

# Recent Advances in the Titanium-Based Catalysts for Ring-Opening Polymerization

Wei Wang\*

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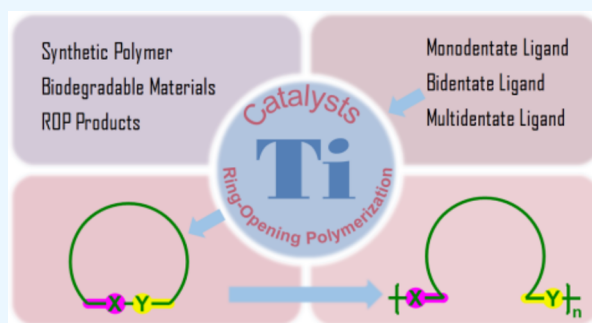
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**ABSTRACT:** At present, economic development and daily life cannot be separated from organic synthetic polymers. However, a large number of nondegradable polymers have caused serious pollution to the environment. It is necessary for sustainable development to use biodegradable materials instead of traditional polymers, but it is not yet comparable in performance and cost to the competitor it will replace. Therefore, there is a long way to go to develop effective synthesis methods. Through ring-opening polymerization, some cyclic monomers, such as  $\epsilon$ -caprolactone or lactide, can be synthesized into biodegradable polymers, which can not only replace traditional synthetic polymers in some fields but also have applications in drug delivery, surgical consumables, human implant materials, bone materials, etc. Ring-opening polymerization is a potential candidate for solving environmental pollution. For ring-opening polymerization, catalysts are very important, among which titanium catalysts have attracted much attention because of their high efficiency, economy, and nontoxicity. In this paper, the development status of organotitanium compounds as ring-opening polymerization catalysts is reviewed, including the effects of different ligand structures on polymerization behavior and polymer structure, and its development trend is prospected. We hope that this review will be helpful for developing efficient ring-opening polymerization catalysts.



## 1. INTRODUCTION

The development of society is increasingly dependent on synthetic materials, especially polymer resins. Per capita resin consumption is an important indicator of a country's economic development.<sup>1,2</sup> The raw materials for synthetic resins come from nature, including renewable and nonrenewable resources, the former represented by raw materials from plants, which can be recovered in a short period of time after consumption, and the latter by petroleum, which cannot be regenerated for a long period of time after human development and utilization. Synthetic resins include biodegradable resins and nonbiodegradable resins. The former is represented by some types of polyester or polycaprolactone and the latter by polyolefin (see Figure 1).<sup>3</sup> The resin will also return to nature after use. Biodegradable materials are decomposed into small molecules through a simple process that has little impact on the environment. On the other hand, nonbiodegradable materials will exist for a long time without human intervention, causing great strain on the environment. Therefore, the demand for the development of biodegradable materials is increasing for the sake of reducing the strain on the environment.<sup>4</sup> It is important to note that raw materials and resin are two-level problems. For specific products, the emphasis on the source of raw materials only indicates whether the resources can be renewable and does not affect the properties of the final product. The biodegradable

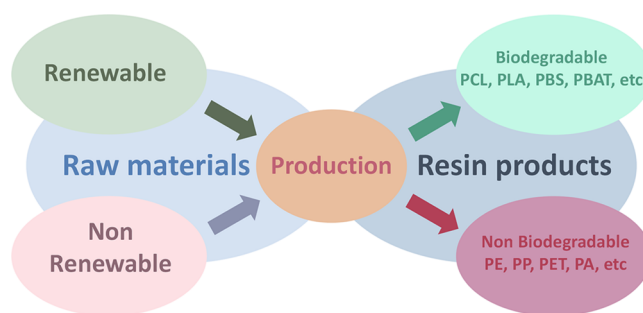


Figure 1. Synthetic resin and its materials.

polyester could be produced from nonrenewable petroleum raw materials, while polyethylene made from bioderived raw materials is not biodegradable.

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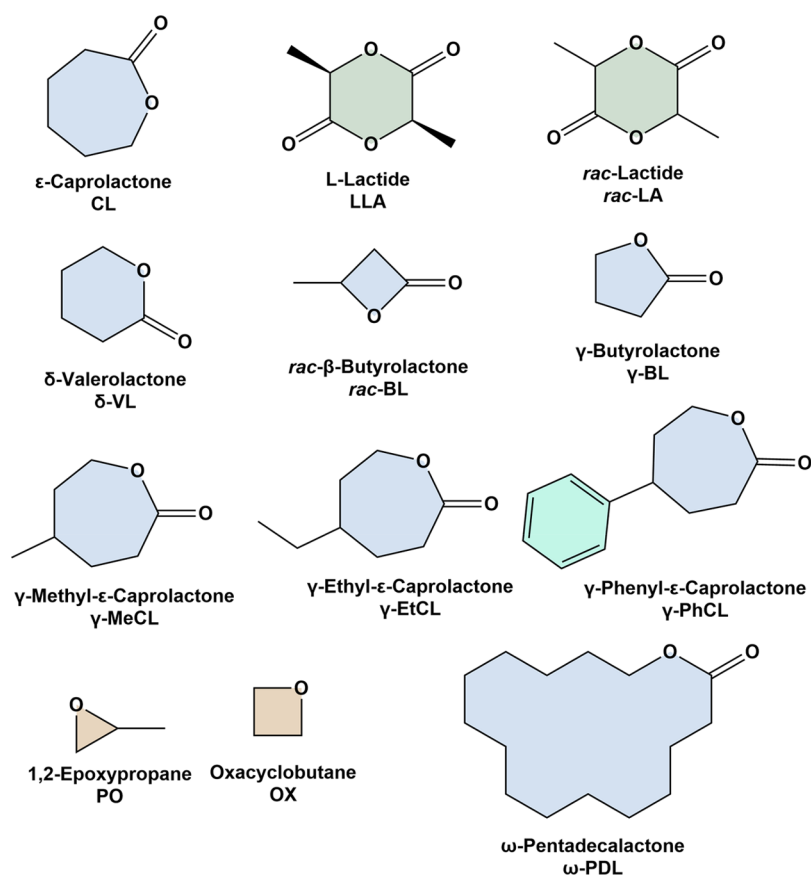


Figure 2. Cyclic ester or cyclic ether monomers.

