

Investigating the Ring-Opening Polymerization Activity of Niobium and Tantalum Ethoxides Supported by Phenoxyimine Ligands

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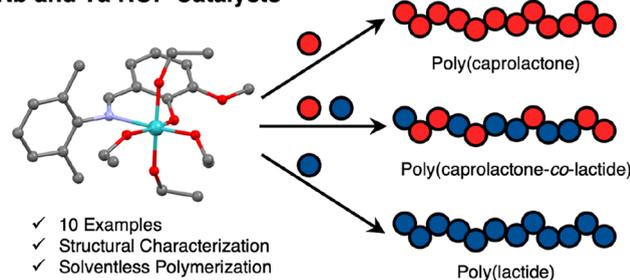
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ABSTRACT: A variety of metal catalysts from around the periodic table have been studied for the ring-opening polymerization (ROP) of cyclic esters. Within this field, group V catalysts have been rarely explored. To better understand the effect the choice of metal and ligand has on ROP activity, a series of 10 niobium and tantalum alkoxide catalysts, supported by a range of phenoxyimine ligands, were synthesized. The electronics and steric bulk of the ligands were varied on the phenoxy group (*t*Bu, Cl, and OMe) and the imine group (Ph; 2,6-diMePh; 2,6-diⁱPrPh; and 2,4,6-tri^tBuPh) to probe their effect on the catalyst structure and activity. Catalysts were characterized with 1D, 2D, and variable-temperature NMR techniques to determine their structure in solution. Single crystal X-ray diffraction studies were conducted to establish their solid-state structure. The 10 catalysts are pseudo-octahedral, and each shows ligand coordination through phenoxy-oxygen and imine-nitrogen (O,N). In the case of the *o*-vanillin ligand set, however, evidence was found for O,O-coordination of the ligand when the steric encumbrance of the imine-nitrogen was increased. Each catalyst was active for the ring-opening polymerization of both *rac*-lactide (LA) and ϵ -caprolactone (CL) in the absence of solvent at 140 °C. In the case of CL, the catalysts supported by chloro-containing ligands showed the most polymerization control based on final polymer molecular weight and dispersity. Ligand trends were less clear for the polymerization of LA, though in all cases the catalysts were more controlled than the parent homoleptic alkoxide [M(OEt)₅; M = Nb or Ta]. The most promising catalyst in the family was tested for copolymerization activity of LA and CL in one pot. Copolymerization of the two monomers was successful and yielded random poly(caprolactone-*co*-lactide).

Nb and Ta ROP Catalysts



INTRODUCTION

Biodegradable polymers comprising ester linkages are an important class of materials used for a range of applications, including packaging and drug delivery.^{1,2} Polyesters derived from ring-opening polymerization (ROP), such as poly(caprolactone) (PCL) and poly(lactide) (PLA), are widely studied in this area as their material properties can be tuned by altering the polymer architecture.^{3–5} The choice of catalyst is integral to the nature of the resulting polymer, and a variety of metal complexes from across the periodic table, including aluminum,^{6,7} tin,^{8,9} magnesium,^{10,11} zinc,^{12,13} and titanium,^{14–16} have been studied in detail. In choosing a catalyst, one must balance primarily the following: (1) rate of polymerization—how quickly the material is produced at a given concentration and temperature; (2) control of polymerization—for example, the distribution of polymer molecular weight and the resulting polymer tacticity; and (3) environmental considerations—how tolerant the catalyst is to oxygen, water, and impurities. The search for new families of ROP catalysts that optimize these factors, through ligand design and the study of underexplored metal centers, remains an active area of research.¹⁷

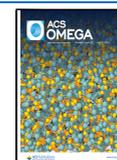
The ROP activity of group V metal alkoxides has been rarely studied compared to their group IV neighbors.^{15,18,19} Indeed,

ROP of lactide (LA) by tantalum ethoxide is slow, and a corresponding (EtO)₂Ta[tris(2-oxy-3,5-dimethylbenzyl)-amine] complex is unreactive in the melt at 130 °C.²⁰ Regardless, there have been some reports of successful polymerization of LA and ϵ -caprolactone (CL) either through the addition of benzyl alcohol to Nb or Ta halide complexes²¹ or *via* a coordination-insertion mechanism with metal alkoxides or hydrides.^{22–24} Of these limited examples, a family of molecules synthesized by Saha and co-workers suggests that phenoxyimine derivatives of heavy group V alkoxides are capable of remarkable polymerization control.²³ Inspired by these results and previous work on group IV phenoxyimines,^{25–27} we sought to explore a new family of Nb and Ta ethoxide catalysts for the ROP of LA and CL. Herein, we report the synthesis, characterization, and polymerization studies of 10 group V catalysts, with the aim of identifying

