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First Example of N-Heterocyclic Carbenes as Catalysts for Living Polymerization: Organocatalytic Ring-Opening Polymerization of Cyclic Esters

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Aliphatic polyesters are an important class of biologically relevant macromolecules.[1] One of the most common synthetic routes to polyesters uses transition metal initiating compounds to effect the ring-opening polymerization (ROP) of cyclic esters.[2] Removal of the metal contaminant, bound to the chain-end, must be considered for application in resorbable biomaterials and in microelectronics. We are interested in metal-free, organocatalytic living polymerization approaches to well-defined macromolecules. Versatile strategies for asymmetric synthesis using organic compounds as reaction catalysts exist;[3] however, efficient polymer-forming reactions via organic catalyzed reactions are not as pervasive. Recently, we reported a purely organic approach to the catalytic living ROP of lactide using either tertiary amines or phosphines as nucleophilic transesterification catalysts.[4] N-heterocyclic carbenes, pioneered by Arduengo,[5] constitute another class of possible nucleophilic compounds that have yet to be exploited as polymerization catalysts. In the area of organometallic chemistry, the use of N-heterocyclic carbenes, in many cases, has replaced the electron-rich phosphine ligands, producing transition metal complexes that exhibit superior catalytic performances.[6] Moreover, nucleophilic N-heterocyclic carbene compounds are readily synthesized with significant structural diversity including chiral derivatives.[7] Herein, we describe the use of nucleophilic N-heterocyclic carbene compounds as organic catalysts for living polymerizations (Scheme 1).

1,3-Bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene (**1**) was prepared by literature methods,[8] and its catalytic behavior for the polymerization of lactide and lactone was studied at 25 °C in THF with assorted alcohols as initiators. Although **1** can be generated in situ, we preferred to use the isolated carbene. The molecular weights of the ring-opened cyclic esters closely tracked the monomer-to-initiator ratio (M/I) with consistently narrow polydispersities (Table 1). The carbene catalyst concentration was varied from 0.008 to 1.5 equiv relative to alcohol initiator and under the conditions explored, higher molecular weights generally required larger catalyst loadings for polymerization times on the order of a couple of hours (samples **2**−**6**). The higher molecular weight polymerizations were conducted in a 1 M THF solution which facilitated both the dissolution of the lactide monomer and narrow polydispersities. The reactivity of **1** is clearly demonstrated in samples **8** and **9**. To prepare lactide oligomers with narrow polydispersities in higher solid contents solutions (2 M THF), a significant reduction in catalyst concentration was required (for sample **9**, a ratio of lactide/initiator/**1** of 1200/120/1).

A plot of molecular weight versus monomer conversion for the ROP of lactide initiated from benzyl alcohol in the presence of **1** shows a correlation typical of a living polymerization (Figure 1). In a chain extension experiment, polylactide **4** having a DP of 92 and a molecular weight of 22 500 g/mol by GPC (PDI 1.15) was charged with an additional 100 equiv of L-lactide. The molecular weight of the sample increased to 39 500 g/mol by GPC (95% yield) with minimal change to the polydispersity (1.17), substantiating the living character of the polymerization. Likewise, the ROP of lactones was accomplished with **1**, giving polymers of predictable molecular weight in near quantitative conversions (20 h) (samples **10**−**14**). To further demonstrate the initiating species and possible macromolecular architecures, star-shaped poly(caprolactones) with narrow, monomodal polydispersities and extremely high molecular weight (samples **12** and **13**, Table 1) were prepared with use of a 6 arm hydroxyl functional poly(propylene glycol), PPG (M_n 3000 g/mol), as an initiator. Poly(β-butyrolactone), an important class of naturally occurring polymers, was prepared in near quantitative yield with exceptional control, **14**.

Scheme 1

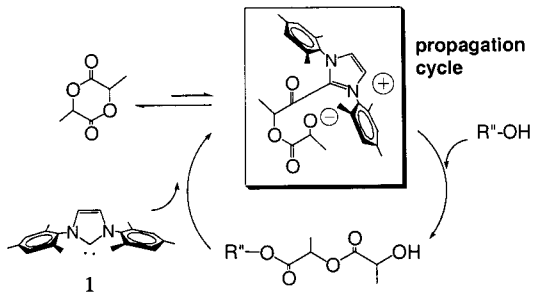

Table 1. Selected Polymerization Data of Cyclic Esters Using N-Heterocyclic Carbene **1** as a Catalyst[a]

no.	monomer	I/(Cat./I)[b]	conv.[c]	(M/I)[d]	DP[e]	PDI[f]
2	L-lactide	$PhCH_2OH$/1.5	90	50	47	1.12
3	L-lactide	$PhCH_2OH$/1.5	98	60	59	1.09
4	L-lactide	$PhCH_2OH$/1.5	92	100	92	1.15
5	L-lactide	$PhCH_2OH$/1.5	60	200	110	1.08
6	L-lactide	$PhCH_2OH$/1.5	63	200	120	1.12
7	L-lactide	Pyrene-butanol/1.5	99	30	30	1.11
8	L-lactide	$PhCH_2OH$/0.016	98	10	12	1.16
9	L-lactide	$PhCH_2OH$/0.0083	98	10	11	1.10
10	ϵ-caprolactone	$PhCH_2OH$/0.5	99	60	56	1.30
11	ϵ-caprolactone	$PhCH_2OH$/0.5	99	100	97	1.33
12	ϵ-caprolactone	6-arm PPG [g]/0.5	95	40 per arm	35	1.15
13	ϵ-caprolactone	6-arm PPG [g]/0.5	90	10 per arm	9	1.05
14	β-butyrolactone	pyrene-butanol/1.5	90	50	44	1.15