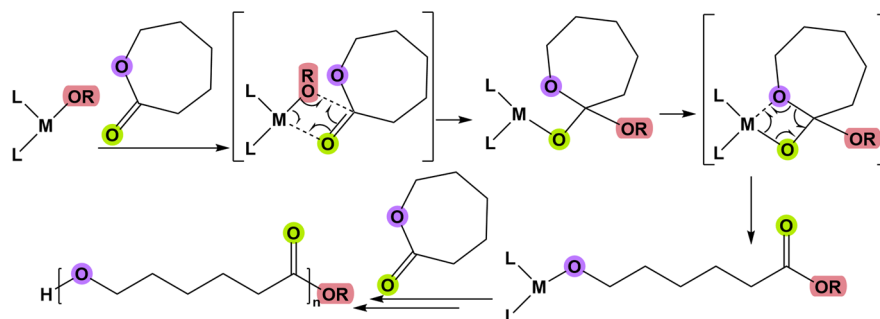


Figure 3. Coordination–insertion mechanism of ROP of  $\epsilon$ -caprolactone catalyzed by an alkoxide organometallic catalyst.

Due to the increasing pressure of environmental protection, researchers are aware of the harm of nonbiodegradable materials and are putting more effort into biodegradable polymers. These materials are not only biodegradable but also biocompatible. This has profound implications for biomedical and pharmaceutical engineering, such as drug delivery, biodegradable surgical sutures, medical implants, bone materials, stents, etc.<sup>5–9</sup>

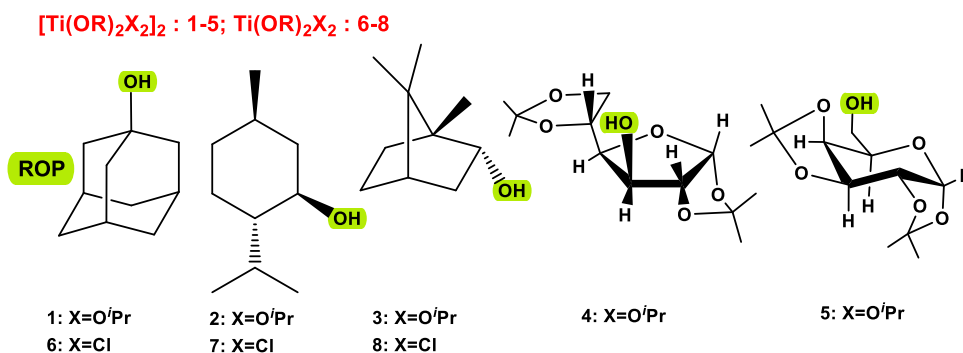
In recent years, people have been developing environmentally friendly synthetic biodegradable polymers,<sup>10,11</sup> such as aliphatic polyesters. These materials have attracted a lot of attention as alternatives to nonbiodegradable plastic and found wide applications in medicine,<sup>12</sup> packaging,<sup>13</sup> film,<sup>14</sup> and thermoplastics.<sup>15</sup> The most representative materials are poly( $\epsilon$ -caprolactone) (PCL)<sup>16</sup> and poly(lactic acid) (PLA).<sup>17</sup> Their corresponding monomers are  $\epsilon$ -caprolactone and lactide, both of which are cyclic esters, and polymers are obtained by ring-opening polymerization (ROP).<sup>18,19</sup> The cyclic ester and cyclic

ether involved in this review article and their abbreviations are illustrated in Figure 2.

ROP using organometallic compounds as catalysts follows a coordination–insertion mechanism. Taking a typical alkoxide organometallic catalyst as an example, the polymerization mechanism is illustrated in Figure 3.<sup>20</sup>

The most frequently and industrially used catalyst is organotin, which is efficient for the ROP of a wide range of cyclic esters. However, the catalyst is also competent for transesterification, which makes the polymerization out of control and broadens the molecular weight distribution of the polyester.<sup>21,22</sup> Although the toxicity of the tin catalyst is controversial,<sup>23</sup> the cytotoxicity, which is generally accepted, prevents the polyester catalyzed by the tin catalyst from being used in pharmaceuticals or biomedicine.<sup>24</sup>

In recent years, many metal compounds have been used as catalysts for ROP,<sup>25,26</sup> among which group 4 metals, especially



**Figure 4.** Titanium compounds with hindered alcohol ligands for ROP in Hierro's work.<sup>30</sup>

titanium complexes,<sup>27</sup> have attracted more attention due to their low cost and noncytotoxicity. Alkoxy ligands are known to be stable in the early and middle transition metal centers of the high oxidation states. Transition metal complexes with large volume alkoxy or aryloxy groups have been widely used in catalysis.<sup>28,29</sup>

The combination of titanium with various alkoxy or aryloxy ligands may yield valuable catalysts suitable for ROP. The application of these catalysts in ROP is reviewed in this paper.

## 2. ALKOXY OR ARYLOXY LIGANDS

Hierro synthesized titanium complexes of type  $\text{Ti}(\text{OR})_2\text{X}_2$  (see Figure 4) and used them as catalysts for ROP of  $\epsilon$ -CL and LLA.<sup>30</sup> At 25 °C and 100 equiv of  $\epsilon$ -CL in dichloromethane, titanium catalyst initiated the polymerization reaction. After 8–24 h, conversions reached 60–100%. Catalysts 2, 3, and 4 all reached 100%  $\epsilon$ -CL conversion within 8 h. Catalysts in which X is an isopropoxy group have a conversion significantly higher than that in which X is a chlorine atom. The molecular weight of the polymer is between 4800 and 10900, and the molecular weight distribution is between 1.45 and 2.28. The molecular weight is in good agreement with the calculated value. In the <sup>1</sup>H NMR spectrum of poly( $\epsilon$ -caprolactone) obtained from catalyst 2, the resonance ascribed to the  $\text{CH}_2\text{OH}$  end group could be observed, which is formed by the oxygen atom connected with the titanium atom after quenching polymerization with alcohol. This resonance could be found in the <sup>1</sup>H NMR spectrum of all polymers. At the same time, the resonances of a terminal isopropyl ester and a terminal menthyl ester also appeared in the NMR spectrum, indicating that the growing end groups are isopropoxy and menthoxy, which meant that different alkoxy groups led to polymers with different structures of chain ends. Thus, the ring opening of  $\epsilon$ -CL occurs between the acyl–oxygen bond to realize monomer insertion and chain propagation. Similar phenomena were observed for other titanium complexes of type  $\text{Ti}(\text{OR})_2(\text{O}'\text{Pr})_2$ . In the NMR of polymers caused by  $\text{Ti}(\text{OR})_2\text{Cl}_2$  (6, 7, and 8), only a single chain end could be observed. These observations are consistent with the coordination–insertion mechanism described above (Figure 3). Catalysts 7 and 8 were used for ROP of LLA in toluene at 100 °C. Within 72 h, the conversions were 76% and 95%, respectively.

