Macromolecules
PERSPECTIVE

Macromolecules **2010**, *43*, 2093–2107 **2093**
DOI: 10.1021/ma9025948

Organocatalysis: Opportunities and Challenges for Polymer Synthesis

Matthew K. Kiesewetter,[‡] Eun Ji Shin,[‡] James L. Hedrick,*[,†] and Robert M. Waymouth*[,‡]

[†]*IBM Almaden Research Center, 650 Harry Road, San Jose, California 95120, and* [‡]*Department of Chemistry, Stanford University, Stanford, California 94305*

Received November 24, 2009; Revised Manuscript Received January 26, 2010

ABSTRACT: Organocatalysis offers a number of opportunities in polymer synthesis and was among the earliest methods of catalyzing the synthesis of polyesters. In the following Perspective we attempt to highlight the opportunities and challenges in the use of organic molecules as catalysts or initiators for polymerization reactions. The ring-opening polymerization of cyclic monomers is used as a representative polymerization process to illustrate some of the features of organic catalysts and initiators and to compare them to metal-based approaches. The convergence of convenience, functional group tolerance, fast rates, and selectivities will continue to drive innovations in polymerization catalysis, and it is our perspective that organocatalysis will continue to play an important role in these developments.

Introduction

Organocatalysis can be traced back at least a century to the enantioselective synthesis of quinine alkaloids.[1,2] Many enzymatic reactions are mediated by precise arrays of organic functional groups, and much of the early work was inspired by an effort to understand and mimic the remarkable rates and selectivities of enzymatic catalysis.[2−7] The application of chiral organocatalysts for enantioselective synthesis has,[1,8,9] particularly in the past decade, spawned an impressive array of new catalysts, processes, and mechanistic insights.[10−30] While the focus of most recent research in organocatalysis has concentrated on enantioselective synthesis of small molecules, organocatalysis offers a number of opportunities in polymer synthesis and was among the earliest methods of catalyzing the synthesis of polyesters.[31]

In the following perspective we attempt to highlight the opportunities and challenges in the use of organic molecules as catalysts or initiators for polymerization reactions. The ring-opening polymerization of cyclic monomers will be used as a representative polymerization process to illustrate some of the features of organic catalysts and initiators and to compare them to metal-based approaches. Polymerization can occur by one of two general enchainment processes: step growth or chain growth.[32] Ring-opening polymerization is an example of a chain-growth process where repeated addition of the monomer to the chain end leads to an increase in the molecular weight. The thermodynamics of ring-opening polymerization (ROP) is driven by the enthalpy of ring-opening; the kinetics and selectivity of the ring-opening process are strongly influenced by the nature of the reactive chain ends, the monomers, and the presence of catalysts.

Catalysis plays a critical role not only in enhancing the rate of chemical reactions but also in controlling the selectivity of the reaction of interest relative to other competing reactions. For fine chemical synthesis, the premium placed on high chemo-, regio-, and stereoselectivities (particularly enantioselectivities) can compensate for modest rates and turnover numbers.[29] For polymerization catalysis, rate and turnover number come to the fore, as catalyst residues are often left in the final material due to the difficulty or added cost of separating these impurities from the resultant material. Furthermore, the selectivities critical for the ideal polymer synthesis include those that enable control over the molecular weight, molecular weight distribution, the nature and number of polymer end groups, the architecture, stereochemistry and topology of the macromolecule (linear, branched, cyclic, degree of cross-linking), and the functionality and sequence of monomers in the chain.[33] Indeed, the number of discrete catalytic steps in a ring-opening polymerization that must occur with the correct relative rates to yield a well-controlled reaction is impressive. Under conditions where the rates of initiation and propagation are higher than termination and inter- and intrachain reactions, exquisite control over the molecular weight and molecular weight distribution is possible.[32]

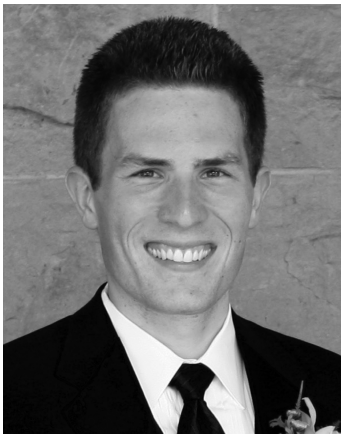
"Living" polymerization reactions are those where termination is absent, enabling control over the molecular weight by control of the monomer/initiator ratio (M/I) and monomer conversion. For living polymerizations where the rate of initiation is faster or comparable to propagation and all other competing reactions are minimized (inter- and intrachain reactions, etc.), very narrow distributions of molecular weights are possible, and a linear relationship between molecular weight and monomer conversion allows for precise tailoring of the molecular weight. Deviations from the living behavior can be attributed to slow initiation or side reactions such as chain transfer and termination reactions,[32] and these processes typically result in the broadening of molecular weight distribution (described by the polydispersity index PDI = M_w/M_n, the weight-average molecular weight and number-average molecular weight, respectively).[34−38]

If we consider the ring-opening polymerization of lactones as a representative example, a variety of general strategies can be envisioned for enhancing the rate and selectivity of enchainment either catalytically or stoichiometrically. For these reactions, the lactone monomer is electrophilic and the initiator/chain end is typically a nucleophile such as an alcohol. The rates of these reactions can be increased by activating the monomer, activating the initiator/chain end, or activating both simultaneously.

Metal alkoxides represent the most widely used set of catalysts for the ROP of cyclic esters, and they typically operate by a "coordination−insertion" mechanism (Scheme 1).[39−47] A typical mechanism for these reactions involves activation of the alcohol initiator (or chain end) by formation of metal alkoxide. Depending on the Lewis acidity of the metal (or the availability of open coordination sites), the metal alkoxide can also activate the

*To whom correspondence should be addressed.

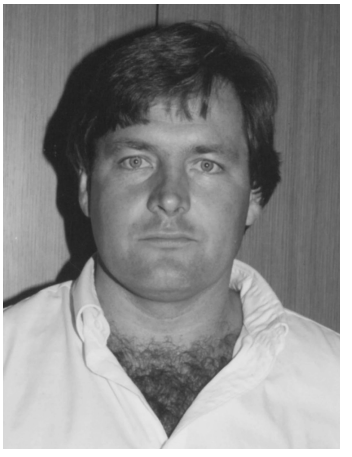
Published on Web 02/16/2010



Matthew K. Kiesewetter was born in 1982 in Bloomington, IL. In 2004, he received his B.S. in chemistry from Illinois State University where he did undergraduate and masters research with Professor Cheryl D. Stevenson. He is currently working toward his Ph.D. in chemistry at Stanford University under the supervision of Professor Robert M. Waymouth and Dr. James L. Hedrick. His current research focuses on the application of organocatalysts for the preparation of biocompatible materials.

Eun Ji Shin was born in 1980 in Busan, Korea. She received her B.S. in 2003 and M.S. in 2005 in chemistry from Seoul National University (Korea) with Professor Do Y. Yoon. She is currently pursuing her Ph.D. in chemistry at Stanford University under the supervision of Professor Robert M. Waymouth and Dr. James L. Hedrick. Her research interests include N-heterocyclic carbenes and their applications to organic and polymer chemistry.

Robert M. Waymouth was born in 1960 in Warner Robins, GA. He received bachelor's degrees in mathematics and chemistry from Washington and Lee University and his Ph.D. from the California Institute of Technology in 1987 with Professor Robert H. Grubbs. Following a year of postdoctoral research with the late Professor Pino at the ETH in Zurich, he joined the faculty at Stanford University in 1988, where he is now the Robert Eckles Swain Professor of Chemistry. His research interests are in homogeneous catalysis and polymer chemistry.



James L. Hedrick was born in 1959 in Blacksburg, VA. He received both his B.S. and Ph.D. from the Virginia Tech in 1981 and 1985, respectively, under the mentorship of Dr. James E. McGrath. He is currently a research staff member at IBM's Almaden Research Center in San Jose, CA, and he is also an investigator in the NSF Center for Polymeric Assemblies and Macromolecular Interfaces. He was the recipient of the 2003 American Chemical Society (ACS) Carl S. Marvel Creative Polymer Chemistry Award and the 2006 ACS Industrial Sponsors Award. His research has focused on new synthetic methodologies for microelectronics, nanotechnology, and biocompatible materials using organic catalysis.

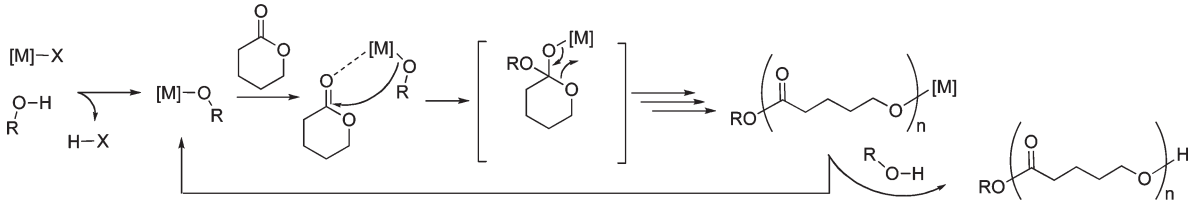
monomer by binding to the carbonyl (Scheme 1).[39−44] In cases where transesterifications of the propagating metal alkoxide are slow, the metal alkoxide functions as an initiator (not a catalyst); however, if the metal alkoxide reacts with alcohols to regenerate a new metal alkoxide, then chain formation is catalytic in M−OR. A wide range of metal complexes, most commonly alkoxides, have been developed using metals such as Al, Mg, Zn, Ca, Sn, Fe, Y, Sm, Lu, Ti, and Zr (turnover frequencies = TOF $\sim 0.01-0.1\ s^{-1}$ for metal alkoxide complexes).[39−42] The applications of polyesters in packaging,[48] biomedical,[44] and microelectronic[49] applications have motivated efforts to develop more biocompatible metal catalysts[50,51] or metal-free organic catalysts.[24]

Organic catalysts and initiators will typically operate by different mechanisms of enchainment than metal alkoxides;[24] this diversity of mechanistic pathways has provided new opportunities for the control of polymerization reactions with organic catalysts. In the following, we outline some general strategies for enhancing the rate and selectivity of ring-opening polymerization by the activation of the monomer, activation of the initiator/chain ends, or cooperative dual activation.

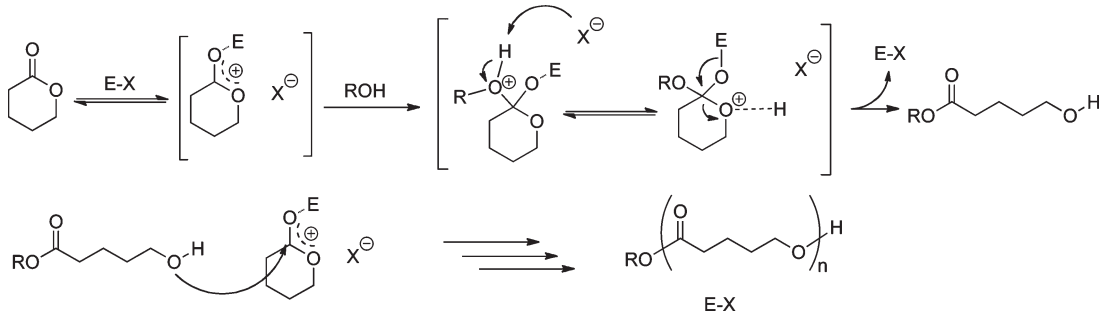
Results and Discussion

Electrophilic Monomer Activation. Electrophiles can activate the monomer toward enchainment. In the case of

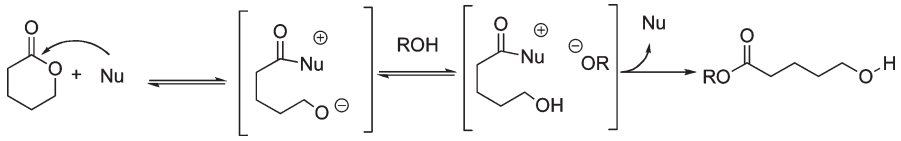
Scheme 1. Coordination−Insertion Mechanism for Metal-Catalyzed ROP



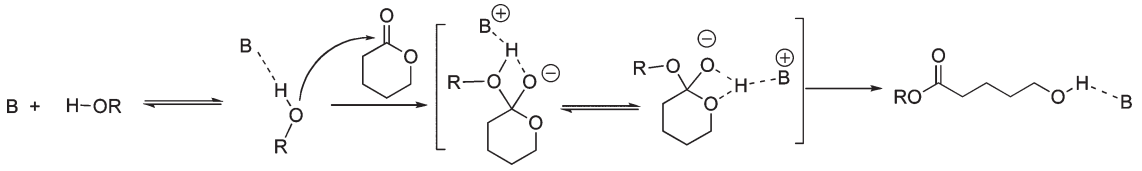
Scheme 2. Electrophilic Monomer Activation Mechanism for ROP



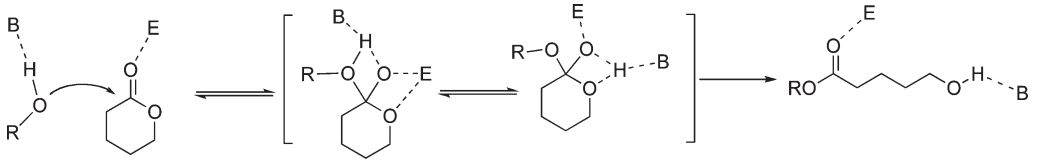
Scheme 3. Nucleophilic Monomer Activation Mechanism for ROP



Scheme 4. Initiator/Chain-End Activation Mechanism for ROP



Scheme 5. Bifunctional Activation Using Hydrogen Bonding for ROP



lactones, activation of the carbonyl by an electrophile facilitates nucleophilic attack by the initiating or propagating alcohol (Scheme 2). This has been achieved by protic acids (catalytic) or methylating agents (stoichiometric).

