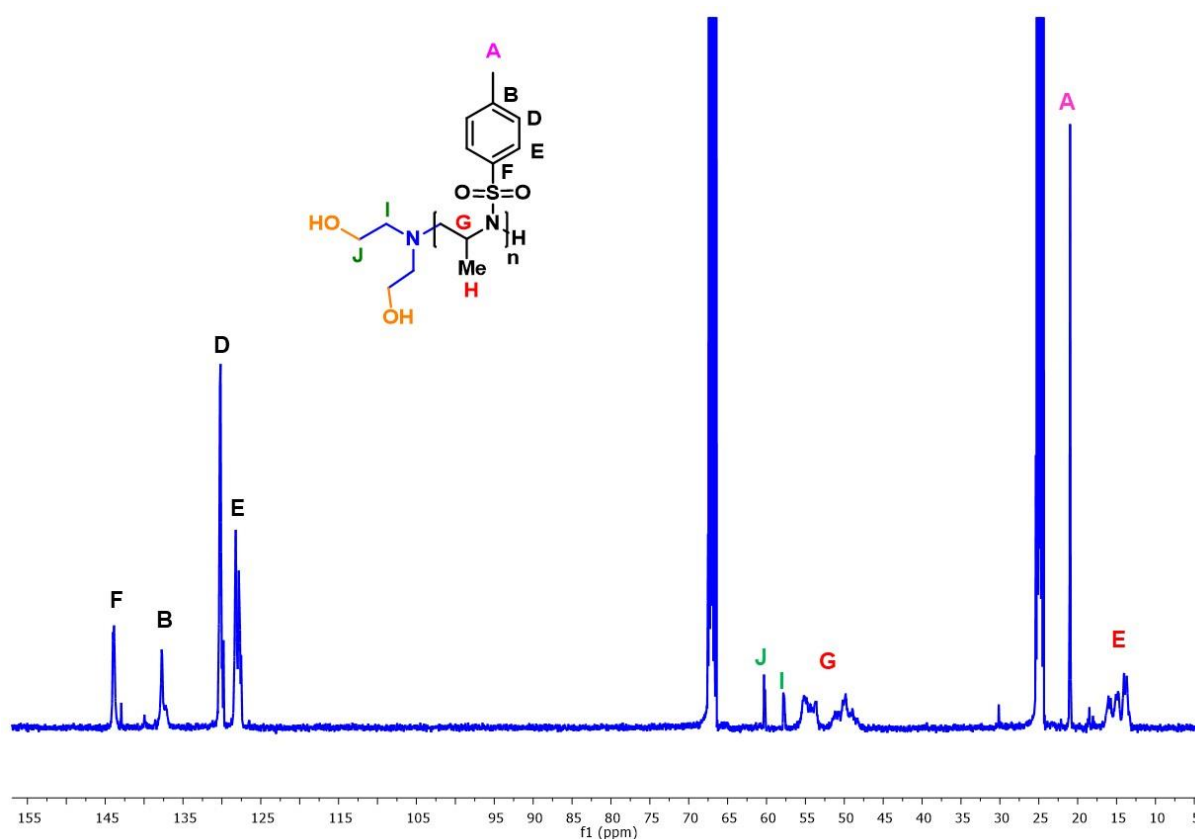
**Figure 24.** SEC traces of  $\alpha$ -hydroxy-poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) and poly(2-methyl *N*-*p*-toluenesulfonyl aziridine)-*b*-poly(L-lactide) obtained by sequential NHC-OROP



**Figure 25.**  $^1\text{H}$  NMR (THF- $d_8$ ) spectrum of a)  $\alpha$ -hydroxy-poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) and b) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine)-*b*-poly(lactide) obtained by sequential NHC-OROP

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We then resorted to another commercially available hydroxyamino-containing compound, namely, diethanolamine (**2**, Scheme 12) to initiate the NHC-OROP of 2-methyl *N*-tosylaziridine. In the latter case, it was expected that  $\alpha,\alpha'$ -bis-hydroxy- $\omega$ -amino PAz telechelics could be synthesized. Different ratios between the monomer and the initiator were employed (entry 6-9, Table 5, Figure 20.b). Remarkably, well-defined polymers could also be obtained in this case, with molar masses in the range 3200-13200 g.mol<sup>-1</sup> and  $\bar{D} < 1.20$ , and with no need for protection of the two hydroxyl groups of **2** (Figure 20.b). As in the case of the  $\alpha$ -OH- $\omega$ -NH(Ts) PAz obtained from **1**, the presence of the primary hydroxyl groups could not be directly evidenced by <sup>1</sup>H NMR but small signals (I and J) in <sup>13</sup>C NMR spectrum presented in Figure 26 can be attributed to the amino alcohol at the  $\alpha$ -position of PAz chains.

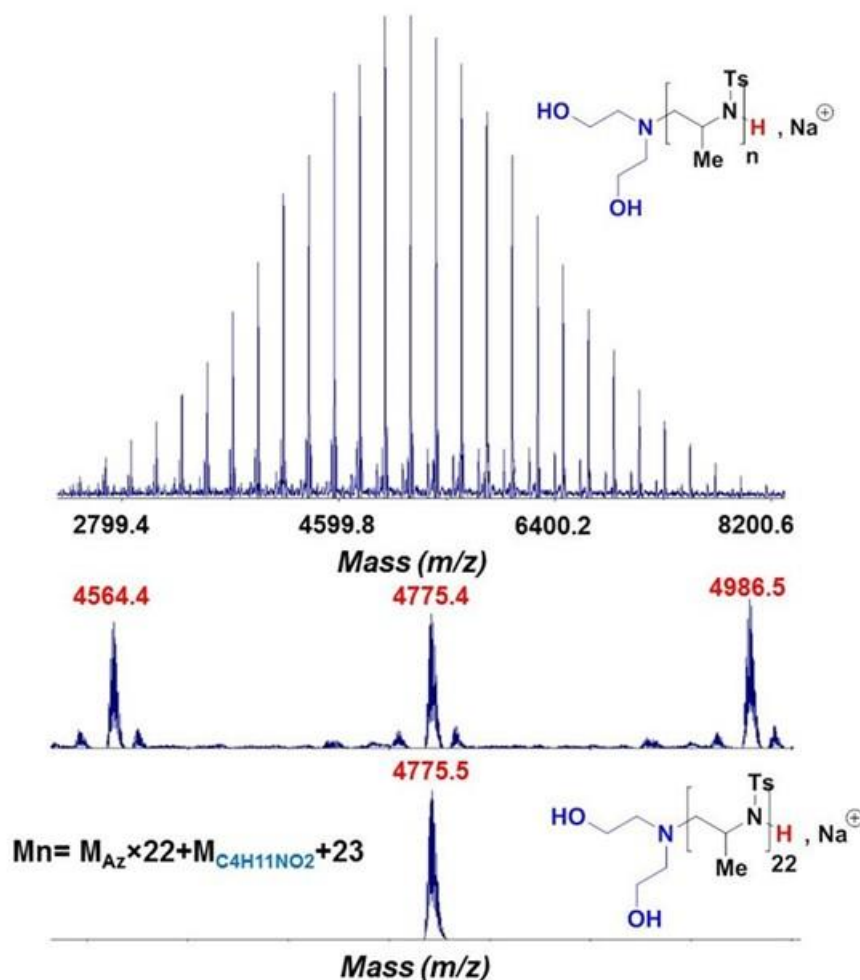


**Figure 26.** <sup>13</sup>C NMR (THF-*d*8) spectrum of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by diethanolamine (Run 6, Table 5)

However, MALDI ToF MS analysis of a low molar mass PAz obtained in this way (entry 7, Table 5) revealed a single population consistent with the formation of a cationized PAz, with a peak-to-peak mass increment of 211.3 g.mol<sup>-1</sup> corresponding to the molar mass of one monomer unit (Figure 27). Discrete peaks appeared at  $m/z = 211.3n + M_{(\text{HOCH}_2\text{CH}_2)_2\text{N}} + M_{\text{H}} + 23$ , where  $n$  was the degree of polymerization, 23 the molar mass of Na<sup>+</sup> generated during ionization,  $M_{(\text{HOCH}_2\text{CH}_2)_2\text{N}}$  and  $M_{\text{H}}$  being the molar mass of end groups introduced in  $\alpha$ - and  $\omega$ -position,

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respectively. Simulations giving the theoretical isotope distributions were in agreement with experimental distributions attributed to the cationized adduct of the  $\alpha$ -diethanolamino,  $\omega$ -NH(Ts) PAz. This result unambiguously attested to the presence of both hydroxyl groups in  $\alpha$ -position of PAz chains, *i.e.* to the formation of a  $\alpha,\alpha'$ -bis-hydroxy PAz telechelic.

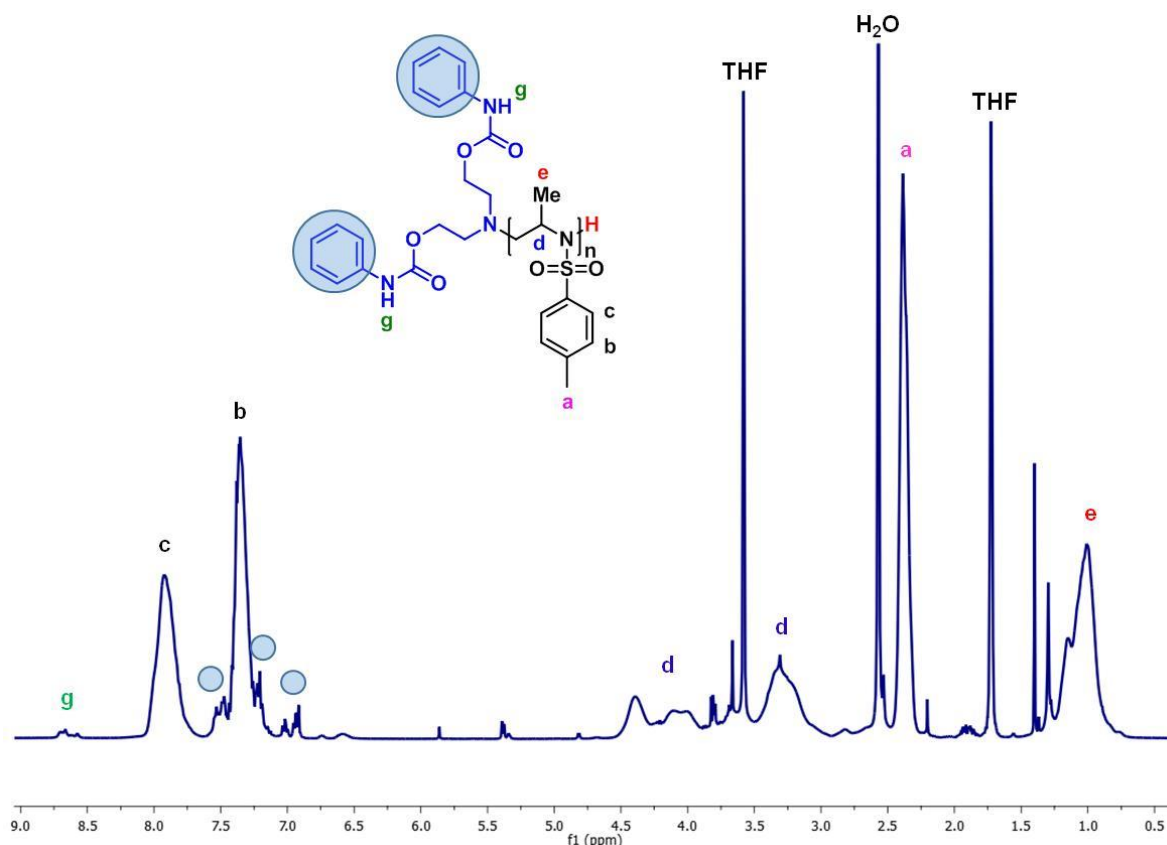


**Figure 27.** Experimental (a) and computed (b) MALDI ToF mass spectrum of a  $\alpha,\alpha'$ -bishydroxy, $\omega$ -NH(Ts) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine). \* The 2 populations at  $\Delta(m/z)=-22$  and  $\Delta(m/z)=+16$  correspond respectively to proton ionization and potassium ionization.

To further illustrate the reactivity of the geminal hydroxy chain ends, the latter PAz was also reacted with 2 eq. of phenyl isocyanate, leading to a telechelic  $\alpha,\alpha'$ -bis-carbamate PAz telechelic. This was supported by  $^1\text{H}$  NMR analysis showing the diagnostic signal at 8.6 ppm, due to the NH of the carbamate group. (Figure 28). In Figure S10 are also displayed SEC traces before and after urethanization, with a slight increase in molar mass after addition of phenyl isocyanate, while the dispersity remains very low. MALDI ToF MS analysis of the low molar

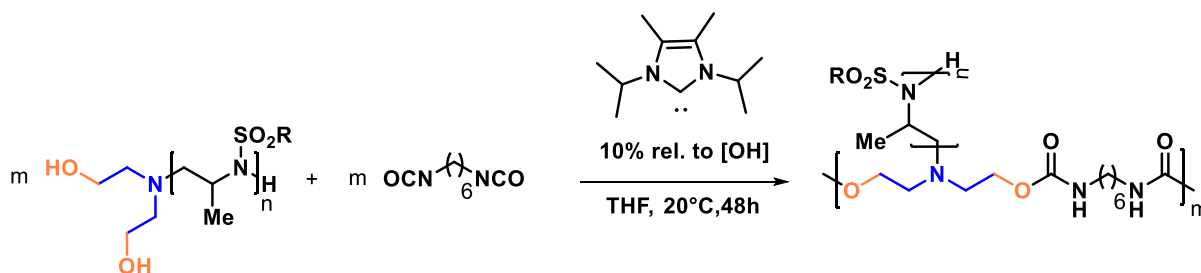
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

mass  $\alpha,\alpha'$ -bis-carbamate PAz telechelic revealed a single population consistent with the formation of a cationized PAz, with a peak-to-peak mass increment of  $211.3 \text{ g.mol}^{-1}$  corresponding to the molar mass of one monomer unit (Figure S11). Simulations giving the theoretical isotope distributions were flawlessly matched experimental distributions attributed to the cationized adduct of the  $\alpha$ -dicarbamate,  $\omega$ -NH(Ts) PAz (Figure S11).



**Figure 28.**  $^1\text{H}$  NMR ( $\text{THF-}d_8$ ) spectrum of  $\alpha,\alpha'$ -bis(phenylisocyanate) derivatized poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) after derivatization by phenylisocyanate.

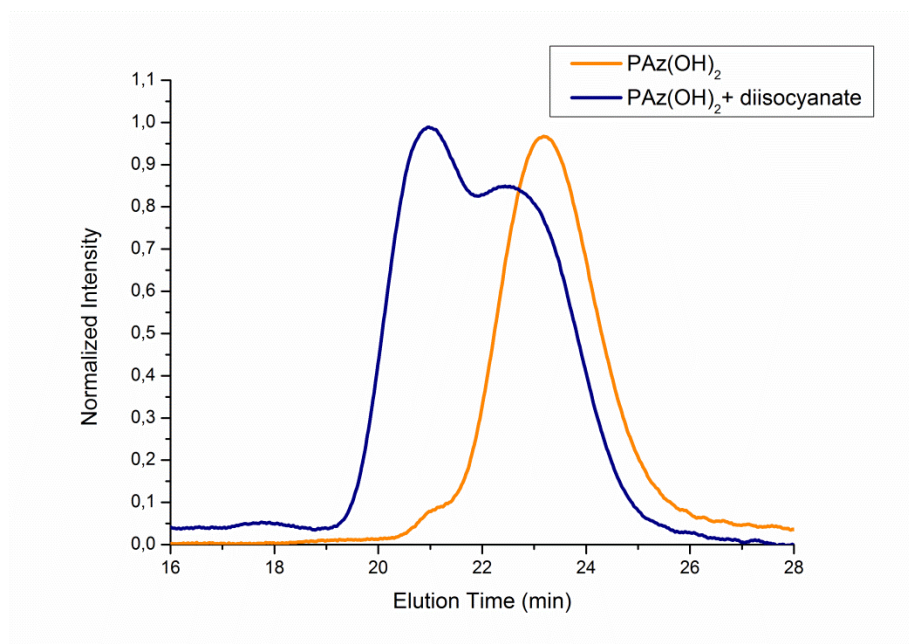
We also envisioned a chain extension experiment using stoichiometric amounts of a diisocyanate, namely, hexamethylene diisocyanate, to react with  $\alpha,\alpha'$ -bis-hydroxy PAz telechelic in a step-growth polymerization process (Scheme 13).



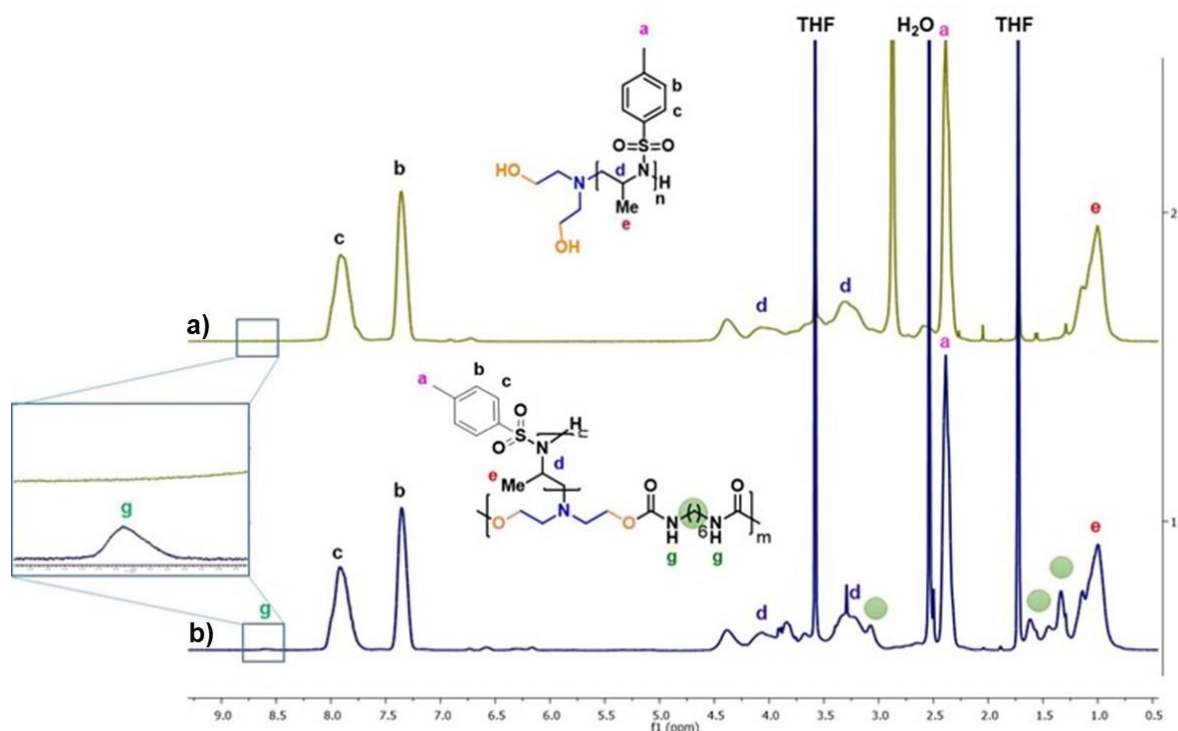
**Scheme 13.** Step-growth polymerization using the  $\alpha,\alpha'$ -bis-hydroxy poly(2-methyl *N*-*p*-toluene sulfonyl aziridine) forming a polyurethane

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After 24h at 20°C, the molar mass of the resulting polymer increased from  $\overline{M}_n = 3\,800\text{ g.mol}^{-1}$  (Run 7, Table 5) to  $\overline{M}_n = 10\,200\text{ g.mol}^{-1}$ , with a significant broadening of the molar mass distribution ( $D \geq 1.6$ ), consistently with the formation of a polyurethane (Figure 29). This was confirmed by analysis by  $^1\text{H}$  NMR spectroscopy of the isolated polyurethane, which showed all expected signals from PAz segments linked by carbamate groups (Figure 30). Despite many attempts to increase the molar mass of the targeted polyurethane, the low amount of  $\alpha,\alpha'$ -bis-hydroxy PAz telechelic engaged in the polymerization process, and consequently the low concentration of hydroxyl function available, only yielded low molar mass polyurethane (Figure 29).



**Figure 29.** SEC traces of  $\alpha,\alpha'$ -bishydroxy-poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) before (in orange) and after (in blue) reaction with hexamethylene diisocyanate



**Figure 30.**  $^1\text{H}$  NMR ( $\text{THF-}d_8$ ) spectrum  $\alpha, \alpha'$ -bishydroxy-poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) before (a) and after (b) reaction with hexamethylene diisocyanate

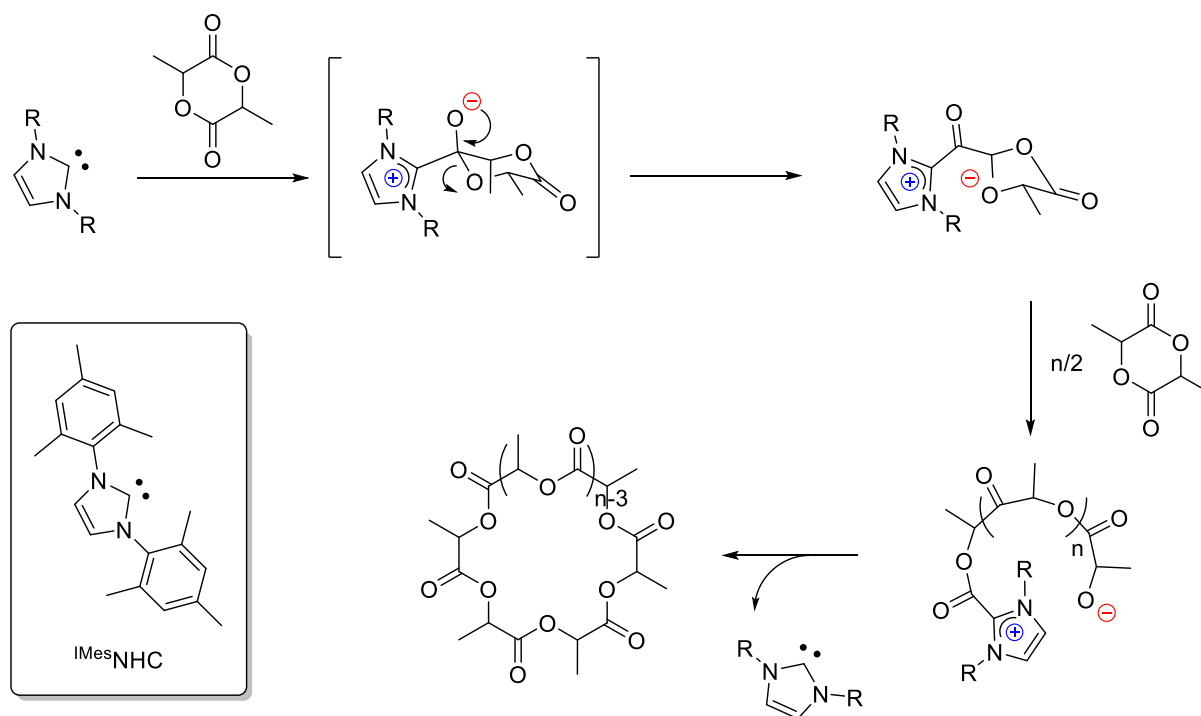
In conclusion, the *N*-heterocyclic carbene organocatalyzed ring-opening polymerization (NHC-OROP) of 2-methyl-*N*-*p*-toluenesulfonyl aziridine can be controlled at 50 °C in THF in presence of aminoalcohols as multifunctional initiators. This provides a facile and direct synthetic access to metal-free  $\alpha$ -hydroxy, $\omega$ -amino and  $\alpha, \alpha'$ -bis-hydroxy, $\omega$ -amino telechelic poly(*N*-tosyl aziridine) telechelics, with no need for tedious protection-deprotection chemistry. As evidenced by combined characterizations, including NMR spectroscopy, SEC and MALDI ToF mass spectrometry, this NHC-OROP process proves highly chemoselective and guarantees high chain-end fidelity, as well as high level of control over molar masses and dispersity. Given the accessibility and versatility of the hydroxyl function, both for post-functionalization reactions and as initiating fragment for a wide range of polymerization reactions, this synthetic strategy utilizing commercially available non-activated hydroxy-containing amines further expands the scope of NHC-mediated polymerizations for macromolecular engineering of polyaziridines. This is demonstrated here with the preparation of poly(*N*-tosyl aziridine)-*b*-poly(L-lactide) block copolymers by sequential and selective NHC-OROP using the same NHC organocatalyst.

## **PART 2.C: Preliminary Results of *N*-Heterocyclic Carbenes Promoted Zwitterionic Ring-Opening Polymerization of *N*-tosyl Aziridines.**

During the course of the investigation on the NHC-OROP of *N*-activated aziridines, we already observed that, in some cases, the polymerization could proceed by the so-called zwitterionic mechanism (see sections 2.A.3.2 and 2.B.1). The zwitterionic ring-opening polymerization (ZROP) involves generally the addition of neutral organic nucleophiles (such as pyridine, amidine, imidazole-based nucleophiles or NHCs) to strained heterocyclic monomers, which can generate, under appropriate conditions, cyclization of the resultant macrozwitterions, thus producing cyclic macromolecules. Among organocatalysts, NHCs were the most investigated in the last two decades for the purpose of polymerization. NHCs have served to catalyze/initiate different polymerization reactions, including step-growth and chain growth polymerizations. As already mentioned, NHCs were mainly used as organic catalyst in chain-growth ROP of cyclic monomers to produce linear as well as cyclic polymers. In 2002, Waymouth, Hedrick and co-workers described for the first time that cyclic PLAs could be obtained by a kinetically controlled zwitterionic ring-opening polymerization (ZROP) through the polymerization of lactide with a peculiar NHC, namely 1,3-dimesitylimidazol-2-ylidene (<sup>IMes</sup>NHC) in total absence of an alcohol initiator (Scheme 14).<sup>21</sup> In other words, the NHC played in this case the role of initiator and molar masses were directly controlled by the initial feed ratio of the monomer to the initiator, *i.e.* the <sup>IMes</sup>NHC.



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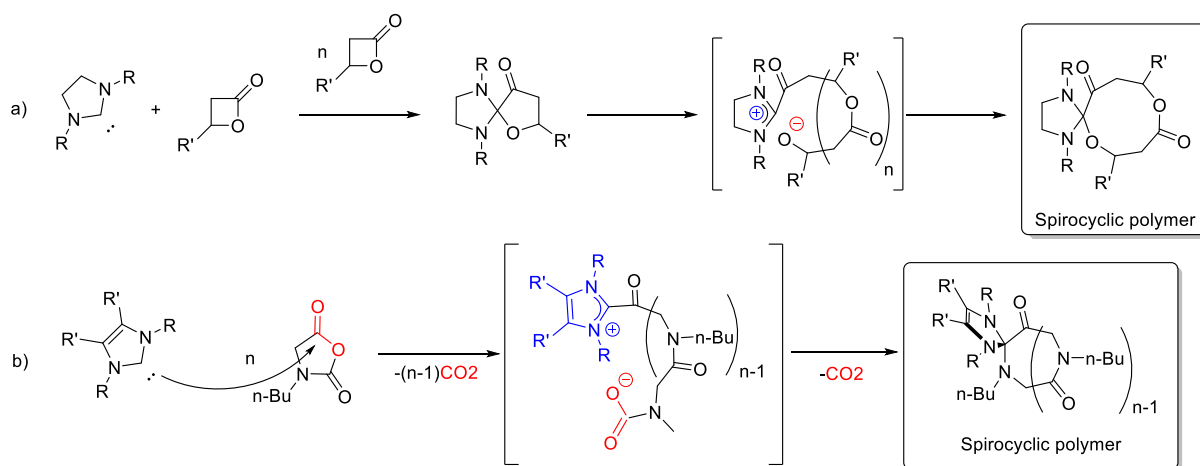
**Scheme 14.** ZROP of *rac*-lactide initiated by IMesNHC and synthesis of cyclic PLAs

ZROP initiated by NHCs were not only applied for the polymerization of carbonyl-containing monomers such as lactide,<sup>22</sup> lactones,<sup>23</sup> cyclic carbonates,<sup>37</sup> *N*-carboxyanhydrides,<sup>32-34</sup> etc. but also for the polymerization of other heterocycles such as epoxides<sup>41,42</sup> or cyclic carbosiloxanes.<sup>38</sup> Interestingly, the macromolecular architectures obtained by the NHC-ZROP were found to be really sensitive to the solvent effect and more generally to the polarity of the medium. Polymerizations carried out in aprotic low- or nonpolar solvent such as THF or toluene generate mainly cyclic topologies due to strong ion-pairing between the imidazolium moiety and the propagating anion. In an opposite way, polymerizations carried out in highly aprotic polar solvents, *e.g.* DMSO or DMF, or in presence of salts (LiCl, LiBr, etc.), induce the ion pair separation and generate specifically linear polymers.<sup>30,33,41,42</sup> The mechanism of ring-closure *via* an intramolecular cyclization depends on both the nature of the monomer substrates and NHCs. As an example, the majority of cyclic polyesters are obtained by intramolecular transesterification reactions (accompanied by the NHC releasing) while the generation of cyclic poly(*N*-carboxy anhydride)s, cyclic poly( $\beta$ -butyrolactone) or poly( $\beta$ -propiolactone) is achieved by addition of the propagating anion directly on the imidazolium chain-end generating a



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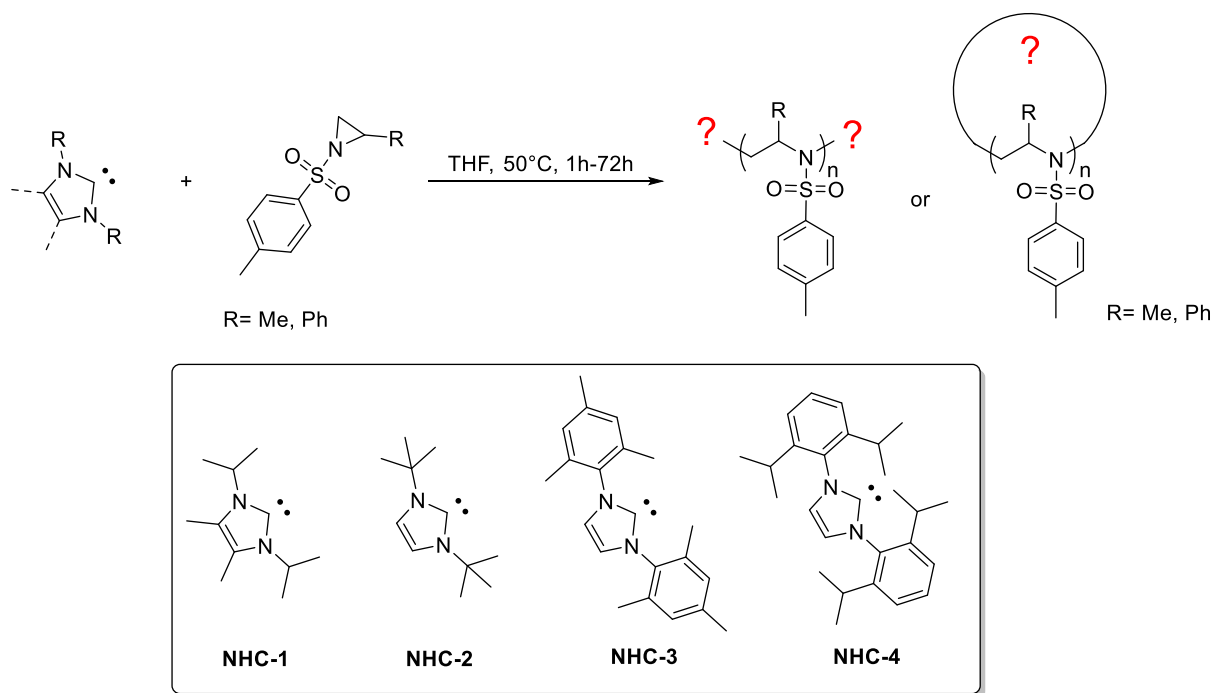
spirocyclic junction. (See Scheme 14 and 15).<sup>33</sup> Logically, we decided to study the NHC-ZROP of the *N*-sulfonyl aziridines in order to synthesize original cyclic polyaziridines architectures.



**Scheme 15.** Ring-closure mechanism *via* an intramolecular addition occurring in the ZROP of a) β-butyrolactone or β-propiolactone and b) NCA initiated by NHCs

During the investigation on the NHC-OROP of *N*-activated aziridines, for the polymerizations initiated by secondary non-activated amine or allylic alcohol, the chain-growth was shown to proceed, in some cases, by the so-called zwitterionic mechanism (see section 2.A.3.2 and 2.B.1). Based on this result, the NHC-mediated zwitterionic ring-opening polymerization behavior of the 2-methyl- and 2-phenyl-*N*-*p*-toluenesulfonyl aziridine was investigated using four different sterically hindered NHCs (NHC 1-4), named respectively 1,3-bis(*tert*-butyl)imidazol-2-ylidene (NHC-1), 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene (NHC-2), 1,3-bis(2,3-diisopropylphenyl)imidazol-2-ylidene (NHC-3) and bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (NHC-4). Polymerizations of *N*-activated aziridines were carried out at 50 °C in THF, keeping the usual conditions of NHC-OROP, in the presence of NHC as initiator (Scheme 16, Table 6). The NHC-ZROP was conducted in THF as a low polar aprotic solvent in order to preserve the strong ion-pairing between the imidazolium moiety and the propagating anion for the purpose of generating cyclic poly(*aziridine*)s.

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**Scheme 16.** NHC-ZROP of 2-alkyl-*N*-*p*-toluenesulfonyl aziridine (THF, 50 °C, 1h-72h)

In any case, regardless of the monomer substrate or the NHC initiator, the polymerization occurs, but depending on the nature of the side substituents of the NHC catalysts, completely different polymerization behaviors were observed. Fast polymerization of 2-methyl-*N*-*p*-toluenesulfonyl aziridine within a few hours, complete conversion and molar masses increasing with the initial ratio  $[Az]_0/[NHC]_0$  were firstly observed for the less-sterically hindered NHC-1 and NHC-2 (Run 1-3 and 6-8, Table 6). As already mentioned, the experimental molar masses are underestimated by the SEC calibration with PS standards. Nevertheless, SEC traces of polymerization initiated by NHC-1 and -2 presented in Figure 31.a and b. exhibited, in both cases, higher molar masses than those predicted by the initial feed ratio  $[Az]_0/[NHC]_0$  and bimodal distribution regardless of the molar mass targeted. The discrepancy between the experimental and theoretical molar masses was already observed for the NHC-ZROP of lactide initiated by <sup>IMes</sup>NHC. The unusual kinetic features of these zwitterionic polymerizations of lactide were illuminated with kinetic and mechanistic investigations and implicate a mechanism that involves a slow and incomplete initiation step and a propagation step that is much faster than initiation.<sup>74</sup> The NHC-ZROP of *N*-activated aziridines initiated by NHC-1 or -2 exhibits probably the same polymerization features, *i.e.* low initiation efficiency and a fast propagation step as compared to the initiation step.

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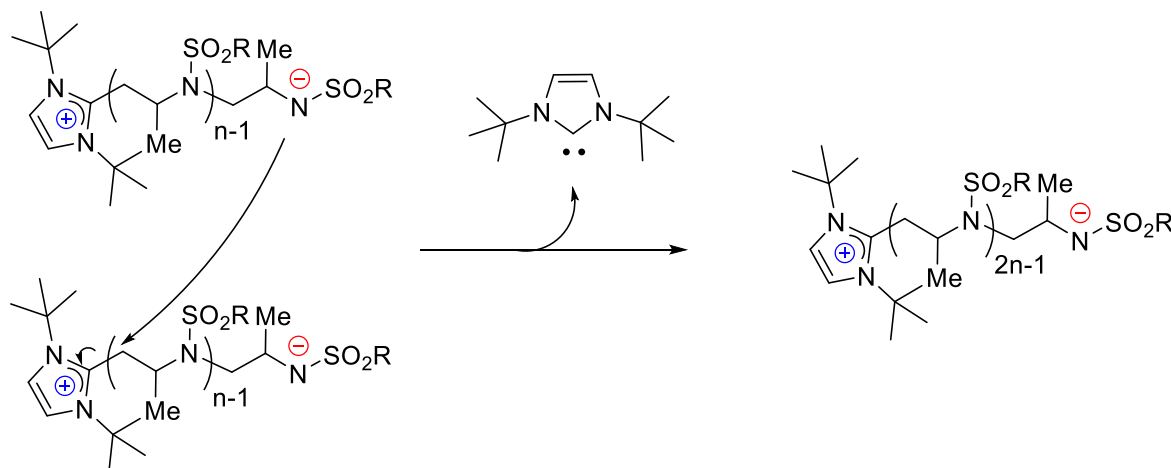
**Table 6.** NHC-ZROP of 2-alkyl-*N*-*p*-toluenesulfonyl aziridine (THF, 50 °C, 1h-48h)

Run	R	NHC	[Az]/[NHC]	Time (h)	Conv(%) <sup>a</sup>	$\overline{Mn}_{calcd}^c$ (g/mol)	$\overline{Mn}_{exp}^b$ (g/mol)	$\overline{D}^b$
1	Me	NHC-1	20/1	6	100	4 200	13 000	1.10 <sup>d</sup>
2	Me	NHC-1	50/1	10	100	10 600	22 000	1.06 <sup>d</sup>
3	Me	NHC-1	100/1	24	100	21 100	32 200	1.06 <sup>d</sup>
4	Ph	NHC-1	20/1	48	95	4 200	9 100	1.29
5	Me	NHC-2	20/1	1	100	4 200	7 100	1.22
6	Me	NHC-2	50/1	4	100	10 600	16 300	1.20
7	Me	NHC-2	200/1	24	100	42 200	60 000	1.25
8	Ph	NHC-2	20/1	24	99	5 400	-	-
9	Me	NHC-3	20/1	48	100	4 200	3 300	1.06
10	Me	NHC-3	50/1	72	57	6 000	4 300	1.12
11	Ph	NHC-3	20/1	72	80	3 400	3 200	1.08
12	Me	NHC-4	20/1	24	100	4 200	3 500	1.06
13	Me	NHC-4	50/1	48	97	10 600	6 000	1.09
14	Me	NHC-4	150/1	72	98	31 700	20 200	1.05

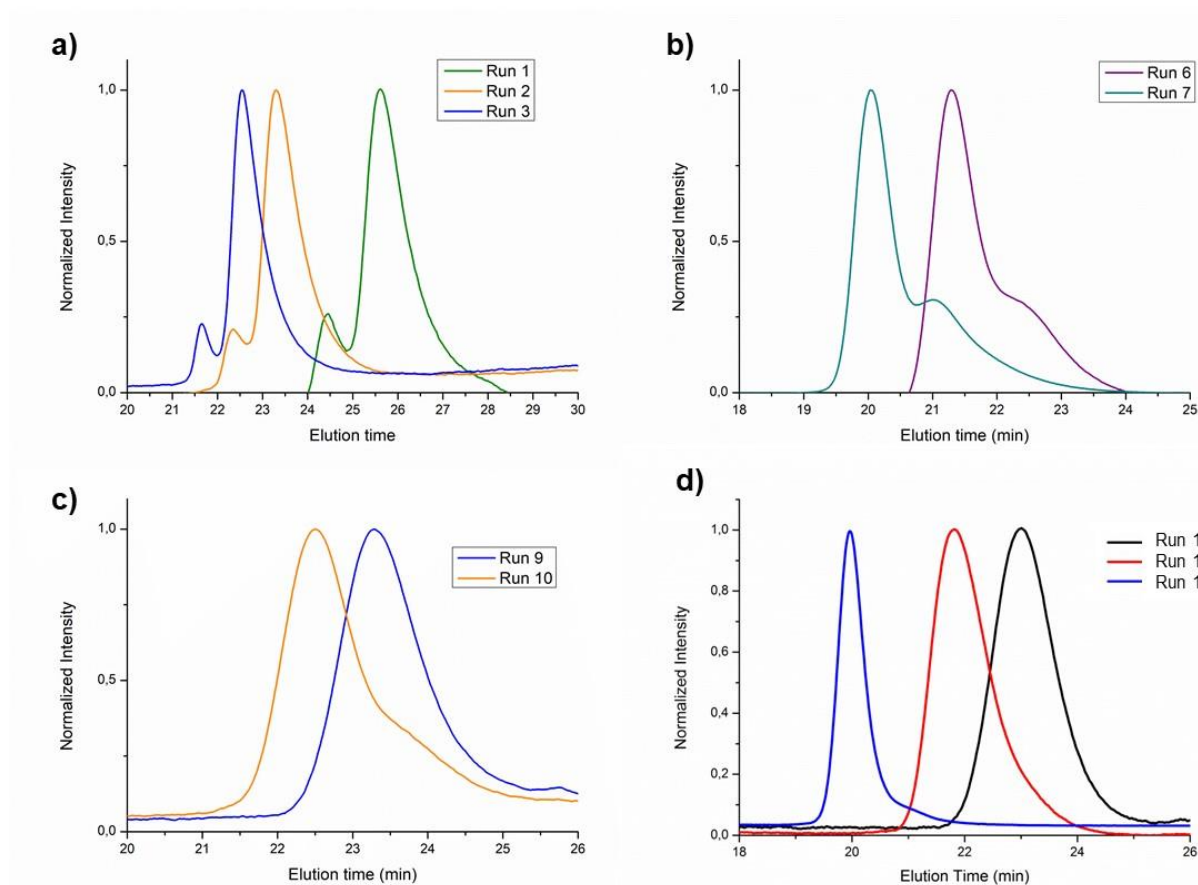
<sup>(a)</sup> Determined by NMR <sup>1</sup>H, <sup>(b)</sup> determined by SEC in THF (PS calibration), <sup>(c)</sup>  $\overline{Mn}_{calcd} = ([Az]/[NHC]) \times M_{Az} \times \text{conv.}$  <sup>(d)</sup> molar mass and dispersity determined for the main population

In the case of ZROP initiated by NHC-1, a second population in the high molar masses region, which corresponds roughly to twice the molar mass (based on the peak molar mass) of the main population is readily observed in Figure 31.a. Indeed, coupling reactions were already observed for the NHC-OROP of the less reactive 2-phenyl-*N*-*p*-toluenesulfonyl aziridine initiated by secondary *N*-sulfonyl amine (see section 2.A.1), and was suggested to occur at high monomer conversion by the intermolecular nucleophilic addition of the “aza-anion” on the imidazolium chain-end of another macrozwitterion (see Scheme 17).

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**Scheme 17.** Proposed zwitterionic coupling for the NHC-ZROP of poly(2-methyl-*N*-*p*-toluenesulfonyl aziridine) initiated by NHC-1

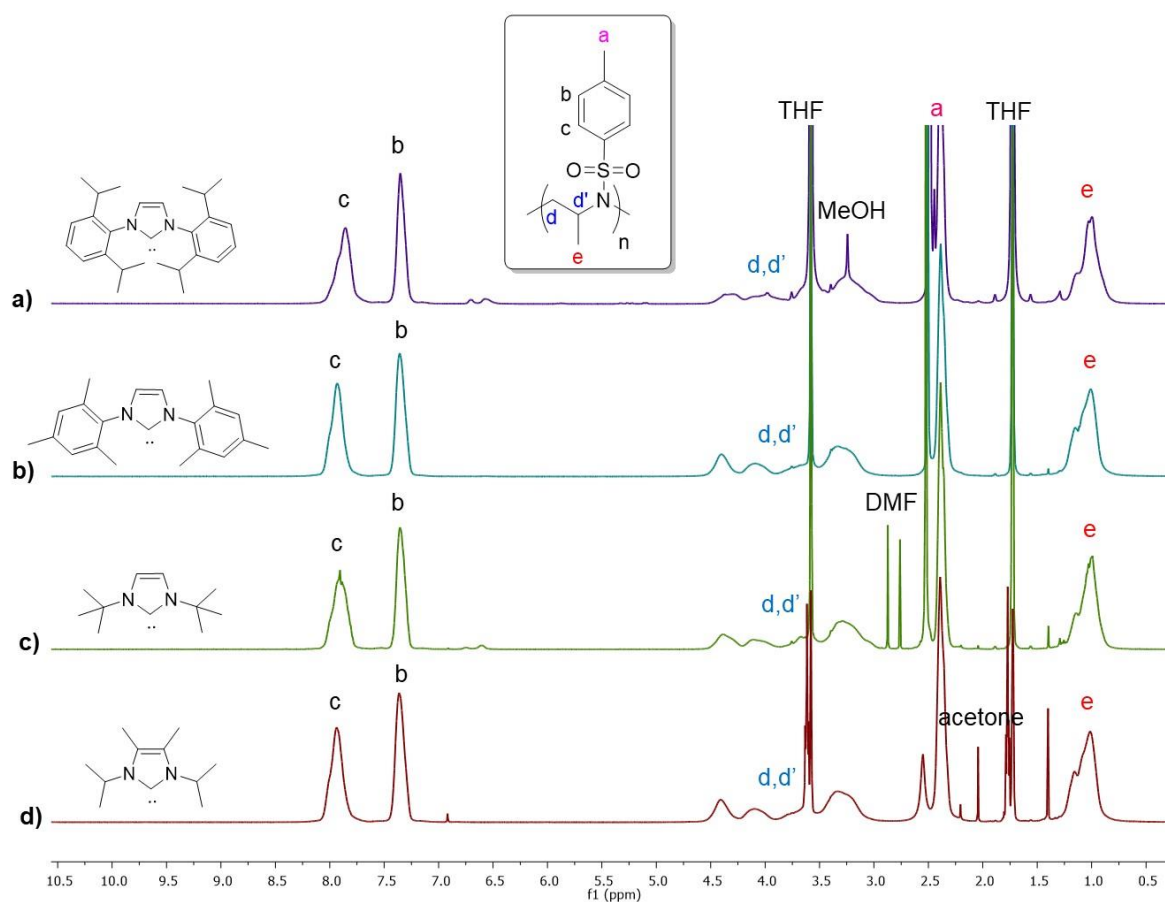


**Figure 31.** NHC-ZROP SEC traces of poly(2-methyl-*N*-*p*-toluenesulfonyl aziridine) initiated by a) NHC-1, b) NHC-2, c) NHC-3 and d) NHC-4

On the other hand, the NHC-ZROP initiated by the sterically hindered NHC-3 and NHC-4 exhibited longer polymerization times, almost complete conversions, monomodal distribution and molar masses close to the values expected by the initial feed ratio  $[Az]_0/[NHC]_0$ . Despite good control over the molar masses and low dispersities ( $\mathcal{D} \leq 1.12$ ), the polymerizations

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initiated by NHC-3 displayed some limitations. Indeed, the attempts to increase the molar mass (by increasing the  $[Az]_0/[NHC]_0$  molar ratio) of the PAz have failed and only incomplete conversions were observed (Run 10, Table 6). In contrast, the NHC-4 bearing dimesityl (IMes) substituent allowed the control of the polymerization of the *N*-tosyl aziridine yielding well-defined PAz up to  $20\,200\text{ g}\cdot\text{mol}^{-1}$  with good control over the molar masses and low dispersities ( $D \leq 1.09$ ). Typical  $^1\text{H}$  NMR spectra of purified PAz initiated by NHCs are presented in Figure 33, and display all the expected signals of PAz though small signals corresponding to residual solvents were observed, no signals corresponding to an imidazolium moiety, spirocyclic junction or other chain-ends are discernable. The absence of chain-end signals could be caused by several reasons such as (i) the formation of cyclic polymers obtained by intramolecular cyclization with the concomitant release of the NHC, (ii) overlapping between the chain-end signals and the broad PAz signals, (iii) the nucleophilic substitution of the imidazolium chain-end by MeOH during the purification step.

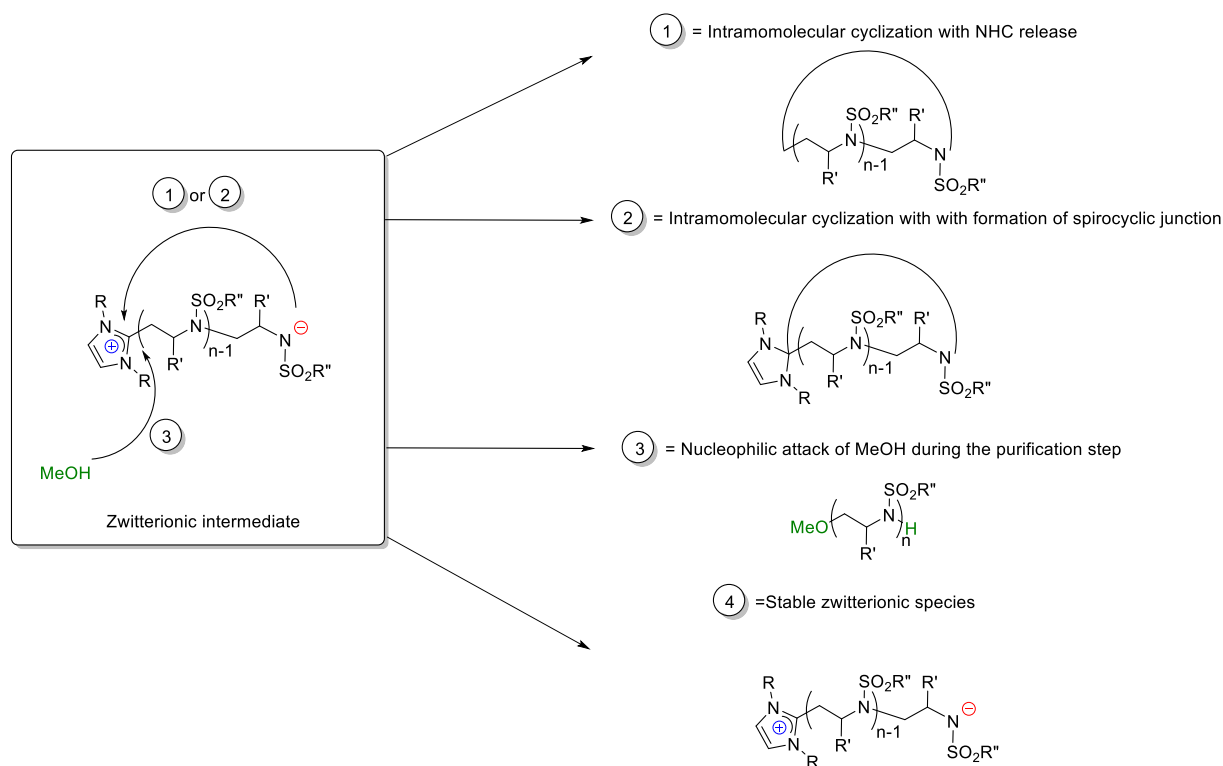


**Figure 32.**  $^1\text{H}$  NMR spectra (THF- $d_8$ ) of poly(2-methyl-*N*-*p*-toluenesulfonyl aziridine) initiated by a) NHC-3 (Run 9, Table 6), b) NHC-4 (Run 12, Table 6), c) NHC-1 (Run 1, Table 6) and d) NHC-2 (Run 5, Table 6)

Based on the background literature regarding other examples of NHC-mediated ZROP, four PAz structures with no or different chain-ends were expected and displayed in Scheme 18. As

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already mentioned the generation of cyclic topologies was observed by two distinct mechanisms through the intramolecular by addition on the NHC moiety or by nucleophilic substitution accompanied by the NHC release (Scheme 18.1 and 2). Generally, PAz were quenched by the addition of large excess of methanol and further precipitated in the latter, which may lead to an  $\alpha$ -methoxy PAz by nucleophilic substitution of the imidazolium chain-end (Scheme 18.3). In addition, *N*-Heterocyclic carbenes are relatively poor leaving groups and the propagating “aza-anion” was found to be relatively stable and insensible to the presence of a large amount of protic impurities such as alcohols and even water (see section 2.B.1.2). Consequently, the generation of a stable macro-zwitterion in which each chain bears one imidazolium-based cation and one “aza-anion” cannot be excluded (Scheme 18.4).

