

Coupling of Propylene Oxide and Lactide at a Porphyrin Chromium(III) Center

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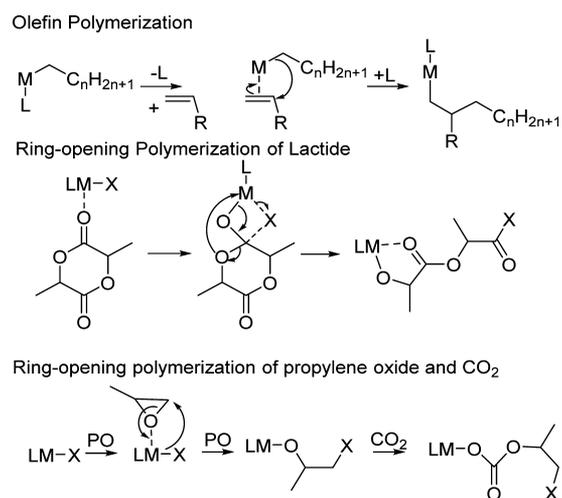
S Supporting Information

ABSTRACT: 5,10,15,20-Tetraphenylporphyrin chromium chloride (TPPCrCl) with added $[\text{Ph}_3\text{P}=\text{N}=\text{PPh}_3]^+\text{Cl}^-$ (PPN⁺Cl⁻) selectively polymerizes lactide (L and *rac*) dissolved in neat propylene oxide (PO) to yield polylactide (PLA) terminated by the $-\text{OCHMeCH}_2\text{Cl}$ group. At 0 °C and below, *rac*-LA yields polymers highly enriched in isotactic tetrads (*iii*). At 25 °C, some stereoselectivity is lost as transesterification becomes significant, and at 60 °C and above, enchainment of PO leads to the formation of 3,6-dimethyl-1,4-dioxan-2-one by a backbiting mechanism. At 0 °C, after the enchainment of L-(*S,S*)-LA in neat (*R*)-(+)-PO, the formation of (3*S*,6*R*)-3,6-dimethyl-1,4-dioxan-2-one occurs, while at higher temperatures the ratio of (3*S*,6*R*)-3,6-dimethyl-1,4-dioxan-2-one to (3*R*,6*R*)-3,6-dimethyl-1,4-dioxan-2-one falls to 3:2.

Ring opening of propylene oxide (PO) by a metal coordinate mechanism can occur by a bimetallic pathway, as demonstrated by Jacobsen in the stereoselective ring opening of *rac*-PO by chiral Schiff base chromium and cobalt complexes.¹ In this mechanism, one metal serves as a Lewis acid to activate PO toward nucleophilic attack by a ligand, typically a halide or alkoxide that is delivered from the other metal center. This type of mechanism may also work efficiently in the copolymerization of PO and CO₂ to form poly(propylene carbonate)s.² However, the ring-opening polymerization (ROP) of PO can also occur at a single metal center, as has been well-documented now by Darensbourg and others.³ In our studies of the reactivity of porphyrin metal(III) catalysts, we have shown that this single-site mechanism can be involved in both the homopolymerization of PO and its copolymerization with CO₂.⁴ The homopolymerization of PO follows the order M = Cr > Al ~ Co, and for TPPCr(III) (TPP = tetraphenylporphyrin), enchainment of PO under ambient conditions is quite rapid with a turnover frequency (TOF) of ~2000 h⁻¹, yielding regioregular (HT)_n poly(propylene oxide) (PPO). When *rac*-PO is employed, this is significantly enriched in isotactic junctions.

The enchainment of PO at a single metal center can be considered to occur by a mechanism akin to a 1,2-migratory addition of the type common for the insertion of alkenes into metal-alkyl bonds in olefin polymerization (Scheme 1).⁵ Although this may not be a commonly accepted view of the

Scheme 1. Mechanisms of Olefin Polymerization, Ring-Opening Polymerization of Lactide, and Copolymerization of Propylene Oxide and CO₂ at a Single-Site Metal Center



homopolymerization of PO, there certainly are some similarities with olefin polymerization. The metal must be coordinatively unsaturated, provide an electrophilic site for activation of the substrate, and have a polar metal-alkyl or -alkoxide bond.