Chakraborty synthesized a series of titanium complexes of type  $[\text{Ti}(\text{OR})_a(\text{iPrO})_b(\text{iPrOH})_c]_2$ , which were listed in Table 1.<sup>31</sup>

By using these complexes as catalysts, the polymerization of  $\epsilon$ -CL or  $\delta$ -VL gave the total consumption within a short reaction time. The molecular weight ranges are  $5\text{--}96 \times 10^3$  for PCL and  $4\text{--}138 \times 10^3$  for PVL, with molecular weight distribution from 2

**Table 1.** Titanium Complexes of Type  $[\text{Ti}(\text{OR})_a(\text{iPrO})_b(\text{iPrOH})_c]_2$ <sup>31</sup>

Catalyst	R	a	b	c
9	2-Me-C <sub>6</sub> H <sub>4</sub>	4	0	0
10	2-F-C <sub>6</sub> H <sub>4</sub>	4	0	1
11	2-Cl-C <sub>6</sub> H <sub>4</sub>	4	0	0
12	2-Br-C <sub>6</sub> H <sub>4</sub>	4	0	0
13	3-F-C <sub>6</sub> H <sub>4</sub>	4	0	1
14	3-CF <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	4	0	1
15	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4	0	1
16	4-Me-C <sub>6</sub> H <sub>4</sub>	4	0	0
17	4-tBu-C <sub>6</sub> H <sub>4</sub>	4	0	0
18	4-CF <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	4	0	1
19	4-F-C <sub>6</sub> H <sub>4</sub>	4	0	1
20	4-I-C <sub>6</sub> H <sub>4</sub>	4	0	1
21	C <sub>6</sub> F <sub>5</sub>	4	0	1
22	C <sub>6</sub> Cl <sub>5</sub>	4	0	1
23	2,4,6-F <sub>3</sub> -C <sub>6</sub> H <sub>2</sub>	2	2	0
24	2,4,6-Cl <sub>3</sub> -C <sub>6</sub> H <sub>2</sub>	2	2	0
25	2,4,6-Br <sub>3</sub> -C <sub>6</sub> H <sub>2</sub>	2	2	0
26	2,4,6-I <sub>3</sub> -C <sub>6</sub> H <sub>2</sub>	2	2	0
27	4-Me-C <sub>6</sub> H <sub>4</sub> -CH <sub>2</sub>	4	0	0
28	4-MeO-C <sub>6</sub> H <sub>4</sub> -CH <sub>2</sub>	4	0	2

to 2.8. Previous studies have shown that the addition of benzyl alcohol (BnOH) to the ROP system can accelerate the polymerization process and give a polymer with higher molecular weight.<sup>32,33</sup> After the addition of benzyl alcohol in the polymerization system in this study, the molecular weight of the polymer is generally improved ( $7\text{--}137 \times 10^3$  for PCL and  $12\text{--}256 \times 10^3$  for PVL), and the molecular weight distribution was narrowed to less than 1.5. In addition, the time to complete monomer consumption is shortened for most polymerizations. Kinetic studies showed that the polymerization rate was a first-order dependence with monomer concentration and no induction period. The calculation of the apparent reaction rate constant showed a faster reaction rate of the polymerization in the presence of BnOH. MALDI-TOF and NMR analysis of the polymer produced by the catalyst 10 showed that the polymer chain end was isopropyl in the absence of BnOH and benzyl in the presence of BnOH, and no isopropyl competing products are observed. This indicated that the initiation efficiency of benzyloxy is much higher than that of isopropoxy.

## 3. BIDENTATE LIGANDS

Metal complexes formed by bidentate ligands are important strategies in catalytic chemistry,<sup>34</sup> especially in terms of polymerization catalysts.<sup>35</sup> As one of the most important design

