SYNTHESIS OF POLY(HYDROXYALKANOATES): ROUTES TO POLY(3-HYDROXYBUTYRATE) AND POLY(3-HYDROXYPROPIONATE) FROM THE CARBONYLATION AND RING-OPENING POLYMERIZATION OF EPOXIDES

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SYNTHESIS OF POLY(HYDROXYALKANOATES): ROUTES TO POLY(3-HYDROXYBUTYRATE) AND POLY(3-HYDROXYPROPIONATE) FROM THE CARBONYLATION AND RING-OPENING POLYMERIZATION OF EPOXIDES

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New methods for the syntheses of poly(3-hydroxybutyrate) (P3HB) and poly(3-hydroxypropionate) (P3HP) from epoxides are reported. Epoxides are readily available, inexpensive starting materials that can be transformed into valuable biodegradable and biocompatible polyesters. We successfully developed a one-pot synthesis of P3HB from propylene oxide and carbon monoxide using a multicatalytic transformation. The intermediate β-butyrolactone was formed and subsequently polymerized in situ. The carbonylation of propylene oxide to β-butyrolactone was accomplished using a catalyst of the form [Lewis acid][Co(CO)₄], and the lactone monomer was then polymerized by a (BDI)ZnOAc (BDI = β-diiminate) catalyst. The two catalysts were found to have orthogonal reactivity, and were compatible with each other as well as with the solvent, substrate, and any reaction side-products. The reaction proceeded with high activity and selectivity to synthesize P3HB with high molecular weights. Furthermore, this dual-catalyst approach eliminated exposure to the toxic β-butyrolactone monomer.
We also report the synthesis of P3HP from ethylene oxide and carbon monoxide. The carbonylation of ethylene oxide proceeded in greater than 99% yield and high selectivity with the bimetallic catalyst \([\text{CITPP} \text{Al} (\text{THF})_2]^+[\text{Co} (\text{CO})_4]^-
\]
(CITPP = meso-tetra(4-chlorophenyl)porphyrinato; THF = tetrahydrofuran). Ring-opening polymerization of \(\beta\)-propiolactone by organic ionic compounds afforded poly(3-hydroxypropionate) (P3HP) in high yields. The catalyst \([\text{P} (\text{N} = \text{P} (\text{N} (\text{CH}_2)_4)_3)_4]^+
\]
\([\text{^7} \text{BuCO}_2^-\] displayed the highest activity for the ring-opening polymerization of propiolactone, and produced polyesters with molecular weights over 100,000 g/mol and narrow molecular weight distributions. P3HP can be pyrolyzed to produce acrylic acid. This method allows for the synthesis of acrylic acid from the inexpensive feedstocks of EO and CO.
BIOGRAPHICAL SKETCH

Erin Whitfield Dunn was born in Raleigh, North Carolina on July 14th, 1985 to Vickie and Charles Dunn. Erin attended William G. Enloe High School, where she participated in the International Baccalaureate program, and where her interest in science was sparked by Mr. Chad Ogren’s AP Environmental Science class and Mrs. Elizabeth Woolard’s AP Physics class. She also had the opportunity to participate in a research program for high-school students sponsored by NC State University.

After graduating Enloe High School, Erin attended the University of North Carolina at Chapel Hill as a Chancellor’s Carolina Scholar. She decided to major in chemistry after considering other branches of the physical and life sciences. She participated in a summer internship at the National Institutes of Health – National Institute of Environmental Health Science. After taking a “Synthesis of Polymers” class taught by Professor Valerie Ashby, she decided to pursue the study of polymer chemistry in greater depth. She began undergraduate research in Professor Joe DeSimone’s lab making polymer electrolyte membranes for fuel cell applications. Erin graduated with highest honors in May 2007, and moved to Ithaca, NY later that summer to continue her study of polymer chemistry at Cornell University.

Erin joined the research group of Professor Geoff Coates in 2008, were she has worked on the synthesis of poly(hydroxyalkanotes), a class of biodegradable and biocompatible polyesters. She was funded by a NSF IGERT fellowship for part of her training. While at Cornell, she has had the opportunity to serve as a teaching assistant for “Organic Chemistry for the Life Sciences,” which gave her a greater appreciation for and deeper understanding of organic chemistry. Upon completion of her Ph.D., Erin will move to the Twin Cities area to begin a position at 3M.
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CHAPTER ONE

Poly(3-hydroxypropionate):

Properties, Synthesis, and Degradation
1.1 Introduction

Bacteria produce polyhydroxyalkanoates (PHAs) in the absence of certain nutrients as energy-storage materials.\(^1\)\(^2\) Polyhydroxyalkanoates are biodegradable and biocompatible polyesters, and have many potential applications as such.\(^3\)\(^-\)\(^7\) The structures of a few common PHAs that will be discussed in this chapter are shown in Figure 1.1. PHAs produced by bacteria are isotactic, and the asymmetric carbons in the polymer backbone all have the \((R)\) configuration.

![Polymer Structure](image)

**Figure 1.1.** Structure of polyhydroxyalkanoates

Poly(3-hydroxybutyrate) (P3HB) was first isolated from *Bacillus megaterium* in the 1920s.\(^8\)\(^9\) P3HB itself is a very brittle material, which limits its possible applications. Furthermore, the decomposition temperature of P3HP is close to the melting temperature (180 °C), and thermal degradation occurs during melt processing of the polymer.\(^10\) The random copolymer P(3HB-\textit{co}-3HV), however, displays significantly improved mechanical properties, and its lower melting temperature facilitates processing. ICI Bioproducts commercialized the P(3HB-\textit{co}-3HV) polymer (with varying 3HV incorporation between 0 and 24%) in the 1980s under the trade name BIOPOL.\(^11\) However, the enterprise failed as a result of the high production cost of the material. Metabolix currently owns the fermentation technology.\(^12\)
The unsubstituted PHA poly(3-hydroxypropionate) (P3HP) has a $T_g$ of -24 °C and a $T_m$ of 93 °C. It exhibits excellent mechanical properties, and high molecular weight samples had tensile strengths of almost 500 MPa in drawn films. In addition to the attractive material properties of P3HP, the pyrolysis of the polyester affords acrylic acid. The remainder of this chapter will focus on the synthesis and degradation of P3HP.

Recombinant *Escherichia coli* has been reported to produce P3HP in up to 92% of cell dry weight. An example of PHA granules in a bacterial cell can be seen in Figure 1.2. Even though fermentation routes have the ability to produce high molecular weight polyester, the large amounts of energy required and the difficult extraction of the polymer from the bacterial culture are two major drawbacks.

![Figure 1.2. PHA Granules in *Azotobacter chroococcum* Cell](image)

The chemical synthesis of P3HP is an attractive alternative to the fermentation method. Although the monomers come from a nonrenewable source, petroleum, the biodegradability of the resulting polyester is maintained. There is significantly more control over the polymer structures formed when a chemically synthetic route is used. The sequence of the polymer can be designed, and random copolymers or block
copolymers with different composition can be synthesized. It is possible to chemically synthesize P3HP by three routes: (1) condensation polymerization of 3-hydroxypropionic acid, (2) copolymerization of ethylene oxide and carbon monoxide, and (3) ring-opening polymerization of β-propiolactone (PL) (Scheme 1.1).

**Scheme 1.1. Synthetic Routes to Poly(3-hydroxypropionate)**

![Scheme 1.1](image)

Although all three methods of synthesizing P3HP are theoretically possible, the ring-opening polymerization of β-propiolactone is the most efficient. It is difficult to obtain high molecular-weight polymer using condensation polymerizations. High temperatures are needed and the water produced as a reaction byproduct must be removed from the system.\(^\text{13}\) In addition, the 3-hydroxy acid monomer has a tendency to undergo elimination reactions. One example of the synthesis of P3HP by the condensation of 3-hydroxypropionic acid used a transesterification catalyst at 70 °C; however, there was a low degree of control over the molecular weight of the polymer formed.\(^\text{16}\)

The alternating copolymerization of ethylene oxide and carbon monoxide catalyzed by dicobalt octacarbonyl and 3-hydroxypyridine produces low molecular weight P3HP (Table 1.1).\(^\text{19}\) The low \(M_n\)s were attributed to chain termination by water;
when the water scavenger dimethoxypropane was added, a higher molecular weight polymer ($M_n = 5,833$ g/mol) was obtained (Table 1.1, Entry 3). The proposed mechanism (Scheme 1.2) begins with Co-Co bond cleavage by the $N$-donor to give Co(CO)$_4^-$ . The Co(CO)$_4^-$ anion then reacts with the hydroxyl group of 3-hydroxypryidine to give HCo(CO)$_4$, which ring opens the epoxide and undergoes CO insertion. The epoxide ring opening and CO insertion repeats to provide P3HP. According to Allmendinger et al., the role of the pyridine is unclear, but may assist in the electrophilic attack on the epoxide.

**Table 1.1. Copolymerization of Ethylene Oxide with Carbon Monoxide**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Monomer</th>
<th>Conv. of Epoxide (%)$^b$</th>
<th>Yield Polyester (g)$^c$</th>
<th>$M_n$ (g/mol)/PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EO/5 mL</td>
<td>80</td>
<td>2.8$^d$</td>
<td>4625/1.6</td>
</tr>
<tr>
<td>2</td>
<td>EO/20 mL</td>
<td>25</td>
<td>7.4</td>
<td>3000/1.7</td>
</tr>
<tr>
<td>3</td>
<td>EO/20 mL$^f$</td>
<td>30</td>
<td>8.8</td>
<td>5833/1.8</td>
</tr>
</tbody>
</table>

$^a$ Diglyme (10 mL), Co$_2$(CO)$_8$ 109 mg, 3-hydroxypyridine 61 mg, 4 h; CO 60 bar, 75 °C. $^b$ Conversion determined by $^1$H NMR of the reaction mixture. $^c$ Yield after precipitation in methanol. $^d$ Melting point of polyester is 62 °C determined by DSC. $^e$ Diglyme (80 mL), 3-hydroxypyridine (760 mg), Co$_2$(CO)$_8$ (684 mg), CO (60 bar), 80 °C, 1 h. $^f$ As in [e] and dimethoxypropane (1.1 g).
Ring-opening polymerization of β-propiolactone overcomes many of the limitations of the previous methods. High molecular weight P3HP with narrow dispersities can be synthesized.\(^ \text{20} \) The ring-opening polymerization of PL and the types of complexes that have been found effective for this reaction will be the focus of this review.

### 1.2 Cationic Initiators for the Polymerization of β-Propiolactone

Cationic initiators fall into four main classes: 1) Lewis acids, 2) protic acids, 3) alkylating reagents and 4) acylating reagents.\(^ \text{21} \) In general, cationically-initiated lactone polymerizations are difficult to control and produce low molecular weight polymers.\(^ \text{13} \) Ferric chloride and sulfuric acid were first used to polymerize β-propiolactone in a very exothermic reaction in 1948.\(^ \text{22} \) Dale et al. reported that the reaction of PL with BF\(_3\),
TiCl₄, and H₂SO₄ in CH₂Cl₂ produced cyclic oligomers. Ring sizes up to n = 10 were formed (Scheme 1.3).

**Scheme 1.3.** Reaction of β-propiolactone with BF₃

Ito claimed the cationic polymerization of PL proceeded solely by acyl-oxygen bond scission. The reaction of PL with a (CH₃CH₂)₃O⁺ initiator made oligomers with ethyl ether end groups. Almost twenty years later, Hofman et al. disputed the mechanistic hypothesis. He published that the ether end groups could result from the reaction of already formed polymer chains with unreacted initiator (Scheme 1.4).

Hofman studied the polymerization of PL with both halonium salts and acylium cations, and found the mode of ring scission depended on the initiator.

**Scheme 1.4.** Reaction of P3HP chain with cationic initiator to form ether end groups

In the reaction of PL and alkylating agents [(CH₃)₂Br]⁺[SbF₆]⁻ and [(CH₃)₂I]⁺[SbF₆]⁻, the exocyclic oxygen attacked the initiator to form an oxonium ion. Propagation occurred by alkyl-oxygen bond cleavage and continued exocyclic oxygen attack in further monomer additions (Scheme 1.5). The propagating species were all determined to be oxonium ions by trapping of the active centers with triphenylphosphine.
Scheme 1.5. Methylation of the exocyclic oxygen atom and subsequent alkyl-oxygen bond scission

\[
\begin{align*}
1 \text{ or } 2 + & \quad 
\begin{array}{c}
\text{H}_3\text{C}^+ \text{SbF}_6^- \\
\text{H}_3\text{C}
\end{array} \\
& \quad \xrightarrow{\text{O}} \\
& \quad \xrightarrow{\text{O}} \\
& \quad \xrightarrow{\text{O}} \\
& \quad \xrightarrow{\text{O}} \\
\text{CH}_3\text{O}^- \text{CH}_2\text{CH}_2\text{O}^- \\
\end{align*}
\]

When acylating agents \([\text{CH}_3\text{CO}]^+\text{[SbF}_6^-]\) and \([\text{CH}_3\text{CH}_2\text{CO}]^+\text{[SbF}_6^-]\) were used to polymerize PL, both exocyclic and endocyclic oxygen attacks were found to occur (Scheme 1.6). Although initiation took place with approximately equal alkyl-oxygen and acyl-oxygen bond scissions, the acylium active species eventually converted into oxonium ions, and oxonium species became the only propagating centers. End group analysis by \(^1\text{H NMR}\) revealed ester and anhydride groups, consistent with both modes of lactone ring opening.

Scheme 1.6. Attack of the acetylium cation (3) at the a) exocyclic oxygen atom and alkyl-oxygen bond scission and b) endocyclic oxygen atom and acyl-oxygen bond scission

\[
\begin{align*}
\text{CH}_3\text{C}^+ \text{SbF}_6^- \\
3 \\
\end{align*}
\]

a) \quad 3 + \xrightarrow{\text{O}} \quad \text{H}_3\text{C}^- \text{CH}_2\text{CH}_2\text{O}^- \\
\]

b) \quad 3 + \xrightarrow{\text{O}} \quad \text{H}_3\text{C}^+ \text{OCH}_2\text{CH}_2\text{C}^+

Słomkowski examined the “primary active centers” formed in the first step of the reaction between PL and \([\text{CH}_3\text{CO}]^+\text{[SbF}_6^-]\) and proposed the reaction sequence shown in Scheme 1.7.\(^{26}\) The reverse reaction of the attack of the exocyclic oxygen on the acylium
cation (path A) is fast, and therefore, attack by the exocyclic oxygen is not effective. The attack of the endocyclic oxygen on the acylium cation (path B) is slower, but effective. The result of path B is a six-membered cyclic intermediate that reacts with the exocyclic oxygen in another PL molecule. The growing polymer chain contains an anhydride end group and oxonium cation at the active end.

**Scheme 1.7. Initiation of β-propiolactone with [CH$_3$CO]$^+$ cations**

The cationic polymerization of PL was also studied by Kricheldorf, who examined the reaction with alkylation reagents [Me-OSO$_2$]$^+$[CF$_3$], [Et-OSO$_2$]$^+$F, and [Et$_3$O]$^+$[BF$_4$]. He found the cationic polymerization proceeded via alkyl-oxygen bond cleavage involving electrophilic attack by the exocyclic oxygen of the PL monomer.$^{21}$ Using a monomer/ratio initiator of 100/1, he synthesized P3HP in 82% yield in 16 hours using [Me-OSO$_2$]$^+$[CF$_3$], and 75-79% yield in 48 hours using [Et-OSO$_2$]$^+$F$^-$ and [Et$_3$O]$^+$[BF$_4$].
1.3 Anionic Initiators for the Polymerization of β-Propiolactone

1.3.1 Alkali Metal Alkoxides

The first report of the anionic polymerization of PL with sodium ethoxide in toluene claimed the reaction occurred primarily through acyl-oxygen fission. In 1977, Iida et al. published the reaction of the unsubstituted PL with sodium methoxide (1 mol%) in THF, which produced polymer in low yield (24%) after 5 days. The addition of dibenzo-18-crown-6 ether improved polymerization activity, and P3HP yields of over 95% were achieved using crowned potassium methoxide in DMF.

Later publications disputed the mechanism of PL ring-opening polymerization with potassium alkoxides. Penczek reported that the polymerization of PL in DMF initiated with potassium methoxide produced both carboxylate and alkoxylate active species at the start of the reaction (Scheme 1.8). However, as the reaction proceeded, the active end groups converted into carboxylate anions completely. The $^1$H NMR showed signals corresponding to methoxy and methyl ester end groups, evidence of the incorporation of the methoxide initiator into the polymer chains. No double bonds were observed.

**Scheme 1.8.** Ambident Reactivity of β-Propiolactone

In contrast to Penczek’s observation of polymer chains containing initiator end groups, Dale identified double bond end groups in the polymer chains produced in the
reaction of PL with potassium tert-butoxide. Instead of tert-butyl ester or ether end groups, which would be expected if the initiator were on the ends of the chains, he saw acrylic acid and oligomers with olefinic endgroups. Jedliński et al. examined the polymerization of PL with potassium methoxide/18-crown-6 in THF. The $^1$H NMR did not show peaks corresponding to methoxy or methyl ester groups, but C=C double bonds and hydroxyl groups were identified. The equimolar model reaction between PL and K$^+\$[OMe]$^-$ revealed methyl acrylate and potassium hydroxide as the initial products formed. Jedliński proposed the polymerization was initiated by acyl-oxygen bond scission followed by K$^+\$[OH]$^-$ elimination. The ester was unreactive and K$^+\$[OH]$^-$ acted as the true initiator. The hydroxide anion opened another PL ring by acyl-oxygen bond cleavage. After rearrangement of the unstable intermediate, propagation occurred via a carboxylate active center, producing polymer chains with both hydroxyl and unsaturated end groups (Scheme 1.9).