Similar requirements pertain to the ROP of cyclic esters such as lactides (*rac*, L, D, and *meso*).⁶ Among the most active coordinate catalysts for the ROP of lactides (LAs) are the lanthanides⁷ and group-2 metals (i.e., Mg and Ca).⁸ The commonly accepted mechanism for the ROP of LA is also shown in Scheme 1. Rather interestingly, though single-site metal catalysis is well-established for the ROP of LA, these sites are not typically active for the ROP of PO despite the ability of PO to bind to these centers. This is nicely seen in the molecular structure of $\text{Tp}^*\text{Ca}(\text{OAr})(\text{PO})$ [Tp^* = tris(*tert*-butylpyrazolyl)borate], where OAr and PO occupy adjacent sites at the five-coordinate Ca²⁺ ion.⁹

We recently reasoned that the greater reactivity of TPPCr(III) toward the homopolymerization of PO is due to its more polar Cr-OR bond relative to Al-OR and Co-OR.⁴ This

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prompted us to investigate the TPPCr(III) system with PO and LA, and herein we report our initial findings.

TPPCrCl, $[\text{Ph}_3\text{P}=\text{N}=\text{PPh}_3]^+\text{Cl}^-$ (PPN^+Cl^-), LA, and PO react at 0 °C to produce initially a polylactide (PLA) with an $-\text{OCHMeCH}_2\text{Cl}$ end group, as determined by mass spectrometry, with some supporting OH group from hydrolysis (see Figures S26 and S27 in the Supporting Information). With *rac*-LA, the formation of isotactic PLA was determined by NMR spectroscopy and powder X-ray diffraction (PXRD) (see Figure 1 for the ^1H NMR spectrum and Figures S18 and S22 in the Supporting Information for the ^{13}C NMR spectrum and PXRD pattern, respectively).

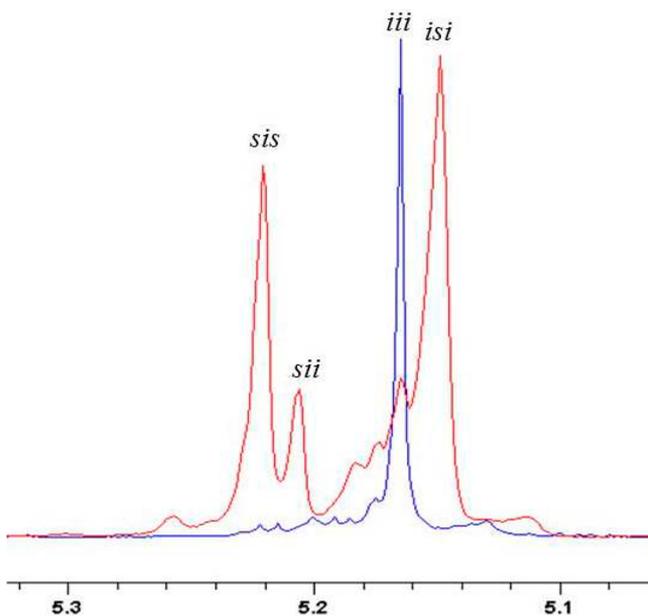
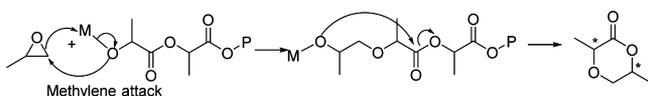


Figure 1. Homodecoupled ^1H NMR (500 MHz, CDCl_3 , 25 °C) spectrum of poly(lactide) (blue) obtained from *rac*-LA catalyzed by TPPCrCl/ PPN^+Cl^- in *rac*-PO ($M_w \approx 3500$ Da, PDI = 1.06) compared with the spectrum of a heterotactic enriched PLA sample (red), $P_r = 0.86$.