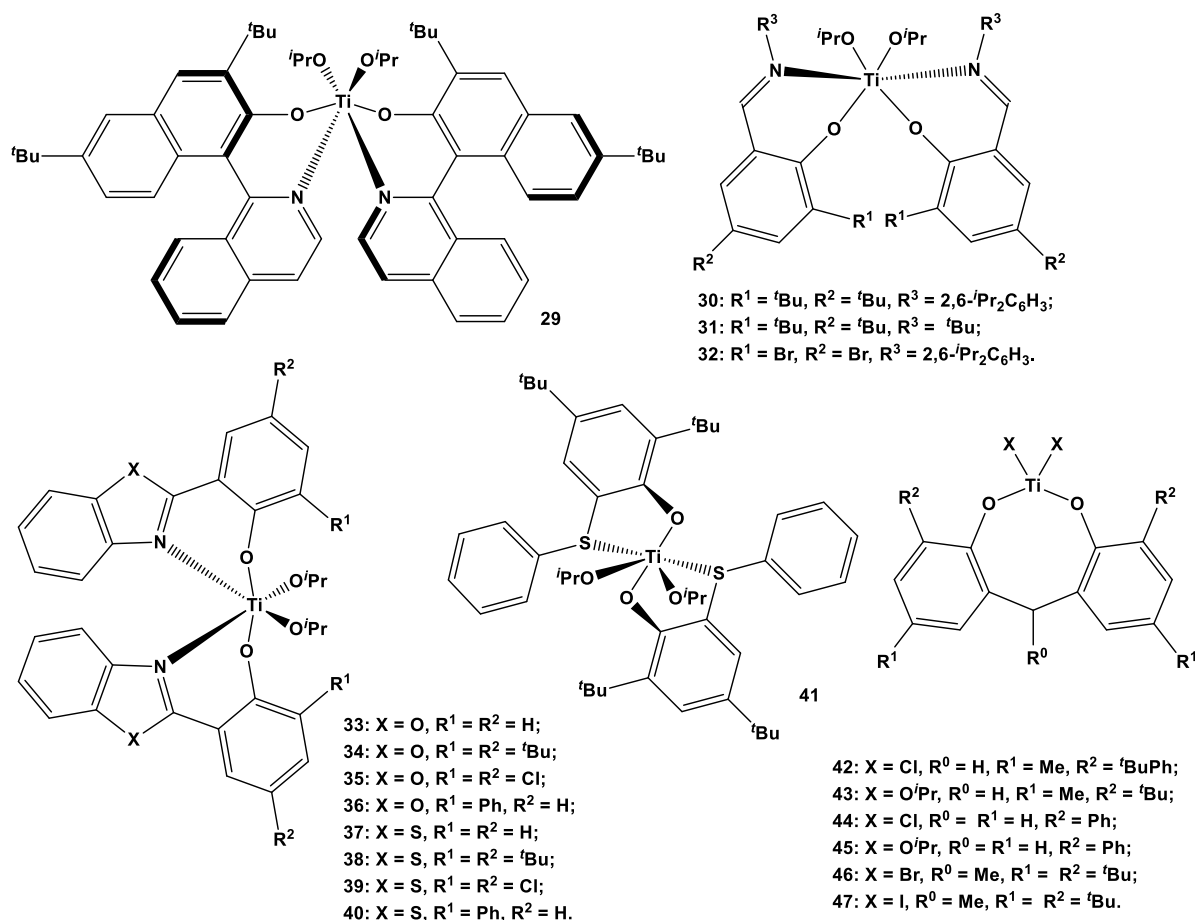


Figure 5. Titanium complexes ligated with bidentate ligand(s).

strategies, metal compounds with bidentate ligands are widely used in ROP.<sup>36</sup>

Titanium complex **29** was used for ROP of  $\epsilon$ -CL and LLA but gave very low conversion.<sup>37</sup> Compounds **30**, **31**, and **32** were used as catalysts for ROP of *rac*-LA, LLA,  $\delta$ -VL, and *rac*-BL (Figure 5).<sup>38</sup> All polymerization achieved almost complete conversion within 20 min, affording polymer with a molecular weight of  $29\text{--}70 \times 10^3$  and a molecular weight distribution below 1.40. When BnOH was used as an additive, the conversion time was shortened, and the molecular weight distribution was narrowed to less than 1.2; however, the molecular weight was reduced to less than  $16 \times 10^3$ . Polymerization of *rac*-LA gave a polymer with the heterotactic-enriched manner of about 70%. The addition of BnOH has virtually no effect on the stereospecificity. With the increase of the  $[\textit{rac}\text{-LA}]/[\text{catalyst}]$  ratio, the molecular weight of the polymer increased significantly, and the molecular weight distribution remained almost unchanged. Kinetic studies showed a fast reaction rate at the initial stage without an induction period. A first order relationship between the reaction rate and the concentration of *rac*-LA and the linear relationship between  $\ln([\textit{rac}\text{-LA}]_0/[\textit{rac}\text{-LA}]_t)$  ( $[\textit{rac}\text{-LA}]_0$  and  $[\textit{rac}\text{-LA}]_t$  are the concentration of *rac*-LA at the initial stage and the stage of time  $t$ ) and time could be observed.

PCL is suitable for controlled drug release because of its biocompatibility, biodegradability, nontoxicity, high permeability, and low glass transition temperature. Increasing the chain length of the polymer helps to increase the drug loading but also increases the crystallinity of the polymer, which is not conducive

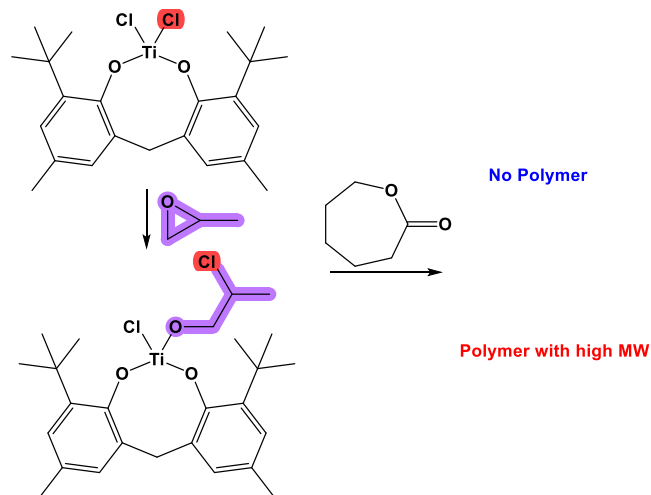
to the controlled release of the drug. In order to reduce the crystallinity, LLA or  $\gamma$ -BL or substituted CL is usually used for copolymerization.<sup>39–41</sup> Hornmiron used titanium complexes of salicylbenzoxazole (complexes **33–36**) and salicylbenzothiazole (complexes **37–40**) ligands as catalysts for ROP of  $\epsilon$ -CL and substituted CL and their copolymerizations.<sup>42</sup> All of the complexes can effectively catalyze ROP of  $\epsilon$ -CL and three substituted  $\epsilon$ -CLs ( $\gamma$ -MeCL,  $\gamma$ -EtCL, and  $\gamma$ -PhCL). Among them, catalyst **37** has the highest activity. The completely random copolymers were formed by the copolymerization of  $\epsilon$ -CL with three kinds of substituted  $\epsilon$ -CL. The polymerization may be carried out through a dissociation coordination–insertion mechanism. Catalytic activity of the salicylbenzothiazole titanium complex is lower than that of its salicylbenzoxazole titanium homologue. In addition, DFT calculations show that the key factors to increase the catalytic rate are the decoordination step of ligands and the small steric hindrance of the titanium center in salicylbenzothiazole titanium complexes.

Milione catalyzed ROP of LLA and  $\epsilon$ -CL using complex **41**.<sup>43</sup> The molecular weight of the polymer was in good agreement with the calculated values, and the molecular weight distribution was very narrow. The copolymerization of LLA and  $\delta$ -VL was performed. The microstructure of the copolymer was analyzed by <sup>13</sup>C NMR. Thermal behavior studied by DSC showed that the two monomers are randomly distributed in the polymer chain.

