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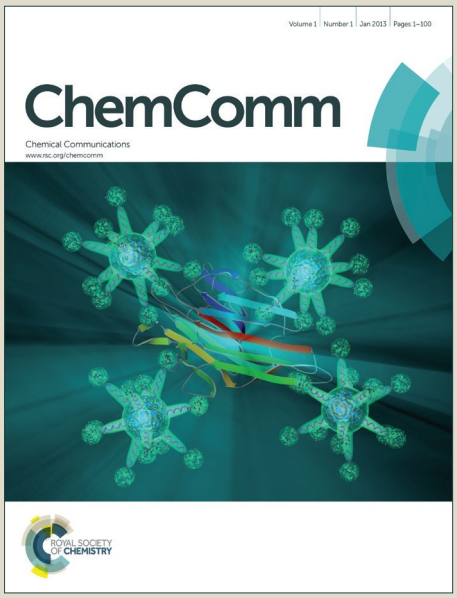

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ARTICLE

Organocatalytic Ring-Opening Polymerization of *N*-Tosyl Aziridines by an *N*-Heterocyclic Carbene

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The ring-opening polymerization of *N*-tosyl aziridines, in presence of 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene as organocatalyst and a *N*-tosyl secondary amine as initiator mimicking the growing chain, provides the first metal-free route to well defined poly(aziridine)s (PAz) and related PAz-based block copolymers.

Owing to their near unlimited structural diversity allowing their steric and electronic properties to be finely tuned, *N*-heterocyclic carbenes (NHCs) have revolutionized organometallic chemistry as ligands for transition metals in the last two decades.[1] NHCs have also gained an increasing popularity as true organic catalysts in molecular chemistry.[1,2] Polymer synthesis has also greatly benefited from the potential of NHCs, providing a straightforward and metal-free synthetic strategy to a wide range of polymers.[3] Cyclic esters (e.g. D,L-lactide and lactones) have been by far the most investigated monomers for the NHC-organocatalyzed ring-opening polymerization (OROP).[3,4] The range of monomers amenable to polymerization by a NHC catalysis has also been expanded, not only to the ROP of other heterocycles[5] (e.g. oxiranes, cyclic carbonates, carbosiloxanes), but also to the group transfer polymerization of alkyl (meth)acrylates,[6] and to some step-growth polymerizations.[7] Besides their role as catalysts, a few NHCs can also serve as direct nucleophilic initiators, for chain-growth polymerization reactions, either through ring-opening of heterocyclic monomers,[8] such as lactide, *N*-carboxyanhydrides or lactams, or through 1,4-conjugate addition of some (meth)acrylics.[9]

In this communication we demonstrate the first OROP of *N*-activated aziridines using a NHC, namely, 1,3-bis(isopropyl)-4,5(dimethyl) imidazol-2-ylidene (^{Me}5-Ipr). 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 (or azacyclopropane) are polymerized by an anionic 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) (PEI) with a broad dispersity (*Đ*). Interestingly, Toste, Bergman *et al.* have reported in 2005 that 2-n-alkyl-*N*-sulfonylaziridines can be subjected to a controlled anionic ROP through monomer activation by *N*-tosylation.[10] Typically, the ROP of the *N*-sulfonylaziridine is performed at 50 °C in DMF, in presence of 1:1 molar of *N*-alkyl-methanesulfonamide: KHMDS as initiating system, which affords substituted polyaziridines (PAz) of narrow molar mass distribution. Corresponding linear 2-n-alkyl substituted PEI derivatives can next be obtained upon deprotection of the *N*-sulfonyl moieties, under mild conditions.[10,11] Ensuing reports by Wurm *et al.* have resorted to the living anionic ROP pathway to achieve "in-chain" functional PAz incorporating vinyl or acetal moieties, from purposely designed functional *N*-sulfonyl aziridines.[12]

As mentioned, this *N*-sulfonylaziridine ROP method employs stoichiometric amount of KHMDS rel. to the *N*-activated amine. Consequently, it also introduces metallic residues in the final PAz compounds. Here, the ^{Me}5-Ipr NHC is used in true catalytic amount (10% mol. rel. to the amine initiator). We thus provide a facile OROP synthesis to well-defined metal-free PAz *via* a novel NHC catalytic pathway, as depicted in Scheme 1. We also report first examples of all PAz-based block copolymer by sequential ^{Me}5-Ipr-mediated OROP of two different *N*-sulfonylaziridines.

