Organic Catalysis:
A Broadly Useful Strategy for Green Polymer Chemistry
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Organic Catalysis:
A Broadly Useful and Environmentally Benign Strategy to Synthetic Polymer Materials

Milestone: The team of Hedrick and Waymouth have pioneered the application of organocatalysis to polymer chemistry as a new and versatile strategy for Green Polymer Chemistry. The discovery and application of highly active organic catalysts as an environmentally responsible synthetic method to generate well-defined biodegradable macromolecules, functional materials and complex macromolecular architectures represent a significant advance and a fundamental paradigm shift to the established methods in this mature field. This team has produced more that 80 manuscripts and 8 patents (2002-2011) on the design of organic catalysts for polymer chemistry with applications in sustainable plastics, biomedical materials, and plastics recycling.

Academic award nomination
Focus area- the use of greener synthetic pathways
All research conducted in United States

Abstract: The nominated technology relates to new organocatalytic methods for generating polyesters, including biodegradable and biocompatible polyesters. Catalysis is a foundational pillar for sustainable chemical processes; the discovery of highly active, environmentally benign catalytic processes is a central goal of Green Chemistry. Plastics are ubiquitous and useful modern materials, but their widespread utility and indiscriminate disposal has left an adverse and enduring environmental legacy. The team of Hedrick and Waymouth have developed a broad class of highly active, environmentally benign organic catalysts for the synthesis of biodegradable and biocompatible plastics. Conventional routes to polyesters rely on metal catalysts such as those derived from tin complexes; residual metal residues for plastics generated on such scales can result in negative environmental impacts in solid waste. For example, the European Union has recently phased out many organotin compounds. As a result, the investigation of organic catalysts to replace the tin-based workhorse catalyst has gained significant prominence in industrial settings, including those related to important commodity polymers such as siloxanes, urethanes, nylons and polyesters. This technology describes the application of metal-free organic catalysts for the synthesis and recycling of polyesters. New organic catalysts have been discovered which rival or exceed metal-based alternatives for polyester synthesis, both in terms of activity and selectivity. This approach provides an environmentally attractive, atom-economical, low energy alternative to traditional metal catalyzed processes. This technology includes organocatalytic approaches to ring-opening, anionic, zwitterionic, group transfer, and condensation polymerization techniques. Monomer feedstocks include those from renewable resources, such as lactides, as well as petrochemical feedstocks. Organic catalysts have been developed to depolymerize poly(ethyleneterephthalate) (PET) quantitatively, allowing a bottle-to-bottle recycling strategy for PET as an approach to mitigate the millions of pounds of PET that plague our landfills. This team also demonstrated that that these catalysts are tolerant to a wide variety of functional groups, enabling the synthesis of well-defined biocompatible polymers for biomedical applications. As these catalysts do not remain bound to the polymer chain, they are effective at low concentrations. These results, coupled with cytotoxicity measurements in biomedical applications have highlighted the environmental and human health benefits of this approach.

Motivated by a desire to generate new classes of metal-free polymeric materials for microelectronic applications, the team of Hedrick and Waymouth have pioneered the design and application of organic catalysts for polymer chemistry.[1,2] A major focus of their efforts has been on ring-opening polymerization, a strategy dominated by metal oxide or metal hydroxide catalysts. They have shown that organic catalysts not only exhibit activities that rival the most active metal-based catalysts, but by virtue of their novel mechanisms of enchainment, provide access to polymer architectures that are difficult to access by conventional approaches.