Aida used a series of titanium catalysts for ROP of  $\epsilon$ -CL, PO, and OX.<sup>44</sup> When 100 equal amounts of  $\epsilon$ -CL were added to  $\text{CH}_2\text{Cl}_2$  solution at 25 °C and complex **43** was used as catalyst,



the polymerization of  $\epsilon$ -CL reached 23, 66, and 100% conversion within 1, 2, and 5 h, respectively. Polymers with average molecular weight of 6500 and molecular weight distribution of 1.15 were obtained. The degree of polymerization of the polymer was almost half the molar ratio of monomer to catalyst, which indicates that each complex **43** molecule can form two polymer chains. Using complex **45** instead of **43** to polymerize  $\epsilon$ -CL resulted in a narrower product of MWD, although the polymerization rate is lower than that of **43**. It took 75 h to achieve 100% conversion, resulting in a polymer with an average molecular weight of 5500 and a molecular weight distribution of 1.1. The UV detection of the polymer showed no absorption at 254 nm, indicating that the initiation of the polymer was independent of the bisphenol group of complex **45**. The polymerization was therefore initiated by an isopropoxy group ligated with titanium, which was consistent with the results of NMR detection. Catalysts **43** and **45** cannot initiate ROP for cyclic ether PO or OX. However, chlorine analogues **42** and **44** have no effect on ROP of  $\epsilon$ -CL but can initiate ROP of PO or OX. However, the reaction only stays in the initiation stage, and the subsequent coordination–insertions could not occur consistently. It was also found that only one chlorine atom was inserted into PO or OX to form chloro-alkoxy. Using this chloro-alkoxy titanium compound as a catalyst to initiate ROP of  $\epsilon$ -CL, catalytic activity similar to that of the isopropoxy titanium compound can be achieved, resulting in a polymer with higher molecular weight (see Figure 6). Similar catalysts were also shown in Redshaw's work.<sup>45</sup> Catalysts **46** and **47** were effective for the ROP of  $\epsilon$ -CL after the addition of BnOH.



**Figure 6.** ROP of  $\epsilon$ -CL catalyzed by a titanium chloride compound assisted by cyclic ether.

#### 4. TRIDENTATE LIGANDS

Metal complexes with tridentate ligands were widely used in the fields of medicine,<sup>46</sup> polymerization,<sup>47</sup> catalysis,<sup>48</sup> luminous material,<sup>49</sup> and so on.

The titanium complex with an imino-benzotriazole phenolate ligand **48** was used as the catalyst for ROP of  $\epsilon$ -CL and LLA (Figure 7).<sup>50</sup> Polymers with high molecular weight and narrow molecular weight distribution were steadily obtained. Additional isopropanol could act as the chain transfer agent and efficiently decrease the molecular weight of the polymer. Titanium

complexes with 2,6-bis(*o*-hydroxyalkyl)pyridine ligand(s) were used for the ROP of  $\epsilon$ -CL and LLA.<sup>51</sup> Catalyst **51** exhibited the highest activity because the electron-donating effect of methyl on the pyridine ring enhanced the coordination ability of nitrogen atoms to titanium. This enhancement weakens the connection between the isopropoxy and titanium atoms to some extent, thus reducing the difficulty of initiating monomer insertion. In monoligand catalysts, **50** is less active than **49** because the steric hindrance of phenyl is higher than that of methyl. The monomer coordination is blocked, and the activity is reduced. The dual-ligand titanium compound **52** exhibits lower activity than all monoligand compounds due to steric hindrance. The results show that the electronic effect and steric hindrance effect in the ligand have an important influence on polymerization.

Titanium complexes **53–59** were used for ROP of  $\epsilon$ -CL. All polymers obtained showed the narrow molecular weight distribution.<sup>52</sup> Complex **59** showed the highest activity and gave the polymer with the highest molecular weight. Complex **53** showed the highest activity of LLA polymerization, while **58** showed the lowest activity. It indicated the important impact of the electron-donating ability of ligand substituents on polymerization activity.

The bulk polymerization of  $\epsilon$ -CL and *rac*-LA was carried out with catalysts **60–62** at 100 and 140 °C, achieving 90% monomer conversion within 10 and 20 min and affording polymer with an average molecular weight of about 20,000 and a narrow molecular weight distribution, respectively.<sup>53</sup> The time required to reach a certain monomer conversion (~90%) decreases in the following order: **62** < **61** < **60**. Polymers of *rac*-LA have 60–70% heterotactic enriched manner. The high activity of the catalysts comes from the increasing Lewis acid of the metal center, resulting from the strong electron-withdrawing cyano group. In addition, the order of the electron-donating groups on the ligands is consistent with the order of activity. The combination of electronic properties in the ligand design results in a robust catalyst.

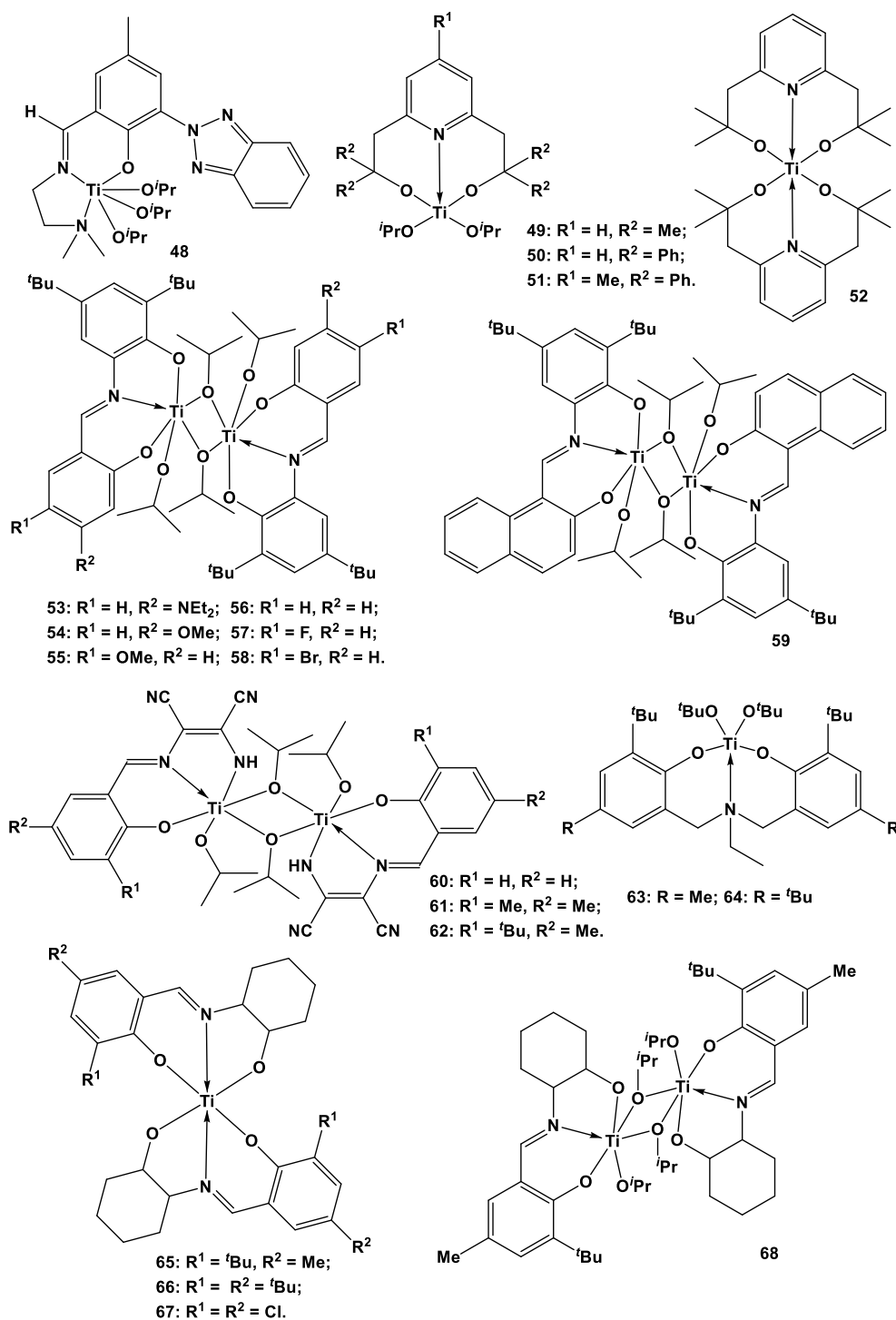
Zaitsev and Karlov synthesized titanium complexes **63** and **64**.<sup>54</sup> According to the X-ray diffraction results, **64** is monomeric in the solid phase. When using  $\epsilon$ -CL as the bulk polymerization catalyst at 100 °C, the activities of both were higher. Low polymerization activity of complex **64** in solution was apparently due to the increased steric hindrance of the alkoxy group.