Nucleophilic Monomer Activation. Nucleophiles can activate the monomer by direct attack on the monomer to generate more reactive chain-carrying intermediates. Protonation of the zwitterionic alkoxide by the initiating or propagating alcohol followed by acylation of the incipient alkoxide leads to the formation of a ring-opened alcohol that can propagate by repeated attack on the activated monomer. This mechanism has been postulated for a variety of nucleophiles including pyridines, imidazoles, phosphines, and N-heterocyclic carbenes.

Initiator or Chain-End Activation by a General Base. Rather than activating the monomer, the initiator or active chain ends can be activated by a variety of mechanisms. In classical anionic polymerization, the initiator or chain end is activated by deprotonation to generate an alkoxide,[52,53] which is reactive enough to mediate ring-opening even with noncoordinating counterions.[54] Attack of the alkoxide at the carbonyl carbon of the monomer is followed by acyl−oxygen bond scission. This forms an ester end group and an active alcoholate species which reacts with the monomer for further propagation. The high reactivity of alkali metal alkoxides often leads to competitive transesterification.

Milder general bases can also activate the initiator or chain end via H-bonding. By hydrogen bonding to the alcohol, a general base can increase the nucleophilicity of the initiating or propagating alcohol to facilitate nucleophilic attack on the lactone monomer (Scheme 4).[55−57]

Bifunctional Activation of Monomer and Initiator/Chain End. Dual activation of both the monomer and the chain end

is a very effective strategy for enhancing the rate and selectivity of ring-opening polymerization; many of the metal alkoxide catalysts are proposed to operate in this way (Scheme 1). The combination of an electrophile to activate the monomer and a general base to activate the initiator/chain end can activate both partners to effect ring-opening (Scheme 5).

The strategies described in Schemes 2−5 are not mutually exclusive, and different catalysts and initiators can operate by a combination of mechanisms; for ring-opening reactions catalyzed or mediated by organic molecules, one or more of these mechanisms may be operative. In the discussion below, we highlight situations where this diversity of mechanistic pathways can provide new opportunities for enhancing the rate of polymerization and influencing the selectivity to generate polymer architectures that are difficult to access by metal-mediated processes.

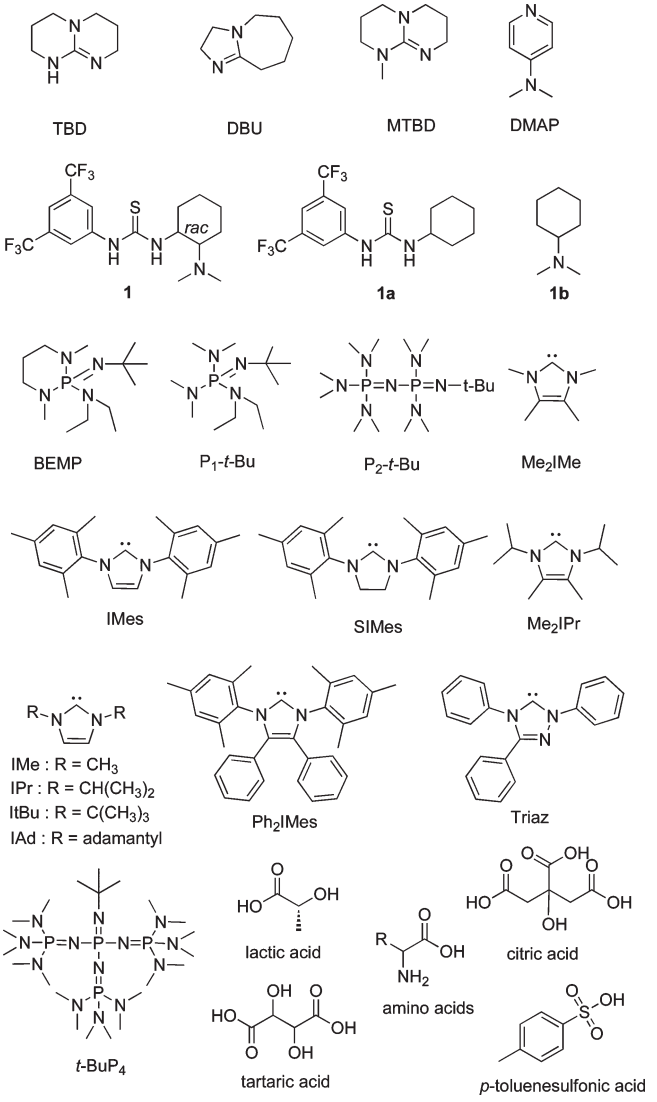


Figure 1. Representative organic catalysts and initiators.

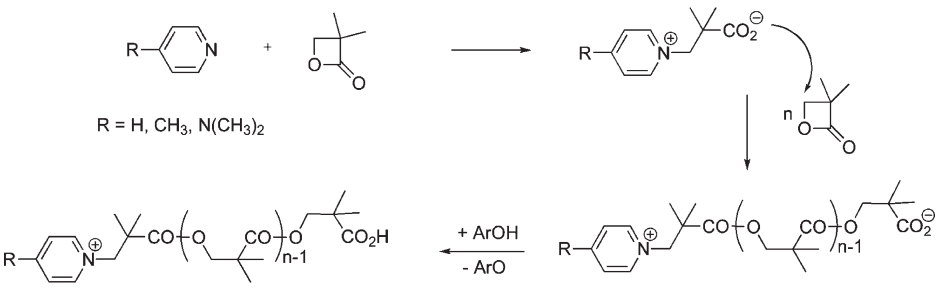
The following discussion will focus primarily on the ring-opening of lactones, but other monomers and processes will also be discussed. Representative organic catalysts and initiators are shown in Figure 1.

Organic Acids. The simplest method to effect ROP is by the employment of a strong organic acid.[32,58] The polymerization is initiated by the protonation of the monomer and subsequent ring-opening by reaction with a nucleophile, such as an alcohol (initiator). The polymerization propagates by the terminal hydroxyl group of the polymer chain acting as the nucleophile toward the protonated monomer. The use of a catalyst that is free from the propagating polymer (whereas metal alkoxides remain attached to the propagating species) represents a fundamental advantage of this strategy: less than one catalyst per monomer chain.[32,59] Stoichiometric activation of the monomer can be achieved with strong methylating agents such as methyl trifluoromethanesulfonate (MeOTf);[58] this strategy has proven particularly effective for the ring-opening of 1,3-oxazolin-2-enes,[32] but for lactones, this procedure requires further optimization to control the molecular weights.

Acid-catalyzed ROP has a distinct advantage in its simplicity and the wide range of acids available, but as with many cationic processes, the selectivity for propagation relative to other chain termination or transfer reactions is dictated by the reactivity of the protonated monomer.[60] In the presence of an alcohol initiator, $HCl \cdot Et_2O$ polymerizes ε-caprolactone (CL) and δ-valerolactone (VL) with controlled molecular weights ($M_n \sim 3000$) and low polydispersity index (< 1.20).[61] Higher molecular weights could be achieved by increasing the initial monomer concentration.[62] Amino acids (L-alanine, L-leucine, L-phenylalanine, L-proline) have also been used as catalysts for the ROP of CL in the absence of initiators. ^{1}H NMR spectroscopy and titration of carboxyl end group showed that the polymerization was initiated by the amino group of the amino acid.[63] Other organic acids such as tartaric acid, lactic acid, citric acid, and fumaric acid have been used as catalysts for δ-valerolactone (VL) and ε-caprolactone (CL) polymerization in the presence of alcohol and carbohydrate initiators.[64] The acid-catalyzed polymerization of lactide (LA) with trifluoromethanesulfonic acid (HOTf)[58] was faster and more highly controlled in the presence of a protic (alcohol) initiator.[65] The low molecular weights, slow rates, and high catalyst loadings associated with organic acids is compensated by the operational simplicity of this approach and the observation that the polymerization of L-lactide was highly stereospecific.[60,65]

Pyridine Bases/Nucleophiles. Pyridines are moderate bases and good nucleophiles;[66] they have been shown to act as

Scheme 6. ROP of Pivalolactone with Pyridine Initiators



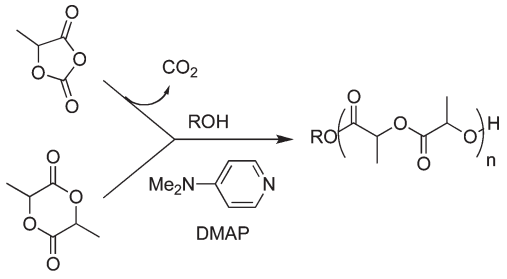
nucleophilic initiators in the zwitterionic ring-opening polymerization of pivalolactone.[32,67] Linear chains having one pyridinium ion and one CO_2^- ion as end groups were observed as products, and no cyclic polymers were observed in the MALDI-TOF mass spectra, which suggests that pyridine functions as a nucleophilic initiator by ring-opening the lactone to generate a zwitterionic carboxylate, which propagates by an anionic mechanism (Scheme 6).

The more nucleophilic 4-(dimethylamino)pyridine (DMAP) and 4-pyrrolidinopyridine (PPY) were shown to be very effective for the ROP of lactide (LA) in solution and in the melt.[54,68−72] In solution, DMAP loadings on the order of initiator concentration produced poly(lactide) (PLA) up to degree of polymerization (DP) = 100 with PDI < 1.13 in days. PPY was shown to effect the ROP of LA only in the melt and significantly slower than DMAP (20 h vs 20 min).[69] DMAP was also shown to be effective for the ROP of substituted lactides and lactide equivalents (Scheme 7).[73−76] DMAP was originally proposed to react via a nucleophilic monomer activation mechanism (Schemes 3 and 8),[69,77] although subsequent computational studies strongly suggest that an alcohol activation mechanism (either concerted or stepwise) may be operative in the DMAP-catalyzed ROP of lactide (Schemes 4 and 9).[78]

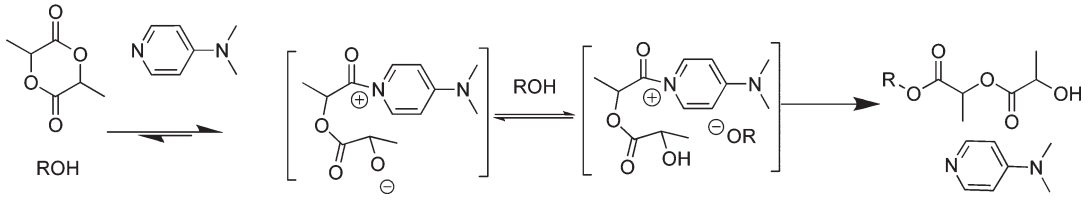
This mechanistic competition between nucleophilic and general-base mechanisms is a recurrent theme for nucleophilic/basic organic catalysts. Calculations suggest that both pathways are energetically accessible[55−57,78] and predict the H-bonded pathway to be lower in energy than the nucleophilic mechanism in the gas phase or in polar aprotic solvents. However, in cases where alcohol initiators are absent (Schemes 6 and 10) or at low concentration (high monomer/initiator ratio), nucleophilic mechanisms can compete.