**Scheme 1.9.** Mechanism of Ring-Opening Polymerization of β-Propiolactone with Potassium Alkoxides

Penczek proposed a solvent effect on PL reactivity, and found the reaction of PL and K$^+\$[OMe]$^-$ in CH$_2$Cl$_2$ produced a polymer with unsaturated, hydroxyl, methyl ester,
and methoxy end groups by $^1$H NMR spectroscopy.\textsuperscript{33} In CH$_2$Cl$_2$, approximately 10\% of all polymer chains contained initiator molecules as end groups.

Shortly after Penczek’s claim that PL reactivity was solvent-dependent, Jedliński reported that the reaction of PL and potassium methoxide in DMF produced polymers with double bond and hydroxyl end groups; also, a very weak signal corresponding to methoxy end groups could be detected.\textsuperscript{34} Therefore, the mechanism of PL ring-opening polymerization carried out in any aprotic solvent is the same as depicted in Scheme 1.9, and initiator segments are not necessarily present in the polymer chains.

In 1995, Kurcok et al. examined the effect of substituents in the $\alpha$ position.\textsuperscript{35} The $\alpha,\alpha$-disubstituted $\beta$-lactone pivalolactone has no protons in the $\alpha$ position, and thus cannot undergo the elimination reaction proposed for PL. $^1$H NMR analysis of the polymer endgroups formed in the reaction of pivalolactone with potassium methoxide suggested attack of the methoxide anion on the carbonyl carbon, breaking the acyl-oxygen bond and creating a methyl ester end group and an active alcoholate propagating end. Propogation continued by acyl-oxygen bond scission. These results suggest the mechanism of ring-opening polymerization of lactone monomers by alkali metal alkoxides depends on the monomer structure. PL and other lactones with hydrogens in the $\alpha$ position undergo a substitution-elimination reaction at the initiation step, while pivalolatone and other $\alpha,\alpha$-disubstituted $\beta$-lactones proceed by a different mechanism.

Kircheldorf stated that the formation of unsaturated end groups occurred in the later stages of the polymerization as well as the initiation step. Sodium methoxide was added to a sample of P3HP in DMF and new acrylate end groups were formed.
Presumably, attack of the methoxide anion on the polyester chain induced an elimination reaction.\textsuperscript{36}

\subsection*{1.3.2 Alkali Metal Acetates}

In 1968, Yamashita et al. reported the polymerization of PL with sodium acetate via alkyl-oxygen fission.\textsuperscript{27} The addition of dibenzo-18-crown-6 ether greatly increased the rate of propagation in the reaction of sodium acetate with PL. When the complexing agent was added in at least three times the amount of Na\textsuperscript{+}[OAc]\textsuperscript{−}, the rate constant of propagation increased by over 100.\textsuperscript{37} Furthermore, the polymerization was shown to have living character. In addition to crown ethers, the use of cryptands also increased polymerization activity. No polymer was produced in the reaction of PL and potassium acetate after 100 hours at room temperature in toluene, but the addition of cryptand [222] (Figure 1.3) resulted in 7.4% conversion of PL to P3HP.\textsuperscript{38} A higher conversion (17.0%) was achieved after changing the solvent to chloroform. Shiota et al. examined the effect of the cation of various alkali metal acetate complexes on the polymerization of PL. The rate of polymerization was found to be fastest for K\textsuperscript{+}, then decreased in the order Na\textsuperscript{+} > Li\textsuperscript{+} > H\textsuperscript{+}.\textsuperscript{39}

\begin{center}
\includegraphics[width=0.5\textwidth]{cryptand.png}
\end{center}

\textbf{Figure 1.3. Cryptand [222]}

Słomkowski studied the rate constants for macroions ($k_p$) and macroion pairs ($k_p^\dagger$) in the anionic polymerization of PL using $\text{K}^+\text{[OAc]}^-\text{-dibenzo-18-crown-6}$ ether in
CH₃Cl₂. As shown in Scheme 1.10a, the carboxylate anion is strongly solvated by the polar PL monomer. In the activated complex, where some bonds are partially broken and some bonds are partially formed, the negative charge is delocalized and thus solvation is less efficient. In the macroion pair (Scheme 1.10b), the charge distribution for both the ground state and activated complex are similar. The shielding effect of the bulky cation results in lower solvation for the macroion pair. The ratio of $k_p^{-}/k_p^{+}$ depended on temperature. At -20 °C, $k_p^{-}/k_p^{+} = 5.6$, and at 35 °C, $k_p^{-}/k_p^{+} = 150$. The activation enthalpy for macroions is larger than for macroion pairs because of the strong solvation by a polar monomer. A follow-up study in the more polar solvent DMF confirmed that macroions were more reactive than macroion pairs, except when [PL] = 1 M at 20 °C, where macroion pairs became more reactive.

Scheme 1.10. a) Formation of the Activated Complex for the Propagation on Macroions and b) Formation of the Activated Complex for the Propagation on Macroion Pairs

Hofman stated that the carboxylate anion was the propagating species in the reaction of PL with $K^+[OAc]^-$ in DMF. Furthermore, the carboxylate anion was the
active end throughout the entire polymerization, starting with the initiation step. Alkyl-oxygen bond cleavage is favored because the desired approach of a nucleophile on a carbonyl (for which $\alpha$ is always greater than 90°) is hindered in the almost-flat PL molecule (Figure 1.4(a)). Moreover, after breaking the C=O double bond, unfavorable synperiplanar interactions are created between the electron pairs of the oxygen in the lactone ring and the polar C-O bonds (Figure 1.4(b)).

![Figure 1.4](image)

**Figure 1.4.** (a) Hindered Nucleophilic Attack on PL Carbonyl Carbon and (b) Unfavorable Conformation of PL with Synperiplanar Interactions

Kricheldorf reported the presence of large amount of acrylate end groups found in the reaction of PL with potassium benzoate. The double bonds could be formed in the initiation step or by an elimination reaction of the polymer chain.\(^{36}\) In 2005, Nanda et al. reported that extensive purification of the PL monomer was necessary to obtain high molecular weight material. He synthesized P3HP with a molecular weight of 251,000 g/mol and a polydispersity of 1.35 from PL using a potassium acetate-dibenzo-18-crown-6 complex.\(^{42}\)

### 1.3.3 Potassium Metal Solutions

Potassium solutions were very found to be very active initiators for PL polymerization. In THF, PL was polymerized to P3HP in 90% yield with a molecular weight of 110,000 g/mol.\(^{43}\) The system displayed living characteristics. Analysis by $^1$H
NMR showed carboxylic acid end groups, which suggested ring opening by alkyl-oxygen cleavage. For low molecular weight polymers, however, acetoxy groups were observed. Jedliński proposed an initiation step consisting of the unusual sigma CH₂-CH₂ bond cleavage by potassium anions. The resultant carbanion was stabilized by the enolate tautomer. The carbanion reacted with another PL molecular by either alkyl-oxygen scission or acyl-oxygen scission to form a carboxylate or alkoxide propagating end, respectively (Scheme 1.11). Eventually all active ends converted into carboxylate anions, which were responsibility for the majority of polymer chain growth.⁴⁴

**Scheme 1.11.** Mechanism of Ring-Opening Polymerization of β-Propiolactone with Potassium Metal Solutions

1.3.4 Other Alkali Metal-Based Initiators

Butyl lithium was reported to polymerize PL with moderate conversions, reaching 64.9% yield in 72 hours in toluene at -78 °C.²⁸,⁴⁵ The reaction of PL with potassium hydride/18-crown-6 complex in THF at room temperature produced P3HP with a $M_n$ of 17,800 g/mol in 85% yield in 4 h (monomer/initiator = 300 and [PL] = 2 M). Acrylic end groups were seen by $^1$H NMR, and the mechanism depicted in Scheme 1.12 was proposed.⁴⁶ Hydride abstraction of the $\alpha$-proton from PL formed H₂ and the cyclic enolate, which rearranged to potassium acrylate. The carboxylate anion was the active species and the polymer chain grew by alkyl-oxygen bond cleavage.
Scheme 1.12. Mechanism of Ring-Opening Polymerization of $\beta$-Propiolactone with Potassium Hydride

\[
\begin{align*}
\text{O} & \xrightarrow{K^+ H^- - H_2} \text{O}^+ \xrightarrow{n} \text{O}^+ \xrightarrow{K^+} \text{O}^+ \xrightarrow{K^+} \text{O}^+ \\
\end{align*}
\]

$K^+ = (K^+, 18$-crown-6) complex

Sodium naphthalene showed very low activity for the polymerization of PL (3.3% conversion after 72 hours), but the use of potassium naphthalenide with cation complexing agents resulted in much higher activities. P3HP with molecular weights up to 120,500 g/mol were synthesized in approximately 90% yield (Table 1.2).

Table 1.2. Results of anionic polymerization of $\beta$-propiolactone initiated by potassium naphthalenide (at 20 °C in THF)

<table>
<thead>
<tr>
<th>Cation complexing agent</th>
<th>$[M]_0/[I]_0$</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>$M_n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>50</td>
<td>20</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>18-crown-6</td>
<td>40</td>
<td>5</td>
<td>92</td>
<td>2,500</td>
</tr>
<tr>
<td>cryptand [2,2,2]</td>
<td>200</td>
<td>10</td>
<td>90</td>
<td>13,600</td>
</tr>
<tr>
<td>cryptand [2,2,2]</td>
<td>2000</td>
<td>24</td>
<td>89</td>
<td>120,500</td>
</tr>
</tbody>
</table>

The mechanism for the polymerization of BBL with potassium naphthalenide was reported to be similar to that of the potassium hydride initiator (Scheme 1.12). $^4$H NMR analysis of the polymer formed in the reaction of PL and potassium naphthalenide/18-crown-6 complex revealed alkene end groups. $^4$ Dilithium benzophenone and potassium benzophenone produce P3HP in low yields (< 12%) after 72 hours, while dipotassium benzophenone gave 50.6% conversion after 26 hours at 15 °C. $^4$
1.3.5 Organocatalysts

Residual metal contaminants in polymers can be harmful or significantly decrease materials’ performances, particularly in biomedical and microelectronic applications. The use of (metal-free) organocatalysts in chemical synthesis has received attention as a way to eliminate such impurities.\textsuperscript{49,50} The reaction of PL with tetraethylammonium pivalate was published in 1969.\textsuperscript{51} PL was polymerized with tetraethylammonium benzoate (1 mol\%) in THF to give 81\% yield of P3HP after 5 days at 30 \degree C.\textsuperscript{28} P3HP has also been synthesized from PL with a tetramethylammonium acetate catalyst in isopropyl chloride at 40 \degree C for 15 hours. The $M_n$ was determined to be 166,000 g/mol.\textsuperscript{52} In the same paper, the ring-opening polymerization of PL with pyridine at 5 \degree C was reported. After 140 hours, P3HP was isolated which had a molecular weight of 153,000 g/mol. The reaction of PL with pyridine produced molecules with vinyl end groups, instead of the expected pyridinium groups. The initiation steps shown in Scheme 1.13a were proposed.\textsuperscript{23,53} Betaine polymerized PL via alkyl-oxygen bond cleavage, and proceeded by zwitterions and macrozwitterions (Scheme 1.13b).\textsuperscript{54} Corley et al. studied the rates of initiation of PL with tertiary phosphines (Scheme 1.13c).\textsuperscript{55} For complex 4a, propagation was found to be fast in comparison with initiation. For the much bulkier phosphine 4b, initiation was much faster than propagation. Kricheldorf examined P3HP end groups, and determined elimination reactions occurred in the polymerization of PL with triethylamine, pyridine, and triphenylphosphine initiators.\textsuperscript{36,56}
Scheme 1.13. Reactions of β-Propiolactone with Organocatalysts: a) Initiation of β-Propiolactone with Pyridine and Elimination to form Acrylate End Groups and b) Reaction of β-Propiolactone with Betaine and c) Initiation of β-Propiolactone with Tertiary Phosphines

\[ \text{N} + \text{O} \rightarrow \text{N}^-\text{CH}_2\text{CH}_2\text{COO}^- \]

\[ \text{N}^-\text{CH}_2\text{CH}_2\text{COO}^- \rightarrow \text{CH}_2\text{CH} \text{COO}^- + \text{H}^+ \]

b) \((\text{CH}_3)_3\text{N}^+\text{-CH}_2\text{COO}^- + \text{O} \rightarrow (\text{CH}_3)_3\text{N}^+\text{-CH}_2\text{COOCH}_2\text{CH}_2\text{COO}^- \)

\[ 4a: R^1 = \text{CH}_3, \quad R^2 = \text{C}_6\text{H}_5, \quad R^3 = \text{C}_3\text{H}_9 \]

\[ 4b: R^1 = R^2 = R^3 = \text{C}_6\text{H}_5 \]

1.4 Tin Catalysts for the Polymerization of β-Propiolactone

1.4.1 Tin(IV) Complexes

The first report of the reaction between PL and Sn(C_3H_7)_4 claimed tin compounds were ineffective for the polymerization of PL. The reaction of PL with 1 mol% Sn(C_3H_7)_4 resulted in 0% conversion of the starting monomer after 24 h, even with the addition of O_2 and water as cocatalysts.\(^{45}\) The reaction of PL with trimethylstannyl (IV) diethyl amine resulted in ring-opening by acyl-oxygen bond cleavage.\(^{57}\) In 1988, Kricheldorf
polymerized PL with \(^{n}\text{Bu}_3\text{SnOMe}, \(^{n}\text{Bu}_3\text{SnO}^{t}\text{Bu}\), and \(^{n}\text{Bu}_3\text{SnOPh}\) (Table 1.3).\(^{58}\) The polymer chains contained ester end groups from acyl-oxygen bond scission. P3HP synthesized by the reaction of PL with \(^{n}\text{Bu}_3\text{SnOMe}\) was determined to have low concentrations of acrylate end groups, which is a common characteristic of insertion mechanisms.\(^{36}\) The reaction of PL with \(^{n}\text{Bu}_3\text{SnOMe}\) proceeded by lactone coordination to tin, followed by ring opening of the acyl-oxygen bond via insertion into the covalent tin-alkoxide bond (Scheme 1.14).

**Table 1.3.** Reaction Conditions and Results of Solution Polymerization of \(\beta\)-Propiolactone Initiated by Various Metal Alkoxides

<table>
<thead>
<tr>
<th>Entry</th>
<th>Initiator</th>
<th>M/I</th>
<th>Solvent</th>
<th>Temp ((^\circ\text{C}))</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(^{n}\text{Bu}_3\text{SnOMe})</td>
<td>100/1</td>
<td>dioxane</td>
<td>95</td>
<td>48</td>
<td>43</td>
</tr>
<tr>
<td>2</td>
<td>(^{n}\text{Bu}_3\text{SnO}^{t}\text{Bu})</td>
<td>25/1</td>
<td>dioxane</td>
<td>25</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>(^{n}\text{Bu}_3\text{SnOPh})</td>
<td>50/1</td>
<td>dioxane</td>
<td>95</td>
<td>48</td>
<td>45</td>
</tr>
</tbody>
</table>

**Scheme 1.14.** Insertion Mechanism with Sn(IV) Complexes

**1.4.2 Distannoxane Complexes**

The reaction of PL with distannoxane compounds has been reported.\(^{59}\) The copolymerization of PL with \((R)\)-BBL using distannoxane complex 2 resulted in high yields of polymer (Table 1.4).\(^{60}\) The composition of repeating groups in the polymer
backbone closely matched the composition of monomers in the feedstock. As anticipated, the melting point of the copolymer was lower than of pure (R)-P3HB.

