Block Copolymers

DOI: 10.1002/anie.200700522

A Distinctive Organocatalytic Approach to Complex Macromolecular Architectures**

Olivier Coulembier, Matthew K. Kiesewetter, Andrew Mason, Philippe Dubois, James L. Hedrick, and Robert M. Waymouth**

The self-assembly of precisely aggregated macromolecular assemblies has largely been the domain of biological systems owing to the exquisite architectural and compositional configuration of natural macromolecules.[1] Modern synthetic methods are beginning to challenge nature's monopoly on the creation of well-defined macromolecules of specific architecture and composition.[2–5] Living-polymerization methods enable the synthesis of a wide variety of block copolymers of different structure and topology.[4] In the case of block copolymers, the molecular architecture or topology of the chain has a pronounced affect on the morphology and interfacial activity. For example, ABC triblock copolymers, dendritic–linear hybrid copolymers, radial star-shaped copolymers, comb, tadpole-shaped, and linear–nanoparticle copolymers all manifest unique morphologies as a result of their distinctive architectures.[5–13] While the synthesis of linear block copolymers is facile with several methods, the introduction of branch points at specific loci is more challenging and requires multiple steps.[4,14–16] H-shaped homopolymers, first reported by Roovers and Toporowski,[17] exhibit unique rheological behavior. Many variations of this architecture (super-H, π-shaped, graft, off-centered graft, etc.) have been prepared with anionic methods,[4] typically from styrene, isoprene, and butadiene monomers. More recently, controlled radical polymerization and ring-opening metathesis methods have expanded the comonomer classes that can be enchained into specifically branched copolymer architectures.[14–16,18] Herein, we report an expedient approach to H-shaped and super-H-shaped polymers by ring-opening polymerization from telechelic diamine or polyamine macroinitiators.

New catalysts beget new patterns of reactivity for the enchainment of monomers to structurally well-defined macromolecules.[2] Organocatalysts complement transition-metal catalysts owing to their different mechanisms for effecting bond constructions.[19] Our research has focused on organocatalytic ring-opening polymerization (ROP) of cyclic esters, primarily motivated to avoid metal contaminants in polymers for microelectronic and biomedical applications.[20–25] Recent studies have shown that these catalysts enable the construction of novel polymer architectures.[21,22] We have reported several classes of ROP organocatalysts, including N-heterocyclic carbenes,[22,24,25] bifunctional thiourea amines,[23] and amidine or guanidine superbases,[20] with user-selectable degrees of activity and selectivity. Herein, we report a simple approach to H-shaped and super-H-shaped architectures enabled by the unique reactivity of the commercially available 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4-triazol-5-ylidene (**1**).[26] Primary amines were found to function as bifunctional initiators for ROP in the presence of **1** to generate imide end groups and two chains per initiating amine, enabling the facile introduction of branch points in block copolymers. This result is in marked contrast to conventional organometallic promoters where only one chain is initiated from a primary amine, generating an amide end group.[27,28]

The triazole carbene **1** is an efficient catalyst for the ROP of lactide in the presence of alcoholic initiators at 50–90 °C.[25,29] Elevated temperatures are required for **1** owing to a competitive O–H insertion reactions of **1** with terminal alcohols of the growing chains. These insertions lead to dormant alcohol adducts that are reactivated reversibly at elevated temperatures (Figure 1).[25,26] As analogous N–H insertion reactions are known for secondary amines,[30–32] we investigated the use of primary amines as initiators for lactide polymerization with **1**.

The polymerization of *rac*-lactide (LA) initiated by 4-pyrene methylamine as an initiator and **1** as catalyst in

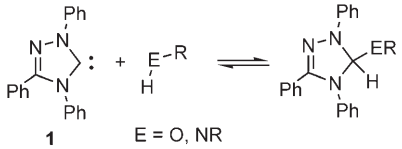


Figure 1. Reversible E–H insertion reactions of **1**.