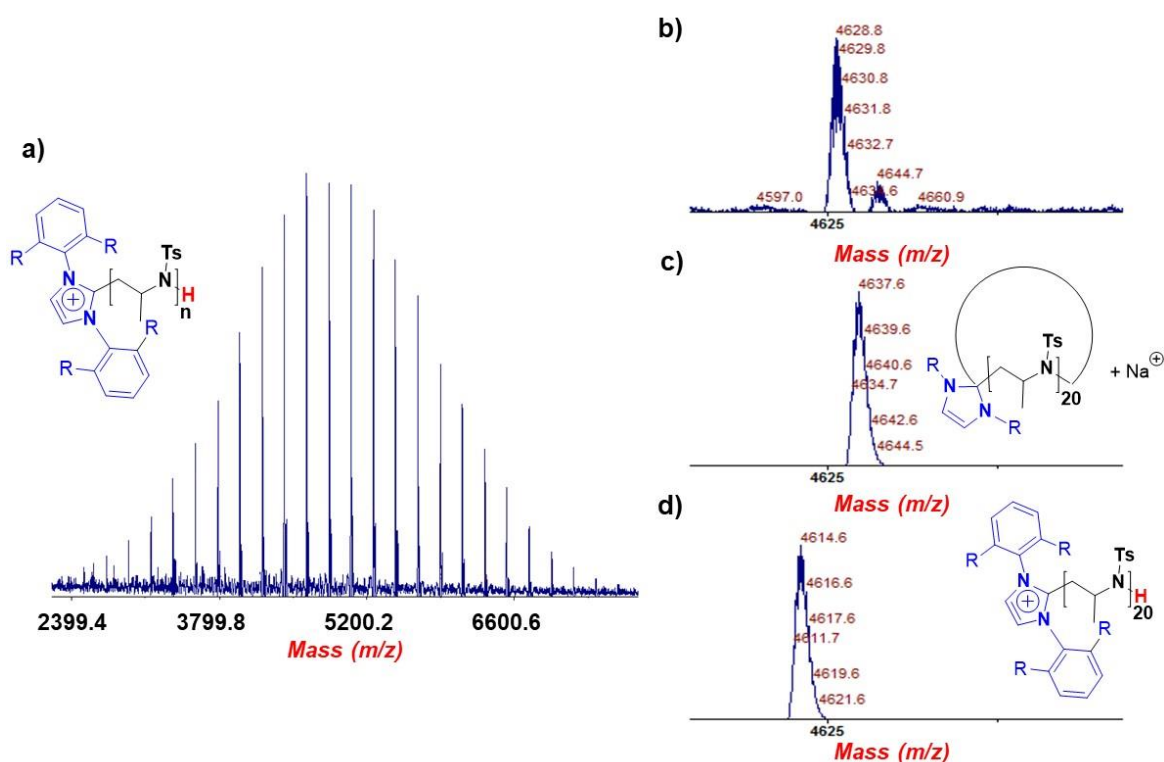


**Scheme 18.** Plausible reactions generating linear and cyclic topologies.

MALDI-Tof mass spectrometry analysis of a purified PAz (Run 9, Table 6) initiated by NHC-3 is presented in Figure 33. A single population, corresponding to a cationized PAz bearing a methyl side chain, with a peak-to-peak mass increment of  $211.3 \text{ g.mol}^{-1}$  (molar mass of one monomer unit) was readily observed. However, a discrepancy between the computed spectra of the expected cyclic or linear structure (Figure 33.c and d) and the experimental data (Figure 33.a and b) was also noted. Indeed, for the expected cationized cyclic structure, a difference of  $\Delta m/z = -9$  was noticed while a difference  $\Delta m/z = +14$  was observed for the linear one. The

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generation of  $\alpha$ -methoxy PAz (simulated spectrum not presented in Figure 33) was also excluded ( $(m/z)_{\text{expected}} = 4699.86$  for a sodium cationized adduct with a  $\overline{\text{DPn}}$  of 21). Exactly the same results were observed for the polymerization initiated by NHC-4. The synthesis of high molar mass PAz ( $\overline{\text{Mn}} \geq 7\,200 \text{ g}\cdot\text{mol}^{-1}$  vs. PS standards) for the polymerization initiated by NHC-1 or-2 prevented any accurate analyses by MALDI ToF mass spectrometry under those conditions. Unfortunately, precise characterization results by  $^1\text{H}$  NMR spectroscopy and mass spectrometry are lacking to conclude about the generation of cyclic or linear topologies. In addition, many key parameters of NHC-ZROP such as the solvent effect, the influence of the NHC concentration as well as kinetic features, need to be further explored.

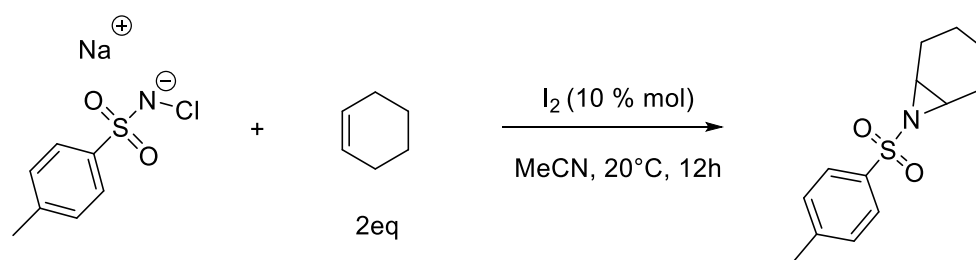


**Figure 33.** Experimental (a, b) and computed (c, d) MALDI ToF mass spectrum of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) initiated by NHC-3 (Run 9, Table 6). \* The second population at  $\Delta(m/z)=+16$  corresponds to potassium ionization.

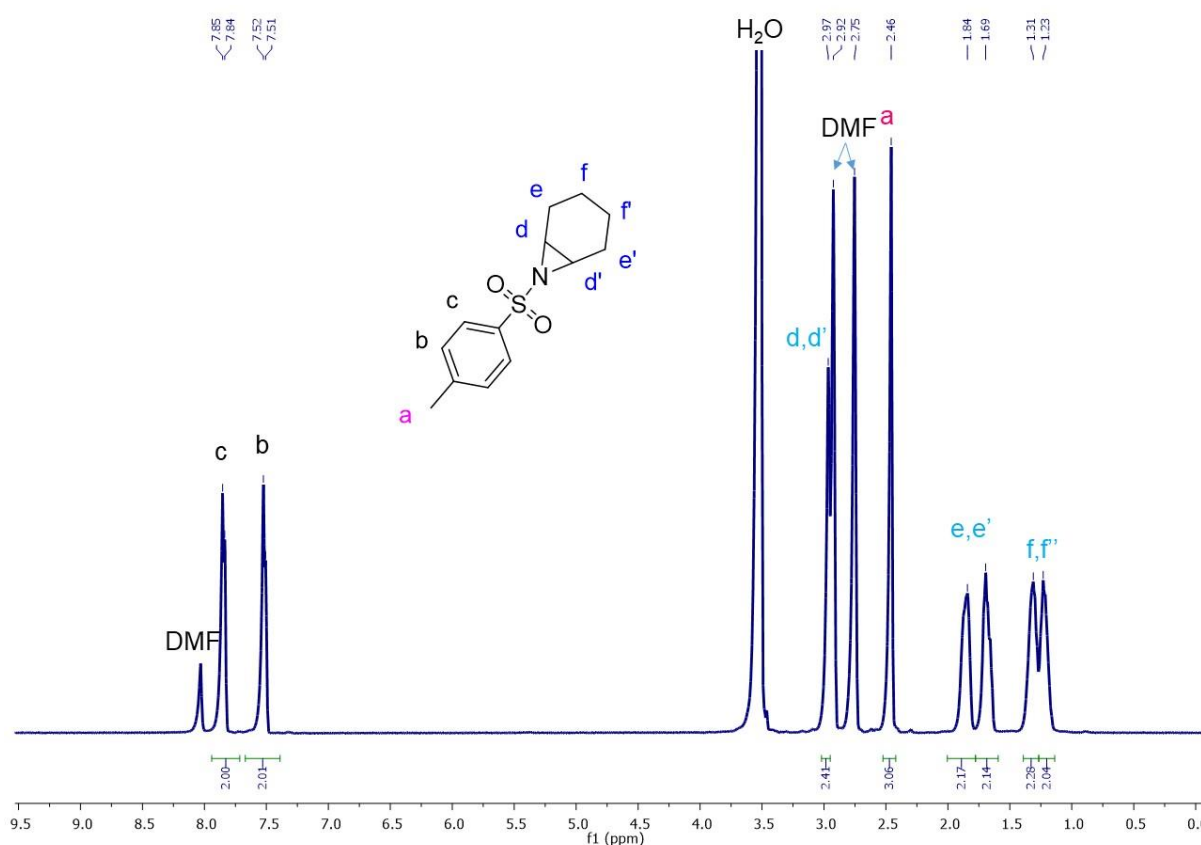
In order to gain a better understanding and to elucidate the mechanism of NHC-ZROP of *N*-tosyl aziridines, molecular model reactions were performed through the ring-opening reaction of a non-polymerizable monomer, namely 7-tosyl-7-azabicyclo[4.1.0]heptane, by the selected NHC-4, in order to isolate the hypothetical zwitterionic intermediate. The synthesis of 7-tosyl-7-azabicyclo[4.1.0]heptane was performed by reacting cyclohexene, *N*-chloro-*N*-sodio-*p*-

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toluenesulfonamide (Chloramine T) and a catalytic amount of iodide ( $I_2$ ) using the same procedure already involved for the synthesis of racemic 2-phenyl *N*-*p*-toluenesulfonyl aziridine (78%, Scheme 19).<sup>66</sup> The efficiency of the aziridination reaction was demonstrated by NMR spectroscopy analysis ( $^1H$  and  $^{13}C$ ), which display all the signals expected for the bicyclic *N*-activated aziridine structure (Figure 34).



**Scheme 19.** Synthesis of 7-tosyl-7-azabicyclo[4.1.0]heptane



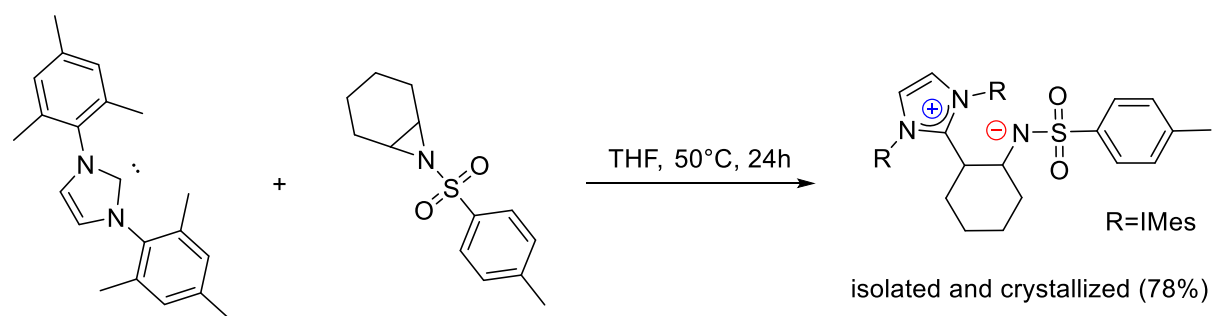
**Figure 34.**  $^1H$  NMR spectrum (DMF- $d_7$ ) of purified 7-tosyl-7-azabicyclo[4.1.0]heptane

The molecular ring-opening reaction was then performed in THF at 50 °C by reacting a equimolar amount of 7-tosyl-7-azabicyclo[4.1.0]heptane and the NHC-4, which was selected for its good performances during the NHC-ZROP (Scheme 20). The resulting imidazolium-



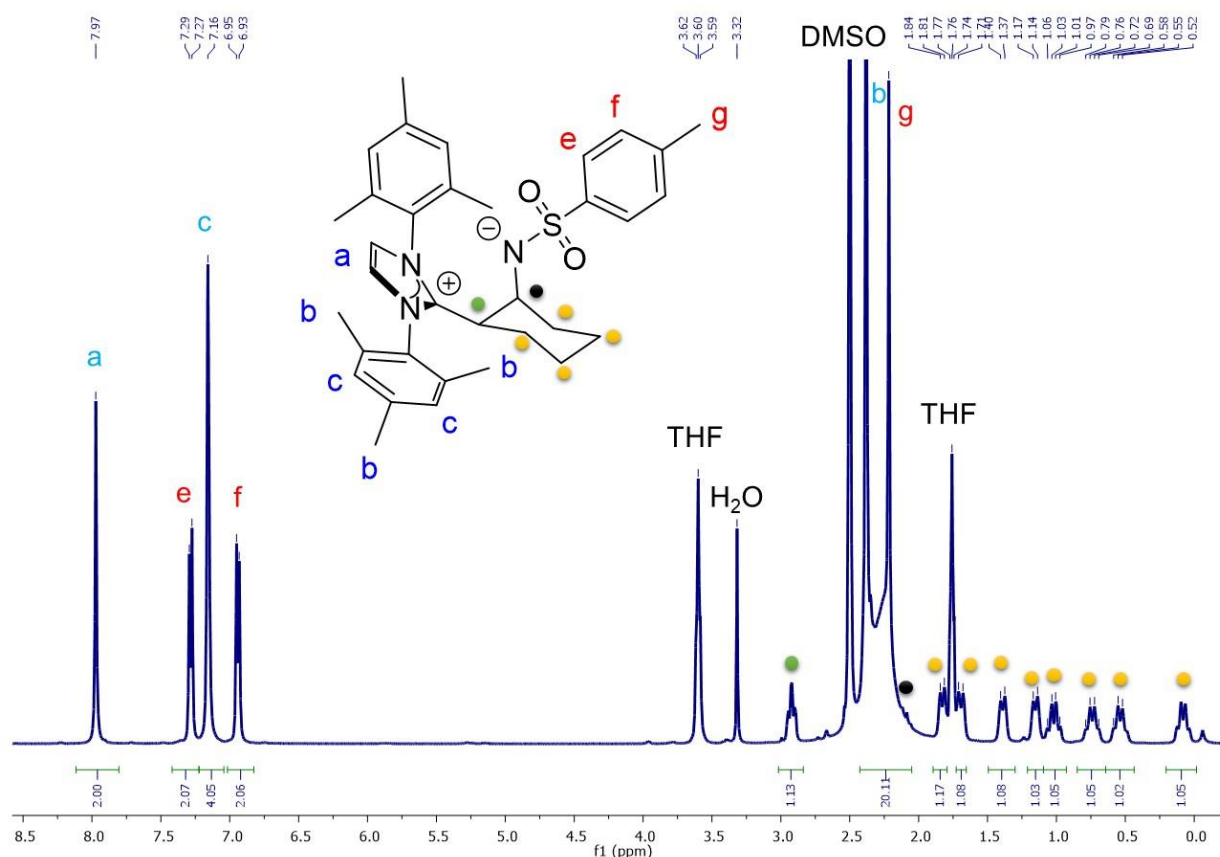
## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

based zwitterion precipitated in THF, was simply purified by washing the white solid with dry THF (yield = 78 %). This isolated mono-adduct was analysed by NMR spectroscopy ( $^1\text{H}$ ,  $^{13}\text{C}$  (Figure S.12), COSY (Figure S.13) and HSQC (Figure S.14)) and further crystallized for XRD analysis (Figure 35 and 36).



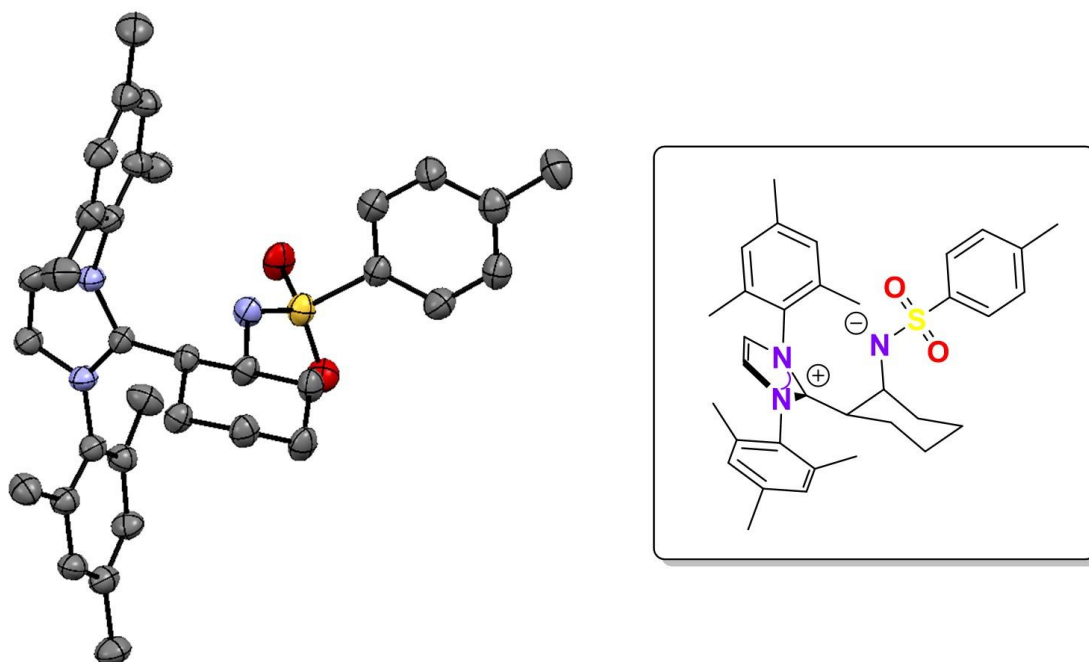
**Scheme 20.** Generation of zwitterionic by mono-addition of the NHC-4 on the 7-tosyl-7-azabicyclo[4.1.0]heptane

$^1\text{H}$  NMR analysis of the isolated zwitterion (presented in Figure 35) obtained by the addition of the NHC-4 on the bicyclic aziridine-based monomer, exhibits all the expected signals and relative integrations for a mono-adduct structure. Signals of the imidazolium moiety are readily observable at  $\delta(\text{ppm}) = 7.97$ ; 7.16 and 2.29. The broad signal observed between 2.0 and 2.5 ppm, which corresponds to the  $\text{CH}_3$  of the mesityl substituent, has been attributed to the existence of different conformations, thus multiplying the chemical environments. The addition of the NHC-4 on the bicyclic structure, which modifies the initial symmetry of the latter, is also characterized by the appearance of diastereotopic signals attributed to the cyclohexane ring at  $\delta(\text{ppm})=1.82$ ; 1.73; 1.38; 1.16; 0.99; 0.77; 0.55 and 0.09.



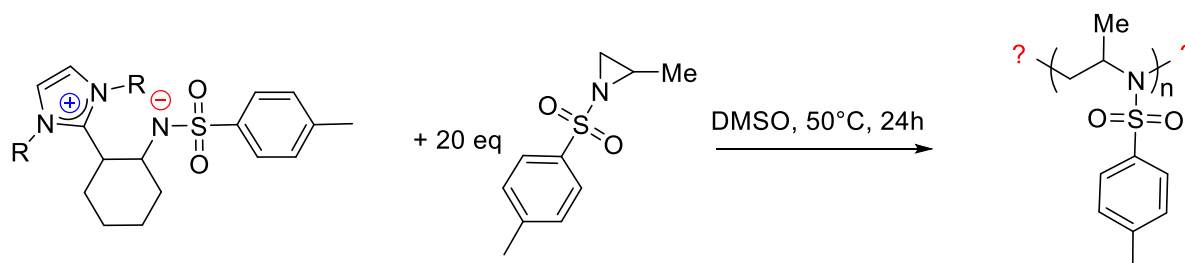
**Figure 35.**  $^1\text{H}$  NMR analysis ( $\text{DMSO-}d_6$ ) of the zwitterionic mono-adduct

The crystallographic structure of the mono-adduct was further obtained by XRD analysis (Figure 36) and confirmed the proposed zwitterionic structure which displayed on the same molecule an imidazolium moiety as cation and the “aza-anion” as counter-cation. To our knowledge, this is the first example of an isolated zwitterionic intermediate obtained by mono-addition of NHC on a monomer substrate. As already mentioned, only spirocyclic compounds were isolated by the addition of saturated carbene, namely dimesitylimidazolin-2-ylidene with four-membered lactones such as  $\beta$ -butyrolactone and  $\beta$ -propiolactone. The isolation of mono-adduct zwitterionic could serve as a model in order to determine its reactivity towards various nucleophiles and to elucidate the particular mechanism occurring in the NHC-ZROP of *N*-tosyl aziridines.



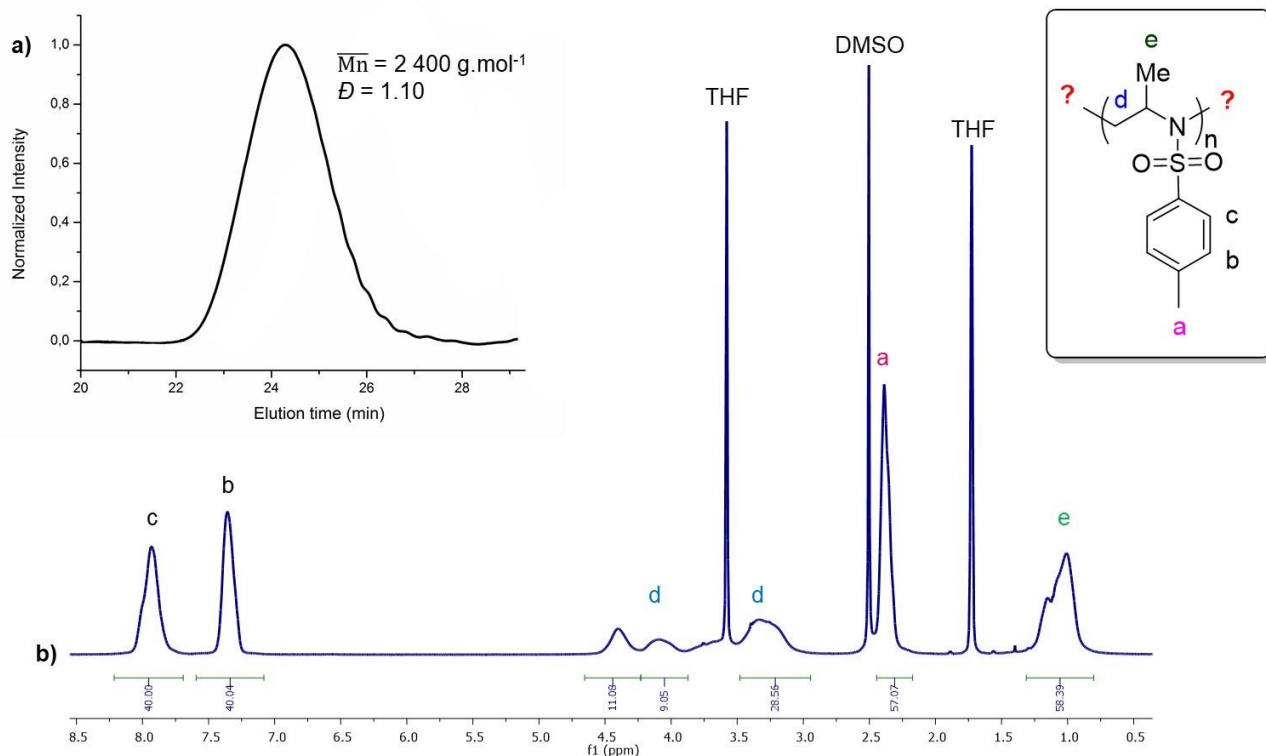
**Figure 36.** DRX analysis of the zwitterionic mono-adduct (hydrogen atoms were omitted for better clarity)

Nonetheless, the so-obtained zwitterion was further used directly as an initiator for the ZROP of 2-methyl *N*-*p*-toluenesulfonyl aziridine in DMSO, instead of THF due to the low solubility of the zwitterion in THF, at 50 °C (See scheme 21).



**Scheme 21.** Polymerization of 2-methyl *N*-*p*-toluenesulfonyl aziridine initiated by the zwitterion mono-adduct (DMSO, 50°C, 24h)

After 24h at 50°C, complete conversion of the aziridine monomer, good control over the molar mass and low dispersity ( $\overline{M}_n = 2\,400\text{ g.mol}^{-1}$ ,  $D = 1.10$ ) were observed, as attested by SEC analysis presented in Figure 37.a. Surprisingly and as observed for the NHC-ZROP initiated by sterically hindered NHC-3 and -4, the signals of the expected imidazolium cyclohexyl chain-end were absent, and only signals of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) were readily observed in the  $^1\text{H}$  spectrum of the purified PAz (Figure 37.b).



**Figure 37.** a) SEC traces (THF) and b)  $^1\text{H}$  NMR spectrum (THF- $d_8$ ) of purified PAZ obtained by polymerization 2-methyl *N*-*p*-toluenesulfonyl aziridine at 50 °C, in DMSO initiated by the zwitterion mono-adduct

In the last part of this chapter dedicated to the organocatalyzed polymerization of *N*-activated aziridine, the preliminary results of the NHC-mediated zwitterionic ring-opening polymerization of 2-methyl *N*-*p*-toluenesulfonyl aziridine and of 2-phenyl *N*-*p*-toluenesulfonyl aziridine were presented. Four different sterically hindered NHCs were employed in order to produce original cyclic PAz structures. Interestingly, regardless of the monomer substrate or the NHC initiator, the ZROP was shown to occur, but depending on the nature of the side substituents of the NHCs, completely different polymerization behavior were observed. Fast polymerization and high molar masses PAz with bimodal distributions were noticed by using less sterically hindered NHC, namely 1,3-bis(*tert*-butyl)imidazol-2-ylidene (NHC-1) and 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene (NHC-2). In contrast, ZROP initiated by highly sterically hindered NHC, namely 1,3-bis(2,3-diisopropylphenyl)imidazol-2-ylidene (NHC-3) and bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (NHC-4), exhibited low polymerization rates, good control over the molar masses and low dispersities. Promising results of ZROP of *N*-activated aziridines were obtained using the so-called bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (NHC-4). Unfortunately, characterizations of PAz by

## Chapter 2. *N*-Heterocyclic carbene organocatalyzed ring-opening polymerization of *N*-tosyl aziridines

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combining NMR spectroscopy and MALDI ToF mass spectrometry analyses, have not allowed the accurate determination of both chain-ends and macromolecular topologies. Model reactions were also performed through the preparation, the isolation and the complete characterization of a zwitterionic intermediate resulting from the addition of the NHC-4 on a non-polymerizable bicyclic *N*-tosyl aziridine monomer. Finally, the zwitterionic mono-adduct was used directly as an initiator for the polymerization of 2-methyl *N*-*p*-toluenesulfonyl aziridine yielding PAz with controlled molar mass and low dispersity ( $\mathcal{D} \leq 1.10$ ). Overall, the NHC-ZROP paves the way to achieve original aziridine-based macromolecular topologies.

However many keys parameters were not investigated in this thesis and need to be further developed in order to complete the promising preliminary results of the NHC-ZROP of those particular monomers, such as:

- A precise determination of the macromolecular topology and accurate determination of the chain-ends.
- The effect of the NHC concentration on the zwitterionic coupling observed for NHC-ZROP initiated by the less strically hindered NHCs.
- Kinetic investigations for each NHC initiator by  $^1\text{H}$  real-time NMR spectroscopy.
- Synthesis of aziridine-based block copolymer.
- Model reactions on the zwitterionic intermediate to determine the sensitivity towards nucleophiles of the active species involves in the NHC-ZROP of *N*-tosyl aziridines.

## Conclusion

One decade after the first description of anionic ring-opening polymerization of *N*-sulfonyl aziridines by Toste, Bergman *et al.*,<sup>53</sup> the potential of *N*-activated aziridines is just starting to develop. As an example, more than 20 papers have been published over the last three years playing around the anionic polymerization of *N*-activated aziridines.

During this thesis work, polyaziridines (PAz) were synthesized for the time by “living/controlled” NHC-OROP of 2-methyl and 2-phenyl-*N*-*p*-toluenesulfonyl aziridine, in the presence of activated secondary amine, functional, non-activated amine and amino-alcohol initiators. Excellent control over the molar masses, high chain-end fidelity and narrow dispersities ( $\bar{D} \leq 1.20$ ) were achieved, as attested by NMR spectroscopy, size exclusion chromatography and MALDI ToF mass spectrometry. This method has also been applied to achieve well-defined all PAz-based block copolymers by sequential OROP using a carbene catalysis. PAz precursors consisting of an alkene or an azide functionality were further derivatized, highlighting the accessibility of those functional groups.

Non-protected and non-activated aminoalcohol initiators were found to provide a direct access to metal-free well-defined  $\alpha$ -hydroxy- $\omega$ -amino- and  $\alpha,\alpha'$ -bishydroxy- $\omega$ -amino telechelics PAz, thus demonstrating the tolerance to the presence of non-protected hydroxyl groups. The as-obtained hydroxyl-ended PAz were further derivatized by reaction with phenylisocyanate. Moreover, block copolymer synthesis were readily achieved by sequential NHC-OROP of 2-methyl-*N*-*p*-toluenesulfonyl aziridine and L-lactide starting from  $\alpha$ -hydroxy- $\omega$ -amino telechelics PAz in a highly chemoselective process and open the way to achieve original block copolymer structures.

The preliminary results of NHC-mediated zwitterionic ring-opening polymerization of the *N*-tosyl aziridines, as a potential synthetic pathway to generate cyclic poly(aziridine)s, has been also reported. Kinetic of polymerization as well as macromolecular dimensions of the so-obtained PAz were found to be sensitive to the nature of the NHCs employed.

As mentioned in the bibliographic chapter, the sulfonyl group can be partially removed by different method of deprotection using strong reducing or strong acidic conditions, thus

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conducting generally to chain scissions and ill-defined linear poly(ethylene imine) derivatives. Very recently, the group of F. R. Wurm proposed a new method combining mild acidic conditions and microwave irradiation, thus demonstrating the potential of poly(aziridines) to generate well-defined poly(ethylene imine)-based architectures.<sup>75</sup>

## Experimental and supporting information

### 1. Instrumentation

NMR spectra were recorded on a Bruker Avance 400 ( $^1\text{H}$ ,  $^{13}\text{C}$ , 400.2 MHz and 100.6 MHz respectively) in appropriate deuterated solvents. Molar masses were determined by size exclusion chromatography (SEC) in THF (1ml/min) with trichlorobenzene as a flow marker, using both refractometric (RI) and UV detectors. Analyses were performed using a three-column TSK gel TOSOH (G4000, G3000, G2000) calibrated with polystyrene standards. MALDI-Tof spectra were performed by the CESAMO (Bordeaux, France) on a Voyager mass spectrometer (Applied Biosystems). Spectra were recorded in the positive-ion mode using the reflectron and with an accelerating voltage of 20kV. Samples were dissolved in THF at 10mg/ml. The matrix solution (trans-3-indoleacrylic acid, IAA) was prepared by dissolving 10mg in 1ml of THF. A MeOH solution of cationisation agent (NaI, 10mg/ml) was also prepared. Solutions were combined in a 10:1:1 volume ratio of matrix to sample to cationisation agent. X-Ray diffraction data were collected on a high flux rotating anode Rigaku FRX (2.9 kW) equipped with a partial chi goniometer and a Dectris<sup>®</sup> Pilatus 200k hybrid detector at the IECB x-ray facility (CNRS UMS 3033 – INSERM US001, University of Bordeaux)

### 2. Materials

THF and THF-*d*8 were dried over sodium/benzophenone and distilled prior to use. Toluene was dried over  $\text{CaH}_2$ , refluxed overnight, distilled, and stored over polystyryllithium. Dibutylamine (Sigma-Aldrich, 99.5%) was dried over refluxed KOH pellets and distilled prior to use. Trimethylsilyl azide was dried over  $\text{CaH}_2$  and distilled prior to use. 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene, denoted as <sup>Me</sup>5-Ipr, was prepared according to the procedure already reported by Kunh *et al.*<sup>63</sup>. Aziridines were prepared according to the procedure described by T. Ando *et al.*<sup>61</sup> (R = Ph) and by F. R. Wurm *et al.* (R=Me).<sup>50</sup> Diethanolamine (Sigma-Aldrich, >98.0%) was dried by azeotropic distillation with dry toluene (three times) and further dried under vacuum overnight at 50 °C. (L)-Lactide (Sigma-Aldrich, 98.0%) was recrystallized three times from dry toluene. Phenyl isocyanate (Sigma-Aldrich, >98.0%) and hexamethylene diisocyanate (Sigma-Aldrich, >99.0%) were used as received. All polymerizations were conducted under Argon atmosphere at 50 °C. Allylamine (Sigma-Aldrich, 99%), propargyl acrylate (Sigma-Aldrich, 98%), N,N,N',N'',N''-Pentamethyldiethylenetriamine



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(PMDETA) (Sigma-Aldrich, 99%), Copper (I) Bromide (Strem, 98%), 1-octanethiol (TCI, 98%), 2,2-dimethoxy-2-phenylacetophenone (DMPA) (Sigma-Aldrich, 99%) and 4-methylbenzene sulfonylchloride (Alfa Aesar, 98%) were used as received. All polymerizations were conducted under Argon atmosphere at 50°C.

### 3. General procedures

#### *N*-hexyl *N*-*p*-toluenesulfonylamine Synthesis.

In a flame-dried Schlenk was introduced 1.0 g (5.25 mmol) of 4-methylbenzene sulfonylchloride under argon flux. Then dried DCM (5 mL) was introduced under vacuum. The solution was cooled to 0°C before added 1.37 mL (10.5 mmol, 2eq) of 1-hexanamine under argon flux. After 24h at RT, the mixture was diluted by adding 5 mL of DCM and 10 mL of water. The organic phases were extracted with DCM (3×20 mL), washed with brine (3×20 mL) and dried over MgSO<sub>4</sub>. After evaporation of the solvent, the product was recovered as a white crystalline powder (98%), dried 12h under vacuum at room temperature, and stored in the glovebox.

**RMN <sup>1</sup>H (400MHz, 298K, THF-*d*8):**  $\delta$ (ppm)= 7.62 (d, 2H, *CH*(Ar), *J*=8Hz); 7.24 (d, 2H, *CH*(Ar), *J*=8Hz); 6.27 (t, 1H, *NH*, *J*=5.6Hz); 2.75 (q, 2H, *CH*<sub>2</sub>, *J*=6.8Hz); 1.34 (m, 2H, *CH*<sub>2</sub>); 1.25-1.1 (m, 6H, *CH*<sub>2</sub>); 0.80 (t, 3H, *CH*<sub>3</sub>, *J*=6.8Hz). **RMN <sup>13</sup>C (100MHz, 298K, THF-*d*8):**  $\delta$ (ppm)= 143.0; 140.0; 130.0; 127.8; 43.8; 32.3; 30.6; 27.2; 23.4; 21.3; 14.28.

#### *2*-methyl *N*-*p*-toluenesulfonylaziridine Synthesis

5 mL 2-methylaziridine were cryo-transferred for purification. 2-Methylaziridine (4.36 g, 76 mmol) and *N,N*-diisopropylethylamine (14.72 g, 145 mmol) were dissolved in anhydrous DCM (180 mL). The solution was cooled to -30 °C and tosylchloride (17.96 g, 94 mmol) in anhydrous DCM (30 mL) was added over a period of 45 minutes. Afterwards the reaction mixture was stirred at -30 °C for 30 minutes. Saturated aqueous sodium bicarbonate (150 mL) was added and the mixture was allowed to reach room temperature and stirred overnight. After washing with saturated aqueous sodium bicarbonate and brine, the organic phases were combined, dried over magnesium sulfate and concentrated at reduced pressure. Recrystallization from petroleum ether/ethyl acetate 5:1 yielded the product as a colorless solid (8.13g, 51%).

**<sup>1</sup>H NMR (400 MHz, 298 K, THF-*d*8):**  $\delta$ (ppm) = 7.89-7.71 (m, 2H, *CH*(Ar)), 7.37–7.28 (m, 2H, *CH*(Ar)), 2.92–2.74 (m, 1H, *CH*), 2.59 (d, *J* = 7.0 Hz, 1H, *CH*<sub>2</sub>), 2.42 (s, 3H, *CH*<sub>3</sub>(tosyl)), 2.00 (d, *J* = 4.6 Hz, 1H, *CH*<sub>2</sub>), 1.23 (d, *J* = 5.6 Hz, 3H, *CH*<sub>3</sub>). **<sup>13</sup>C NMR (100 MHz, 298 K,**

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**THF-*d*8**):  $\delta(\text{ppm}) = 144.47; 135.41; 129.75; 127.85; 35.92; 34.79; 21.68; 16.84$ .

### *2-phenyl N-p-toluenesulfonylaziridine Synthesis*

Styrene (2.0 mmol, 2.30 mL) was added to a solution of iodine (0.1 mmol, 10 mol%), Chloramine-T (1.0 mmol, 2.28g), in acetonitrile/buffer solution (1.5 mL/1.5 mL). The solution was allowed to stir at room temperature under argon atmosphere. After the addition of dichloromethane (40 mL) and water (20 mL), the phases were separated and the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (20 mL). The combined organic extracts were washed with water (20 mL x 3) and brine (20 mL), dried over  $\text{K}_2\text{CO}_3$  and concentrated to give the crude product. Purification by recrystallization (Toluene/Pentane (1/1)) gave the aziridine as a white crystalline powder (2.49g, 91% (as compared to the amount of Chloramine-T)).

**$^1\text{H}$  NMR (400 MHz, 298 K, THF-*d*8)**:  $\delta(\text{ppm}) = 7.84$  (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ), 7.36 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ), 7.24 (m, 5H,  $\text{CH}(\text{Ph})$ ) 3.76 (dd, 1H,  $\text{CH}$ ,  $J_1=7.2\text{Hz}$ ,  $J_2=4.4\text{Hz}$ ), 2.88 (d,  $J=7.2\text{ Hz}$ , 1H,  $\text{CH}_2$ ), 2.40 (s, 3H,  $\text{CH}_3(\text{tosyl})$ ), 2.34 (d,  $J=4.4\text{ Hz}$ , 1H,  $\text{CH}_2$ ).  **$^{13}\text{C}$  NMR (100 MHz, 298 K, THF-*d*8)**:  $\delta(\text{ppm}) = 137.9; 134.8; 133.6; 129.0; 128.5; 128.3; 127.8; 126.5; 41.0; 35.9; 26.7$ .

### *7-tosyl-7-azabicyclo[4.1.0]heptane Synthesis*. Same procedure (yield=78%)

**$^1\text{H}$  NMR (400 MHz, 298 K, DMF-*d*7)**:  $\delta(\text{ppm}) = 7.84$  (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ), 7.52 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ), 2.97 (m, 2H,  $2\times\text{CH}$ ), 2.46 (s, 3H,  $\text{CH}_3(\text{tosyl})$ ), 1.84 (m, 2H,  $\text{CH}_2$ ), 1.69(m, 2H,  $\text{CH}_2$ ), 1.31 (m, 2H,  $\text{CH}_2$ ), 1.23 (m, 2H,  $\text{CH}_2$ ).

### *Synthesis of N-allyl N-p-toluenesulfonylamine*

In a flame-dried Schlenk was introduced 1.0 g (5.25 mmol) of 4-methylbenzene sulfonylchloride under argon flux. Then dried DCM (5 mL) was introduced under vacuum. The solution was cooled to  $0^\circ\text{C}$  before added 0.79 mL (10.5 mmol, 2eq) of allylamine under argon flux. After 24h at RT, the mixture was diluted with 5 mL of DCM and 10 mL of water. Organic phases were extracted with DCM ( $3\times 20\text{ mL}$ ), washed with brine ( $3\times 20\text{ mL}$ ) and dried over  $\text{MgSO}_4$ . After evaporation of the solvent, the product was recovered as a yellow crystalline powder (95%), dried 12h under vacuum at room temperature, and stored in the glovebox.

**$^1\text{H}$  NMR (400 MHz, 298K, THF-*d*8)**:  $\delta(\text{ppm})= 7.70$  (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.2\text{Hz}$ ); 7.31 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.2\text{Hz}$ ); 6.61 (s, 1H,  $\text{NH}$ ); 5.71 (m, 1H,  $\text{CH}(\text{allyl})$ ); 5.12 (dd, 1H,  $\text{CH}(\text{allyl})$ ,  $J_1=1.2\text{Hz}$ ,  $J_2=17.2\text{Hz}$ ); 4.99 (dd, 1H,  $\text{CH}(\text{allyl})$ ,  $J_1=1.2\text{Hz}$ ,  $J_2=10.0\text{Hz}$ ); 3.47 (t, 2H,  $\text{CH}_2$ ,  $J=5.7\text{Hz}$ ); 2.38 (s, 3H,  $\text{CH}_3$ ).  **$^{13}\text{C}$  NMR (100 MHz, 298K, THF-*d*8)**:  $\delta(\text{ppm})= 143.1; 139.6; 135.2; 130.0; 127.6; 116.4; 46.4; 21.2$ .

***Synthesis of mono-adduct between NHC-4 and 7-tosyl-7-azabicyclo[4.1.0]heptane.***

30.0 mg (0.098 mmol) of NHC-4 and 1.0 mL was added in a flame-dried Schlenk flask in the glovebox. After removal of the Schlenk, 1.0 mL of dried THF was added under vacuum. After homogenization, the solution was cooled to 0°C, and a solution containing 24.8 mg (0.098 mmol) of 7-tosyl-7-azabicyclo[4.1.0]heptane in 1 mL of THF was added under argon flux. After 24h at 50°C, the solution (slightly orange) was filtrated under argon flux and the white solid was further washed with 3×5 mL of dried THF. The white solid (42.4 mg, yield=78%) was further crystalized by slow evaporation of THF and subsequent freezing.

**<sup>1</sup>H NMR (400 MHz, 298K, DMSO-*d*6):** δ(ppm)= 7.97 (s, 2H, CH(IMes)); 7.28 (d, 2H, CH(*tosyl*), J=7.8Hz); 7.16 (s, 4H, CH(IMes)) 6.94 (d, 2H, CH(*Ar*), J=7.8Hz); 2.82 (td, 1H, J<sub>1</sub>=17.6Hz, J<sub>2</sub>=7.2Hz); 2.29 (s, 18H, CH<sub>3</sub>(IMes)); 2.12 (s, 3H, CH(*tosyl*)); 1.83 (d, 1H, CH<sub>2</sub>(*cyclo*), J=7.6Hz); 1.72 (d, 1H, CH<sub>2</sub>(*cyclo*), J=7.6Hz); 1.37 (d, 1H, CH<sub>2</sub>(*cyclo*), J=12.4Hz); 1.15 (d, 1H, CH<sub>2</sub>(*cyclo*), J=12.4Hz); 1.03 (q, 1H, CH<sub>2</sub>(*cyclo*), J=12.8Hz); 0.75 (q, 1H, CH<sub>2</sub>(*cyclo*), J=12.8Hz); 0.56 (q, 1H, CH<sub>2</sub>(*cyclo*), J=12.8Hz) 0.08 (q, 1H, CH<sub>2</sub>(*cyclo*), J=12.8Hz). **<sup>13</sup>C NMR (100 MHz, 298K, DMSO-*d*6):** δ(ppm)= 151.87; 151.75; 140.49; 136.86; 131.71; 129.63; 129.35; 128.13; 125.58; 124.51; 67.48; 58.73; 46.61; 35.44; 27.41; 25.92; 25.58; 24.58; 21.12; 18.14.

***General polymerization procedure***

In a typical procedure, 1.0 mg (5.7 μmol) of <sup>Me</sup>5-Ipr and 14.6 mg (57 μmol) of *N*-tosylhexylamine (**3**) were added in a flame-dried Schlenk flask in the glovebox. After removal of the Schlenk, 1 mL of dried THF was added under vacuum. After homogenization, the solution was cooled to 0°C, and a solution containing 120 mg (0.57 mmol) of 2-methyl *N*-tosylaziridine in 1 mL of THF was added under argon flux. After 24h at 50°C, an aliquot of the polymerization mixture was taken to determine the conversion by <sup>1</sup>H NMR (THF-*d*8). The reaction was quenched with 1 mL of degassed MeOH and stirred 30 min. The crude product was analyzed by SEC (THF) and purify by precipitation in MeOH (twice) then wash with ether. PAz was recovered as a white solid after drying under vacuum at room temperature (12h).

**RMN <sup>1</sup>H PAz(1) (400MHz, 298K, THF-*d*8):** δ(ppm)= 8.10-7.70 (br, 2H, CH(*Ar*)); 7.50-7.20 (br, 2H, CH(*Ar*)); 4.50-3.80 (br, 1H, CH(*backbone*)); 3.80-3.00 (br, 2H, CH<sub>2</sub>(*backbone*)); 2.38 (s, 3H, CH<sub>3</sub>(*tosyl*)); 1.20-0.90 (br, 3H, CH<sub>3</sub>); 1.30-0.70 (br, 11H, *hexyl chain 3*). **RMN <sup>1</sup>H PAz(2) (400MHz, 298K, THF-*d*8):** δ(ppm)= 8.00-6.00 (br, 9H, CH(*Ar*)) ; 5.5-4.5 (br, 1H, CH(*backbone*)) ; 4.00-3.10 (br, 2H, CH<sub>2</sub>(*backbone*)) ; 2.33 (s, 3H, CH<sub>3</sub>(*tosyl*)) ; 1.30-0.70 (br, 11H, *hexyl chain 3*).

***Kinetic of polymerization***

In this procedure, 0.3 mg (1.5  $\mu\text{mol}$ ) of <sup>Me</sup>5-Ipr and 3.6 mg (15  $\mu\text{mol}$ ) of *N*-tosylhexylamine (**3**) were added in a flame-dried Schlenk flask in the glovebox, then 0.5 mL of dried THF-*d*8 was added and the solution was transferred in a flame-dried young tube. A solution containing 60 mg (0.285 mmol) of 2-methyl *N*-tosylaziridine in 0.5 mL of THF-*d*8 was added in the young tube. Conversion was determined by *in-situ* <sup>1</sup>H NMR at 50 °C during 16h by recording 1 spectrum/hour. NMR spectrum overlay and curves are presented in Fig. S9 and S10.

***Thiol-ene click chemistry***

In a Schlenk, 100.0 mg of allyl-functionalized PAz (Run 1, Table S1) and 11.5  $\mu\text{L}$  (66  $\mu\text{L}$ , 3eq) of octanethiol were added followed by 2.0 mL of THF. DMPA (0.8mg, 5% mol) was then added and the solution was irradiated during 15 min at 365 nm. The reaction was monitoring by <sup>1</sup>H NMR (THF-*d*8), the crude product was purified by precipitation twice in MeOH and dried under vacuum at room temperature (8h).

***CuAAC click chemistry***

In a flame-dried Schlenck, were added under argon 50.0 mg of azide-functionalized PAz (Run 7, Table S1), dry THF (1ml), propargyl acrylate (4 $\mu\text{L}$ , 35.2  $\mu\text{mol}$ ) and PMDETA (5.0  $\mu\text{L}$ , 24  $\mu\text{mol}$ ). The solution was then degassed by five freeze-thaw cycles and added to a degassed solution of CuBr (3.4 mg, 24  $\mu\text{mol}$ ) in THF (0.5ml). After 24h at room temperature, the crude product was purified by precipitation twice in MeOH and dried under vacuum during 12h.

***General polymerization procedure***

In a typical procedure, 0.5 mg (2.9  $\mu\text{mol}$ ) of <sup>Me</sup>5-Ipr, 150  $\mu\text{L}$  (0.2 M in THF) of 2-(methylamino) ethanol and 850  $\mu\text{L}$  of dried THF were added in a flame-dried Schlenk flask in the glovebox. After homogenization, the solution was cooled down to 0 °C, and a solution containing 120 mg (0.57 mmol) of 2-methyl *N*-tosylaziridine in 1 mL of THF was added under an argon flux. After 24h at 50 °C, an aliquot of the polymerization mixture was taken to determine the conversion by <sup>1</sup>H NMR (THF-*d*8). The reaction was quenched with 1 mL of degassed MeOH and stirred 30 min. The crude product was analyzed by SEC in THF and purified by precipitation in MeOH

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(twice) then wash with ether. The PAz derivative was recovered as a white solid after drying under vacuum at room temperature (12h). The same procedure was used for NHC-ZROP.

**<sup>1</sup>H NMR PAz (400 MHz, 298K, THF-*d*8):**  $\delta$ (ppm) = 8.10-7.70 (br, 2H, CH(Ar)); 7.50-7.20 (br, 2H, CH(Ar)); 4.50-3.80 (br, 1H, CH(backbone)); 3.80-3.00 (br, 2H, CH<sub>2</sub>(backbone)); 2.38 (s, 3H, CH<sub>3</sub>(tosyl)); 1.20-0.90 (br, 3H, CH<sub>3</sub>). **<sup>13</sup>C NMR PAz (100.6 MHz, 298K, THF-*d*8; see Fig. S2 and S3):**  $\delta$ (ppm) = 143.90; 137.75; 130.20; 127.84; 55.18; 49.82; 16.05; 14.83; 13.70.

### *Functionalization of $\alpha$ -hydroxy- $\omega$ -aminotelechelic PAz using phenyl isocyanate.*

In a flame-dried Schlenk was added 40 mg (9.5  $\mu$ mol) of  $\alpha$ -hydroxy- $\omega$ -aminotelechelic PAz (Run 1, Table 1) dried by three azeotropic distillations with toluene. Phenyl isocyanate (21  $\mu$ L, 0.19 mmol, 20 eq) was then added under an argon flux and the mixture was heated up to 70 °C during 24h. The reaction was monitoring by <sup>1</sup>H NMR (THF-*d*8) and the crude product was purified by precipitation twice in MeOH and dried under vacuum at room temperature (8h).

**<sup>1</sup>H NMR (400 MHz, 298K, THF-*d*8):**  $\delta$ (ppm) = 8.66 (br, NH, 1H) 8.10-7.70 (br, 40H, CH(tosyl)); 7.50-7.20 (br, 40H, CH(tosyl)+ 4H (phenyl)); 6.90 (m, 1H, CH(phenyl)) 4.50-3.80 (br, 20H, CH(backbone)); 3.80-3.00 (br, 40H, CH<sub>2</sub>(backbone)); 2.38 (s, 60H, CH<sub>3</sub>(tosyl)); 1.20-0.90 (br, 60H, CH<sub>3</sub>).

### *Polymerization of L-lactide initiated from the $\alpha$ -hydroxy- $\omega$ -aminotelechelic PAz.*

In the glove-box, 40.0 mg of  $\alpha$ -hydroxy- $\omega$ -aminotelechelic PAz (Run 1, Table 1), dried by three azeotropic distillations with toluene, 0.2 mg (1.1  $\mu$ mol) of <sup>Me</sup>5-Ipr and 1 mL of dried THF were added in a flame-dried Schlenk flask. After homogenization, the solution was cooled down to 0 °C, and a solution containing 130 mg (0.91 mmol) of (L)-lactide in 1 mL of THF was added under argon. After 24h at 50 °C, an aliquot of the polymerization mixture was taken to determine the conversion by <sup>1</sup>H NMR in THF-*d*8 (conv. 52% after 24h). The reaction was quenched with a solution containing 10 mg of benzoic acid in 1 mL MeOH and stirred 30 min. The crude product was analyzed by SEC (THF) and purified by precipitation in MeOH at low temperature (0°C) then washed with ether. PAz-*b*-poly(lactide) was recovered as a white solid after drying under vacuum at room temperature (12h).

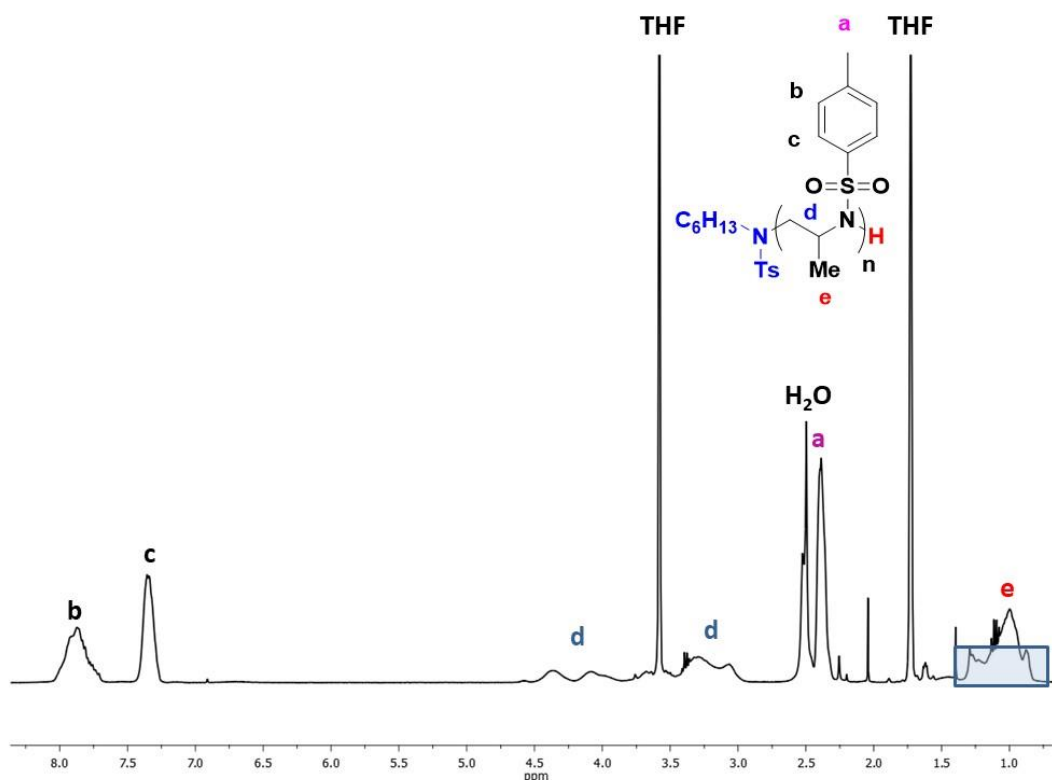
**<sup>1</sup>H NMR PAz-*b*-PLA (400 MHz, 298K, THF-*d*8):**  $\delta$ (ppm) = 8.10-7.70 (br, 40H, CH(tosyl)); 7.50-7.20 (br, 40H, CH(tosyl)); 5.16 (m, 30H, CH(PLA)); 4.50-3.80 (br, 20H, CH(PAz)); 3.80-3.00 (br, 40H, CH<sub>2</sub>(PAz)); 2.38 (s, 60H, CH<sub>3</sub>(tosyl)); 1.51 (m, 90H, CH<sub>3</sub>(PLA)); 1.20-0.90 (br, 60H, CH<sub>3</sub>).