At 0 °C, when the reaction goes toward completion of the formation of PLA, a further reaction occurs, yielding a six-membered ring by incorporation of PO via a backbiting mechanism (Scheme 2). This does not polymerize at this

Scheme 2. Possible Pathway for the Formation of Six-Membered Lactones 3,6-Dimethyl-1,4-dioxan-2-one by a Backbiting Mechanism



temperature. The formation of this ring can be achieved by a procedure involving *L*-ethyl lactate and allyl bromide. Indeed, this reaction was used to make authentic samples of the products (Scheme 3).

The reaction involving *L*-ethyl lactate and allyl bromide yielded the four stereoisomers shown in Figure 2. These were determined by ^1H and ^{13}C NMR spectroscopy and by gas chromatography (GC) using columns with achiral and chiral stationary phases. At 0 °C, the reaction between *L*-LA [(3*S*,6*S*)-3,6-dimethyl-1,4-dioxan-2,5-dione] and (*S*)-(–)- or (*R*-

Scheme 3. Synthetic Route for 3,6-Dimethyl-1,4-dioxan-2-one from *L*-Ethyl Lactate and Allyl Bromide

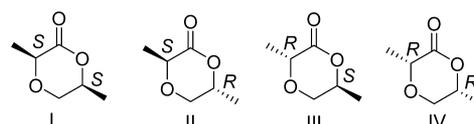
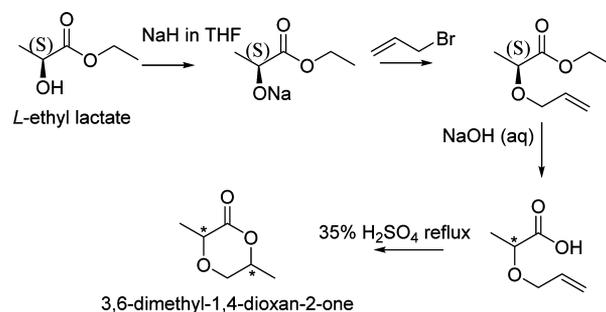


Figure 2. Isolated stereoisomers of 3,6-dimethyl-1,4-dioxan-2-one.

(+)-PO yielded one product, namely, (3*S*,6*S*)-3,6-dimethyl-1,4-dioxan-2-one (I) or (3*S*,6*R*)-3,6-dimethyl-1,4-dioxan-2-one (II), respectively, as the major product. This indicates that the stereocenter of the (*R*)-(+) or (*S*)-(–)-PO remains the same. However, when the reactions were repeated at elevated temperature, the reaction between *L*-LA and (*S*)-(–)- or (*R*)-(+)PO yielded two isomers (I and III or II and IV, respectively). At 60 °C, each compound produced a mixture of PO–LA oligomers (Figure 25 in the Supporting Information) and cycles, as shown in Figure 3.