Chakraborty used titanium complexes **65–68** as catalysts for the ROP of *rac*-LA, LLA, and  $\epsilon$ -CL.<sup>55</sup> All the polymerizations achieved complete monomer conversion in a short time, resulting in the polymer with a high molecular weight and narrow molecular weight distribution. When the feed ratio of monomer to catalyst was increased, the molecular weight of the polymer increased almost linearly and maintained a narrow distribution.

#### 5. TETRADENTATE LIGANDS AND MULTINUCLEAR COMPOUNDS

Tetradentate ligands have various structures and forms. Typical tetradentate ligands include salen/salan ligands,<sup>56,57</sup> atrane ligands,<sup>58,59</sup> and calixarene ligands.<sup>60</sup>

Titanium complexes with salen ligand **69** gave almost no polymer (Figure 8).<sup>61</sup> Salen ligand ligated titanium complexes **70–74** were used to catalyze the ROP of  $\epsilon$ -CL and LLA.<sup>62</sup> The activity was higher for LLA than for  $\epsilon$ -CL. The interaction between the coordinating atoms of the ligands and the central metal ion has a considerable influence on the resulting catalyst.



**Figure 7.** Titanium complexes ligated with tridentate ligand(s).

Kinetic results show a first-order dependence on the concentration of LLA and  $\epsilon$ -CL, respectively. The substituents on the ligand have a great influence on the polymerization activity. The benzyl-substituted salen-Ti catalyst **76** exhibited much higher activity for  $\epsilon$ -CL polymerization than the methyl-substituted catalyst **75**.<sup>63</sup> The molecular weight of the polymer obtained by the former was also higher than that of the latter. For the solution polymerization of  $\epsilon$ -CL or LLA in toluene, complexes **77** and **79** did not show any observable activity, while complex **78** gave the polymer with low molecular weight and broad molecular weight distribution.<sup>64</sup> It may be the effect

of the ortho substituent on the phenolic hydroxyl group on the ligand. All three complexes were inefficient for the solution copolymerization of  $\epsilon$ -CL and LLA. However, complexes **77**–**79** showed high conversion of *rac*-LA when polymerization was conducted under melt condition without using solvent and gave atactic PLA with high molecular weight and broad molecular weight distribution.

In an atrane ligand (see **Figure 9** left), there are three arms (*X*, *Y*, and *Z*) on an atom (*A*), and the atom itself and the three arms can coordinate with the central atom to form a pocket-shaped surrounding structure.<sup>58</sup> The titanium complex with an atrane

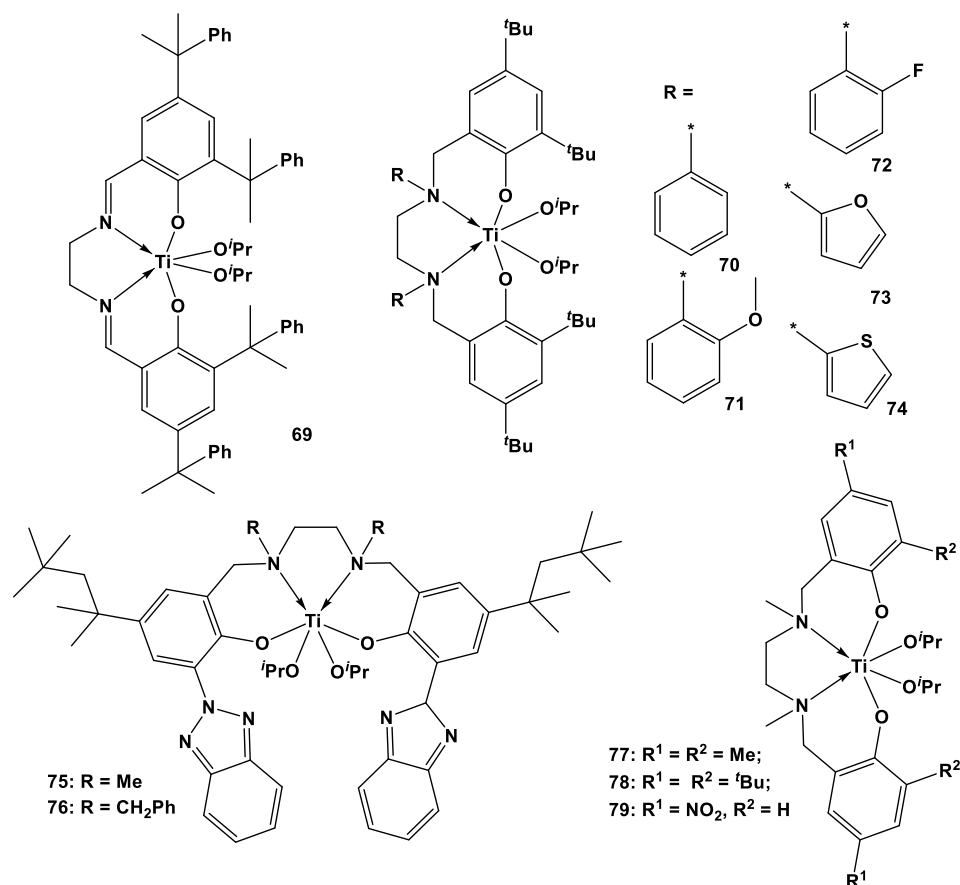


Figure 8. Titanium complexes ligated with salen/salan ligands.