[*] M. K. Kiesewetter, Prof. R. M. Waymouth
Center for Polymer Interfaces and Macromolecular Assembies
Stanford University
Stanford, CA 94305 (USA)
Fax: (+1) 650-736-2262
E-mail: waymouth@stanford.edu
A. Mason, Dr. J. L. Hedrick
Center for Polymer Interfaces and Macromolecular Assembies
IBM Almaden Research Center
650 Harry Road, San Jose, CA 95120 (USA)
Fax: (+1) 650-736-2262
E-mail: hedrick@almaden.ibm.com
O. Coulembier, Prof. P. Dubois
Chimie des Matériaux Polymères et Composites
Université de Mons-Hainaut
Place du Parc 10, 7000 Mons (Belgium)

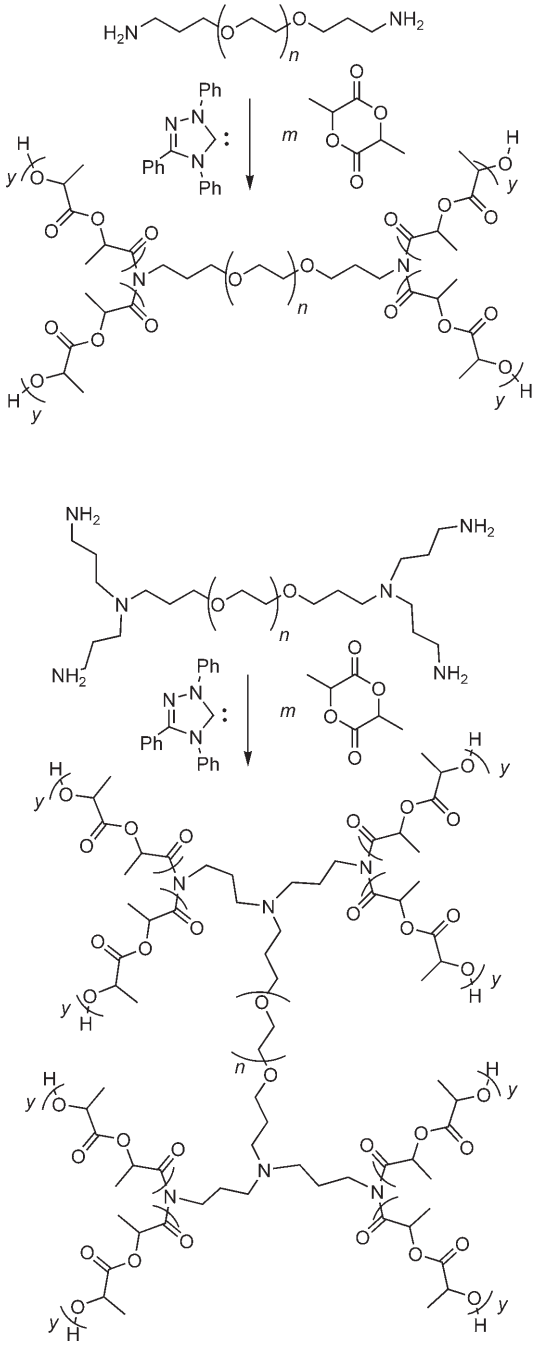
[**] R.M.W., M.K.K., and J.L.H. acknowledge support from the NSF (CPIMA: NSF-DMR-0213618, GOALI: NSF-CHE-0313993). O.C. acknowledges the FRIA for financial support. This work was partially supported by the Belgian Federal Office of Science Policy (SSTC-PAI-5/3). We thank Purac for the donation of lactide.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

deuterated benzene (C_6D_6) was carried out at an initial monomer-to-initiator ratio ($[M]_0/[I]_0$) of 100 at 90 °C. After 15 h (conv. = 72.6 %), the reaction was cooled to room temperature and directly quenched with a few drops of carbon disulfide. The polymer was precipitated twice from cold methanol and dried under vacuum until constant weight to give polylactide with a $M_n = 10600\ g\,mol^{-1}$ and $M_w/M_n = 1.1$. Analysis of the ^1H NMR spectrum, MALDI-TOF mass spectra, (see Supporting Information) and gel permeation chromatography (GPC) with a UV detector clearly show the presence of the 4-pyrene methylamino end group. Surprisingly, integration of the signals for the methine end groups versus the pyrene aromatic signals revealed approximately two end groups per pyrene, suggesting that lactide polymerization was initiated from both N–H groups of the initiator (i.e., both the amine and resulting amide functionality). This result is surprising, as it suggests that the N-heterocyclic carbene **1** can initiate lactide polymerization both from primary amines and from amides.