***Step-growth polymerization of a  $\alpha,\alpha'$ -bishydroxy- $\omega$ -aminotelechelic PAz with hexamethylene diisocyanate.***

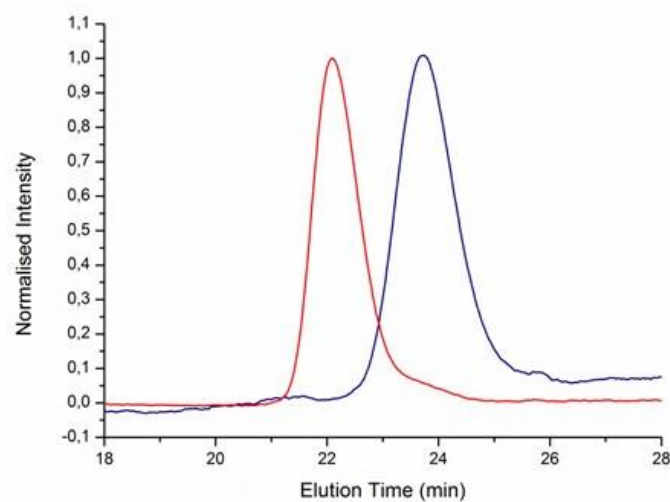
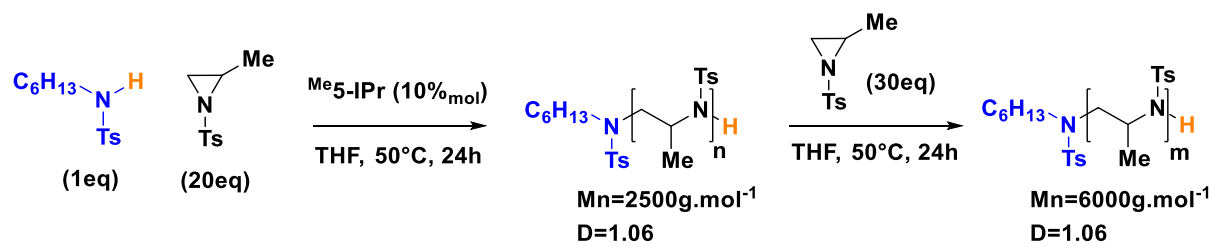
In the glovebox, 40.0 mg of  $\alpha,\alpha'$ -bishydroxy- $\omega$ -aminotelechelic PAz (Run 6, Table 1), dried by three azeotropic distillations with toluene, 0.2 mg (1.1  $\mu$ mol) of <sup>Me</sup>5-Ipr and 1 mL of dried THF were added in a flame-dried Schlenk flask. After homogenization, the solution was cooled down to 0 °C, and a solution containing 3.2  $\mu$ L (0.02 mmol) of hexamethylene diisocyanate in 1 mL of THF was added under an argon flux. After 24h at room temperature, an aliquot of the polymerization mixture was taken to determine the conversion by <sup>1</sup>H NMR (THF-*d*8). The reaction was quenched by addition of 1 mL MeOH. The crude product was analyzed by SEC (THF) and purified by precipitation in MeOH (m=32mg; 76%).

**<sup>1</sup>H NMR Paz-*b*-PLA (400 MHz, 298K, THF-*d*8):**  $\delta$ (ppm) = 8.60 (NH, urethane); 8.10-7.70 (br, 40H, CH(*tosyl*)); 7.50-7.20 (br, 40H, CH(*tosyl*)); 4.50-3.80 (br, 20H, CH(PAz)); 3.80-3.00 (br, 40H, CH<sub>2</sub>(PAz)); 2.38 (s, 60H, CH<sub>3</sub>(*tosyl*)); 1.75-1.20 (br, CH<sub>2</sub>(urethane)); 1.20-0.90 (br, 60H, CH<sub>3</sub>).

#### 4. Analyses



**Figure S1.**  $^1\text{H}$  NMR (THF- $d_8$ ) of poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) entry 1 (Table 1).

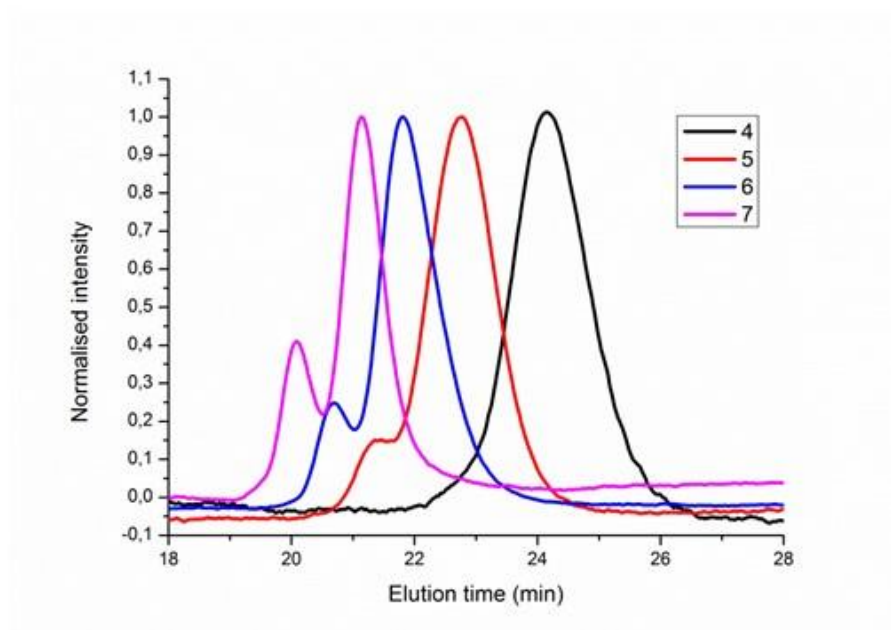


**Figure S2.** SEC traces of chain extension experiment of poly(2-methyl *N*-*p*-toluenesulfonyl aziridines)

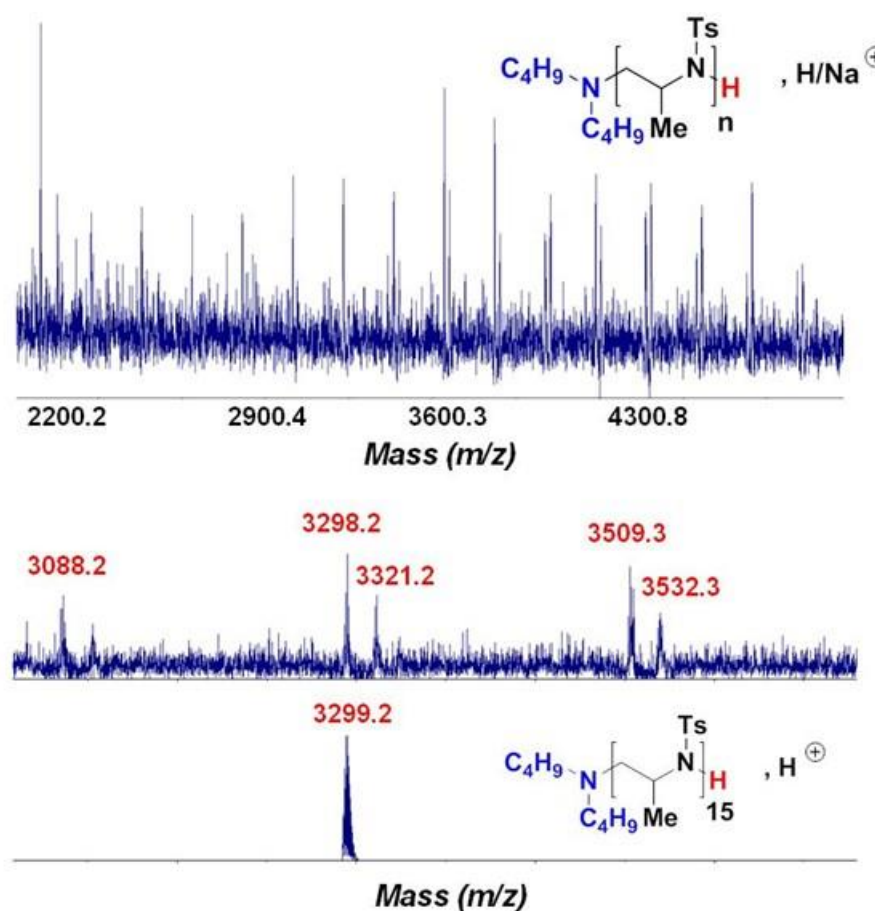
SEC chromatogram showing the elution of PAz (Me) and PAz (Me) thiol-ene. The x-axis is Elution Time (min) from 18 to 28. The y-axis is Normalised RI Intensity from -0.1 to 1.1. Both curves show a single peak at approximately 23.2 minutes, indicating similar molecular weights.

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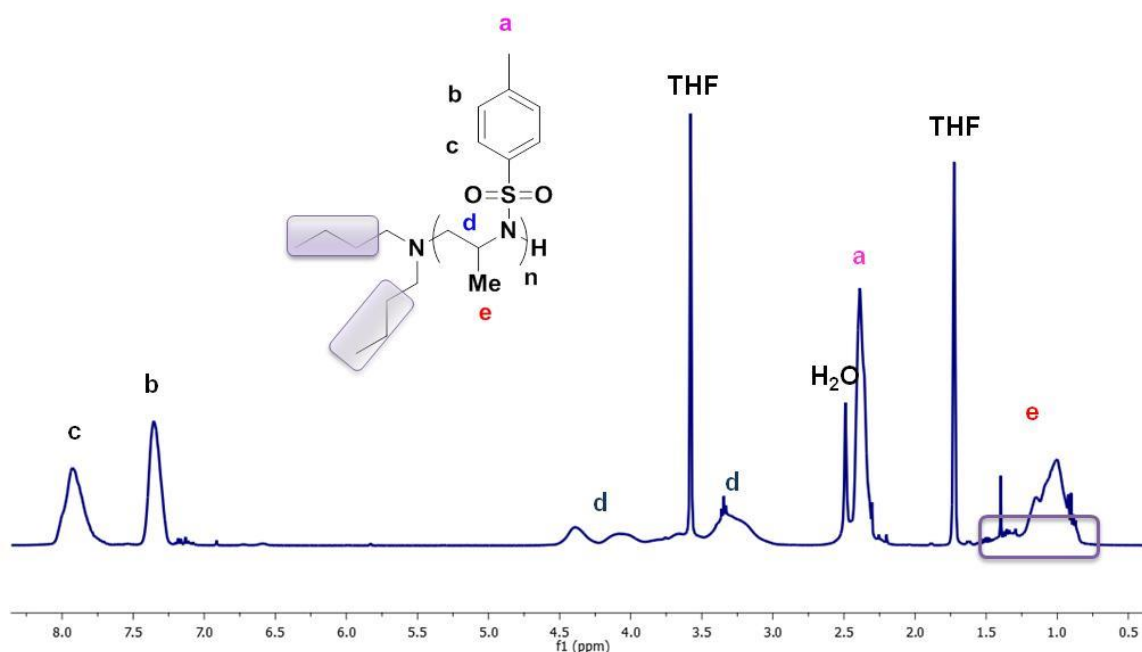




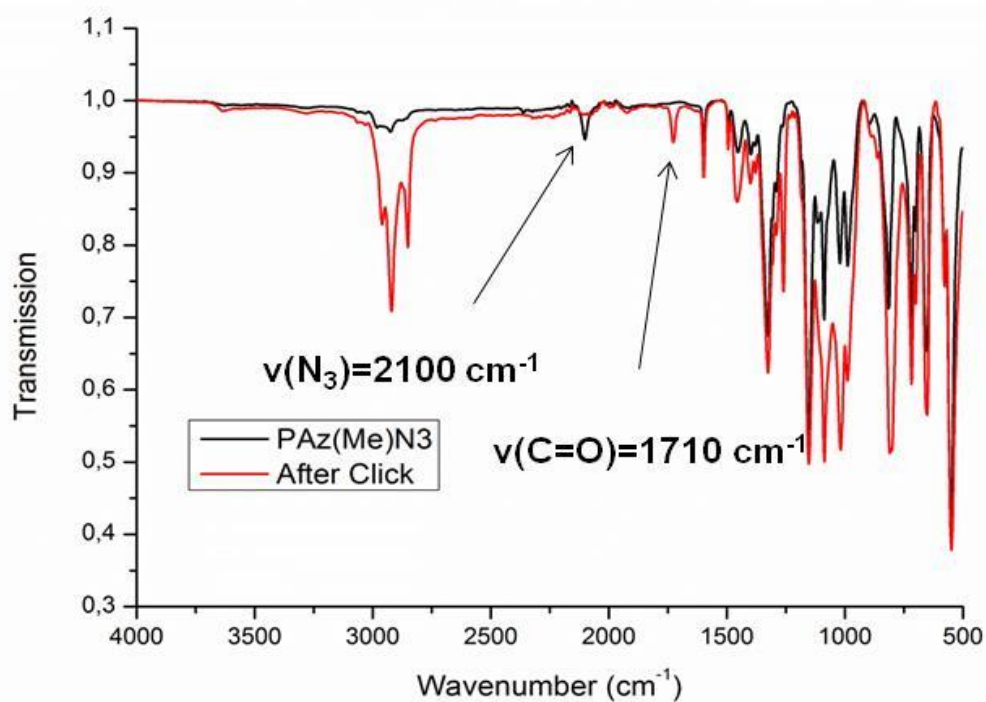
**Figure S5.** SEC traces of poly(2-phenyl *N*-*p*-toluene sulfonyl aziridine)s from di-*n*-butylamine (Run 10-13, Table 3)



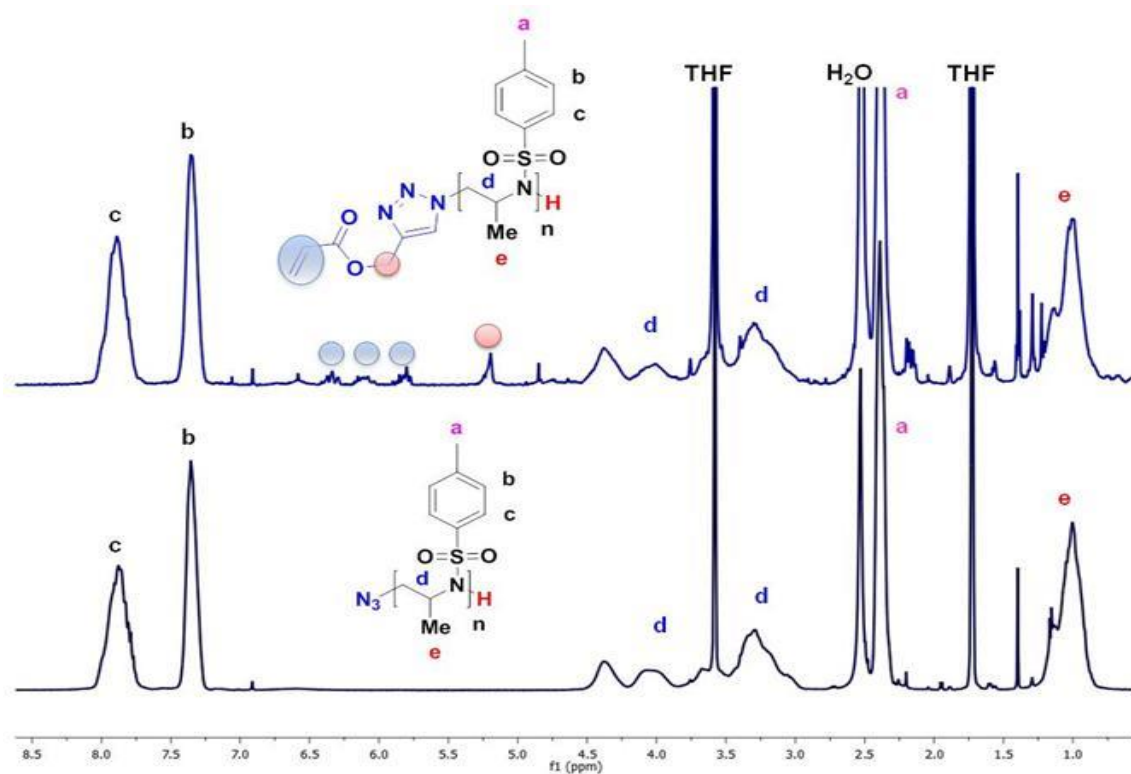
**Figure S6.** MALDI ToF mass spectrum of poly(2-methyl *N*-*p*-toluene sulfonyl aziridine)s (Table 3, entry 10).<sup>\*</sup> The second population ( $\Delta m=23$ ) corresponds to sodium ionization



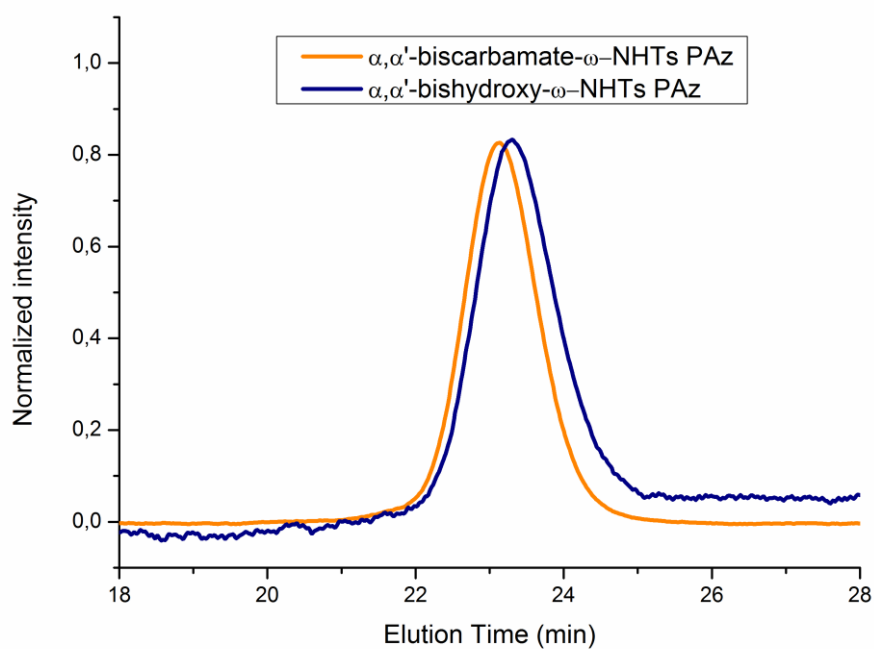
**Figure S7.**  $^1\text{H}$  NMR ( $\text{THF-}d_8$ ) spectrum of the poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) (run 7, Table 3).



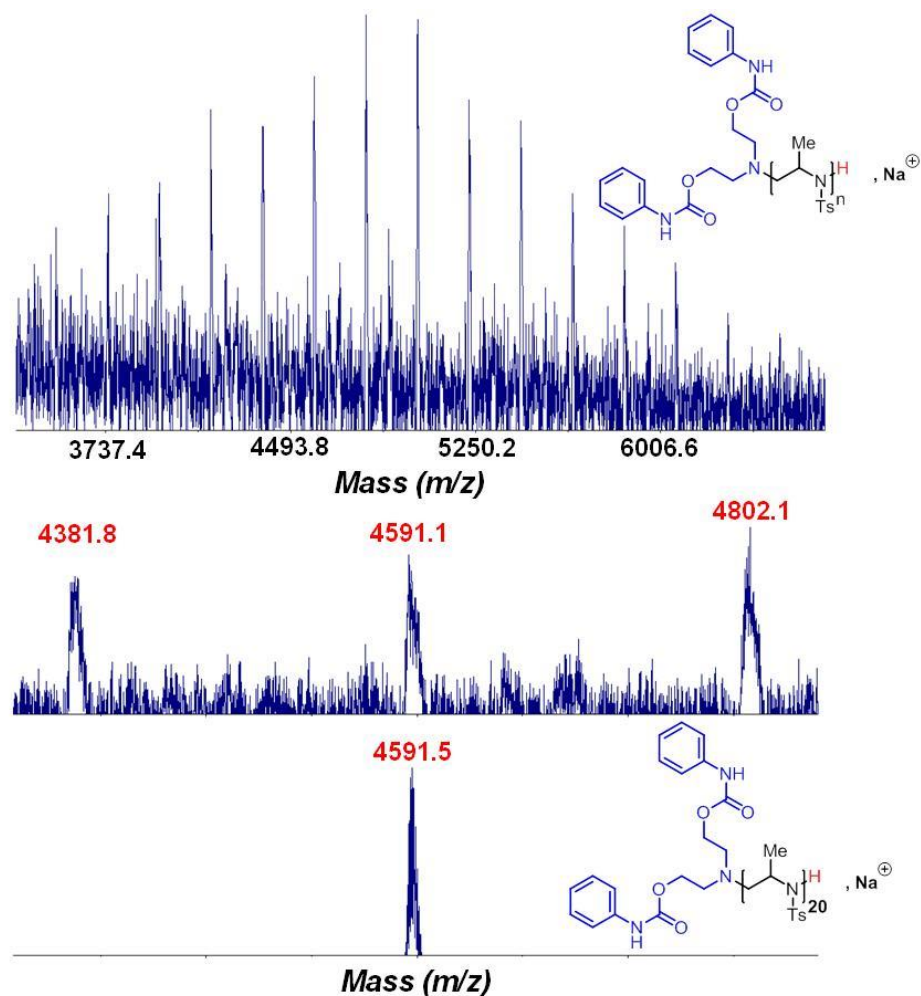
**Figure S8.** FTIR spectra before (in black) and after (in red) CuAAC click reaction



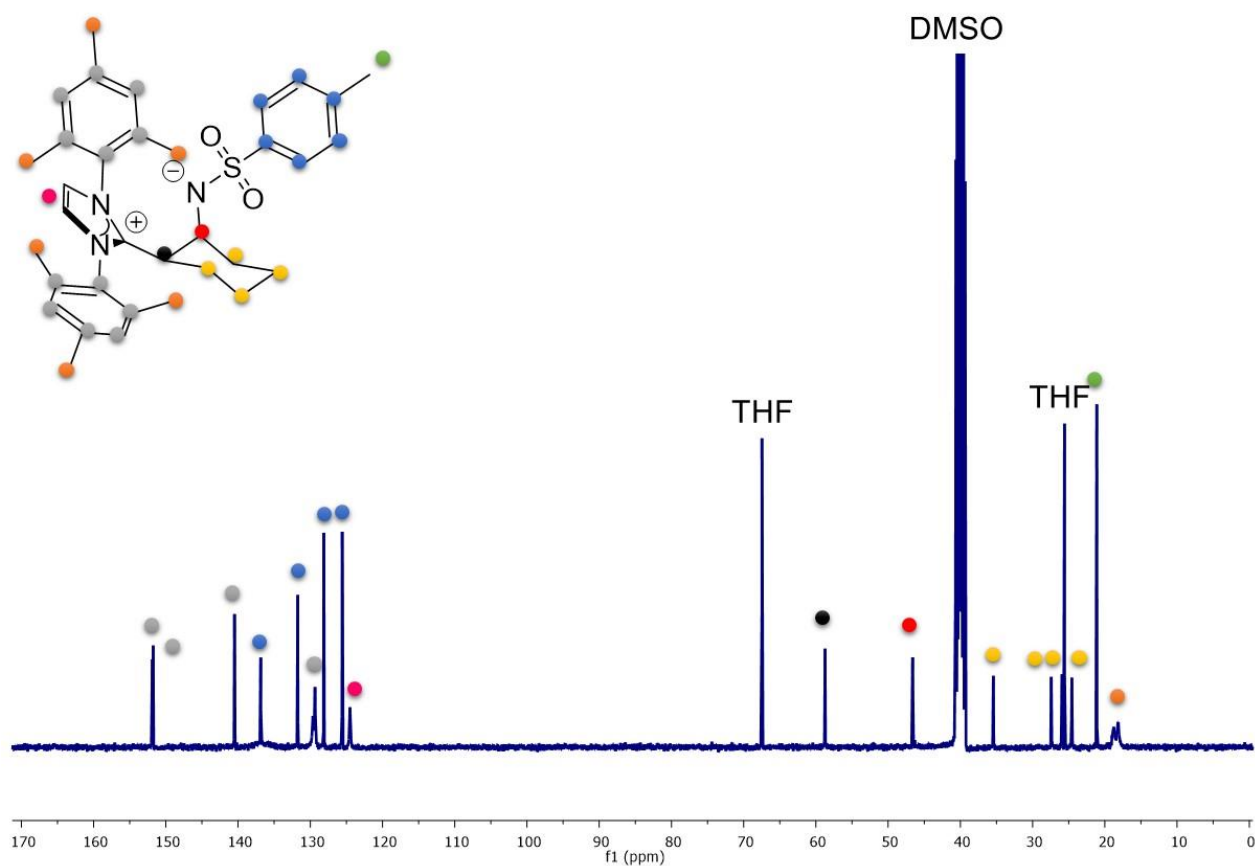
**Figure S9.**  $^1\text{H}$  NMR (THF- $d_8$ ) spectrum of the poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) (entry 14, Table 4) before and after CuAAC click reaction



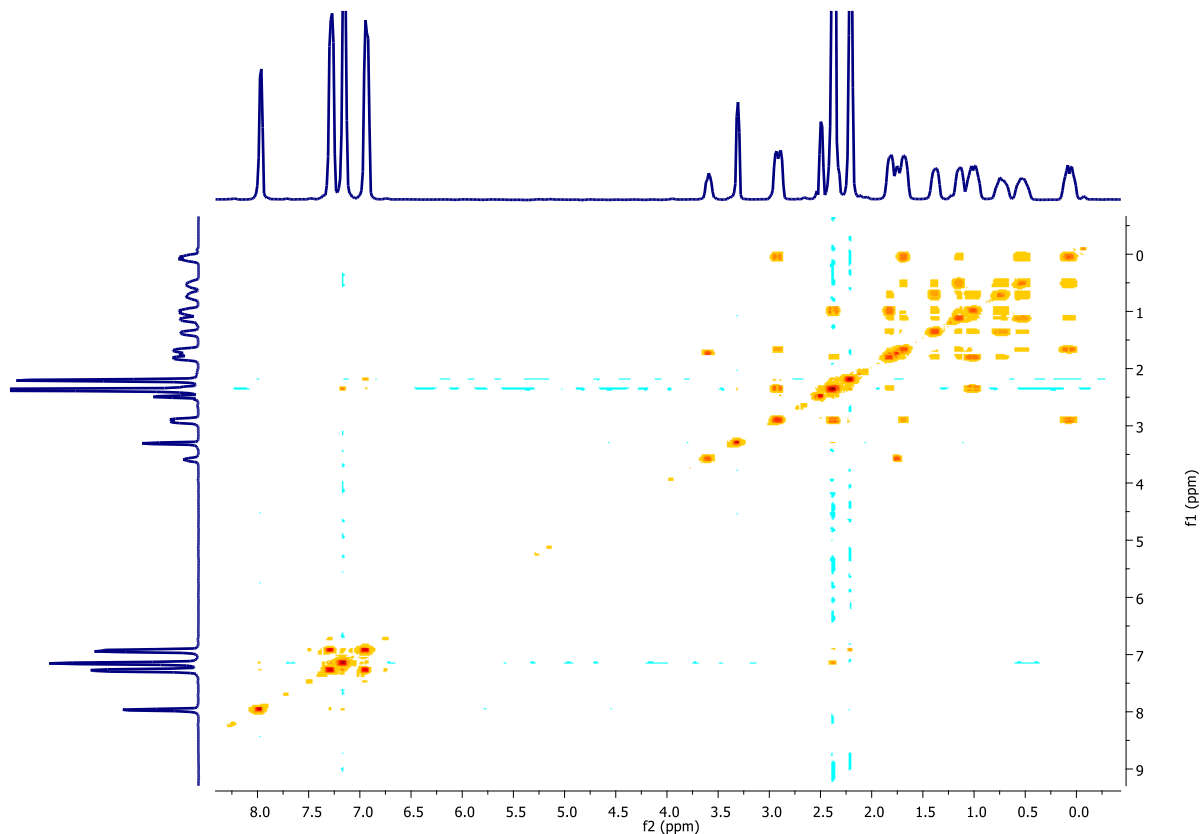
**Figure S10.** SEC traces of  $\alpha, \alpha'$ -bishydroxy-poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) before (in blue) and after (in orange) derivatization by phenylisocyanate



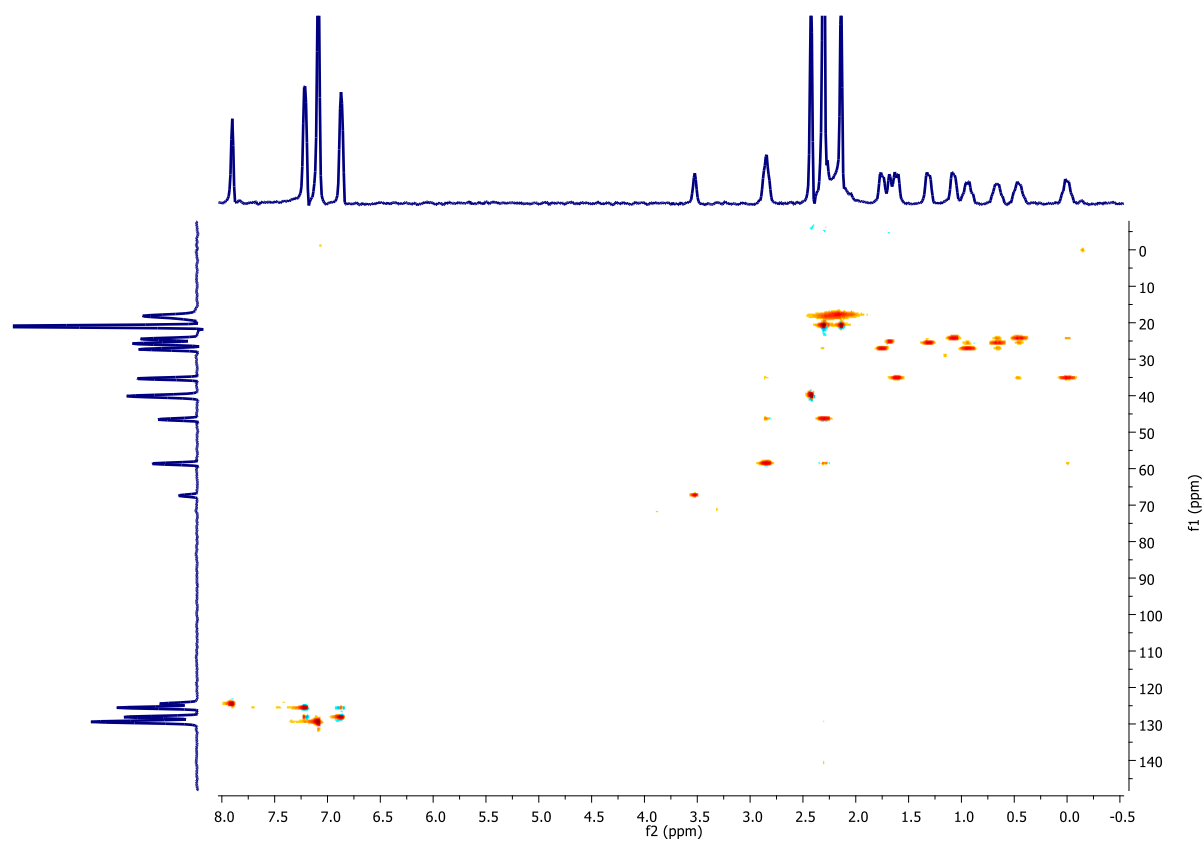
**Figure S11.** Experimental (a) and computed (b) MALDI ToF mass spectrum of a  $\alpha, \alpha'$ -biscarbamate,  $\omega$ -NH(Tosyl) poly(2-methyl *N*-*p*-toluenesulfonyl aziridine) obtained by post-functionalization with phenyl isocyanate



**Figure S12.**  $^{13}\text{C}$  NMR analysis ( $\text{DMSO-}d_6$ ) of the zwitterionic mono-adduct



**Figure S13.** COSY  $^1\text{H}$ - $^1\text{H}$  NMR analysis ( $\text{DMSO-}d_6$ ) of the zwitterionic mono-adduct



**Figure S14.** COSY  $^1\text{H}$ - $^1\text{H}$  NMR analysis (DMSO-*d*<sub>6</sub>) of the zwitterionic mono-adduct

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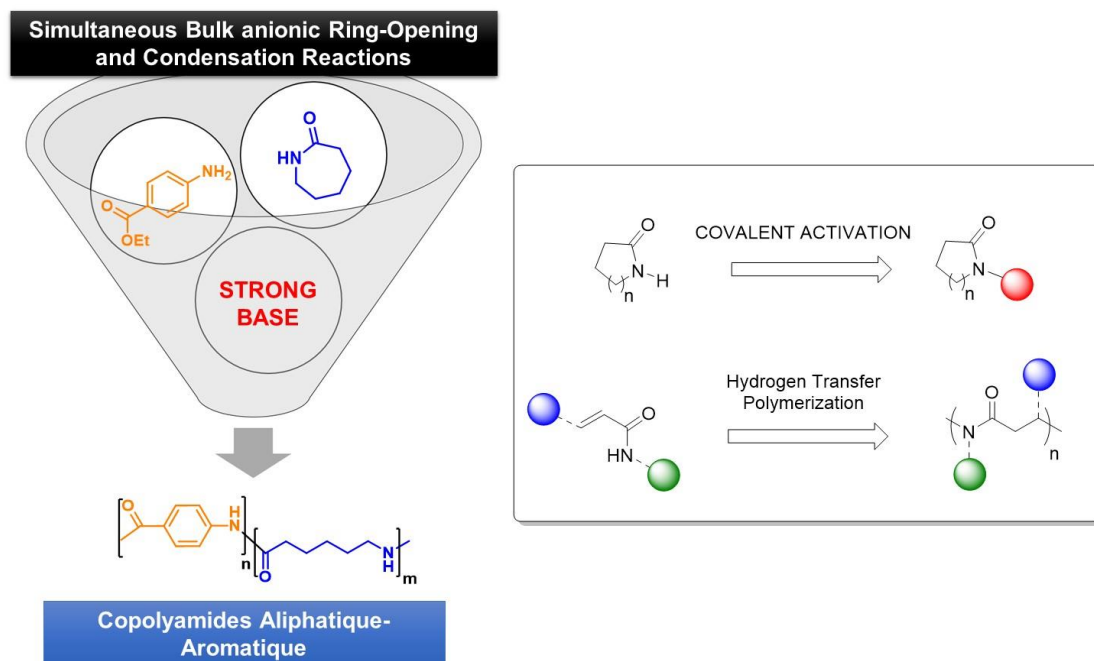
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# Chapter 3.

## Monomer Activation Strategy for the Synthesis of New Polyamides



### Publications:

1. Bakkali-Hassani, C.; Tunc, D.; Roos, K.; Planes, M.; Carlotti, S, *Macromolecules* **2017**, *51*, 175-181.
2. Bakkali-Hassani, C.; Planes, M.; Roos, K.; Wirotius, A.-L.; Ibarboure, E.; Carlotti, S, *European Polymer Journal* **2018**, *102*, 231-237.

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3. Carlotti, S.; Bakkali-Hassani, C.; Planes, M.; Roos, K. Synthèse de polyamides riche en aromatiques. **2017**, FR1659918, EP2017/076226.

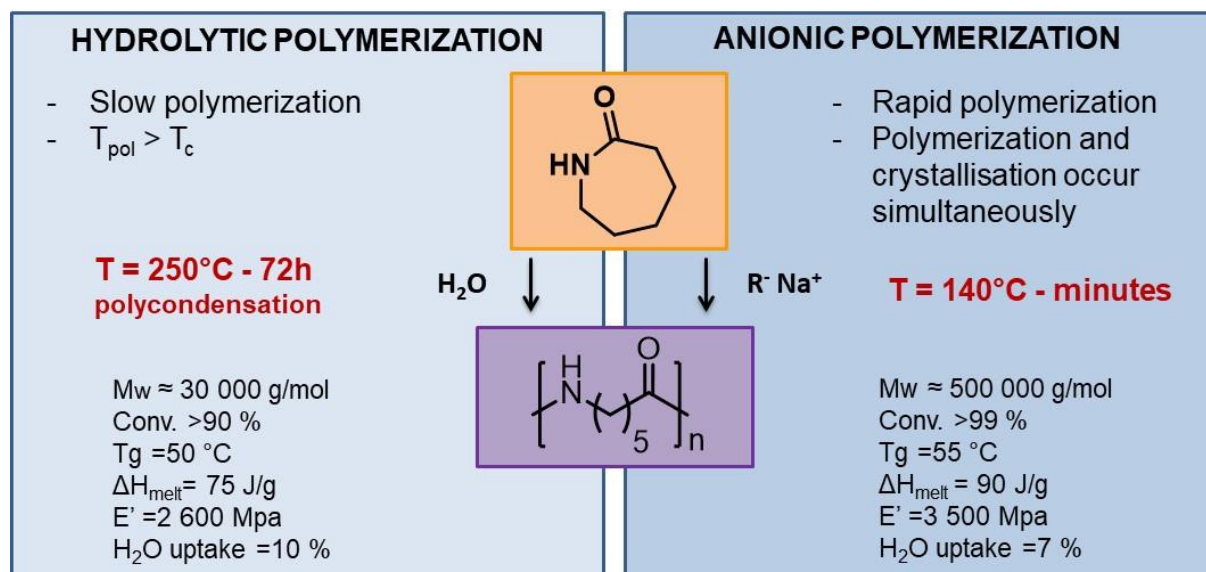
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## Introduction

Polyamides are widely used as engineering thermoplastics in a broad range of application areas due to their good mechanical properties such as tensile, flexural, and compressive strengths as well as resistance to abrasion and chemicals.<sup>1,2</sup> Polyamide 6 (PA6) is one of the most common aliphatic polyamide and represents itself roughly half of the worldwide consumption of the polyamide market ( $\approx 1.1$  million tons/year in 2012 without fiber application). Polyamide 6 is synthesized either by hydrolytic polymerization<sup>3-6</sup> or anionic ring-opening polymerization.<sup>5-9</sup> The first method requires water to ring-open  $\epsilon$ -caprolactam (CL). Reactions between amine chain-ends and the lactam and/or carboxylic group of its hydrolyzed derivative occur. This route is used industrially to form polyamide 6, though polyamides 6-6, 4-6, 6-10 are synthesized by step growth reactions between diacid and diamine monomers. Anionic ring-opening polymerization (AROP) following an activated monomer mechanism is also used to prepare polyamides 6 and 12 directly from the corresponding lactams.<sup>5-16</sup> It is the fastest method due to the low activation energy needed.

Interestingly, PA6 prepared by polycondensation (hydrolytic polymerization) or AROP are not the same materials. Differences in polymerization temperature and kinetics modify its macromolecular dimension (molar masses,  $\bar{D}$ , etc) and consequently its thermo-mechanical properties (Figure 1). AROP favors for instance the monomer conversion, the crystallinity, the elastic modulus, or decrease the water uptake and has been naturally chosen as the method of choice with the idea to play around this chemistry and to modify PA6 thermo-mechanical properties.



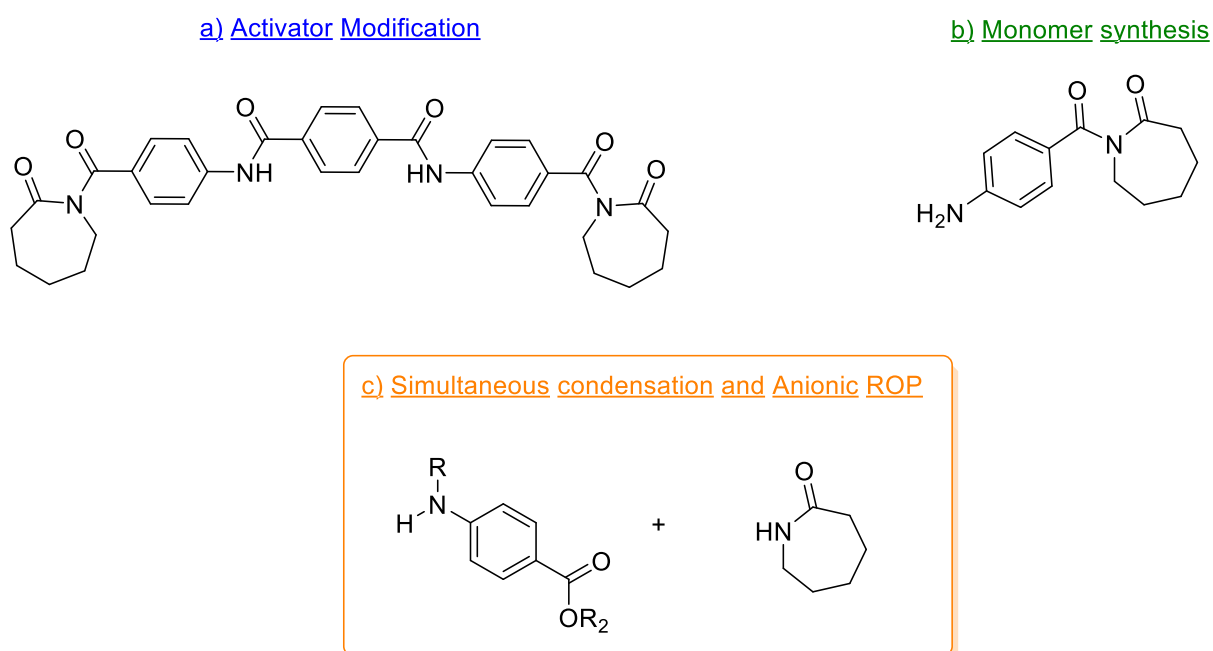
**Figure 1.** Comparison between hydrolytic polymerization and anionic ring-opening polymerization for the synthesis of polyamide 6 from  $\epsilon$ -caprolactam

Despite their high melting temperature ( $T_m=200-220^\circ\text{C}$ ) and crystallinity, PA6s exhibit relatively low glass transition temperature ( $T_g=50-55^\circ\text{C}$ ) which is a limitation for many applications. In contrast to PA6, aramids (contraction of “aromatic polyamide”) are considered as high performance organic material with outstanding thermo-mechanical properties.<sup>17</sup> Fully aromatic polyamides are also known to increase the crystallinity due to strong interaction, *i.e.* intermolecular highly directional hydrogen bonding between amide bonds and  $\pi$ – $\pi$  stacking of aromatic structures. However, their thermal degradation is generally observed before reaching their high glass transition temperature, which is problematic for processing, by injection or compression molding. To a synthetic point of view, fully aromatic polyamides are basically obtained by step-growth condensation polymerization<sup>18-20</sup> and can be also obtained in a controlled way by chain-growth condensation polymerization (CGCP) of *N*-alkyl aminobenzoate followed by deprotection.<sup>21-31</sup>

Introducing aromatic moiety in an aliphatic polyamide backbone by anionic ring-opening polymerization generally required the design of new cyclic monomers or activators to be able to introduce aromatic units.<sup>32,33</sup> The synthesis of alternating and block aliphatic-aromatic copolyamides was described using *N*-(*p*-aminobenzoyl)caprolactam. Aromatic unit can be also introduced in a polyamide backbone using a *N*-acyl lactam activator containing aromatic units (Figure 2).<sup>33</sup> Those

two examples required the modification of  $\epsilon$ -caprolactam or the activator to be able to introduce aromatic moieties into the aliphatic polymer chains.

During this thesis, we developed the combination of anionic ring-opening and condensation reactions which occurred simultaneously in a one-step bulk copolymerization between  $\epsilon$ -caprolactam (CL) and *p*-aminobenzoate derivatives (containing an alkyl chain or not) leading aliphatic-aromatic copolyamides. This work follows the Ph.D. works of D. Tunc at the LCPO.<sup>34</sup> In the part A of this third chapter, the synthesis of aliphatic-*N*-butyl-aromatic copolyamides will be described and we will further demonstrate that aliphatic-aromatic copolyamides without any alkyl side group can be directly obtained by using the usual PA6 synthesis procedure enhancing the thermal properties and more specifically the transition glass temperature of PA6.

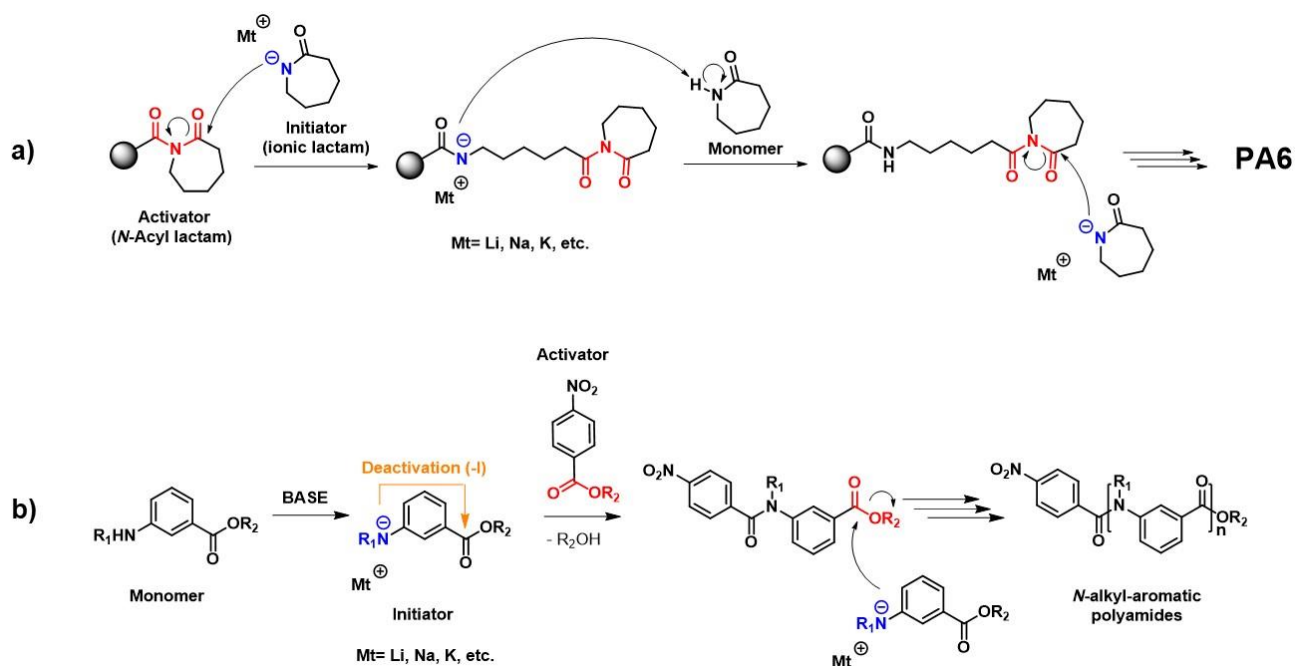


**Figure 2.** Introducing aromatic moieties in a PA6 backbone by AROP using a) the design of the activator<sup>33</sup>, b) the design of monomer<sup>32</sup> and c) by simultaneous ring-opening and condensation reactions



## PART 3.A : Simultaneous Anionic Ring-opening and Condensation Reactions for the Synthesis of Aliphatic-Aromatic Copolyamides

Looking at the mechanisms of both chemistries (Scheme 1), *i.e.* anionic ring-opening polymerization (AROP) and chain-growth condensation polymerization (CGCP), similarities are first observed such as the need of a base which acts as deprotonating agent, the monomer carrying the anionic charge, the need of an activator able to start the polymerization (N-acyllactam or a reactive aromatic ester) and a functionalized chain end (lactam or ester). Since the “initiator” of CGCP and “activator” of AROP have the same role on each polymerization system, “initiator” of CGCP is called as an “activator” in this work.



**Scheme 1.** Activated monomer mechanism for a) AROP of  $\epsilon$ -caprolactam and b) CGCP of N-alkyl-aminobenzoate compounds.

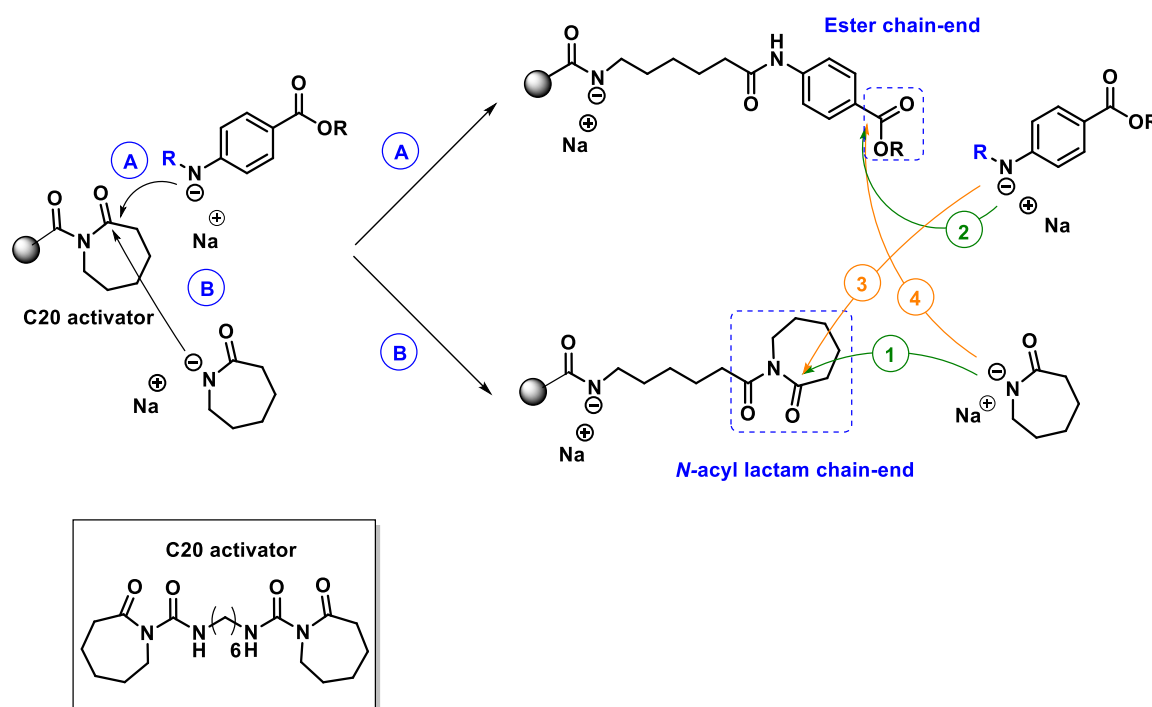
Differences also exist like the difference between the monomers reactivity, the living or controlled character as well as polymerization conditions, *i.e.* solvent vs. bulk or polymerization temperature (Table 1).

**Table 1.** Differences between CGCP and AROP reaction conditions

Methodology	CGCP	AROP
Reaction temperature	-78°C to 25°C	130°C-180°C
Reaction medium	solvent (THF, etc)	bulk
Reaction time	2h-24h	15s – 300s
Living/Controlled	YES	NO

## 3.A.1. Model Reactions

The combination of AROP and CGCP was examined by using different types of initiators and activators. Model reactions were proposed to demonstrate the feasibility or the limitations of the chemical reactions. The expected mechanism of the reaction between chain ends and deprotonated monomers is depicted in Scheme 2. A nucleophilic attack of both activated (deprotonated) monomers is envisaged to react with ester and lactam chain ends (reactions 1-4 presented in Scheme 2). Metal alkoxides and amidates are expected to be formed and then to deprotonate CL or aromatic monomers. Finally, an aliphatic-aromatic polyamide should be synthesized.



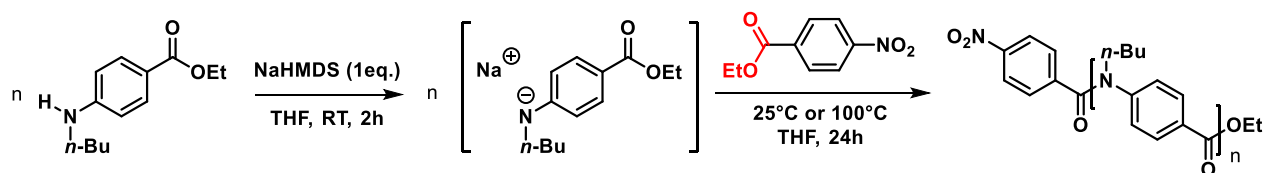
**Scheme 2.** Anionic-based strategy proposed for the synthesis of aliphatic-aromatic copolyamides

In CGCP, the deprotonation of the aromatic/amine monomer by strong bases creates amide anions which deactivate its own ester carbonyl function minimizing/suppressing the self-condensation. Besides, the initiator, now called activator, favors the synthesis of controlled polymers since this molecule bears an electron withdrawing group activating the ester carbonyl group more prone to be attacked by a deprotonated monomer. The polymerization continues by addition of deprotonated monomers onto the chain-ends as terminal ester groups are activated by the electron withdrawing amide groups (Scheme 1b).