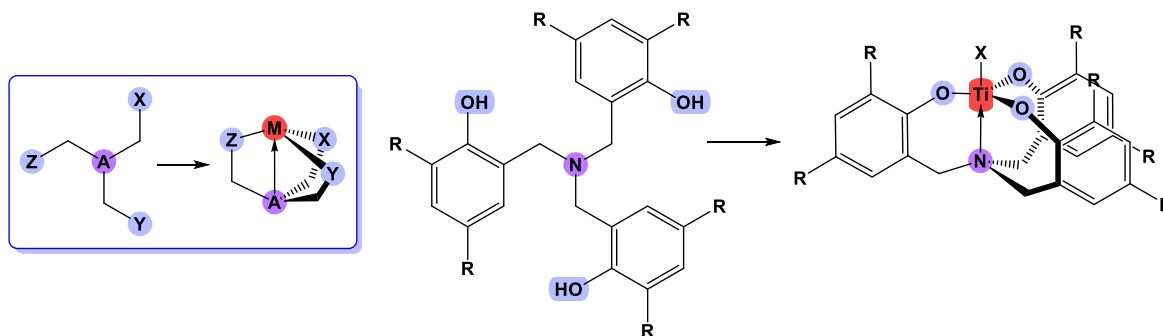


Figure 9. Model of the atrane ligand and its complex.

ligand, named titanatrane, was proved as an efficient catalyst for olefin polymerization (Figure 9 right).<sup>65</sup> Under melt conditions, complex **80** efficiently catalyzed the polymerization of *rac*-LA to give atactic PLA with high molecular weight but was inefficient for the solution polymerization of  $\epsilon$ -CL or LLA in toluene (Figure 10).<sup>64</sup> Complexes **81–84** were efficient for the ROP of  $\epsilon$ -CL in the solution polymerization conditions.<sup>66</sup> Isopropoxy compounds (**82** and **84**) required a shorter time to achieve complete monomer consumption, but polymer molecular weight was lower. From molecular weight analysis, each isopropoxy catalyst (**82** and **84**) molecule initiated two polymer chains, while each dimethylamine-based catalyst (**81** and **83**) molecule initiated only one polymer chain. For comparison and further investigation, additional atrane titanium compounds (**85** and **86**) and some analogues with a tridentate ligand (**87–91**) were synthesized.<sup>67</sup> The solution polymerization of  $\epsilon$ -CL was

carried out with these compounds as catalysts. For titanium complexes ligated with both atrane and tridentate ligands, dimethylamine-based catalysts showed the slowest polymerization rates, and each catalyst molecule initiated only one polymer chain. The polymerization rate of dimethylamine-based catalyst **89** was 200 times slower than that of isopropoxy catalyst **90**. This may indicate that the dimethylamine group that does not initiate polymerization has a negative effect on the insertion growth of  $\epsilon$ -CL in dimethylamine-based catalysts. The strong electron-donating ability of  $\text{NMe}_2$  inhibited the coordination of the monomer. This can be found by comparing the polymerization rates of dimethylamine and isopropoxy catalysts. To verify this interpretation, compound **91** was synthesized. When polymerization was initiated with this compound, the propagation chain only grew from the isopropoxy group, which was known from the NMR of the end-chain structure.

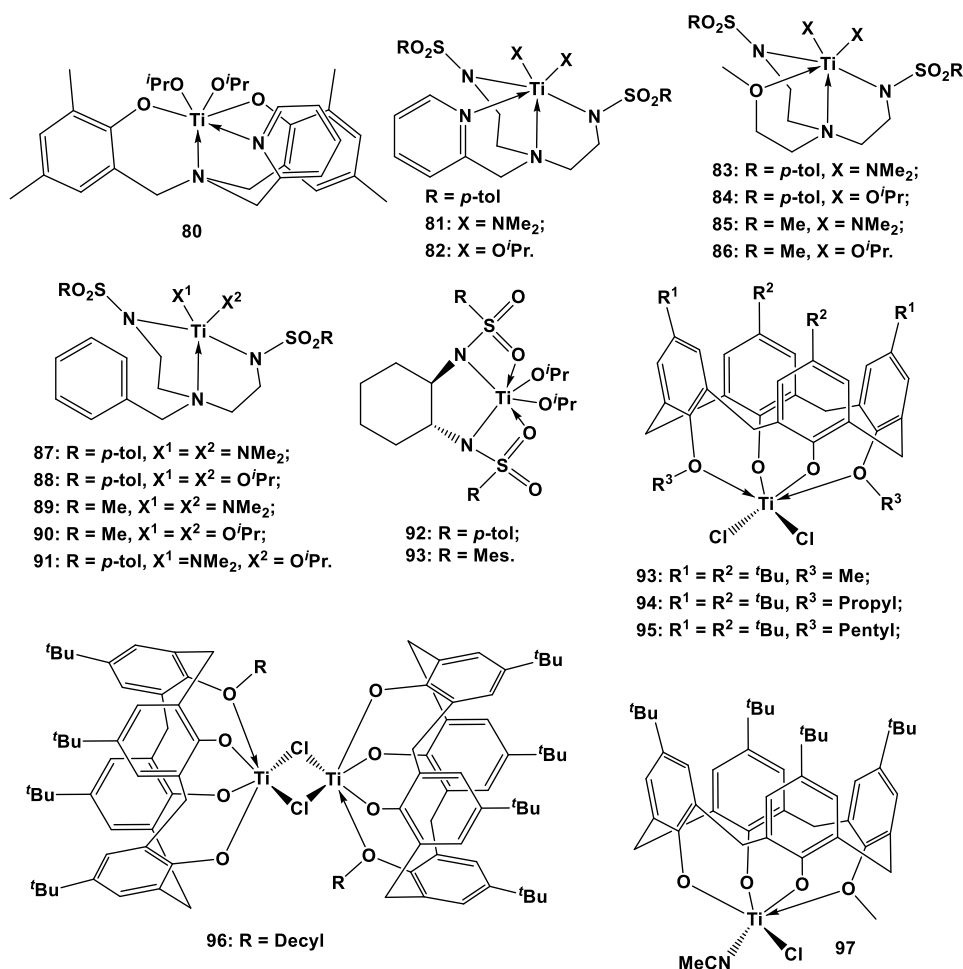


Figure 10. Titanium complexes with atrane and calixarene ligands.