To establish the competence of amides as initiators in the presence of **1**, we investigated the polymerization of *rac*-lactide (LA) initiated from the cyclic amide ε-caprolactam (CLa) ($[LA]_0/[CLa]_0 = 10$). After 22 h in C_6D_6 at 90 °C, the reaction was quenched with acetic acid and the resulting polymer analyzed by ^1H and ^{13}C NMR spectroscopy and by electrospray ionization mass spectrometry (ESI-MS). The ESI-MS yields a series of peaks corresponding to CLa–$(LA)_n$ with a parent ion at m/z 1121.3 (m/z 1122.03 for CLa–$(LA)_7$) and the ^1H- and ^{13}C NMR spectra clearly demonstrate the presence of the CLa end group. The observation that amides can serve as initiators for the polymerization of lactide with **1** is intriguing as initiation from both N–H bonds of primary amines provides a facile means of generating branched polymers in a single step.

To test the latter hypothesis, the polymerization of *rac*-lactide was carried out with poly(ethylene glycol) bis(3-aminopropyl) (PEO-$(NH_2)_2$) as initiator and **1** as catalyst ($[M]_0/[I]_0 = 100$, $[\mathbf{1}]_0/[I]_0 = 4$) in C_6D_6 at 90 °C (Scheme 1). Analysis of aliquots of the reaction mixture revealed a linear dependence of molecular weight (M_n) versus conversion. Plots of $\ln(([LA]_0\text{-}[LA]_{eq})/([LA]_t\text{-}[LA]_{eq}))$ versus time are linear with zero intercepts (see Supporting Information), indicating a first-order dependence on LA concentration and an absence of termination. The linear nature of the plot, in conjunction with the narrow polydispersities ($M_w/M_n < 1.1$), suggests that the polymerization of LA from the amino adduct of **1** is living, as previously described for LA ROP from the alcohol adduct of **1**.[25,29] At 71 h, the reaction had reached 85 % conversion, and a ^1H NMR spectrum (see Supporting Information) of the purified polymer taken after quenching with CS_2 revealed the formation of the [poly(lactide)]$_2$-poly(ethylene glycol)-[poly(lactide)]$_2$ (PLA_2-PEO-PLA_2) triblock polymer with $DP_{PLA} = 48$ (degree of polymerization, determined by comparison of the PLA and PEO resonances at $\delta = 5.14$ and 3.61 ppm, respectively). Integration of the signals of the methine end group ($\delta = 4.34$ ppm) versus those of the PEO segment confirmed the presence of 4.0 end groups and indicated that polymerization had occurred off all four N–H bonds of the initiator.



Scheme 1. Polymerization of LA initiated with PEO-$(NH_2)_2$ (upper) and PEO-$(NH_2)_4$ (lower) forming H-shaped and super-H-shaped polymers, respectively.

To confirm the initiation from all four N–H groups of the telechelic initiator PEO-$(NH_2)_2$, we compared the kinetics of ROP from PEO-$(NH_2)_2$ to those of PEO-$(OH)_2$ in the presence of **1**. The kinetics are consistent with the rate law: $-d[LA]/dt = k_{obs}[LA]$ for $k_{obs} = k_1[PEO][\mathbf{1}]$, where [PEO] = PEO-$(OH)_2$ or PEO-$(NH_2)_2$. These studies reveal that the rate constant for monomer consumption (k_1) is approximately two-times higher when LA is polymerized from PEO-$(NH_2)_2$ ($k_{1\text{-}NH_2}$) compared to when LA is polymerized from PEO-$(OH)_2$ ($k_{1\text{-}OH}$), $k_{1\text{-}NH_2}/k_{1\text{-}OH} = 1.97$, consistent with the doubling of the number of propagating O–H end groups when