Despite its low monomer scope and slow reaction times, DMAP marked two fundamental advances in the development of polymerization catalysts: (1) these catalysts show a high selectivity for transesterification of the monomer (propagation) relative to the open chain esters of the polymer (chain shuttling), and (2) these catalysts are compatible with

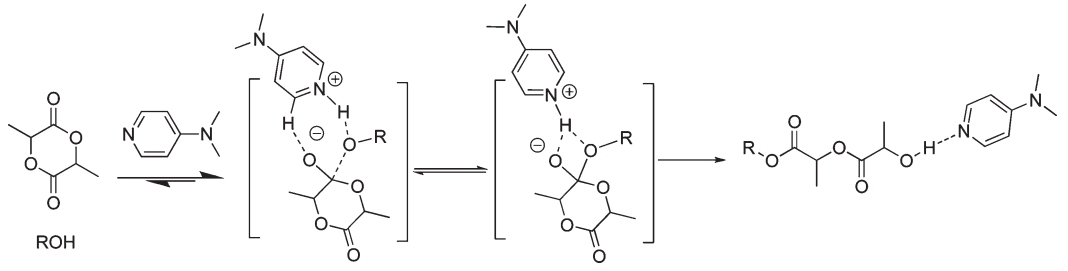
Scheme 7. DMAP-Catalyzed ROP of LA and lac-OCHA To Produce PLA



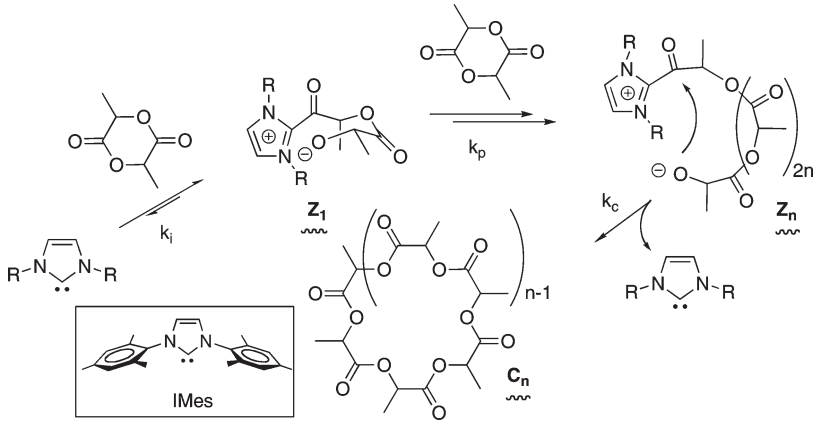
Scheme 8. Proposed Nucleophilic Mechanism for ROP of Lactide with DMAP



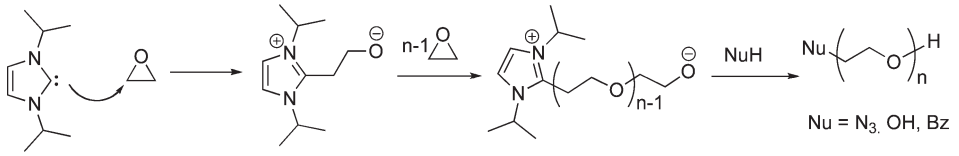
Scheme 9. Proposed General-Base Mechanism for ROP of Lactide with DMAP



Scheme 10. Zwitterionic Ring-Opening Polymerization of Lactide by IMes



Scheme 11. Zwitterionic Polymerization of EO



a range of different initiators and cocatalysts. DMAP does not catalyze the transesterification of esters with secondary alcohols, which mitigates transesterification of the PLA backbone by the propagating alcohol end groups, resulting in narrow polydispersities.[68] This idea would be developed further, in much more widely applicable catalysts, later (see Bifunctional Activation section). Also, DMAP was used in the successful ROP of LA from a metalloinitiator when $Al(OiPr)_3$ and $Sn(Oct)_2$ failed to produce the desired polymer.[79] This trait, broadly denoted herein as compatibility with functionality, was also to become a defining attribute of organocatalysts (see Chemoselectivity section).

Phosphine and Carbene Bases/Nucleophiles. Phosphines, such as $P(Bu)_3$, $PPheMe_2$, PPh_2Me, and PPh_3, catalyze the ROP of lactide in the presence of an alcohol initiator.[80] The substitution on the phosphine controls the reactivity of the catalyst such that the alkyl-substituted phosphines are more active (they are more basic and more nucleophilic) than the aryl-containing ones. Polymerizations are effective at high temperatures (135 °C) and in bulk (on the order of 0.01 s^{-1} for $P(Bu)_3$), which shows the potential for phosphine catalysts to be used in industrial processes.[80]

N-Heterocyclic carbenes (NHCs) are another class of potent neutral bases and nucleophiles.[18,81−84] They are widely used in place of phosphines in organometallic complexes.[85−88] Early work by Breslow,[6] Wanzlick,[89] Sheehan,[90] and Stetter[91] demonstrated that they are also potent organocatalysts.[18,24] In 2002, the groups of Nolan[92] as well as Hedrick and Waymouth[93] demonstrated that NHCs were potent organocatalysts for transesterification reactions, studies which led to their investigation as catalysts for the ring-opening polymerization of lactones.[94,95]

The ROP of lactide by the NHC IMes is considerably faster than that catalyzed by DMAP. The polymerization of lactide is extremely rapid (TOF ~ 18 s^{-1}) and well-controlled and exhibits features of a living polymerization.[24,94−96] A variety of cyclic monomers can be polymerized with NHCs, including lactones,[94−97] cyclic carbonates,[98,99] cyclic siloxanes,[100,101] acrylates,[102−104] dialdehydes,[105] and epoxides.[106]

Both a nucleophilic mechanism (Scheme 3)[94,95] and a H-bonding alcohol activation mechanism (Scheme 4)[57] have been proposed for the NHC-catalyzed transesterifications[92,93,107] and ring-opening polymerizations of lactide. Theoretical calculations predicted that the H-bond alcohol activation mechanism has a lower barrier than the nucleophilic mechanism.[57] Mechanistic studies to test for the viability of the nucleophilic mechanism demonstrated that in the absence of alcohol initiators the carbene IMes could mediate the zwitterionic ring-opening polymerization of lactide to generate cyclic polylactides (Scheme 10).[108] These studies strongly support that a nucleophilic activation of the monomer by NHC's is viable; moreover, these studies provided a new strategy to generate well-defined cyclic polyesters. Kinetic and mechanistic investigations[108b] indicate that the NHC acts as a catalyst/initiator; because of a slower rate of initiation relative to propagation, only a small fraction (approximately 30−50%) of the carbenes are converted to active zwitterions which propagate rapidly and extrude the carbene to generate cyclic macrolactones.

In the presence of alcohol initiators, it is likely that the NHC-catalyzed ROP operates by a combination of both mechanisms, particularly at high monomer/initiator ratios. The carbenes are active for the polymerization of a variety of lactones, and the rates and selectivities depend sensitively on both the nature of the carbene and the lactone monomer;[24,95] for example, the aryl-substituted carbene IMes is very active for lactide but much less active for CL. For CL, the more basic and less sterically hindered carbenes Me_2IMe and Me_2IPr are more effective than IMes.[97]

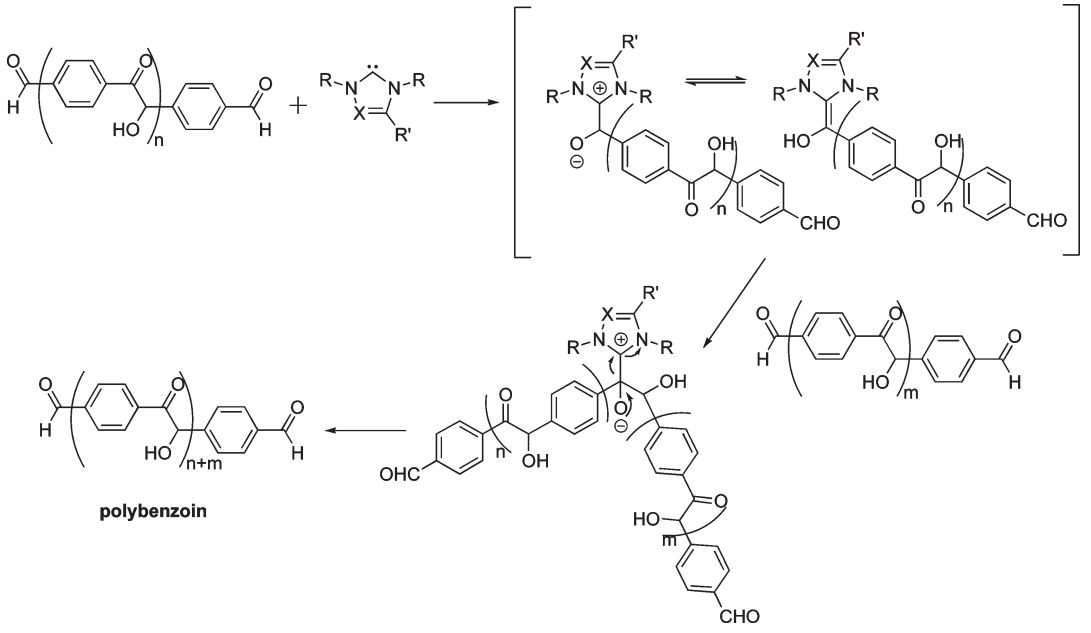
The ring-opening polymerization of ethylene oxide can also be catalyzed by NHC's such as IPr (Scheme 11).[106] Under the conditions described (DMSO, 50 °C), linear PEO was exclusively obtained, unlike the zwitterionic polymerization of LA described above. A nucleophilic mechanism to generate a zwitterionic imidazol-2-ylidinium alkoxide was proposed. The appropriate choice of the terminating agent gave a variety of α,ω-difunctionalized PEOs,[106] and dendrimer-like PEOs could be obtained by zwitterionic polymerization of EO followed by slow, semicontinuous addition of glycidol and propylene oxide (sequentially or randomly) during the arborization of the PEO chain ends.[110]

In addition to chain-growth ring-opening polymerizations, carbenes are effective for the step-growth polymerization of diesters and diols[93] and the depolymerization of polyesters, including poly(ethylene terephthalate) (PET).[93,111] Poly(glycolide) and PCL, biodegradable and commodity polymers, were synthesized by polycondensation of ethyl glycolate and ethyl 6-hydroxyhexanoate, respectively, using IMe generated *in situ*.[93]

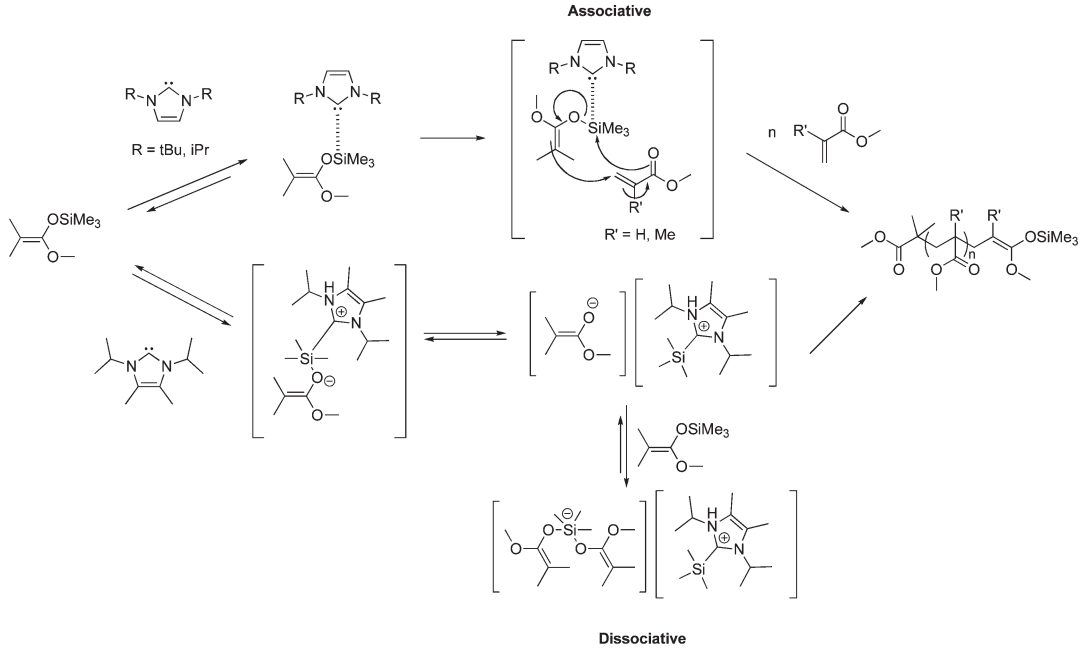
Carbenes are known to catalyze the benzoin and formoin condensation reactions.[18] This reactivity has been exploited for the step-growth polymerization of dialdehydes to obtain polybenzoin polymers.[105] Various carbenes, such as IPr, ItBu, IAd, and Triaz, were used in the step-growth polymerization of terephthaldehyde to produce poly(1,4-phenylene-1-oxo-2-hydroxyethylene) under mild conditions (THF + DMSO solution, 40 °C) (Scheme 12).[105] Optimization of reaction conditions to achieve higher molecular weights, minimize possible cyclic byproducts, and expanding the catalyst and monomer scope are some of the challenges of step-growth polymerization.