Catalysts with different structures had different induction periods. The induction period of dimethylamine-based catalyst **89** was the longest (up to 1 h); that of the isopropoxy catalyst **88** was about 10 min; and that of the induction period of the hybrid catalyst **91** was about 30 min. The isopropoxy catalysts, **82**, **84**, **88**, and **90**, were used for *rac*-LA polymerization and gave the atactic PLA. In this study, compounds **92** and **93** were also synthesized. When used for  $\epsilon$ -CL polymerization, it was found that the polymerization of **92** was dual-chain initiation, while that of **93** was single-chain initiation. The reason may be the larger steric hindrance of the ligand of **93**. In the polymerization of *rac*-LA, there is no significant difference in the performances of these two catalysts.

The ability of titanium complexes ligated with tetrahydroxycalix[4]arene (**93**–**98**) as catalysts for ROP of  $\epsilon$ -CL,  $\delta$ -VL, *rac*-LA, and  $\omega$ -PDL with and without BnOH was screened.<sup>68</sup> The solution polymerization of  $\epsilon$ -CL in toluene or acetonitrile by complexes **93**, **94**, and **95** in the presence or absence of BnOH resulted in a satisfactory conversion within 24 h, but the polymer obtained in acetonitrile has a higher molecular weight and narrower molecular weight distribution. In a shorter polymerization time (1 h), conversion was sharply decreased. The complete conversion of  $\epsilon$ -CL by complexes **93**–**97** could also be achieved by polymerization in air, but the molecular weight of the polymer was changed. Lowering the polymerization temperature reduced the conversion, especially for catalysts **93**–**95**. Conversions of  $\delta$ -VL or *rac*-LA were lower

than that of  $\epsilon$ -CL. Only catalyst **97** achieved moderate activity of  $\omega$ -PDL polymerization at 130 °C and 24 h, and the activity of polymerization in the air was considerably reduced. Other catalysts (**93**–**96**) were inactive. The copolymerization by using complex **97** of  $\epsilon$ -CL with  $\delta$ -VL or *rac*-LA was also studied. Both copolymerizations achieved complete monomer conversion within 24 h, and the same conversion rate was observed in the copolymerization in air. The products were generated as random copolymers. In the copolymer of  $\epsilon$ -CL and  $\delta$ -VL, the average sequence length of the two monomers was 2.22 and 1.82. In the copolymers of  $\epsilon$ -CL and *rac*-LA, the average sequence lengths of the two monomers were 3.04 and 2.42.

The activity of  $\epsilon$ -CL or LLA polymerization catalyzed by the multinuclear titanium compound **98** (Figure 11) was lower than that of the corresponding mononuclear catalysts (**49** and **52**), but the molecular weight of the polymers was slightly improved.<sup>51</sup>

## 6. SUMMARY AND OUTLOOK

There are many studies on catalysts and polymerization methods of ring-opening polymerization for different monomers.<sup>19,69</sup> Through the analysis of catalyst, polymerization behavior, and polymer structure, it is hoped that the general law of catalyst design is obtained. It can be concluded that:

1. The catalytic effect of catalysts is closely related to the structure of ligands. The electronic effect and steric hindrance effect of the ligand greatly affect the polymer-



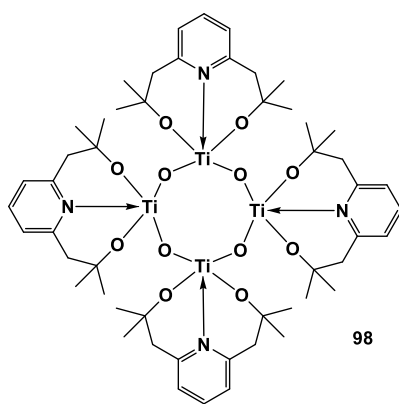


Figure 11. Multinuclear complex.

ization activity, molecular weight, and distribution of polymers and the stereoselectivity of individual monomers.

- Polymerization conditions have an important impact on the polymerization results, such as polymerization temperature, time, solvent or not, and feeding sequence, etc. If the catalyst structure determines the range of polymerization effects, then the optimum polymerization conditions can find the upper limit of this range.
- The matching of catalyst and monomer is very important. No single catalyst works best for all monomers. What fits is the best.
- The design of the catalyst should be simple. Too complex a structure brings the difficulty of synthesis and separation, thus causing the cost to increase.

It is hoped that the summary of the titanium catalyst in this paper can inspire the design and application of the ROP catalyst.

In the study of various metal catalyst residues, the titanium catalyst is considered to have good biocompatibility and safety.<sup>70–73</sup> However, from a certain point of view, it can only be said that there is no experiment to prove that the residue of titanium is harmful to the human body. For example, nano-TiO<sub>2</sub> has been proved to be harmful to the human liver, circulatory system, and genetic systems.<sup>74</sup> Therefore, a safer catalytic system should be transition metal free. Many metal-free ROP catalytic systems have been developed.<sup>75,76</sup> It is expected that the wide application of harmless polymer products will improve the quality of human life.

## AUTHOR INFORMATION

### Corresponding Author

Wei Wang – Sinopec (Beijing) Research Institute of Chemical Industry Co., Ltd., Sinopec Key Laboratory of Research and Application of Medical and Hygienic Materials, Beijing 100013, China; [orcid.org/0000-0001-5210-4432](https://orcid.org/0000-0001-5210-4432); Email: [wangw.bjhy@sinopec.com](mailto:wangw.bjhy@sinopec.com)

Complete contact information is available at:  
<https://pubs.acs.org/10.1021/acsomega.4c00048>

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