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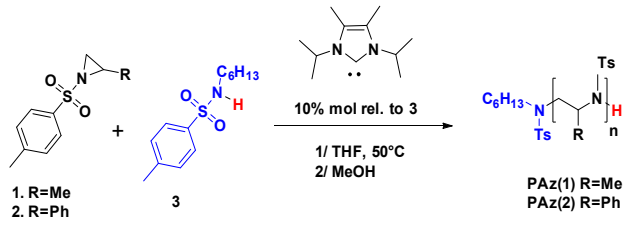

Scheme 1. OROP of *N*-tosylaziridines induced by ^{Me}**5-Ipr**

Both 2-methyl-*N*-*p*-toluenesulfonyl aziridine (**1**) and 2-phenyl-*N*-*p*-toluenesulfonyl aziridine (**2**) were investigated as monomer substrates for the ^{Me}5-Ipr-OROP. The polymerization of (**1**) was first carried out at 50 °C in THF -instead of DMF used in previous work[10,12]- in presence of *N*-hexyl-*p*-toluenesulfonylamine (**3**) as initiator and ^{Me}5-Ipr as catalyst (Scheme 1). Under those conditions, well-defined PAz(**1**) with excellent control over molar masses (up to 20,000 g.mol^{-1}) and low dispersities ($Đ$ < 1.10) were obtained (entries 1-4, Table 1 and Fig. S1). While 100 eq. of **1** could be quantitatively converted within 24h, 5 days were needed to reach completion of the OROP of **2**, witnessing 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 (entries 5–7, Table 1) 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**) (Fig. S2 in ESI), as the initial $[\mathbf{2}]_0/[\mathbf{3}]_0$ was increased, *i.e.* for higher molar masses targeted.

Table 1. Polymerization of 2-alkyl-*N*-*p*-toluenesulfonyl aziridines **1** and **2** in THF at 50 °C (see Scheme 1).

Run	R	[M]/[3]/[^{Me}5-Ipr]	Time (h)	Conv (%)[a]	$\overline{Mn}_{calcd}$[b] (g/mol)	$\overline{Mn}_{exp}$[c] (g/mol)	$Đ$[c]
1	Me	10/1/0.1	24	100	2100	1880	1.07
2	Me	20/1/0.1	24	100	4200	2500	1.06
3	Me	50/1/0.1	24	100	10600	6000	1.06
4	Me	100/1/0.1	24	100	21100	11700	1.04
5	Ph	20/1/0.1	120	97	5300	2600	1.06
6	Ph	50/1/0.1	120	98	13400	6250	1.12
7	Ph	100/1/0.1	120	99	27000	10800	1.15

[a] Determined by ^{1}H NMR; [b] Theoretical molar masses: $\overline{Mn}_{calcd}$ = ([M]/[3]) x M_{Az} x conv. (M_{Az}= molar mass of one monomer unit); [c] Determined by size exclusion chromatography in THF (PS calibration)

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 by ^{1}H NMR spectroscopy (5,200 and 27,000 g.mol^{-1}, entries 5 and 7, Table 1, respectively) indeed closely matched theoretical values. Fig. 1a) shows a typical ^{1}H NMR of a purified PAz(**2**) (entry 5), with the presence, in particular, of the characteristic signals of the hexyl group from the amine initiator at 0.7-1.3 ppm. Relative integration of these signals with those corresponding to the main chain protons (**d**) of PAz(**2**) allowed estimation of PAz(**2**) molar mass (Table 1). The agreement between experimental and theoretical molar masses attested to the complete initiation of polymer chains by the 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 backbone precluded an accurate determination of molar masses of these compounds (Fig S7 in ESI).

The presence of the *N*-hexyl-*p*-toluenesulfonylamino group from **3** in α-position could yet be evidenced by MALDI-ToF MS analysis of a low molar mass PAz(**1**) (entry 1, Table1). A single population, corresponding to a cationized PAz(**1**), with a peak-to-peak mass increment of 211.3 g.mol^{-1} corresponding to the molar mass of one monomer unit derived from **1**, was indeed unambiguously observed, as shown in Fig. 1b) and c).