Plastics are ubiquitous and extremely useful modern materials; polyesters constitute a significant fraction of commercial plastics. The widespread application of polyesters in packaging and fiber applications has motivated efforts to craft a new vision for sustainable packaging.[3] To achieve this vision, major scientific and technological challenges include the conversion of renewable resources to products that exhibit cost/performance characteristics equal or superior to existing materials, the development of more environmentally benign catalytic processes, and recycling or biodegradation strategies that would enable a "closed-loop" life cycle for materials that meet the needs of the marketplace while minimizing the environmental footprint left for future generations. The synthesis of polyesters is traditionally carried out with metal oxide or metal alkoxide catalysts. While these processes are highly efficient, the search for more sustainable packaging materials[3] has motivated the search of more active and less toxic catalysts. Organocatalytic methods developed by Hedrick and Waymouth for polyester synthesis avoid metal residues in the resultant material. The leaching of toxic antimony residues from commercial poly(ethyleneterephthalate) (PET) has stimulated Victor Innovatex to develop new classes of polyester fibers,[4] and has led to increased concerns regarding residual antimony in bottled water.[5] The use of natural enzymes to catalyze the synthesis of polyesters is another approach identified as a promising strategy for Green Polymer Chemistry.[6] The team of Hedrick and Waymouth have taken a different approach. Inspired by enzymatic catalysis, they have devised several families of organic catalysts that mimic the mechanistic pathways of enzymes, but catalyze polymerization at rates and turnover numbers that match or exceed those of metal or enzyme catalysts.[1,6]

Significant achievements of this team include organocatalytic strategies for the synthesis of polyesters,[1,7] polycarbonates[8,9] polysiloxanes,[10] and polyacrylates,[11] chemical recycling of polyesters,[12-17] the use of metal-free polymers to template inorganic nanostructures for microelectronics applications,[18,19] the development of new synthetic strategy for the synthesis of high molecular weight cyclic polyesters,[20-22] and the generation of new families biocompatible polymers for biomedical applications.[23-25]

A key innovation of this group was the demonstration that N-Heterocyclic carbenes, as well as neutral organic “superbases”, such as amidines, guanidines,[26,27] and phosphazenes[28,29] are exceedingly active and in some cases highly stereoselective catalysts for ring-opening polymerization reactions (Fig 1). The activity of the commercially available cyclic guanidine 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD) in comparison to the other superbases is striking; TBD is among the most active catalysts known for the ring-opening polymerization of lactide. At room temperature in THF solution, TBD catalyzes the ring-opening polymerization of lactide with turnover frequencies of 80 s^{-1} for turnover numbers of 100.[27] Following our work, others have shown that TBD catalyzes the ring-opening polymerization of unpurified trimethylene carbonate (TMC) at 150°C in neat monomer with turnover frequencies of 1.6 s^{-1} for turnover numbers up to 91,000.[30] The guanidine TBD is commercially available and is effective in a variety of solvents, including hydrocarbons (toluene), chlorinated solvents (CH_2Cl_2) or in neat

monomer at 90 -120 °C (lactide, caprolactone, TMC). In addition to ring-opening reactions, organic catalysts such as the N-heterocyclic carbenes are also effective catalysts for step growth polymerizations: the condensation of ethyl 6-hydroxyhexanoate in the bulk generated poly(e-caprolactone) with turnover numbers of 3 x 10^5.[31]