Table 1.4. Copolymerization results of (R)-β-butyrolactone and β-propiolactone with Distannoxane Complex 5 at 100 °C (monomer/initiator = 2000)

<table>
<thead>
<tr>
<th>Monomer (feed ratio)</th>
<th>Observed ratio in polymer</th>
<th>$T_m$ (°C)</th>
<th>$T_g$ (°C)</th>
<th>$M_w$</th>
<th>$M_n$</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBL/PL (90/10)</td>
<td>90/10</td>
<td>135</td>
<td>3.1</td>
<td>96,000</td>
<td>54,000</td>
<td>99</td>
</tr>
<tr>
<td>BBL/PL (60/40)</td>
<td>59/41</td>
<td>93</td>
<td>-11.7</td>
<td>60,000</td>
<td>36,000</td>
<td>89</td>
</tr>
</tbody>
</table>

1.5 Aluminum Catalysts for the Polymerization of β-Propiolactone

Triethylaluminum was found to be inactive for PL ring-opening polymerization, but the addition of O$_2$ or ethanol cocatalysts resulted in low activity.$^{45}$ B(C$_4$H$_9$)$_3$, another group 13 compound, was found to give 0% conversion of the PL monomer after 24 h.$^{45}$ The polymerization of PL using a heterogeneous aluminum-alkyl/water system was reported in 1962. The optimum ratios of initiators (in terms of highest conversions of PL and highest molecular weight polymer) were determined to be [H$_2$O]/[Al(C$_2$H$_5$)$_3$] = 0.66, [H$_2$O]/[Al(C$_2$H$_5$)$_2$Cl] = 0.33, and [H$_2$O]/[AlC$_2$H$_5$Cl$_2$] = 0.16.$^{61}$ P3HP synthesized for enzymatic hydrolysis studies was prepared by ring-opening polymerization of PL using a polymethylaluminoxane catalyst.$^{62}$ Mixed aluminum-zinc oxo-alkoxides ZnAl$_2$O$_2$(OCHMe)$_2$$_4$ were also reported to be active for the polymerization of PL.$^{63}$
The living polymerization of PL with (tetraphenylporphinato)aluminum chloride (TPPAICl) (Figure 1.5) was reported in 1983. The reaction of PL with 1 mol% TPPAICl completely converted to P3HP in 13 days, and made polymer with a $M_n$ of 2800 g/mol and a $M_w/M_n$ of 1.13. The reaction proceeded by attack of the chloride from the catalyst on the lactone carbon next to the ester oxygen. Insertion of PL resulted in a (tetraphenylporphinato)aluminum carboxylate (Scheme 1.15). The polymerization continued by nucleophilic attack of the carboxylate on another PL molecule with alkyl-oxygen bond scission. Yasuda and colleagues took advantage of the living nature of the TPPAICl catalyst to make block copolymers of BBL and PL with narrow molecular weight distributions and well-controlled chain lengths.

In 1990, Sugimoto examined the effects of substituents on the aryl rings in TPPAICl on the polymerization of PL. A series of catalysts were synthesized, and the
reactivity was studied (Table 1.5). Although all catalysts gave polymers with narrow molecular weight distributions, the most active catalysts were (tetrakis(2’ ,4’ ,6’-trimethoxyphenyl)porphinato)aluminum chloride (7a), (tetrakis(2’ ,6’-dimethoxyphenyl)porphinato)aluminum chloride (9a), and (tetrakis(2’ ,6’-dichlorophenyl)porphinato)aluminum chloride (14a) (Figure 1.6).
Table 1.5. (Porphinato)Aluminum Chloride Complexes with Various Aryl Substituents

![Diagram](image)

<table>
<thead>
<tr>
<th>Formula No.</th>
<th>Abbreviation</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>time (h)</th>
<th>conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>(TPP)AlX</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>3.5</td>
<td>32</td>
</tr>
<tr>
<td>7a</td>
<td>(T(2,4,6-MeO)PP)AlX</td>
<td>OMe</td>
<td>H</td>
<td>OMe</td>
<td>H</td>
<td>OMe</td>
<td>0.3</td>
<td>50</td>
</tr>
<tr>
<td>8a</td>
<td>(T(3,4,5-MeO)PP)AlX</td>
<td>H</td>
<td>OMe</td>
<td>OMe</td>
<td>OMe</td>
<td>H</td>
<td>3.8</td>
<td>30</td>
</tr>
<tr>
<td>9a</td>
<td>(T(2,6-MeO)PP)AlX</td>
<td>OMe</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>OMe</td>
<td>0.25</td>
<td>40</td>
</tr>
<tr>
<td>10a</td>
<td>(T(2,4-MeO)PP)AlX</td>
<td>OMe</td>
<td>H</td>
<td>OMe</td>
<td>H</td>
<td>H</td>
<td>0.7</td>
<td>20</td>
</tr>
<tr>
<td>11a</td>
<td>(T(2-MeO)PP)AlX</td>
<td>OMe</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>1.3</td>
<td>21</td>
</tr>
<tr>
<td>12a</td>
<td>(T(4-MeO)PP)AlX</td>
<td>H</td>
<td>H</td>
<td>OMe</td>
<td>H</td>
<td>H</td>
<td>3.8</td>
<td>31</td>
</tr>
<tr>
<td>13a</td>
<td>(T(2,3,4,5,6-F)PP)AlX</td>
<td>F</td>
<td>F</td>
<td>F</td>
<td>F</td>
<td>F</td>
<td>3.6</td>
<td>39</td>
</tr>
<tr>
<td>14a</td>
<td>(T(2,6-Cl)PP)AlX</td>
<td>Cl</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>Cl</td>
<td>1</td>
<td>55</td>
</tr>
<tr>
<td>15a</td>
<td>(T(2,4,6-Me)PP)AlX</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>H</td>
<td>Me</td>
<td>3.5</td>
<td>12</td>
</tr>
<tr>
<td>16a</td>
<td>(T(2,4,6-Ph)PP)AlX</td>
<td>Ph</td>
<td>H</td>
<td>Ph</td>
<td>H</td>
<td>Ph</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
Kricheldorf et al. polymerized PL with Al(O\text{Pr})\textsubscript{3} to P3HP in 59% yield\textsuperscript{58}. Of the two possible ring-opening mechanisms depicted in Scheme 1.16, the reaction proceeded by acyl-oxygen bond cleavage. The \textsuperscript{1}H NMR analysis of polymer end groups revealed only isopropyl ester end groups. Inoue found the reaction between Al(O\text{Pr})\textsubscript{3} and PL at 0 °C for 20 hours gave 62.2% conversion to P3HP\textsuperscript{45}. 

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{conversion_curve.png}
\caption{Polymerizations of β-Propiolactone Initiated with (Porphinato)Aluminum Chlorides Shown in Table 1.5 at 30 °C in CH\textsubscript{2}Cl\textsubscript{2}. [PL]/[initiator] = 50 ([initiator] = 76.1 mM). Time-Conversion Curve.}
\end{figure}
Scheme 1.16. Reaction of Al(O^iPr)_3 with β-Propiolactone: a) Acyl-Oxygen Bond Scission and b) Alkyl-Oxygen Bond Scission

1.6 Zinc (and Other Transition Metal) Catalysts for the Polymerization of β-Propiolactone

A heterogeneous diethylzinc-water catalyst system was reported to be active for the ring-opening polymerization of PL in benzene at 60 °C. The reaction of PL with only diethylzinc resulted in very low yields of P3HP (1.3% conversion after 24 hours at 15 °C). Under the same conditions, adding O_2 as a cocatalyst (1:1 mol ratio of O_2:ZnEt_2) increased the conversion to 96.5%. The use of a H_2O cocatalyst (H_2O/ZnEt_2 = 0.25) gave 23.9% conversion and ethanol (EtOH/ZnEt_2 = 2) resulted in 87.7% conversion. The use of Zn(O^nBu)_2 as an initiator with PL resulted in P3HP (55% yield) with n-butyl ester end groups. In addition to zinc, Ti(O^nBu)_4 and Zr(O^nPr)_4 were also active for the polymerization of PL, and made polyester in 53% yield and 48% yield, respectively (monomer/initiator = 200 in dioxane at 95 °C for 48 hours). The use of Cd(C_2H_5)_2 for the ring-opening polymerization of PL resulted in 1% conversion after 24...
hours at 15 °C. Hg(C₄H₉)₂ was inactive for the same reaction after a period of 69 hours.⁴⁵

Tert-butyl chromate polymerized PL by a coordinated anionic mechanism similar to that of metal alkoxides. The reaction of PL with (′BuO₂)CrO₂ at 50 °C for 3 days gave 70% yield of P3HP.⁶⁸

Zhang et al. reported the synthesis of P3HP from macrocyclic esters using a zinc alkoxide catalyst (Scheme 1.17).⁶⁹ The ring-opening polymerization proceeded with high conversions and produced polyesters with molecular weights up to 66,500 g/mol. However, the macrocyclic esters were made from 3-hydroxypropionic acid in low yields (20-60%).

Scheme 1.17. Synthesis of P3HP from the Ring-Opening Polymerization of Macroyclic Esters made from 3-Hydroxypropionic Acid

1.7 Rare Earth Catalysts for the Polymerization of β-Propiolactone

Yamashita et al. published that lanthanide alkoxides showed good activity for PL polymerization, although organolanthanide alkyls were inactive for the same reaction.⁷⁰ The complexes SmOEt(C₅Me₃)₂(OEt₂), [YOMe(C₅H₅)₂], and YOMe(C₅Me₅)₂(THF)
made P3HP in 86-91% yields with high molecular weights (60,000-63,000 g/mol) in toluene at 0 °C after 10 hours. As depicted in Scheme 1.18a, the lanthanide akyl-lactone adduct is stabilized, and not active for polymerization. The reaction between PL and SmOEt(C_5Me_3)_2(OEt)_2, however, proceeds by acyl-oxygen scission and the initial product is active to continue propagation (Scheme 1.18b).

Scheme 1.18. β-Propiolactone with Rare Earth Initiators: a) LuMe(C_5Me_3)_2/β-Propiolactone Adduct and b) Reaction of β-Propiolactone with SmOEt(C_5Me_3)_2(Et_2O)

1.8 Magnesium Catalysts for the Polymerization of β-Propiolactone

Kricheldorf reported the polymerization of PL using Mg(OEt)_2 in diethylene glycol methyl ether at 95 °C produced P3HP in 77% yield after 24 hours. The reaction between Mg(C_2H_3)_2·MgI_2 and PL at -78 °C in toluene for 72 hours gave 39% conversion to polymer.
1.9 Biodegradability of Poly(3-hydroxypropionate)

Tokiwa first reported the hydrolysis of P3HP by the lipase *Rh. Delemar*. In addition to enzymatic degradation, P3HP can be degraded microbially. Nishida studied the ability of microorganisms found in natural environments to degrade P3HP. Essentially complete degradation was seen after 10 days in 6 out of 10 cultures (Figure 1.7). The polyester was metabolized to CO$_2$ and H$_2$O, as evidenced by the lack of change in pH values of the microorganisms culture’s media after cultivation.

![Figure 1.7](image)

**Figure 1.7.** Weight loss of fibrous P3HP after second enrichment culture at 30 °C for 10 days in yeast extract medium. Inocula: environmental samples collected in winter.
1.10 Pyrolysis of Poly(3-hydroxypropionate) to Acrylic Acid

The pyrolysis of P3HP to acrylic acid was reported to proceed at 200 °C at 80 mm Hg. Anhydrous copper acetate was added to inhibit acrylic acid polymerization. Several other publications describing the polyester thermolysis to acrylic acid in high yields and purity followed. Iwabuchi et al. studied the mechanism of thermal degradation and found the initial decrease in molecular weight of the polymer was followed by the rapid formation of acrylic acid. Chain scission occurs by ester pyrolysis involving a cyclic transition state, and produces one fragment containing an unsaturated end group and a second fragment containing a carboxylic acid chain end (Scheme 1.19a). Further chain scission of a polymer fragment with a carboxylic acid group results in acrylic acid (Scheme 1.19b). The relationship between polymer weight loss and time was studied in the thermal degradation of P3HP at 180-220 °C and 80 mm Hg. Loss of polymer weight was slow at first, then rapidly accelerated as more acrylic acid (a catalyst for ester cleavage) was formed (Figure 1.8).

**Scheme 1.19.** Chain scission of P3HP: a) Ester cleavage to form fragments with carboxylic acid and double bond end groups and b) Formation of acrylic acid
Figure 1.8. Thermal degradation of P3HP. Relationship between time and weight loss of the polymer.\textsuperscript{a}

\textsuperscript{a} Conditions: P3HP under nitrogen at 180-220 °C and 80 mm Hg in small tubes. \( W = \) weight of the nonvolatile polymer in the residue; \( W_0 = \) original weight of the polymer.

1.11 Crystalline Structure of Poly(3-hydroxypropionate)

P3HP can exist in different crystalline forms depending on the method of polymerization and the preparation of the sample. Theoretical calculations predicted that nearly all PHAs existed in a \( 2_1 \) helix and/or a trans crystalline phase.\textsuperscript{79} Four polymorphs of P3HP have been identified. The \( \alpha \textsuperscript{80} \) and \( \delta \textsuperscript{81} \) forms exist as a \( 2_1 \) helix, while the \( \beta \textsuperscript{82} \) and solution-cast \( \gamma \textsuperscript{83} \) polymorphs crystallize in an all-trans configuration with planar zigzag structures. Furuhashi et al. studied the degradation of the various crystalline structures of
P3HP with PHB depolymerase and found the β form was the fastest to degrade, followed by the α form and then the γ form.\textsuperscript{80}

1.12 Conclusion

Replacing nondegradable petroleum-based plastics with biodegradable polymers is a noble goal. Polyhydroxyalkanotes display promising mechanical properties, and in some cases are comparable to polyolefins. The choice between a biological synthesis and a chemical synthesis of polyhydroxyalkanoates is not obvious. Bacterial fermentation routes produce high-molecular weight polyesters, yet materials made with this method are not cost competitive with petroleum-based plastics. PHAs currently find applications in biomedical devices, where the high production cost is justified.\textsuperscript{84} Technological advances are needed, however, in order for PHAs to become commercially viable for use as commodity plastics.

The chemical synthesis of polyhydroxyalkanotes also has the ability to produce high molecular weight polyester, and offers much greater control over polymer composition. The stereochemistry and monomer sequence along a polymer chain can be controlled, and there is large potential to synthesize unique copolymers. New catalysts and/or synthetic methods may give rise to the discovery of new PHA architectures with exceptional material properties.

Numerous types of initiators have been found active for the ring-opening polymerization of β-propiolactone to give poly(3-hydroxypropionate). These include cationic and anionic initiators as well as complexes of tin, aluminum, zinc, yttrium, and magnesium. Organocatalysts also show a great deal of promise as a way to synthesize
P3HP without leaving metal contaminants in the final material. The mechanism of ring opening has been widely studied, and found to depend on the type of initiator used.

Furthermore, poly(3-hydroxypropioniate) can be pyrolyzed into acrylic acid. Acrylic acid is an important commodity chemical, and is currently made from the two-step oxidation of propylene. With rising propylene prices, it is becoming important to develop alternative synthetic methods to acrylic acid. The use of P3HP as a precursor to acrylic acid would allow for easy transport and handling of the solid polymer. The synthesis of acrylic acid from ethylene oxide and carbon monoxide (via β-propiolactone and P3HP) allows the use of a new two-carbon feedstock instead of propylene.
References

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(12) www.metabolix.com


36


(84) www.tepha.com
CHAPTER TWO

Carbonylative Polymerization of Propylene Oxide:

A Multicatalytic Approach to the Synthesis of Poly(3-hydroxybutyrate)

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2.1 Introduction

Poly(3-hydroxybutyrate) (P3HB) is a naturally occurring biodegradable and biocompatible polyester that exhibits properties similar to polyolefins.¹ Current methods to synthesize P3HB include bacterial fermentation, direct copolymerization of propylene oxide (PO) and carbon monoxide (CO), and ring-opening polymerization of β-butyrolactone (BBL). Fermentation produces high molecular weight P3HB with the potential to incorporate various pendant functionality into the polyester, however, the process is energy-intensive and necessitates polymer separation from the bacterial culture.² In contrast, the direct copolymerization of CO and PO is atom-economical, yet it suffers from low monomer conversion and polymers of low molecular weight are generally produced.³⁻⁵ Finally, the living ring-opening polymerization of BBL yields high molecular weight polyester, although it requires the rigorous purification of a toxic lactone.⁶ We have initiated a research effort to synthesize P3HB via a one-pot tandem catalytic transformation, where BBL is synthesized from PO and CO and subsequently polymerized in situ (Scheme 2.1). A multicatalytic approach would eliminate the need to isolate and purify the toxic lactone monomer, while still maintaining the atom economy of the CO and PO copolymerization and providing the high-molecular weight polymer achieved by BBL polymerization. Tandem catalysis⁷ is a valuable method for synthesizing small molecules⁸ but has rarely been utilized for polymer synthesis.⁹

**Scheme 2.1.** One-Pot Carbonylative Polymerization of (R)-Propylene Oxide to (R)-Poly(3-hydroxybutyrate)
Developing a one-pot catalytic system is challenging, as the two catalysts must not only be compatible with each other, but also with the solvent, substrate, and reaction side-products in order to achieve high activity and selectivity.\textsuperscript{10} We have previously reported several catalysts of the form [Lewis acid]\textsuperscript{+}[Co(CO)\textsubscript{4}]\textsuperscript{-} to be highly active for the carbonylation of epoxides.\textsuperscript{11} Furthermore, (BDI)ZnO\text{Pr} (BDI = \textbeta-diiminate) has been shown to be an active catalyst for \textbeta-lactone polymerization.\textsuperscript{12} We anticipated that the catalysts had orthogonal reactivity and could be combined to create an efficient system for the one-pot carbonylative polymerization of PO.