Group transfer polymerization (GTP) employs silyl ketene acetals as initiators in the presence of either nucleophilic or Lewis acid catalysts for controlled polymerization of acrylic monomers.[112] NHCs such as Me_2IPr,[102] IPr, and ItBu[103,104] were found to be effective neutral nucleophilic catalysts for the GTP of methacrylates and acrylates. Methyl methacrylate and *tert*-butyl acrylate were successfully polymerized in a controlled manner showing living characteristics enabling synthesis of block copolymers. Such high degree of control was proposed to come from the modulation of the concentration of the propagating enolates via reversible activation/deactivation equilibrium involving dormant bis(enolate) siliconates in the case of the Me_2IPr (dissociative mechanism in Scheme 13).[102] Later, for the case of IPr and I*t*Bu, the associative mechanism (an initiator activation mechanism) was proposed. The first-order dependence of the initial polymerization rate on the initiator concentration

Scheme 12. NHC-Catalyzed Polybenzoin Condensation



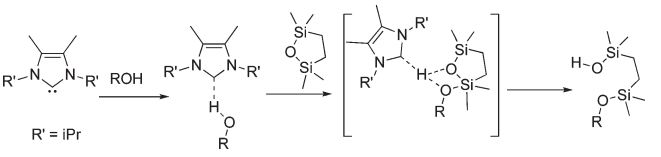
Scheme 13. Mechanisms of Group Transfer Polymerization of Acrylic Monomers



and the absence of enolate type species were offered to support the associative mechanism.[104]

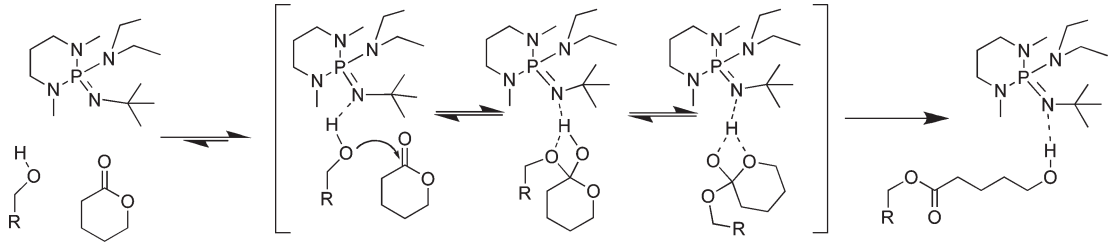
NHCs were also shown to catalyze the ring-opening polymerization of carbosiloxanes in the presence of initiating alcohols.[100,101] The ROP of 2,2,5,5-tetramethyl-1-oxa-2,5-disilacyclopentane (TMOSC) with Me_2IPr was proposed to occur by an alcohol activation mechanism where the strongly basic NHC activates the alcohol toward nucleophilic attack by H-bonding (Scheme 14), but a nucleophilic mechanism is also possible. The ROP reaction of TMOSC with 1 mol % Me_2IPr is extremely fast (99% conversion in 1 min or 1.65 s^{-1}) and yields poly(carbosiloxane) with a molecular weight $M_n = 10\,200$ and a polydispersity of $M_w/M_n = 1.19$. The aryl-substituted carbene IMes is slower (80% after 30 min or 0.044 s^{-1}) but provides a similar degree of control (M_w/M_n = 1.14).[100]

Scheme 14. ROP of TMOSC with Me_2IPr

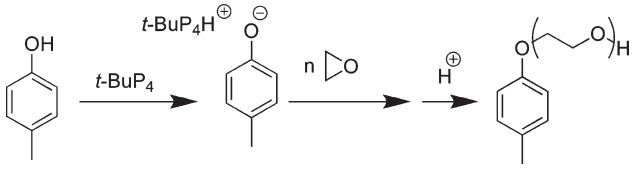


Strong Neutral Bases: Phosphazenes. The phosphazene bases P_1-*t*-Bu, P_2-*t*-Bu, *t*-BuP_4, and BEMP (Figure 1) developed by Schwesinger and Schlemper[113,114] are potent neutral bases in aprotic solvents ($^{MeCN}pK_a$ P_1-*t*-BuH^+=27.6, $^{DMSO}pK_a$ *t*-BuP_4H^+ = 32).[115] These bases are effective catalysts for the ring-opening polymerization of lactones in the presence of alcohol initiators. Both BEMP ($^{MeCN}pK_a$ BEMPH^+ = 27.6)[116] and P_1-*t*-Bu are active for the polymerization of LA and VL,

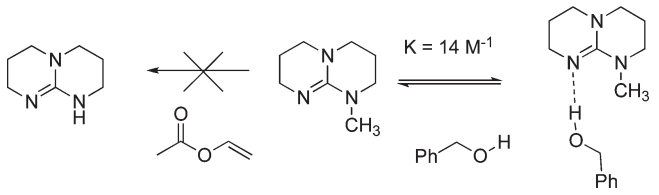
Scheme 15. Alcohol Activation Mechanism for the BEMP-Catalyzed ROP of VL



Scheme 16. Mechanism for the ROP of Ethylene Oxide by *t*-BuP$_4$



Scheme 17. MTBD Reversibly Associates with Benzyl Alcohol but Does Not React with Vinyl Acetate



producing comparable polymers, but BEMP offered enhanced rates (1 day vs several days). The ROP of CL was exceedingly slow (> 10 days for 14% conversion). The BEMP-catalyzed ROP of L-LA was shown to evolve M_n linearly with time and exhibited excellent chain end control,[116] which is consistent with a living polymerization. On the basis of experimental evidence, an alcohol activated mechanism was proposed whereby the catalyst activates the alcohol toward nucleophilic attack on the monomer (Scheme 15). BEMP is inert toward polymer except at high conversion when broadening of PDI occurs due to transesterification of the polymer backbone.[116]

These bases have been shown to be effective for the polymerization of siloxanes. The catalyst P$_1$-*t*-Bu offered improvement in reaction time over alkali metal alkoxide alternatives, as is typical of softer cations, but retained the broad PDIs.[114] A similar catalyst, *t*-BuP$_4$, was shown to be effective for the ROP of ethylene oxide in the presence of acidic initiators (a phenol or benzyl cyanide); in these cases, it was proposed that the phosphazene deprotonates the initiator which concomitantly attacks monomer and produces short oligomers ($M_w \sim 3000$) of narrow PDI < 1.09 (Scheme 16).[117] Similar reports were made for propylene oxide monomer.[118]

Nitrogen Bases. The guanidines and amidines *N*-methyl-1,5,7-triazabicyclododecene (MTBD, pK_a MTBDH$^+$ = 25.5)[115] and diazabicycloundecene (DBU, ^{MeCN}pK_a DBUH$^+$ = 24.3)[115] have similar basicities. Both MTBD[119] and DBU[120] are effective for the polymerization of LA, producing polymers of up to DP = 500 with narrow PDI < 1.1 in less than 1 h (TOF $\sim$ 0.05 s^{-1}). As with the phosphazenes, transesterification of the polymer backbone and accompanying broadening of PDI occur at high conversion.[120] An alcohol-activated mechanism was proposed for the MTBD- or DBU-catalyzed polymerization of LA.[120] In such a mechanism, MTBD would activate the initiating alcohol but be inert toward the monomer, and this was shown to be the case in some model reactions. MTBD was shown to associate strongly with benzyl alcohol (K_{eq} = 14 ± 2 M^{-1} at 298 K, $\Delta H°$ = −3.82 ± 0.24 kcal mol^{-1}, $\Delta S°$ = −7.17 ± 0.24 cal mol^{-1}), and neither MTBD nor DBU is a potent enough nucleophile to be acylated by vinyl acetate (Scheme 17).[121−124] While the alcohol activation executed by MTBD and DBU is sufficient for the ROP of LA,[100] DBU produced poly(ethylene oxide) in very poor yield;[117] neither catalyst is active for the polymerization of BL, VL, or CL at up to 20 mol % catalyst loading.[120]

Bifunctional Activation. The previous sections have highlighted the selective activation of monomer *or* initiator, but the dual implementation of an electrophile and nucleophile should allow for the simultaneous activation of both; the attenuation of the strength of each interaction required to effect the transformation can lead to higher selectivities. Catalytic reactions using weak electrophilic interactions (hydrogen bonding) to activate the substrate have been demonstrated for small molecule transformations;[21,125] this motif is also a powerful strategy for ring-opening polymerization. For lactones, bifunctional activation of the monomer by an electrophile and the initiator by a nucleophile has been shown to facilitate the ROP of esters. Both unimolecular and bimolecular catalysts have been employed.

Thiourea/Amines. A variety of ureas and thioureas activate carbonyl substrates[7,21] in a fashion similar to the hydrogen-bonding motifs in enzyme active sites.[7,21,125−130] One particular example combined the hydrogen-bonding capabilities of a thiourea (TU) H-bond donor and an amine base in a discrete catalyst, **1** (Figure 1).[127−131] In the ROP of LA, the thiourea **1** produced PLA of narrow PDI (< 1.08) whose M_n is dictated by the monomer-to-initiator ratio and evolves linearly with time (TOF $\sim$ 0.8 h^{-1}). The thiourea and amine need not be linked; a combination of the thiourea **1a** and the tertiary amine **1b** was also active.[132] Catalytic activity was modulated by changing the architecture of the thiourea; **1a** was the most effective of the thioureas tested,[121] but amido-indoles can also be used.[133]

Catalytic activity was significantly augmented when stronger bases are substituted for **1b**. Whereas DBU and MTBD alone or any TU-tertiary amine combination are only active for the ROP of LA, TU/MTBD and TU/DBU were shown to be active for the ROP of VL, CL, trimethylene carbonate (TMC) and 2-methyltrimethylene carbonate (MTC).[99,120,134] The combination of MTBD or DBU and **1a** (5 mol % each) produced PVL with predictable molecular weights up to DP $\sim$ 200 (TOF$_{MTBD/1a} \sim$ TOF$_{DBU/1a} \sim$ 5 h^{-1}). However, MTBD/TU and DBU/TU required days (TOFs $\sim$ 0.13 h^{-1}) to reach 80% conversion in the ROP of CL.[120] The DBU/TU system demonstrated a higher TOF for the ring-opening polymerization of the cyclic carbonates MTC-OR (Figure 2, TOF$_{MTC-OBn} \sim$ 19 h^{-1}) than for TMC.[99] The proposed bifunctional mechanism of action (Scheme 19) was

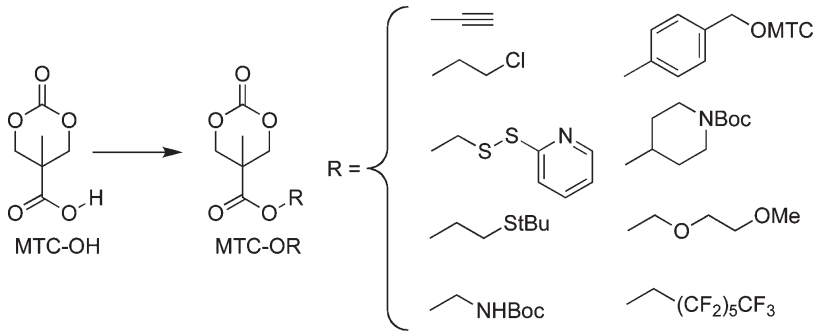
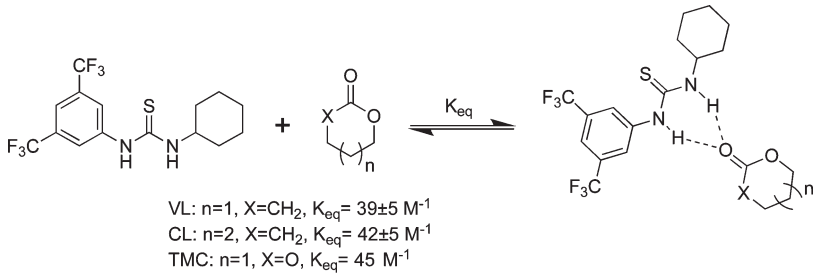
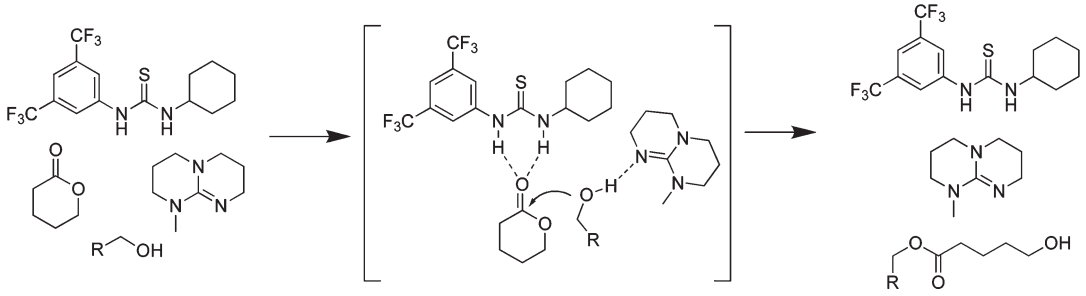


Figure 2. A selection of the MTC-OR monomers accessible from MTC-OH.