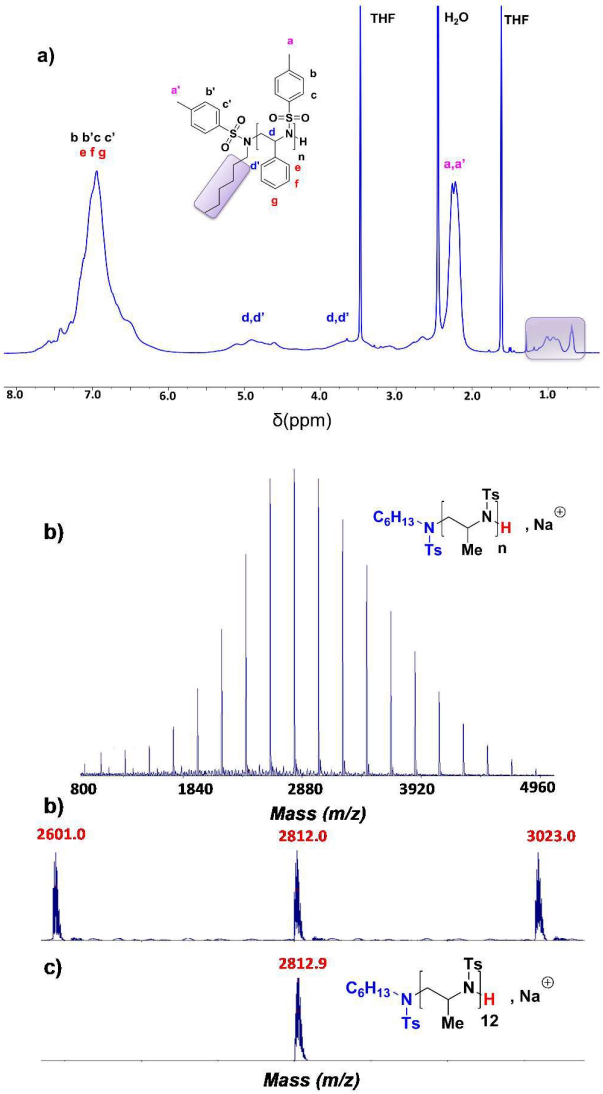

Fig. 1.a) ^{1}H NMR spectrum of PAz(**2**) (entry 5, Table 1). Experimental **b)** and computed **c)** MALDI ToF MS of PAz(**1**) (entry 1, Table 1)

In combination, characterizations by SEC, NMR and MALDI-ToF MS are consistent with a controlled OROP of *N*-tosyl aziridines. This was also supported by the perfectly linear evolution of $\ln([M]_0/[M])$ *vs.* time, when monitoring the ^{Me}5-Ipr-OROP of **2** by real-time ^{1}H NMR spectroscopy a (Fig. S9 and S10).

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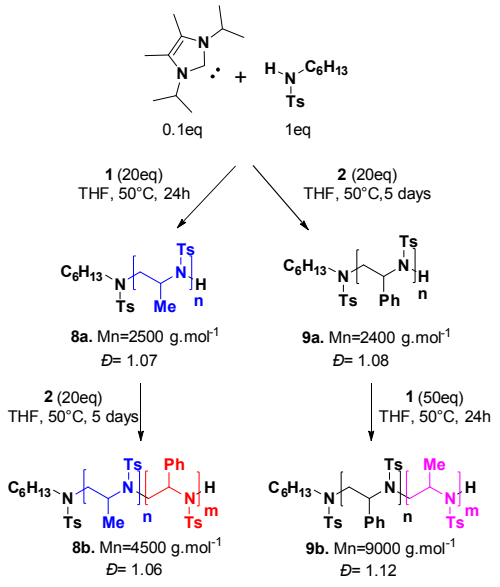
Based on background literature regarding other examples of NHC-mediated OROP,[3-5] either a nucleophilic or a basic mechanism, *i.e.* through the aziridine or the amine activation by the ^{Me}5-Ipr NHC, respectively (*vide infra*) could be operative (see Scheme S1 in ESI). The former mechanism would involve ring opening of the aziridine by direct attack by ^{Me}5-Ipr, forming an imidazolium amide zwitterionic intermediate that would be further displaced by the secondary amine (**3**). However, given the high basicity of ^{Me}5-Ipr (pK_a = 24 in DMSO[13]), in particular compared to that of the sulfonylamine group (pK_a ≈16 in DMSO[14]), a basic mechansim where the amine initiator/chain end would be deprotonated by ^{Me}5-Ipr cannot be ruled out. Data are lacking at this stage to state on the correct mechanism, and both experimental and theoretical investigations on these NHC-mediated OROP's of *N*-sulfonylaziridines are in progress.