In a preliminary work, exploring of suitable activators, initiators and reaction temperatures for adapting CGCP to AROP is reported in order to synthesize the targeted aliphatic/aromatic copolymers. Their synthesis is strongly dependent on the implementation of similar experimental conditions. AROP of  $\epsilon$ -caprolactam in bulk is known to be conducted at 140 °C while CGCP of ethyl (4-alkylamino)benzoate in solution is generally carried out up to 25 °C. Polymerization of CL in bulk can still be run at 100 °C with a slower polymerization rate. In any case, the polymerization of CL has to be higher than 80 °C which is the melting temperature of the lactam. The decreasing of the temperature below 130 °C favors the crystallization, resulting in a lower monomer conversion due to entrapment of the monomers in the crystalline phase. On the other hand, increasing the temperature higher than 170 °C is not also favorable for AROP of CL due to more side reactions which are reducing the crystallization degree and therefore decreasing the material stiffness.<sup>35</sup> Finally, conducting of CL polymerization in solution is not preferable because of a slow rate of polymerization limiting the conversion or economic concerns for industrial producing.

Considering the need to run the polymerization in bulk at 140 °C, CGCP of aromatic monomers and their possible self-condensation were investigated at such a temperature. CGCP of ethyl 4-(octylamino)benzoate was previously reported in a temperature range from -78 °C to 25 °C.<sup>21-31</sup> A good control of the molar masses was generally observed. At low reaction temperatures (< 0 °C), the slow rate of the proton abstraction from the monomer can give a small amount of deprotonated monomer, which caused the dimerization between deprotonated and non-deprotonated species. These dimers can act as an initiator and lead to self-initiated chain-growth condensation polymerization.<sup>36</sup> A broadening of the distribution was also shown at room temperature.

In this work, the polymerization of ethyl 4-(butylamino)benzoate was first carried out in THF at 25 °C and 100 °C for 24h in the presence of NaHMDS as a base and ethyl 4-nitrobenzoate or *N*-acetyl caprolactam as an activator (Scheme 3 and 4.a, Table 2).



**Scheme 3.** CGCP of sodium activated ethyl 4-(butylamino)benzoate initiated by ethyl 4-nitrobenzoate

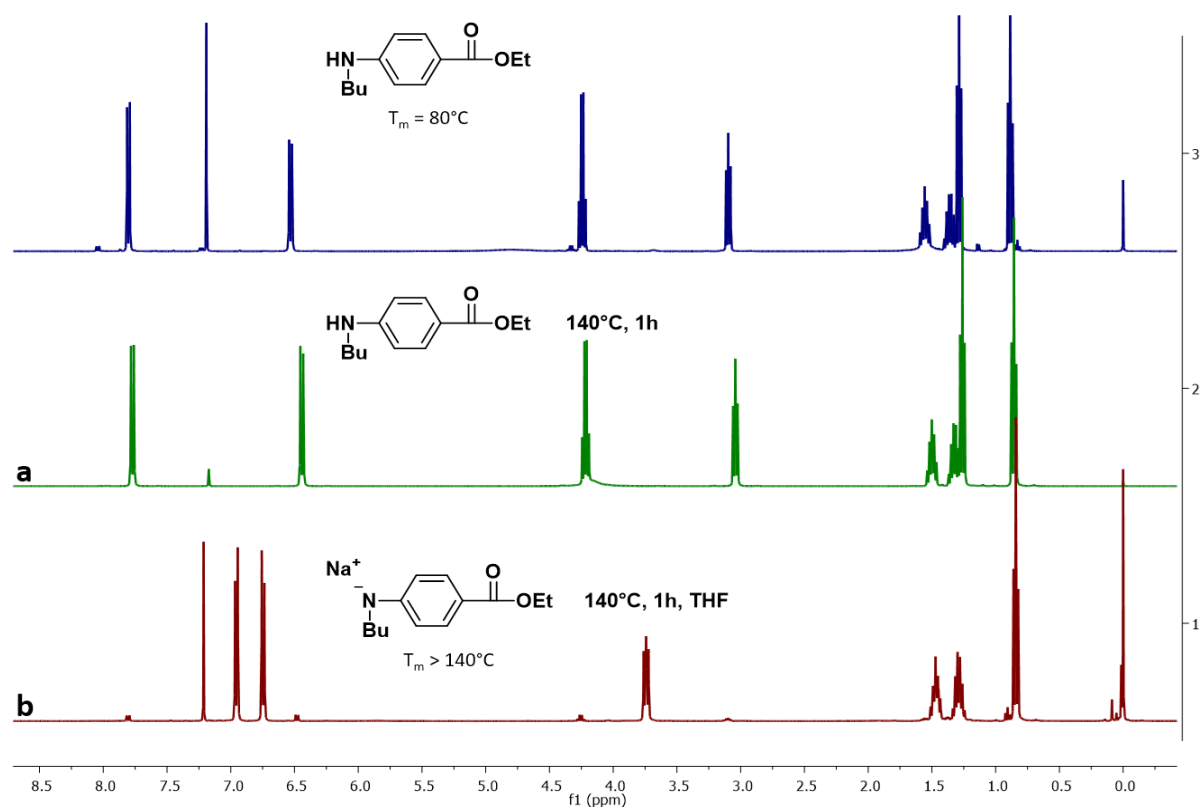
**Table 2.** Polymerization of sodium-activated ethyl 4-(butylamino)benzoate with ethyl 4-nitrobenzoate for the synthesis of aromatic polyamide (THF, 24h)

Run	Activator	Temp. (°C)	time (h)	$\overline{M}_n^{\text{THEO}}$ (g.mol <sup>-1</sup> )	$\overline{M}_n^{\text{SEC}^a}$ (g.mol <sup>-1</sup> )	Conv. <sup>b</sup> (%)	$\overline{D}^a$
1	Ethyl 4-nitrobenzoate	25	24	3 000	2 500	72	1.25
2	Ethyl 4-nitrobenzoate	100	24	10 000	1 380	88	1.12
3 <sup>c</sup>	<i>N</i> -acetyl caprolactam	25	24	10 000	1 850	45	1.10

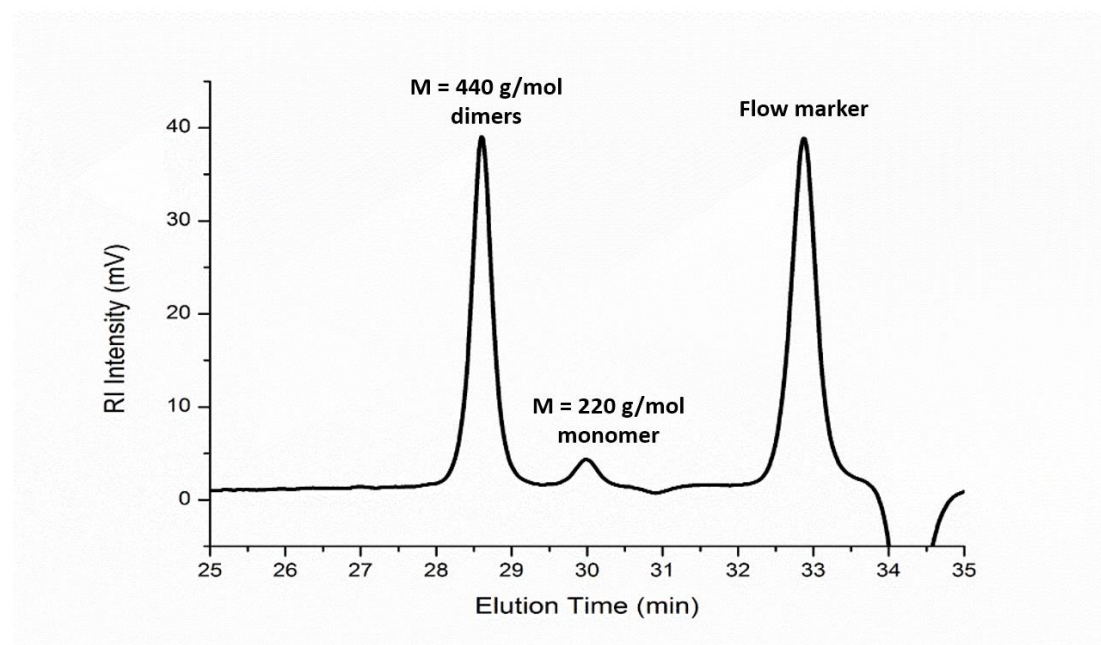
<sup>(a)</sup> Determined by SEC in THF using PS standards <sup>(b)</sup> Conversion was calculated by <sup>1</sup>H NMR in CDCl<sub>3</sub>

<sup>(c)</sup> Polymerization initiated by *N*-Acetyl caprolactam.

Low molar mass polymers and non-complete conversions were observed and was explained by the occurrence of side reactions and a lack of solubility of the resulting polymer which precipitated in THF. Self-condensation cannot be excluded, in particular at high temperatures, and has been checked in the copolymerization conditions, *i.e.* in bulk at 140 °C for 1h. Melted ethyl 4-(butylamino)benzoate did not polymerize as only the monomer was recovered (Figure 3.a). The sodium salt of this monomer was then solubilized in a minimum of THF and cured in similar conditions. Surprisingly, mainly dimers were formed as demonstrated by <sup>1</sup>H NMR spectroscopy and size exclusion chromatography (Figure 3.b and 4). No self-condensation leading to aromatic homopolymers was observed under this conditions.



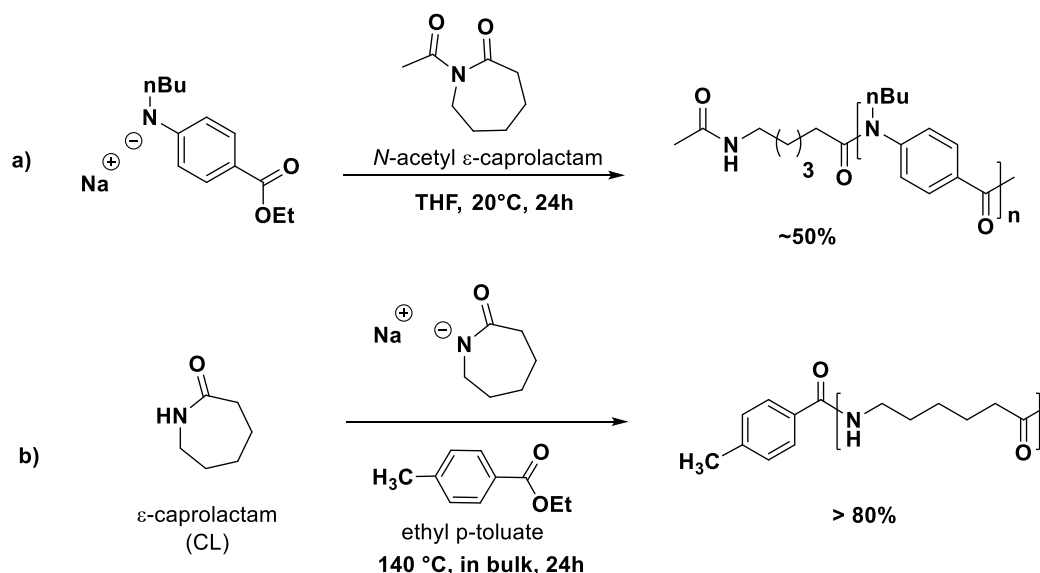
**Figure 3.** Overlay of  $^1\text{H}$  NMR (in  $\text{CDCl}_3$ ) spectra of ethyl 4-(butylamino)benzoate (in blue) (a) of ethyl 4-(butylamino)benzoate left 1h at  $140^\circ\text{C}$  and (b) sodium-activated ethyl 4-(butylamino)benzoate left 1h at  $140^\circ\text{C}$ .



**Figure 4.** SEC trace of sodium-activated ethyl 4-(butylamino)benzoate left 1h at  $140^\circ\text{C}$  in THF

The nucleophilicity of aromatic amidate toward a *N*-acyl lactam moiety was also demonstrated by reacting fully deprotonated ethyl 4-(butylamino)benzoate with *N*-acetyl  $\epsilon$ -caprolactam (*N*-AcCL) (Scheme 4.a). A polymer was indeed obtained (run 3, Table 2) when no polymerization occurs without the *N*-acyllactam activator.

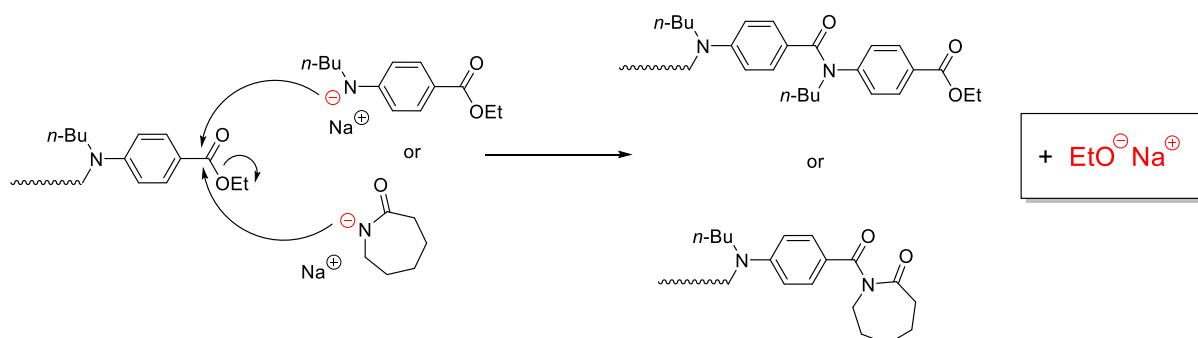
The nucleophilicity of sodium  $\epsilon$ -caprolactamate toward an aromatic ester was then studied by reacting CL with ethyl *p*-toluate as activator in bulk at 140 °C in the presence of this amidate (C10) without hexamethylene-1,6-dicarbamoylcaprolactam (C20) which is the standard activator of PA6 chemistry. Polymerization was shown to proceed with good yield (80-85 %; Scheme 4b). For both model reactions, we observed a non-complete yield or conversion which may lead to some limitations. It's worth noting that nitrobenzoate derivatives, well known as efficient CGCP activators,<sup>21-31</sup> did not enable the polymerization in similar conditions. A reduction of the nitro group to primary amine in the presence of the lactamate is envisaged as referred in the literature for an alkoxide.<sup>37</sup>



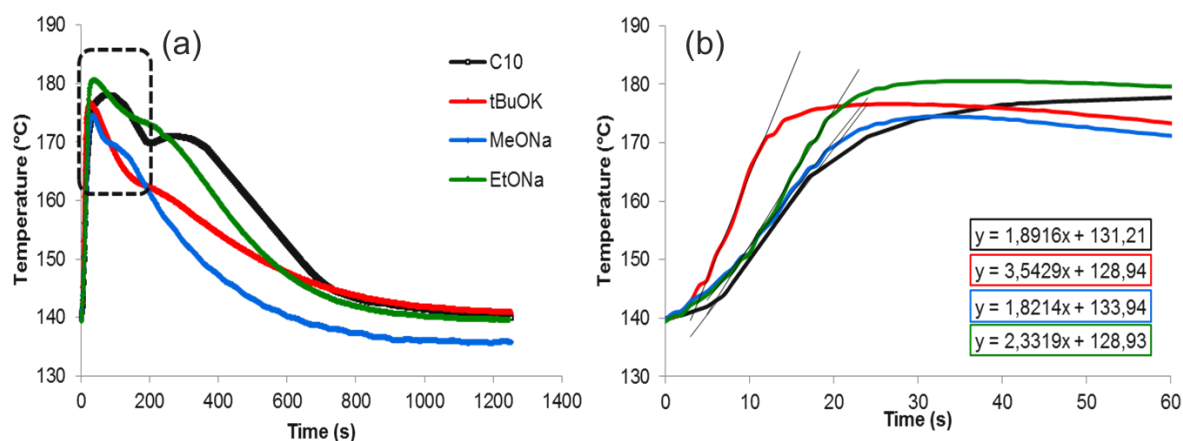
**Scheme 4.** Model reactions: **a)** Chain growth condensation polymerization of ethyl 4-(butylamino)benzoate activated by *N*-acetyl  $\epsilon$ -caprolactam; **b)** Anionic ring-opening polymerization of  $\epsilon$ -caprolactam initiated by sodium  $\epsilon$ -caprolactamate and activated by ethyl *p*-toluate

For the AROP of CL, the caprolactamate anion is formed by the proton transfer from CL to strong bases such as alkali metal hydrides but also alkoxides.<sup>38</sup> In the proposed novel polymerization system, the nucleophilic attack of the aromatic ester is expected to release a sodium alkoxide as described for CGCP methodology (Scheme 5). This leaving group is also supposed to deprotonate the lactam. Indeed, this feature was verified by

the occurrence of the AROP of CL in the presence of EtONa, and also MeONa or tBuOK as an initiator and compared to C10. As demonstrated by the plot temperature *vs.* time presented in Figure 5.a, a rapid polymerization of CL is observed regardless of the nature of the deprotonating agents used, *i.e.* caprolactamate or alkoxide. One can note that the polymerization using t-BuOK as deprotonating agent exhibits the highest propagation rates as expected for this larger counter-cation (Figure 5.b).



**Scheme 5.** Generation of sodium ethoxide by condensation between the ester chain-end and the activated monomers (aromatic amidate or caprolactamate)

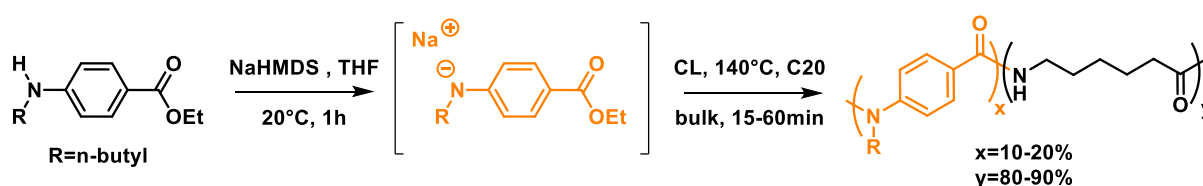


**Figure 5.** Temperature-time diagrams ((a) overall polymerization time and (b) enlargement to short times) of the polymerization of ε-caprolactam initiated by C10, tBuOK, MeONa and EtONa (activator = C20, 20 min, 140 °C, in bulk, yield > 98 %).

To summarize and despite some limitations, we demonstrated by different model reactions that all the plausible cross-reactions, *i.e.* the nucleophilic attack of both activated monomers on the ester or *N*-acyl lactam chain-ends and the deprotonation of ε-CL by the alkoxide generated by the reaction of condensation, occur under the usual conditions for anionic polymerization of ε-caprolactam (bulk, 140°C, *N*-acyllactam as activator).

### 3.A.2. Copolymerization of $\epsilon$ -caprolactam with ethyl 4-(butylamino)benzoate

In the following part, the copolymerization of CL with ethyl 4-(butylamino)benzoate in the presence of C20 as activator and sodium salts is investigated. Copolyamides with different percentages of aromatic/aliphatic units were synthesized in a one-step bulk copolymerization (Scheme 6, Table 3).



**Scheme 6.** Copolymerization of CL with sodium-activated ethyl 4-(butylamino)benzoate in the presence of C20 (activator)

**Table 3.** Synthesis of aliphatic/aromatic copolyamides at 140°C in bulk and in the presence of N-acetyl lactam as activator

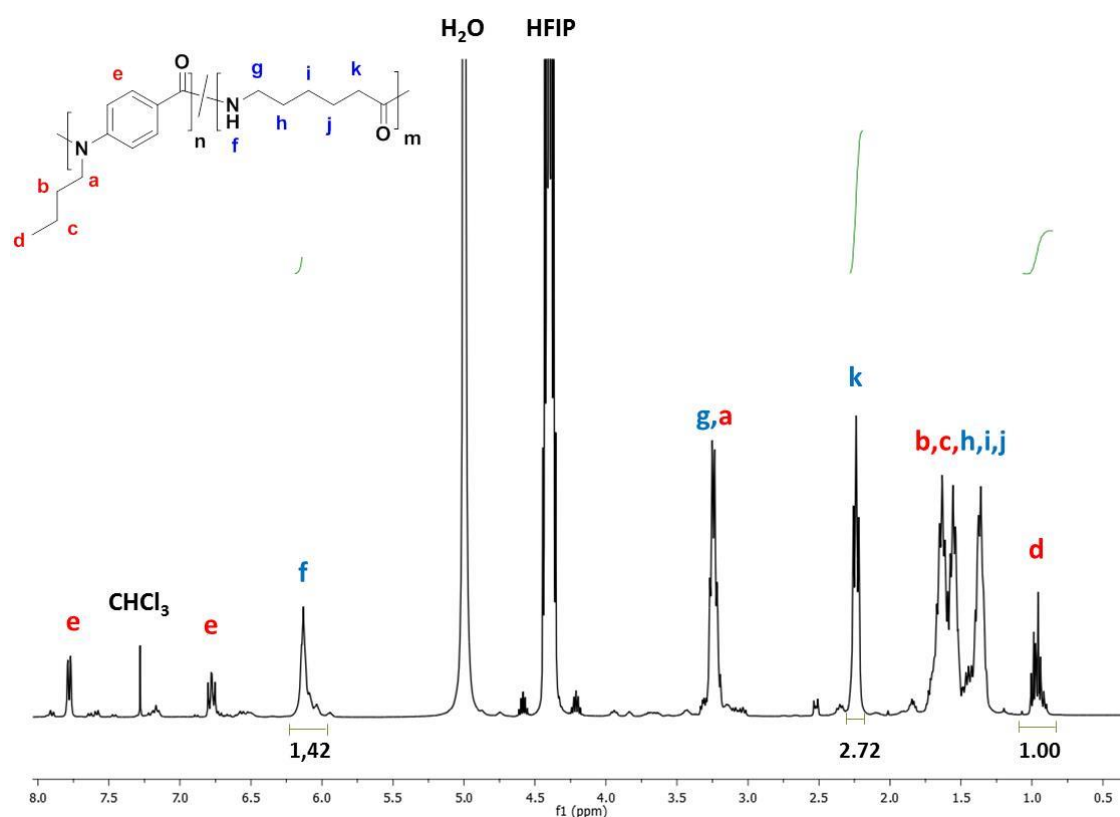
Run	NaHMDS <sup>a</sup> (eq)	C10 (mol%)	Theor. Composition Al/Ar (mol%)	Exp. Composition Al/Ar (mol%) <sup>b</sup>	Time (min)	Yield <sup>c</sup> (%)	$\overline{M}_n^d$ (g/mol)	$\overline{D}^d$
1	1	-	90/10	90/10	15	98	10 200	2.4
2	0.5	-	90/10	90/10	15	98	16 500	1.7
3	0.1	-	90/10	97/3	60	80	12 500	2.2
4	-	2	90/10	97.5/2.5	60	72	9 400	2.2
5	1	-	75/25	78/22	15	98	2 500	2.6
6	0.5	-	75/25	82/18	15	90	1 750	2.6
7	0.1	-	75/25	95/5	60	70	7 500	2.5
8	-	2	75/25	94/6	60	65	7 900	2.6
9 <sup>e</sup>	1	-	90/10	90/10	15	98	22 000	1.8
10 <sup>f</sup>	1	-	90/10	90/10	15	98	32 000	1.6

(a) Equivalent of NaHMDS as compared to ethyl 4-(butylamino)benzoate, (b) % of aromatic monomer incorporated in the copolymer calculated by  $^1\text{H}$  NMR, (c) Determined by gravimetric analysis (d) Determined by SEC in HFIP (MALLS/RI detection),  $\overline{M}_n$  theo = 10,000 g.mol<sup>-1</sup> for all copolymers (e)  $\overline{M}_n$ (théo)= 50,000 g.mol<sup>-1</sup> (f)  $\overline{M}_n$ (théo)= 100,000 g.mol<sup>-1</sup>

In order to characterize the reaction equilibria involved during the copolymerization, different experiments were performed by varying the amount and the nature of the active species (NaHMDS or C10). Experiments carried out in this work are listed in Table 3. The more detailed experimental conditions are given in the experimental part Table S1.



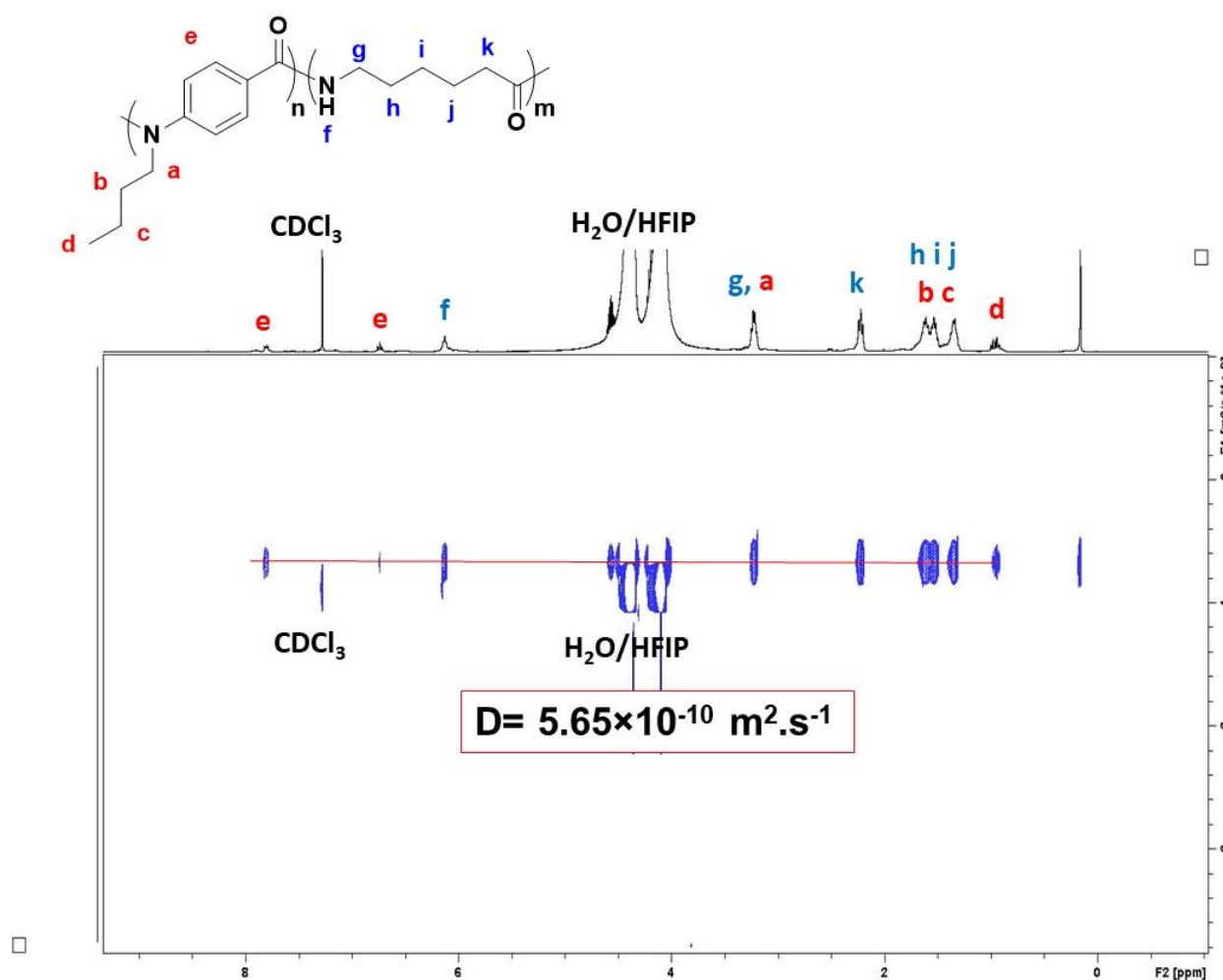
The copolymerization of ethyl 4-(butylamino)benzoate and CL could be obtained for 10 to 25 mol%, which correspond respectively to about 15 and 35 weight% of aromatic units in polyamides. Unreacted monomers and other reagents were removed by refluxing the polymers in H<sub>2</sub>O/THF during 24h. As shown in Figure 6, characteristic proton signals of CL repeating units appeared at  $\delta$  (ppm) 6.20-5.90 (f), 3.20 (g), 2.22 (k), and between 1.75-1.25 (h, i, j). As an example, the copolymer 25% Ar-PA6 (Run 5, Table 3) exhibits the aromatic repeating units of ethyl 4-(butylamino)benzoate at 7.85 and 6.76 ppm (e) and butyl pendant groups were seen at 3.22 ppm (a), 1.25-1.75 ppm (b, c) and at 0.88 ppm (d). Molar ratios of monomer units could be calculated from integrated intensity ratio at 2.22 ppm (k) and 0.88 ppm (d) and are given in Table 1



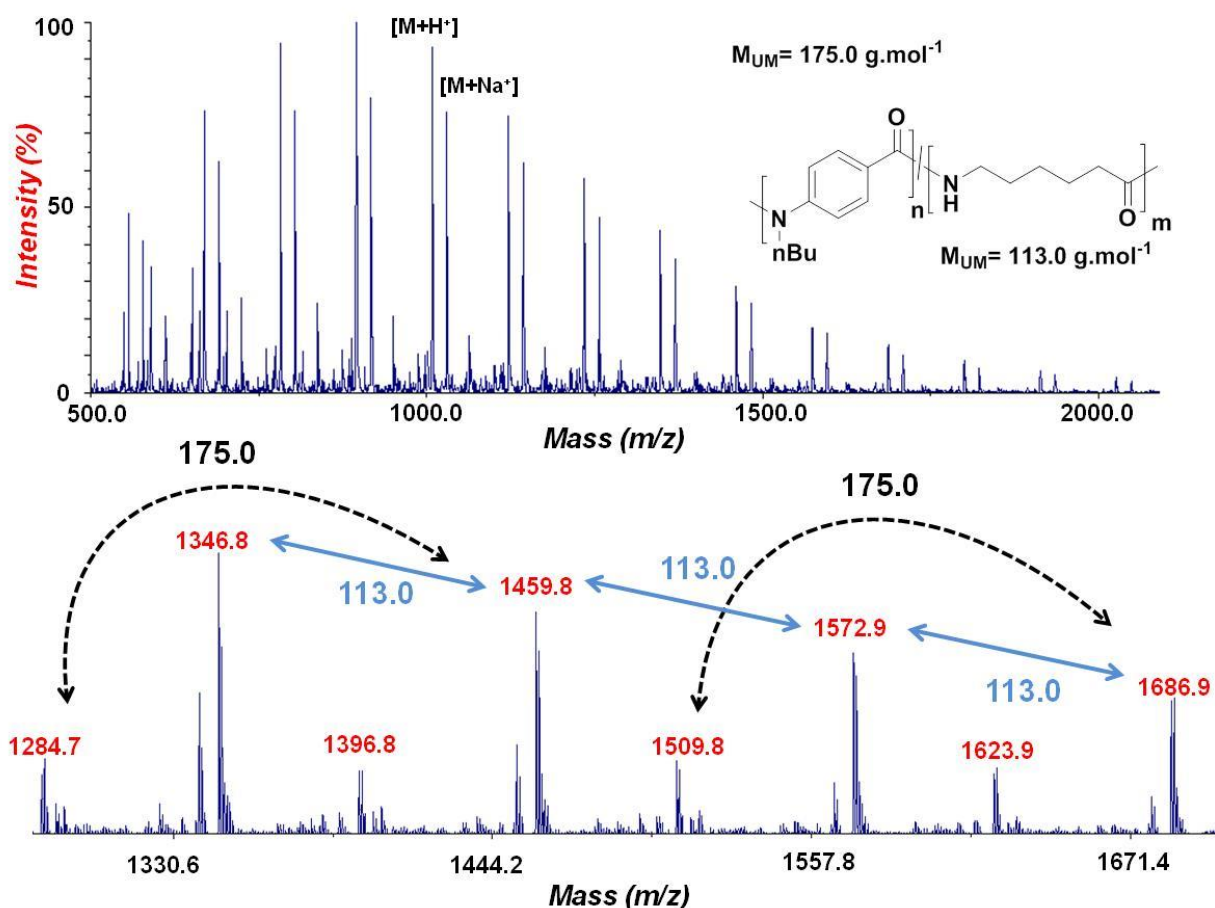
**Figure 6.** <sup>1</sup>H NMR spectrum of 25% Ar-PA6 copolyamide in CDCl<sub>3</sub>/HFIP (Run 5, Table 3)

A 2D DOSY NMR spectrum performed on the copolyamide containing 22% of aromatic units (Run5, Table 3, Figure 7) showed only one population with a diffusion coefficient  $D = 5.65 \cdot 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$  attesting the presence of a copolymer and the efficiency of coupling AROP and CGCP. Maldi ToF mass spectrometry analysis (Figure 8) exhibits two different populations, without taking into account H<sup>+</sup> and Na<sup>+</sup> ionizations, with a peak to peak mass increment corresponding to  $m/z = 113.0$  for an  $\epsilon$ -caprolactam unit and  $m/z$

= 175.0 for the aromatic one. Interestingly, consecutive peaks with a gap of  $m/z = 175.0$  were not observed revealing that there are no aromatic sequences into the copolymer structure.



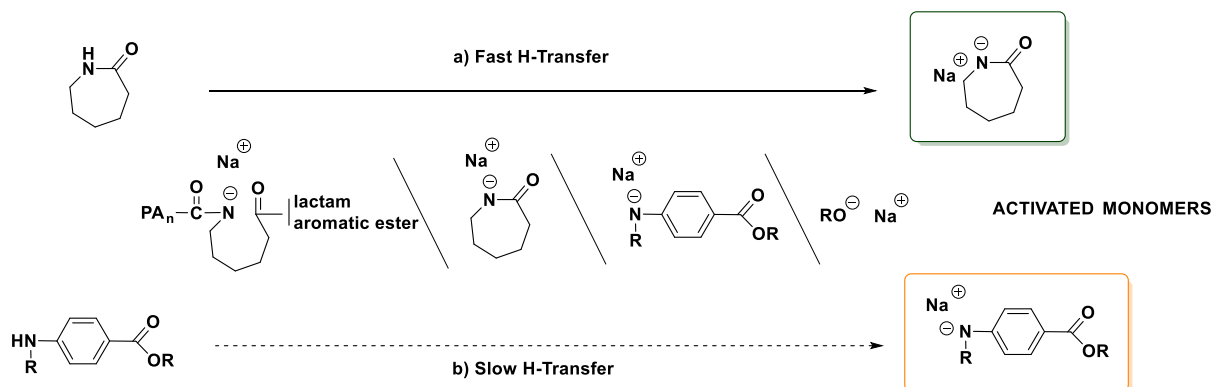
**Figure 7.** 400 MHz 2D DOSY NMR spectrum obtained at 298K ( $D=5.65 \cdot 10^{-10} \text{ m}^2/\text{s}$ ) of copolyamide 25%Ar-PA6 (Run 5, Table 1).



**Figure 8.** Maldi-ToF MS spectrum of 25% Ar copolyamide (Run 5, Table 3)

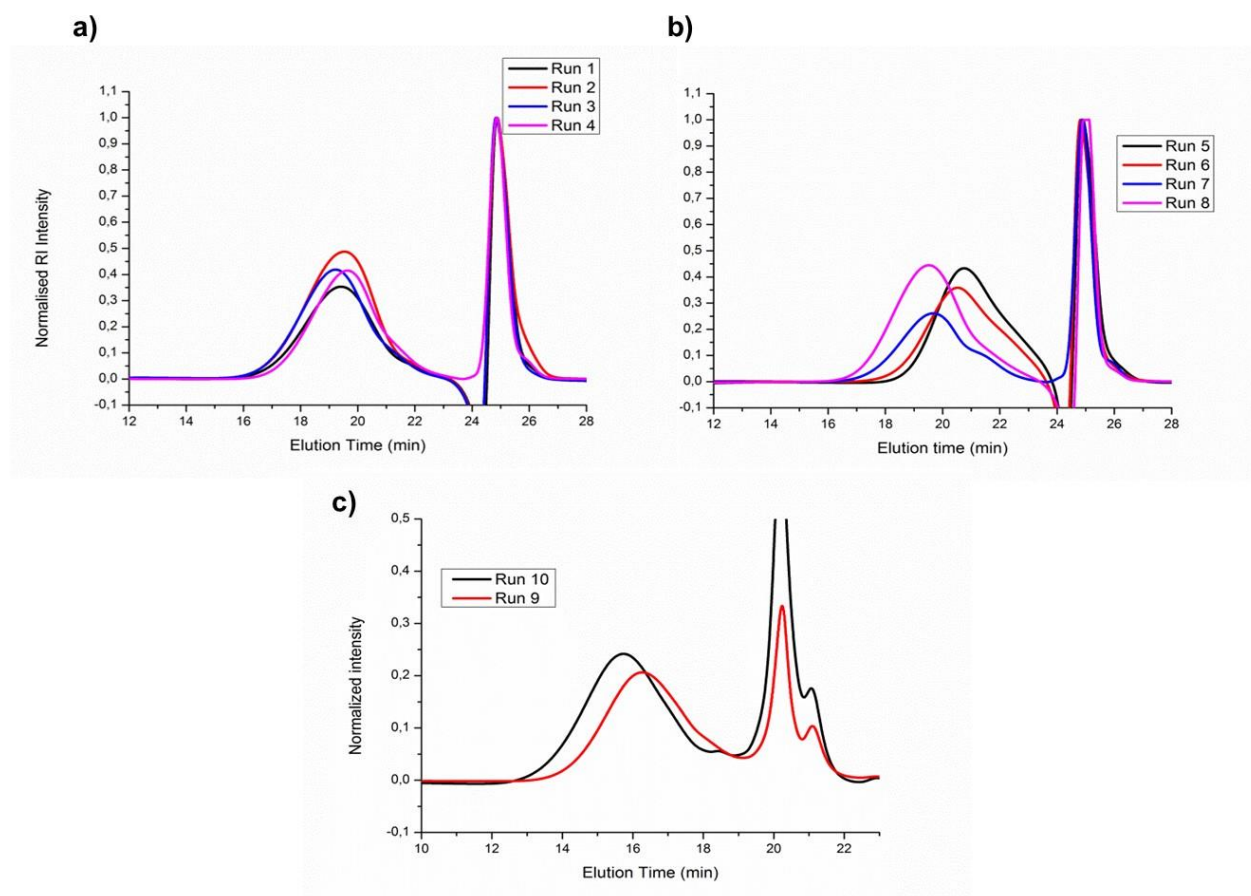
The copolymerization using fully deprotonated ethyl (4-butylamino)benzoate proceeded in a few minutes with a high yield ( $\geq 98\%$ ). The incorporation of the aromatic monomer in the polymer chain was demonstrated by  $^1\text{H}$  NMR spectroscopy of the purified material. The experiments show that most of the benzamide monomers were incorporated into the polyamide structure (run 1 and 5, Table 3). To a mechanistic point of view, sodium  $\epsilon$ -caprolactamate can be generated by direct H-transfer with *N*-acyl lactam anion moiety, benzamide, or also alkoxide formed in-situ as proposed in Scheme 7.a. Furthermore, the polymerizations performed with 0.5 eq of NaHMDS as compared to ethyl 4-(butylamino)benzoate exhibit quite similar characteristics, high conversion (90-98 %), and almost complete incorporation of aromatic units (Table 3, Run 2 and 6) pointing out again various possibilities of deprotonation reactions. Nonetheless, the copolymers prepared with 10 % of activated aromatic monomer highlight the limitation of this approach (Run 3 and 7, Table 3). In this case, a decrease of the reaction yield and the incorporation of aromatic units was observed despite a longer reaction time (1h). The

same results were obtained for the polymerization performed without an activation of ethyl 4-(butylamino)benzoate, but using only sodium  $\epsilon$ -caprolactamate as deprotonating agent (run 4 and 8, Table 1). The deprotonation of the aromatic monomer is believed to be very slow (Scheme 7.b).



**Scheme 7.** Activated monomers formation by H-transfer during the anionic copolymerization of  $\epsilon$ -caprolactam and ethyl 4-(butylamino)benzoate

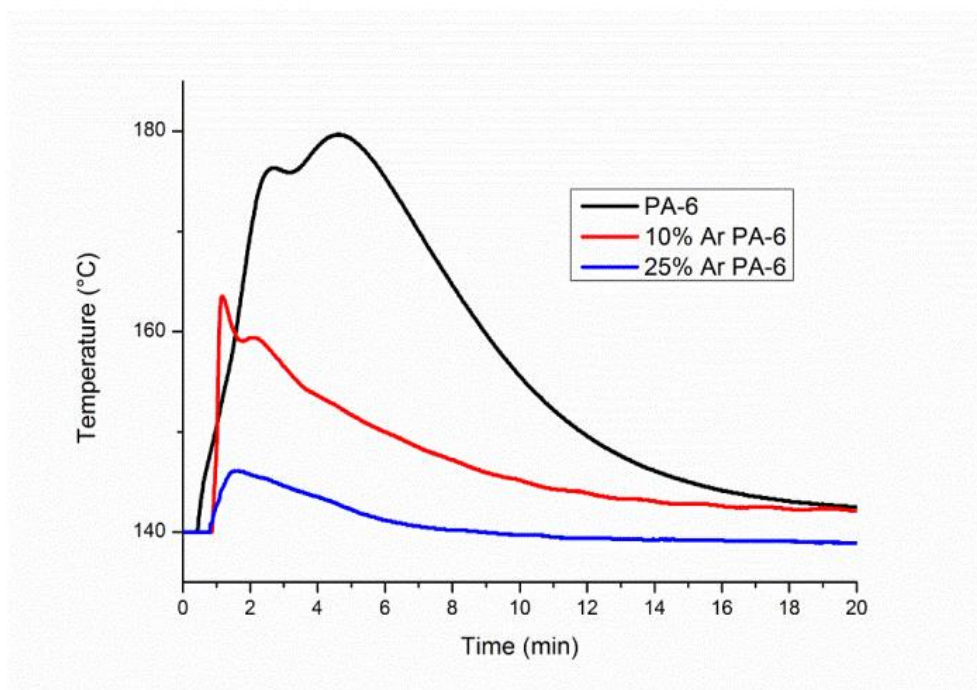
Interestingly, the amount of active species has also a strong influence on the molar masses. Copolymerization using a high amount of deprotonated ethyl 4-(butylamino)benzoate (Run 5 and 6, Table 3 and Figure 9.b) yields only low molar mass copolyamides. Side reactions previously described for AROP of  $\epsilon$ -caprolactam in strongly basic conditions, such as transacylation or cyclization, can explain this observation.<sup>39</sup> The high basicity and concentration of aromatic amidates probably increase all the possible side reactions occurring generally for the bulk AROP of CL and the dispersity values in the range 1.6 - 2.6 which are typical for this chemistry.



**Figure 9.** SEC traces in HFIP of copolyamides (a) PA6/10%Ar (Run 1-4, Table 3) and (b) PA6/25%Ar (Run 5-8, Table 3) and (c) High molar mass copolyamides (Run 9,10, Table 3)

High molar masses copolyamides (run 9 and 10, Table 3, Figure 9.c) up to  $32\,000\text{ g}\cdot\text{mol}^{-1}$  were also prepared by this approach for 10 mol% or aromatic units by varying the initial ratio  $([\text{Ar}]_0 + [\epsilon\text{-CL}]_0)/[\text{C20}]_0$ . Almost complete conversions and incorporation of the aromatic comonomer were observed in both cases.

The evolution of the temperature of the polymerization medium was monitored for the PA6 reference as well as for the copolymers 10 % and 25 % Ar-PA6 (run 1 and 5, Table 3). During the bulk PA6 synthesis started at  $140\text{ }^{\circ}\text{C}$ , exothermic polymerization and crystallization occur almost simultaneously with a maximum temperature of  $180\text{ }^{\circ}\text{C}$ . The copolymerization of CL with ethyl 4-(butylamino)benzoate led to a decrease of this value, down to  $163\text{ }^{\circ}\text{C}$  and  $146\text{ }^{\circ}\text{C}$  when increasing the amount of activated aromatic monomers (Figure 10).



**Figure 10.** Temperature-time diagrams of PA6 (in black), 10%Ar-PA6 (in red, Run 1, Table 3) and 25%Ar-PA6 (in blue, Run 5, Table 3)

Such an exotherm decrease was also observed in the case of the copolymerization of CL with functionalized amino- $\epsilon$ -caprolactam<sup>40,41</sup> and can be explained here by the decrease of the crystallinity of the obtained polymers. DSC analyses of those copolyamides (Run 1 and 5, SI Figures S1 and S2) show a melting temperature of 190°C ( $\Delta H_m = 30.7$  J/g) and 177°C ( $\Delta H_m = 22.2$  J/g) respectively for the copolymers containing 10 % and 22 % of aromatic moieties. Moreover, only one glass transition temperature below 50°C was observed in both cases due the presence of a butyl side group and probable chain irregularities induced by the statistical copolymerization. Interestingly, the high molar mass copolymer (run 10, Table 3) exhibits higher  $T_g$  (62°C), crystallinity ( $\Delta H_m = 51.0$  J/g) and melting temperature (208°C) (SI Figure S3).

Combining both Maldi-ToF MS, DOSY 2D NMR and DSC analysis, results are consistent with a statistical copolyamides with aromatic amide distributed along the aliphatic polyamide backbone.

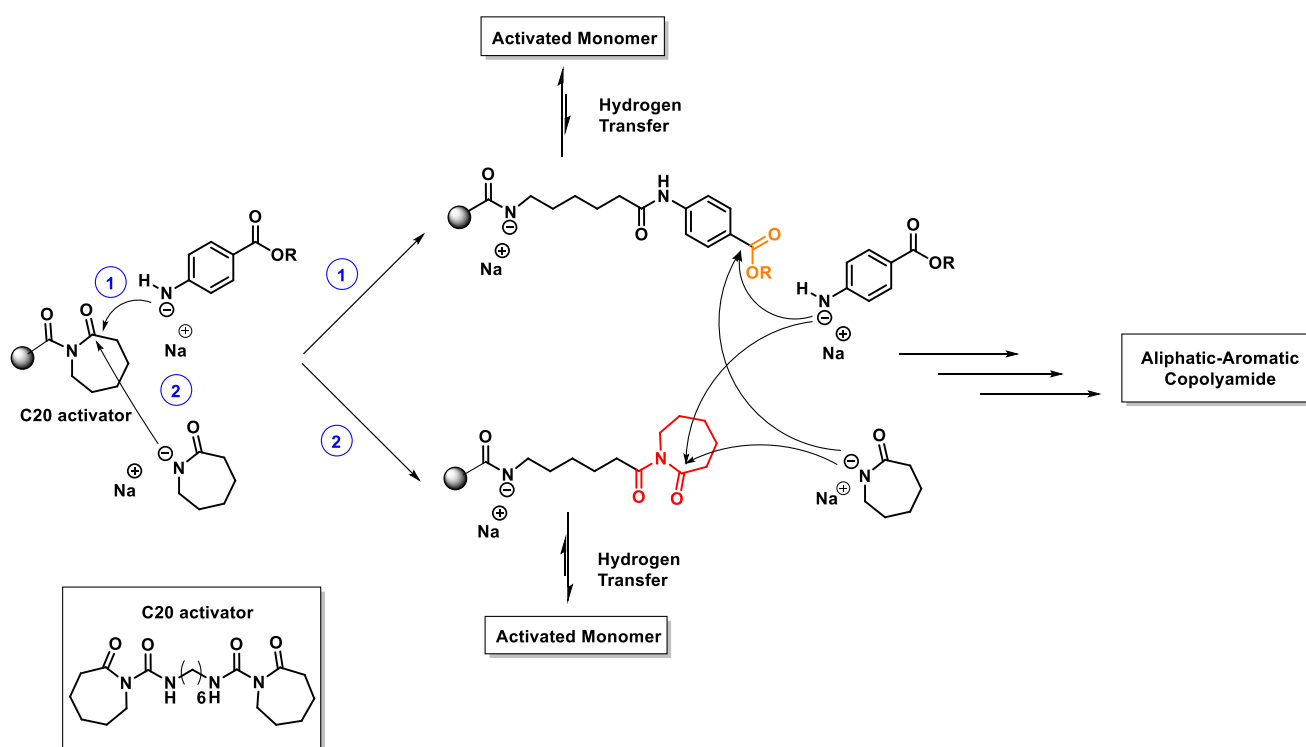
In summary, this study intends to demonstrate that the copolymerization between  $\epsilon$ -caprolactam (CL) and ethyl 4-(butylamino)benzoate, combining both ring-opening and condensation reactions, occurs in a one-step bulk reaction at 140 °C enabling the synthesis of aliphatic-aromatic copolyamides. Polyamides 6 with 3 to 22 mol% of aromatic units were prepared. A base acting as deprotonating agent of both  $\epsilon$ -

caprolactam and ethyl 4-(butylamino)benzoate was first needed to form the activated monomers, *i.e.* sodium  $\epsilon$ -caprolactamate and the aromatic ester amidate and a *N*-acyllactam was used to start their copolymerization. Characterizations of the copolyamides indicated that no aromatic sequences were present in the final material attesting that there is no or negligible reaction of deprotonated aromatic monomer on the ester chain-end. Interestingly and similarly to CL AROP, we could also demonstrate that the complete deprotonation of the aromatic monomers was not mandatory as the copolymerization occurred with half or less activated monomers. This methodology based on a simultaneous anionic ring opening and condensation reactions, affords a new synthetic pathway to introduce aromatic moieties and to tune the thermo-mechanical properties of polyamides. Finally, the thermal characterizations of the so-obtained copolyamides demonstrated that the introduction of a butyl side chain induced chain-irregularities and no- or slight improvement of the thermal properties despite the introduction of “rigid” aromatic units. Consequently, we decided to replace the butyl-containing aromatic comonomer by a non-alkylated aminobenzoate derivative, namely ethyl 4-aminobenzoate, in order to introduce aromatic unit without any alkyl side chains.

#### 3.A.3. Copolymerization of $\epsilon$ -caprolactam with ethyl 4-aminobenzoate

The copolymerization between  $\epsilon$ -caprolactam and ethyl 4-aminobenzoate, in bulk at 140°C, was then investigated in order to introduce aromatic units capable to create hydrogen bonding and  $\pi$ - $\pi$  stacking interactions into a PA6 backbone. Expected simultaneous activated anionic ring-opening and condensation reaction mechanism is proposed in Scheme 8. Polymerization can be initiated either by nucleophilic attack of 1) the activated aromatic salt or by 2) sodium  $\epsilon$ -caprolactamate, both activated monomers formed by deprotonation with a strong base (NaHMDS), on the *N*-acyllactam activator (C20). After the first addition, two active chain-ends, *i.e.* ester and *N*-acyllactam, are generated. Both activated monomers can then react on the acyllactam enabling the ring-opening of the lactam moiety or on the ester chain-end by condensation reaction releasing sodium ethoxide. This novel synthetic route, keeping the usual PA6 experimental conditions is expected to offer the possibility to tune thermo-mechanical properties of polyamide 6 by introducing aromatic moiety in the polymer backbone starting from two commercially available products.