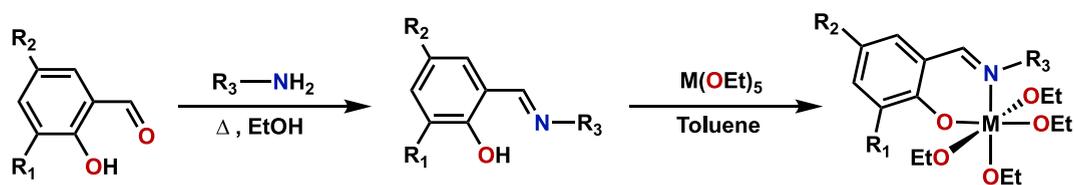
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Scheme 1. Synthesis of HL_{1-3d} Adapted from the Literature,^{26,28–33} Followed by Metalation to Form the Desired Catalyst, 1–6d^a



L						
M	HL ₁	HL ₂	HL _{3a}	HL _{3b}	HL _{3c}	HL _{3d}
Nb	1	2	3a	3b	3c	3d
Ta	4	5	6a	6b	6c	6d

^a(M = Nb or Ta; R₁ = ^tBu, Cl, or OMe; R₂ = ^tBu, Cl, or H; R₃ = Ph, 2,6-diMePh, 2,6-diⁱPrPh, or 2,4,6-tri^tBuPh)

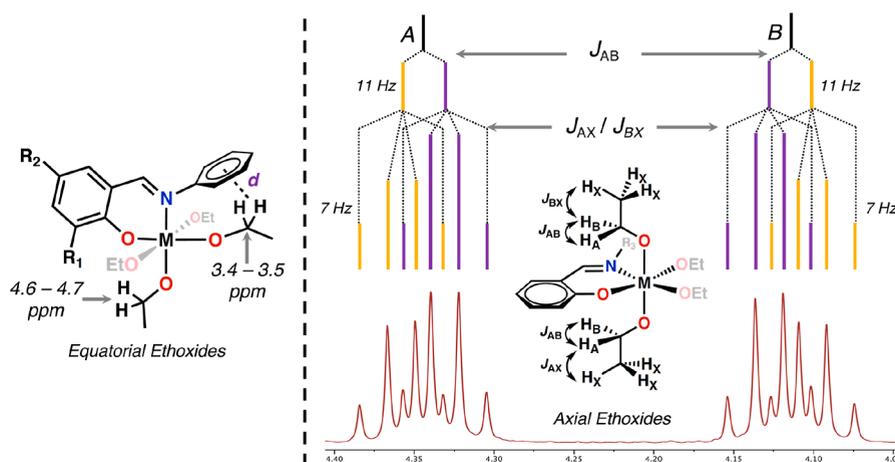


Figure 1. Structural considerations in catalyst 4 giving rise to the observed ¹H NMR shifts for equatorial (left) and axial (right) ethoxide methylene units.

how altering the metal or the steric and electronic properties of the ligand affects polymerization activity and control. In addition, we report initial findings on the ability of the catalysts to produce copolymers of the two monomers in a one-pot reaction.

RESULTS AND DISCUSSION

Catalyst Synthesis. The catalyst family 1–6d is synthesized *via* a 1-to-1 addition of the desired ligand to the commercially available homoleptic metal alkoxide, Nb(OEt)₅ or Ta(OEt)₅, in dry toluene (Scheme 1). The resulting yellow product has an oily consistency after removal of volatiles under vacuum. Addition of pentane followed by drying under vacuum produced a yellow powder or, in the case of 3b and 6b, an oil that could be recrystallized from pentane or tetrahydrofuran (THF) at –35 °C to yield X-ray quality crystals. Most complexes required no further purification; however, 3a and 6c

showed trace amounts of starting material in the ¹H NMR, which could be removed by recrystallization. Full synthetic details can be found in the Supporting Information. The identity of each catalyst was determined in solution by ¹H and ¹³C{¹H} NMR as well as by several 2D techniques, including COSY, HSQC, and HMBC (Figures S7–S64). In addition, all catalysts, except 3d and 6d, were able to be crystallized and their solid-state structures determined by single crystal X-ray diffraction (SCXRD) experiments (Figures S65–S76).

The metathesis reaction between M(OEt)₅ (M = Nb or Ta) and the ligand to form the desired catalyst is likely driven by the relative basicity of ethoxide as compared with the resulting phenoxide as well as by the chelate effect. This procedure is similar to the synthesis of analogous group IV²⁶ and group V phenoxyimine chelates^{34,35} and provides a straightforward route to a variety of ROP catalysts containing ethoxide initiating groups. Starting from commercially available metal

alkoxides and proceeding through an alcohol metathesis route has advantages over salt metathesis reactions with metal halides, as this approach eliminates the need to first deprotonate the ligand and does not require the separation of metal salts from the final reaction mixture, simplifying the synthesis and increasing atom economy.