[a] Typical lactide reaction, sample **4**. Under an inert atmosphere, a 1.0 M THF solution of lactide (2 g, 100 equiv to alcohol) was added to a 0.088 mM THF solution of **1** and benzyl alcohol for 2 h at 25 °C. The reaction was terminated by the addition of 2 drops of 1.0 M aqueous acetic acid and exposure to air. Reactions **8** and **9**: 2.0 M THF solution of lactide was used. Reactions of lactones (e.g. **10**) were similar, except: 24 h, 20% solids. [b] Initiator/catalyst-to-initiator ratio. [c] Conversion, experimentally measured by ^{1}H NMR spectroscopy. [d] Monomer-to-initiator ratio. [e] Degree of polymerization; experimentally measured by end group analysis from ^{1}H NMR spectroscopy. [f] Polydispersity index; experimentally measured by gel permeation chromatography. [g] PPG: poly(propylene glycol).

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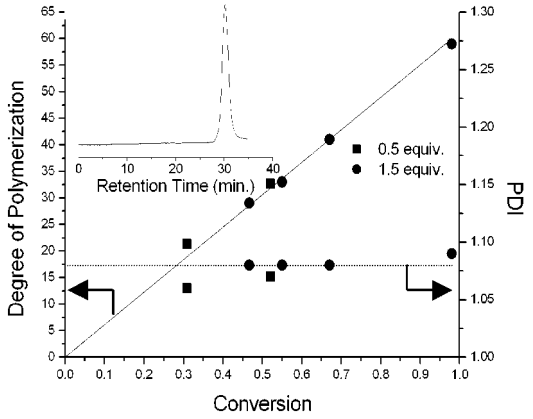

Figure 1. DP and PDI versus conversion for two catalyst concentrations along with a typical GPC trace ($M_w/M_n = 1.08$).

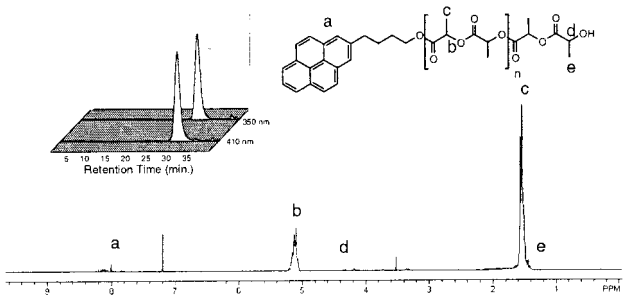

Figure 2. ^{1}H NMR spectrum of polylactide initiated from 1-pyrene butanol in the presence of **1** together with GPC scans using both RI (410 nm) and UV (350 nm) detectors.

There are two likely mechanisms by which N-heterocyclic carbene can catalyze polymerization: (a) a monomer-activated mechanism, analogous to the ROP of cyclic esters with biocatalysts,[9] or (b) an anionic mechanism. Since the carbene is basic with a pK_a value of 24 in DMSO, the possibility of a "catalytic anionic" reaction is a possible propagating route, i.e., protonation of the carbene with the initiating alcohol, followed by nucleophilic addition of the anion from the initiating alcohol.[10] However, since the pK_a value of the alcohol in DMSO is 29, we believe the nucleophilic N-heterocyclic carbene activates the substrate toward attack from the initiating/propagating alcohol (Scheme 1).[11] This proposed mechanism is similar to the widely studied benzoin condensation reaction, where Breslow, Stetter, and others postulated acyl activation by carbene.[12] Moreover, Murry et al. suggested a similar mechanism in the thiazolium-catalyzed cross coupling of aldehydes with acylimines.[13] Although in several related thiazolium-catalyzed transformations the mechanism was postulated to proceed through the bis(thiazolin-2-ylidene) reactive intermediate, these catalysts were formed in situ.[14] Initiation occurs when a nucleophile such as an alcohol reacts with the lactide carbene complex to form the ring-opened adduct. With this mechanism the α-chain end of the polylactide bears the ester from the initiating alcohol and the ω-chain end is a secondary alcohol and serves as the nucleophile to propagate the chain. Consistent with this mechanism, the ^{1}H NMR spectrum of the polylactide, **6**, initiated with 1-pyrenebutanol in the presence of **1** shows the resonances associated with the pyrenebutyl ester as well as the hydroxyl chain-end, and the GPC measurements with use of the RI and UV detectors show quantitative and statistical distribution of pyrene in the sample (Figure 2). The feasibility of N-heterocyclic carbenes as reactive organic catalysts for the living ROP of cyclic esters was demonstrated. Current efforts focus on extending the catalyst pool to thiazolium and triazolium carbenes, in situ catalyst formation and chiral carbene catalysts to elaborate enantioselective complex targets including asymmetric synthesis and stereochemically controlled polymerization.

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