Scheme 18. Binding Constants of 1a with Selected Monomers



Scheme 19. ROP of VL by the Dual Activation of Monomer and Initiator by 1a and MTBD



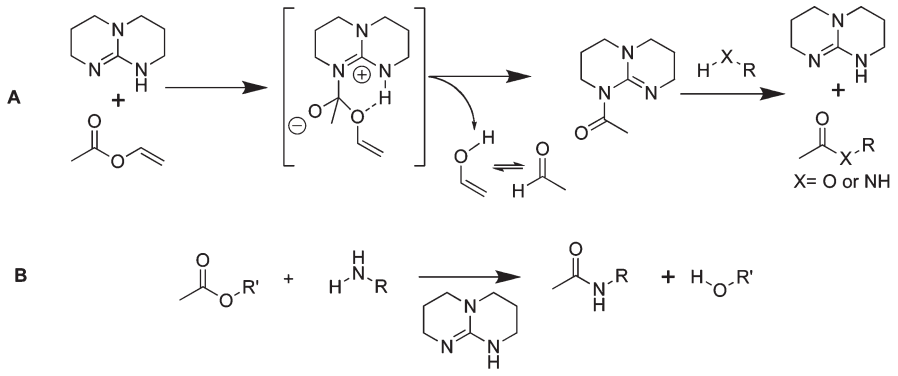
supported by observed interactions between benzyl alcohol and MTBD (Scheme 17) and between **1a** and various monomers (Scheme 18).[120,121,132]

While the activities of the TU/amine (TU/A) catalysts are lower than that of the carbenes, these catalysts are remarkably tolerant and selective, leading to polymers of very narrow polydispersities. Transesterification of the polymer chain was shown to be minimal; when fully converted reaction solutions were allowed to sit for days in the presence of the catalyst, the polydispersities did not increase.[120,121,132] The origin of this high selectivity was investigated by NMR experiments measuring the binding constants of lactones and esters with the thioureas. Cyclic lactones and cyclic carbonates bind to the thiourea **1a** (Scheme 18). In contrast, the open chain ester ethyl acetate exhibited no measurable binding affinity for **1a** under similar conditions.[120] The higher H-bond basicity of *s-cis* esters of lactones/cyclic carbonates[135] relative to that of the acyclic *s-trans* esters of the polymer chain is the likely origin of this high selectivity for ring-opening relative to transesterification of the chain. This high selectivity is a defining attribute of the TU/A organic catalysts. The selectivity of these catalysts, coupled with their broad substrate tolerance, has created new opportunities for generating highly functionalized polymers with well-defined molecular weights (*vide infra*).

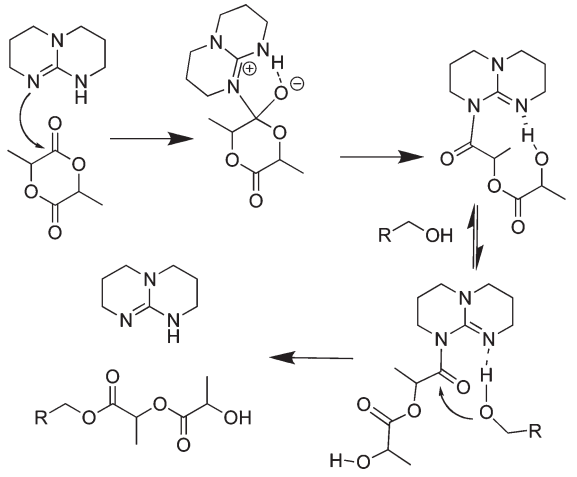
1,5,7-Triazabicyclododecene (TBD). The bicyclic guanidine TBD has a slightly higher basicity (pK_a $TBDH^+$ = 26.0)[115] than its substituted analogue MTBD (Figure 1 and Scheme 17), but its activity in ring-opening polymerization reactions is considerably higher. The ROP of lactide requires ~30 min in the presence of 0.5 mol % MTBD (an average turnover frequency of TOF ~0.002 s^{-1}), whereas TBD is much more active. At 0.1 mol % TBD, the ROP of lactide is complete in 1 min (TOF ~81 s^{-1}).[120] Similarly, the ring-opening polymerization of the cyclic carbonate TMC (Figure 2) requires 6 days (TOF < 0.1 h^{-1}) for MTBD, but in the presence of TBD complete conversion is achieved in 15 min (TOF ~ 0.1 s^{-1}).[134] This commercially available catalyst has been shown to be active in the ROP of LA, VL, CL, MTC, TMC, and carbosiloxanes with rates that exceed any other organocatalyst or, in some cases, any other *catalyst* known. For all monomers tested, TBD exhibited characteristics of a living polymerization, but its higher transesterification activity results in the broadening of the molecular weight distribution upon full conversion for all monomers except carbosiloxanes.[99,119,120,134] This is in marked contrast to the NHC-catalyzed ROP of carbosiloxanes that, while faster, broaden the PDI by transetherification. The methylated analogue, MTBD, was inactive in the ROP of carbosiloxanes.[100]

The much higher reactivity of TBD relative to DBU and MTBD stimulated mechanistic and theoretical studies to illuminate the origin of the higher rates. Treatment of TBD with vinyl acetate led to the rapid formation of acyl-TBD

Scheme 20. TBD-Catalyzed Acyl-Transfer Reaction for Alcohols and Amines



Scheme 21. Nucleophilic Mechanism for the TBD-Catalyzed ROP of LA



which subsequently reacted with benzyl alcohol to regenerate TBD and the ester (Scheme 20A).[119] This led to the proposal that TBD might function as a bifunctional nucleophilic catalyst for transesterification (Scheme 21). A nucleophilic mechanism was also proposed for the TBD-catalyzed formation of amides from esters (Scheme 20B);[136] kinetic studies provide strong support for a nucleophilic mechanism involving an acyl-TBD intermediate.[137]

Theoretical studies[55,56] implied that while a nucleophilic mechanism for TBD-catalyzed ring-opening polymerization is feasible, a H-bonding mechanism (Scheme 22) exhibited a lower calculated barrier for transesterification. Binding of the alcohol to TBD[100] simultaneously activates the alcohol and creates an incipient guanidinium ion, which can function as a H-bond donor to the lactone carbonyl (analogous to a thiourea). The unique structural and electronic features of TBD enable it to catalyze transacylation reactions by a variety of mechanisms[137] with high rates and selectivities. Because TBD is commercially available, it is also operationally quite simple and convenient.

Chemoselectivity and Substrate Tolerance. While achieving fast rates and high turnover numbers is highly desirable, the selectivity and tolerance of the catalyst to other functional groups are also important. For example, DMAP catalysts are effective for the ring-opening of lactones[75,76] or *O*-carboxyanhydrides[73−76] functionalized with pendant esters. The TU/A catalyst systems are particularly chemoselective and tolerant to a wide variety of functionalized monomers.

The high selectivity of the TU/A catalysts for transesterification of cyclic lactones and carbonates relative to open-chain *s-cis* esters has created new opportunities for generating highly functionalized polylactones and polycarbonates with a diverse range of functionalities. For example, a wide range of functionalized carbonates (MTC-OR) can be prepared from 2,2-bis(methylol)propionic acid (bis-MPA);[99,138,139] these functionalized carbonates are readily polymerized or copolymerized in the presence of the TU/A catalysts to generate a family of functionalized carbonates with a range of pendant functional groups (Figure 2).[99]

The ring-opening polymerization can be initiated from a wide variety of functional groups including alcohols, thiols, primary amines, and silanols.[99,121,134] These highly controlled polymerizations led to a new synthesis of well-defined guanidinylated oligocarbonates that were shown to act as molecular transporters[140] that traverse cell membranes (Scheme 23).[141]

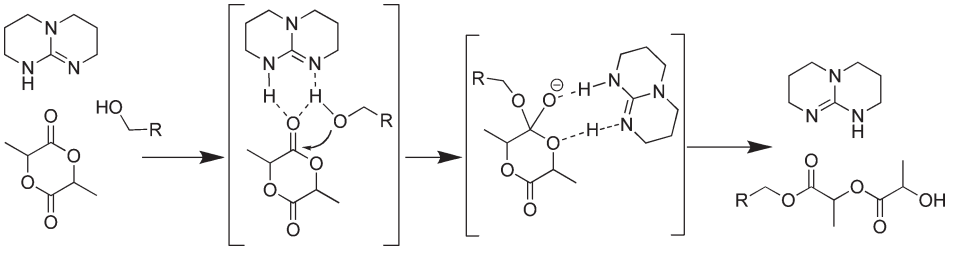
The high chemoselectivity of the TU/A catalysts also creates additional opportunities for tandem polymerizations from multifunctional initiators. Hydroxy-functionalized nitroxides or dithioesters can be used as initiators for tandem free-radical and ring-opening polymerization reactions (Scheme 24).[134] This is one strategy for the synthesis of complex, multifunctional polymer architectures that is enabled by the high functional group tolerance of the TU catalysts.

Architectural Control. The mechanistic diversity of organocatalytic polymerization reactions has created new opportunities and strategies to control the architecture of macromolecules. The zwitterionic polymerization with NHC's to make cyclic polymers (Scheme 10)[108,109,142] and the step-growth benzoin condensations (Scheme 12)[105] are two examples; below we highlight several other examples where the selectivity of organic catalysts has provided new strategies for macromolecular design.

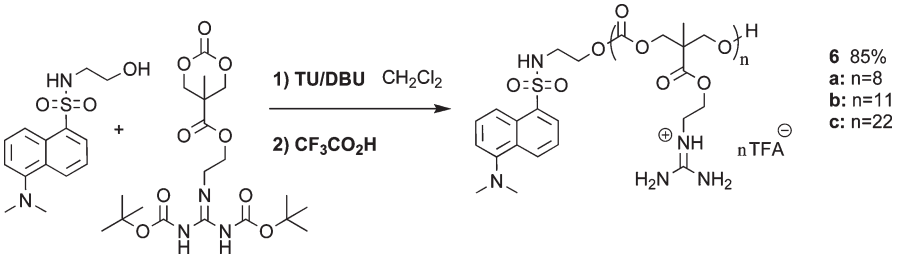
Stereoselectivity is critically important in fine-chemical synthesis; it is also very important in polymerization catalysis as the relative stereochemistry of stereogenic centers along the chain influences the physical properties of the polymer.[143,144] The stereoselective polymerization of the chiral monomer lactide has attracted considerable interest and can be carried out with a variety of metal catalysts.[143,145−150]

Several organic catalysts have been shown to influence the stereoselectivity of enchainment of lactide. The sterically encumbered carbene, Ph_2IMes, is very active for the ROP of LA at room temperature (1.58 s^{-1}), producing atactic poly(LA) from *rac*-LA; however, when the temperature is lowered (−40 to −70 °C), highly isotactic (from *rac*-LA) and heterotactic (from *meso*-LA) polylactides are generated.[151] Similar stereoselectivities were observed with sterically demanding phosphazenes.[116,121,152] The stereoselectivity of these polymerization catalysts was proposed to be due to a

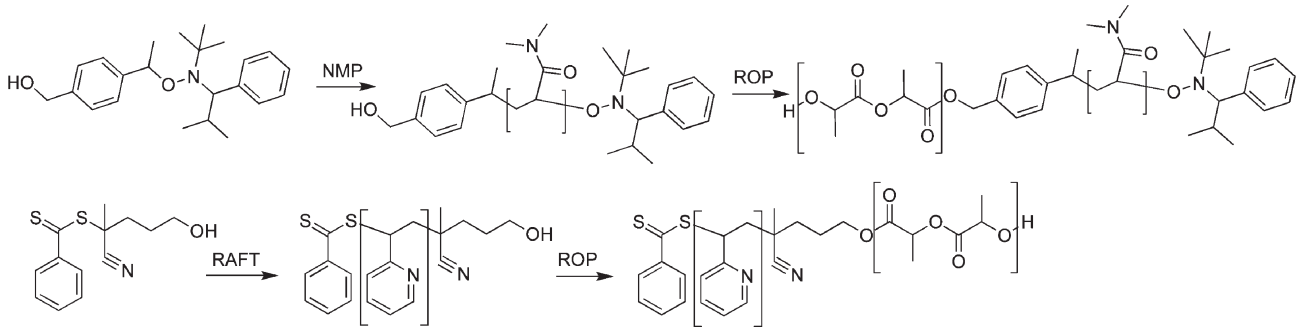
Scheme 22. TBD-Catalyzed ROP of LA by the Hydrogen-Bonding Mechanism



Scheme 23. Synthesis of Guanidinylated Oligocarbonate Molecular Transporters



Scheme 24. Use of Dual-Function Initiators To Generate (Upper) Poly(*N*,*N*-dimethylacrylamide)-*block*-PLA by Tandem NMP-ROP and (Lower) Poly(vinylpyridine)-*block*-PLA by Tandem RAFT-ROP



chain-end control mechanism whereby the growing chain selectively attacks the activated monomer of the same stereochemistry leading to isotactic enchainment.