### 2.2 Results and Discussion

We initially investigated four catalysts (complexes 1-4) for the carbonylation step of the one-pot reaction while using (BDI)ZnO\text{Pr} (5) for the polymerization (Table 2.1). Both complex 1 and complex 2 used with (BDI)ZnO\text{Pr} resulted in incomplete conversions for the carbonylation and polymerization reactions (entries 1 and 2). Catalyst 3 used with 5 completely transformed PO to BBL, but resulted in incomplete conversion of BBL to P3HB (entry 3). Finally, complex 4 [(CITPP)Al(THF)\textsubscript{2}]\textsuperscript{+}[Co(CO)\textsubscript{4}]\textsuperscript{-} (CITPP = \textit{meso}-tetra(4-chlorophenyl)porphyrinato) used with 5 showed high activities for both the carbonylation and polymerization stages of the reaction, respectively (entry 4).
Table 2.1. Optimization of One-Pot P3HB Synthesis

\[
\begin{align*}
\text{carbonylation catalyst} & \rightarrow \text{polymerrization catalyst} \\
\text{O} + \text{CO} & \rightarrow \text{[O-C(O)-O]_n}
\end{align*}
\]

Carbonylation Catalysts:

<table>
<thead>
<tr>
<th>M</th>
<th>Catalyst Structure</th>
<th>( \text{M} = \text{Al}; ) 1</th>
<th>( \text{M} = \text{Cr}; ) 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>![Image of catalyst 1]</td>
<td>![Image of catalyst 2]</td>
<td>![Image of catalyst 3]</td>
</tr>
</tbody>
</table>

Polymerization Catalysts:

<table>
<thead>
<tr>
<th></th>
<th>Catalyst Structure</th>
<th>( \text{Ar} = 4\text{-Cl phenyl} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>![Image of catalyst 5]</td>
<td>![Image of catalyst 6]</td>
</tr>
<tr>
<td>6</td>
<td>![Image of catalyst 7]</td>
<td>![Image of catalyst 8]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>carbonylation catalyst</th>
<th>polymerization catalyst</th>
<th>PO</th>
<th>BBL</th>
<th>P3HB</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>5</td>
<td>66</td>
<td>5</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>9</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>5</td>
<td>-</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>5</td>
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<td>1</td>
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</tr>
<tr>
<td>5</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td>64</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>7</td>
<td>&gt;99</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

\( ^a \) Reaction conditions: 0.1 mol\% carbonylation catalyst, 0.1 mol\% polymerization catalyst, [PO] = 2.0 M in THF, 850 psi CO, 10 h, 50 °C. Product distribution determined by \(^1\)H NMR of crude reaction.
Equipped with a highly efficient and selective carbonylation catalyst for the one-pot synthesis of P3HB, we screened two additional polymerization catalysts. Complexes 6 and 7 were selected based on literature reports of high activities and their ability to produce high molecular weight polymer. Ethylzinc isopropoxide\textsuperscript{13} (6) was a poor catalyst for this system, as it resulted in incomplete conversions for both reactions (entry 5). Distannoxane 7, reported by Hori and co-workers,\textsuperscript{14} impeded the carbonylation catalyst such that no BBL was formed (entry 6). Thus, the original polymerization catalyst (5) was the most efficient and selective of the three catalysts studied.

Minor changes in the sterics and electronics of the BDI zinc catalysts have significant effects on their activity,\textsuperscript{15} therefore we explored alternative BDI zinc complexes and reaction conditions to optimize the one-pot carbonylative polymerization of PO (Table 2.2). Although complex 5, in combination with 4, proceeded to high conversion of P3HB, the molecular weight of the isolated polyester was low (entry 1). Complexes 8 and 9 with catalyst 4 resulted in incomplete formation of P3HB (entries 2 and 3). Complexes 10 and 11 used with 4 displayed both high activities and produced high molecular weight polymer (entries 4-7).
Table 2.2. Screening of β-Diiminate Zinc Polymerization Catalysts

<table>
<thead>
<tr>
<th>entry</th>
<th>(BDI)Zn (mol %)</th>
<th>[PO] (M)</th>
<th>time (h)</th>
<th>BBL (%)</th>
<th>P3HB (%)</th>
<th>$M_n$ (kDa)</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 (1.0)</td>
<td>3</td>
<td>10</td>
<td>1</td>
<td>99</td>
<td>7</td>
<td>1.5</td>
</tr>
<tr>
<td>2</td>
<td>8 (1.0)</td>
<td>3</td>
<td>15</td>
<td>29</td>
<td>55</td>
<td>4</td>
<td>1.1</td>
</tr>
<tr>
<td>3</td>
<td>9 (1.0)</td>
<td>3</td>
<td>15</td>
<td>2</td>
<td>41</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>4</td>
<td>10 (1.0)</td>
<td>2</td>
<td>6</td>
<td>&lt;1</td>
<td>&gt;99</td>
<td>38</td>
<td>1.3</td>
</tr>
<tr>
<td>5</td>
<td>10 (1.0)</td>
<td>2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>6</td>
<td>&lt;1</td>
<td>&gt;99</td>
<td>43&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.1</td>
</tr>
<tr>
<td>6</td>
<td>11 (1.0)</td>
<td>2</td>
<td>10</td>
<td>&lt;1</td>
<td>&gt;99</td>
<td>25&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.3</td>
</tr>
<tr>
<td>7&lt;sup&gt;e&lt;/sup&gt;</td>
<td>11 (0.5)</td>
<td>2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10</td>
<td>&lt;1</td>
<td>&gt;99</td>
<td>52&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.1</td>
</tr>
</tbody>
</table>

<sup>a</sup> General conditions: 0.1 mol% 4, $T_{rxn} = 50$ °C. Product distribution determined by $^1$H NMR of crude reaction. <sup>b</sup> $M_n$ and PDI values determined by GPC in THF with polystyrene standards. <sup>c</sup> (R)-PO. <sup>d</sup> $M_n$ and PDI values determined by GPC in CHCl$_3$ vs. polystyrene standards. <sup>e</sup> 0.05 mol% 4.

Under the reaction conditions of entry 4, the number-average molecular weight ($M_n$) of the polymer grew linearly with conversion and the polydispersity remained narrow throughout the reaction, suggesting living behavior (Figure 2.1). Naturally occurring P3HB is isotactic with all stereocenters in the (R) configuration, resulting in
semicrystalline morphology.\textsuperscript{1} To produce isotactic P3HB, we carbonylatively polymerized (\textit{R})-PO to (\textit{R})-P3HB with a molecular weight of 43 kDa (entry 5). Complex 11 with 4 made polymer with a lower $M_n$ (entry 6) than complex 10 with 4 under the same conditions and we attribute this to decomposition of the polyester under prolonged exposure to the reaction environment.\textsuperscript{12} Finally, we decreased the moles of 4 and 11 to roughly double $M_n$, and synthesized (\textit{R})-P3HB with a molecular weight of 52 kDa in 10 h using 0.5 mol\% catalyst 4 and 0.05 mol\% catalyst 11 at 50 °C (entry 7).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Plot of $M_n$ vs. Conversion of BBL (Table 2.2, entry 4). PO was not detected in the $^1$H NMR spectra of the reaction mixture aliquots.}
\end{figure}

To confirm that the reaction proceeded by a two-step mechanism, we monitored the reaction by in situ IR spectroscopy.\textsuperscript{11d} A plot of absorbance as a function of time
confirmed formation of the BBL intermediate that subsequently was consumed to produce P3HB (Figure 2.2).

![Figure 2.2](image-url) In situ IR spectroscopy of carbonylative polymerization showing formation and subsequent conversion of \(\beta\)-butyrolactone intermediate to poly(3-hydroxybutyrate) (Table 2.2, entry 4).

We planned to eliminate exposure to the toxic BBL molecule by using tandem catalysis. In order to ensure the lactone was completely transformed over the course of the reaction, we used \(^1\)H NMR spectroscopy and gas chromatography to verify the absence of BBL in the crude product. Figure 2.3 shows the \(^1\)H NMR spectrum of racemic \(\beta\)-butyrolactone. No peaks corresponding to the lactone intermediate can be seen in the crude product mixture (Figure 2.4).
After determining the percent monomer conversion to poly(3-hydroxybutyrate) in
the crude reaction mixture by $^1$H NMR analysis, the crude reaction mixture was analyzed
by gas chromatography in order to confirm the absence of $\beta$-butyrolactone. As seen in
Figure 2.5, the BBL monomer elutes from the gc at approximately 6.76 minutes. There is
no peak present between 6 and 8 minutes in the crude reaction mixture (Figure 2.6); therefore, no BBL is left in the reaction mixture.

![Figure 2.3. $^1$H NMR spectrum of rac-BBL](image)
Figure 2.4. $^1$H NMR spectrum of crude reaction mixture (Table 2.2, entry 6)

Figure 2.5. Gas chromatogram of rac-BBL
The effect of the initiator of the \((\text{Et,EtBDI})\text{ZnR}\) complex on the carbonylative polymerization of propylene oxide was examined (Table 2.3). All the complexes tested showed activity for the polymerization reaction, but produced P3HB with varying molecular weights. The trimethylsilyl amido initiator (entry 1) formed the lowest molecular-weight polymer \((M_n = 2,200 \text{ g/mol})\). The methoxide group also produced low molecular weight polymer (entry 2); however, the use of an isopropanoxide initiator made P3HB with a molecular weight of 6,900 g/mol (entry 3). The \((\text{Et,EtBDI})\text{Zn}\) complexes with carboxylate initiators produced the highest molecular weight polymer. The acetate complex made P3HB with a molecular weight of 11,000 g/mol in over 99% conversion (entry 4), while the catalyst containing a benzoate initiator was used to synthesize the highest molecular weight polyester \((M_n = 11,900 \text{ g/mol}, \text{entry 5})\).
Table 2.3. Effect of the (BDI)Zn initiator on the carbonylative polymerization of propylene oxide

\[
\text{O} + \text{CO} \xrightarrow{4 + (\text{Et,EtBDI})ZnR} \left[\begin{array}{c}
\text{C} \\
\text{O}
\end{array}\right]_n
\]

\[
\begin{array}{cccc}
\text{entry} & \text{R} & \text{conversion (\%)}^b & \text{M}_n \text{ (g/mol)} \\
1 & \text{N(TMS)}_2 & 98 & 2,200 \\
2 & \text{OMe} & 99 & 2,600 \\
3 & \text{O} \text{Pr} & 99 & 6,900 \\
4 & \text{OAc} & >99 & 11,000 \\
5 & \text{OBz} & 99 & 11,900 \\
\end{array}
\]

\(^a\) General conditions: 0.1 mol\% 4, 1.0 mol\% (\text{Et,EtBDI})ZnR, 850 psi CO, \(T_{\text{rxn}} = 50 \degree \text{C}, t = 15 \text{ h}, [\text{propylene oxide}] = 2.9 \text{ M in THF}. \)

\(^b\) As determined by the \(^1\text{H} \text{NMR}\) of the crude reaction.

P3HB was successfully synthesized in one pot from propylene oxide and carbon monoxide in high yields and high molecular weights; furthermore, the toxic lactone intermediate quantitatively reacted to make polymer. As the commercially produced
Biopol™ material is the copolymer poly(hydroxybutyrate-co-valerate) (PHBV), we attempted to synthesize PHBV in one pot from propylene oxide, 1-butene oxide, and carbon monoxide. Using 0.1 mol% catalyst 4 and 1 mol% catalyst 11, PHBV with 5% ethyl branches was synthesized in 12 hours at 50 °C (Scheme 2.2). The \(^1\)H NMR spectrum is shown in Figure 2.7.

**Scheme 2.2.** Copolymerization of propylene oxide and 1-butene oxide with carbon monoxide to make PHBV

\[
\begin{align*}
\text{COP} + \text{PB} + \text{CO} & \rightarrow \begin{array}{c}
\text{O} \\
\text{5\%}
\end{array} \\
\text{0.1 mol\% CITPPAI(CO)}_4 & + \begin{array}{c}
\text{1 mol\% } \text{PBDIZnOAc} \\
\text{[PO]} = 2 \text{ M in THF} \\
\text{12 h, 50 °C}
\end{array}
\end{align*}
\]

\[\text{PHBV} 5\%\]
2.3 Conclusion

We have reported a new atom-economical and highly efficient method for the synthesis of P3HB from the carbonylative polymerization of propylene oxide. The use of compatible catalysts allows for a one-pot reaction that eliminates the need to isolate and purify the toxic BBL intermediate. Future studies will focus on expanding this methodology to include the incorporation of new monomers.

2.4 Experimental Section

2.4.1 General Considerations

All manipulations of air and water sensitive compounds were carried out under
dry nitrogen using a Braun Labmaster glovebox or standard Schlenk line techniques. $^1$H NMR spectra were recorded on a Varian Mercury ($^1$H, 300 MHz) or Varian INOVA 400 ($^1$H, 400 MHz) spectrometers and referenced with residual non-deuterated solvent shifts (CHCl$_3$ = 7.26 ppm). In situ IR data were collected using a 100-mL Parr stainless steel high-pressure reactor modified for use with a Mettler-Toledo ReactIR 4000 Reaction Analysis System fitted with a Sentinel DiComp high-pressure probe, and analyzed with ReactIR software version 2.21. Gas chromatography (GC) analyses were carried out using a Hewlett-Packard 6890 series gas chromatograph using a HP-5 (Crosslinked 5% PH ME Siloxane) capillary column (30 m x 0.32 mm), a flame ionization detector, and He carrier gas.

### 2.4.2 Polymer Characterization

Gel permeation chromatography (GPC) analyses were carried out using a Waters instrument, (M515 pump, 717+ Autosampler) equipped with a Waters UV486 and Waters 2410 differential refractive index detectors, and three 5 µm PSS SDV columns (Polymer Standards Service; 50 Å, 500 Å, and Linear M porosities) in series. The GPC columns were eluted with tetrahydrofuran or chloroform at 40 °C at 1 mL/min and were calibrated using 20 monodisperse polystyrene standards.

### 2.4.3 Materials

HPLC grade tetrahydrofuran was purchased from Fisher Scientific and dried by passing over columns of alumina and degassed via repetitive freeze-pump-thaw cycles. Propylene oxide (PO) was purchased from Aldrich and dried over calcium hydride,
degassed via three freeze-pump-thaw cycles, and then vacuum transferred under nitrogen before use. \((R)\)-Propylene oxide was prepared from the hydrolytic kinetic resolution of \(\text{rac}\)-propylene oxide as described in section 2.4.4. All other reagents were purchased from commercial sources and used as received. \(((\text{salph})\text{Al(THF)}_2)^+\text{[Co(CO)}_4^-\) \((1),^{16} \((\text{salph})\text{Cr(THF)}_2)^+\text{[Co(CO)}_4^-\) \((2),^{17} \,(\text{OEP})\text{Cr(THF)}_2)^+\text{[Co(CO)}_4^-\) \((3),^{18} \,(\text{TPP})\text{Cr(THF)}_2)^+\text{[Co(CO)}_4^-\) \((4),^{19} \,(\text{BDI})\text{ZnO}^\text{Pr} \) complex \(5,^{20} \) ethylzinc isopropoxide \(6,^{21} \) distannoxane complex \(7,^{22} \) and \((\text{BDI})\text{ZnOAc} \) complexes \(8-11^{23} \) were synthesized according to literature procedures as described in section 2.4.6.

2.4.4 Hydrolytic Kinetic Resolution of Propylene Oxide

\[
\begin{align*}
\text{O} + 0.5 \text{ mol\% } (R,R)-1\text{OAc} + 0.55 \text{ equiv H}_2\text{O} & \rightarrow \text{O} + \text{HO-CH}_2-\text{OH} \\
M = \text{Co: } (R,R)-1 & \\
M = \text{Co(OAc): } (R,R)-1\text{OAc} & 
\end{align*}
\]

The hydrolytic kinetic resolution procedure published by Jacobsen et al. was followed.\(^{24} \) \((R,R)-(\text{--})\text{-N,N'-Bis(3,5-di-\text{-tert-} \)butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (380.0 mg, 0.63 mmol) was dissolved in 8 mL toluene. Glacial acetic acid (0.4 mL, 6.6 mmol) was added. The solution was stirred at room temperature open to air for 30 minutes. The solvent was evaporated to give a brown solid, which was dissolved in propylene oxide (22.0 mL, 314.0 mmol). The solution was cooled
to 0 °C and 3.4 mL H₂O (188.0 mmol) was added dropwise over 5 minutes. The reaction was allowed to warm to room temperature and stirred 14 hours. The product was isolated by distillation at 40 °C from the reaction mixture. The ee was determined to be >99% by chiral gas chromatography.