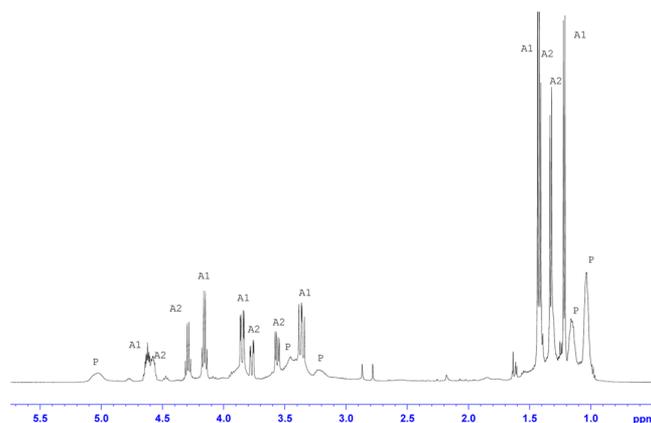


Figure 3. ^1H NMR (500 MHz, CDCl_3) spectrum of the crude product obtained from *rac*-PO and *rac*-LA catalyzed by TPPCrCl/ PPN^+Cl^- . A1 and A2 denote diastereomeric pairs of 3,6-dimethyl-1,4-dioxan-2-one. P denotes oligomers of $\text{H}(1/2\text{LA})_n(\text{PO})_m\text{Cl}$.

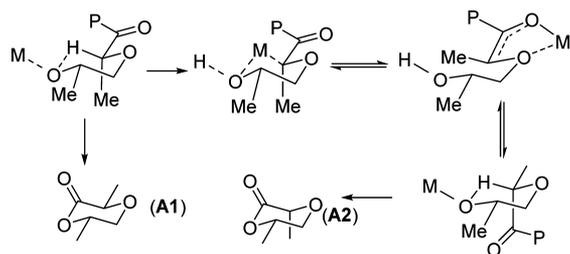
At 60 °C, the compounds of composition (*R/S*)-1/2LA and (*R/S*)-PO are formed as a mixture of four products, two from (*R*)-(+)PO and two from (*S*)-(–)-PO, as indicated in Table 1. The ratios of products were determined by chiral-stationary-phase (CSP) GC, and each compound was identified by extraction with hexane and analysis by ^1H and ^{13}C NMR spectroscopy and CSP and achiral stationary phase (ASP) GC. The six-membered ring can be described as 3,6-dimethyl-1,4-dioxan-2-one and can be formed by the reaction shown in Scheme 2.

Table 1. Percentages of 3,6-Dimethyl-1,4-dioxan-2-one Isomers Obtained with Different Combinations of LA and PO at 60 °C

	(3 <i>R</i> ,6 <i>S</i>)	(3 <i>S</i> ,6 <i>R</i>)	(3 <i>R</i> ,6 <i>R</i>)	(3 <i>S</i> ,6 <i>S</i>)
Retention Times Observed in CSP GC (rt, in min)				
	4.71	15.45	17.15	18.42
Isomer Yields (%)				
<i>rac</i> -LA + <i>rac</i> -PO	28	28	22	22
<i>rac</i> -LA + (<i>R</i>)-(+)-PO	–	58	42	–
L-LA + <i>rac</i> -PO	26	29	21	24
L-LA + (<i>R</i>)-(+)-PO	–	58	42	–
L-LA + (<i>R</i>)-(+)-PO ^a	–	100	–	–
L-LA + (<i>S</i>)-(–)-PO ^a	–	–	–	100
monomer ^b	18	39	19	24

^aReactions were carried out at 0 °C. ^b3,6-Dimethyl-1,4-dioxan-2-one was obtained from the reaction of L-ethyl lactate and allyl bromide according to Scheme 3.

While at 0 °C the reaction between enantiopure LA and enantiopure PO (e.g., between (*R*)-(+)- or (*S*)-(–)-PO and L-LA) proceeds to form one enantiomer, at higher temperatures the formation of two diastereomers arises because of the stereo sequence shown in Scheme 4. At 25 °C, the ratio of the two

Scheme 4. Possible Mechanism of Racemization at the Chiral Center of the Lactide Unit in the Polymer Chain

isomers is smaller than that produced at 60 °C and above, where the 3:2 pattern emerges, as shown in Figure 4A. In the