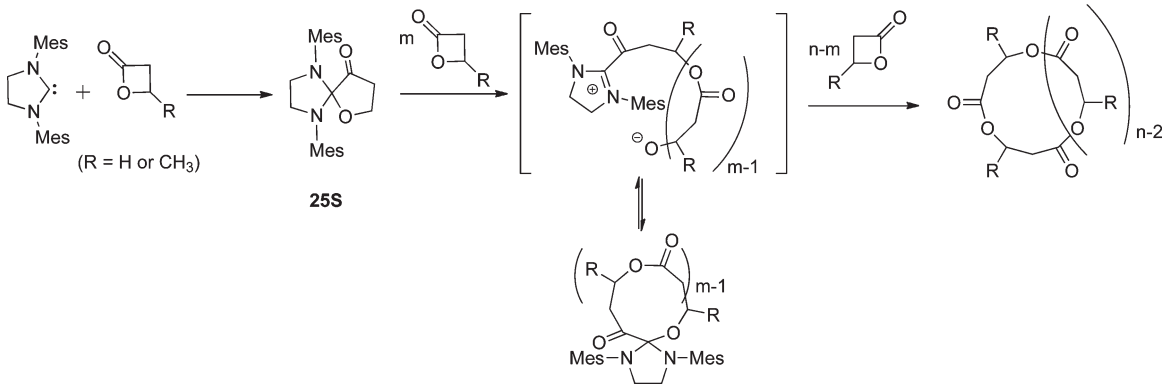
In addition to the stereochemistry, the comonomer sequence is also an important determinant for polymer properties. Because of their different mechanisms of enchainment, organic catalysts exhibit a different chemoselectivity for copolymerization than typical metal alkoxide catalysts.[153−159] The catalysts MTBD/TU, DBU/TU, and TBD all show a selectivity for monomer wherein the fastest propagating monomer ($k_{LA} \gg k_{VL} > k_{CL}$) is ring-opened to >95% conversion before ring-opening of the second monomer begins.[120] While extensive studies on the copolymerization selectivity have not been done, these selectivities imply that block copolymers might be accessible in one step. In the case of the cyclic carbonates MTC-OR, more random copolymers were observed. Accordingly, block and random MTC-OR copolymers could be generated simply by varying reaction conditions.[99,160]

Unsaturated carbenes such as IMes generate cyclic polyesters or polyamides in the zwitterionic ring-opening of lactide[108] or *N*-carboxyanhydrides.[142] The saturated carbene SIMes (Figure 1) also generates cyclic polyesters from β-lactones,[109] but subtle differences in the reactivity between the unsaturated and saturated carbenes[81] lead to different mechanisms. Treatment of the saturated carbene SIMes with 1 equiv of β-butyrolactone generates the novel spirocycle **25S**. This spirocycle initiates the ring-opening polymerization of β-lactones to yield cyclic polyesters.[109] A novel mechanism involving reversible collapse of the zwitterionic intermediate to a neutral imidazolidine spirocycle was proposed (Scheme 25).[109,142] The polymerization is highly selective due to the generation of small amount of zwitterionic intermediate by the reversible formation of the spiromacrocycles.

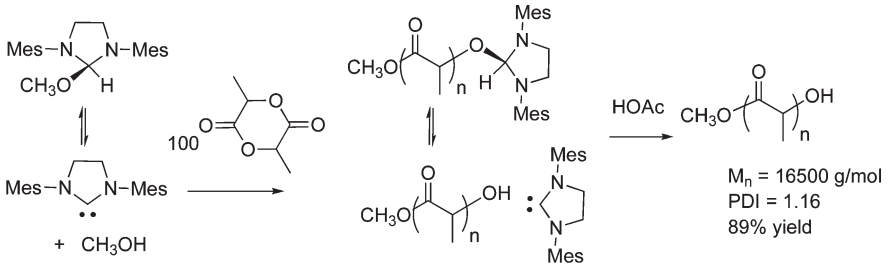
Organic catalysts can also be used to generate telechelic poly(valerolactone) or poly(THF) that could be cyclized into large cyclic polymers.[161,162] These new strategies for generating macromolecules with a cyclic topology offer new opportunities for generating these architectures.[163]

Alkyl[164] and alcohol[165] adducts of saturated N-heterocyclic carbenes have been used in the ROP of LA as a convenient method for generating the NHC catalyst *in situ*. Chloroform and pentafluorobenzene adducts of saturated imidazolinylidene are stable at room temperature but eliminate the carbene at elevated temperature.[164,166] These NHCs polymerize LA in the presence of an alcohol initiator at elevated temperatures (65−144 °C). In contrast, alcohol adducts of the saturated carbene SIMes eliminate the alcohol reversibly at room temperature.[165] In these adducts, the alcohol initiator is liberated with the carbene; thus, the adducts of SIMes act as single-component catalyst/initiators for the ROP of LA (Scheme 26). The liberation of the alcohol is rapid in solution at room temperature and PLA is obtained within minutes in high yield with narrow polydispersity.

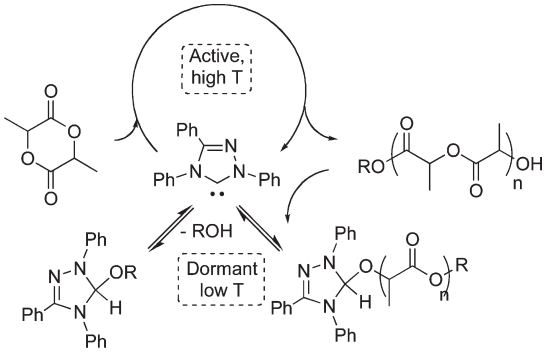
Scheme 25. ROP of β-Lactones Using SIMes



Scheme 26. Reversible Activation and Deactivation of SIMes



Scheme 27. Reversible Activation of Triazolylidene Carbenes



In contrast to the alcohol adducts of the saturated imidazolinylidene carbenes, alcohol adducts of Enders' triazol-5-ylidene are stable at room temperature and reversibly eliminate the alcohol only at 90 °C.[167,168] At room temperature in the presence of alcohols, the triazolylidenes are inactive; at 90 °C they polymerize lactide to give polymers of narrow polydispersities. This provides a means of regulating the polymerization with temperature: at elevated temperature, polymerization proceeds; at lower temperature the alcohol "clicks"[169] back onto the alcohol terminus of the polymer to give the dormant alcohol adduct (Scheme 27).[168,170] The reversible formation of the active and dormant carbene species is the key factor that contributes to the exceptional control observed in these polymerizations.

The triazol-5-ylidene is also tolerant to a variety of initiators and, in conjunction with telechelic macroinitiators, has been used to produce complex architectures such as block copolymers, star copolymers,[168] and (super-) H-shaped copolymers.[171]

Outlook and Summary

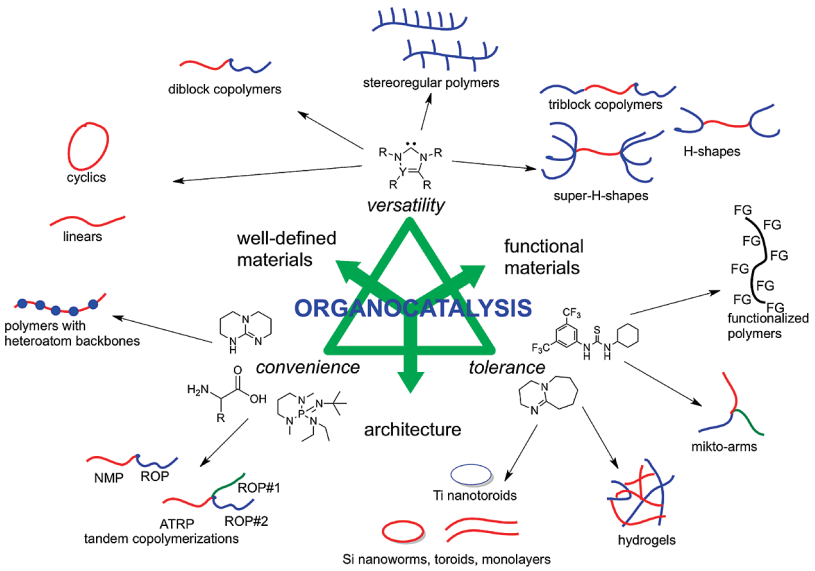
The activity, selectivity, convenience, and diverse reactivity of organic catalysts have expanded the armamentarium of synthetic methods for polymer synthesis. Organic catalysts have proven of broad utility for the generation of an ever-increasing array of polymer architectures that have interesting properties in their own right or can be programmed to assemble into larger nanostructures of defined size, shape, and function (Scheme 28).[24,60,98,121,160,172−174]

The application of organocatalysts to polymer synthesis has provided new mechanistic insights, new strategies for enchaining monomers, and new families of materials with a range of structure and function that continues to evolve. In the past decade, the development of new families of organic catalysts has led to impressive advances in the catalytic rates (DMAP to TBD) and selectivities (acids to TU/base). Some organocatalysts exhibit rates that compare or exceed those of organometallic catalysts.[175]

The development of new families of metal catalysts[51] and enzymes[176] for ring-opening polymerization continues apace;[47,50,60] recent advances in metallic, enzymatic, and organic catalysts have highlighted the important role of catalyst development for advancing our ability to generate well-defined macromolecules with specific structure and function.[177] In this Perspective, we have attempted to highlight where investigations of organic catalysts have provided mechanistic insights and strategies for activating monomers and chain-ends to generate new opportunities for macromolecular design. Organic catalysts in many cases are complementary to metal or enzyme catalysts; choosing between a particular catalyst will depend on a variety of factors relevant to the specific challenge at hand. The use of organic catalysts can provide advantages in microelectronic[178−181] or biomedical applications where the presence of metal residues in the final material can be deleterious to their end use.[50,141,160,174,182] An additional advantage of organic species that activate monomers or chain ends catalytically is that they can be used in concentrations lower than that of the polymer chains, further minimizing the amount of catalyst residues in the final material.[50,183]

The wide substrate tolerance and exquisite selectivity of the thiourea organic catalysts[120,121,132] for ring-opening versus transesterification of open chain esters provides a new strategy for

Scheme 28. Organocatalysts Possess the Triad of Versatility, Convenience, and Functional Group Tolerance and Yield Well-Defined Polymers of Precise Architecture Structures for a Specific Function



precision polymer synthesis. The reversible capping of end groups with triazolylidene carbenes[168,170,171] and the zwitterionic polymerization to generate cyclic polymers[108,109,142] are just a few examples of new strategies to complex molecular architectures and topologies.

While the foregoing discussion highlights some of the advantages of organocatalytic approaches, challenges remain. Melt polymerizations are industrially attractive and compliant with the tenets of green chemistry.[184,185] However, organocatalysts have not been widely investigated in melt polymerizations, and this remains an attractive target for future research. Chiral phosphines have been used to great success in small molecule reactions,[186] but chiral phosphines for stereoselective polymerization is an area still to be explored. The trifunctional catalyst for ROP may be just around the corner. A trifunctional organocatalyst modeled on serine hydrolases combines electrophilic activation, nucleophilic activation, and a nucleophile in a discrete catalyst and exhibits a million-fold enhancement in acyl-transfer rate from vinyl trifluoroacetate to alcohols.[187] A polymerization strategy can be envisaged. This system extends concepts in multifunctional activation by precise arrays of functional groups that mimics the behavior of many enzymatic processes. New catalyst families that combine the attributes of organic and metal catalysis[146] or that employ new combinations of activation mechanisms (or a new mechanism entirely) will create new opportunities for polymer synthesis. Many cues are evident from nature; the extraordinary rates, selectivities, and exquisite multicomponent catalytic cascades of natural catalysts inspire emulation. The convergence of convenience, functional group tolerance, fast rates, and selectivities will continue to drive innovations in polymerization catalysis, and it is our perspective that organocatalysis will continue to play an important role in these developments.