2.4.5 Representative Carbonylative Polymerization Procedure

\[
\text{[O]} + \text{CO} \xrightarrow{\text{carbonylation catalyst}} \left[ \text{\text{O}} \right]_n \xrightarrow{\text{polymerization catalyst}} \text{[\text{p}]}_n
\]

Under nitrogen, a 100-mL Parr high-pressure reactor was charged with 14 µmol carbonylation catalyst, 0.14 mmol polymerization catalyst, 29 mmol propylene oxide, and 14 mL THF. The reactor was pressured to 850 psi CO followed by rapid stirring and heating to 50 °C. After the appropriate time, the reactor was cooled to rt, and slowly vented. A small aliquot was removed for crude \(^1\)H NMR analysis to determine monomer conversion. The viscous reaction mixture was then dissolved in a minimum amount of dichloromethane and precipitated into an excess of hexane. The polymer was collected and dried \textit{in vacuo} to give a purple (from residual porphyrin catalyst) solid typically in 90-95% recovery by weight.
2.4.6 Complex Synthesis

2.4.6.1 \([\text{(Salph)Al(THF)}_2]^+[\text{Co(CO)}_4]^-\) (1).

\[
\begin{align*}
\text{(Salph)H}_2 & \quad \text{3,5-di-tert-butyalsalicylaldehyde (5.6 g, 24.0 mmol)} \\
\text{1,2-phenylenediamine (1.3 g, 12.0 mmol)} & \quad \text{were dissolved in 60 mL methanol. The solution} \\
& \quad \text{was refluxed for 15 hours. After cooling, a yellow precipitate formed which was filtered,} \\
& \quad \text{washed with methanol, and dried under vacuum.} \\
& \quad \text{^1H NMR (C}_6\text{D}_6, 300 MHz) \delta \text{ 14.03 (2H, s, OH), 8.13 (2H, s, CH=N), 7.64 (2H, d, J = 3.0 Hz, ArH), 7.05 (2H, d, J = 3.0 Hz,} \\
& \quad \text{ArH), 7.00 (2H, q, J = 3.0 Hz, ArH), 6.74 (2H, q, J = 3.0 Hz, ArH), 1.66 (18H, s,} \\
& \quad \text{Ph'}Bu'Bu'), 1.34 (18H, s, Ph}^\text{t}\text{Bu'}Bu').
\end{align*}
\]
(Salph)AlCl. (Salph)H₂ (502.9 mg, 0.9 mmol) was dissolved in 10 mL dry dichloromethane. A 1 M solution of diethylaluminum chloride (0.9 mL, 0.9 mmol) was added dropwise under N₂. The solution was stirred at room temperature for 10 hours, and then the solvent was evaporated under vacuum to give a solid. The product was rinsed with hexanes. (516.5 mg, 92% yield) ¹H NMR (C₆D₆, 400 MHz) δ 8.15 (2H, s, CH=N), 7.90 (2H, d, J = 4.0 Hz, ArH), 7.03 (2H, d, J = 4.0 Hz, ArH), 6.89 (2H, q, J = 4.0 Hz, ArH), 6.71 (2H, q, J = 4.0 Hz, ArH), 1.90 (18H, s, PhᵗBuᵗBu’), 1.41 (18H, s, PhᵗBuᵗBu’).

\[
\text{Co}_2(\text{CO})_8 + \text{NaOH} \rightarrow \text{NaCo(CO)}_4
\]

NaCo(CO)₄. A procedure by Edgell et al. was followed.²⁵ In the glovebox, Co₂(CO)₈ (6.8 g, 20 mmol) was weighed into a schlenk tube. The schlenk tube was removed from the glovebox and NaOH pellets (5.6 g, 140 mmol) were added under the flow of N₂(g). THF (80 mL) was cannula transferred into the schlenk tube to dissolve the solids. The schlenk tube was wrapped in foil and the solution was stirred overnight at room temperature. The yellow solution was cannula filtered. The solvent was evaporated.
under reduced pressure and became a yellow oil, and upon further evaporation, a white solid. (3.5 g, 90% yield)

\[
\begin{align*}
\text{[(Salph)Al(THF)\textsubscript{2}]\textsuperscript{+}[Co(CO)\textsubscript{4}]\textsuperscript{-}} & \quad (1).
\end{align*}
\]

(Salph)AlCl (140.7 mg, 0.2 mmol), NaCo(CO)\textsubscript{4} (45.4 mg, 0.2 mmol), and THF (8 mL) were added to a schlenk tube under nitrogen. The dark red solution was stirred for 15 hours at room temperature, and was then cannula filtered to remove NaCl precipitate. The solvent was evaporated under reduced pressure to give a red solid. The crude product was crystallized by dissolving in approximately 5 mL THF and layering ~20 mL hexanes above the THF. The schlenk tube was wrapped in foil. After several hours, bright red crystals formed, which were filtered and rinsed with hexanes. (119.1 mg, 58 % yield) \textsuperscript{1}H NMR (C\textsubscript{6}D\textsubscript{6}, 400 MHz) \( \delta \)

9.41 (2H, s, \( \text{CH=N} \)), 8.21 (2H, q, \( J = 4.0 \text{ Hz, ArH} \)), 8.06 (2H, d, \( J = 4.0 \text{ Hz, ArH} \)), 7.91 (2H, d, \( J = 4.0 \text{ Hz, ArH} \)), 7.43 (2H, q, \( J = 4.0 \text{ Hz, ArH} \)), 3.22 (8H, m, THF), 1.68 (18H, s, Ph\textsuperscript{'Bu}Bu\textsuperscript{'}), 1.45 (18H, s, Ph\textsuperscript{'Bu}Bu\textsuperscript{'}), 0.86 (8H, m, THF).
2.4.6.2 [(Salph)Cr(THF)$_2$]$^+$/[Co(CO)$_4$]$^-$(2). This compound was provided by Dr. John Kramer (as synthesized in Org. Lett. 2006, 8, 3709-3712).

2.4.6.3 [(OEP)Cr(THF)$_2$]$^+$/[Co(CO)$_4$]$^-$(3). This compound was provided by Dr. Joe Schmidt (as synthesized in J. Am. Chem. Soc. 2005, 127, 11426-11435).
2.4.6.4 [(TPP)Cr(THF)$_2$]$^+$/[Co(CO)$_4$]$^-$ (4).

$\text{(ClTPP)H}_2$. 4-Chlorobenzaldehyde (28.1 g, 0.2 mmol) was dissolved in propionic acid (750 mL). Pyrrole (13.9 mg, 0.2 mmol) was added. The solution was refluxed for 3 hours. Upon cooling, a dark purple solid formed, which was isolated by filtration. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 8.91 (8H, s), 7.87 (8H, d, $J = 8.0$ Hz), 7.48 (8H, d, $J = 8.0$ Hz), -2.16 (2H, s, NH).

$\text{(ClTPP)AlCl}$. $\text{(ClTPP)H}_2$ (1.5 g, 2.0 mmol) was weighed into a schlenk tube. Approximately 110 mL of CH$_2$Cl$_2$ was cannula transferred into the schlenk tube to
dissolve the ligand. A 1 M solution of diethylaluminum chloride (2.2 mL, 2.2 mL) was added via syringe. The red solution was stirred for 3 hours, and then the solvent was removed under vacuum. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 9.09 (8H, s), 8.12 (8H, d, $J = 6.0$ Hz), 7.76 (8H, d, $J = 6.0$ Hz).

$\text{Cl}_2\text{AlCl}_2 + \text{NaCo(CO)}_4 \rightarrow \text{THF} \rightarrow \text{Cl}_2\text{TPP} \text{Co(CO)}_4^2\text{THF}_2^2 \text{Co(CO)}_4^- (4)$. $(\text{Cl}TPP)\text{AlCl}$ (1.0 g, 1.2 mmol) and NaCo(CO)$_4$ (262.5 mg, 1.4 mmol) were added to a schlenk tube under nitrogen. Approximately 100 mL of THF was added to dissolve the solids. The solution was stirred for 15 hours at room temperature, and then was cannula filtered to remove the NaCl precipitate. The solution was concentrated and the THF was layered with hexanes. After several days, diffusion of the hexanes through the THF resulted in purple crystals that were isolated and dried under vacuum. $^1$H NMR (THF-d$_8$, 300 MHz) $\delta$ 9.22 (8H, s), 8.21 (8H, d), 7.85 (8H, d), 3.61 (8H, m, THF), 1.77 (8H, m, THF).
2.4.6.5 [(iPr,iPrBDI)ZnOiPr] (5).

(iPr,iPrBDI)H. 2,4-pentanedione (5.0 mL, 48.7 mmol), 2,6-diisopropylaniline (22.1 mL, 117.1 mmol), and concentrated hydrochloric acid (4.0 mL) were refluxed in ethanol (150 mL) for 12 hours. Upon cooling, a white precipitate formed which was dissolved in dichloromethane. The organic layer was washed with saturated NaHCO₃ and saturated NaCl, dried over Na₂SO₄, filtered, and evaporated under reduced pressure to give a gray solid. The crude product was purified by recrystallization from acetonitrile to give white crystals. (7.2 g, 35% yield) ¹H NMR (CDCl₃, 300 MHz) δ 12.11 (1H, s, NH), 7.12 (6H, m, ArH), 4.87 (1H, s, CH), 3.11 (4H, m, J = 6.0 Hz, CHMe₂), 1.71 (6H, s, CH₃), 1.21 (12H, d, J = 6.0 Hz, CHMeMe’), 1.12 (12H, d, J = 9.0 Hz, CHMeMe’).

ZnCl₂ + 2 NaN(SiMe₃)₂ → Zn(N(SiMe₃)₂)₂

Zn(NTMS)₂. Zn(NTMS)₂ was prepared according to a literature procedure.²⁶
Zinc chloride (4.0 g, 29.3 mmol) and sodium bis(trimethylsilyl)amide (10.7 g, 58.6 mmol) were dissolved in diethyl ether (75 mL) and heated in a 50 °C oil bath for 3 hours under N₂. The colorless solution was cannula filtered and distilled to give a clear, colorless liquid. (8.3 g, 73% yield) ¹H NMR (C₆D₆, 400 MHz) δ 0.20 (36H, s, CH₃).
\[(\text{^{iPr}_{iPr}BDI})\text{ZnN(TMS)}_2\]. \(\text{Zn(NTMS}_2\) (2.4 mL, 6.0 mmol) was added to a solution of \((\text{^{iPr}_{iPr}BDI})\text{H}\) ligand (2.3 g, 5.4 mmol) in a schlenk tube under \(\text{N}_2\) in xylens (5.0 mL). The reaction was stirred at 150 °C for 4 days. White crystals formed upon cooling. The crystals were isolated and washed with hexanes while maintaining an air-free atmosphere. (1.7 g, 49% yield) \(^1\)H NMR (C\(_6\)D\(_6\), 300 MHz) \(\delta\) 7.13 (6H, m ArH), 4.85 (1H, s, CH), 3.24 (4H, m, \(J = 6.0\) Hz, C\(_{\text{CHMe_2}}\)), 1.66 (6H, s, CH\(_3\)), 1.37 (12H, d, \(J = 6.0\) Hz, CH\(_{\text{MeMe'}}\)), 1.12 (12H, d, \(J = 6.0\) Hz, CH\(_{\text{MeMe'}}\) ), -0.01 (18H, s, SiCH\(_3\)).

\[\text{[^{iPr}_{iPr}BDI]ZnO'Pr} \] (5). Isopropyl alcohol (78 µL, 1.0 mmol) was added dropwise to a solution of \((\text{^{iPr}_{iPr}BDI})\text{ZnN(TMS)}_2\) (687.8 mg, 1.1 mmol) in toluene (11 mL) in a schlenk tube under \(\text{N}_2\). The colorless solution was stirred for 15 hours at room temperature. The volatiles were evaporated under reduced pressure to give a white powder. The crude product was recrystallized from toluene and dried under vacuum. (309.8 mg, 56% yield) \(^1\)H NMR (C\(_6\)D\(_6\), 300 MHz) \(\delta\) 7.08 (6H, m ArH), 4.90 (1H, s, CH), 3.84 (1H, m, \(J = 6.0\) Hz, OCH\(_{\text{Me_2}}\)), 3.16 (4H, m, \(J = 6.0\) Hz, CH\(_{\text{Me_2}}\)), 1.63(6H, s, CH\(_3\)).
1.38 (12H, d, \( J = 6.0 \, \text{Hz}, \text{CHMeMe}' \)), 1.15 (12H, d, \( J = 6.0 \, \text{Hz}, \text{CHMeMe}' \)), 0.90 (6H, d, \( J = 6.0 \, \text{Hz}, \text{OCHMe}_2 \)).

2.4.6.6 Ethylzinc isopropoxide (6). A solution of isopropyl alcohol (1.7 mL, 22.5 mmol) in toluene (20 mL) was added to a solution of diethyl zinc (1 M in hexane, 25.0 mL, 25 mmol) at -78 °C in a schlenk tube under \( \text{N}_2 \). Stirred at -78 °C for 15 minutes and at room temperature for 3 hours. The solvent was evaporated under reduced pressure to give a white solid. The crude product was recrystallized from toluene to give a white powder. \( ^1\text{H} \) NMR (\( \text{C}_6\text{D}_6 \), 400 MHz) \( \delta \) 4.00 (1H, m, \( J = 8.0 \, \text{Hz}, \text{OCHMe}_2 \)), 1.55 (3H, t, \( J = 8.0 \, \text{Hz}, \text{CH}_3 \)), 1.20 (6H, d, \( J = 4.0 \, \text{Hz}, \text{OCHMe}_2 \)), 0.58 (2H, q, \( J = 8.0 \, \text{Hz}, \text{CH}_2 \)).
2.4.7.7 ClBu₂SnOSnBu₂OEt (7). Dibutyltin oxide (12.3 g, 49.4 mmol) and dibutyltin dichloride (5.0 g, 16.5 mmol) were refluxed in ethanol (160 mL) for 6 hours. The solvent was evaporated under reduced pressure to give a white powder. More ethanol was added to dissolve the solid, and the solution was refluxed for 12 hours. The ethanol was removed and the crude product was crystallized from hexanes. $^1$H NMR (C₆D₆, 400 MHz) δ 3.43 (4H, q, $J = 8.0$ Hz, OCH₂CH₃), 1.97 (16H, m, CH₂CH₂CH₂CH₃), 1.52 (32H, m, CH₂CH₂CH₂CH₃), 1.07 (12H, t, $J = 8.0$ Hz, CH₂CH₂CH₂CH₃), 0.99 (12H, t, $J = 8.0$ Hz, CH₂CH₂CH₂CH₃), 0.96 (6H, t, $J = 8.0$ Hz, OCH₂CH₃).
2.4.7.8 \([ i^\text{Pr}, E^\text{t} BDl^{CF3}] ZnOAc \) (8).

\[
\begin{array}{c}
\text{Et} \quad \text{H} \\
\text{N} \quad \text{Et} \\
\text{Et} \quad \text{MeO} \quad \text{OMe} \\
\end{array}
\rightarrow
\begin{array}{c}
\text{Et} \\
\text{N} \\
\text{Et}
\end{array}
\]

**2,6-diethyl-\( N \)-\( \text{propan-2-ylidene} \)aniline**

**2,6-Diethyl-\( N \)-\( \text{propan-2-ylidene} \)aniline.** 4 Å sieves and toluene (20 mL) were added to a schlenk tube. 2,6-diethylaniline (20 mL, 128.5 mmol) and 2,2-dimethoxypropane (78.8 mL, 624.6 mmol) were added to the solvent. The red solution was heated to 100 °C for 15 hours without stirring. The solution was cooled, the liquid was filtered away from the sieves, and the solvent was evaporated under reduced pressure. The crude product was distilled in a 75 °C oil bath under vacuum. (9.7 g, 40 % yield) \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \) 7.04 (2H, d, \( J = 4.0 \) Hz, ArH), 6.98 (1H, t, \( J = 4.0 \) Hz, ArH), 2.38 (2H, m, CH\(_2\)CH\(_3\)), 2.30 (2H, m, CH\(_2\)CH\(_3\)), 2.25 (3H, s, CH\(_3\)), 1.66 (3H, s, CH\(_3\)), 1.13 (6H, t, CH\(_2\)CH\(_3\)).

\[
\begin{array}{c}
\text{iPr} \\
\text{H} \\
\text{N} \\
\text{iPr}
\end{array}
\rightarrow
\begin{array}{c}
\text{iPr} \\
\text{F} \\
\text{O} \\
\text{H}
\end{array}
\]

\((E)-N-(2,6-\text{diisopropylphenyl})-2,2,2\text{-trifluoroethanimidoyl \underline{\text{chloride}}}\).

\((E)-N-(2,6-\text{Diisopropylphenyl})-2,2,2\text{-trifluoroethanimidoyl \underline{\text{chloride}}.}\)

Triphenylphosphine (31.7 g, 120.8 mmol), triethylamine (6.7 mL, 48.3 mmol), carbon tetrachloride (38.9 mL, 402.5 mmol), and trifluoroacetic acid (3.0 mL, 40.3 mmol) were
added to a round bottom flask. The flask was cooled to 0 °C and diisopropylaniline (9.1 mL, 48.3 mmol) dissolved in 11 mL CCl₄ was slowly added to the reaction mixture. The light red solution was refluxed in a 80 °C oil bath for 6 hours. While still warm, the solution was poured into 200 mL hexanes. After the solution completely cooled, the solid was filtered out and rinsed with cold hexanes. The solvent was evaporated under reduced pressure and the crude product was distilled in a 80 °C oil bath under vacuum. (8.3 g, 71 % yield) \(^1\)H NMR (CDCl₃, 300 MHz) \(\delta\) 7.20 (3H, m, ArH), 2.62 (2H, m, \(J = 6.0\) Hz, \(\text{CH}_3\)Me₂), 1.18 (12H, d, \(J = 6.0\) Hz, CH₃).

\[\text{(tPr,EtBDI}^{\text{CF}3}\text{)H} \]

Diisopropylamine (3.1 mL, 22.1 mmol) was dissolved in approximately 200 mL dry THF under nitrogen. The flask was cooled to 0 °C. A solution of \(n\)-butyl lithium (1.6 M in hexanes, 13.8 mL, 22.1 mmol) was added dropwise and stirred for 20 minutes. The solution was cooled to -78 °C. 2,6-Diethyl-N-(propan-2-ylidene)aniline (2.0 g, 10.5 mmol) was added and the solution was stirred for 20 more minutes, then warmed to 0 °C and stirred for 2 hours. \((E)\)-N-(2,6-diisopropylphenyl)-2,2,2-trifluoroethanimidoyl chloride was added at 0 °C and stirred for 2 hours. The reaction was quenched with 50 mL saturated NH₄Cl solution. The crude product was added to a separatory funnel with 100 mL water and 100 mL ethyl acetate. The organic
layer was isolated, dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The resulting yellow solid was recrystallized from acetonitrile. $^1$H NMR (C$_6$D$_6$, 400 MHz) $\delta$ 12.21 (1H, s, NH), 7.08 (6H, m, ArH), 5.38 (1H, s, CH), 3.26 (2H, m, $J = 8.0$ Hz, $CHMe_2$), 2.49 (2H, m, $J = 8.0$ Hz, $CH_2CH_3$), 2.38 (2H, m, $J = 8.0$ Hz, $CH_2CH_3$), 1.42 (3H, s, CH$_3$), 1.31 (6H, m, $J = 8.0$ Hz, $CH_2CH_3$), 1.08 (12H, m, $J = 8.0$ Hz, CH($CH_3$)$_2$).