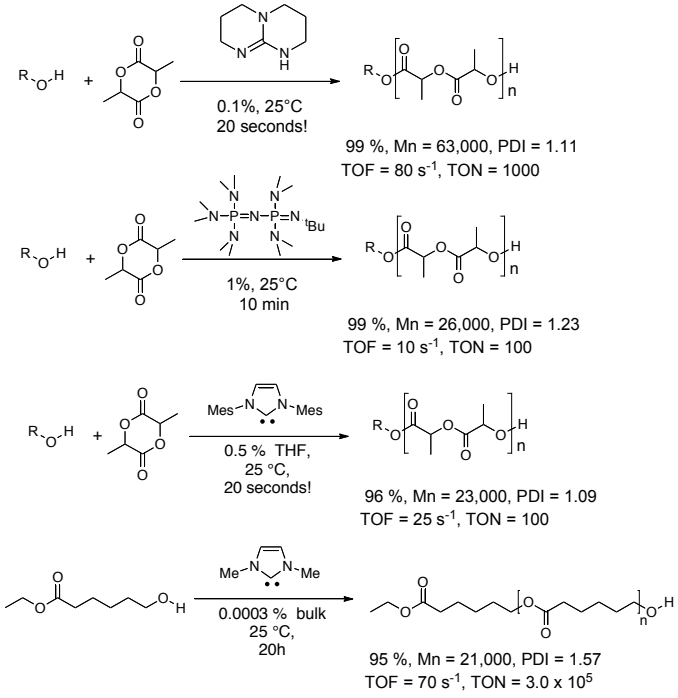

Figure 1. Organocatalytic Synthesis of Polyesters

Mechanistic[26,32] and theoretical[33] studies showed that TBD behaves simultaneously as both a hydrogen bond donor to the monomer via the N-H site and also a hydrogen bond acceptor to the hydroxylic proton of the propagating alcohol, achieving activation of both the electrophile and nucleophile. TBD is active not only for ring-opening polymerization, but for the melt polymerization[34] and depolymerization[35] of poly(ethyleneterephthalate) PET and for the catalytic formation of amides from esters.[32]

The innovation of the scientific approach is evidenced in the diversity of mechanistic pathways they have identified for organocatalytic polymerization reactions and the opportunities these new insights have provided for the generation of well-defined polymer architectures and functional materials.

Mechanistic and kinetic investigations of the N-heterocyclic carbene mediated ring-opening polymerization of lactide led to the discovery of a conceptually novel strategy for generating high molecular weight cyclic polyesters (Figure 2),[20-22,36] H-shaped[37] and mikto-arm branched block copolymers.[38]

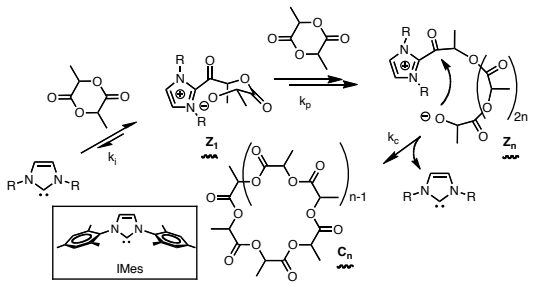

Figure 2. Zwitterionic Polymerization of Lactide

The team also developed a class of bifunctional thiourea / amine catalysts that represent one of the most selective catalyst systems for ring-opening polymerization, generating polyesters with polydispersities below $M_w/M_n = 1.05$, comparable to the polystyrene molecular weight standards (Figure 2).[39] Mechanistic studies of the H-bonding affinity of linear and cyclic esters to thiourea catalysts provided new fundamental insights on the design of ring-opening polymerization catalysts that are highly selective for propagation relative to transesterification of the product polyester. Thioureas used as catalysts for ring-opening were observed to bind to cyclic lactones and carbonates through H-bonding, but exhibited no binding affinity for linear esters.[26] This high selectivity, coupled with the high tolerance of the thiourea catalysts to functional groups was a key advance to enable the synthesis of precise functional carbonate oligomers for cell-penetrating polymers.[24]

The team of Hedrick and Waymouth have also exploited their organocatalytic strategies as a means of generating well-defined metal-free materials for biomedical applications.[23-25,40,41] They have shown that the stereocomplexation of lactide provides a means of generating polymeric micelles with low critical micelle concentrations that encapsulate therapeutic agents such as paclitaxel.[25,38] The organocatalytic ring-opening of carbonates can generate highly functionalized biocompatible polycarbonates with a range of functionalities that mimic the rich functionality of polypeptides.[8,9] These strategies were exploited to develop a novel approach to biocompatible hydrogels with a defined network structure,[42] and a novel class of guandinylated oligocarbonates which function as novel biodegradable "molecular transporters" which readily traverse cell membranes to deliver drugs or fluorescent or luminescent probes.[23,24] These studies demonstrate the potential of organocatalytic strategies for biomedical applications.