References and Notes

(1) Bredig, G.; Fiske, P. S. *Biochem. Z.* **1912**, *46*, 7.
(2) Langenbeck, W. *Die Organische Katalysatoren und ihre Beziehungen zu den Fermenten*, 2nd ed.; Springer: Berlin, 1949.
(3) Detar, D. F.; Westheimer, F. H. *J. Am. Chem. Soc.* **1959**, *81*, 175–178.
(4) Hamilton, G. A.; Westheimer, F. H. *J. Am. Chem. Soc.* **1959**, *81*, 6332–6333.
(5) Westheimer, F. H. *Tetrahedron* **1995**, *51*, 3–20.
(6) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719–3726.
(7) Zhang, Z. G.; Schreiner, P. R. *Chem. Soc. Rev.* **2009**, *38*, 1187–1198.
(8) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615.
(9) Eder, U.; Sauer, G.; Weichert, R. *Angew. Chem., Int. Ed.* **1971**, *10*, 496.
(10) Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243–4244.
(11) Jen, W. S.; Wiener, J. J. M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 9874–9875.
(12) Notz, W.; Tanaka, F.; Barbas, C. F. *Acc. Chem. Res.* **2004**, *37*, 580–591.
(13) Hanessian, S.; Auzzas, L. *Acc. Chem. Res.* **2008**, *41*, 1241–1251.
(14) Erkkila, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416–5470.
(15) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471–5569.
(16) Wurz, R. P. *Chem. Rev.* **2007**, *107*, 5570–5595.
(17) Gaunt, M. J.; Johansson, C. C. C. *Chem. Rev.* **2007**, *107*, 5596–5605.
(18) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655.
(19) Hashimoto, T.; Maruoka, K. *Chem. Rev.* **2007**, *107*, 5656–5682.
(20) Atodiresei, I.; Schiffers, I.; Bolm, C. *Chem. Rev.* **2007**, *107*, 5683–5712.
(21) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713–5743.
(22) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744–5758.
(23) Davie, E. A. C.; Mennen, S. M.; Xu, Y.; Miller, S. J. *Chem. Rev.* **2007**, *107*, 5759–5812.
(24) Kamber, N. E.; Jeong, W.; Waymouth, R. M.; Pratt, R. C.; Lohmeijer, B. G. G.; Hedrick, J. L. *Chem. Rev.* **2007**, *107*, 5813–5840.
(25) McGarrigle, E. M.; Myers, E. L.; Illa, O.; Shaw, M. A.; Riches, S. L.; Aggarwal, V. K. *Chem. Rev.* **2007**, *107*, 5841–5883.
(26) List, B. *Chem. Rev.* **2007**, *107*, 5413–5415.
(27) Berkessel, A.; Gröger, H. *Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*; Wiley-VCH: Weinheim, 2005.
(28) Barbas, C. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 42–47.
(29) Bertelsen, S.; Jorgensen, K. A. *Chem. Soc. Rev.* **2009**, *38*, 2178–2189.
(30) MacMillan, D. W. C. *Nature* **2008**, *455*, 304–308.
(31) Flory, P. J. *J. Am. Chem. Soc.* **1940**, *62*, 2261–2264.
(32) Odian, G. *Principles of Polymerization*, 4th ed.; Wiley-Interscience: Hoboken, NJ, 2004.
(33) Ober, C. K.; Cheng, S. Z. D.; Hammond, P. T.; Muthukumar, M.; Reichmanis, E.; Wooley, K. L.; Lodge, T. P. *Macromolecules* **2009**, *42*, 465–471.
(34) Penczek, S.; Duda, A.; Szymanski, R.; Biela, T. *Macromol. Symp.* **2000**, *153*, 1.
(35) Szymanski, R. *Macromol. Theory Simul.* **1998**, *7*, 27.

(36) Pepper, D. C. *Eur. Polym. J.* **1980**, *16*, 407.
(37) Gold, L. *J. Chem. Phys.* **1958**, *28*, 91.
(38) Beste, L. F.; Hall, H. K. *J. Phys. Chem.* **1964**, *68*, 269.
(39) Gibson, V. C.; Marshall, E. L. *Compr. Coord. Chem. II* **2004**, *9*, 1.
(40) Kricheldorf, H. R.; Berl, M.; Scharnagl, N. *Macromolecules* **1988**, *21*, 286.
(41) Degee, P.; Dubois, P.; Jerome, R.; Jacobsen, S.; Fritz, H.-G. *Macromol. Symp.* **1999**, *144*, 289.
(42) O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *J. Chem. Soc., Dalton Trans.* **2001**, 2215.
(43) Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. *Chem. Rev.* **2004**, *104*, 6147–6176.
(44) Albertsson, A. C.; Varma, I. K. *Biomacromolecules* **2003**, *4*, 1466–1486.
(45) Kowalski, A.; Libiszowski, J.; Majerska, K.; Duda, A.; Penczek, S. *Polymer* **2007**, *48*, 3952–3960.
(46) Penczek, S.; Cypryk, M.; Duda, A.; Kubisa, P.; Slomkowski, S. *Prog. Polym. Sci.* **2007**, *32*, 247–282.
(47) Dove, A. P. *Chem. Commun.* **2008**, 6446–6470.
(48) Drumright, R. E.; Gruber, P. R.; Henton, D. E. *Adv. Mater.* **2000**, *12*, 1841–1846.
(49) Hedrick, J. L.; Magbitang, T.; Connor, E. F.; Glauser, T.; Volksen, W.; Hawker, C. J.; Lee, V. Y.; Miller, R. D. *Chem.—Eur. J.* **2002**, *8*, 3308.
(50) Platel, R. H.; Hodgson, L. M.; Williams, C. K. *Polym. Rev.* **2008**, *48*, 11–63.
(51) Kricheldorf, H. R. *Chem. Rev.* **2009**, *109*, 5579–5594.
(52) Jedlinski, Z.; Walach, W.; Kurcok, P.; Adamus, G. *Makromol. Chem.* **1991**, *192*, 2051.
(53) Kricheldorf, H. R.; Boettcher, C. *Makromol. Chem.* **1993**, *194*, 1665.
(54) Kricheldorf, H. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 5752–5784.
(55) Simon, L.; Goodman, J. M. *J. Org. Chem.* **2007**, *72*, 9656–9662.
(56) Chuma, A.; Horn, H. W.; Swope, W. C.; Pratt, R. C.; Zhang, L.; Lohmeijer, B. G. G.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L.; Rice, J. E. *J. Am. Chem. Soc.* **2008**, *130*, 6749–6754.
(57) Lai, C.-L.; Lee, H. M.; Hu, C.-H. *Tetrahedron Lett.* **2005**, *46*, 6265–6270.
(58) Kricheldorf, H. R.; Dunsing, R. *Makromol. Chem. Phys.* **1986**, *187*, 1611–1625.
(59) Saegusa, T. *Angew. Chem., Int. Ed.* **1977**, *16*, 826–835.
(60) Bourissou, D.; Moebs-Sanchez, S.; Martin-Vaca, B. *C. R. Chim.* **2007**, *10*, 775–794.
(61) Shibasaki, Y.; Sanada, H.; Yokoi, M.; Sanda, F.; Endo, T. *Macromolecules* **2000**, *33*, 4316.
(62) Lou, X. D.; Detrembleur, C.; Jerome, R. *Macromolecules* **2002**, *35*, 1190.
(63) Liu, J. Y.; Liu, L. J. *Macromolecules* **2004**, *37*, 2674.
(64) (a) Persson, P. V.; Schroder, J.; Wickholm, K.; Hedenstrom, E.; Iversen, T. *Macromolecules* **2004**, *37*, 5889. (b) Casas, J.; Persson, P. V.; Iversen, T.; Cordova, A. *Adv. Synth. Catal.* **2004**, *346*, 1087. (c) Cordova, A.; Hafren, J. *Nordic Pulp Paper Res. J.* **2005**, *20*, 477.
(65) Bourissou, D.; Martin-Vaca, B.; Dumitrescu, A.; Graullier, M.; Lacombe, F. *Macromolecules* **2005**, *38*, 9993–9998.
(66) Murugan, R.; Scriven, E. F. V. *Aldrichim. Acta* **2003**, *36*, 21–27.
(67) Kricheldorf, H. R.; Garaleh, M.; Schwarz, G. *J. Macromol. Sci., Pure Appl. Chem.* **2005**, *42A*, 139–148.
(68) Nederberg, F.; Connor, E. F.; Glausser, T.; Hedrick, J. L. *Chem. Commun.* **2001**, 2066–2067.
(69) Nederberg, F.; Connor, E. F.; Moller, M.; Glauser, T.; Hedrick, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 2712–2715.
(70) Kricheldorf, H. R.; Lomadze, N.; Schwarz, G. *Macromolecules* **2008**, *41*, 7812–7816.
(71) Kricheldorf, H. R.; Lomadze, N.; Schwarz, G. *Macromolecules* **2007**, *40*, 4859–4864.
(72) Kricheldorf, H. R.; Von Lossow, C.; Schwarz, G. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 4680–4695.
(73) Thillaye Du Boullay, O.; Marchal, E.; Martin-Vaca, B.; Cossio, F. P.; Bourissou, D. *J. Am. Chem. Soc.* **2006**, *128*, 16442.
(74) Thillaye du Boullay, O.; Bonduelle, C.; Martin-Vaca, B.; Bourissou, D. *Chem. Commun.* **2008**, 1786–1788.
(75) Trimaille, T.; Gurny, R.; Moeller, M. *Chimia* **2005**, *59*, 348.
(76) Trimaille, T.; Moeller, M.; Gurny, R. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4379.
(77) du Boullay, O. T.; Marchal, E.; Martin-Vaca, B.; Cossio, F. P.; Bourissou, D. *J. Am. Chem. Soc.* **2006**, *128*, 16442–16443.
(78) Bonduelle, C.; Martin-Vaca, B.; Cossio, F. P.; Bourissou, D. *Chem.—Eur. J.* **2008**, *14*, 5304–5312.
(79) Johnson, R. M.; Fraser, C. L. *Biomacromolecules* **2004**, *5*, 580–588.
(80) Myers, M.; Connor, E. F.; Glauser, T.; Mock, A.; Nyce, G.; Hedrick, J. L. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 844–851.
(81) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39–91.
(82) Herrmann, W. A.; Kocher, C. *Angew. Chem., Int. Ed.* **1997**, *36*, 2163–2187.
(83) Arduengo, A. J. *Acc. Chem. Res.* **1999**, *32*, 913–921.
(84) Alder, R. W.; Allen, P. R.; Williams, S. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1267–1268.
(85) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309.
(86) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.
(87) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674–2678.
(88) Weskamp, T.; Schattenmann, W. C.; Spielger, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1998**, 37.
(89) Wanzlick, H. W. *Angew. Chem., Int. Ed.* **1962**, *1*, 75–80.
(90) Sheehan, J. C.; Hunneman, D. H. *J. Am. Chem. Soc.* **1966**, *88*, 3666–3667.
(91) Stetter, H. *Angew. Chem., Int. Ed.* **1976**, *15*, 639–647.
(92) Grasa, G. A.; Kissling, R. M.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 3583–3586.
(93) Nyce, G. W.; Lamboy, J. A.; Connor, E. F.; Waymouth, R. M.; Hedrick, J. L. *Org. Lett.* **2002**, *4*, 3587–3590.
(94) Connor, E. F.; Nyce, G. W.; Myers, M.; Mock, A.; Hedrick, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 914–915.
(95) Nyce, G. W.; Glauser, T.; Connor, E. F.; Mock, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 3046–3056.
(96) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Culkin, D. A.; Hagberg, E. C.; Nyce, G. W.; Waymouth, R. M.; Hedrick, J. L. *Polymer* **2006**, *47*, 4018.
(97) Kamber, N. E.; Jeong, W.; Gonzalez, S.; Hedrick, J. L.; Waymouth, R. M. *Macromolecules* **2009**, *42*, 1634–1639.
(98) Nederberg, F.; Trang, V.; Pratt, R. C.; Mason, A. F.; Frank, C. W.; Waymouth, R. M.; Hedrick, J. L. *Biomacromolecules* **2007**, *8*, 3294–3297.
(99) Pratt, R.; Nederberg, F.; Waymouth, R. M.; Hedrick, J. L. *Chem. Commun.* **2008**, 114–116.
(100) Lohmeijer, B. G.; Dubois, G.; Leibfarth, F.; Pratt, R. C.; Nederberg, F.; Nelson, A.; Waymouth, R. M.; Wade, C.; Hedrick, J. L. *Org. Lett.* **2006**, *8*, 4683.
(101) Rodriguez, M.; Marrot, S.; Kato, T.; Sterin, S.; Fleury, E.; Baceiredo, A. *J. Organomet. Chem.* **2007**, *692*, 705–708.
(102) Scholten, M. D.; Hedrick, J. L.; Waymouth, R. M. *Macromolecules* **2008**, *41*, 7399–7404.
(103) Raynaud, J.; Ciolino, A.; Baceiredo, A.; Destarac, M.; Bonnette, F.; Kato, T.; Gnanou, Y.; Taton, D. *Angew. Chem., Int. Ed.* **2008**, *47*, 5390–5393.
(104) Raynaud, J.; Gnanou, Y.; Taton, D. *Macromolecules* **2009**, *42*, 5996–6005.
(105) Pinaud, J.; Vijayakrishna, K.; Taton, D.; Gnanou, Y. *Macromolecules* **2009**, *42*, 4932–4936.
(106) Raynaud, J.; Absalon, C.; Gnanou, Y.; Taton, D. *J. Am. Chem. Soc.* **2009**, *131*, 3201–3209.
(107) Movassaghi, M.; Schmidt, M. A. *Org. Lett.* **2005**, *7*, 2453–2456.
(108) (a) Culkin, D. A.; Jeong, W.; Csihony, S.; Gomez, E. D.; Balsara, N. P.; Hedrick, J. L.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 2627–2630. (b) Jeong, W.; Shin, E. J.; Culkin, D. A.; Hedrick, J. L.; Waymouth, R. M. *J. Am. Chem. Soc.* **2009**, *131*, 4884–4891.
(109) Jeong, W.; Hedrick, J. L.; Waymouth, R. M. *J. Am. Chem. Soc.* **2007**, *129*, 8414–8415.
(110) Feng, H.; Dong, C. M. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5353–5361.
(111) Hedrick, J. L.; Nyce, G. W.; Waymouth, R. M. U.S. Patent 7,053,221 B2, **2006**.
(112) Webster, O. W. *Adv. Polym. Sci.* **2004**, *167*, 1–34.
(113) Schwesinger, R.; Schlemper, H. *Angew. Chem., Int. Ed.* **1987**, *26*, 1167.
(114) Molenberg, A.; Moller, M. *Macromol. Rapid Commun.* **1995**, *16*, 449.
(115) Kaljurand, I.; Kutt, A.; Soovali, L.; Rodima, T.; Maemets, V.; Leito, I.; Koppel, I. A. *J. Org. Chem.* **2005**, *70*, 1019–1028.
(116) Zhang, L.; Nederberg, F.; Pratt, R. C.; Waymouth, R. M.; Hedrick, J. L.; Wade, C. G. *Macromolecules* **2007**, *40*, 4154–4158.