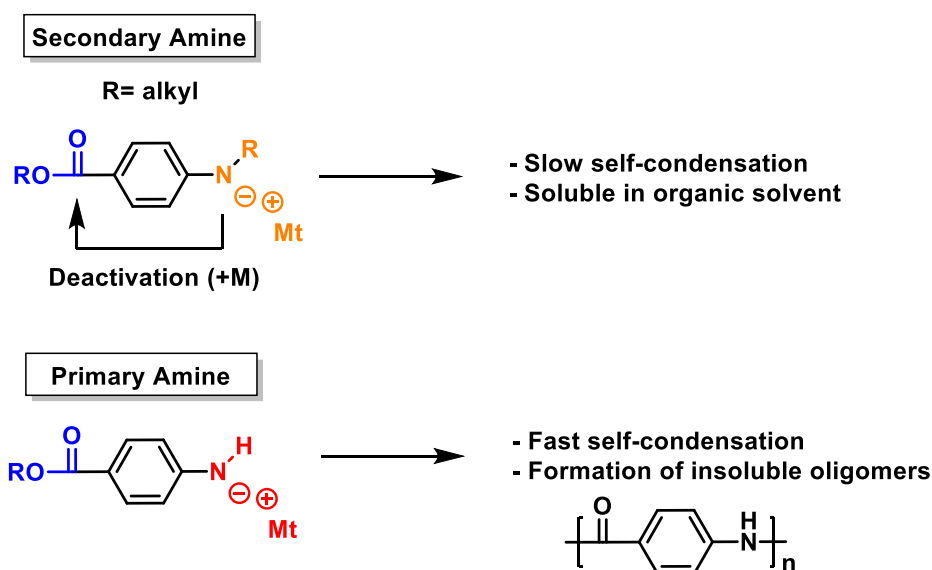


**Scheme 8.** Mechanism of copolymerization of  $\epsilon$ -caprolactam and ethyl 4-aminobenzoate in the presence of a di-N-acyllactam as activator

Copolymerizations were first performed by pre-activation of the ethyl 4-aminobenzoate, which consists of its complete deprotonation, using 1 equivalent of NaHMDS in THF and yielding the corresponding activated aromatic salt (see Scheme 10). Interestingly, a precipitation occurred in THF rapidly after the addition of the strong base.  $^1\text{H}$  NMR analysis of the soluble part of the crude product demonstrates a fast oligomerization of the benzamine salt by reaction of the activated amine on an ester function (Figure S4). In chain-growth condensation polymerization of *N*-(alkylamino)benzoate, the deprotonation of the aromatic monomers by strong bases creates amidate anions, which deactivate their own ester carbonyl functions avoiding/minimizing the self-condensation.<sup>21-31</sup> In the present case, the primary amine used instead of a secondary one tends to promote a self-condensation reaction (Scheme 9). This reaction was also investigated in bulk at 140°C by reacting a stoichiometric amount of NaHMDS and ethyl 4-aminobenzoate in order to mimic the copolymerization conditions. The oligomerization takes place in a few seconds yielding a yellow solid, which was purified by refluxing in THF/H<sub>2</sub>O mixture. The oligo(*p*-benzamide) was obviously non soluble in common organic solvents and also in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP). Thermo-gravimetric

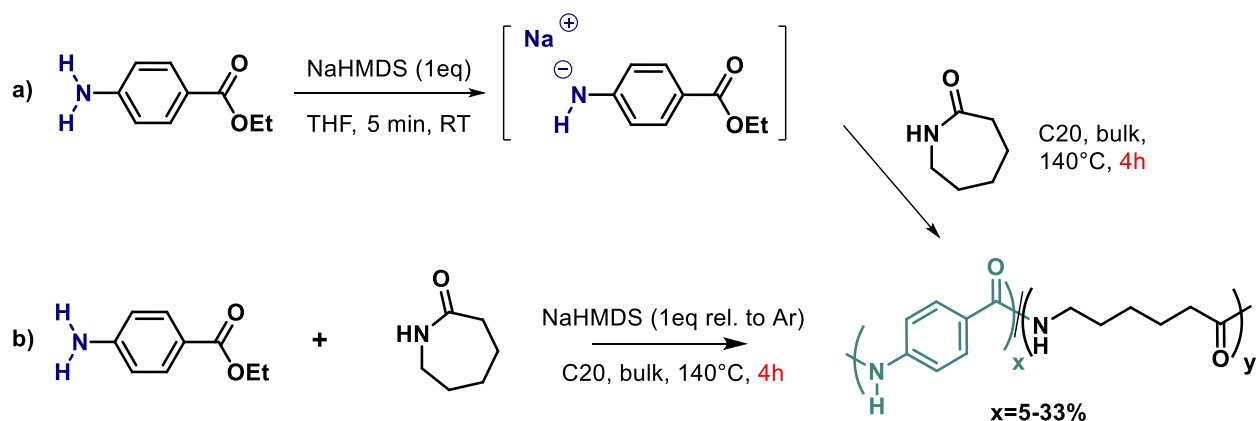


analysis of the purified product shows a high degradation temperature ( $T_d=436^\circ\text{C}$ ) generally observed for poly(*p*-benzamide) (Figure 3 and Table 4).



**Scheme 9.** Reactivity of activated *N*-alkyl aminobenzoate<sup>21-31</sup> vs. *N*-H aminobenzoate

Two different copolymerization processes were performed in order to determine the influence of the pre-activation of the aromatic primary amine on the polymerization results (Scheme 10). The aromatic monomer was first activated by reacting with 1 equivalent of NaHMDS in THF. CL was then quickly added to form a homogeneous yellow mixture after evaporation of the solvent (Table 4, P1-3). On the other hand, NaHMDS was added in a melt mixture of CL and ethyl 4-aminobenzoate (Table 4, P'4-6). All the copolymerizations were performed using C20 as an activator and NaHMDS as a base. Copolyamides with different percentages of aromatic/aliphatic units, up to 20 mol% of aromatics, were prepared in a one-step bulk copolymerization at  $140^\circ\text{C}$  during 4h and results are summarized in Table 4.

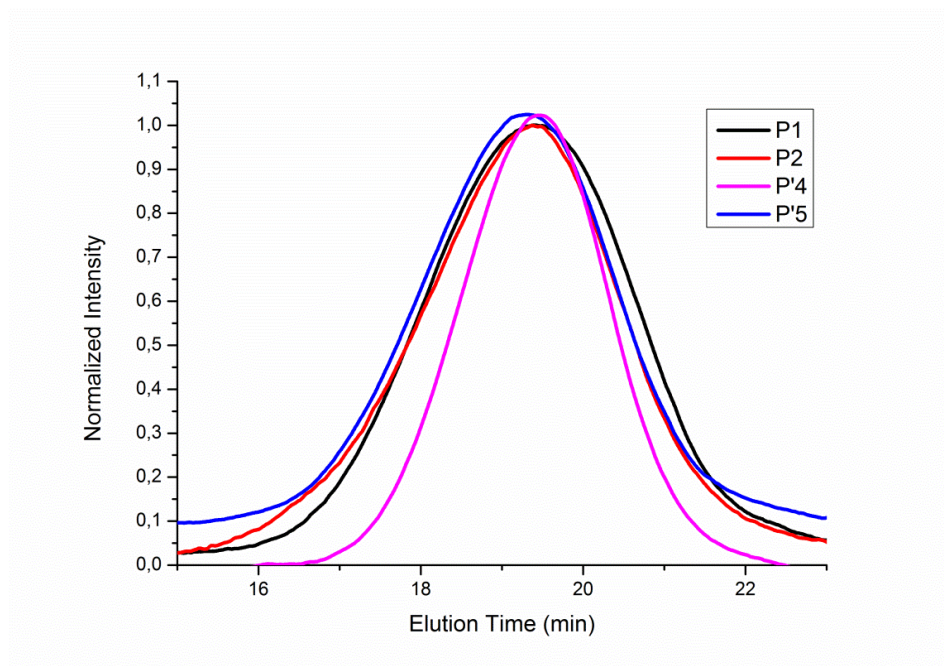


**Scheme 10.** Copolymerization processes performed a) with and b) without “preactivation” of the aromatic comonomer for the synthesis of aromatic-aliphatic copolyamides

**Table 4.** Copolyamides prepared by a one-step bulk copolymerization at 140°C (4h) with (P1-P3) and without (P’4-P’6) pre-activation of ethyl 4-aminobenzoate.

Copolymer	Conversion <sup>a</sup> (%) Al/Ar	Composition Al/Ar (%mol) <sup>a</sup>		$\overline{M}_{n \text{ theo}}^b$ (g.mol <sup>-1</sup> )	$\overline{M}_{n \text{ exp}}^c$ (g.mol <sup>-1</sup> )	$\overline{D}^c$
		Theo	exp			
P1	92/100	95/5	95/5	20000	22500	1.54
P2	72/100	90/10	86/14	20000	23800	1.54
P3 <sup>d</sup>	nd	80/20	nd	20000	nd	nd
P’4	90/100	95/5	93/7	20000	22000	1.36
P’5	73/100	90/10	83/17	20000	25000	1.52
P’6 <sup>d</sup>	nd	80/20	nd	20000	nd	nd

a) Conversion and composition were calculated by <sup>1</sup>H NMR ; b)  $\overline{M}_{n \text{ theo}} = ([\text{ethyl 4-aminobenzoate}] + [\text{CL}]) / (2[\text{C20}] \times M_0)$  ; c) Molar masses and dispersities were determined by SEC in HFIP, 0.05% KTFA (vs. PMMA standards) ; d) insoluble.



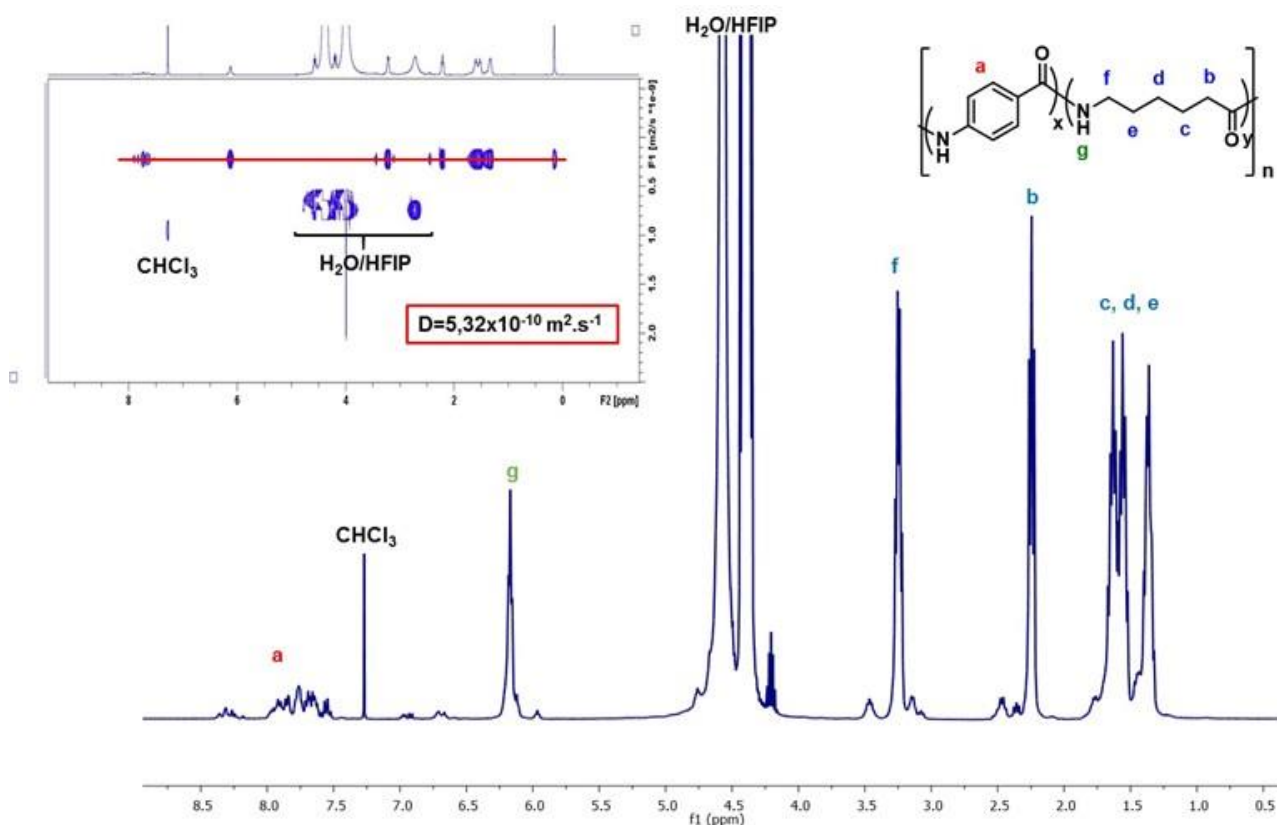
**Figure 11.** SEC traces of copolyamides P1, P2, P'4 and P'5 in HFIP (Table 4)

As a difference with conventional bulk polymerization of CL that occurs in a few minutes at 140°C, a few hours were necessary to observe a high conversion due to the presence of a primary amine in the polymerization medium and possible equilibrium between protonation and deprotonation. This point was also investigated by starting the polymerization of CL in presence of a slight excess of isopropylamine as compared to the active species (C10, sodium  $\epsilon$ -caprolactamate). Indeed, the exotherm measured during the first seconds of polymerization significantly decreased in the presence of isopropylamine (Figure S5). A polymer could still be obtained. Interestingly, in all cases, the conversion of the aromatic comonomer was quantitative; it was not the case of CL, attesting the higher reactivity of the aromatic amine salt as compared to the sodium  $\epsilon$ -caprolactamate toward chain ends (Table 4). The crude products were analysed by  $^1\text{H}$  NMR spectroscopy to determine the conversion of both monomers and the unreacted monomers were then removed by refluxing the polymers in  $\text{H}_2\text{O}/\text{THF}$  mixture for 24h. Results summarized in Table 4 demonstrated that there was no influence of the pre-activation of the aromatic co-monomer on the conversion of either monomers, molar masses or dispersities (SEC trace in Figure S6), probably due to a fast hydrogen-exchange with CL and the aromatic co-monomer. Dispersity values in the range of 1.5-1.9 are quite low in comparison with typical values observed in the AROP of CL (generally 1.6-3.0) and have been attributed to the longer reaction time needed to achieve high conversion related to a less exothermic

polymerization, which disfavoured side reactions such as transacylation, transamidation or cyclization<sup>38</sup>.

<sup>1</sup>H NMR analysis of a purified product exhibits characteristic signals of PA6 monomer units at  $\delta(\text{ppm}) = 6.20\text{--}5.90$ , 3.20, 2.22 and 1.75–1.25 and a broad signal between 8.25–7.5 ppm corresponding to the aromatic repeating units of ethyl 4-aminobenzoate (Figure 12). The relative proportion of both monomers in the polyamide structure could be calculated from integrated intensity ratio at 2.22 ppm and 8.25–7.50 ppm. 2D DOSY NMR spectra were also performed on different copolyamides and demonstrated the efficiency of the copolymerization. As an example, DOSY 2D NMR spectrum of the copolymer P5 showed only one population with a diffusion coefficient  $D = 5.32 \times 10^{-10} \text{ m}^2 \cdot \text{s}^{-1}$  (Figure 12).

For the copolymerization performed with a targeted composition of 80/20 aliphatic/aromatic in the polyamide, a self-initiation is expected. Indeed, with or without pre-activation of the aromatic monomer, a precipitate was observed in melt CL before the addition of the activator (C20).



**Figure 12.** <sup>1</sup>H NMR analysis and 2D DOSY analysis of a purified copolyamide (P'5, Table 1)

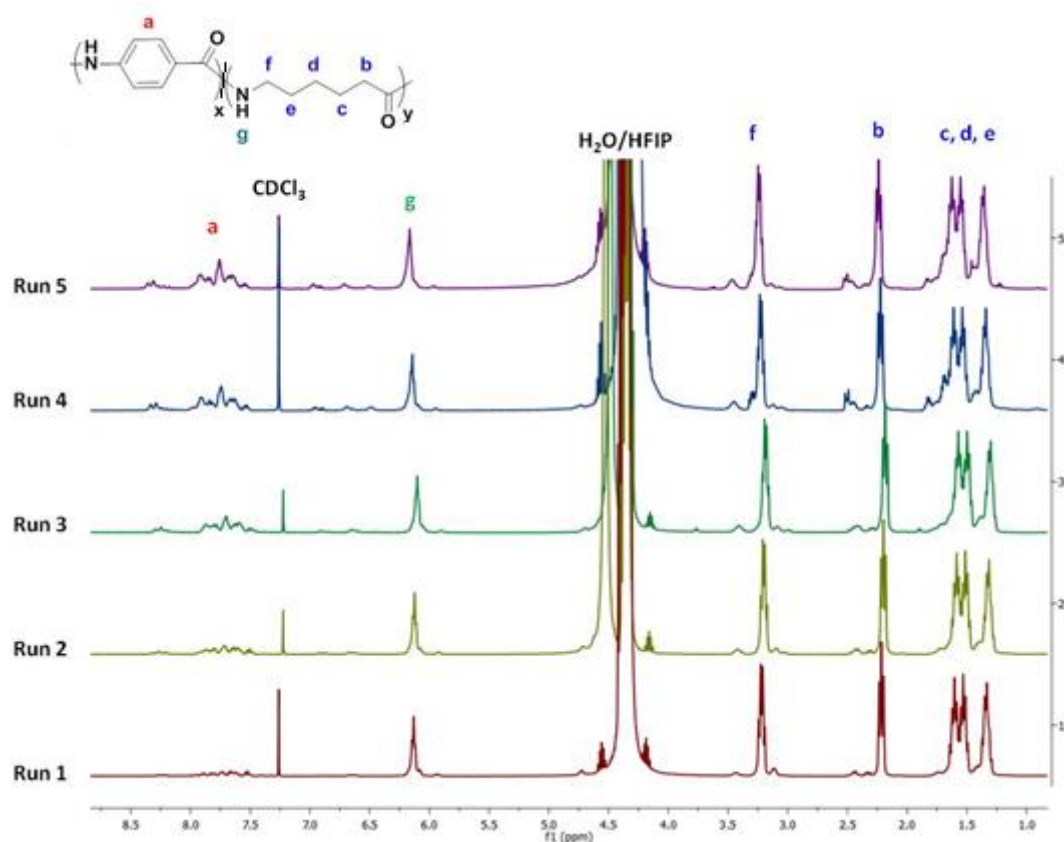
Dimensional characteristics were also studied by preparing different copolyamides containing an initial composition of 90/10 and 95/5 aliphatic/aromatic (%mol). Though increasing the

molar mass of copolymer with a targeted composition of 95/5 (Run 8, Table 5, Figure S6) was successful, copolymerization with initial feed ratio of 10% in aromatic was found to be more complex (Run 1-7, Table 5). High conversion in CL (73-98%) and almost complete conversion of the aromatic co-monomer was observed when theoretical molar masses were below 20 000 g.mol<sup>-1</sup>. In this case, the proportion of the aromatic moieties introduced in the final copolyamide was close to theoretical values (Run 1-2, Table 5 and Figure 14.a). However, when the molar mass targeted is higher than 20 000 g.mol<sup>-1</sup>, the conversion of CL dramatically dropped down and bimodal distribution are observed in size exclusion chromatography traces (Run 3-5, Table 5 and Figure 14.b). Interestingly, the high content of aromatic unit in the final copolyamide (more than 30%) can be clearly observed by the increase of the intensity of aromatic signals between 7.50-8.25ppm (Figure 13) and demonstrated a faster insertion of ethyl 4-aminobenzoate as compared to CL during the copolymerization process. Indeed, as observed for a copolymerization performed with a high amount of ethyl 4-aminobenzoate, the low reactivity of activated CL toward the ester chain-end seems to stop the chain-growth. In order to verify this hypothesis, copolymerizations were performed by adding active species (sodium  $\epsilon$ -caprolactamate, C10, run 6, Table 5) or activator (C20) (run 7, Table 5) after 2 hours, *i.e.* the half time of the polymerization. After addition of C10, a slight and negligible increase of the conversion of CL was observed. On the contrary, the addition of the N-acyllactam activator induced a high conversion in CL meaning that activated monomers are still present but could not react with the polymer chain ends. Those two results agree with a low reactivity of sodium  $\epsilon$ -caprolactamate toward the ester chain end which is responsible for a non-complete conversion of CL. <sup>1</sup>H NMR coupled with 2D NMR analyses (Figures S7, S8 and S9) revealed different chemical shifts for the aliphatic signals, whose intensity increases with the aromatic content. This effect can be clearly observed for the signal of methylene proton in  $\alpha$ -position of the NH group at 3.20 ppm, with the appearance of new signals at 3.28 and 2.95 ppm probably induced by branching reactions due to the higher acidity of the aromatic amide as compared to CL. Moreover, aromatic amide signals are more complicated than those observed previously for copolymerization using ethyl 4-butylaminobenzoate (see above) which is apparently indicating the formation of branched copolyamides. Those small signals could also be assigned to the aliphatic units bounded to aromatic units in different sequences in line with a random distribution of aromatic units along the aliphatic polyamide backbone.

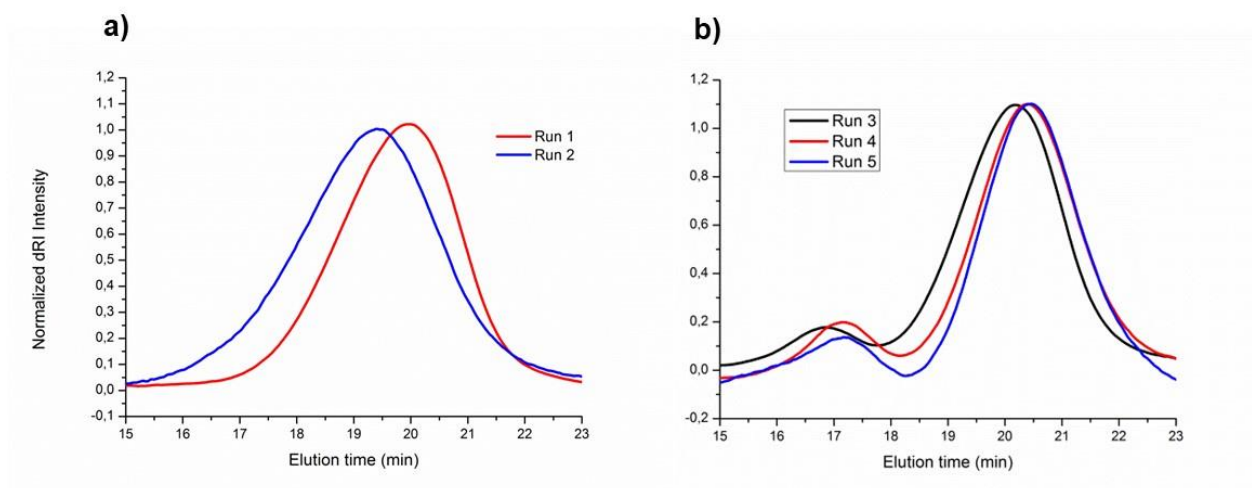
**Table 5.** Anionic bulk copolymerization of ethyl 4-aminobenzoate and  $\epsilon$ -caprolactam at 140°C (4h) with a targeted composition of 90/10 aliphatic/aromatic.

Run	$\overline{Mn}_{theo}$ (g.mol <sup>-1</sup> )	Conv CL <sup>a</sup> (%)	Conv Ar <sup>a</sup> (%)	Exp. Composition Al/Ar (mol%) <sup>a</sup>	$\overline{Mn}_{exp}^b$ (g.mol <sup>-1</sup> )	$\overline{D}^b$
1	10 000	85	100	89/11	17 000	1.56
2	20 000	73	100	83/17	25 000	1.75
3	30 000	33	100	74/26	20 700 (144 000)	1.50 <sup>f</sup>
4	40 000	25	100	67/33	18 200 (127 000)	1.45 <sup>f</sup>
5	50 000	20	100	68/32	16 300 (140 000)	1.42 <sup>f</sup>
6 <sup>c</sup>	50 000	30	100	nd	nd	nd
7 <sup>d</sup>	50 000	80	100	85/15	30 000	1.89
8 <sup>e</sup>	50 000	85	100	93/7	36 000	1.62

a) Conversion and composition were calculated by <sup>1</sup>H NMR; b) Molar masses and dispersities were determined by SEC in HFIP, 0.05% KTFA (vs. PMMA standards) ; c) Addition of C10 (2% mol) after 2h of polymerization ; d) Addition of C20 (0.02% mol) after 2h of polymerization ; e) Copolyamide with a targeted composition of 95/5 aliphatic/aromatic ; f) Dispersity measured for the main population.



**Figure 13.** <sup>1</sup>H NMR analysis of purified copolyamides (Table 5, Run 1-5)

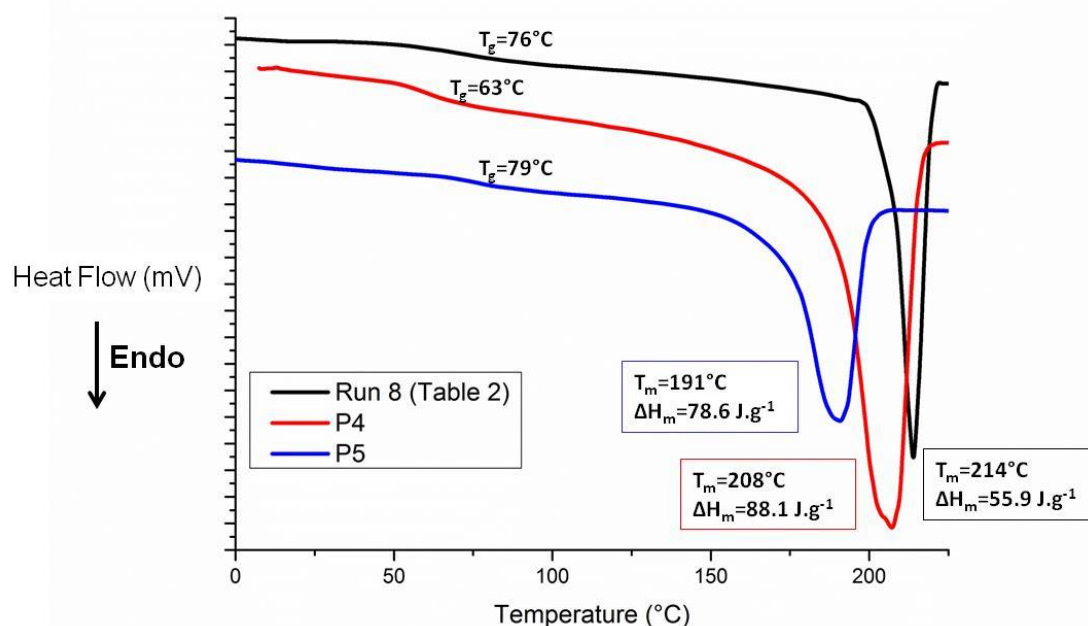


**Figure 14.** SEC traces of a) copolyamides in HFIP (Run 1 and 2, Table 2) and b) of copolyamides in HFIP (Run 3-5, Table 2)

The thermo-mechanical properties of aliphatic/aromatic of selected copolyamides (monomodal distribution and relatively good control over molar masses) having 7% and 17% of aromatic units quantified by  $^1\text{H}$  NMR analysis (P'4 and P'5, Table 4) were investigated by differential scanning calorimetry (DSC), dynamic mechanical analysis (DMA) and thermogravimetric analysis (TGA). The results are presented in Table 6.

Glass transition temperature of PA6 reference prepared by AROP in bulk is observed at  $53^\circ\text{C}$  and melting temperature at  $217^\circ\text{C}$  ( $\Delta H_m = 90 \text{ J.g}^{-1}$ ). The DSC (second heating) results are shown in Table 6 and Figure 15. Synthesized aliphatic/aromatic copolyamides exhibited increased  $T_g$  values up to  $79^\circ\text{C}$  and a slight decrease of the melting temperature ( $T_m = 191\text{--}208^\circ\text{C}$ ) and melting enthalpies ( $\Delta H_m = 78\text{--}88 \text{ J.g}^{-1}$ ) as compared to PA6 reference. A copolyamide with higher molar mass ( $\overline{M}_n = 36\,000 \text{ g.mol}^{-1}$ , Run 8, Table 5) and with an aromatic content equal to 7% was also investigated by DSC (Figure 15). An increase of the glass transition temperature up to  $76^\circ\text{C}$  and a melting temperature at  $214^\circ\text{C}$  were observed accompanied by a decrease of the melting enthalpy ( $\Delta H_m = 55.9 \text{ J.g}^{-1}$ ).





**Figure 15.** DSC curves (second heating) of copolyamides containing 7% (P'4), 17% (P'5) of aromatic content and Run 8 in Table 5.

Dynamic mechanical analysis demonstrated also an increased temperature of the  $\alpha$ -transition ( $\tan\delta$ ) from 71°C for the neat PA6 to 92°C for the copolymer containing 17% of aromatic amide moieties. The elastic modulus ( $E'$ ) measured below  $\tan\delta$  at 25 °C exhibited a slight decrease down to  $6 \cdot 10^8$  or  $9 \cdot 10^8$  Pa, for respectively PA6-7%Ar and PA6-17% Ar, instead of  $2 \cdot 10^9$  Pa for neat PA6 in line with a more branched structure or some irregularities of the repeating units sequences (Figures S10, S11 and S12). This is in agreement with  $E'$  values, measured above  $\tan\delta$ , which were also below the reference in agreement with some decrease of the crystallinity.

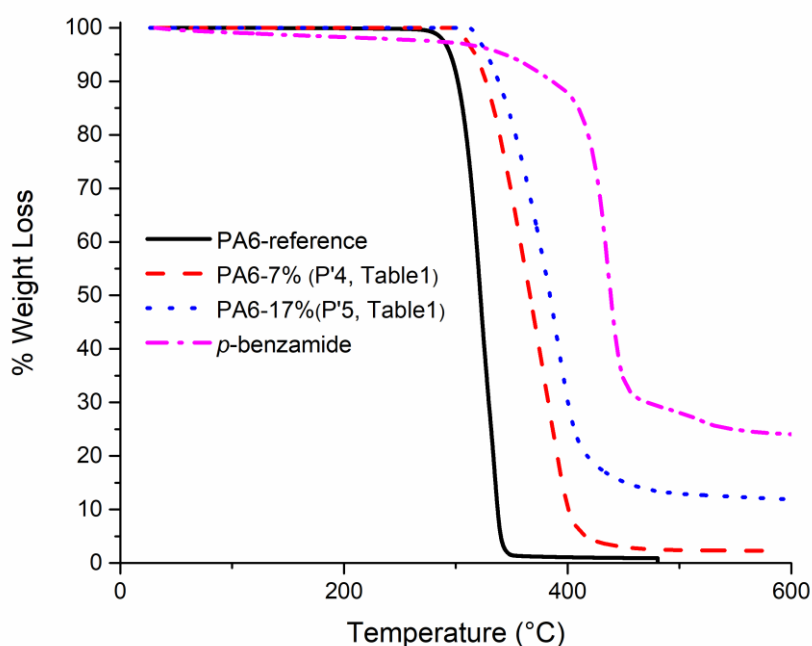
**Table 6.** Thermo-mechanical properties of aliphatic/aromatic copolyamides prepared by one-step bulk copolymerization at 140°C.

Polymer	T <sub>g</sub> (°C)	T <sub>m</sub> (°C)	ΔH <sub>m</sub> (J.g <sup>-1</sup> )	T <sub>d5%</sub> (°C) <sup>a</sup>	T <sub>dmax</sub> (°C) <sup>b</sup>	%res. <sup>c</sup>	E' <sup>d</sup> (GPa)	Tan δ (°C)
Neat PA6	53	216	90.0	290	300	1.0	2.15	72
PA6-7% (P'4)	63	208	88.1	310	376	2.2	0.60	84
PA6-17% (P'5)	79	191	78.6	328	393	12.2	0.90	92
100%Ar	-	-	-	344	436	23.0	-	-

a) Decomposition temperature at 5% weight loss ; b) Maximum of the peak decomposition temperature determined from DTG curves ; c) Residue % at 600°C ; d) measured at 25°C



The thermal stability of aliphatic/aromatic copolyamides was also investigated by thermogravimetric analysis ( $10^{\circ}\text{C min}^{-1}$  under  $\text{N}_2$  atmosphere). The thermograms of PA6, copolyamides with 7 and 17% of aromatic units (P'4 and P'5, Table 4) and aromatic oligomers are displayed in Figure 16. Introduction of aromatic moieties into the PA6 backbone induced an increase of the degradation temperature obtained at 5% of weight loss ( $T_{d5\%}$ ), from  $310^{\circ}\text{C}$  to  $328^{\circ}\text{C}$  ( $290^{\circ}\text{C}$  for the PA6 reference) and the  $T_{d\text{max}}$ , obtained at maximum of the peak decomposition temperature, from  $356^{\circ}\text{C}$  to  $393^{\circ}\text{C}$  ( $300^{\circ}\text{C}$  for PA-6 reference) demonstrating the higher thermal stability of modified PA6.



**Figure 16.** TGA thermograms of neat PA6, PA6-7%Ar, PA6-17%Ar and product of self-condensation (*p*-benzamide) in bulk at  $140^{\circ}\text{C}$ .

In conclusion, the combination of anionic ring-opening and condensation reactions offers a new synthetic route to tune the thermo-mechanical properties of aliphatic polyamides. In this study, polyamides 6 containing various aromatic content were prepared from a mixture of  $\epsilon$ -caprolactam and ethyl 4-aminobenzoate in a one-step procedure. Molar masses up to  $36\,000\text{ g.mol}^{-1}$  with aromatic content up to 33% are reported in those experimental conditions. Characterizations by NMR spectroscopy and thermal analysis are consistent with a statistical distribution of aromatic amide along the aliphatic polyamide chain. As compared to neat PA6, the copolyamides prepared exhibit higher glass transition temperature, up to  $79^{\circ}\text{C}$ , and better

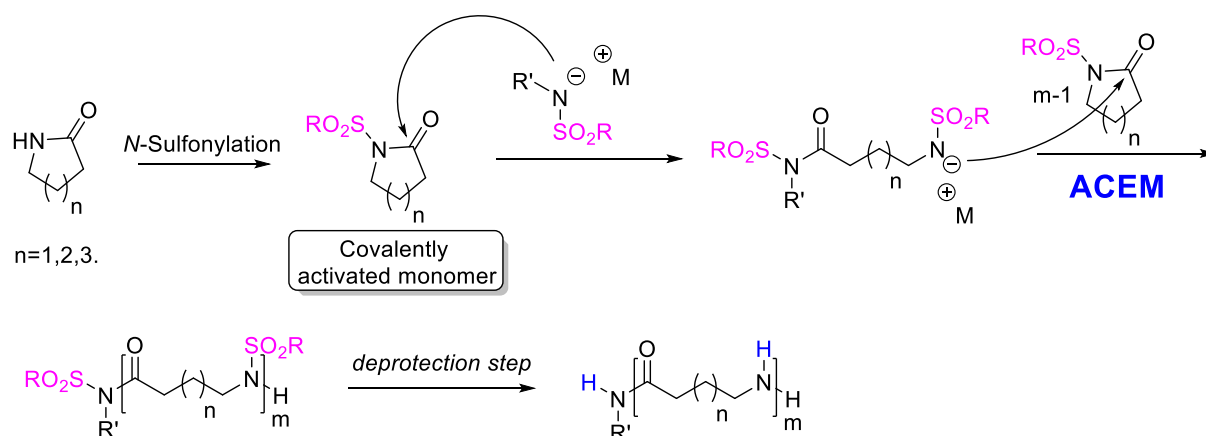
thermal stability. We also demonstrated the limitation of this approach such as the synthesis of high molar mass copolyamides containing more than 10% of aromatic units. Beyond the preparation of new polyamides, we demonstrated the possibility to “marry” anionic ring-opening polymerization of a cyclic amide and condensation reactions of aminobenzoate derivatives keeping the standard and simple experimental conditions of PA6 synthesis, following an activated monomer mechanism.

## **PART 3.B: Monomer Activation Strategy for the Synthesis of Polyamides.**

In this part, we have studied approaches for the synthesis of polyamides *via* a monomer activation strategy. A first part will be devoted to the covalent activation of lactams including the 2-pyrrolidone,  $\delta$ -valerolactam (or 2-piperidone) and  $\epsilon$ -caprolactam, respectively the 5-, 6- and 7-membered cyclic amide, using different tosyl-based activating groups in order to facilitate their ROP. In a second part, the hydrogen transfer polymerization (HTP) and copolymerization of acrylamide derivatives have been applied for the synthesis of polyamide 3-based (co)polymers and polyamide 3/polyamide 6 cross-linked networks.

### **3.B.1. Covalent activation of lactams derivatives**

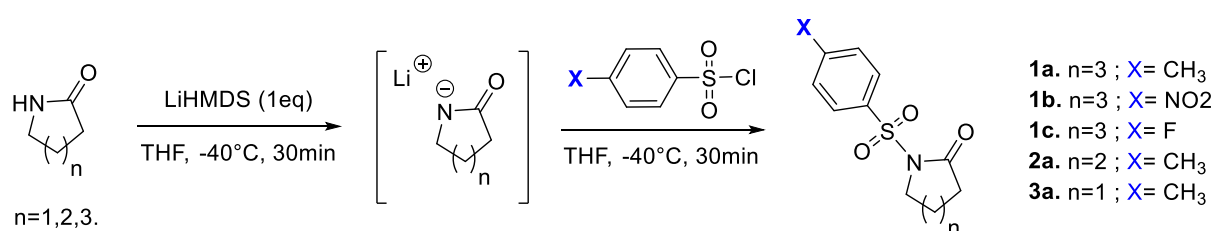
In the chapter 2 of this thesis, we have reported on the NHC-OROP of covalently activated aziridines. In this case, the activation by grafting electron withdrawing group (mainly sulfonyl groups) in a covalent manner allows to switch the mechanism of polymerization (from cationic to anionic).<sup>42,43</sup> Inspired by the activation of aziridines, three representative members of the lactam family, *i.e.* 2-pyrrolidone, 2-piperidone and the  $\epsilon$ -caprolactam, were activated by *N*-sulfonylation on the amide group in order to prepare, in a controlled manner, polyamide precursors in solution *via* an active chain-end mechanism (See Scheme 11). As previously mentioned, the AROP of lactams proceeds generally over an activated monomer mechanism under relatively harsh conditions (bulk, high temperature, etc.) despite the addition of an activator (generally an *N*-acyl lactam moiety). With this proposed “monomer activation strategy”, the introduction of an activating sulfonyl group on the nitrogen of the amide group is expected to achieve the *sine qua non* conditions established by Hashimoto for the living polymerization of lactams,<sup>7</sup> *i.e.* polymerization in solution, with highly reactive lactams under mild conditions. Apart from some  $\alpha,\alpha'$ -di-substituted  $\beta$ -lactams described in the bibliographic chapter, no example of living/controlled polymerization of lactams by AROP or related mechanism has been reported in the literature and still appeared today as a challenge for polymer chemists.



**Scheme 11.** Expected mechanism for the anionic ring-opening polymerization of *N*-sulfonyl activated lactams.

## 3.B.1.1. Monomer synthesis

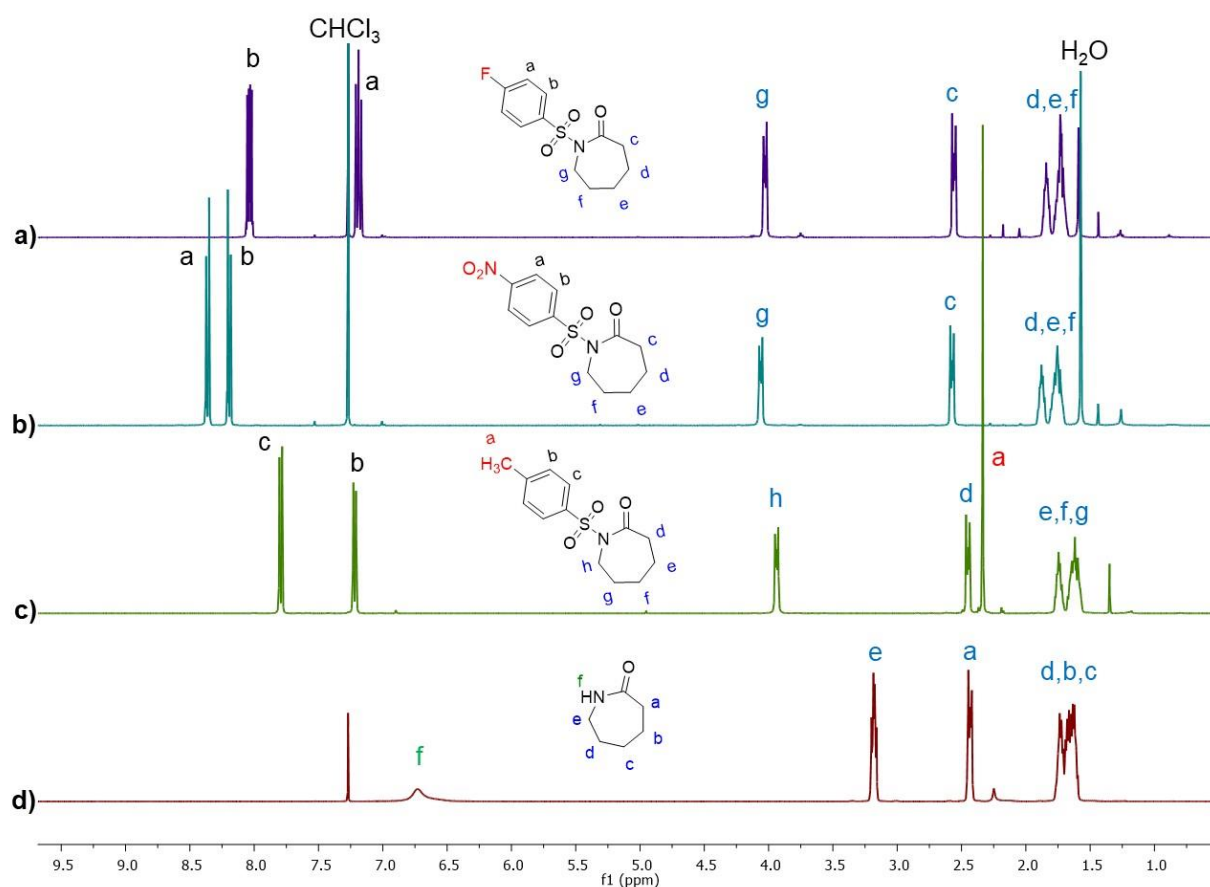
All the activated lactams were prepared according to the procedure already reported by Suarez del Villar *et al.* who used the tosylation as protecting group of the amide function for further modification.<sup>44</sup> This synthesis consists to a complete deprotonation of the corresponding lactam using a strong base (LiHMDS) at  $-40^{\circ}\text{C}$  follow by the addition of *p*-toluenesulfonyl chloride (Scheme 12). For  $\epsilon$ -caprolactam, three different tosyl-based activating groups were grafted by varying the electron withdrawing capacity of the substituent in para position of the aromatic sulfonyl group in the order  $\text{NO}_2$  (nosyl)  $\geq$  F  $\geq$   $\text{CH}_3$  (tosyl).



**Scheme 12.** Synthesis of *N*-sulfonyl lactams.

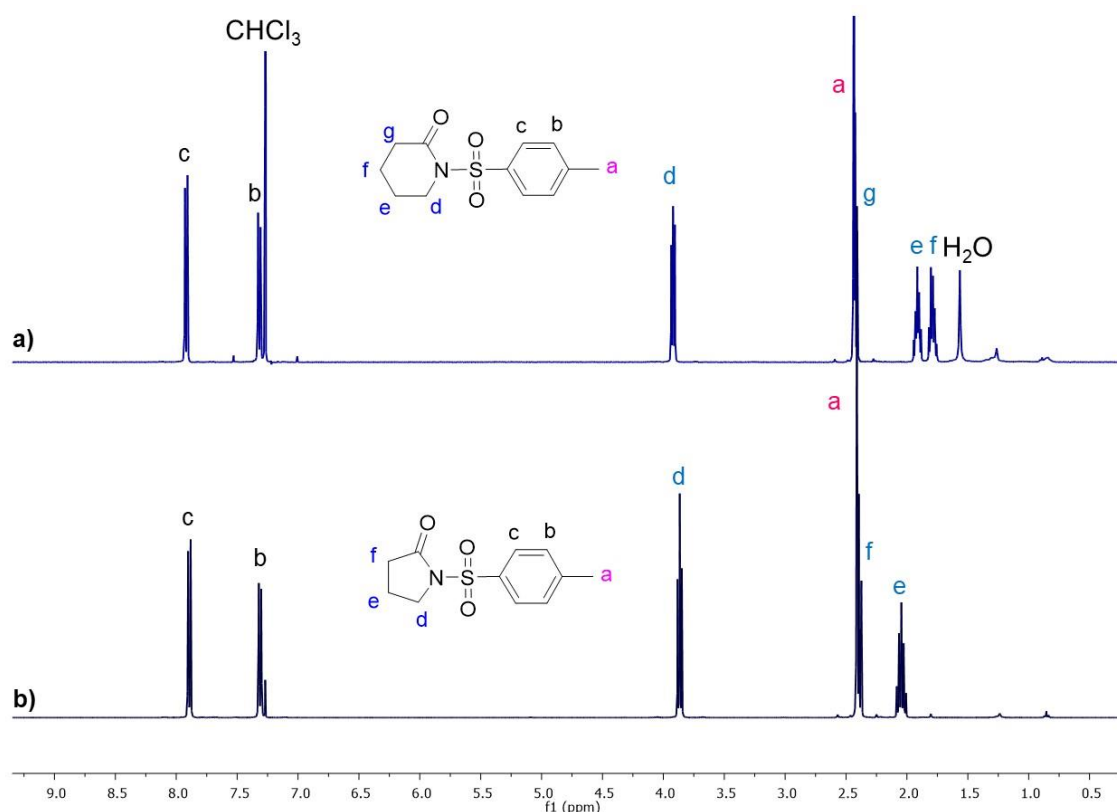
The lactam monomers were purified by chromatographic column using a mixture of pentane/ethyl acetate (from 8/2 to 7/3 depending on the activating group) with relatively good yield ( $R=60$ -95%), further recrystallized and stored in the glovebox. Typical  $^1\text{H}$  NMR spectra of *N*-sulfonyl  $\epsilon$ -caprolactam are presented in Figure 17. The grafting of the electron withdrawing group can be unambiguously observed by the disappearance of NH signal of the amide function at 6.70 ppm and the appearance of aromatic signals of the tosyl-based activating

group between 7 and 8.5 ppm. A large signal shift of the proton in the  $\alpha$ -position of the nitrogen from 3.30 to around 4.00 ppm, which is consistent with the functionalization by a strong electron withdrawing group, is also observed for the *N*-activated lactams.



**Figure 17.**  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ) of a) *N*-*p*-fluorobenzenesulfonyl  $\epsilon$ -caprolactam b) *N*-nosyl  $\epsilon$ -caprolactam, c) *N*-tosyl  $\epsilon$ -caprolactam and d)  $\epsilon$ -caprolactam.

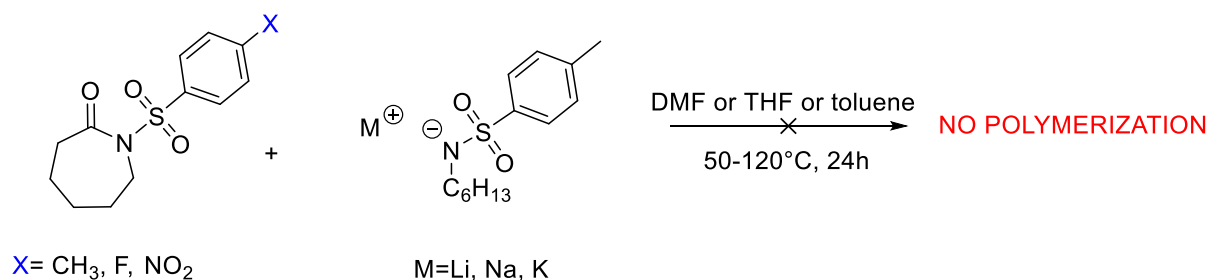
In a similar way, the 2-piperidone and  $\delta$ -valerolactam, respectively the 5- and 6-membered lactams were activated by sulfonylation using the same procedure, *i.e.* deprotonation using LiHMDS at  $-40^\circ\text{C}$  following by the addition of *p*-toluenesulfonyl chloride. High yield (85-97%) were obtained after purification by chromatographic column. The  $^1\text{H}$  NMR spectra of the two sulfonyl lactams are presented in Figure 18 and exhibit all the characteristic signals of the sulfonyl group at 7.90, 7.30 (aromatic signals) and 2.37 ppm (methyl group), demonstrating the versatility of this method for the grafting of tosyl activating groups on a lactam ring.



**Figure 18.**  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ) of tosyl-activated a) 2-piperidone (**2a**) and b) 2-pyrrolidone (**3a**)

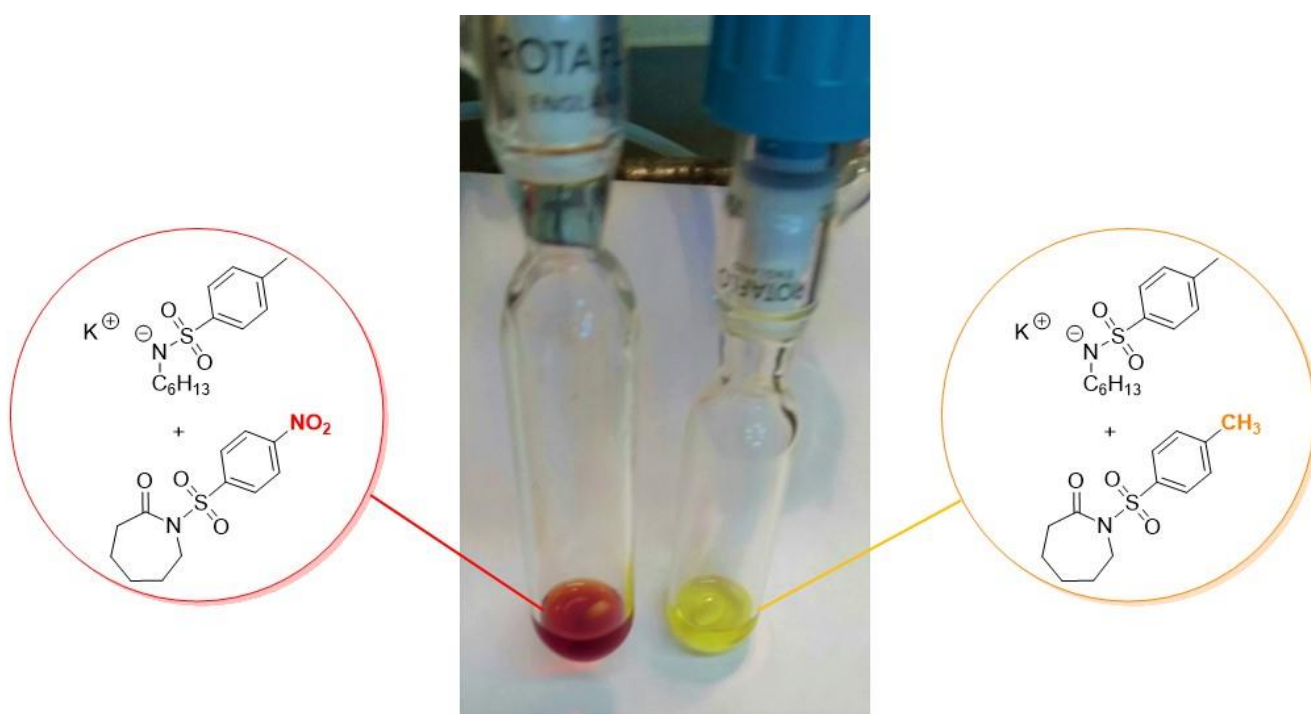
### 3.B.1.2. Preliminary results of the anionic ring-opening polymerization of *N*-activated lactams

Based on the “aza-anionic” polymerization of activated aziridines described by F. R. Wurm and co-workers,<sup>45</sup> we firstly investigated the AROP of activated  $\epsilon$ -caprolactams derivatives using secondary amine salts as initiator in DMF by varying the temperature and the nature of the counter cation (Li, Na or K). We decided to select the initiator previously synthesized for the NHC-OROP of aziridines, namely *N*-hexyl *N*-*p*-toluenesulfonylamine. In the AROP of activated aziridines, highly polar aprotic solvents such as DMSO or DMF were shown to be the best candidates for aza-anionic polymerization (highest propagation rates).<sup>45</sup> Unfortunately, no polymerization was observed under those conditions regardless of the nature of the counter-cation (Li, Na or K), the range of temperature employed (from 50°C to 120°C) or the nature of the solvent (DMF, toluene and THF) (Scheme 13). Different *N*-heterocyclic carbenes as well as *s*-butyllithium were also employed directly as initiators without any improvement.

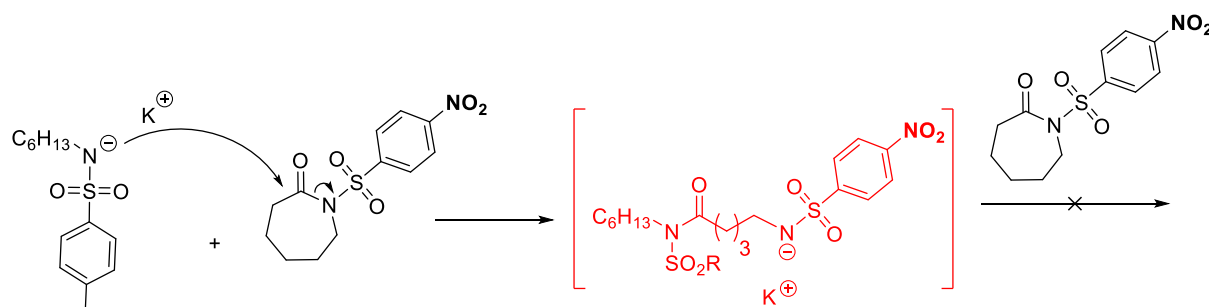


**Scheme 13.** Anionic polymerization of activated  $\epsilon$ -caprolactams initiated by various secondary sulfonamide salts

Interestingly, after the addition of the secondary sulfonamide salt on the monomer solution, a strong coloration appears depending on the nature of the activating group (Figure 19). This result suggests that probably the first addition of the initiator on the lactam ring occurred yielding the colourful “aza-anion” already observed in the AROP of activated aziridines (Scheme 14).<sup>45</sup>



**Figure 19.** Photography of the polymerization media (DMF and *N*-nosyl or *N*-tosyl  $\epsilon$ -caprolactam) after addition of the potassium secondary sulfonamide salt.



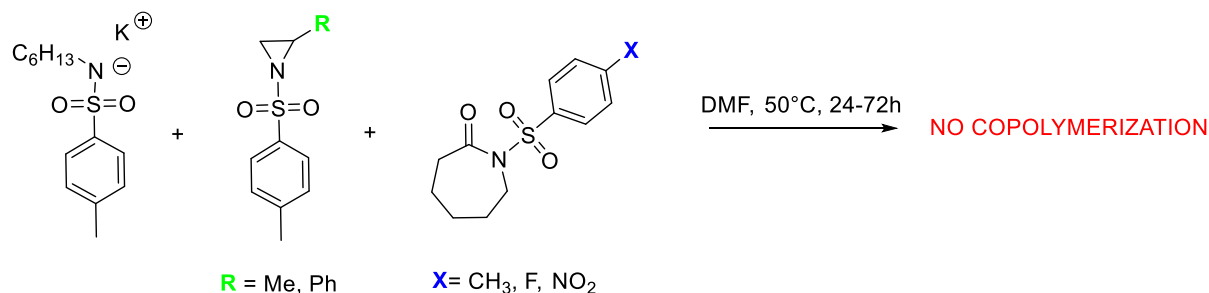
**Scheme 14.** Addition of the potassium secondary sulfonamide salt on the activated lactam exemplified for the *N*-nosyl- $\epsilon$ -caprolactam.

