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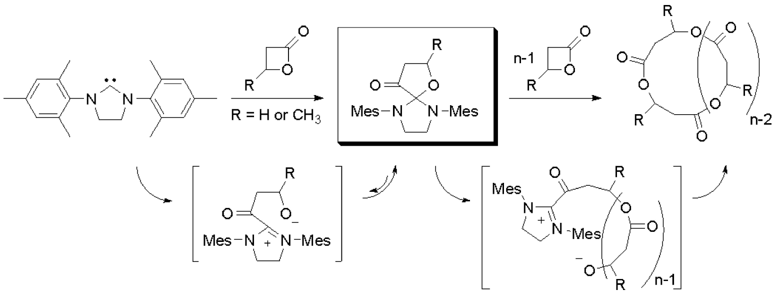

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COMMUNICATIONS

Organic Spirocyclic Initiators for the Ring-Expansion Polymerization of *β*-Lactones

Wonhee Jeong,[†] James L. Hedrick,[#] and Robert M. Waymouth*,[†]

Department of Chemistry, Stanford University, Stanford, California 94305, and IBM Almaden Research Center, 650 Harry Road, San Jose, California 95120

Received April 3, 2007; E-mail: waymouth@stanford.edu

Modern methods have allowed the synthetic chemist to begin to challenge nature's monopoly on the creation of well-defined macromolecules.[1−6] Many of these developments were spawned by new classes of catalysts, whose unique mechanisms of enchainment have enabled the rapid construction of well-defined block, star, comb, and cyclic polymers.[1−6] Szwarc's development of living ionic polymerization methods is arguably one of the most significant conceptual advances for the synthesis of complex polymer architectures.[4] Zwitterionic polymerizations are a special class of ionic polymerizations where the propagating ions and counterions are both part of the same polymer chain.[7,8] As early as 1960, Swarc proposed that zwitterionic polymerizations could produce macrocycles by the intramolecular coupling of the reactive cationic and anionic chain ends.[9] We recently reported the zwitterionic[8−10] ring-opening polymerization of lactide by the N-heterocyclic carbene 1,3-dimesitylimidazol-2-ylidene (IMes)[11] to generate high-molecular-weight cyclic poly(lactide) with predictable molecular weights and narrow polydispersities (Scheme 1).[11]

The zwitterionic ring-opening polymerization was proposed to occur by nucleophilic attack of the carbene on lactide to generate an alkoxide and acylimidazolium zwitterion which subsequently propagates by the addition of the monomer to the alkoxide of the zwitterionic intermediate. Herein, we report that the saturated carbene 1,3-dimesitylimidazolin-2-ylidene (SIMes) mediates the ring-opening polymerization of four-membered lactones to give cyclic polyesters through a novel mechanism involving the reversible collapse of zwitterionic intermediates to neutral imidazolidine spirocycles.

During the course of mechanistic studies to provide support for the intermediacy of acylimidazolium zwitterions, we discovered that the carbene SIMes reacts with an equimolar amount of *β*-butyrolactone to generate the spiro imidazolidine compound **1** (Scheme 2). The diagnostic downfield shift of 214 ppm in the ^{13}C NMR spectra is observed for the ketone resonance of **1**. Crystallographic analysis of **1** shows that the spiro ring is situated nearly perpendicular to the N-heterocycle, flanked by two mesityl groups (Figure 1). NOE NMR spectroscopy experiments and DFT-optimized geometry[12] at the level of B3LYP/6-31G* are in good agreement with the observed X-ray structure. The formation of **1** can be rationalized by nucleophilic attack of SIMes on *β*-butyrolactone to generate the zwitterion **2**, followed by collapse to **1**. DFT calculations indicate that the generation of the spiro compound can be attributed to the release of ring strain from the four-membered *β*-lactone to the five-membered spiro ring; the strain energy released by the generation of the spiro compound is estimated to be 21 kcal/mol.

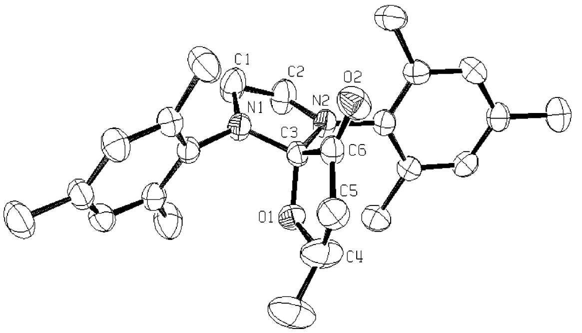
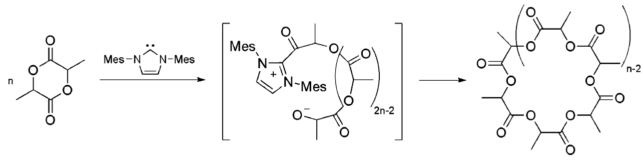
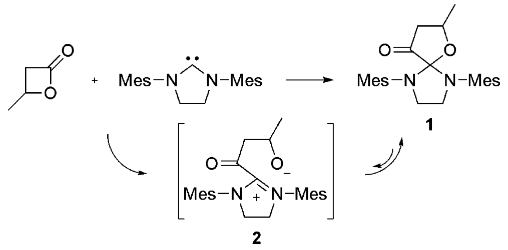


Figure 1. ORTEP drawing of **1**. Ellipsoids are drawn at the 50% probability level. Selected bond lengths (Å) and angles (deg): N1−C3, 1.438(3); N2−C3, 1.420(4); C3−C6, 1.553(4); O1−C3, 1.441(3); O2−C6, 1.203(4); N1−C3−N2, 102.3(2); O1−C3−C6, 101.8(2).