[($^{iPr,Et}BDI^{CF_3}$)ZnOAc] (8). In a glovebox, ($^{iPr,Et}BDI^{CF_3}$)H (173.7 mg, 0.4 mmol) was added to a schlenk tube and dissolved in 7.5 mL toluene. A 1 M solution of diethylzinc (0.6 mL, 0.6 mmol) was added and the solution was stirred at 75 °C for 23 hours. The solvent and excess diethylzinc were evaporated under reduced pressure at 50 °C to give a yellow solid. The crude product was dissolved in 10 mL dry CH$_2$Cl$_2$ and cooled to 0 °C. Acetic acid (22 µL, 0.4 mmol) was added dropwise via a syringe. The solution was stirred overnight at room temperature. The solvent was removed under vacuum, and the crude product was recrystallized from toluene to give a white powder. $^1$H NMR (C$_6$D$_6$, 400 MHz) $\delta$ 7.10-6.96 (18H, m, ArH, monomer + dimer), 5.51 (1H, s, CH, monomer), 5.26 (2H, s, CH, dimer), 3.37 (2H, m, $J = 8.0$ Hz, $CHMe_2$, monomer), 3.26 (4H, m, $J = 8.0$ Hz, $CHMe_2$, dimer), 2.62 (4H, q, $J = 8.0$ Hz, $CH_2CH_3$, monomer),
2.38 (8H, q, $J = 8.0$ Hz, $CH_2CH_3$, dimer), 1.52-1.32 (54H, m, CH$_3$ and OCOCH$_3$ and CHMeMe’ and CHMeMe’, monomer + dimer), 1.17 (6H, t, $J = 8.0$ Hz, CH$_2CH_3$, monomer), 1.03 (6H, t, $J = 8.0$ Hz, CH$_2CH_3$, dimer), 0.86 (6H, t, $J = 8.0$ Hz, CH$_2CH_3$, dimer).
(E)-N-(2,6-dimethylphenyl)-2,2,2-trifluoroethanimidoyl chloride

2.4.7.9 [(Me,EtBDI(CN,CF3)] ZnOAc (9). This compound was provided by Dr. Ryan Jeske.
2.4.7.10 \((^{\text{Et,Et}}\text{BDI})\text{ZnOAc}\) (10).

\((^{\text{Et,Et}}\text{BDI})\text{H}\). 2,4-pentanedi酮 (5.0 mL, 48.7 mmol), 2,6-二乙基胺iline (19.3 mL, 116.9 mmol), and concentrated hydrochloric acid (4.0 mL) were refluxed in ethanol (150 mL) for 12 hours. Upon cooling, a white precipitate formed which was dissolved in dichloromethane (~100 mL). The organic layer was washed with saturated NaHCO\(_3\) and saturated NaCl, dried over Na\(_2\)SO\(_4\), filtered, and evaporated under reduced pressure to give a gray solid. The crude product was purified by recrystallization from acetonitrile to give white crystals. (8.4 g, 47% yield) \(^1\text{H NMR (C}_6\text{D}_6, 400 MHz)} \delta 12.37 (1H, s, NH), 7.08 (6H, m, ArH), 4.84 (1H, s, CH), 2.65 (4H, m, \(J = 8.0\) Hz, \(CH_2\text{CH}_3\)), 2.52 (4H, m, \(J = 8.0\) Hz, \(CH_2\text{CH}_3\)), 1.61 (6H, s, CH\(_3\)), 1.16 (12H, t, \(J = 8.0\) Hz, \(CH_2\text{CH}_3\)).

\([^{\text{Et,Et}}\text{BDI})\text{ZnOAc}\] (10). A solution of diethyl zinc (1 M in hexane, 14.1 mL, 14.1 mmol) was added to a solution of \((^{\text{Et,Et}}\text{BDI})\text{H}\) ligand (3.7 g, 9.4 mmol) in toluene (30 mL) in a schlenk tube under N\(_2\). The solution was heated to 85 °C with stirring for 15 hours. The volatiles were removed under vacuum to give a black liquid.
The black liquid was dissolved in ~40 mL dry hexanes and cooled to 0 °C. Acetic acid (0.54 mL, 9.4 mmol) was added dropwise to the solution. The solution was allowed to warm to room temperature and stirred for 15 hours. The solvent was evaporated under reduced pressure to give a white solid. The crude product was recrystallized from toluene and dried under vacuum. (2.2 g, 48% yield) $^1$H NMR (C$_6$D$_6$, 300 MHz) δ 7.06 (6H, m, ArH), 4.72 (1H, s, CH), 2.56 (8H, q, $J = 6.0$ Hz, CH$_2$CH$_3$), 1.56 (9H, s, CH$_3$ and OCOCH$_3$), 1.17 (12H, t, $J = 6.0$ Hz, CH$_2$CH$_3$).
2.4.7.11 [(iPr,iPrBDI)ZnOAc] (11). In the glovebox, the (iPr,iPrBDI)H ligand (4.0 g, 9.6 mmol), toluene (30 mL), and 1 M diethylzinc (14.3 mL, 14.3 mmol) were added to a schlenk tube. The solution was stirred at 85 °C for 15 hours. The solvent was evaporated under reduced pressure. The crude product was dissolved in ~40 mL dry hexanes and cooled to 0 °C. Acetic acid (0.55 mL, 9.6 mmol) was added dropwise and the solution was stirred at room temperature for 15 hours. The product was recrystallized from toluene and dried under vacuum. $^1$H NMR (C$_6$D$_6$, 300 MHz) δ 7.22 (18H, m, ArH, monomer + dimer), 5.01 (1H, s, CH, monomer), 4.72 (2H, s, CH, dimer), 3.37 (12H, m, $J$ = 6.0 Hz, $CHMe_2$, monomer + dimer), 1.80 (6H, s, OC(O)CH$_3$, dimer), 1.75 (6H, s, $CH_3$, monomer), 1.63 (12H, s, $CH_3$, dimer), 1.49 (12H, d, $J$ = 6.0 Hz, CHMeMe’, monomer), 1.44 (3H, s, OC(O)CH$_3$, monomer), 1.27 (24H, d, $J$ = 6.0 Hz, CHMeMe’, dimer), 1.22 (24H, d, $J$ = 6.0 Hz, CHMeMe’, monomer), 0.95 (12H, d, $J$ = 6.0 Hz, CHMeMe’, monomer).
References


(5) In contrast, the living copolymerization of aziridines and CO has been reported: Jia, L.; Sun, H.; Shay, J. T.; Allgeier, A. M.; Hanton, S. D. *J. Am. Chem. Soc.* 2002, 124, 7282-7283.


CHAPTER THREE

Carbonylation of Ethylene Oxide to Propiolactone:

A Facile Route to Poly(3-hydroxypropionate) and Acrylic Acid
3.1 Introduction

Acrylic acid (AA) production is approximately 3 million metric tons annually, and U.S. demand is predicted to grow at 4% per year.\(^1\) Acrylic acid and its ester derivatives are used in the manufacture of fibers, polymers, coatings, adhesives, and super absorbers.\(^2\) The current production method for AA is the oxidation of propylene in a two-step sequence (Scheme 3.1a);\(^3\) however, increasing propylene prices make alternate synthetic routes attractive.\(^4\) In the past, ethylene cyanohydrin, \(\beta\)-propiolactone (PL), acetylene, and acrylonitrile have been employed industrially for the synthesis of AA (Scheme 3.1b), but are not currently cost-competitive with propylene.\(^5\)

Other routes to AA have been reported but have not been used commercially. The oxidative carbonylation of ethylene using a palladium catalyst is a potential route to make AA, but the reaction displays low selectivities for the desired product (Scheme 3.1c).\(^6\) Propane oxidation with molecular oxygen provides AA in low yields and with poor selectivity.\(^3\) In addition, AA can be synthesized from the renewable feedstock lactic acid by a catalytic dehydration (Scheme 3.1c),\(^7\) yet the reaction suffers from low yields and requires high temperatures.\(^8\) Finally, a fermentation route can produce AA; however, the product is toxic to most potential host organisms and is produced in low yields.\(^9\) Alternatively, 3-hydroxypropionic acid made from a biosynthetic pathway can be derivatized to yield AA.\(^10\) Recombinant *Escherichia coli* has been reported to produce P3HP,\(^11\) which could be pyrolyzed to provide acrylic acid.\(^12\) However, fermentation routes are energy-intensive and require separation of the reaction product from the bacterial culture.\(^13\)
We hypothesized that AA could be prepared from ethylene oxide and carbon monoxide via β-propiolactone (Scheme 3.1c). PL could be synthesized from the high-yielding ring expansion of ethylene oxide using a bimetallic carbonylation catalyst. Furthermore, the ring-opening polymerization of PL results in P3HP, allowing for easy transport and handling of the solid polymer. P3HP can be thermolyzed to provide AA. Herein, we report the synthesis of acrylic acid from ethylene oxide and CO.
Scheme 3.1. Synthetic Routes to Acrylic Acid: a) Industrial Process; b) Historically-Used Methods; c) Proposed Alternate Methods

a) Propylene Oxidation: Current Method of Acrylic Acid Production

\[
\begin{align*}
\text{H}_2\text{C} = \text{CH} - \text{CH}_3 \xrightarrow{\text{O}_2 \text{cat.}} \text{H}_2\text{C} = \text{CH} - \text{CHO} \xrightarrow{1/2 \text{O}_2 \text{cat.}} \text{HO} - \text{C} = \text{O} \\
\end{align*}
\]

b) Previously Commercialized Methods of Acrylic Acid Production

Ethylene Cyanohydrin Dehydration and Hydrolysis:

\[
\begin{align*}
\text{O} \xrightarrow{\text{HCN}} \text{HO} - \text{C} = \text{O} \xrightarrow{\text{H}_2\text{SO}_4} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]

β-Propiolactone Thermolysis:

\[
\begin{align*}
\text{H}_2\text{C} = \text{C} = \text{O} + \text{HCHO} \xrightarrow{\text{Cu}} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]

Reppe Process:

\[
\begin{align*}
\text{HC} = \text{CH} + \text{CO} + \text{H}_2\text{O} \xrightarrow{\text{Ni(CO)}_4} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]

Acrylonitrile Hydrolysis:

\[
\begin{align*}
\text{H}_2\text{C} = \text{CH} - \text{CN} \xrightarrow{\text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{H}_2\text{C} = \text{CHCONH}_2 \cdot \text{H}_2\text{SO}_4 \xrightarrow{\text{ROH}} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]

c) Alternate Synthetic Routes to Acrylic Acid

Oxidative Carbonylation of Ethylene:

\[
\begin{align*}
\text{H}_2\text{C} = \text{CH}_2 + \text{CO} + 0.5 \text{O}_2 \xrightarrow{\text{cat.}} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]

Lactic Acid Dehydration:

\[
\begin{align*}
\text{OH} \xrightarrow{-\text{H}_2\text{O}} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]

EO Carbonylation, PL Polymerization, and P3HP Pyrolysis:

\[
\begin{align*}
\text{CO} \xrightarrow{\text{cat.}} \text{C} = \text{O} - \text{H}_2\text{O} \xrightarrow{[\text{C}]^+ [\text{A}]^-} \text{C} = \text{O} - \text{H}_2\text{O} \\
\end{align*}
\]
3.2 Results and Discussion

Initially, we examined the carbonylation of ethylene oxide, the first step of the reaction sequence. As a side reaction, EO can doubly react with CO to produce succinic anhydride (SA), which has been shown to retard the polymerization of PL.\textsuperscript{14} Therefore, efforts were undertaken to find reaction conditions that suppress the formation of SA (Table 3.1). The mechanism of double carbonylation is shown in Figure 3.1.\textsuperscript{15}

![Mechanism of the double carbonylation of an epoxide to an anhydride](image)

**Figure 3.1.** Mechanism of the double carbonylation of an epoxide to an anhydride (as published in *J. Am. Chem. Soc.* 2007, 129, 4948-4960.)

We have reported several well-defined bimetallic catalysts of the form [Lewis acid][Co(CO)\textsubscript{4}]\textsuperscript{-} for the carbonylation of epoxides, including [(salph)Al(THF)\textsubscript{2}][Co(CO)\textsubscript{4}]\textsuperscript{-} (1; salph = \textit{N,N’}-bis(3,5-di-\textit{t}ert-butylsalicylidene)-1,2-}
The carbonylation reaction catalyzed by 1 occurred with 44% conversion of EO after 8 hours (Table 3.1, entry 1). 

\[ \text{[(OEP)Cr(THF)}_2]\text{[Co(CO)}_4]\text{]}^- \] (2; OEP = octaethylporphyrinato), showed higher activity, but left 26% of EO unreacted in the same reaction time (entry 2). The reaction in the presence of \[ \text{[(ClTPP)Al(THF)}_2]\text{[Co(CO)}_4]\text{]}^- \] (3; ClTPP = meso-tetra(4-chlorophenyl)porphyrinato) occurred with full conversion of EO and gave a mixture of PL and SA (entry 3). Based on mechanistic studies, we expected solvent choice to affect the amount of double carbonylation, and therefore optimized the reaction conditions to prevent SA formation. Two additional solvents, 1,4-dioxane and tetrahydrofuran, were screened. As shown in entry 4, dioxane favors SA synthesis, while THF prevents the reaction of PL to SA (entry 5). This result is consistent with solvent studies on the carbonylation of propylene oxide, where the rate of epoxide carbonylation was found to be fastest in strongly donating solvents. The rate of lactone carbonylation was found to be fastest in non-donating solvents; therefore, a solvent with intermediate donicity such as 1,4-dioxane promotes the double carbonylation of ethylene oxide to succinic anhydride. By using a solvent with strong donicity such as THF, we are able to cleanly obtain the lactone product. Decreased catalyst loadings demonstrate the high activity of complex 3 to make PL without further reaction to SA (entries 6 and 7).
Table 3.1. Carbonylation of Ethylene Oxide to β-Propiolactone

[ balanced Eqn]

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst (mol %)</th>
<th>solvent</th>
<th>lactone</th>
<th>anhydride</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 (0.1)</td>
<td>toluene</td>
<td>44&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;1</td>
</tr>
<tr>
<td>2</td>
<td>2 (0.1)</td>
<td>toluene</td>
<td>74&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;1</td>
</tr>
<tr>
<td>3</td>
<td>3 (0.1)</td>
<td>toluene</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>3 (0.1)</td>
<td>dioxane</td>
<td>43</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>3 (0.1)</td>
<td>THF</td>
<td>&gt;99</td>
<td>&lt;1</td>
</tr>
<tr>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3 (0.05)</td>
<td>THF</td>
<td>&gt;99</td>
<td>&lt;1</td>
</tr>
<tr>
<td>7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3 (0.02)</td>
<td>THF</td>
<td>96&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: [epoxide] = 2.0 M in solvent, 850 psi CO, 8 h, 60 °C. Product distribution determined by <sup>1</sup>H NMR spectroscopy of crude reaction. <sup>b</sup> Remainder is starting epoxide. <sup>c</sup> 12 h. <sup>d</sup> 24 h.
After optimizing the synthesis of PL, the ring-opening polymerization of the lactone was examined. Although high conversion of PL to P3HP was the primary goal, we sought catalysts that would provide high molecular-weight polyester with narrow dispersities, as P3HP is a biodegradable and biocompatible material\textsuperscript{19} with excellent mechanical properties.\textsuperscript{20} Various initiators, including (tetraphenylporphinato)aluminum chloride,\textsuperscript{21} alkali-metal alkoxides,\textsuperscript{22} alkali-metal carboxylates,\textsuperscript{23} and organolanthanides\textsuperscript{24} have been used for the ring-opening polymerization of PL. Propiolactone undergoes homo-polymerization to high molecular weights, but with broad molecular weight distributions.\textsuperscript{25} In addition to the ring-opening polymerization of PL, P3HP has been synthesized through the polymerization of macrocyclic esters with a zinc alkoxide catalyst.\textsuperscript{26} However, the synthesis of the macrocyclic esters from 3-hydroxypropionic acid proceeds in low yields. Another route to P3HP is the copolymerization of ethylene oxide and carbon monoxide; however, this copolymerization occurs in low conversions to produce low-molecular weight materials.\textsuperscript{27}

Previous reports of polymerizing PL with alkali-metal acetate salts led us to examine organic ionic compounds for the lactone ring-opening reaction. Organocatalysts have received attention as valuable metal-free synthetic tools to make biocompatible polymers.\textsuperscript{28} For example, small molecules such as 4-(dimethylamino)pyridine, tertiary phosphines, \textit{N}-heterocyclic carbenes, thiourea-amines, triazabicyclodecene, and phosphazene bases have been used to activate cyclic ester monomers for ring-opening reactions.\textsuperscript{29} The reactions of tetraalkylammonium pivalates with various lactones, including PL, have also been reported.\textsuperscript{30}
We hypothesized that nucleophilic anions paired with base-stable cations would be effective catalysts for the ring-opening polymerization of PL. Initiators containing carboxylate anions were chosen to best mimic the propagating species of the growing polymer chain. Bis(triphenylphosphine)iminium ([PPN]+) and the more soluble phosphonium and phosphazenium salts were initially tested. [PPN]+Cl has been shown to be an active cocatalyst for the copolymerization of propylene oxide and carbon dioxide, and we proposed that [PPN]+ acetate (4) might catalyze the ring opening of PL. Phosphonium salts have been used in the anionic ring-opening polymerization of propylene oxide and phosphazenium salts have been proven effective for the ring-opening reactions of epoxides. Based on prior results in our group where the use of more base-stable and soluble ionic cocatalysts led to improved activity in the polymerization of epoxides, we believed that similar complexes should be advantageous in the polymerization of PL. We tested the reactivity of PL with a series of ionic compounds containing carboxylate anions and base-stable, non-coordinating cations.