The polymerization of tosyl-activated  $\epsilon$ -caprolactam initiated by secondary amine potassium salts in bulk at 135°C has allowed the synthesis of oligomers under those harsh conditions, thus demonstrating the possibility to ring-open the activated lactam (See  $^1\text{H}$  NMR spectra and SEC traces respectively Figure S13 and S14). The “low polymerisability” of the *N*-tosyl activated seven-membered lactams towards AROP can be explained by the high stability of the lactams ring but also by the introduction of an electron withdrawing group on the nitrogen atom which decreases the nucleophilicity of the propagating anion. The AROP of activated 2-pyrrolidone (**3a**) and 2-piperidone (**3b**), respectively the 5- and 6-membered cyclic amide monomers is currently under investigation and is not described in this manuscript.

In order to overcome the lack of reactivity of the activated lactams, the anionic copolymerization of *N*-activated  $\epsilon$ -caprolactam with the 2-methyl- or 2-phenyl-*N*-*p*-toluenesulfonyl aziridines synthesized previously, were performed using the standard conditions for AROP of activated aziridines (secondary sulfonamide salts, DMF, 50°C, see Scheme 15). The results of the copolymerization are reported in Table 7. We first investigated the copolymerization using the most reactive activated aziridine, namely the 2-methyl *N*-*p*-toluenesulfonyl aziridine. In any case, a complete conversion of the aziridine comonomer was observed independently of the activated lactams used (Table 7, Run 1-3). Typical  $^1\text{H}$  NMR spectrum and SEC traces of the crude copolymerization product are presented in Figure 20 and 21 demonstrated the very low or inexistent conversion of the *N*-tosyl lactams derivatives. The  $^1\text{H}$  NMR spectrum presented Figure 20, exhibits all the diagnostic “broad” signals of the poly(2-methyl-*N*-*p*-toluenesulfonyl aziridine) chains at 7.00-8.00ppm (CH, tosyl); 2.75-4.50ppm (CH<sub>2</sub> and CH backbone); 2.30 ppm (CH<sub>3</sub>, tosyl) and 0.70-1.25 ppm (CH<sub>3</sub>) and also well-defined signals characteristic of the activated lactam monomer at  $\delta(\text{ppm})$ = 8.37; 8.19; 4.06; 2.57; 1.88; 1.76. Interestingly, the AROP of *N*-sulfonyl aziridines is not disturbed by the presence of the activated lactam comonomer and proceeds smoothly yielding well-defined poly(aziridine)s



with low dispersities ( $\bar{D} \leq 1.20$ ). As an example, the SEC trace of the crude (co)polymerization media (Run 2, Table 7) presented in Figure 21 exhibits two populations corresponding respectively to the poly(aziridine) and to the unreactive nosyl-activated lactam in the low molar mass region.



**Scheme 15.** Anionic copolymerization of activated aziridines and activated lactams initiated by secondary sulfonamide salts.

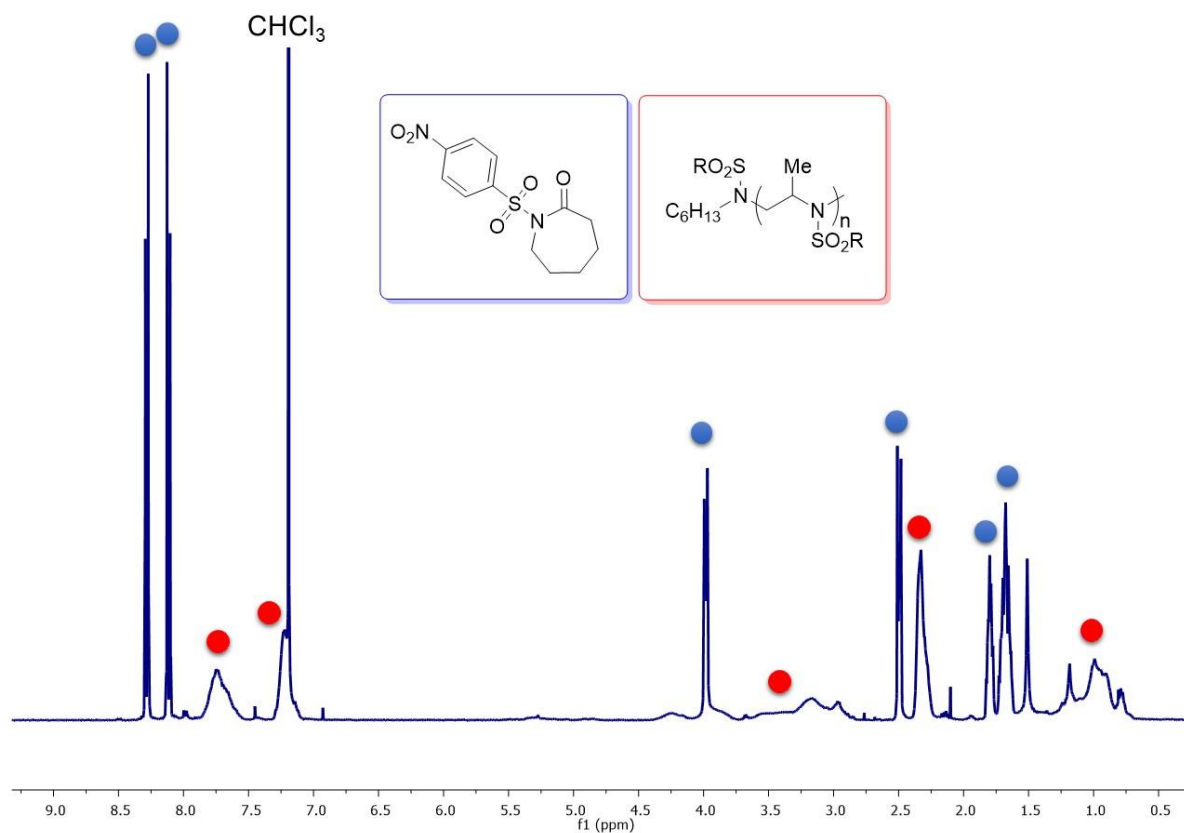
**Table 7.** Anionic copolymerization of activated aziridines and activated lactams initiated by potassium secondary sulfonamide salts (DMF, 50°C, 24-72h).

Run	R	X	[I]/[Az]/[CL]	Conv. % <sup>a</sup> (Az/CL)	$\overline{Mn}_{\text{exp.}}^b$ (g.mol <sup>-1</sup> )	$\bar{D}^b$
1	Me	CH <sub>3</sub>	1/10/10	100/0	1 600	1.06
2	Me	NO <sub>2</sub>	1/10/10	100/0	1 500	1.16
3	Me	F	1/10/10	100/0	1 750	1.08
4	Ph <sup>c</sup>	CH <sub>3</sub>	1/10/10	85/0	1 300	1.10
5	Ph <sup>c</sup>	NO <sub>2</sub>	1/10/10	80/0	1 450	1.20
6	Ph <sup>c</sup>	F	1/10/10	88/0	1 600	1.13

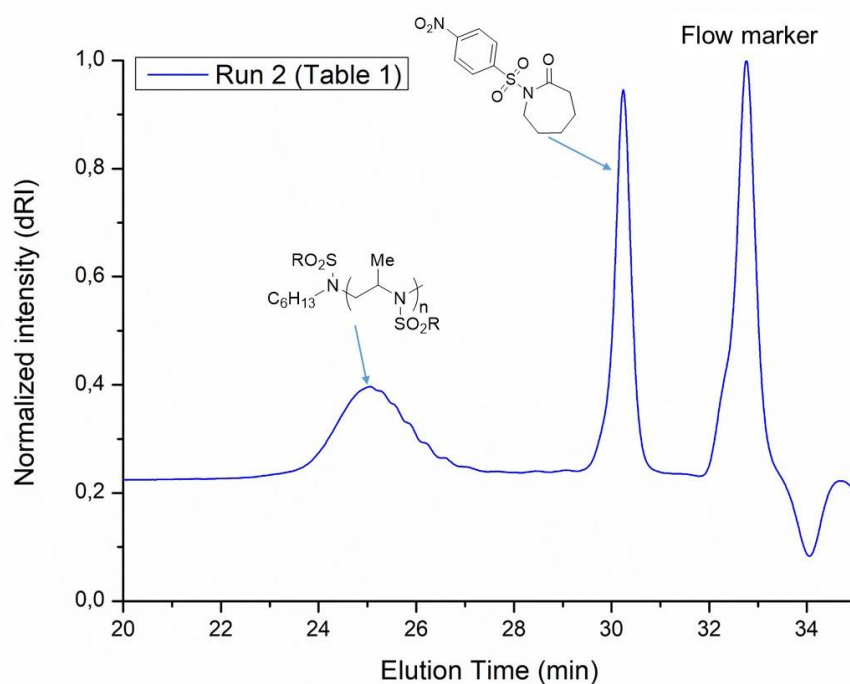
a) Determined by <sup>1</sup>H NMR, b) Determined by size exclusion chromatography in THF (PS standards), c) After 72h at 50°C.

The copolymerization was also investigated by using the less reactive aziridine containing a phenyl group as lateral substituent. Similarly, the anionic polymerization of the 2-phenyl *N*-*p*-toluenesulfonyl aziridine proceeds smoothly without any incorporation of the activated lactams. Despite expected lower conversion, due to the bulky phenyl substituent (80-88%, see PART 2), as compare to the aziridine bearing a methyl side chain, a good control of the polymerization was also observed. MALDI-ToF mass spectrometry experiments need to be further performed

and investigated in order to determine if there is no- or only very low incorporation of the *N*-sulfonyl lactams derivatives into the polyaziridine backbone.



**Figure 20.**  $^1\text{H}$  spectrum ( $\text{CDCl}_3$ ) of the crude copolymerization mixture (Run 2, Table 7).



**Figure 21.** SEC traces (THF) of the crude copolymerization mixture (Run 2, Table 7).

In conclusion, despite the synthesis of original activated lactams using various sulfonyl groups as electron withdrawing group activators, the preliminary polymerization tests performed have highlighted the no- or low reactivity toward anionic ring-opening polymerization of the *N*-activated  $\epsilon$ -caprolactam derivatives. This low reactivity can be explained by the strong delocalisation of the resulting “aza-anion” which seems to be not able to ring-open the stable seven-membered cyclic amide even it is activated. The activation of the 5- and 6-membered cyclic amide by *N*-tosylation has been also performed but their polymerization behaviour has not yet been explored. Nonetheless, the covalent activation of lactams by EWG still appears as promising strategy to achieve the *sine qua non* conditions to attain living ring-opening polymerization of lactams.

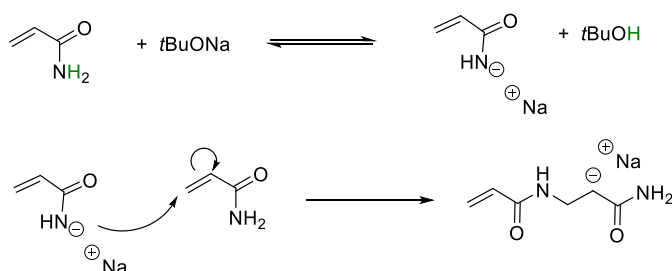
### 3.B.2. Hydrogen Transfer Polymerization of acrylamides derivatives

Polyamide-3 (PA3), also called *nylon 3* or *poly( $\beta$ -alanine)* depending on the precursors used, differs from the other commercial polyamides due to its particular molecular structure in which each repeating unit contains only two methylene groups for one amide function. PA3 exhibits generally high melting temperature (320-355°C), crystallinity (30-40%), glass transition temperature in the range of 110°C-125°C and a good capacity to uptake moisture.<sup>46-53</sup> Despite good thermo-mechanical properties (quite similar to that of silk), only few applications of PA3 derivatives are referenced in the literature, *e.g.* the synthesis of PA3 can be achieved by i) polycondensation of  $\beta$ -alanine and its derivatives,<sup>54,55</sup> ii) the ring-opening polymerization of substituted  $\beta$ -lactams or unsubstituted  $\beta$ -propiolactam using anionic or enzymatic approaches<sup>47,56-62</sup> and iii) the hydrogen transfer polymerization (HTP) of acrylamides derivatives.<sup>63-71</sup>

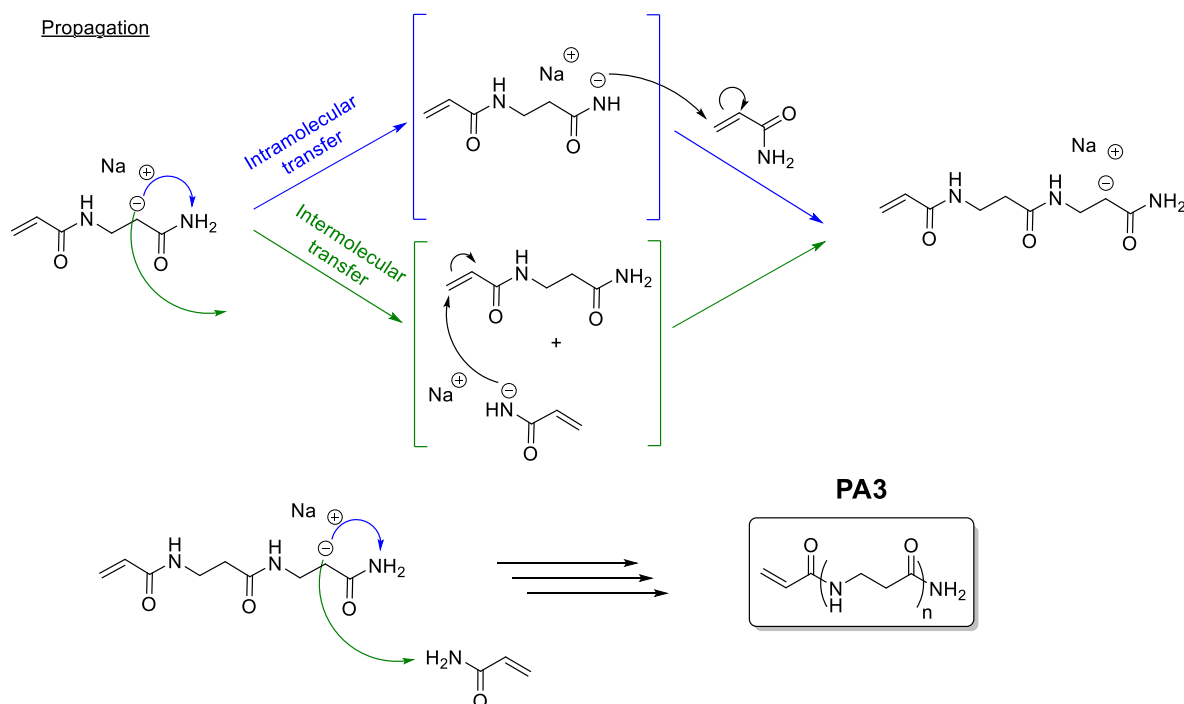
The hydrogen transfer polymerization, following an activated monomer mechanism, of acrylamide has been firstly investigated by Matlack and co-workers using various metal catalyst as an initiator.<sup>72,73</sup> As described in Scheme 16, the polymerization is initiated by abstraction of the primary amide proton from acrylamide by a *tert*-butoxide anion yielding the corresponding amidate, *i.e.* the activated monomer. The propagation occurs by multiple Michael addition (1,4 addition) of the amidate on the double bond of another acrylamide molecule followed by a rapid proton transfer thus regenerating the activated monomer. The chain growth can occur by (i) a chain-transfer type mechanism (intermolecular transfer) or (ii) by poly(1,4 addition) mechanism (intramolecular transfer) (See scheme 16).

Tertiary alkoxides were found to be the best metal catalyst for the HTP of acrylamide in the order  $t\text{-BuOK} \approx t\text{-BuONa} > t\text{-BuOLi}$ . Most of the time the polymerizations were performed between 80-150°C (from a few minutes to hours) in aprotic solvent such as pyridine, benzene and its derivatives, DMF, or DMAc to favour the polymer solubility.<sup>63-73</sup> In all cases, HTP of acrylamides in solution conducts to an incomplete conversion of the monomer and the formation of low molar mass polyamide 3.

### Initiation

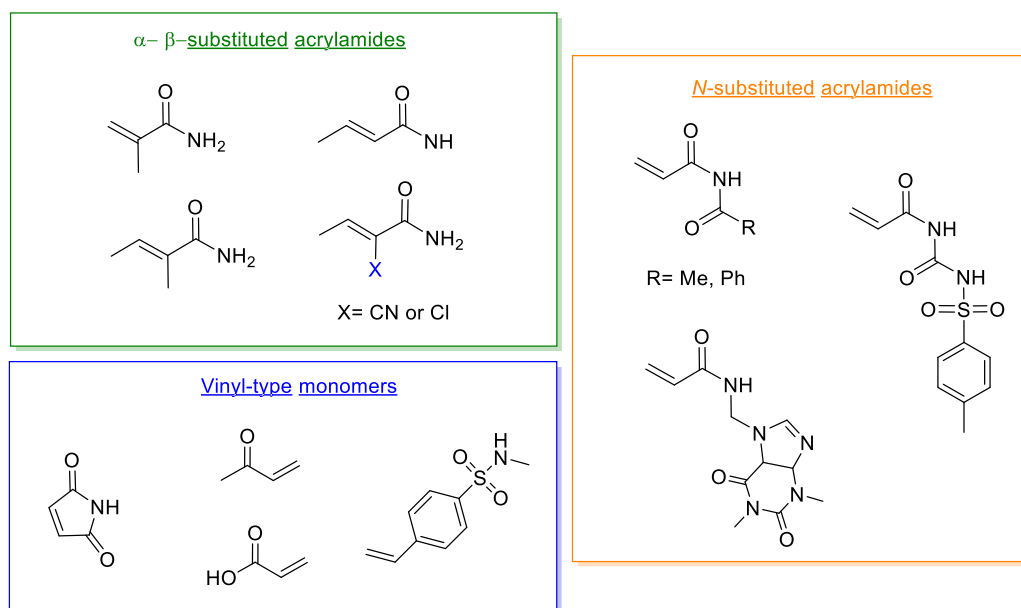


### Propagation



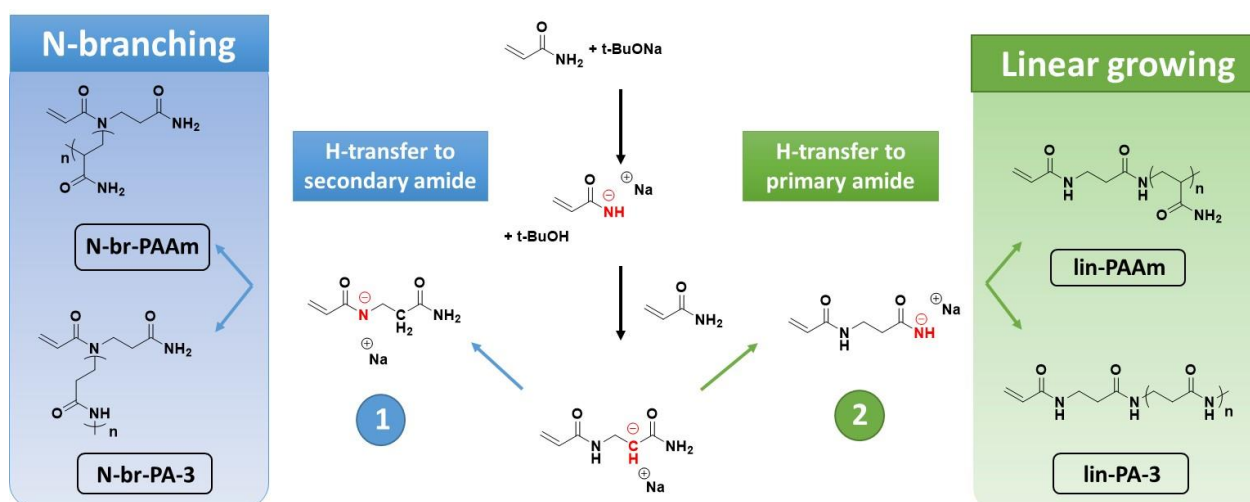
**Scheme 16.** Proposed mechanism for the hydrogen transfer polymerization of acrylamide initiated by  $t\text{-BuONa}$ .

Despite this limitation, HTP in solution has been extended to other acrylamides derivatives such as  $\alpha$ - and/or  $\beta$ -substituted acrylamide or  $N$ -substituted acrylamides (Figure 22).<sup>74-78</sup> The number and the position of the substitution in the monomer structure significantly affected both the rate of polymerization and the molar mass of the resulting polyamide. Vinyl-type monomers such as maleimide,<sup>74</sup> cinnamide,<sup>75,76</sup> methyl vinyl ketone or acrylic acid<sup>78</sup> were also investigated as monomer substrates for the HTP but only low conversion, low molar mass polymer and low selectivity (vinyl vs. HTP growth) were observed.



**Figure 22.** Scope of the  $\alpha$ - and/or  $\beta$ -substituted acrylamide, *N*-substituted acrylamides and vinyl-type monomers polymerized by HTP in solution

In the laboratory, K. Roos *et al.* proposed the anionic bulk HTP of acrylamides in order to overcome the solubility and reactivity issues.<sup>79</sup> The polymerization was initiated by *t*-BuONa and polyamide 3 up to 23 600 g.mol<sup>-1</sup> were obtained in bulk at 90°C within a few seconds. A precise mechanistic study combining NMR spectroscopy, MALDI ToF mass spectrometry and size exclusion chromatography has demonstrated the occurrence of side reactions such as branching, transfer to the monomer and formation of acrylamide units depending on the amount of base used (Scheme 17).

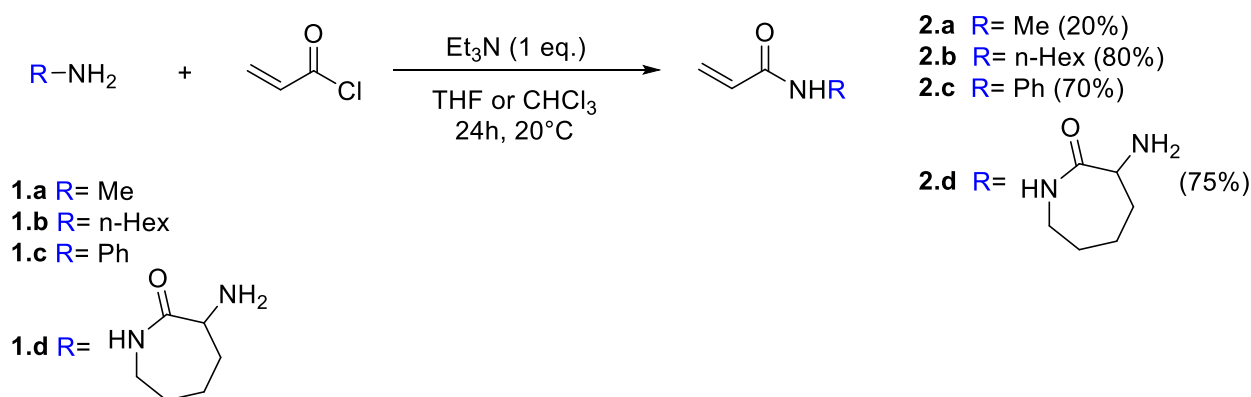


**Scheme 17.** Possible hydrogen-transfer and propagation reactions for bulk HTP of acrylamides.

Based on this result and in order to tune the properties of PA3- or PA6-PA3-based materials. We decided to extend the scope of monomer amenable to polymerize by HTP in bulk through anionic bulk (co)polymerization of *N*-substituted and  $\beta$ -substituted acrylamide.

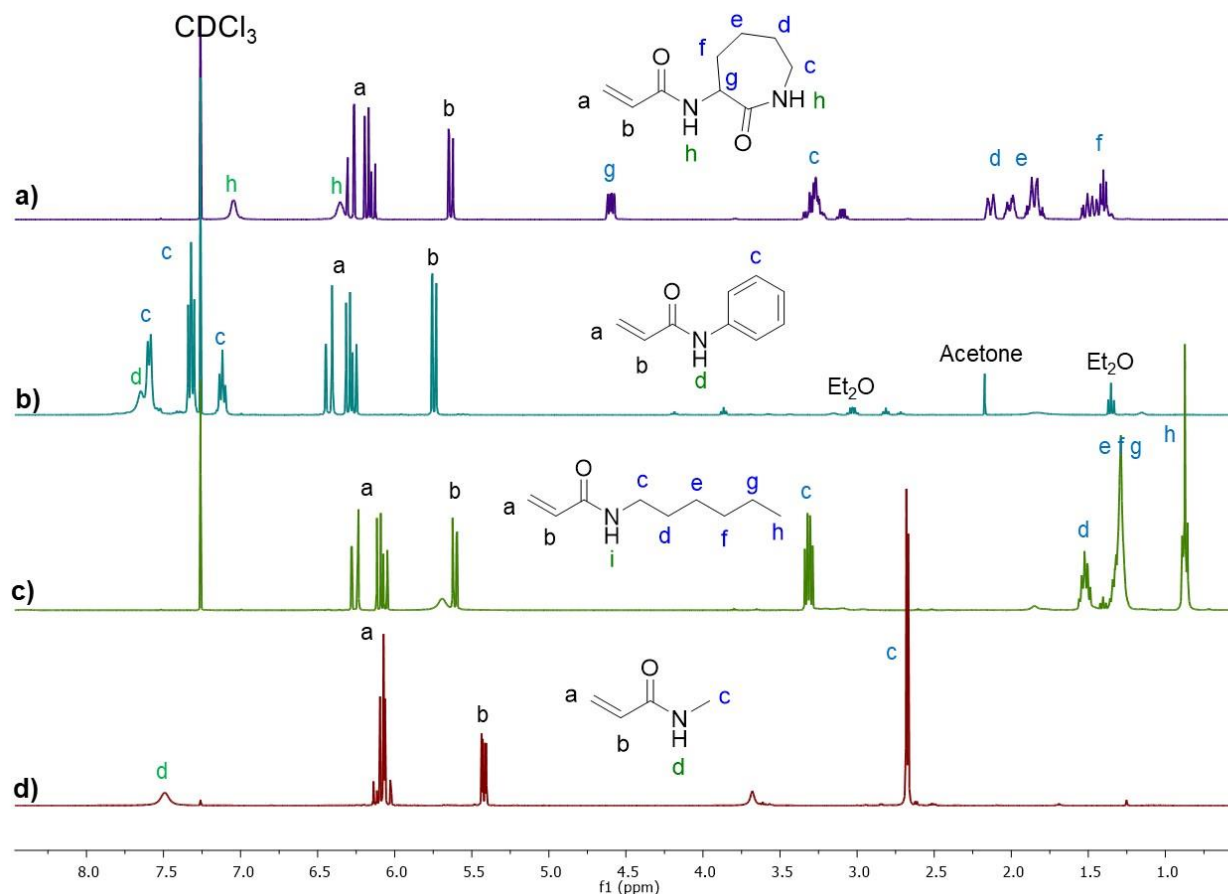
### 3.B.2.1 Monomer Synthesis

Four different *N*-substituted acrylamide compounds were synthesized by reacting primary amine such as *N*-methylamine (**1a**), *N*-hexylamine (**2a**), aniline (**3a**) or DL- $\alpha$ -amino- $\epsilon$ -caprolactam (**4a**) with acryloyl chloride in presence of tri-ethylamine (NEt<sub>3</sub>) in THF or CHCl<sub>3</sub> (Scheme 18).

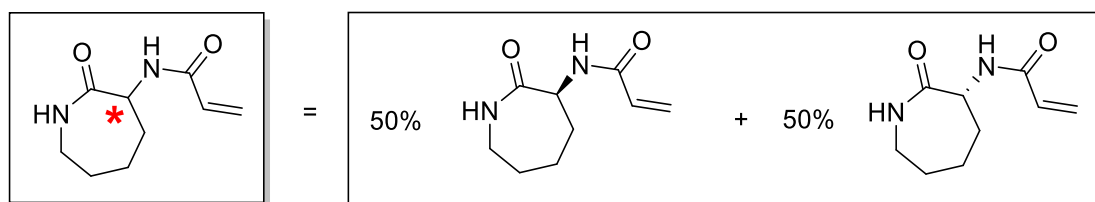


**Scheme 18.** Synthesis of *N*-substituted acrylamide derivatives

Apart from the *N*-methyl acrylamide (**2.a**) which was only obtained in low yield (20%) due to arduous purifications, the *N*-substituted acrylamides **2.b**, **2.c** and **2.d** were obtained in good yield (70-80%). The <sup>1</sup>H NMR spectra of the purified *N*-substituted acrylamide monomers, displayed in Figure 23, attested the efficiency and the versatility of the coupling reaction between a primary amine and acryloyl chloride. Characteristic signals of the alkyl side chain are clearly visible for *N*-methyl and *N*-hexyl acrylamide, respectively at 2.70 ppm and between 0.80-1.70 ppm. For the *N*-phenyl acrylamide monomer, diagnostic signals of the aromatic substituent are readily observed between 7.00-7.75 ppm. The presence of an asymmetric carbon (racemic mixture) for the monomer **2.d** bearing a  $\epsilon$ -caprolactam moiety slightly complexify the signals of the caprolactam ring at 4.60, 3.20, and between 1.27 and 2.05 ppm observed by <sup>1</sup>H NMR (Figure 23 and 24).



**Figure 23.**  $^1\text{H}$  NMR spectra (in  $\text{CDCl}_3$ ) of a)  $N$ -(DL- $\alpha$ -amino- $\epsilon$ -caprolatam) acrylamide, b)  $N$ -phenyl acrylamide, c)  $N$ -hexyl acrylamide and d)  $N$ -methyl acrylamide



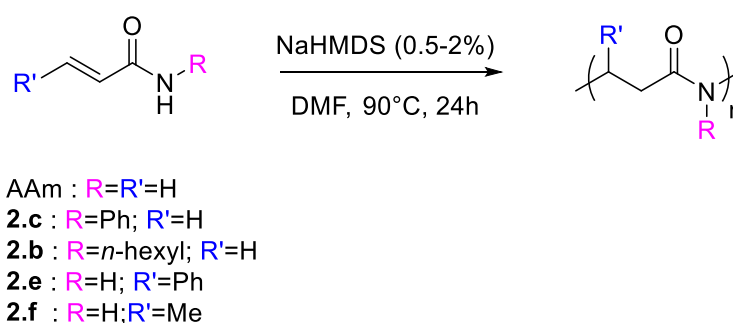
**Figure 24.** Racemic mixture of the  $N$ -(DL- $\alpha$ -amino- $\epsilon$ -caprolatam) acrylamide monomer

Two commercially available  $\beta$ -substituted acrylamide monomers containing a phenyl or a methyl at the  $\beta$ -position of the double bond moiety, namely respectively the cinnamide (**2.e**) and the crotonamide (**2.f**) were also used to study the influence of the substitution on the reactivity of the acrylamide derivatives.



### 3.B.2.2. PA3-based copolyamides by hydrogen transfer polymerization

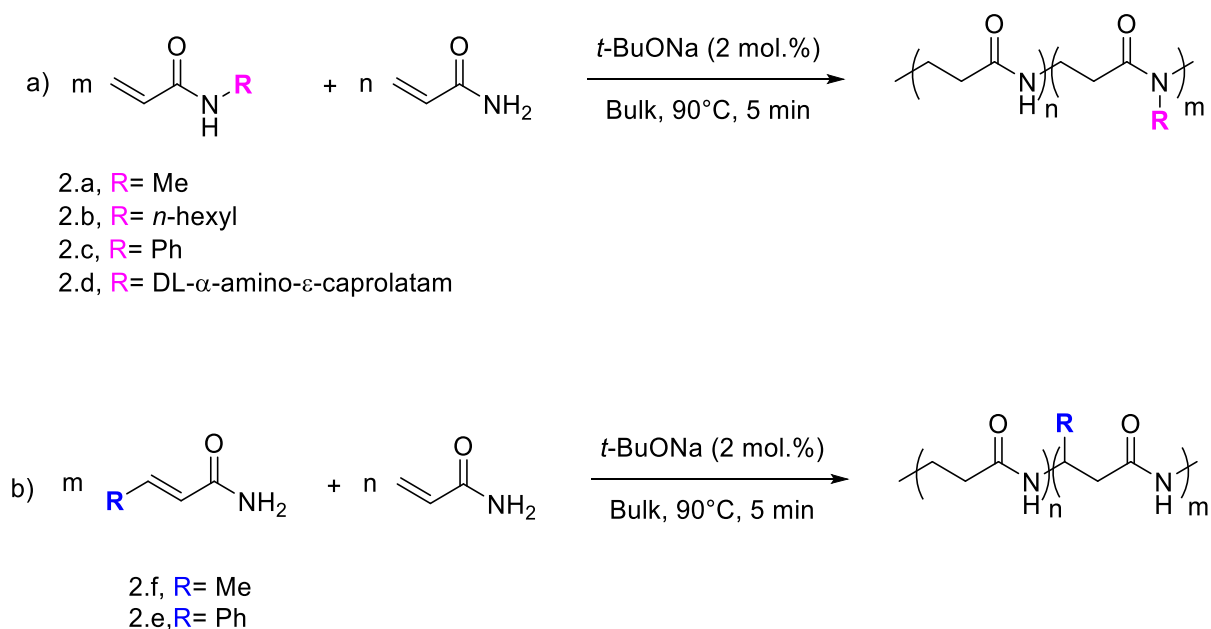
In a preliminary work, the homo-polymerization of acrylamide and selected derivatives abovementioned (**2.b**, **2.c**, **2.e** and **2.f**), *i.e.* the *N*-substituted and  $\beta$ -substituted acrylamides, have been investigated in solution in order to evaluate the monomer reactivity. All the polymerizations were performed in DMF using NaHMDS as deprotonating agent and have been reported in the experimental part (Table S2 and Scheme 19). The anionic hydrogen transfer polymerization of acrylamide (AAm) in solution is generally run at 90°C in DMF with high conversion (> 98%) after 24h for low molar masses targeted. In any case, the polymerization of acrylamide and its derivatives has been observed in solution except for the **2.e** (Table S2, run 2-10). In this case, the presence of phenyl group on the double bond not allowed the nucleophilic attack from the activated monomer under those conditions. As expected for HTP in solution, decreasing the amount of NaHMDS as compared to the monomer concentration, has not afforded higher molar mass polyamide 3 due to the early precipitation of polymer in solution. Given the high melting temperature of some of the acrylamides derivatives such as the crotonamide (158°C), the cinnamide (150°C) or the  $\epsilon$ -caprolactam containing monomer (**2.d**, 177°C), we decided to investigate the bulk copolymerization of such monomers with acrylamide (AAm). All the results of copolymerization are reported in Table 8.



**Scheme 19.** Hydrogen transfer polymerization of acrylamide derivatives in DMF at 90°C initiated by NaHMDS

Based on our previous work on the bulk-HTP of acrylamide,<sup>79</sup> the hydrogen transfer polymerization and copolymerization were performed in bulk with 2% mol. of *t*-BuONa as activator at 90°C, which was found to be the best conditions for the homopolymerization of acrylamide, *i.e.* molar masses closed to theoretical values and low amount of branching reactions. In a typical experiment, the comonomer is solubilized in the melted acrylamide before the addition of the activator. Copolymerization proceeds in a few seconds and the unreactive monomers and other

reagents were removed by refluxing the crude polymer in THF during 24h. Two different initial ratios  $[\text{acrylamide}]_0/[\text{comonomer}]_0$  ([5/1] and [2/1] which correspond respectively to 20 mol% and 50% mol of comonomer initial feed ratio as compared to the amount of acrylamide) were explored depending on the solubility of the comonomer in the melted acrylamide. Indeed, the comonomer **2.c** and **2.d** were found to be only partially soluble in acrylamide at 90°C if the initial feed ratio  $[\text{AAM}]_0/[\text{comonomer}]_0$  was higher than ([5/1], corresponding to 20 mol%). As a difference with the HTP of acrylamide derivatives in solution, which required 24h to achieve high conversion, the bulk copolymerization proceeded in a few seconds or minutes at 90°C with conversion from 30% to 97% depending on the nature and the position of the substitution. *N*-substituted acrylamide derivatives (**2.a-d**, Run 2-6, Table 8) were found to be less reactive than the  $\beta$ -substituted acrylamides. Indeed, despite almost complete conversion, low yield (30-60%) were observed for the copolymerization of acrylamide with *N*-methyl and *N*-hexyl acrylamide. This result might be explained by i) the formation of low molar mass copolyamides (oligomers) removed during the purification or ii) a better solubility in THF induced by the presence of alkyl side chains on the PA3 backbone.



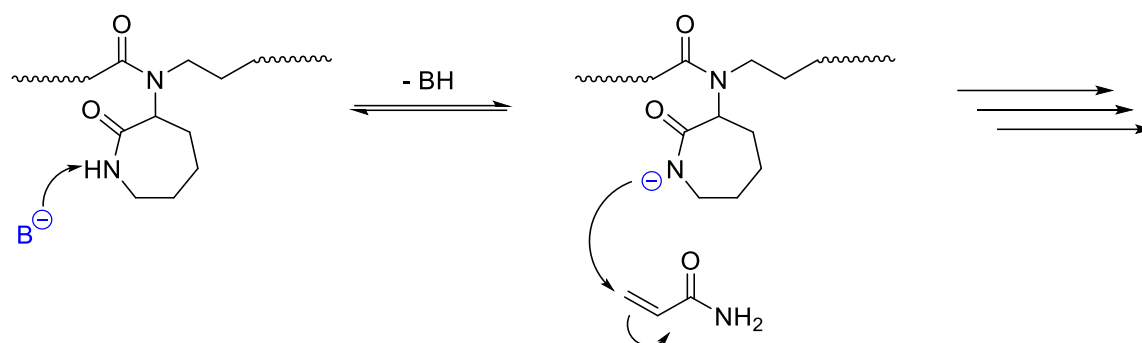
**Scheme 20.** Hydrogen transfer bulk copolymerization of acrylamide with a) *N*-substituted and b)  $\beta$ -substituted acrylamides at 90°C, using *t*-BuONa (2%mol) as initiator

**Table 8.** Bulk copolymerization of Acrylamide (AAM) with *N*-substituted and  $\beta$ -substituted acrylamides at 90°C, using *t*-BuONa (2%mol) as initiator (5 min).

Run	Copolymer	Theor. (mol%) Composition [AAM/2.x]	Exp. (mol%) Composition <sup>a</sup> [AAM/2.x]	Branch. <sup>a</sup> (%)	Yield <sup>b</sup> (%)	$\overline{M}_n^c$ (g/mol)	$\mathcal{D}^c$
1	AAM	100/0	100/0	3.0	98	3 300	3.1
2	AAM/2.a	83/17	89/11	9.0	30	-	-
3	AAM/2.b	83/17	85/15	8.0	50	1 200	2.6
4	AAM/2.b	67/33	75/25	7.0	58	1 450	2.4
5	AAM/2.c	83/17	83/17	14.0	91	1 600	2.6
6	AAM/2.d	83/17	82/18	16.0	77	15 900	3.3
7	AAM/2.e	83/17	80/20	3.0	90	550	1.3
8	AAM/2.e	67/33	55/45	9.0	75	600	1.4
9	AAM/2.f	83/17	86/14	3.0	93	3 800	1.6
10	AAM/2.f	67/33	62/38	2.0	97	4 500	1.7
11 <sup>d</sup>	2f	0/100	0/100	2.0	95	2 600	1.7

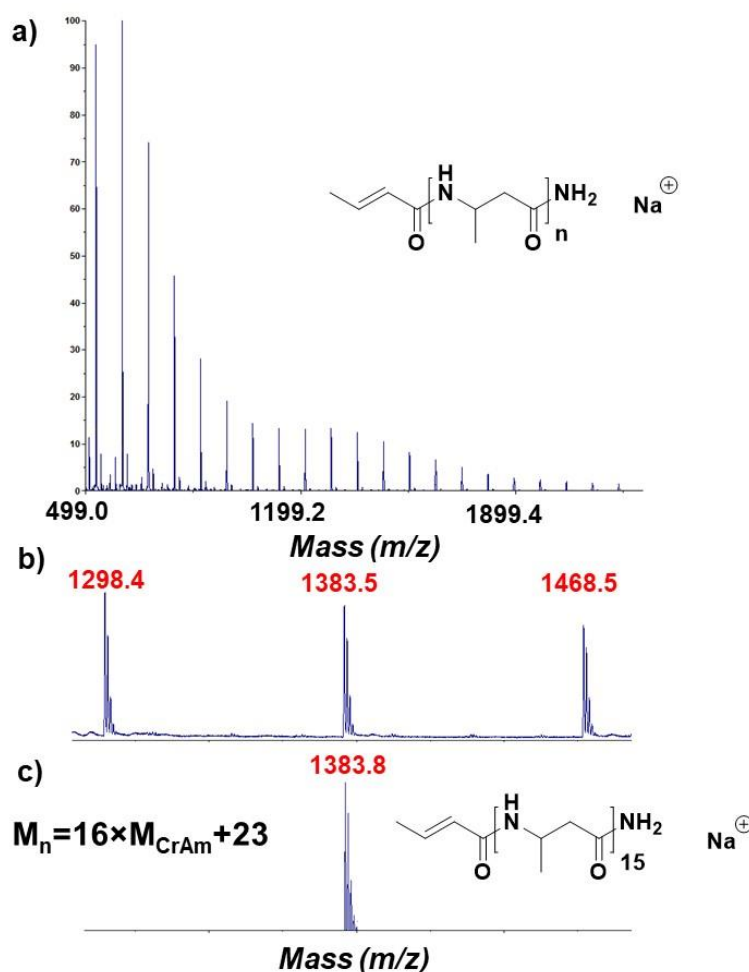
a) Determined by <sup>1</sup>H NMR, b) determined by gravimetry, c) determined by size exclusion chromatography in HFIP (PMMA standards)

Furthermore, the polymerizations performed with 20 mol.% of *N*-substituted or  $\beta$ -substituted (**2a-2f**) as comonomer compared to neat PA3 exhibit similar characteristics than the homopolymerization of acrylamide like a very low reaction time ( $t \leq 5$  min) and a strong exothermic polymerization (Table 8, run 2-10, Figure 28). However, only low molar mass polyamides have been obtained for **2.b**, **2.c** and **2.e** up to 1,600 g.mol<sup>-1</sup> which may be explained the steric hindrance of the phenyl/hexyl group. For the crotonamide (**2.f**) monomer, copolyamides with higher molar mass up to 3,800 g.mol<sup>-1</sup> have been synthesized. Regarding the reaction control, it has been already shown in previous studies that the strongly exothermic HTP of AAM leads to numerous side reactions and consequently to a broader molar mass distribution.<sup>79</sup> In contrast, the monomer bearing a  $\epsilon$ -caprolactam side chain (Run 6, Table 8) exhibits higher molar mass ( $\overline{M}_n = 15\,900$  g.mol<sup>-1</sup>) induced probably by the presence of the endocyclic amide groups. Indeed, the deprotonation of the latter during the copolymerization process generates an amidate anion capable of attacking an acrylamide molecules, leading to branched structures and can explain the formation of a higher molar mass copolyamide (see scheme 21).



**Scheme 21.** Branching reaction during the bulk-HTP copolymerization of acrylamide with monomer **2.d**

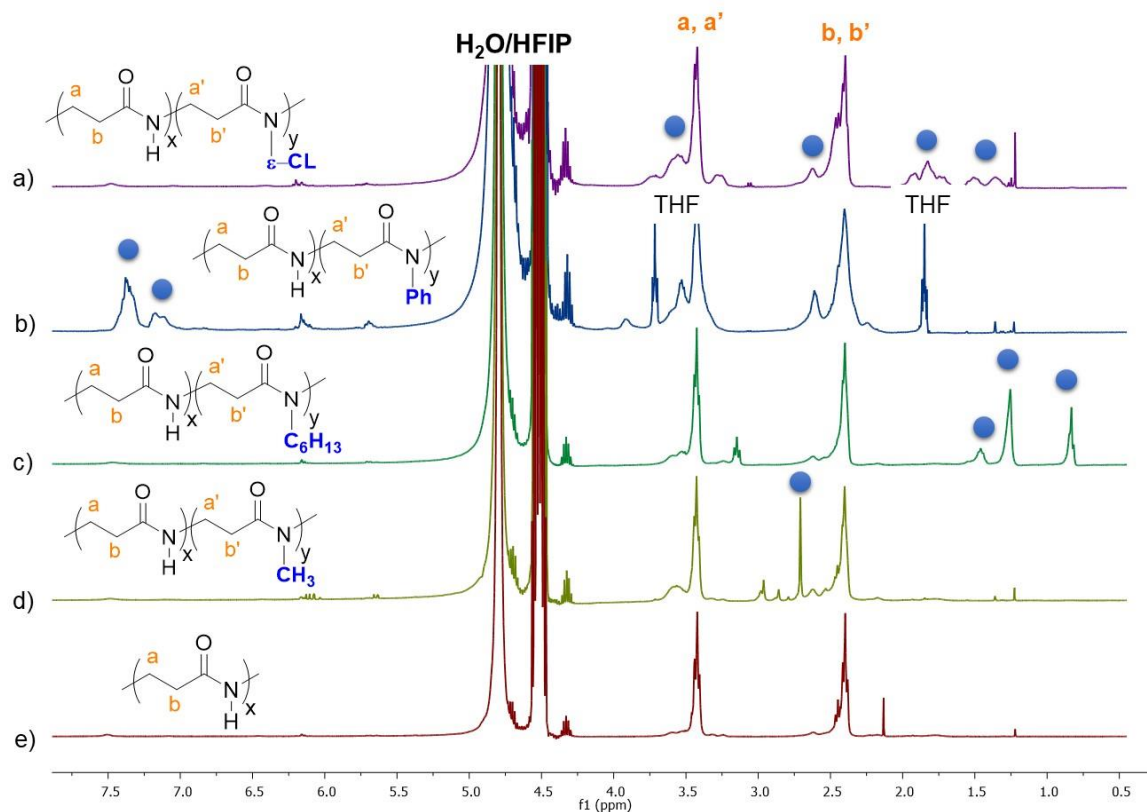
The copolymers prepared with 50 mol.% initial feed ratio of comonomer (**2.b**, **2.e** and **2.f**, Run 4, 8 and 10, Table 8) as compare to AAm highlight the limit of this approach pointing out the various monomer reactivity's (Table 8, run 6 to 9). In the case of phenyl-containing acrylamide (**2.c** and **2.e**) copolymerized with AAm (Table 8, run 5, 7 and 8), the presence of a phenyl group leads to a decrease of monomer conversion for the **2.e**-AAm (75%). This decrease could be explained by a less efficient initiation step due to the steric hindrance issue from the phenyl groups and thus might be explain the low conversion when the amount of cinnamide increase (Table 8, run 8). Interestingly, copolymerization with crotonamide (**2f**, Run 9 and 10) exhibited high conversion, relatively good control over the molar mass, good control of the comonomer incorporation and low amount of branching side reactions. Based on this result, we performed the homopolymerization of crotonamide in bulk at 160°C (Run 11, Table 8). In this case, the polymerization exhibits also good control over molar mass and almost complete conversion under this condition but the attempts to increase the molar mass, but changing the initial ratio  $[2.f]_0/[t\text{-BuONa}]_0$  of this polyamide 3 derivatives have failed. MALDI ToF of the poly(crotonamide) obtained by bulk-HTP is presented in Figure 25. The presence of the double bond at one chain-end and a primary amine at the other suggests that the propagation occurs by multiple Michael addition through the terminal amine with subsequent deprotonation reactions.



**Figure 25.** Experimental (a and b) and computed (c) MALDI ToF spectra of poly(crotonamide) (Run 11, Table 8).

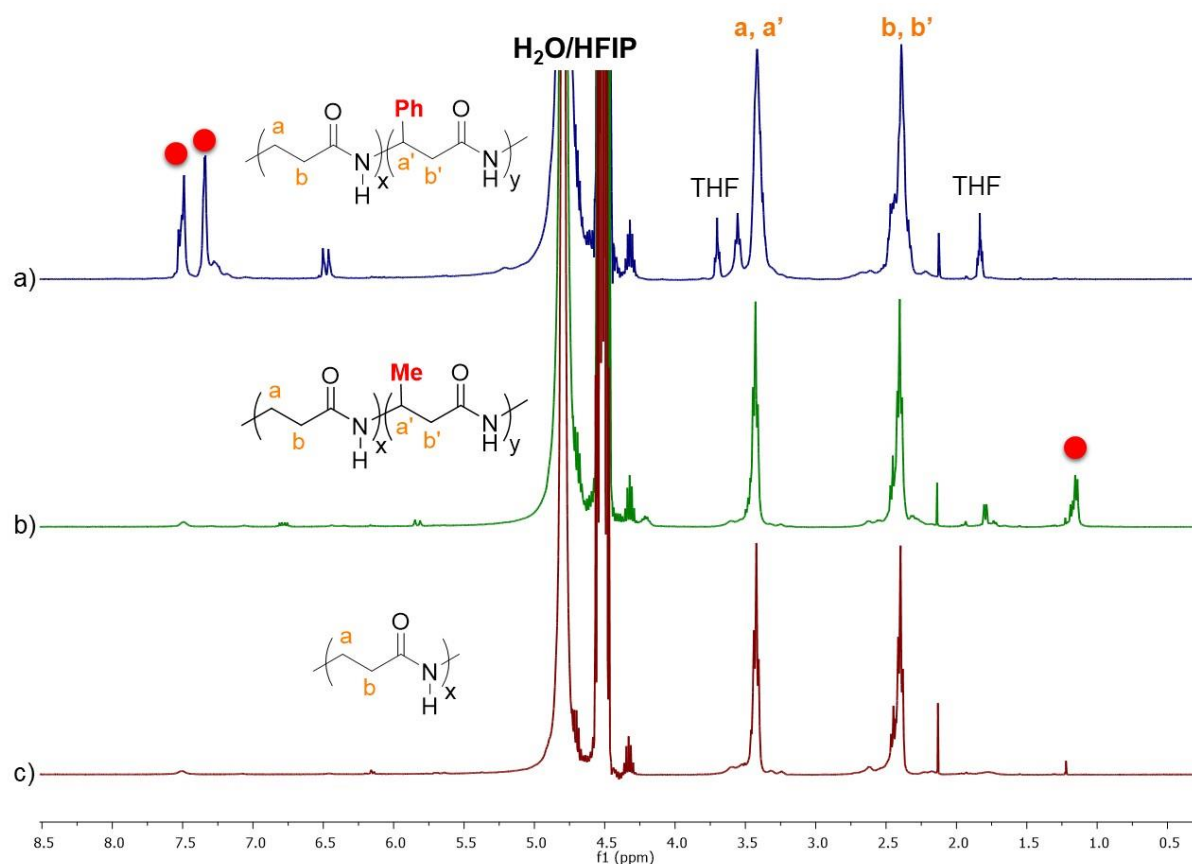
The incorporation of the comonomer in the polyamide chains was demonstrated by  $^1\text{H}$  NMR spectroscopy of the purified material (See figure 26 and 27) thus demonstrating that most of the acrylamide comonomer were incorporated into the polyamide structure. Diagnostic signals of the polyamide 3 methylene groups are observed at  $\delta(\text{ppm}) = 2.4$  and  $3.4$  ppm and signals of the side chains are clearly visible in the aliphatic (0-2ppm) or aromatic region (7-8ppm) depending on the nature of the substituent. One can note that for low molar masses copolyamides AAm-2.e, small signals between 5 and 6.5 ppm corresponding to the double bond chain-end can be observed (Fig. 26.b and 27.a) As previously mentioned, numerous side reactions such as branching reactions (*N*- or *C*-branching, see Scheme 17) were shown to occur for the polymerization of acrylamide in bulk and were evidenced by the appearance of small signals at 3.5 and 2.5 ppm. In the case of copolymerization of acrylamide with *N*- or  $\beta$ - substituted acrylamides, those signals are readily recognizable at 3.5 and 2.5 ppm and the amount of branching is higher (2-16%) than for the homopolymerization of acrylamide (around 3%). High amount of branching were also observed for the bulk-HTP of acrylamide when the amount of

activator (*t*-BuONa) were lower than 0.25mol% and was correlated to a longer and less exothermic polymerization which favors transfer to the polymer side reactions.<sup>79</sup>



**Figure 26.**  $^1\text{H}$  NMR spectra ( $\text{D}_2\text{O}/\text{HFIP}$ ) of purified a) P(AAm-2.d), b) P(AAm-2.c), c) P(AAm-2.b), d) P(AAm-2.a) and e) PA3

Thanks to the thermal probe directly dipped in the melted acrylamide, it was possible to record the exotherm of the polymerization reaction immediately triggered by the base addition. Figure 28.a) and b) represents the thermal evolution of the reaction medium as a function of the polymerization time and the nature of the comonomer. One can note that the bulk anionic polymerization of acrylamide is highly exothermic with a maximal temperature of 275 °C, which is reached in a few seconds. The nature and the amount of the comonomer, *i.e.* *N*-substituted or  $\beta$ -substituted acrylamide, clearly affect the exothermy (from 275°C to 225°C) and the time of the reaction as the polymerization is slowing down when increasing the amount of comonomer particularly for the *N*-substituted comonomer, thus explaining also the higher amount of branching observed by  $^1\text{H}$  NMR.