Scheme 1. Zwitterionic Polymerization of Lactide by IMes



Scheme 2. Formation of Spirocycle from SIMes and *β*-Butyrolactone



The spirocycle **1** is a competent initiator for the ring-opening polymerization of both *β*-propiolactone and *β*-butyrolactone and exhibits similar polymerization behavior to that of the carbene SIMes. The observation that the spirocycle is formed upon mixing of the lactones with SIMes implicates the spirocycle as the initiating species in the polymerization. The initiation of the polymerization occurs rapidly, and the carbene is quantitatively consumed at the early stage of polymerization.

The polymerization of *β*-propiolactone by SIMes is faster than that of *β*-butyrolactone. Kinetic studies on the polymerization of *β*-propiolactone initiated by SIMes were performed varying the initial monomer-to-initiator (M/I) molar ratios. As shown in Figure 2a, the polymerization is first-order in monomer and carbene concentration (see Supporting Information). The linear dependence of $\ln([M]_0/[M])$ on time over a wide range of conversion implicates that the initiation step is fast and the amount of active species is constant during the polymerization.

Analysis of the aliquot taken during the polymerization by high-resolution electrospray ionization (ESI) spectrometry indicates that

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[†] Standford University.
[#] IBM Almaden Research Center.

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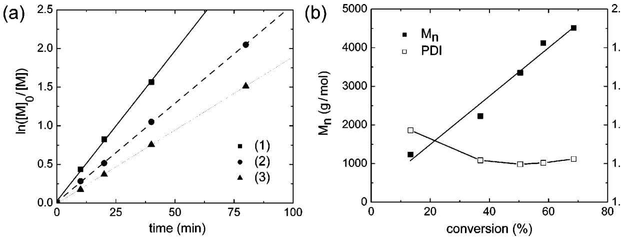
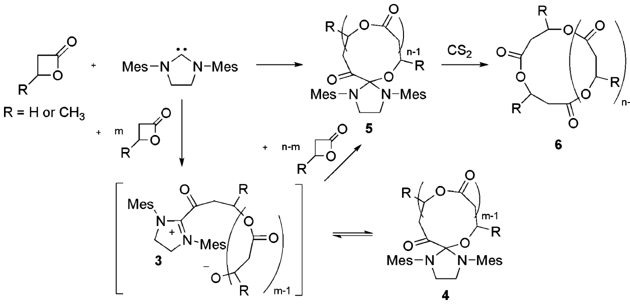


Figure 2. (a) First-order kinetic plot; $[M]_0 = 1$ M, M/I = 30 (1), M/I = 50 (2), and M/I = 70 (3) and (b) plots of number average molecular weight (M_n) and polydispersity index (PDI) as a function of monomer conversion (M/I = 50).

Scheme 3. Ring-Expansion Polymerization of β-Lactones with SIMes



the predominant species in solution are macrocyclic spirocycles (**5**) (Scheme 3). Addition of CS_2 liberates cyclic polyesters,[11] but the mechanism by which the spirocycles react with CS_2 to generate the cyclic polyesters is not well understood and merits further study. The formation of **5** in the presence of excess monomer strongly suggests that the spirocycles are resting states that are in equilibrium with propagating zwitterions. Thus, this system is a novel example of a ring-expansion polymerization mediated by zwitterions. Kricheldorf and Grubbs have shown that ring-expansion of spirocyclic tin initiators[13] or cyclic Ru carbenes[14] is an effective method for generating cyclic polymers.

The SIMes-mediated zwitterionic polymerization of β-propiolactone displays characteristics of a living polymerization; molecular weights linearly track monomer conversion and the molecular weight distributions remain lower than 1.3 to high conversions (Figure 2b). Analysis of crude polymers by ^{1}H NMR spectroscopy shows a negligible amount of acrylate groups formed by elimination reactions, which are common in the polymerization of β-lactones.[15] The remarkable degree of control of this polymerization is presumably due to the generation of a small amount of reactive zwitterionic intermediates (**3**) by the reversible formation of spiro macrocycles (**4**). The low concentration of reactive alkoxides during polymerization suppresses side reactions such as termination and elimination reactions analogous to modern controlled polymerizations.[6,16]

Further evidence for the mechanism of enchainment of β-lactones was provided by polymerization of optically active (R)-β-butyrolactone. Polymerization of (R)-β-butyrolactone with SIMes in THF at room temperature ($[M]_0 = 2.5$ M, M/I = 100) proceeded to 24% conversion after 4 h to yield poly(β-butyrolactone) after treatment with CS_2. Isolation of the cyclic polymer by column chromatography and analysis by high-resolution ESI mass spectrometry, ^{1}H NMR, and circular dichroism (CD) spectroscopy[17] (as well as acidic methanolysis to methyl (R)-3-hydroxybutyrate)[18] revealed it to be cyclic poly[(R)-β-butyrolactone],[17] indicating that the generation of the cyclic polymer[19] proceeds with retention of configuration. These results imply that the generation of the cyclic polymer occurs by acyl-oxygen cleavage with retention, in contrast to the anionic polymerization of β-butyrolactone mediated by carboxylates (which proceeds with inversion of configuration),[20] as observed in amine-initiated (pyridine, R_3N) zwitterionic ring-opening polymerization of β-lactones.[21]

In summary, the saturated carbene SIMes mediates the ring-expansion polymerization of β-lactones to generate cyclic polyesters. Mechanistic studies implicate a novel mechanism involving the reversible opening of spirocyclic imidazolidines. Further efforts are directed toward expanding the synthetic utility of spirocycles and synthesizing macrocycles with interesting functional groups and topology.

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Supporting Information Available: Complete reference 12, experimental procedures, characterization data, polymerization data, DFT calculation data, and X-ray structure data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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