(117) Schlaad, H.; Kukula, H.; Rudloff, J.; Below, I. *Macromolecules* **2001**, *34*, 4302–4304.
(118) Rexin, O.; Mulhaupt, R. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 864.
(119) Pratt, R. C.; Lohmeijer, B. G.; Long, D. A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 4556–4557.
(120) Lohmeijer, B. G. G.; Pratt, R. C.; Leibfarth, F.; Logan, J. W.; Long, D. A.; Dove, A. P.; Nederberg, F.; Choi, J.; Wade, C.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 8574–8583.
(121) Pratt, R. C.; Lohmeijer, B. G. G.; Long, D. A.; Lundberg, P. N. P.; Dove, A. P.; Li, H.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 7863–7871.
(122) Bensa, D.; Rodriguez, J. *Synth. Commun.* **2004**, *34*, 1515.
(123) Schuchardt, U.; Vargas, R. M.; Gelbard, G. J. *J. Mol. Catal. A: Chem.* **1995**, *99*, 65–70.
(124) Heldebrant, D. J.; Jessop, P. G.; Thomas, C. A.; Eckert, C. A.; Liotta, C. L. *J. Org. Chem.* **2005**, *70*, 5335–5338.
(125) Schreiner, P. R. *Chem. Soc. Rev.* **2003**, *32*, 289–296.
(126) Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901–4902.
(127) Hoashi, Y.; Okino, T.; Takemoto, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 4032.
(128) Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12672.
(129) Okino, T.; Nakamura, S.; Furukawa, T.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 625.
(130) Berkessel, A.; Cleemann, F.; Mukherjee, S.; Muller, T. N.; Lex, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 807–811.
(131) Zhu, R. X.; Wang, R. X.; Zhang, D. J.; Liu, C. B. *Aust. J. Chem.* **2009**, *62*, 157–164.
(132) Dove, A. P.; Pratt, R. C.; Lohmeijer, B. G. G.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 13798.
(133) Koeller, S.; Kadota, J.; Deffieux, A.; Peruch, F.; Massip, S.; Leger, J. M.; Desvergne, J. P.; Bibal, B. *J. Am. Chem. Soc.* **2009**, *131*, 15088.
(134) Nederberg, F.; Lohmeijer, B. G. G.; Leibfarth, F.; Pratt, R. C.; Choi, J.; Dove, A. P.; Waymouth, R. M.; Hedrick, J. L. *Biomacromolecules* **2007**, *8*, 153.
(135) Laurence, C.; Brameld, K. A.; Graton, J.; Le Questel, J. Y.; Renault, E. *J. Med. Chem.* **2009**, *52*, 4073–4086.
(136) Sabot, C.; Kumar, K. A.; Meunier, S.; Mioskowski, C. *Tetrahedron Lett.* **2007**, *48*, 3863–3866.
(137) Kiesewetter, M. K.; Scholten, M. D.; Kirn, N.; Weber, R. L.; Hedrick, J. L.; Waymouth, R. M. *J. Org. Chem.* **2009**, *74*, 9490–9496.
(138) Al-Azemi, T. F.; Bisht, K. S. *Macromolecules* **1999**, *32*, 6536–6540.
(139) Al-Azemi, T. F.; Harmon, J. P.; Bisht, K. S. *Biomacromolecules* **2000**, *1*, 493–500.
(140) Wender, P. A.; Galliher, W. C.; Goun, E. A.; Jones, L. R.; Pillow, T. H. *Adv. Drug Delivery Rev.* **2008**, *60*, 452–472.
(141) Cooley, C. B.; Trantow, B. M.; Nederberg, F.; Kiesewetter, M. K.; Hedrick, J. L.; Waymouth, R. M.; Wender, P. A. *J. Am. Chem. Soc.* **2009**, *131*, 16401–16403.
(142) Guo, L.; Zhang, D. *J. Am. Chem. Soc.* **2009**, *131*, 18072.
(143) Coates, G. W. *Dalton* **2002**, 467–475.
(144) Brintzinger, H. H.; Fischer, D.; Mulhaupt, R.; Rieger, B.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **1995**, *34*, 1143–1170.
(145) Chamberlain, B. M.; Cheng, M.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 3229–3238.
(146) Jensen, T. R.; Breyfogle, L. E.; Hillmyer, M. A.; Tolman, W. B. *Chem. Commun.* **2004**, 2504.
(147) Thakur, K. A. M.; Kean, R. T.; Zell, M. T.; Padden, B. E.; Munson, E. J. *Chem. Commun.* **1998**, 1913–1914.
(148) Zell, M. T.; Padden, B. E.; Paterick, A. J.; Hillmyer, M. A.; Kean, R. T.; Thakur, K. A. M.; Munson, E. J. *J. Am. Chem. Soc.* **1998**, *120*, 12672–12673.
(149) Chisholm, M. H.; Patmore, N. J.; Zhou, Z. P. *Chem. Commun.* **2005**, 127–129.
(150) Chisholm, M. H.; Iyer, S. S.; McCollum, D. G.; Pagel, M.; Werner-Zwanziger, U. *Macromolecules* **1999**, *32*, 963–973.
(151) Dove, A. P.; Li, H.; Pratt, R. C.; Lohmeijer, B. G.; Culkin, D. A.; Waymouth, R. M.; Hedrick, J. L. *Chem. Commun.* **2006**, 2881.
(152) Zhang, L.; Nederberg, F.; Messman, J. M.; Pratt, R. C.; Hedrick, J. L.; Wade, C. G. *J. Am. Chem. Soc.* **2007**, *129*, 12610–12611.
(153) Bero, M.; Kasperczyk, J. *Macromol. Chem. Phys.* **1996**, *197*, 3251–3258.
(154) Parrish, B.; Quansah, J. K.; Emrick, T. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 1983–1990.
(155) Stassin, F.; Jerome, R. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 2777–2789.
(156) Wahlberg, J.; Persson, P. V.; Olsson, T.; Hedenstrom, E.; Iversen, T. *Biomacromolecules* **2003**, *4*, 1068–1071.
(157) Kurcok, P.; Penczek, J.; Franek, J.; Jedlinski, Z. *Macromolecules* **2002**, *25*, 2285–2289.
(158) Mosnacek, J.; Duda, A.; Libiszowski, J.; Penczek, S. *Macromolecules* **2005**, *38*, 2027–2029.
(159) Kricheldorf, H. R.; Bornhorst, K.; Hachmann-Thiessen, H. *Macromolecules* **2005**, *38*, 5017–5024.
(160) Fukushima, K.; Pratt, R. C.; Nederberg, F.; Tan, J. P. K.; Yang, Y. Y.; Waymouth, R. M.; Hedrick, J. L. *Biomacromolecules* **2008**, *9*, 3051–3056.
(161) Misaka, H.; Kakuchi, R.; Zhang, C.; Sakai, R.; Satoh, T.; Kakuchi, T. *Macromolecules* **2009**, *42*, 5091–5096.
(162) Tezuka, Y.; Ohtsuka, T.; Adachi, K.; Komiya, R.; Ohno, N.; Okui, N. *Macromol. Rapid Commun.* **2008**, *29*, 1237–1241.
(163) Semlyen, J. A. In *Cyclic Polymers*, 2nd ed.; Semlyen, J. A., Ed.; Kluwer: Dordrecht, 2000; p 790.
(164) Nyce, G. W.; Csihony, S.; Waymouth, R. M.; Hedrick, J. L. *Chem.—Eur. J.* **2004**, *10*, 4073.
(165) Csihony, S.; Culkin, D. A.; Sentman, A. C.; Dove, A. P.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 9079–9084.
(166) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T. L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546–2558.
(167) Enders, D.; Breuer, K.; Raabe, G.; Runsink, J.; Teles, J. H.; Melder, J. P.; Ebel, K.; Brode, S. *Angew. Chem., Int. Ed.* **1995**, *34*, 1021.
(168) Coulembier, O.; Dove, A. P.; Pratt, R. C.; Sentman, A. C.; Culkin, D. A.; Mespouille, L.; Dubois, P.; Waymouth, R. M.; Hedrick, J. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4964–4968.
(169) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021.
(170) Coulembier, O.; Lohmeijer, B. G. G.; Dove, A. P.; Pratt, R. C.; Mespouille, L.; Culkin, D. A.; Benight, S. J.; Dubois, P.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 5617–5628.
(171) Coulembier, O.; Kiesewetter, M. K.; Mason, A.; Dubois, P.; Hedrick, J. L.; Waymouth, R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 4719–4721.
(172) Kim, S. H.; Tan, J. P. K.; Nederberg, F.; Fukushima, K.; Yang, Y. Y.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2008**, *42*, 25–29.
(173) Kim, S. H.; Nederberg, F.; Zhang, L.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L. *Nano Lett.* **2007**, *8*, 294–301.
(174) Nederberg, F.; Appel, E.; Tan, J. P. K.; Kim, S. H.; Fukushima, K.; Sly, J.; Miller, R. D.; Waymouth, R. M.; Yang, Y. Y.; Hedrick, J. L. *Biomacromolecules* **2009**, *10*, 1460–1468.
(175) McLaughlin, M.; Garcia Rubio, S.; Muthyala, R.; Antunes, O. A. C.; Tilstam, U.; Zlota, A.; Yadav, G. D.; Laird, T. *Org. Process Res. Dev.* **2006**, *10*, 687–702.
(176) Kobayashi, S.; Makino, A. *Chem. Rev.* **2009**, *109*, 5288–5353.
(177) Percec, V. *Chem. Rev.* **2009**, *109*, 4961–4962.
(178) Hermans, T. M.; Choi, J.; Lohmeijer, B. G. G.; Dubois, G.; Pratt, R. C.; Kim, H. C.; Waymouth, R. M.; Hedrick, J. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 6648–6652.
(179) Choi, J.; Hermans, T. M.; Lohmeijer, B. G. G.; Pratt, R. C.; Dubois, G.; Frommer, J.; Waymouth, R. M.; Hedrick, J. L. *Nano Lett.* **2006**, *6*, 1761–1764.
(180) Kim, S. H.; Park, O. H.; Nederberg, F.; Topuria, T.; Krupp, L. E.; Kim, H. C.; Waymouth, R. M.; Hedrick, J. L. *Small* **2008**, *4*, 2162–2165.
(181) Kim, S. H.; Nederberg, F.; Zhang, L.; Wade, C. G.; Waymouth, R. M.; Hedrick, J. L. *Nano Lett.* **2008**, *8*, 294–301.
(182) Tan, J. P. K.; Kim, S. H.; Nederberg, F.; Appel, E. A.; Waymouth, R. M.; Zhang, Y.; Hedrick, J. L.; Yang, Y. Y. *Small* **2009**, *5*, 1504–1507.
(183) Williams, C. K.; Hillmyer, M. A. *Polym. Rev.* **2008**, *48*, 1–10.
(184) Horvath, I. T.; Anastas, P. T. *Chem. Rev.* **2007**, *107*, 2169–2173.
(185) Anastas, P. T.; Kirchhoff, M. M. *Acc. Chem. Res.* **2002**, *35*, 686–694.
(186) Methot, J. L.; Roush, W. R. *Adv. Synth. Catal.* **2004**, *346*, 1035.
(187) Ema, T.; Tanida, D.; Matsukawa, T.; Sakai, T. *Chem. Commun.* **2008**, 957–959.