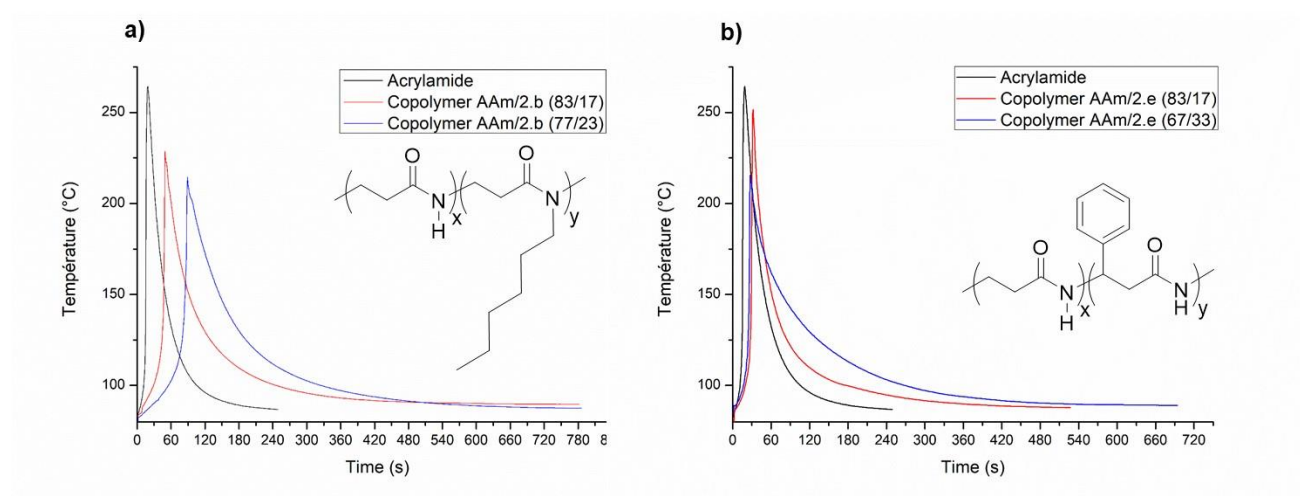
**Figure 27.**  $^1\text{H}$  NMR spectra ( $\text{D}_2\text{O}/\text{HFIP}$ ) of purified a) PA3-*stat*-poly(cinnamide), b) PA3-*stat*-poly(crotonamide) and c) PA3.

Moreover, all the copolyamides synthesized exhibits only one glass transition temperature in the ranging from  $56^\circ\text{C}$  to  $100^\circ\text{C}$  depending on the nature of the side chain (Table 9). The introduction of an alkyl chain (Run 2-4 and 9-10, Table 9), regardless of the position of the substitution (on the  $\beta$ -position or the nitrogen atom), induced a decrease of the glass transition temperature from  $88^\circ\text{C}$  for the PA3 reference to  $56\text{--}79^\circ\text{C}$  depending on the amount of comonomer. In the case of phenyl substituent (Run 5, 7-8, Table 9) the values observed are relatively closed to the PA3 reference except for the copolymer with a high amount of cinnamide. These values contrast with the one obtained by Zhang *et al.* ( $T_g = 126^\circ\text{C}$ ), where they gave evidence of a linear polyamide 3 structure obtained by anionic ring-opening polymerization of  $\beta$ -propiolactam.<sup>47</sup> The formation of branched structures can explain those lower values. As also referenced, no melting of the polymer was observed as it is concomitant with the thermal decomposition.

**Table 9.** Transition glass temperature of the copolyamides prepared by Anionic bulk HTP at 90°C using *t*-BuONa as initiator.

Run	(Co)polymer	Exp. (mol%) Composition [AAm/2.x] <sup>a</sup>	T <sub>g</sub> <sup>b</sup> (°C)
1	AAm	100/0	88
2	AAm-2.a	89/11	79
3	AAm-2.b	85/15	69
4	AAm-2.b	75/25	56
5	AAm-2.c	83/17	91
6	AAm-2.d	82/18	100
7	AAm-2.e	80/20	83
8	AAm-2.e	55/45	69
9	AAm-2.f	86/14	75
10	AAm-2.f	62/38	70

a) Determined by <sup>1</sup>H NMR d) determined by DSC analysis (second heating)

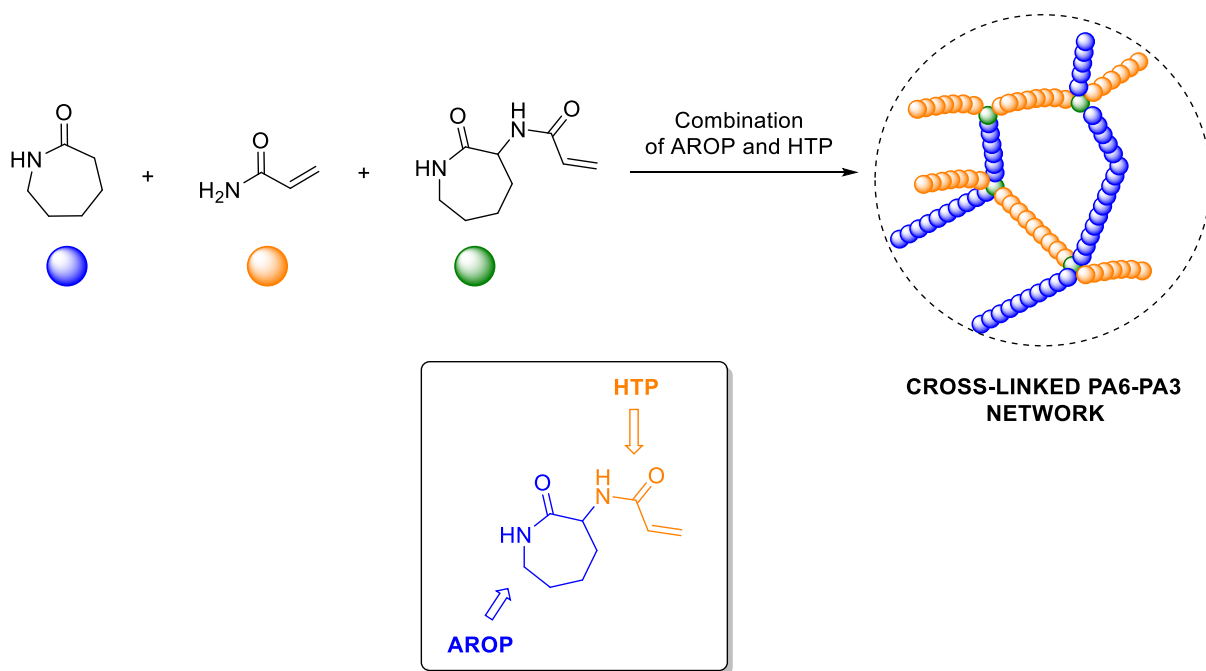


**Figure 28.** Temperature vs time diagram of bulk anionic copolymerization of a) Copolymer AAm-2.b and b) AAm-2.e initiated by *t*-BuONa at 90°C.



### 3.B.2.3. Combining hydrogen-transfer polymerization and anionic ring-opening polymerization for the synthesis of cross-linked copolyamides

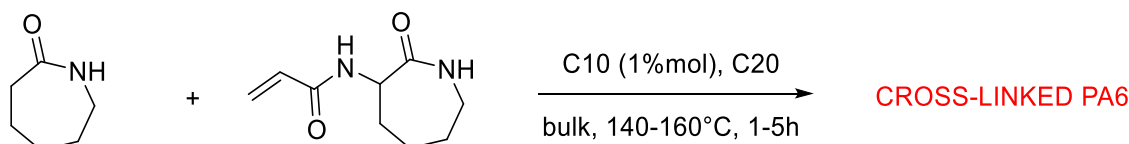
In parallel with the synthesis of copolyamides by hydrogen transfer polymerization, we investigated the terpolymerization of  $\epsilon$ -caprolactam, acrylamide and the  $\epsilon$ -caprolactam-containing acrylamide monomer (**2.d**) in order to synthesize PA-3/PA6 cross-linked network. The strategy, presented in Scheme 22, was to combine in a “one-pot” process the anionic ring-opening polymerization of  $\epsilon$ -caprolactam and the hydrogen transfer polymerization of acrylamide thanks to the synthesis of the bi-functional monomer **2.d** which incorporated on the same structure an acrylamide and a caprolactam moiety. As mentioned before for the combination of AROP and condensation reactions (see PART 3, Chapter 1), the anionic polymerization of  $\epsilon$ -caprolactam was needed to be run at 140°C in bulk in the presence of an activator, generally an *N*-acyllactam moiety.



**Scheme 22.** Strategy combining the anionic ring-opening and the hydrogen transfer polymerization for the synthesis PA6-PA3 crosslinked copolyamides

In a preliminary work, the anionic ring-opening copolymerization of the monomer **2.d** and  $\epsilon$ -caprolactam have been studied keeping the usual PA6 experimental conditions, *i.e.* polymerization in bulk at 140°C using C10 (sodium  $\epsilon$ -caprolactamate) as initiator and C20 as activator (Scheme 23). The result of the anionic copolymerization of the monomer **2.d** and  $\epsilon$ -

caprolactam are displayed in Table 10. As already reported in the literature, the copolymerization of lactams and functionalized lactams (bearing fluorinated groups or cinnamide side chain) required generally a longer reaction time to obtain reasonable conversion.<sup>40,41</sup> In the present case, a few hours (1-5h) were necessary to observe the solidification of the polymerization media depending on the temperature (from 140°C to 160°C) and on the amount of comonomer introduced. Surprisingly, all the copolymer synthesized were found to be insoluble in HFIP, thus indicating the formation of a cross-linked network.



**Scheme 23.** Anionic ring-opening copolymerization of the monomer **2.d** and  $\epsilon$ -caprolactam (bulk, 140-160°C) using C10 as initiator and C20 as activator.

**Table 10.** Anionic ring-opening copolymerization of the monomer **2.d** and  $\epsilon$ -caprolactam (bulk, 140-160°C) using C10 as initiator and C20 as activator.

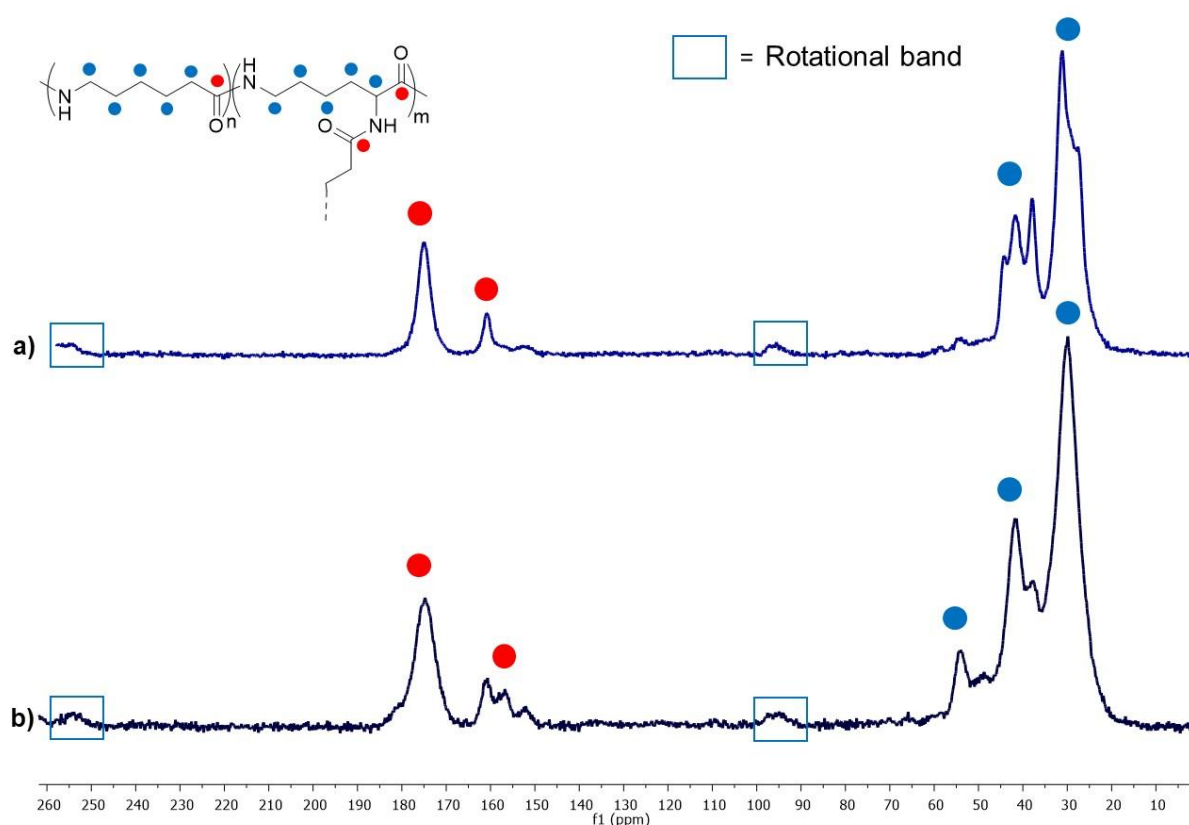
Run	T <sub>pol</sub> (°C) <sup>a</sup>	2.d (mol.%)	t <sub>sol</sub> (min) <sup>b</sup>	Swelling%	T <sub>g</sub> <sup>c</sup>	T <sub>d</sub> max <sup>d</sup>
1	140	5	180	-	-	-
2	140	10	240	-	-	-
3	140	20	300	-	-	-
4	160	5	60	4 560	55	398
5	160	10	120	2 540	61	405
6	160	20	150	1 570	84	418
7	140	0	2	-	53	328

a) Polymerization temperature, b) time before solidification, c) Glass transition temperature determined by DSC (second heating) and d) Maximum of the peak decomposition temperature determined from DTG curves

The PA6 cross-linked network obtained by anionic ring-opening polymerization at 160°C have been characterized by thermal analyses (TGA and DSC), solid <sup>13</sup>C NMR and swelling test.. The synthesized PA6 network exhibited higher thermal stability and higher transition glass temperature (T<sub>g</sub>= 55-84°C) than the PA6 reference (T<sub>g</sub>= 53°C) as expected for increasing the amount of the comonomer **2.d**.

<sup>13</sup>C solid NMR analysis of two purified PA6 networks presented in Figure 29, exhibits all the characteristic signals expected for a PA6 backbone at 175 ppm for the carbonyl of the amide group and between 50 and 20 ppm for the aliphatic chain. Other signals between 150-160 ppm,

whose intensity increases by increasing the initial feed ratio of comonomer **2.d**, can be attributed to the carbonyl of the amide group. Interestingly, no characteristic signals of the double bonds are observed in both spectra. In a typical  $^{13}\text{C}$  solid NMR experiment, the sample is rotated at high frequencies (often called as “magic angle spinning”) in order to average the dipolar interaction between carbon 13 and hydrogen. The rotation causes the appearance of artefacts at 95 and 215 ppm (noted rotational bands on the spectra) which correspond to the rotation frequency (8 000 Hz) used for the experiment.

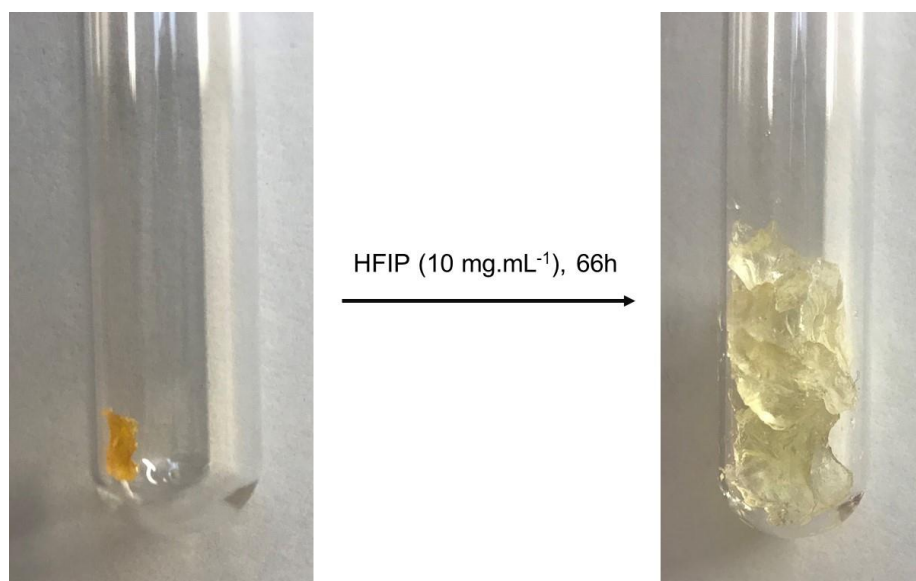


**Figure 30.** Solid  $^{13}\text{C}$  NMR of the cross-linked PA6 obtained by anionic copolymerization of  $\epsilon$ -caprolactam and the monomer **2.d** (Run 4 and 6, Table 10).

The swelling tests were performed in HFIP ( $10 \text{ mg.mL}^{-1}$ , See Figure 30). The dry mass ( $m_d$ ) was determined after purification and subsequent drying (24h at  $100^\circ\text{C}$ ) of the sample. The swollen mass of the cross-linked copolyamides ( $m_s$ ) was measured after 66h in HFIP. The swelling ratio ( $S(\%)$ ) was then determined using the following equation.

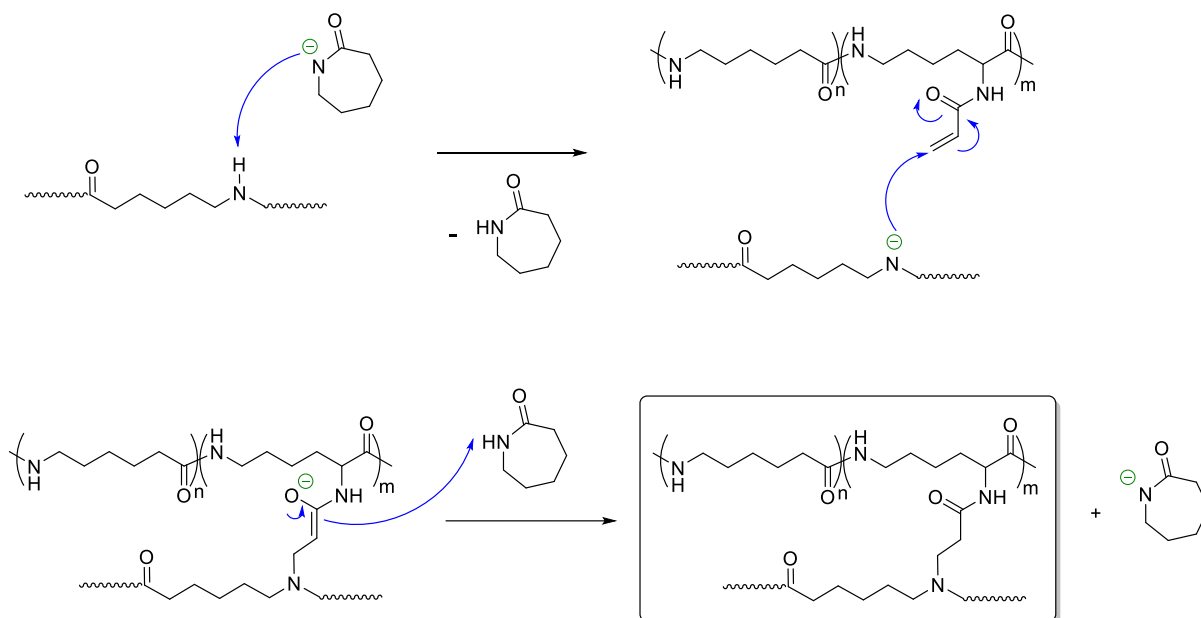
$$S(\%) = \frac{m_s - m_d}{m_d} \times 100$$

avec  $m_s$  : swollen mass and  $m_d$  : dry mass



**Figure 30.** Swelling test (HFIP, 66h, 25°C) for the copolyamide run 5 (Table 8)

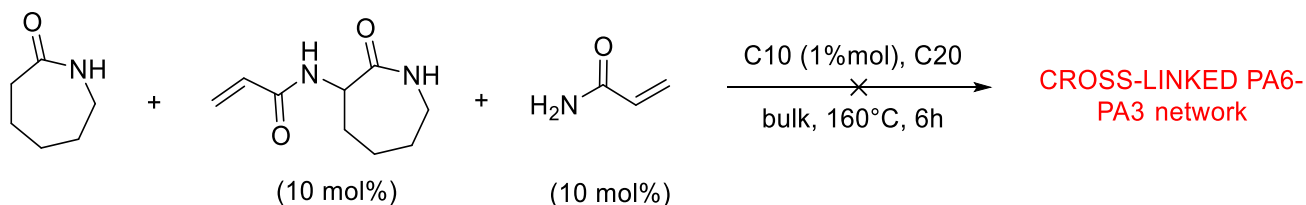
As expected, the swelling ratio measured from 1570 to 4560 % was also shown to be inversely related to the amount of comonomer **2.d** introduced in the PA6 network. To a mechanistic point of view, the cross-linking reaction is probably induced by Mikael addition between an amidate anion and the pendant double bond coming from the incorporation of the monomer **2.d** (Scheme 24) thus explaining the disappearance of the double bond in the  $^{13}\text{C}$  NMR spectrum.



**Scheme 24.** Plausible mechanism of cross-linking by Mikael-type addition reaction.

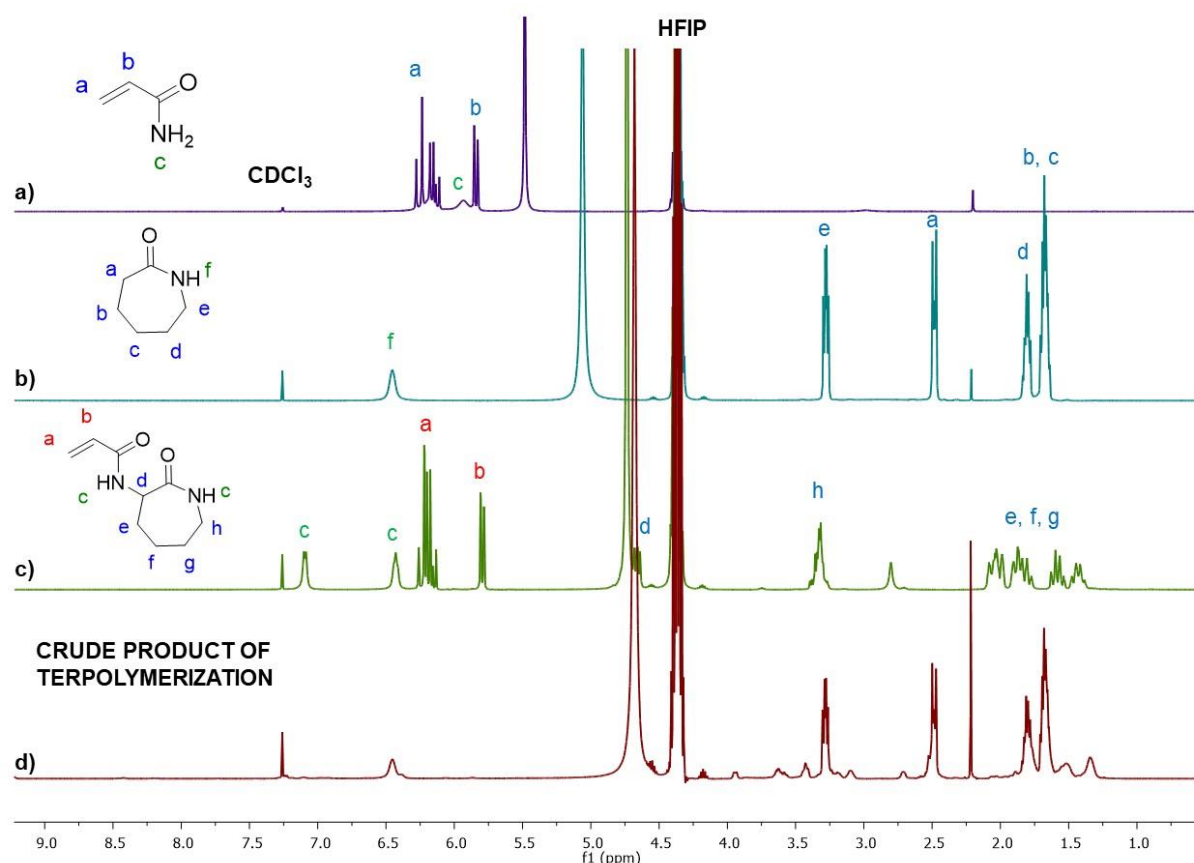
The terpolymerization of acrylamide,  $\epsilon$ -caprolactam and monomer **2.d** was further investigated in presence of sodium  $\epsilon$ -caprolactamate as initiator and C20 as activator in bulk at 160°C. The

polymerization was carried out in the presence of 10 mol% of acrylamide and 10 mol% of the comonomer **2.d** as compared to the  $\epsilon$ -caprolactam concentration (Scheme 25).

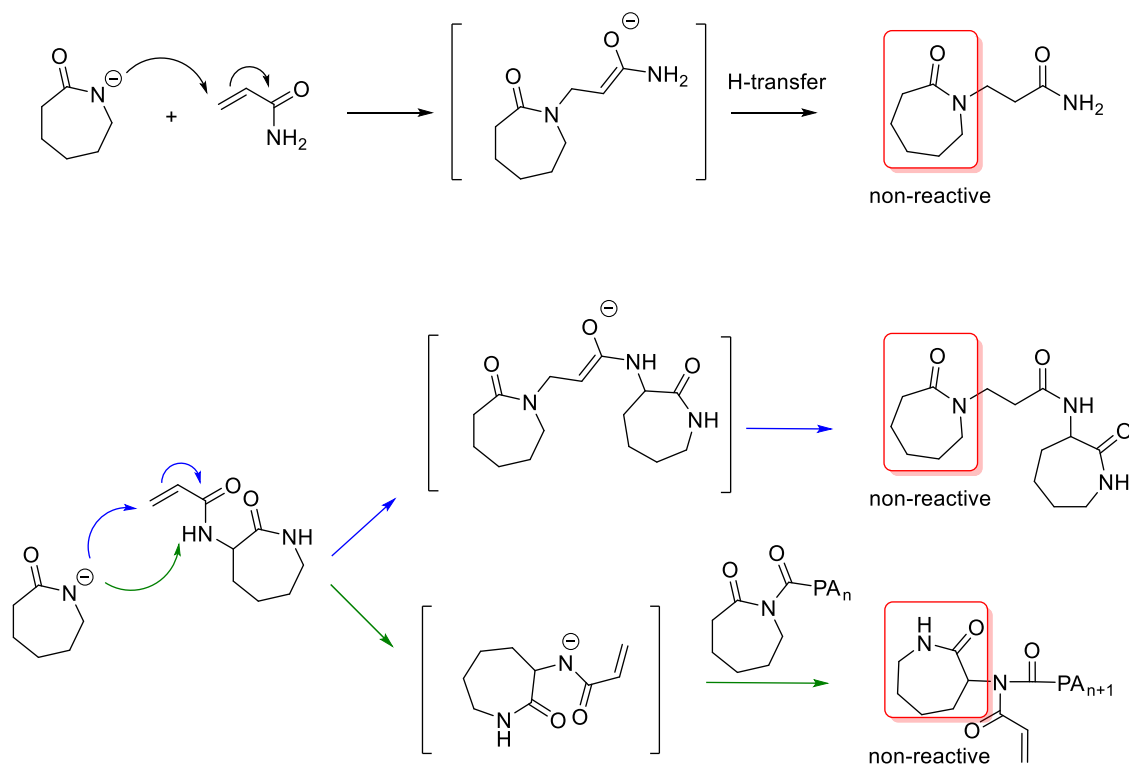


**Scheme 25.** Anionic terpolymerization of acrylamide,  $\epsilon$ -caprolactam and monomer **2.d** in presence of sodium caprolactamate as initiator and C20 as activator in bulk at 160°C

Unfortunately, after 6h of reaction at 160°C, no solidification of the polymerization medium was observed and the crude product, totally soluble in HFIP, was analysed by  $^1\text{H}$  NMR. In Figure 31 are displayed, the NMR spectra (in a mixture HFIP/ $\text{CDCl}_3$ ) of each monomers and of the crude product of the terpolymerization. Characteristics signals of the  $\epsilon$ -caprolactam monomer are readily observed at  $\delta(\text{ppm}) = 6.45; 3.27; 2.48, 1.80$  and  $1.67$  demonstrating a low conversion in  $\epsilon$ -caprolactam under those conditions. Interestingly, no signals of double bonds were observed on the spectrum of the crude product (Figure 31.d)), thus attesting a complete conversion of monomer **2.d** and the acrylamide monomer. This result suggests that the hydrogen transfer polymerization occurs rapidly (generally in a few seconds at 90°C) and consume all the active species or activator. Indeed, the propagation reaction involved in the chain-growth of  $\epsilon$ -caprolactam requires the presence of a reactive *N*-acyllactam chain-end. Many plausible side reactions, induced by the presence of the comonomer **2.d** and the acrylamide, are depicted in Scheme 26 and proposed the formation of non-reactive chain-ends, thus explaining the low conversion in  $\epsilon$ -caprolactam.



**Figure 31.**  $^1\text{H}$  NMR spectra (HFIP/  $\text{CDCl}_3$ ) of a) acrylamide, b)  $\epsilon$ -caprolactam, c) N-DL- $\alpha$ -amino  $\epsilon$ -caprolactam acrylamide and d) crude product of terpolymerization after 6h at  $160^\circ\text{C}$



**Scheme 26.** Plausible side reactions occurring in the terpolymerization of acrylamide,  $\epsilon$ -caprolactam and monomer **2.d.** in bulk at  $160^\circ\text{C}$ .

To summarize this part, we have described the anionic bulk copolymerization of acrylamide with N- and  $\beta$ -substituted acrylamide derivatives at 90°C in order to prepared polyamide 3-based copolymers. As observed for the homopolymerization of acrylamide, the copolymerization occurs in a few seconds with a strong exotherm (up to 275°C) depending on the amount of the comonomer introduced. The incorporation of the comonomer into the PA3 backbone as well as the occurrence of side reactions such as *N*-branching were demonstrated by  $^1\text{H}$  NMR spectroscopy. During the course of our investigation on the HTP of acrylamide derivatives, we also reported synthesis of a particular bi-functional monomer **2.d** which incorporated on the same structure an acrylamide and a caprolactam moiety. For the purpose of synthesize PA-3/PA6 cross-linked network, we investigated the terpolymerization of  $\epsilon$ -caprolactam, acrylamide and this peculiar monomer. The strategy was to combine in a “one-pot” process the anionic ring-opening polymerization of  $\epsilon$ -caprolactam and the hydrogen transfer polymerization of acrylamide. The so-obtained bi-functional monomer were found to be reactive towards the two mechanisms of polymerization, *i.e.* HTP and AROP, but the occurrence of side reactions induces by the terpolymerization have not yet allowed the synthesis of the PA3/PA6 cross-linked networks.

### Conclusion

This third chapter has been dedicated to different approaches for the synthesis of new polyamide-based materials through (i) the simultaneous anionic ring-opening and condensation reactions for the synthesis of aliphatic-aromatic copolyamides (ii) the covalent activation of lactams by electron withdrawing groups and (iii) the synthesis polyamide 3-based materials by hydrogen transfer polymerization of acrylamide derivatives.

In a first part, the combination of anionic ring-opening and condensation reactions has been proposed as a new synthetic route to tune the thermo-mechanical properties of aliphatic polyamides. In this study, polyamides 6 containing various aromatic content were prepared from a mixture of  $\epsilon$ -caprolactam and ethyl 4-aminobenzoate derivatives in a one-step procedure. Molar masses up to 36 000 g.mol<sup>-1</sup> with aromatic content up to 33% are reported in those experimental conditions. Characterizations by NMR spectroscopy and thermal analysis are consistent with a statistical distribution of aromatic amide along the aliphatic polyamide chain. As compared to neat PA6, the copolyamides prepared exhibit higher glass transition temperature, up to 79°C, and better thermal stability. We also demonstrated the limitation of this approach such as the synthesis of high molar mass copolyamides containing more than 10% of aromatic units. Beyond the preparation of new polyamides, we demonstrated the possibility to “marry” anionic ring-opening polymerization of a cyclic amide and condensation reactions of aminobenzoate derivatives keeping the standard and simple experimental conditions of PA6 synthesis, following an activated monomer mechanism.

In the second part, new approaches for the synthesis of polyamides *via* a monomer activation strategy have been investigated through the covalent activation of lactams and the hydrogen transfer (co)polymerization of acrylamides derivatives. The covalent activation of lactams including 2-pyrrolidone,  $\delta$ -valerolactam (or 2-piperidone) and  $\epsilon$ -caprolactam, respectively the 5-, 6- and 7-membered cyclic amides, has been investigated using different tosyl-based activating groups. The preliminary results of AROP of the activated lactams demonstrated a low reactivity probably due to strong stabilization of the resulting aza-anion by delocalization on the sulfonyl activating group. Nonetheless, the covalent activation of lactams by EWG still



appears as promising strategy to achieve the *sine qua non* conditions to attain living ring-opening polymerization of lactams.

The hydrogen transfer polymerization (HTP) and copolymerization of acrylamide derivatives in bulk or solution have been studied for the synthesis of polyamide 3-based (co)polymers and polyamide 3/polyamide 6 cross-linked networks. As observed for the homopolymerization of acrylamide, the copolymerization occurs in a few seconds in a strong exothermic process (up to 275°C), depending on the amount of the comonomer introduced. The incorporation of the comonomer into the PA3 backbone as well as the occurrence of side reactions such as *N*-branching were demonstrated by <sup>1</sup>H NMR spectroscopy. In parallel, we also investigated the terpolymerization of ε-caprolactam, acrylamide and the ε-caprolactam-containing acrylamide monomer in order to synthesize PA3/PA6 cross-linked network. The strategy was to combine in a “one-pot” process the anionic ring-opening polymerization of ε-caprolactam and the hydrogen transfer polymerization of acrylamide thanks to the synthesis of a bi-functional monomer which incorporated on the same structure an acrylamide and a caprolactam moiety. The results presented in this manuscript, have demonstrated the reactivity of this particular monomer towards hydrogen transfer polymerization and anionic ring-opening polymerization. The preliminary results of the terpolymerization have also highlighted the occurrence of numerous plausible side reactions.

### Supplementary information

#### 1. Instrumentation

NMR spectra were recorded on a Bruker Avance III 400 spectrometer ( $^1\text{H}$ ,  $^{13}\text{C}$ , 400.2 MHz and 100.6 MHz respectively) in appropriate deuterated solvents at 298 K. DOSY (Diffusion Ordered Spectroscopy) measurements were performed at 298 K on a Bruker Avance III 400 spectrometer operating at 400.33 MHz and equipped with a 5 mm Bruker multinuclear z-gradient direct cryoprobe-head capable of producing gradients in the z direction with strength  $53.5 \text{ G.cm}^{-1}$ . Each sample was dissolved in 0.4 ml of  $\text{CDCl}_3/\text{HFIP}$  for internal lock and spinning was used to minimize convection effects. Polymer molar masses were determined by Size Exclusion Chromatography (SEC) using hexafluoroisopropanol (HFIP + 0.05 %mol potassium trifluoroacetate KTFA) as the eluent. Measurements in HFIP were performed on a PL GPC50 integrated system equipped with RI, UV (280 nm) and two PL HFIP gel columns (300 x 7.5 mm) (exclusion limits from 100 Da to 1 500 000 Da) at a rate of 1 mL/min using PMMA standards. Columns temperature was held at 40 °C. Differential scanning calorimetry analyses (DSC) were carried out on a DSC Q100 LN2 TA Instrument. Copolyamides samples (5 mg) were heated from -20 to 240 °C at a rate of  $10 \text{ }^\circ\text{C.min}^{-1}$ . The instrument was calibrated with indium sample. Thermo-gravimetric analysis (TGA) was performed on a Perkin-Elmer Diamond TA/TGA with a heating rate of  $10 \text{ }^\circ\text{C.min}^{-1}$  under nitrogen flow. Dynamic mechanical analyses (DMA) were performed on a TA Instrument RSA3. Polyamides samples (prepared by heat pressing) were heated from -10 to 150 °C under nitrogen atmosphere, at a rate of  $5 \text{ }^\circ\text{C.min}^{-1}$ . The measurements were performed in three point bending mode at a frequency of 1 Hz, with an initial static force of 0.5 N and strain sweep of 0.1%.

#### 2. Materials

$\epsilon$ -Caprolactam (CL) (BASF, 99 %) was recrystallized from dry cyclohexane prior to use. Brüggolen® C20 (17 % w/w of isocyanate in CL, N, N'-hexamethylenebis(2-oxo-1-azepanylcarboxamide) or hexamethylene-1,6-dicarbamoylcaprolactam in CL, Brüggemann Chemical), Brüggolen® C10 (~18 % w/w of sodium  $\epsilon$ -caprolactamate in CL, Brüggemann Chemical) were used as received. Ethyl 4-(butylamino)benzoate (98 % Aldrich), ethyl *p*-toluate (or ethyl 4-methylbenzoate, 99 % Aldrich) and Ethyl 4-aminobenzoate (98 % Aldrich) were dried by azeotropic distillation with toluene and further dried under vacuum during 12h. *N*-Acetyl  $\epsilon$ -caprolactam (99%, Aldrich) was

dried over  $\text{CaH}_2$  and distilled prior to use. Tetrahydrofuran was dried over sodium/benzophenone and distilled prior to use. Toluene was dried over  $\text{CaH}_2$ , refluxed overnight, distilled, and stored over polystyrylithium. Lithium, sodium and potassium bis(trimethylsilyl)amide (LiHMDS, NaHMDS, KHMDS 1.0 M in THF) was purchased from Sigma-Aldrich and used as received. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) (Acros Organics,  $\geq 99.7\%$ ) was used without any further purification. 4-methylbenzene sulfonylchloride (Alfa Aesar, 98%), 4-fluorobenzene sulfonylchloride (Alfa Aesar, 95%) and 4-fluorobenzene sulfonylchloride (Alfa Aesar, 98%) were used as received

### 3. General procedures

#### *Anionic ring-opening polymerization of $\epsilon$ -caprolactam with C20 or ethyl p-toluate.*

Polyamide 6 was prepared in bulk by anionic ring-opening polymerization.  $\epsilon$ -Caprolactam (CL) (8.35 g, 73.8 mmol) and sodium  $\epsilon$ -caprolactamate (C10) (0.23 g, 1.7 mmol) were added in a glass reactor at 140 °C under argon atmosphere. After hexamethylene-1,6-dicarbamoylcaprolactam (C20, structure presented in SI) (0.5 g, 1.3 mmol) (or 1.3 mmol of ethyl p-toluate) was added to the molten mixture, the mixture was let to react for several hours. Once a solid polymer was formed, it was crushed and refluxed 24h in water and then dried in an oven overnight at 90 °C under vacuum before analysis. The yield was determined gravimetrically.

#### *Copolymerization of $\epsilon$ -caprolactam and ethyl 4-butylaminobenzoate (25%Ar-PA6 synthesis, run 5 Table 1).*

In a flame-dried schlenk was introduced under argon atmosphere 610 mg (2.75 mmol) of ethyl 4-(butylamino)benzoate. Then, 2 mL of dried THF was added under vacuum. After homogenization, the solution was cooled down to 0°C and 2.75 mL of NAHMDS (1M in THF) was added dropwise under argon flux. The solution (1) was waited overnight at 20 °C. The reactor was heated up to 140 °C under argon atmosphere.  $\epsilon$ -Caprolactam (CL) (933 mg, 8.75 mmol) was added and stirred until its melting. The solution (1) was then added and copolymerization was started, after evaporation of THF (about 10 minutes), by addition of hexamethylene-1,6-dicarbamoylcaprolactam (C20) (47 mg, 0.120 mmol). The reaction was completed after a few minutes (< 15 min). The

obtained copolymer was purified by a reflux of THF, then filtered and dried under vacuum for 24h (Yield = 98%).

**<sup>1</sup>H NMR (400MHz, 298K, CDCl<sub>3</sub>/HFIP)** δ (ppm) = 7.90-7.75; 6.76; 6.20-5.90; 3.22; 2.22; 1.75-1.25; 0.88. **<sup>13</sup>C NMR (100MHz, 298K, CDCl<sub>3</sub>/HFIP)** δ (ppm) = 183.6; 177.8; 176.6; 151.3; 130.8; 114.1; 113.8; 43.3; 39.6; 36.1; 30.5; 29.6; 28.1; 25.8; 24.9; 19.4; 12.3

The copolymer compositions were calculated following the relation:

$$\text{Aliphatic (\%)} = \frac{\frac{I_{2.22}}{2}}{\frac{I_{2.22}}{2} + \frac{I_{0.88}}{3}} \times 100$$

#### ***Copolymerization of ε-caprolactam and ethyl 4-aminobenzoate.***

In a flame-dried schlenk was introduced under argon atmosphere 1.0 g (6.0 mmol) of ethyl 4-aminobenzoate. Then, 4 mL of dried THF was added under vacuum. After homogenization, the solution was cooled down to 0°C and 3.0 mL of NaHMDS (2M in THF) was added dropwise under argon flux (solution (1)). The reactor was heated up to 140 °C under argon atmosphere. ε-Caprolactam (5.80g, 50 mmol) was added and stirred until its melting. The solution (1) was then added and copolymerization was started, after evaporation of THF (about 10 minutes), by addition of hexamethylene-1,6-dicarbamoylcaprolactam (C20) (380 mg, 0.164 mmol). The reaction was stopped after 4h and the crude product was analyzed to determine the conversion of both monomers. The obtained copolymer was crushed and purified by a reflux of THF/H<sub>2</sub>O (1/1) mixture, then filtered and dried under vacuum for 24h.

**<sup>1</sup>H NMR (400MHz, 298K, CDCl<sub>3</sub>/HFIP)** δ (ppm) = 8.25-7.50 (CH(Ar)); 6.20 (NH); 3.22 (CH<sub>2</sub>); 2.22 (CH<sub>2</sub>); 1.75-1.25 (3×CH<sub>2</sub>). **<sup>13</sup>C NMR (100MHz, 298K, CDCl<sub>3</sub>/HFIP)** (Figure S1) δ (ppm) = 180.37 (C=O); 177.75 (C=O); 128.66 (C(Ar)); 125.14 (C(Ar)); 122.42 (C(Ar)); 121.51 (C(Ar)); 119.76 (C(Ar)); 118.61 (C(Ar)); 40.53 (CH<sub>2</sub>); 36.87 (CH<sub>2</sub>); 28.86 (CH<sub>2</sub>); 26.57 (CH<sub>2</sub>); 25.83 (CH<sub>2</sub>).

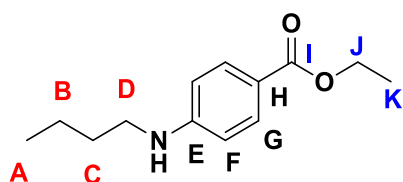
The copolymer compositions were calculated following the relation:

$$\%Ar = \frac{(I_{8.25-7.5}/4)}{(I_{8.25-7.5}/4) + (I_{2.22}/2)} \times 100$$

### *Chain-growth condensation polymerization of ethyl 4-(butylamino)benzoate.*

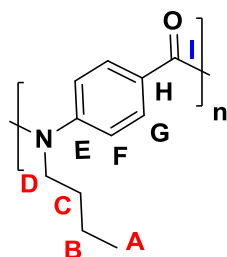
As an example, 1.0 g (4.52 mmol) of ethyl 4-(butylamino)benzoate and dry THF (4 mL) were introduced in a flame-dried Schlenk under argon atmosphere. The solution was cooled down to 0°C and 4.6 ml of NaHMDS solution (1M in THF) was added dropwise under argon atmosphere. The solution was stirred at room temperature for 4h and then added to a solution containing 15 mg of ethyl 4-nitrobenzoate (75  $\mu$ mol) in THF (1ml) at 0°C under argon flux. The mixture was stirred at 25°C or 100°C (in appropriate glassware) for 24 h, and then the reaction was quenched with sat.  $\text{NH}_4\text{Cl}$ . The whole was extracted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with 1 M NaOH and dried over anhydrous  $\text{MgSO}_4$ . Concentration in vacuum gave the crude product as a yellow viscous oil.

**$^1\text{H}$  NMR ethyl 4-(butylamino)benzoate (400 MHz, 298K,  $\text{CDCl}_3$ ) :**  $\delta(\text{ppm}) = 7.87$  (2H, m,  $\text{CH}(\text{Ar})$ ) ;  $6.60$  (2H, m,  $\text{CH}(\text{Ar})$ ) ;  $4.31$  (2H, q,  $\text{O}-\text{CH}_2-\text{CH}_3$ ,  $J=7.0\text{Hz}$ ) ;  $3.17$  ( 2H, t,  $\text{N}-\text{CH}_2$ ,  $J=7.6\text{Hz}$ ) ;  $1.62$  (2H, m,  $\text{CH}_2(\text{butyl})$ ) ;  $1.43$  (2H, m,  $\text{CH}_2(\text{butyl})$ ) ;  $1.35$  (3H, t,  $\text{O}-\text{CH}_2-\text{CH}_3$ ,  $J=7.0\text{Hz}$ ) ;  $0.95$  (3H, t,  $\text{CH}_3(\text{butyl})$ ,  $J=6.4\text{Hz}$ ).



**$^{13}\text{C}$  NMR ethyl 4-(butylamino)benzoate (100 MHz, 298K,  $\text{CDCl}_3$ ) :**  $\delta(\text{ppm}) = 166.9$  (I),  $152.0$  (H),  $131.6$  (G),  $118.4$  (E),  $111.4$  (F),  $60.2$  (J),  $43.2$  (D),  $31.3$  (K),  $20.2$  (C),  $14.4$  (B),  $13.8$  (A).

**$^1\text{H}$  NMR poly(ethyl 4-(butylamino)benzoate) (400 MHz, 298K,  $\text{CDCl}_3$ ) :**  $\delta(\text{ppm}) = 6.99$  (2H, m,  $\text{CH}(\text{Ar})$ ) ;  $6.79$  (2H, m,  $\text{CH}(\text{Ar})$ ) ;  $3.78$  ( 2H, br,  $\text{N}-\text{CH}_2$ ) ;  $1.55$ - $1.40$  (4H, m,  $2 \times \text{CH}_2(\text{butyl})$ ) ;  $0.88$  (3H, m,  $\text{CH}_3(\text{butyl})$ ).



**$^{13}\text{C}$  NMR poly(ethyl 4-(butylamino)benzoate) (100 MHz, 298K,  $\text{CDCl}_3$ ) :**  $\delta(\text{ppm}) = 170.5$  (I),  $142.7$  (H),  $136.0$  (E),  $128.7$  (G),  $128.0$  (H),  $48.7$  (D),  $29.5$  (C),  $19.9$  (B),  $13.7$  (A).

#### *Anionic ring-opening polymerization of $\epsilon$ -caprolactam with different initiators.*

Polyamide 6 was prepared in bulk by anionic ring opening polymerization.  $\epsilon$ -Caprolactam (CL) (8.35 g, 73.8 mmol) and sodium  $\epsilon$ -caprolactamate (C10) (0.23 g, 1.7 mmol) (or 1.7 mmol of EtONa; MeONa; tBuOK) were added in a glass reactor at 140 °C under nitrogen atmosphere. After hexamethylene-1,6-dicarbamoylcaprolactam (C20) (0.5 g, 1.3 mmol) was added to the molten mixture, the polymerization started. After reaction, the polymer obtained was crushed and refluxed in water and then dried in an oven overnight at 90 °C under vacuum before analysis. The yield was determined gravimetrically.

#### *Polymerization of 4-ethyl(butylamino)benzoate initiated by N-Acetyl $\epsilon$ -caprolactam*

In a flame dried Schlenk was introduced under Argon atmosphere, 1 g (4.52 mmol) of 4-ethyl(butylamino)benzoate followed by 4.6 mL of NaHMDS (1M in THF). The mixture was stirred during 1h at RT and 13  $\mu$ l (90  $\mu$ mol) of N-Acetyl  $\epsilon$ -caprolactam in THF was added under Argon flux. The reaction was stirred at RT during 24 h. The reaction was quenched with sat.  $\text{NH}_4\text{Cl}$ . The whole was extracted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with 1 M NaOH and dried over anhydrous  $\text{MgSO}_4$ . Concentration in vacuum gave the crude product as a yellow viscous oil.

**N-tosyl  $\epsilon$ -caprolactam synthesis.** In a flame-dried Schlenk was introduced 2.0 g (17.70 mmol) of  $\epsilon$ -caprolactam and 100mL of dried THF, follow by the addition of 18.0 mL of LiHMDS in THF (1M, 18.0 mmol) under argon flux at -40°C. After 30 min at -40°C, 3.37g (17.70mmol) of 4-methylbenzene sulfonylchloride in dried THF (20ml) was introduced under argon flux. After 45 min at -40°C, the mixture was quenched by adding 10 mL of aqueous HCL solution (1M). The organic phases were extracted with ethyl acetate (3 $\times$ 20 mL), washed with saturated  $\text{NaHCO}_3$  aqueous solution (2 $\times$ 10ml) and brine (2 $\times$ 10 mL), and dried over  $\text{MgSO}_4$ . The product is purified by chromatographic column (heptane/ethyl acetate (70/30)) and recrystallize from heptane, dried 12h under vacuum at room temperature, and stored in the glovebox (Yield= 90%).

**RMN  $^1\text{H}$  (400MHz, 298K,  $\text{CDCl}_3$ ):**  $\delta$ (ppm)= 7.79 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ); 7.22 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8\text{Hz}$ ); 3.94 (t, 2H,  $\text{CH}_2\text{-N}(\text{Ts})$ ,  $J=4.0\text{Hz}$ ); 2.45 (t, 2H,  $\text{CH}_2$ ,  $J=4.0\text{Hz}$ ); 2.34 (s, 3H,  $\text{CH}_3(\text{Ts})$ ); 1.75 (m, 2H,  $\text{CH}_2$ ); 1.63 (m, 4H, 2 $\times$  $\text{CH}_2$ ). **RMN  $^{13}\text{C}$  (100MHz, 298K,  $\text{THF-d}_8$ ):**  $\delta$ (ppm)= 173.78; 143.45; 135.56; 128.22; 127.45; 45.40; 37.73; 28.28; 28.12; 21.87; 20.60.

*N-nosyl  $\epsilon$ -caprolactam synthesis.* Same procedure (Yield= 60%)

**RMN  $^1\text{H}$  (400MHz, 298K,  $\text{CDCl}_3$ ):**  $\delta(\text{ppm})$ = 8.37 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ); 8.19 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8\text{Hz}$ ); 4.06 (t, 2H,  $\text{CH}_2\text{-N}(\text{Ts})$ ,  $J=4.0\text{Hz}$ ); 2.57 (t, 2H,  $\text{CH}_2$ ,  $J=4.0\text{Hz}$ ); 1.88 (m, 2H,  $\text{CH}_2$ ); 1.76 (m, 4H,  $2\times\text{CH}_2$ ). **RMN  $^{13}\text{C}$  (100MHz, 298K, THF- $d_8$ ):**  $\delta(\text{ppm})$ = 174.01; 149.44; 144.11; 128.91; 122.83; 45.68; 37.60; 28.43; 28.11; 21.82.

*N-(4-fluorobenzene sulfonyl)  $\epsilon$ -caprolactam synthesis.* Same procedure (Yield= 85%)

**RMN  $^1\text{H}$  (400MHz, 298K,  $\text{CDCl}_3$ ):**  $\delta(\text{ppm})$ = 8.04 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8.0\text{Hz}$ ); 7.19 (d, 2H,  $\text{CH}(\text{Ar})$ ,  $J=8\text{Hz}$ ); 4.03 (t, 2H,  $\text{CH}_2\text{-N}(\text{Ts})$ ,  $J=4.0\text{Hz}$ ); 2.56 (t, 2H,  $\text{CH}_2$ ,  $J=4.0\text{Hz}$ ); 1.84 (m, 2H,  $\text{CH}_2$ ); 1.75 (m, 4H,  $2\times\text{CH}_2$ ). **RMN  $^{13}\text{C}$  (100MHz, 298K, THF- $d_8$ ):**  $\delta(\text{ppm})$ = 173.92; 145.58; 140.56; 129.01; 127.62; 45.52; 37.82; 28.30; 28.14; 21.85.