We initially studied the reaction of PL with catalysts of the form [C][OAc] to investigate the effect of various cations (Table 3.2). Sodium acetate and potassium acetate were inactive for the ring opening of PL in THF after 2 h at high concentrations (entries 1 and 2). The addition of dibenzo-18-crown-6 ether to potassium acetate resulted in a slight increase in activity for the ring-opening transformation, but gave a broad molecular weight distribution, most likely due to slow initiation (entry 3). Tetrabutylammonium acetate displayed low activity (entry 4), which may be a result of the ionic compound’s instability to base. Furthermore, ammonium salts are known to be difficult to dry. [PPN][OAc] (4) showed high activity, and produced high-molecular
weight polymer (entry 5). Phosphonium and phosphazenium salts 5 and 6 both displayed high activities (entries 6 and 7) similar to complex 4. These data suggest that other catalysts containing an acetate ion and a stable organic cation might also exhibit activity for the ring-opening polymerization reaction of PL.
Table 3.2. Screening of Acetate-Based Ionic Catalysts for the Polymerization of PL: Effect of Cation

![Diagram of polymerization]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>time (h)</th>
<th>conv(^b) (%)</th>
<th>(M_n) (kDa)(^c)</th>
<th>(M_w/M_n)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^d)</td>
<td>Na(^+)[OAc(^-)]</td>
<td>2</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2(^d)</td>
<td>K(^+)[OAc(^-)]</td>
<td>2</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3(^e)</td>
<td>K(^+)[OAc(^-)]-crown ether</td>
<td>2</td>
<td>15</td>
<td>17.3</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>[(Bu)(_4)N(^+)][OAc(^-)]</td>
<td>2</td>
<td>29</td>
<td>26.0</td>
<td>1.5</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>1</td>
<td>&gt;99</td>
<td>66.2</td>
<td>1.2</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>1</td>
<td>&gt;99</td>
<td>63.0</td>
<td>1.1</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>1</td>
<td>&gt;99</td>
<td>66.3</td>
<td>1.1</td>
</tr>
</tbody>
</table>

\(^a\) General reaction conditions: [PL]:[catalyst] = 1000:1 and [PL] = 1.0 M in THF, \(T_{rxn} = 24^\circ\text{C}\), quenched by addition of acetic acid. \(^b\) Determined by \(^1\text{H}\) NMR spectroscopy of crude reaction mixture. \(^c\) Determined by GPC calibrated with polystyrene standards in CHCl\(_3\) at 30 \(^\circ\text{C}\). \(^d\) Reaction conditions: [PL] = 3.8 M in THF. \(^e\) Reaction conditions: [PL]:[K[OAc]-dibenzo-18-crown-6 ether complex] = 1000:1.
Given the improved solubility of the phosphazenium acetate complex and the reported base stability of the phosphazenium cation, a series of phosphazenium salts with various anions were investigated as catalysts for the ring-opening polymerization of PL (Table 3.3). Complex 7 showed good activity, although results were very similar to catalyst 4 (entry 1). Chloride-containing catalyst 8a resulted in low conversion to P3HP, even after longer reaction times (entry 2). The more sterically bulky triphenylacetate anion (8b) displayed a longer reaction time for the ring-opening polymerization of β-propiolactone and produced a lower molecular weight material (entry 3). Use of a benzoate anion (8c) resulted in good activity, whereas the more electron-deficient perfluorobenzoate anion (8d) increased the reaction time and resulted in polymer with a decreased molecular weight and broader molecular weight distribution (entries 4 and 5). Complex 8e, which contains a bulky pivalate anion, resulted in the highest activity for PL polymerization (entry 6). Decreasing the amount of 8e led to an increase in the molecular weight of the P3HP (entries 7 and 8). These results suggest that the most active organic ionic catalysts contain moderately nucleophilic anions with moderate steric bulk. Complex 8e was also tested for the ring-opening polymerization of a bulkier substrate, methyl-substituted β-butyrolactone monomer, but low activity was observed (entry 9).
Table 3.3. Screening of Ionic Catalysts for the Polymerization of PL: Effect of Anion$^a$

![Chemical structure](image)

Table:

<table>
<thead>
<tr>
<th>entry</th>
<th>monomer</th>
<th>catalyst</th>
<th>time (h)</th>
<th>conv$^b$ (%)</th>
<th>$M_n$ (kDa)$^c$</th>
<th>$M_w/M_n$</th>
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<td>7</td>
<td>1</td>
<td>&gt;99</td>
<td>59.4</td>
<td>1.1</td>
</tr>
<tr>
<td>2</td>
<td>PL</td>
<td>8a</td>
<td>2</td>
<td>32</td>
<td>3.5</td>
<td>1.2</td>
</tr>
<tr>
<td>3</td>
<td>PL</td>
<td>8b</td>
<td>2</td>
<td>&gt;99</td>
<td>40.7</td>
<td>1.2</td>
</tr>
<tr>
<td>4</td>
<td>PL</td>
<td>8c</td>
<td>1</td>
<td>&gt;99</td>
<td>64.1</td>
<td>1.1</td>
</tr>
<tr>
<td>5</td>
<td>PL</td>
<td>8d</td>
<td>2</td>
<td>&gt;99</td>
<td>33.5</td>
<td>1.3</td>
</tr>
<tr>
<td>6</td>
<td>PL</td>
<td>8e</td>
<td>0.5</td>
<td>&gt;99</td>
<td>67.3</td>
<td>1.1</td>
</tr>
<tr>
<td>7$^d$</td>
<td>PL</td>
<td>8e</td>
<td>2</td>
<td>&gt;99</td>
<td>105.8</td>
<td>1.3</td>
</tr>
<tr>
<td>8$^e$</td>
<td>PL</td>
<td>8e</td>
<td>5</td>
<td>&gt;99</td>
<td>135.0</td>
<td>1.3</td>
</tr>
<tr>
<td>9</td>
<td>BBL</td>
<td>8e</td>
<td>24</td>
<td>27</td>
<td>20.9</td>
<td>1.1</td>
</tr>
</tbody>
</table>

$^a$ General reaction conditions: [lactone]:[catalyst] = 1000:1 and [lactone] = 1.0 M in THF, $T_{rxn} = 24 ^\circ C$, quenched by addition of acetic acid. $^b$ Determined by $^1$H NMR spectroscopy of crude reaction mixture. $^c$ Determined by GPC calibrated with polystyrene standards in CHCl$_3$ at 30 $^\circ C$. $^d$ Reaction conditions: [PL]:[catalyst] = 2000:1. $^e$ Reaction conditions: [PL]:[catalyst] = 4000:1.
The reaction between PL and phosphazenium chloride 8a was examined in more detail using MALDI-TOF-MS. A MALDI mass spectrum of the low molecular weight polyester formed in entry 2 was obtained (Figure 3.2). No chains with chloride end groups were seen; the structure was either a cyclic polymer (Figure 3.3a) or a polymer with unsaturated end groups (Figure 3.3b). Chloride is a labile end group that can easily be substituted or eliminated. Upon close inspection of the $^1$H NMR spectrum, peaks in the alkene region were observed, suggesting the polymer had double bond end groups (Figure 3.3b). In contrast to the chloride initiator, the use of phosphazenium acetate (6) led to polymer chains containing acetate end groups (Figure 3.4 and Figure 3.5).

**Figure 3.2** MALDI-TOF-MS Spectra of the Na$^+$ adducts of poly(3-hydroxypropionate) synthesized using 8a (Table 3.3, Entry 2).
Figure 3.3. (a) Cyclic P3HP and (b) P3HP with an unsaturated end group made with catalyst 8a

Figure 3.4 MALDI-TOF-MS Spectra of the Na$^+$ adducts of poly(3-hydroxypropionate) synthesized using 6 (Table 3.2, Entry 7).

Figure 3.5. P3HP with acetate end group made by catalyst 6.
Finally, we pyrolyzed P3HP to synthesize AA. The thermolysis of P3HP is known in the literature.\textsuperscript{38} The mechanism of chain scission is shown in Scheme 3.2.\textsuperscript{38d} The ester bond breaks apart via a cyclic transition state to produce a fragment with a carboxylic acid end group and a fragment with a double bond end group. The polymer chain containing the carboxylic acid end group can further break apart to form acrylic acid.

**Scheme 3.2** Chain scission of P3HP: a) Ester cleavage to form fragments with carboxylic acid and double bond end groups and b) Formation of acrylic acid

3.3 Conclusion

In conclusion, we developed the synthesis of acrylic acid from the inexpensive feedstocks ethylene oxide and carbon monoxide. The synthesis was comprised of the carbonylation of EO to make β-propiolactone, the ring-opening polymerization of PL with organic ionic catalysts to make P3HP, and the thermolysis of the polyester to give AA. The carbonylation and ring-opening polymerization may be conducted in a one-pot synthesis or separately. This represents a new, non-propylene based route to the commodity chemical acrylic acid.

3.4 Experimental Section
3.4.1 General Considerations

All manipulations of air and water sensitive compounds were carried out under dry nitrogen using a Braun Labmaster glovebox or standard Schlenk line techniques. $^1$H NMR spectra were recorded on Varian Mercury ($^1$H, 300 MHz) or Varian INOVA 400 ($^1$H, 400 MHz) spectrometers and referenced with residual non-deuterated solvent shifts (CHCl$_3$ = 7.24 ppm). In situ IR data were collected using a 100-mL Parr stainless steel high-pressure reactor modified for use with a Mettler-Toledo ReactIR 4000 Reaction Analysis System fitted with a Sentinel DiComp high-pressure probe, and analyzed with ReactIR software version 2.21.

3.4.2 Materials

Tetrahydrofuran was dried by passing over columns of alumina and degassed via repetitive freeze-pump-thaw cycles. Ethylene oxide was dried over n-butyllithium, vacuum transferred, and degassed via repetitive freeze-pump-thaw cycles before use. β-Propiolactone and β-butyrolactone were synthesized from the carbonylation of ethylene oxide and propylene oxide, respectively, as described in section 3.4.4. Both lactones were dried over calcium hydride and vacuum transferred before use. All other reagents were purchased from commercial sources and used as received. The catalysts [(salph)Al(THF)$_2$][Co(CO)$_4$] $^-$ (salph = N,N’-bis(3,5-di-tert-butylsalicylidene)-1,2-phenylenediamine) (1),$^{39}$ [(OEP)Cr(THF)$_2$][Co(CO)$_4$] $^-$ (OEP = octaethylporphyrinato) (2),$^{40}$ and [(CITPP)Al(THF)$_2$][Co(CO)$_4$] $^-$ (CITPP = meso-tetra(4-chlorophenyl)porphyrinato) (3)$^{41}$ were synthesized according to literature procedures. Bis(triphenylphosphine)iminium acetate ([PPN]$^+$[OAc]$^-$, 4)$^{42}$ was synthesized according
to a published procedure as described in section 3.4.6. Bis(triphenylphosphine)iminium pivalate ([PPN][OPiv], 7)\textsuperscript{43} was prepared according to a literature procedure. Tetrakis[cyclohexyl(methyl)amino]phosphonium acetate (5), tetrakis[(tri-1-pyrrolidinylphosphoranylidene)amino]phosphonium acetate (6), tetrakis[(tri-1-pyrrolidinylphosphoranylidene)amino]phosphonium chloride (8a), tetrakis[(tri-1-pyrrolidinylphosphoranylidene)amino]phosphonium triphenylacetate (8b), tetrakis[(tri-1-pyrrolidinylphosphoranylidene)amino]phosphonium benzoate (8c), tetrakis[(tri-1-pyrrolidinylphosphoranylidene)amino]phosphonium pentafluorobenzoate (8d), and tetrakis[(tri-1-pyrrolidinylphosphoranylidene)amino]phosphonium pivalate (8e) were prepared by a procedure reported by Coates and coworkers.\textsuperscript{44} The potassium acetate-dibenzo-18-crown-6 ether complex was synthesized following a published procedure, as described in section 3.4.5.\textsuperscript{45}

### 3.4.3 Polymer Characterization

Gel permeation chromatography (GPC) analyses were carried out using a Waters M515 pump, a Waters 717+ Autosampler, a Waters 2410 differential refractive index detector, and three 5 μm PSS SDV columns (Polymer Standards Service; 50 Å, 500 Å, and Linear M porosities) in series. The GPC columns were eluted with chloroform at 30 °C at 1 mL/min and were calibrated using 20 monodisperse polystyrene standards.

### 3.4.4 MALDI-TOF-MS Analysis

MALDI analysis was performed on a MALDI micro MX. The P3HP samples were dissolved in CHCl\textsubscript{3} (5 mg/mL). Sodium iodide dissolved in methanol (2 mg/mL)
was the cationization agent. The matrix was dihydroxybenzoic acid (DHB) dissolved in THF (2.5 mg DHB/100 µL THF). The matrix, polymer, and salt were mixed together in a 100:10:1 ratio, respectively. The solution was hand spotted on a stainless steel MALDI target and allowed to dry. The spectra were recorded in the positive ion reflectron mode.

3.4.5 Synthesis of β-Propiolactone

General Procedure for EO Carbonylation (Table 1, Entry 5)

Under nitrogen, a 100-mL Parr high-pressure reactor was charged with catalyst 3 (110.5 mg, 101.0 µmol), ethylene oxide (4.41 g, 100.1 mmol), and 40 mL THF. The reactor was pressured to 850 psi CO followed by rapid stirring and heating to 60 °C. After the appropriate time, the reactor was cooled to room temperature, and slowly vented. β-propiolactone was isolated by vacuum transfer and dried over calcium hydride and vacuum transferred before use. The spectrum is shown in Figure 3.6.
3.4.6 Synthesis of Potassium Acetate-Dibenzo-18-Crown-6 Ether Complex

Potassium acetate (1.0 g, 10.0 mmol) and dibenzo-18-crown-6 ether (3.6 g, 10.0 mmol) were weighed into a schlenk tube. Dry methanol was added until the solids dissolved (~50 mL). The solution was stirred at room temperature for 15 hours, and then the solvent was evaporated under reduced pressure to give a white solid. The product was dried under vacuum at 80 °C for 15 hours. $^1$H NMR (C$_6$D$_6$, 300 MHz) δ 6.81 (4H, m, ArH), 6.66 (4H, m, ArH), 3.86 (8H, m, CH$_2$CH$_2$), 3.75 (8H, m, CH$_2$CH$_2$), 2.61 (3H, s,
COCH₃). As seen in the ¹H NMR (Figure 3.7), the integration value for the acetate peak at 2.61 ppm was significantly lower than expected. Heating the sample to 80 °C resulted in the disappearance of the acetate peak at 2.61 ppm (Figure 3.8). When potassium acetate (1.0 g, 10.0 mmol) and dibenzo-18-crown-6 ether (1.2 g, 3.3 mmol) were mixed in a 3:1 mol ratio and stirred in dry methanol, the integration of the acetate peak was still considerably less than expected value of 3 (Figure 3.9).

Figure 3.7. ¹H NMR spectrum of reaction product of potassium acetate with dibenzo-18-crown-6 ether (1:1 mol ratio) in C₆D₆ at room temperature
Figure 3.8. $^1$H NMR spectrum of reaction product of potassium acetate with dibenzo-18-crown-6 ether (1:1 mol ratio) in C$_6$D$_6$ at 80 °C
3.4.7 Synthesis of Bis(triphenylphosphine)iminium acetate ([PPN][OAc]) (4)

\[
\begin{align*}
\left[ \begin{array}{c}
\text{Ph} \\
\text{Ph} = \text{N} = \text{Ph} \\
\text{Ph} \\
\text{Ph}
\end{array} \right]^{+} \text{Cl}^{-} + \left[ \begin{array}{c}
\text{Ph} \\
\text{Ph} = \text{N} = \text{Ph} \\
\text{Ph} \\
\text{Ph}
\end{array} \right]^{-} \rightarrow \left[ \begin{array}{c}
\text{Ph} \\
\text{Ph} = \text{N} = \text{Ph} \\
\text{Ph} \\
\text{Ph}
\end{array} \right]^{+} \left[ \begin{array}{c}
\text{H}_{3}\text{C} \\
\text{O}
\end{array} \right]^{-}
\end{align*}
\]

A solution of sodium acetate (5.7 g, 69.7 mmol) in 8 mL H₂O was added to a solution of bis(triphenylphosphoranylidene)ammonium chloride (4.0 g, 7.0 mmol) in 20
mL H₂O. The solution was brought to a boil with stirring, and then allowed to cool. A white solid formed upon cooling. The solid was isolated by filtration, washed with cold H₂O, and dried in vacuo at 70 °C. ¹H NMR (CDCl₃, 300 MHz) δ 7.67 (5H, m, ArH), 7.47 (25H, m, ArH), 1.99 (3H, s, [OCH₃]).