The environmental and human health benefits of organocatalytic polymerization derive from the use of renewable resources (biomass-derived monomers such as lactide, cyclic carbonates) as feedstocks, the high activities and turnover numbers observed which minimizes the amount of catalyst residues in the materials, and their demonstration that organocatalysts are effective depolymerization catalysts, enabling strategies for the chemical recycling of both biomass-derived (PLLA)[43] and petrochemically-derived (PET) polyesters (Figure 3).[12-16,44]

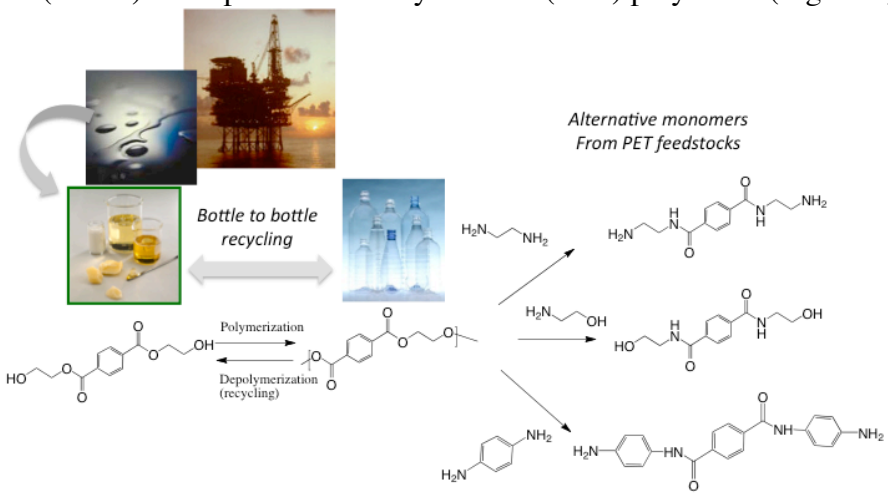

Figure 3. Catalytic Depolymerization and Transformation of PET

The team was inspired to develop organocatalysts for polymerization to avoid metal residues in microelectronic applications;[18] the potential health and environmental benefits of a metal-free approach are also significant. While extensive toxicological experiments on the wide range of organic catalysts have not been carried out, the high activities and low catalyst loadings minimize the impact of catalyst residues. While thioureas[45] and some classes of imidazolium salts[46] (the products of protonation of N-heterocyclic carbenes) have been shown to be toxic, the guanidine and phosphazene superbases have found wide application in organic and pharmaceutical chemistry.[47] In addition, preliminary cytotoxicity measurements (Institute of Bioengineering and Nanotechnology, Singapore) on organocatalytically prepared polylactides and polycarbonates on more that six cell lines show near quantitative cell viability. Several patents have issued on technology of the organocatalytic recycling of polyesters;[13-15,44] in addition, this team developed an undergraduate laboratory experiment to demonstrate the use of organocatalysts for the chemical recycling of polyesters.[12]

Organocatalytic polymerization offers a practical and cost effective approach to Green Polymer Chemistry.[6] For example, at 0.1 mol% of the commercially available cyclic guanidine 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD), the polymerization of lactide is complete in 1 min (TOF ~81 s^{-1})[26] a rate that exceeds that of metal (TOF ~ 2 s^{-1})[48] or enzyme[6] catalysts. The scientific impact of the teams work is evidenced by the degree to which the broader community is recognizing the potential of organocatalytic strategies for polymer synthesis(over 1000 citations since 2002).[49] The technology is broadly applicable not just for polymerization reactions, but for a variety of organic transformations, including transesterification reactions,[31] the formation of amides,[32] the templating of inorganic nanostructures,[18,19] and the generation of new families of well-defined materials for biomedical applications.[23-25,40]

In summary, highlights of the nominated technology include:

- Introduction of organic catalysis to synthetic Green Polymer Chemistry.
- Investigation of organic catalysts to replace organotin compound that are being phased out in Europe for siloxanes, ureathanes, coating materials, nylons and polyesters.
- Broadly applicable technology with demonstrations in ring-opening, anionic, zwitterionic, group transfer, and condensation polymerization techniques.
- Wide monomer scope including those from renewable resourses as well as petrochemical feedstocks.
- Demonstrated that PET plastic refuse can be as a feedstock via organocatalytic depolymerization back to monomer or to other high value monomers
- Demonstrated application in microelectronics and medicine where residual metal catalysts compromise performance or the environment and human health

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