#### *Anionic copolymerization of activated lactams and activated aziridines.*

In a typical procedure, 7.7 mg (30  $\mu\text{mol}$ ) of *N*-tosylhexylamine and 6.0 mg (30  $\mu\text{mol}$ ) of KHMD were added in a flame-dried Schlenk flask in the glovebox. After removal of the Schlenk, 1 mL of dried DMF was added under vacuum. After homogenization, the solution was cooled to 0°C, and a solution containing 64 mg (0.3 mmol) of 2-methyl *N*-tosylaziridine and 80 mg of *N*-tosyl  $\epsilon$ -caprolactam (0.03 mmol) in 2mL of DMF was added under argon flux. After 24h at 50°C, an aliquot of the polymerization mixture was taken to determine the conversion by  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ). The reaction was quenched with 1ml of degassed MeOH and stirred 30 min. The crude product was analyzed by SEC (THF).

#### *Synthesis of N-substituted acrylamide derivatives.*

##### *N-(DL- $\alpha$ -amino- $\epsilon$ -caprolactam) acrylamide synthesis.*

In a flame-dried Schlenk, 10 g (78 mmol) of DL- $\alpha$ -amino- $\epsilon$ -caprolactam was introduced under argon atmosphere followed by the addition of 150 mL of dried  $\text{CHCl}_3$ . After homogenization, 10.52 mL (78 mmol) of dried triethylamine was added and 6.30 mL (78 mmol) of acryloyl chloride was added dropwise at 0°C under argon flux. After 24h at room temperature, 30 mL of water was added and the organic phases were extracted with diethyl ether ( $3\times 50\text{ mL}$ ), washed with brine ( $3\times 30\text{ mL}$ ), and dried over  $\text{MgSO}_4$ . After evaporation of the solvent, the product was

recovered as a white crystalline powder (10.6g, 75%), dried 12h under vacuum at room temperature, and stored under inert atmosphere.

**RMN  $^1\text{H}$  (400 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 7.04$  (s, 1H, NH); 6.36 (s, 1H, NH); 6.22 (ddd, 2H,  $J_1 = 27.1\text{Hz}$ ,  $J_2 = 17.0\text{Hz}$ ,  $J_3 = 5.9\text{Hz}$ ), 5.75 – 5.54 (m, 1H), 4.68 – 4.52 (m, 1H), 3.41 – 3.03 (m, 2H), 2.05 (m, 2H), 1.92 – 1.73 (m, 2H), 1.58 – 1.27 (m, 2H). **RMN  $^{13}\text{C}$  (100 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 175.76$ ; 164.50; 130.84; 126.37; 52.11; 42.01; 31.49; 28.79; 27.93.

***N-methyl acrylamide synthesis.*** Same procedure, N-methylamine (60 mL, 120 mmol), triethylamine (16,19 mL, 120 mmol), acryloyl chloride (9,62 mL, 120 mmol). Orange liquid (2.0 g, yield = 19.6%).

**RMN  $^1\text{H}$  (400 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 7.49$  (s, 1H, NH), 6.17 – 5.99 (m, 2H), 5.42 (dd, 1H  $J_1 = 9.0\text{Hz}$ ,  $J_2 = 3.0\text{Hz}$ ), 2.67 (d, 3H,  $J = 4.9\text{Hz}$ ). **RMN  $^{13}\text{C}$  (100 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 166.88$ ; 130.87; 125.31; 25.96.

***N-hexyl acrylamide synthesis.*** Same procedure N-hexylamine (15 mL, 110 mmol), triethylamine (14,84 mL, 110 mmol), chlorure d'acryloyle (8,89 mL, 110 mmol), white crystalline powder (13.5g, yield= 79%)

**RMN  $^1\text{H}$  (400 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 6.17$  (ddd, 2H,  $J_1 = 27.2\text{Hz}$ ,  $J_2 = 17.0\text{Hz}$ ,  $J_3 = 5.9\text{Hz}$ ), 5.69 (s, 1H), 5.63 – 5.58 (m, 1H), 3.40 – 3.24 (m, 2H), 1.59 – 1.46 (m, 2H), 1.37 – 1.22 (m, 6H), 0.87 (t, 3H,  $J = 6.9\text{Hz}$ ). **RMN  $^{13}\text{C}$  (100 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 165.66$ ; 131.06; 125.84; 39.63; 31.46; 29.46; 26.61; 22.51; 13.93.

***N-phenyl acrylamide.*** Same procedure aniline (15.0 mL, 160 mmol), triethylamine (21,6 mL, 160 mmol), acryloyl chloride (12,9 mL, 160 mmol). orange crystalline powder (16,50g, yield = 70.1%).

**RMN  $^1\text{H}$  (400 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 7.65$  (s, 1H, NH), 7.61 – 7.51 (m, 2H), 7.36 – 7.28 (m, 2H), 7.20 – 7.08 (m, 1H), 6.48 – 6.22 (m, 2H), 5.74 (dd, 1H,  $J_1 = 10.1\text{Hz}$ ,  $J_2 = 1.4\text{Hz}$ ). **RMN  $^{13}\text{C}$  (100 MHz, 298K,  $\text{CDCl}_3$ )**  $\delta(\text{ppm}) = 164.27$ ; 137.90; 131.42; 128.95; 127.57; 124.54; 120.43.



#### 4. Supplementary Analyses

**Table S1.** Synthesis of aliphatic/aromatic copolyamides at 140°C in bulk.

Run	n <sub>NaHMDS</sub> (mmol)	n <sub>Ar</sub> (mmol)	n <sub>CL</sub> (mmol)	n <sub>C20</sub> (mmol)	n <sub>C10</sub> (mmol)
1	1.77	1.77	16.0	0.120	-
2	0.88	1.77	16.0	0.120	-
3	0.17	1.77	16.0	0.120	-
4	-	1.77	16.0	0.120	0.360
5	4.52	4.52	13.6	0.120	-
6	2.26	4.52	13.6	0.120	-
7	0.45	4.52	13.6	0.120	-
8	-	4.52	13.6	0.120	0.360
9	1.77	1.77	16.0	0.024	-
10	1.77	1.77	16.0	0.012	-

**Table S2.** Hydrogen transfer polymerization of acrylamide and its derivatives in DMF at 90°C (24-120h).

Run	Monomer	[Monomer] (mmol)	[NaHMDS] (mmol)	Time (hours)	Conversion <sup>a</sup> (%)	$\overline{M}_n$ THEO g.mol <sup>-1</sup>	$\overline{M}_{n,exp}$ <sup>c</sup> g.mol <sup>-1</sup>	$\overline{D}^c$
1	AAM	2.8	0.08	24	> 98	2500	2000	2.5
2	AAM	2.8	0.02	120	95	10000	2200	2.8
3	2.e	1.36	0.08	24	92	2500	2400	1.8
4	2.e	1.36	0.02	120	0	10000	-	-
5	2.f	2.35	0.08	24	92	2500	500	1.3
6	2.f	2.35	0.02	48	0	10000	-	-
7	2.c	1.36	0.08	24	75	2500	1000	1.4
8	2.c	1.36	0.02	120	30	10000	-	-
9	2.b	1.3	0.08	24	81	2500	1400	2.1
10	2.b	1.3	0.02	120	0	10000	-	-

(a) Conversion calculated by <sup>1</sup>H NMR, (b)  $\overline{M}_{n,THEO} = ([M]_0 / [NaHMDS]_0) \times M_{monomer}$  (c) Determined by SEC in HFIP (MALLS/RI detection)

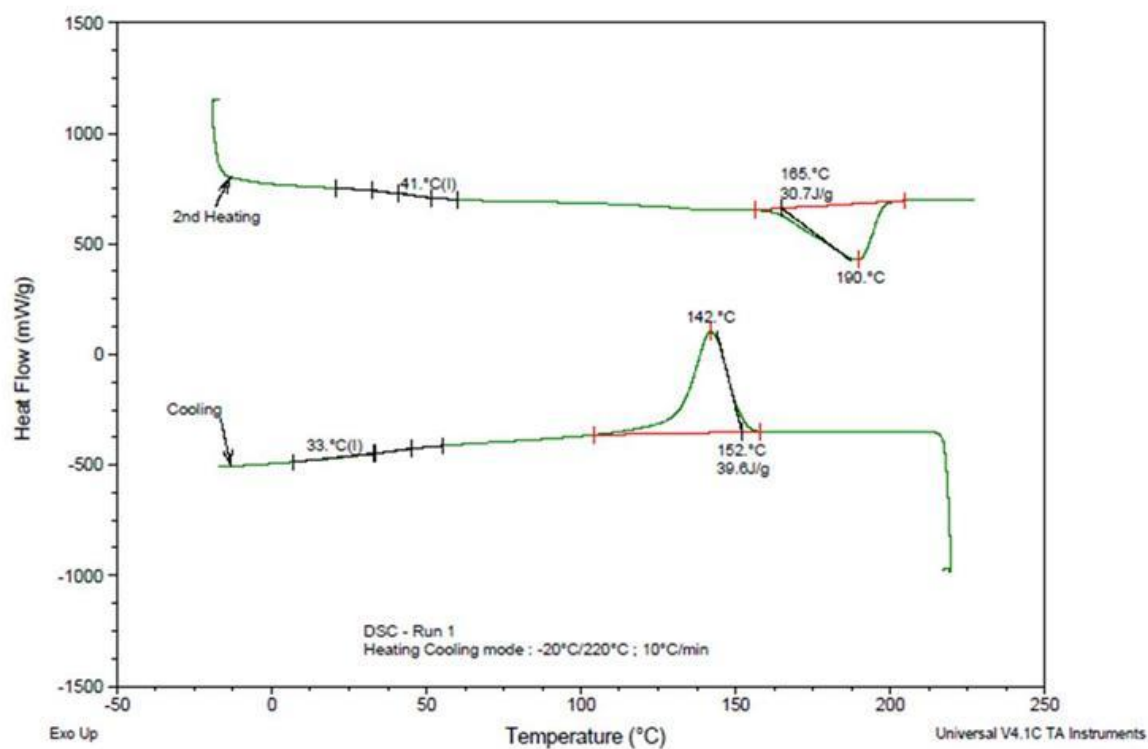


Figure S1. DSC analysis of copolyamides Run 1 (Table 3)

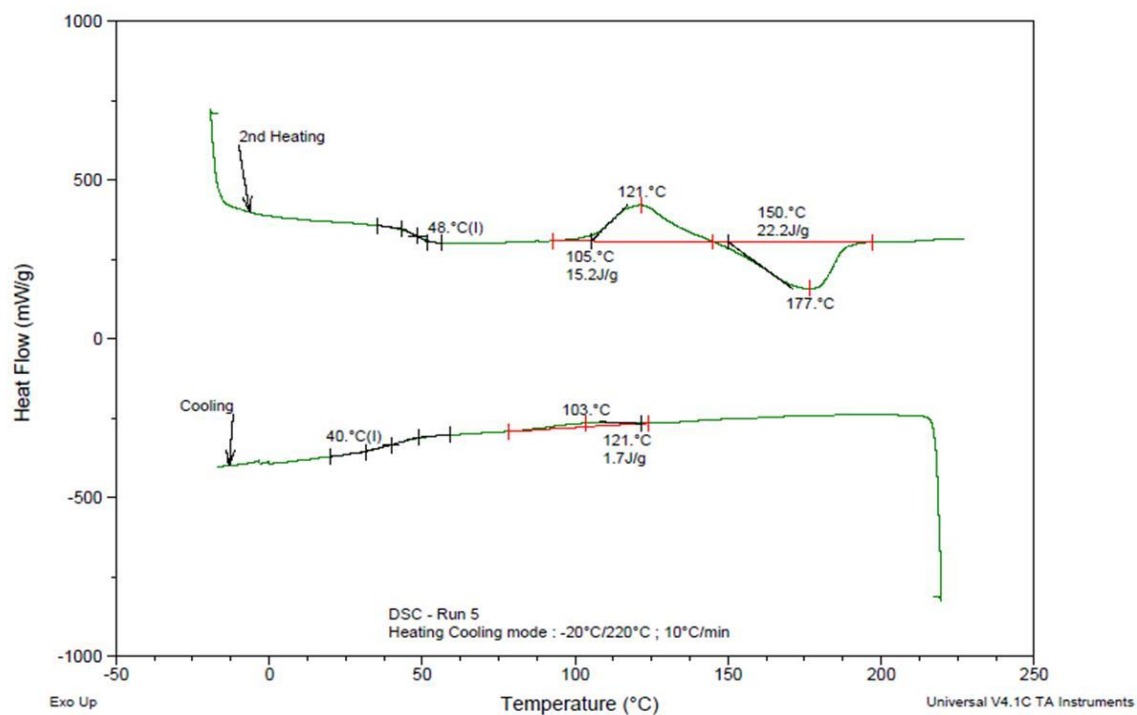


Figure S2. DSC analysis of copolyamides Run 5 (Table 1).

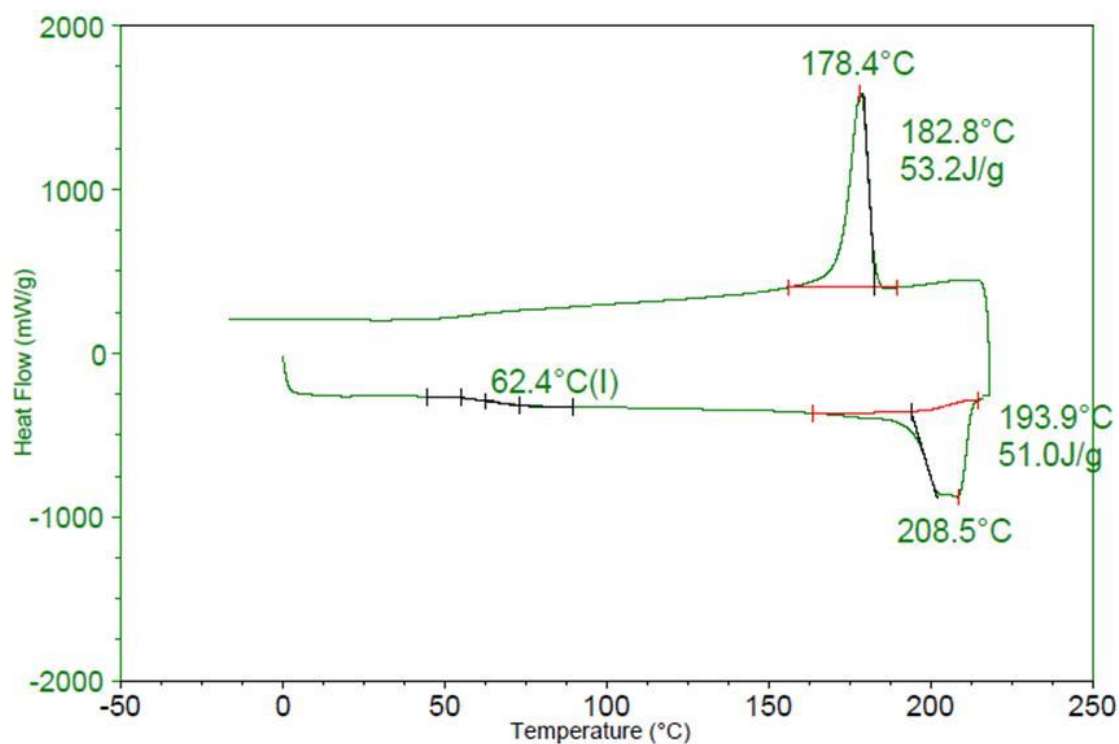


Figure S3. DSC analysis of copolyamides Run 10 (Table 1).

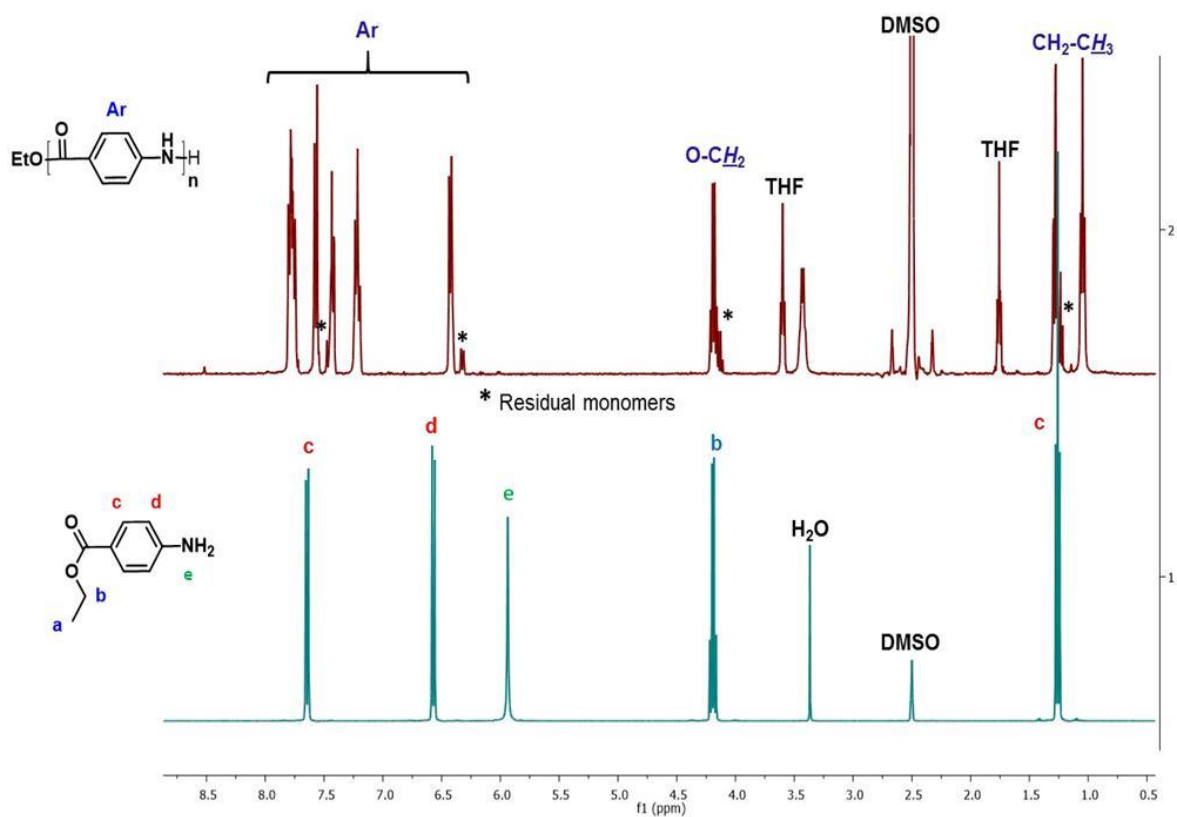
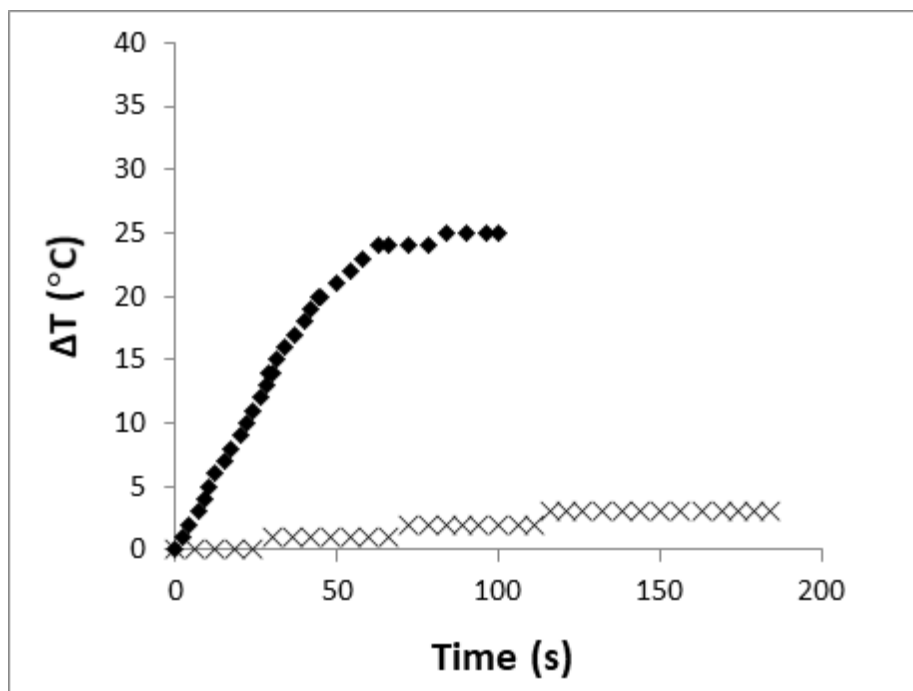
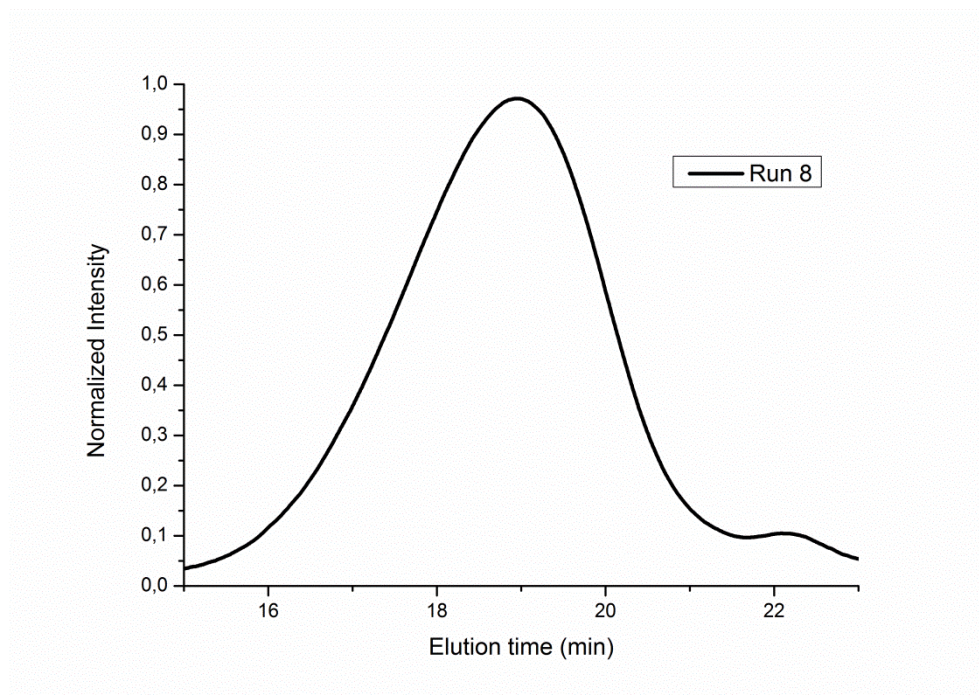


Figure S4.  $^1\text{H}$  NMR analysis of 1) 4-ethyl aminobenzoate and 2) soluble part of crude product of 4-ethyl aminobenzoate reacting with 1 eq. of NaHMDS in THF



**Fig S5.** Rate of polymerization of CL in the presence of isopropylamine, [CL]=8.75M, [C10]=0.158M, [iPrNH<sub>2</sub>]=0.316M, [C20]=23.8mM



**Figure S6.** SEC traces of high molar mass copolyamide with a theoretical composition of 95/5 in HFIP (Run 8, Table 2).

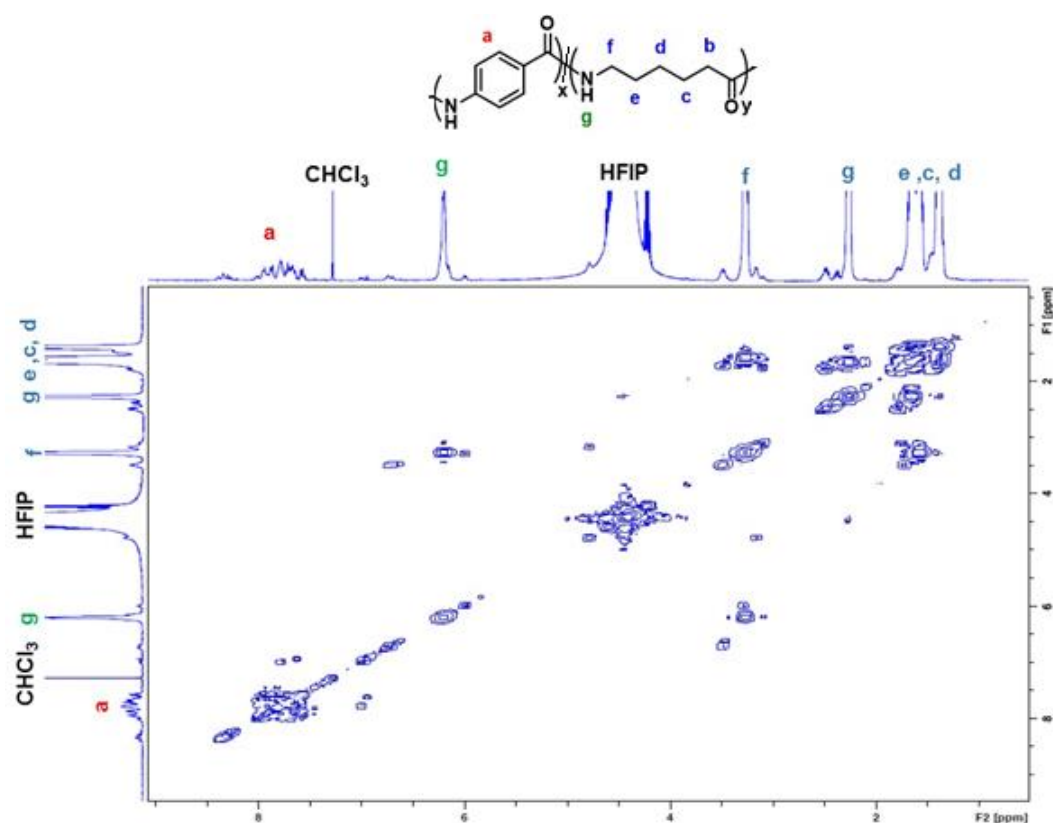


Figure S7. COSY spectrum in  $\text{CDCl}_3/\text{HFIP}$  of copolyamide P'5

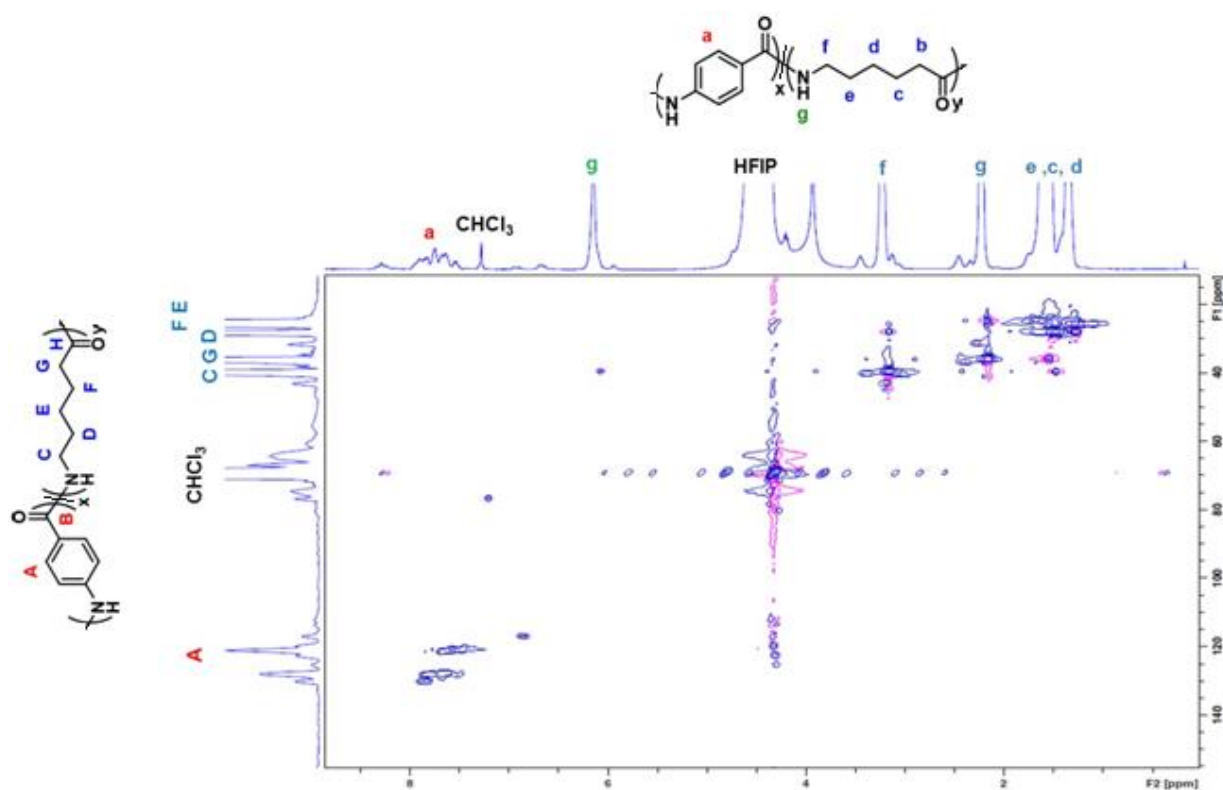


Figure S8. HSQC spectrum in  $\text{CDCl}_3/\text{HFIP}$  of copolyamide P'5

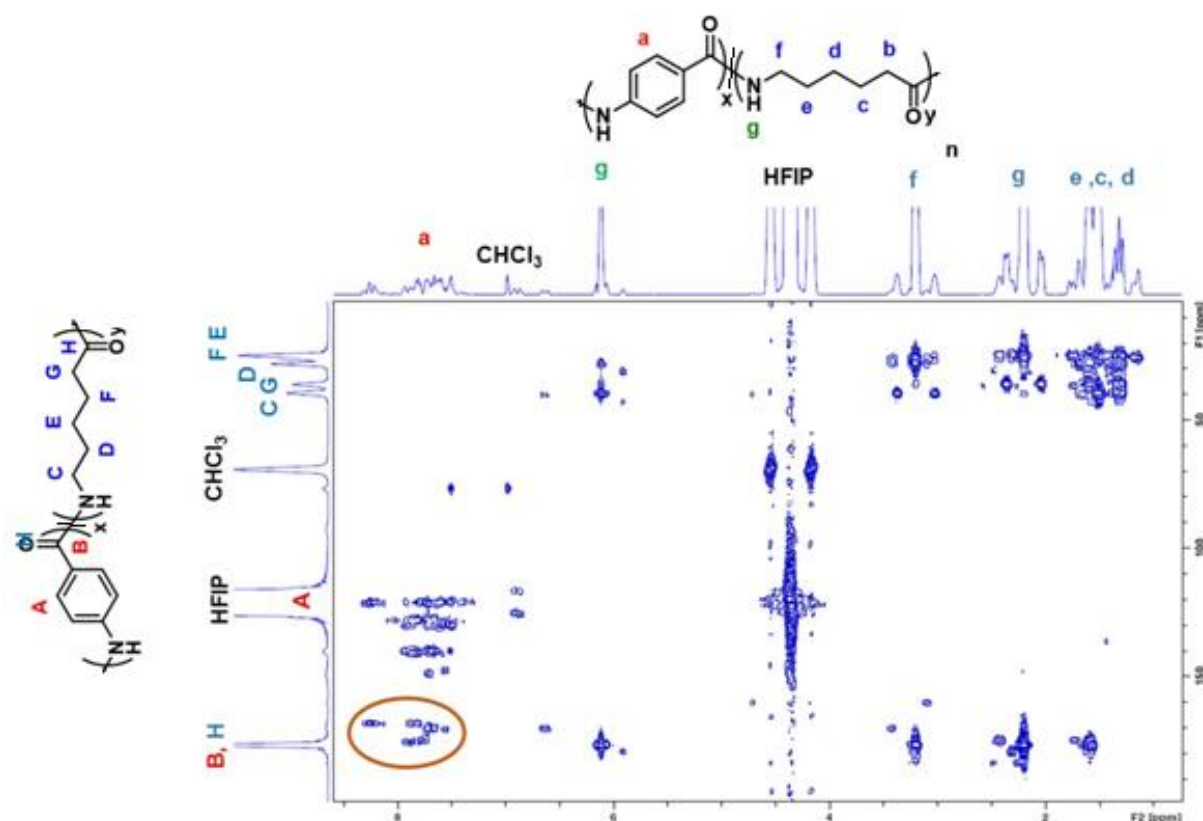


Figure S9. HMBC spectrum in  $\text{CDCl}_3/\text{HFIP}$  of copolyamide P'5

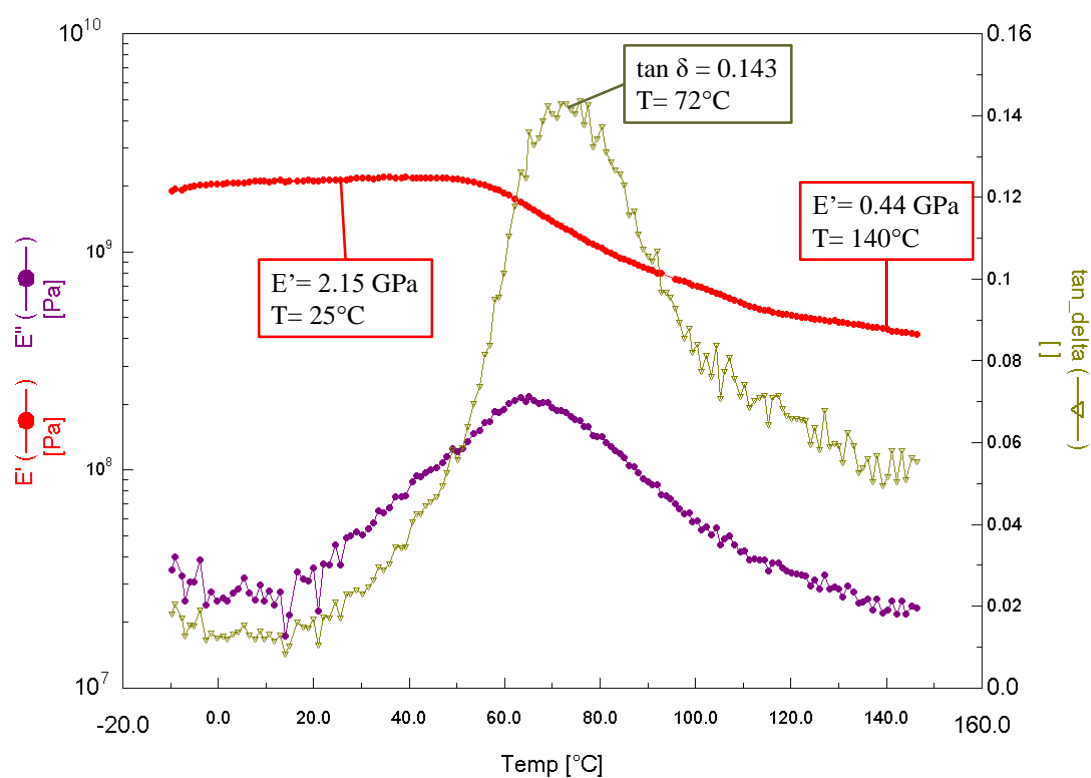


Figure S10. DMA analysis of PA6 reference obtained by anionic polymerization in bulk

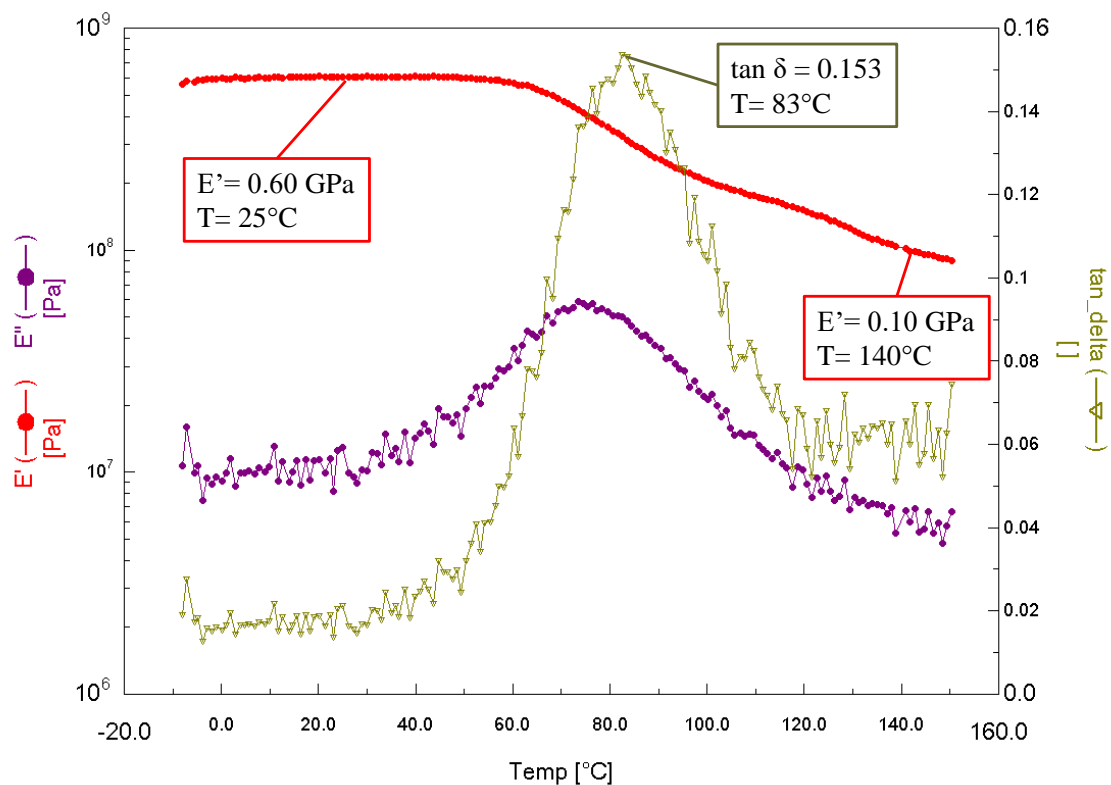


Figure S11. DMA analysis of PA6-7%Ar (P'4) obtained by anionic bulk copolymerization

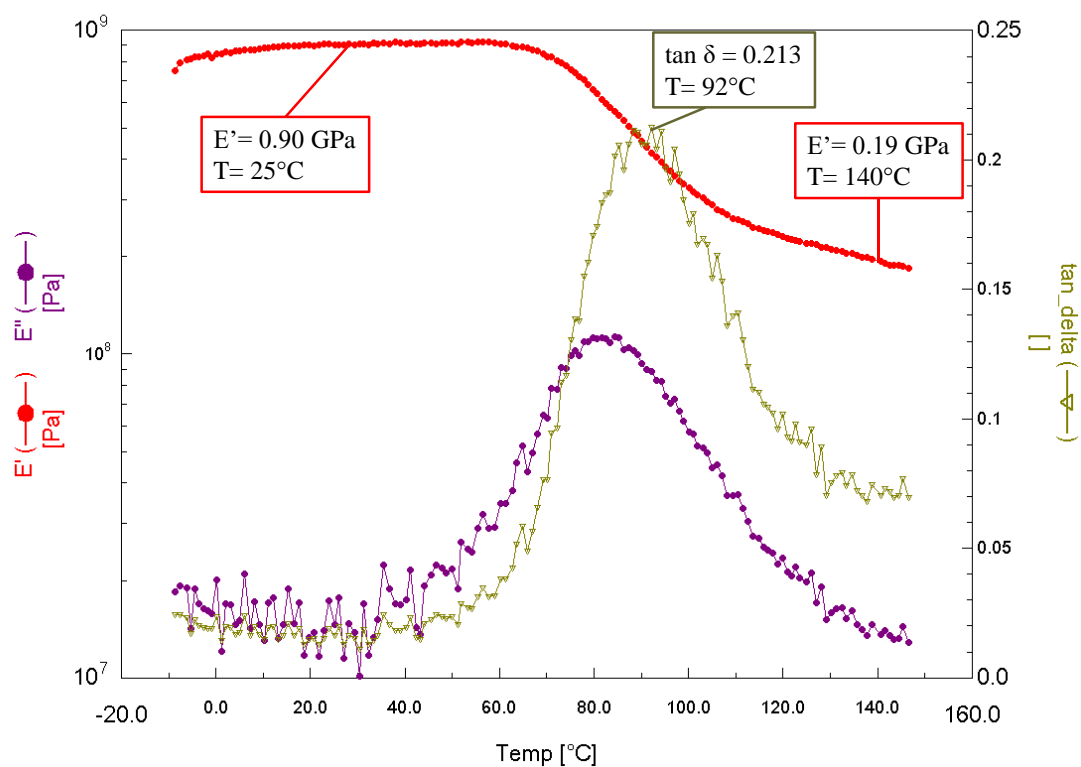
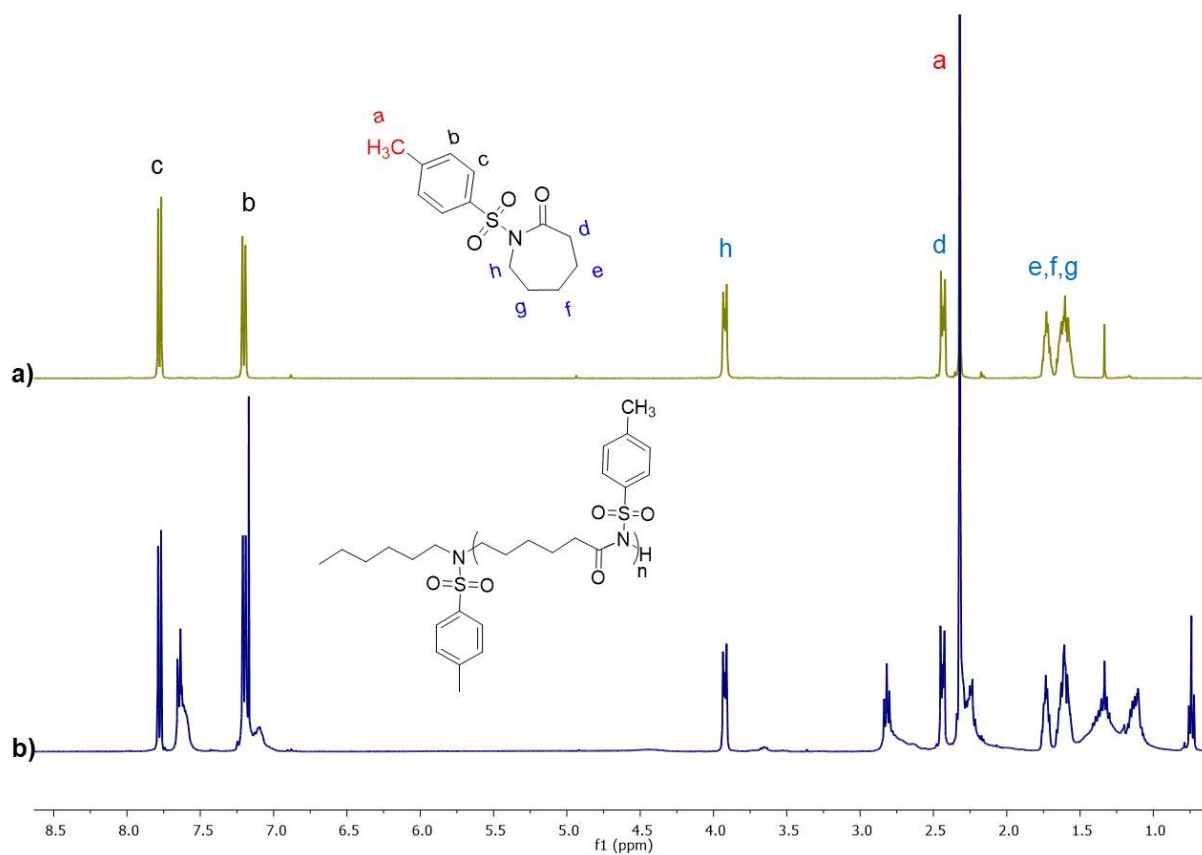
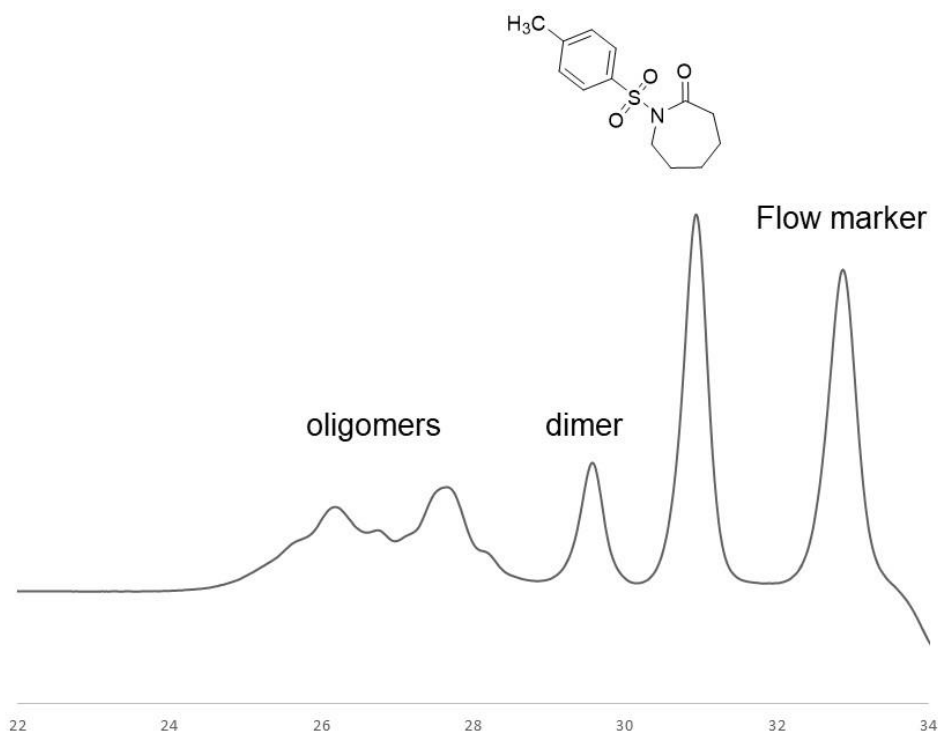


Fig S12. DMA analysis of PA6-17%Ar (P'5) obtained by anionic bulk copolymerization



**Figure S13.**  $^1\text{H}$  NMR spectra (CDCl<sub>3</sub>) of a) N-tosyl  $\epsilon$ -caprolactam and b) the crude product of polymerization initiated by secondary amine potassium salts in bulk at 135°C during 12h



**Figure S14.** SEC traces of the crude product of polymerization initiated by secondary amine potassium salts in bulk at 135°C during 12h



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## General conclusion

In their effort to mimic perfectly defined biological macromolecules materials such as DNA or proteins which are characterized by precise sequence of repeating units, monodispersity, and ability to form highly ordered three-dimensional structure, polymer chemist have developed several methods to prepare well-defined polymer-based architectures for numerous applications. Anionic polymerization, often considered as the “mother” of all living polymerization, was the first step towards the control of the macromolecular architecture. Over the last decades, numerous polymerization methodologies were developed for the purpose of attain the “livingness” in other areas of polymerization, including the ring-opening polymerization of heterocycles. As a typical example, the concept of monomer activation in ROP which consists to generate, more reactive species by the addition of a catalyst or by the appropriate design of the monomer substrates, has been applied for the synthesis of a wide range of polymers such as polyamides, polyethers, polyesters, polycarbonates, etc.

In this context, the objectives of this thesis works were to study the ring-opening polymerization by monomer activation of *N*-activated aziridines and lactams. The first part of this thesis manuscript was dedicated to the organocatalyzed ring-opening polymerization of *N*-activated aziridines by *N*-heterocyclic carbenes. Poly(aziridine)s were synthesized for the time by “living/controlled” OROP of 2-methyl and 2-phenyl-*N*-*p*-toluenesulfonyl aziridine, in the presence of activated secondary amine, functional, non-activated amine and amino-alcohol initiators. Excellent control over the molar masses, high chain-end fidelity and narrow dispersities ( $D \leq 1.20$ ) were achieved. This method has also been applied to achieve well-defined all PAz-based block copolymers by sequential OROP using a carbene catalysis. The high tolerance of the NHC-OROP of *N*-activated aziridines has been further applied to the metal-free synthesis of well-defined  $\alpha$ -hydroxy- $\omega$ -amino- and  $\alpha,\alpha'$ -bishydroxy- $\omega$ -amino telechelics PAz. Alternatively, the preliminary results of NHC-mediated zwitterionic ring-opening polymerization of the *N*-tosyl aziridines offered a potential synthetic pathway to generate original and unprecedented cyclic poly(aziridine)s. Overall, the NHC-OROP of *N*-activated aziridines provided an alternative pathway to the living cationic ring-opening

polymerization of oxazoline for the purpose to generate novel metal-free poly(ethylene imine) architectures.

In the second part of this thesis, different approaches based on the concept of monomer activation were investigated for the synthesis mainly by an anionic mechanism of new polyamides. The combination of anionic ring-opening and condensation reactions as a new synthetic route, to tune the thermo-mechanical properties of aliphatic polyamides, was explored. In this study, polyamide 6 containing various aromatic content were prepared from a mixture of  $\epsilon$ -caprolactam and ethyl 4-aminobenzoate derivatives (containing an alkyl side chain or not) in a one-step procedure. Beyond the preparation of new polyamides, we demonstrated the possibility to “marry” anionic ring-opening polymerization of a cyclic amide and condensation reactions of aminobenzoate derivatives keeping the standard and simple experimental conditions of PA6 synthesis, following an activated monomer mechanism.

With the idea to tend to a living/controlled polymerization of lactams by AROP which still appears today as a challenge for polymer chemists, we applied the concept of monomer activation through the covalent grafting of electron withdrawing group on the nitrogen center of the lactam ring. Despite the synthesis of original activated lactams, only low reactivity toward anionic ring-opening polymerization were observed. Nonetheless, the covalent activation appears as an elegant way to activate various lactam monomers towards living ring-opening polymerization.

In a last part, the hydrogen transfer polymerization (HTP) and copolymerization of acrylamide derivatives in bulk or solution has been studied for the synthesis of polyamide 3-based (co)polymers and polyamide 3/polyamide 6 cross-linked networks. The (co)polymerization occurring in a few seconds/minutes by the so-called activated monomer mechanism was shown to be really sensitive to the substitution on the nitrogen atom or on the double bond of the acrylamide moiety. The synthesis of a peculiar monomer bearing on the same structure reactive functions for the HTP and AROP has been employed for the synthesis of polyamide 3-polyamide 6 cross-linked materials.





# **Titre: Polymérisation par activation du monomère: application à la synthèse de polyaziridines et polyamides**

## **Résumé**

Les travaux de cette thèse portent sur l'étude de la polymérisation par ouverture de cycle de monomère hétérocycliques tels que les lactames et les aziridines par une stratégie d'activation du monomère. Dans une première partie, la polymérisation organocatalysée par des carbènes *N*-hétérocycliques de monomères originaux activés par greffage covalent de groupement électro-attracteur, les *N*-sulfonyl aziridines, a été étudiée en présence d'amorceurs de nature chimique variée. Des amines secondaires tosylées, des amines secondaires non-activées ainsi que des amorceurs comportant des fonctions réactives pour des réactions de post-modifications, ont ainsi démontrés leur potentiel pour le contrôle de la polymérisation des aziridines. La nature vivante/contrôlée et la grande tolérance de cette méthode de polymérisation ont également permis la synthèse de copolymères à blocs originaux. Dans une seconde partie, la combinaison simultanée des réactions d'ouverture de cycle de l' $\epsilon$ -caprolactame et des réactions de condensation des dérivés d'aminobenzoate a permis la synthèse en une étape de copolymères aliphatique-aromatique aux propriétés thermiques améliorées (notamment la température de transition vitreuse). En parallèle, d'autres méthodologies de synthèses telles que la polymérisation par transfert d'hydrogène des dérivés acrylamides ou encore l'activation d'amides cycliques par des groupements électro-attracteurs ont été étudiés pour obtenir de nouveaux polyamides.

**Mots clés :** Activation du monomère, polyaziridines, polyamides, organocatalyse, polymérisation anionique

# **Title: Polymerization by monomer activation : application to the synthesis of polyaziridines and polyamides**

## **Abstract**

In this thesis, the ring-opening polymerization by a monomer activation strategy of heterocyclic monomers such as lactams and aziridines was investigated. In the first part, we described that covalently activated aziridines, *i.e.* *N*-sulfonyl aziridines, could be subjected to the *N*-heterocyclic carbene organocatalyzed ring-opening polymerization (NHC-OROP) in a living/controlled manner. Secondary activated amine, non-activated secondary amine as well as functional initiators were used to promote the ring-opening polymerization of *N*-activated aziridines. The high tolerance to various chemical functions and the high level of control of the so-called NHC-OROP have allowed the synthesis of well-defined and original aziridine-based block copolymers. On the other hand, the simultaneous combination of anionic ring-opening of  $\epsilon$ -caprolactam and condensation reactions of aminobenzoate derivatives was shown to occur in a « one-step » bulk copolymerization allowing the preparation of aliphatic-aromatic copolyamides with enhanced thermal properties (including the glass transition temperature). Alternatively, other methodologies such as covalent activation of lactams with electron withdrawing group or the hydrogen transfer polymerization of acrylamide derivatives were investigated for the synthesis of new polyamides.

**Keywords :** Monomer activation, polyaziridines, polyamides, organocatalysis, anionic polymerization