3.4.8 Polymerization of β-Propiolactone

General Procedure for Propiolactone (PL) Polymerization (Table 2, Entry 5)

Under a nitrogen atmosphere, complex 4 (4.0 mg, 6.7 µmol), 6.7 mL tetrahydrofuran, and PL (0.48 g, 6.7 mmol) were added to a 20 mL vial containing a teflon-coated stir bar. The vial was sealed with a teflon-lined cap and allowed to stir at room temperature. After the appropriate time, the reaction was quenched by the addition of acetic acid. A small aliquot was removed for crude ¹H NMR analysis to determine monomer conversion. The viscous reaction mixture was then dissolved in dichloromethane and precipitated into an excess of hexane. The polymer was collected and dried in vacuo to give a solid in 90% recovery by weight. The ¹H NMR spectrum is shown in Figure 3.10.
Figure 3.10. $^1$H NMR spectrum of crude reaction mixture (Table 2, entry 5) showing complete conversion of propiolactone to poly(3-hydroxypropionate) in CDCl$_3$. 
3.4.9 In situ IR Spectroscopy of Propiolactone (PL) Polymerization (Table 2, Entry 5)

Propiolactone was added to a Parr reactor charged with [PPN][OAc] (4) and THF and the reaction was monitored by FTIR (Figure 3.11).

**Figure 3.11.** In situ IR spectrum of propiolactone polymerization
3.4.10 Mechanism of Ring Opening

The ring opening of β-propiolactone can proceed by cleavage of the acyl-oxygen bond or the alkyl-oxygen bond. Many papers have been published debating the mechanism of PL ring opening with alkali metal alkoxides. Hofman et al. examined the reaction of PL with potassium acetate in DMF (dimethylformamide) and claimed carboxylate anions were the propagating species. To study the regiochemistry of PL ring opening with 4, an oligomerization of PL ([PL]/[PPN][OAc] \(\approx 20\)) was carried out and the endgroups were analyzed by \(^1\)H NMR. Benzyl bromide was added as an electrophilic quenching agent to give a diagnostic endgroup in the \(^1\)H NMR spectrum. In an acyl-oxygen bond opening, the benzyl bromide-quenched polymer chains would be terminated by an anhydride and benzyl ether group (Scheme 3.3, path a). In an alkyl-oxygen bond opening, the benzyl bromide-quenched polymer chain endgroups would be an ester and benzyl ester (Scheme 3.3, path b). The oligomerization resulted in ester and benzyl ester endgroups, as observed by \(^1\)H NMR (Figure 3.12), indicative of alkyl-oxygen bond cleavage as the event for polymerization initiation and propagation.

**Scheme 3.3.** Possible routes for the ring-opening polymerization of propiolactone
Figure 3.12. $^1$H NMR spectrum of the product of the oligomerization of PL in CDCl$_3$. Residual [PPN]$^+$ is seen in the 7.3-7.7 ppm region.
References


(37) The polyester P3HP could be made in high yields from EO via a one-pot carbonylative polymerization using catalyst 3 in THF followed by injection of 4, but low molecular weight materials were obtained. Therefore, the PL monomer was distilled prior to ring-opening polymerization. See Appendix A for experimental details.


(47) See 46(a)
APPENDIX A

Additional Routes to Poly(3-hydroxypropionate):

(A) Ring-Opening Polymerization of β-Propiolactone with (BDI)Zn Catalysts

and (B) One-Pot Carbonylative Polymerization of Ethylene Oxide to P3HP
A.1 Ring-Opening Polymerization of β-Propiolactone with (BDI)Zn Catalysts

In Chapter 3, organic ionic compounds were found to be highly active for the ring-opening polymerization of β-propiolactone to poly(3-hydroxypropionate). Other catalysts were also examined for the ring-opening polymerization; the results of the reactions of PL with several (BDI)Zn complexes are summarized in Table A.1. Complexes 1 and 2 both contain acetate initiators and show very low activities for the polymerization of PL. After 70 minutes, the reactions with 1 and 2 resulted in 3% and 11% conversion of PL, respectively (entries 1 and 2). The ring-opening polymerization of PL with catalyst 3 occurred with 99% conversion of PL after 5 minutes (entry 3). In the same amount of time, complexes 4 and 5 showed no activity for the polymerization (entries 4 and 5). Therefore, the symmetrical, all isopropyl BDI ligand with isopropoxide as an initiator is a very active catalyst for the ring-opening polymerization of PL. However, it doesn’t offer the advantages of “metal-free” catalysts that the organic ionic compounds do.
Table A.1. Reactions of β-propiolactone with (BDI)Zn complexes

![Reaction Scheme]

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>[lactone]/[Zn]</th>
<th>temp (°C)</th>
<th>time (min)</th>
<th>conversion (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>200</td>
<td>24</td>
<td>70</td>
<td>3</td>
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<tr>
<td>2</td>
<td>2</td>
<td>200</td>
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<td>70</td>
<td>11</td>
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<tr>
<td>3</td>
<td>3</td>
<td>200</td>
<td>24</td>
<td>5</td>
<td>&gt;99</td>
</tr>
<tr>
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<td>4</td>
<td>200</td>
<td>24</td>
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</tr>
<tr>
<td>5</td>
<td>5</td>
<td>200</td>
<td>24</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup> All polymerizations run in benzene-<i>d</i><sub>6</sub>; [lactone] = 3.8 M.  <sup>b</sup> As determined by the integration of <sup>1</sup>H NMR methylene resonances of PL and PHP; polymerizations were quenched with acetic acid.

A.2 One-Pot Carbonylative Polymerization of Ethylene Oxide to P3HP

Attempts were made to synthesize P3HP in a one-pot reaction from ethylene oxide and carbon monoxide. Although the polyester could be made in high conversions, the molecular weights of the materials formed were low. EO was carbonylated with 0.05
mol% [(CITPP)Al(THF)$_2$][Co(CO)$_4$] in a Parr reactor. After the carbonylation, the Parr reactor was vented to release the CO pressure and 0.5 mol% (iPr,iPrBDI)ZnO'iPr dissolved in THF was injected into the reactor. The conversion of PL to P3HP was high (97%), but the $M_n$ of the polymer was 9,000 g/mol and the molecular weight distribution was broad (Scheme A.1a). The catalyst loading was decreased in an effort to increase the molecular weight of the polymer formed. However, using 0.025 mol% of [(CITPP)Al(THF)$_2$][Co(CO)$_4$] and 0.25 mol % of (iPr,iPrBDI)ZnO'iPr gave a polymer with a lower molecular weight ($M_n = 5,700$ g/mol) in 92% conversion (Scheme A.1b). The molecular weight was significantly lower than the theoretical molecular weight; in addition, the molecular weight distribution was extremely broad (PDI = 5.4).

**Scheme A.1.** Modified one-pot carbonylative polymerization of ethylene oxide to P3HP with (BDI)ZnO'iPr as the polymerization catalyst.
The modified one-pot procedure with organic ionic catalysts for the polymerization step was also studied. EO was carbonylated with 0.05 mol% \([\text{CITPP} \text{Al(THF)}_2]^+[\text{Co(CO)}_4]^+\), after which 0.5 mol% \([\text{PPN}]^+\text{[OAc]}^-\) dissolved in dichloromethane was injected into the Parr reactor. The reaction proceeded in 86% conversion, and made P3HP with a molecular weight of 6,900 g/mol and a PDI of 1.4 (Scheme A.2a). Decreasing the catalyst loading to 0.025 mol% \([(\text{CITPP})\text{Al(THF)}_2]^+[\text{Co(CO)}_4]^+\) and 0.25 mol% of \([\text{PPN}]^+\text{[OAc]}^-\) gave a polymer with a molecular weight of 14,600 g/mol in 80% conversion (Scheme A.2b). This P3HP sample \((M_n = 14,600 \text{ g/mol})\) was the highest molecular weight sample synthesized in a one-pot procedure. Phosphazenium acetate dissolved in THF was also used as the polymerization catalyst in a modified one-pot synthesis, but made low molecular-weight polyester as well. The highest molecular weight polymer made in a one-pot process was significantly lower than the P3HP made from distilled PL using the same catalysts \((M_n = 135,000 \text{ g/mol})\). In order to make high molecular weight P3HP, the PL monomer had to be purified by distillation. This is most likely due to trace succinic anhydride in the crude reaction mixture, made from the double carbonylation of ethylene oxide side reaction. Control reactions showed that the presence of succinic anhydride inhibited the polymerization of PL. Even though anhydride was not detected by \(^1\text{H NMR}\), trace amounts (< 48 ppm) were seen by gas chromatography, even at low (50%) conversions of EO. If the P3HP will be pyrolyzed to synthesize acrylic acid, the properties of the polymer are extraneous, and the P3HP can be made in high yields using a one-pot route from ethylene oxide and carbon monoxide.
Scheme A.2. Modified one-pot carbonylative polymerization of ethylene oxide to P3HP with [PPN][OAc] as the polymerization catalyst

A.3 Experimental Section

A.3.1 General Considerations

All manipulations of air and water sensitive compounds were carried out under dry nitrogen using a Braun Labmaster glovebox or standard Schlenk line techniques. $^1$H NMR spectra were recorded on Varian Mercury ($^1$H, 300 MHz) or Varian INOVA 400 ($^1$H, 400 MHz) spectrometers and referenced with residual non-deuterated solvent shifts ($\text{CHCl}_3 = 7.24 \text{ ppm}$).

A.3.2 Materials

Tetrahydrofuran and dichloromethane was dried by passing over columns of alumina and degassed via repetitive freeze-pump-thaw cycles. Ethylene oxide was dried over $n$-butyllithium, vacuum transferred, and degassed via repetitive freeze-pump-thaw
cycles before use. The β-propiolactone used in Table A.1 was synthesized from the carbonylation of ethylene oxide as described in section 3.4.4. The PL was dried over calcium hydride and vacuum transferred before use. All other reagents were purchased from commercial sources and used as received.

**A.3.3.3 Polymer Characterization**

Gel permeation chromatography (GPC) analyses were carried out using a Waters M515 pump, a Waters 717+ Autosampler, a Waters 2410 differential refractive index detector, and three 5 µm PSS SDV columns (Polymer Standards Service; 50 Å, 500 Å, and Linear M porosities) in series. The GPC columns were eluted with chloroform at 30 °C at 1 mL/min and were calibrated using 20 monodisperse polystyrene standards.

**A.3.4 Complex Synthesis**

**A.3.4.1** For the synthesis of complex 1, see section 2.4.7.10.

**A.3.4.2** For the synthesis of complex 2, see section 2.4.7.11.

**A.3.4.3** For the synthesis of complex 3, see section 2.4.7.5.

**A.3.4.4** $[	ext{Pr}^t-	ext{EtBDI}]ZnO^tPr]$ (4).
\((\text{iPr,EtBDI})\text{H}\). This ligand was provided by Dr. Ryan Jeske (as synthesized in J. Am. Chem. Soc. 2001, 123, 8738-8749).

\([\text{iPr,EtBDI}Zn(N\text{SiMe}_3)_2]\). The \((\text{iPr,EtBDI})\text{H}\) ligand (2.0 g, 5.1 mmol), \(\text{Zn(NTMS}_2\) (2.3 mL, 5.6 mmol), and xylene (5 mL) were added to a schlenk tube under \(\text{N}_2\). The solution was stirred at 150 °C for 4.5 days. The reaction was cooled and the solvent was evaporated under vacuum to give a white solid. The crude product was recrystallized from xylenes, filtered, and rinsed with hexanes several times to give tan crystals. (3.2 g, 33% yield) 

\(^1\text{H NMR (C}_6\text{D}_6, 300 MHz) \delta 7.12 (6H, m, ArH), 4.87 (1H, s, CH), 3.30 (2H, m, J = 6.0 Hz, \text{C}H\text{Me}_2), 2.73 (2H, m, J = 6.0 Hz, \text{CH}_2\text{CH}_3), 2.64 (2H, m, J = 6.0 Hz, \text{CH}_2\text{CH}_3), 1.68 (3H, s, \text{CH}_3), 1.59 (3H, s, \text{CH}_3), 1.40 (6H, d, J = 6.0 Hz, \text{CHMeMe'}), 1.21 (6H, t, J = 9.0 Hz, \text{CH}_2\text{CH}_3), 1.17 (6H, d, J = 9.0 Hz, \text{CHMeMe'}), 0.00 (18H, s, \text{SiCH}_3).\)
[(iPr,EtBDI)ZnO\textsuperscript{iPr}] (4). Under N\textsubscript{2}, [(iPr,EtBDI)ZnN(TMS)\textsubscript{2}] (1.1 g, 1.7 mmol) was added to a schlenk tube and dissolved in 18 mL toluene. Isopropyl alcohol (124 \( \mu \)L, 1.6 mmol) was added to the solution. The reaction was stirred for 15 hours at room temperature, and then the solvent was evaporated under reduced pressure to give a yellow solid. The crude product was recrystallized from toluene. (0.2 g, 24% yield) \textsuperscript{1}H NMR (C\textsubscript{6}D\textsubscript{6}, 400 MHz) \( \delta \) 7.34-7.00 (6H, m, ArH), 4.78 (1H, s, CH), 3.97 (1H, m, \( J = 6.0 \) Hz, OCHMe\textsubscript{2}), 3.57 (1H, m, \( J = 6.0 \) Hz, CHMe\textsubscript{2}), 3.10 (1H, m, \( J = 6.0 \) Hz, CHMe\textsubscript{2}), 2.82 (2H, m, \( J = 6.0 \) Hz, CH\textsubscript{2}CH\textsubscript{3}), 2.61 (2H, m, \( J = 6.0 \) Hz, CH\textsubscript{2}CH\textsubscript{3}), 1.44 (6H, d, \( J = 3.0 \) Hz, CH(CH\textsubscript{3})\textsubscript{2}), 1.39-1.03 (18H, m, CHMeMe’ and CHMeMe’ and CH\textsubscript{2}CH\textsubscript{3}).

A.3.4.5 [(Et,EtBDI)ZnO\textsuperscript{iPr}] (5).

\[(Et,EtBDI)H\]. For ligand synthesis, see section 2.4.7.10.
\[ ([^{\text{Et,EtBDI}}]\text{ZnN(TMS)}_2] \]. In a glovebox, \((^{\text{Et,EtBDI}})\text{H} (2.0 \text{ g}, 5.4 \text{ mmol}), \text{Zn(NTMS)}_2 (2.4 \text{ mL}, 6.0 \text{ mmol}), \) and xylenes (5 mL) were added to a schlenk tube. The solution was stirred for 4 days at 150 °C. The solvent was evaporated under vacuum to give a white solid. The crude product was recrystallized from xylenes and rinsed with hexanes. \(^1\text{H NMR} (\text{C}_6\text{D}_6, 300 \text{ MHz}) \delta 7.11 (6\text{H, m, ArH}), 4.87 (1\text{H, s, CH}), 2.71 (4\text{H, m, } J=6.0 \text{ Hz, } \text{CH}_2\text{CH}_3), 2.57 (4\text{H, m, } J=6.0 \text{ Hz, } \text{CH}_2\text{CH}_3), 1.57 (6\text{H, s, CH}_3), 1.20 (12\text{H, t, } J=6.0 \text{ Hz, } \text{CH}_2\text{CH}_3), 0.01 (18\text{H, s, SiCH}_3).\]

\[ ([^{\text{Et,EtBDI}}]\text{ZnO}^{\text{OPr}}] \text{ (5).} \] \((^{\text{Et,EtBDI}})\text{ZnN(TMS)}_2 (487.5 \text{ mg}, 0.8 \text{ mmol})\) was dissolved in 8 mL toluene under N\(_2\). Dry isopropyl alcohol (62 \(\mu\)L, 0.8 mmol) was added to the solution. The reaction was stirred at room temperature for 12 hours. The solvent was evaporated under vacuum, and the crude product was recrystallized from toluene. White crystals were isolated and rinsed with hexanes two times. (129 mg, 33% yield) \(^1\text{H NMR} (\text{C}_6\text{D}_6, 300 \text{ MHz}) \delta 7.12 (6\text{H, m, ArH}), 4.75 (1\text{H, s, CH}), 3.74 (1\text{H, m, } J=6.0 \text{ Hz,}}\)
OCH\textsubscript{2}Me\textsubscript{2}, 2.63 (4H, m, $J = 6.0$ Hz, $CH_2CH_3$), 2.16 (4H, m, $J = 6.0$ Hz, $CH_2CH_3$), 1.41 (6H, s, CH$_3$), 1.11 (12H, t, $J = 6.0$ Hz, CH$_2CH_3$), 1.09 (6H, d, 6.0 Hz, CH(CH$_3$)$_2$).