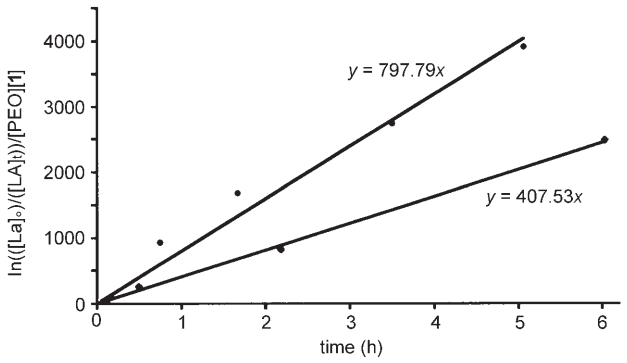


Figure 2. Comparison of rates of LA polymerization with PEO-$(NH_2)_2$ (upper plot) and PEO-$(OH)_2$ (lower plot) catalyzed by **1**.

polymerization is initiated from the amine initiators (Figure 2). In addition, polymerization of lactide from a 1:1 mixture of PEO-$(OH)_2$ and PEO-$(NH_2)_2$ at 90 °C with **1** in C_6D_6 yielded a mixture of diblock copolymers of $M_n =$ 20,000 g mol^{-1} and 9000 g mol^{-1} (GPC vs. polystyrene), consistent with the generation of a mixture of an H-shaped block polymer of approximately twice the molar mass of the linear block copolymer.

This strategy also enables a facile synthesis of super-H-shaped copolymers[33] from a telechelic tetramino-functionalized PEO oligomer (Scheme 1). Tetra-amine-functionalized PEO was synthesized by cyanoethylation of PEO-$(NH_2)_2$ and subsequent nitrile reduction using BH_3·THF. Polymerization of LA initiated from poly(ethylene glycol) octa(3-aminopropyl) (PEO-$(NH_2)_4$) with eight equivalents of **1** and 100 equivalents of LA ($[LA]_0 = 1$ M) in C_6D_6 was carried out at 90 °C until near complete conversion after 16 h (Scheme 1). ^{1}H NMR spectroscopic analysis confirms the polymerization off each N–H bond (integration of the end group signals versus those of the PEO segment suggests 8.15 end groups) and DP = 93 (integration of PLA versus PEO fragment). These results indicate that **1** with any of a host of commercially available amino-functionalized macroinitiators provides a general procedure for the generation of a variety of precisely branched block copolymer architectures. In addition, these results suggest a novel means of functionalizing polyamides or proteins.[34] Further studies are underway to investigate the interfacial and self-assembly properties of these hydrophilic/hydrophobic branched copolymer architectures.

Received: February 6, 2007
Published online: May 15, 2007

Keywords: block copolymers · H-shaped copolymers · N-heterocyclic carbenes · organocatalysis · ring-opening polymerization