In order to verify that a majority of ^{Me}5-Ipr-OROP-derived PAz chains could be reactivated, chain extension experiments were performed as follows (see also Fig. S3). Polymerization in THF at 50 °C of 20 eq. of **1**, using 10%mol. of ^{Me}5-Ipr, afforded a PAz(**1**) precursor (M_n = 2,500 g.mol^{-1}; $Đ$ = 1.06). Addition of 30 eq. of **1** increased the molar mass to M_n = 6,000 g.mol^{-1} while maintaining a low dispersity ($Đ$ = 1.06) after 24h of reaction at 50 °C (Fig. S3), confirming quantitative reinitiation of the OROP from the PAz(**1**) precursor. These results prompted us to further investigate the synthesis of PAz-based block copolymers, *via* a sequential NHC-OROP of **1** and **2**. As displayed in Scheme 2, both monomers were added either in this order (**1** then **2**) or in the other (**2** then **1**).



Scheme 2. Synthesis of PAz(**1**)-*b*-PAz(**2**) and PAz(**2**)-*b*-PAz(**1**) block copolymers by sequential OROP catalyzed by ^{Me}5-Ipr

Synthesis of a well-defined PAz(**1**)-*b*-PAz(**2**) block copolymer (**8b**) was first achieved, *i.e.* using the more reactive aziridine (**1**) first (20 eq.), giving a PAz(**1**) precursor (**8a**, M_n = 2,500 g.mol^{-1}; $Đ$ = 1.06; Scheme 2) 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 the compound collected after 5 days of reaction at 50 °C in THF, showing a clear shift to the higher molar masses (M_n = 4,500 g.mol^{-1}; $Đ$ = 1.06) compared with the SEC trace of the PAz(**1**) macroinitiator (Fig. 3a), Scheme 2), thus attesting to an effective crossover reaction. Interestingly, the PAz(**1**)-*b*-PAz(**2**) block copolymer (**9b**) could also be obtained by reversing the order of addition of the two monomers (**2** then **1**; see Scheme 2). A shoulder in the high molar mass region was observed though, presumably to some coupling reactions at high monomer conversions, as shown in Fig. 3b).

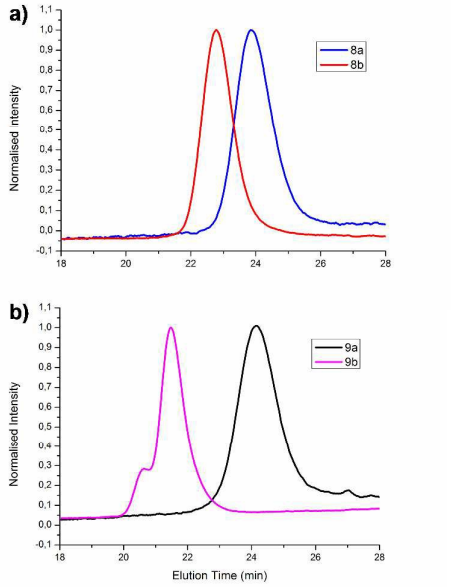


Fig. 2. SEC traces (refractometric detection) of a) PAz(**1**)-*b*-PAz(**2**) and b) PAz(**2**)-*b*-PAz(**1**) block copolymers (see Scheme 2.).

In summary, we describe for the first time the "controlled/living" organocatalyzed ring-opening polymerization (OROP) of *N*-activated aziridines by a *N*-heterocyclic carbene (NHC), namely, 1,3-bis(isopropyl)-4,5(dimethyl)imidazol-2-ylidene. Reactions can be conducted in THF at 50 °C in presence of a *N*-activated secondary amine as 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. This method can also be applied to achieve well-defined all PAz-based block copolymers by sequential OROP utilizing a carbene catalysis. Overall, this work further expands the monomer substrate diversity in NHC-mediated polymerization reactions.

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