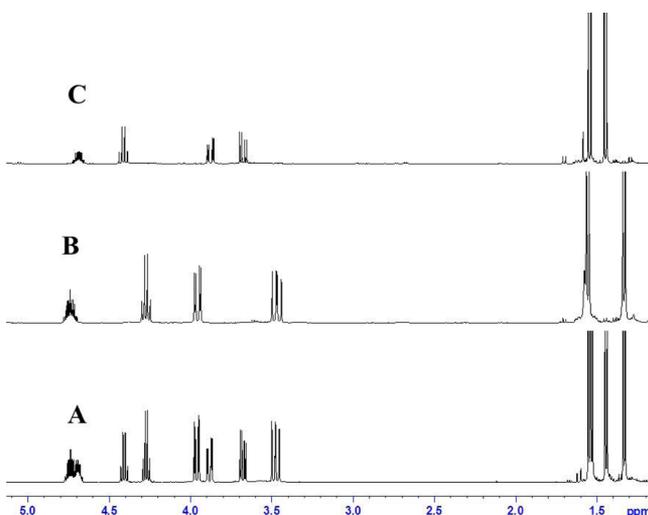


Figure 4. ¹H NMR spectra (400 MHz, CDCl₃) of the hexane-soluble products obtained from the reactions of (A) *rac*-PO and *rac*-LA at 60 °C, (B) (*R*)-(+)-PO and L-LA at 0 °C, and (C) (*S*)-(–)-PO and L-LA at 0 °C catalyzed by TPPCrCl/PPN⁺Cl[–].

formation of isotactic PLA at 0 °C we encounter a factor that limits high *M_w*. Typically, using (TPPCrCl + PPN⁺Cl[–]):LA = 1:80 we obtain a *M_w* of 3500–5000 Da. With a higher catalyst:substrate ratio (e.g., 1:400) we obtain a *M_w* of ~10 400 Da. We also see observations of [(PO)_{*m*}(1/2LA)_{*n*}] with *m* = 2 and *n* = 10–20. Thus, the formation of [Cr]OCHMeCH₂–(LA)_{*n*}–OCHMeCH₂Cl by attack at the terminal chain may prevent the formation of long chains.

Finally, it is worth noting that most coordinate catalysts that are achiral, such as β-diiminates of Mg and Zn, favor the formation of heterotactic PLA in the ROP of *rac*-LA.^{8a,b,10} The conversion of *rac*-LA to isotactic chains having *iii* tetrads is much rarer and generally has involved chiral metal centers, as in the original report by Baker and Smith¹¹ employing *rac*-salen aluminum alkoxide initiators. An exception to this is seen in the work of Williams¹² employing a pentadentate N₃O₂ ligand, even though here the introduction of a chiral alkoxide could introduce chirality in the binding of the N₃O₃ ligand. In the present case of TPPCr, the porphyrin is relatively inflexible, and thus, any stereoselectivity must be due to the alkoxide bound to the metal. Assignment of the stereoplex polymer (P-L-LA + P-D-LA) is expected because of the chiral end group (CrOCHMeCH₂–), as in the formation of poly-*iii*-PPO from *rac*-PO. Presumably this end-group control will lead to a blocky polymer involving alternating sections of –(L-LA)_{*n*}(D-LA)_{*m*}–,¹³ and this needs to be determined. Also, in the development of an understanding of the reaction profile, we noted that in the reaction between TPPCrCl and PO + LA at room temperature only the formation of PPO is favored. Presumably here the [Cr] center acts in a bimetallic manner to form PPO, and the [Cr]–OR bonds do not react with LA that is present in solution. With a TPPCrCl/PPN⁺Cl[–] ratio of 1:1, we see that H–(LA)_{*n*}–OCHMeCH₂Cl is formed at low temperature (0 °C), with small amounts of the six-membered ring as the cyclization nears completion and [LA] goes to zero. We have found that the rate of formation is proportional to the TPPCrCl/PPN⁺Cl[–] ratio, where the order is 1.5 (see Figures S23 and S24 in the Supporting Information). Clearly we need to learn more about the mechanism. Further work is in progress.

■ ASSOCIATED CONTENT

📄 Supporting Information

Experimental procedures and polymer and monomer synthesis and characterization. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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