[1] V. Percec, G. Ungar, M. Peterca, *Science* **2006**, *313*, 55.
[2] C. J. Hawker, K. L. Wooley, *Science* **2005**, *309*, 1200.
[3] P. Wu, A. K. Feldman, A. K. Nugent, C. J. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Fréchet, K. B. Sharpless, V. V. Fokin, *Angew. Chem.* **2004**, *116*, 4018; *Angew. Chem. Int. Ed.* **2004**, *43*, 3928.
[4] N. Hadjichristidis, H. Iatrou, M. Pitsikalis, J. Mays, *Prog. Polym. Sci.* **2006**, *31*, 1068.
[5] V. Percec, C. H. Ahn, G. Ungar, D. J. P. Yeardley, M. Moller, S. S. Sheiko, *Nature* **1998**, *391*, 161.
[6] Y. Kim, J. Pyun, J. M. J. Fréchet, C. J. Hawker, C. W. Frank, *Langmuir* **2005**, *21*, 10444.
[7] T. Magbitang, V. Y. Lee, J. N. Cha, H. L. Wang, W. R. Chung, R. D. Miller, G. Dubois, W. Volksen, H. C. Kim, J. L. Hedrick, *Angew. Chem.* **2005**, *117*, 7746; *Angew. Chem. Int. Ed.* **2005**, *44*, 7574.
[8] J. C. M. Vanhest, D. A. P. Delnoye, M. W. P. L. Baars, M. H. P. Vangenderen, E. W. Meijer, *Science* **1995**, *268*, 1592.
[9] Y. Cong, B. Y. Li, Y. C. Han, Y. G. Li, C. Y. Pan, *Macromolecules* **2005**, *38*, 9836.
[10] S. P. Gido, C. Lee, D. J. Pochan, S. Pispas, J. W. Mays, N. Hadjichristidis, *Macromolecules* **1996**, *29*, 7022.
[11] C. Lee, S. P. Gido, Y. Poulos, N. Hadjichristidis, N. B. Tan, S. F. Trevino, J. W. Mays, *J. Chem. Phys.* **1997**, *107*, 6460.
[12] Z. Y. Chen, H. G. Cui, K. Hales, Z. B. Li, K. Qi, D. J. Pochan, K. L. Wooley, *J. Am. Chem. Soc.* **2005**, *127*, 8592.
[13] J. Pyun, C. B. Tang, T. Kowalewski, J. M. J. Fréchet, C. J. Hawker, *Macromolecules* **2005**, *38*, 2674.
[14] Y. G. Li, P. J. Shi, C. Y. Pan, *Macromolecules* **2004**, *37*, 5190.
[15] Y. Tezuka, F. Ohashi, *Macromol. Rapid Commun.* **2005**, *26*, 608.
[16] X. F. Yu, T. F. Shi, G. Zhang, L. J. An, *Polymer* **2006**, *47*, 1538.
[17] J. Roovers, P. M. Toporowski, *Macromolecules* **1981**, *14*, 1174.
[18] D. H. Han, C. Y. Pan, *J. Polym. Sci. Part A* **2006**, *44*, 2794.
[19] P. Kočovský, A. V. Malkov, *Tetrahedron* **2006**, *62*, 255 (Symposium in print).
[20] R. C. Pratt, B. G. G. Lohmeijer, D. A. Long, R. M. Waymouth, J. L. Hedrick, *J. Am. Chem. Soc.* **2006**, *128*, 4556.
[21] T. M. Hermans, J. Choi, B. G. G. Lohmeijer, G. Dubois, R. C. Pratt, H. C. Kim, R. M. Waymouth, J. L. Hedrick, *Angew. Chem.* **2006**, *118*, 6800; *Angew. Chem. Int. Ed.* **2006**, *45*, 6648.
[22] A. P. Dove, H. B. Li, R. C. Pratt, B. G. G. Lohmeijer, D. A. Culkin, R. M. Waymouth, J. L. Hedrick, *Chem. Commun.* **2006**, 2881.
[23] A. P. Dove, R. C. Pratt, B. G. G. Lohmeijer, R. M. Waymouth, J. L. Hedrick, *J. Am. Chem. Soc.* **2005**, *127*, 13798.
[24] S. Csihony, D. A. Culkin, A. C. Sentman, A. P. Dove, R. M. Waymouth, J. L. Hedrick, *J. Am. Chem. Soc.* **2005**, *127*, 9079.
[25] O. Coulembier, A. P. Dove, R. C. Pratt, A. C. Sentman, D. A. Culkin, L. Mespouille, P. Dubois, R. M. Waymouth, J. L. Hedrick, *Angew. Chem.* **2005**, *117*, 5044; *Angew. Chem. Int. Ed.* **2005**, *44*, 4964.
[26] D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J. P. Melder, K. Ebel, S. Brode, *Angew. Chem.* **1995**, *107*, 1119; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1021.
[27] A. Kowalski, J. Libiszowski, T. Biela, M. Cypryk, A. Duda, S. Penczek, *Macromolecules* **2005**, *38*, 8170.
[28] Q. Cai, Y. L. Zhao, J. Z. Bei, F. Xi, S. G. Wang, *Biomacromolecules* **2003**, *4*, 828.
[29] O. Coulembier, B. G. G. Lohmeijer, A. P. Dove, R. C. Pratt, L. Mespouille, D. A. Culkin, S. J. Benight, P. Dubois, R. M. Waymouth, J. L. Hedrick, *Macromolecules* **2006**, *39*, 5617.
[30] D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534.
[31] R. W. Hoffmann, B. Hagenbruch, D. M. Smith, *Chem. Ber.* **1977**, *110*, 23.
[32] J. Hocker, R. Merten, *Angew. Chem.* **1972**, *84*, 1022; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 964.
[33] H. Iatrou, A. Avgeropoulos, N. Hadjichristidis, *Macromolecules* **1994**, *27*, 6232.
[34] T. L. Schlick, Z. B. Ding, E. W. Kovacs, M. B. Francis, *J. Am. Chem. Soc.* **2005**, *127*, 3718.