Nuclear Magnetic Resonance. The successful synthesis of catalysts 1–3c and 4–6c was determined from several diagnostic signals in the ^1H NMR spectra: (1) the ligand imine signal shifts downfield relative to the ligand upon coordination with the metal center, (2) the ligand phenolic proton disappears, and (3) the metal ethoxide signals shift and split into four distinct chemical environments. The degree of substitution in each catalyst was confirmed through integration of the ligand and ethoxide signals, which in all cases confirmed a 1:4 ratio, as expected. Full ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR assignments can be found in the Supporting Information along with COSY, HSQC, and HMBC spectra (Figures S7–S64). Minor species were found to contaminate 3d and 6d despite efforts to purify them. This is likely due to hydrolysis with adventitious water and facilitated by the alternative bonding mode discussed below.

Catalysts 1–3c and 4–6c had the same gross features in their ^1H NMR spectra. There are four distinct methylene signals resulting from the four alkoxide moieties, which lends insights into the molecular structure. Six of the 10 complexes have sharp signals in the methylene region, while the remaining four are broadened at room temperature, likely due to fluxionality. The broad signals exhibited by the three Nb species (2, 3b, and 3c) could be sharpened at a low temperature ($-50\text{ }^\circ\text{C}$) to show a pattern similar to that of the rest of the family (Figures S13, S24, and S30). As the features of all 10 ^1H NMR spectra are consistent, complex 4 is discussed here as a case study. The two *trans* ethoxide ligands of 4 appear at 4.30 and 4.09 ppm, both as doublets of quartets (Figure 1, right). This splitting pattern suggests that the methylene protons are diastereotopic, and COSY analysis confirms that they couple to one another in addition to their neighboring methyl group (Figure S41). This set of signals is flanked by two additional signals, which both appear as quartets. These resonances correspond to the two remaining ethoxide ligands that are in chemically unique environments. One is significantly more deshielded (4.60 ppm) than the other (3.44 ppm). Previous studies of group V 23 and titanium phenoxyimines 25 have suggested that this difference comes from the orientation of the alkoxide protons above the π -system of the ligand aryl group, leading to an upfield shift. Structural analysis (*vide infra*) of the catalysts confirms a similar arrangement of the methylene unit *trans* to the phenoxide moiety. In all cases, these protons are pointed at the ligand aryl ring at a distance that ranges from ~ 2.64 – 3.01 \AA , as measured from the aryl plane to the closest methylene proton, within the range of previous reports. 23,25 This would suggest that the signals with higher ppm (4.6–4.7) belong to the ethoxide ligand *trans* to the imine, and those at lower ppm (3.4–3.5) correspond to the ethoxide ligand *trans* to the phenoxide (Figure 1, left). It should be noted, however, that the ligand phenoxide and imine have a dissimilar *trans* effect that likely also plays a smaller role in the shift of the methylene signal. The interplay between *trans* effect and ligand/aryl interactions may play a role in the reactivity of the molecules—however, due to the lack of reports in this area, more investigation is required for full confirmation.

Compounds 3d and 6d are supported by the *o*-vanillin ligand with the most extreme steric encumbrance. Past investigation into *o*-vanillin phenoxyimines has shown that this encumbrance can cause the ligand to shift from *O,N*-coordination (between phenoxy and imine) to *O,O*-coordination (between phenoxy and methoxy). 26 If this were the case in 3d and 6d, we would expect a significantly different ^1H NMR spectrum than for the other compounds in the series. For instance, because the imine phenyl ring would be positioned distal to the metal alkoxides, we would not anticipate the downfield shift of one equatorial alkoxide ligand due to interaction with the π -system. We would also expect to see a significant shift in the imine proton's NMR signal, as the neighboring nitrogen is no longer involved in metal coordination. Indeed, ^1H NMR analysis of 3d appears to support the finding of *O,O*-coordination in solution (Figure S35). The alkoxide methylenes collapse into one broad signal at 4.3 ppm, and the imine-CH is shifted significantly downfield relative to the other *O,N*-coordinated compounds. However, despite numerous purification attempts, both 3d and 6d showed evidence of minor side products that could not be removed. As such, their catalytic activities were not tested.

Catalyst Structure. To further understand the coordination chemistry—and thus the nature—of the catalytic metal center, an attempt was made to recrystallize each compound at low temperatures from a concentrated solution in THF or pentane. Despite numerous attempts, 3d and 6d did not crystallize, though a hydrolysis product of 3d (3e) and a doubly substituted side product (3f) were isolated. Ten of the catalysts were crystallized, and SCXRD demonstrates that 1–3c and 4–6c are all isostructural, each adopting a distorted octahedral geometry around the metal center (Figures 2 and S65–S76). Moreover, most of the Nb and Ta complexes supported by the same ligand (1/4, 2/5, 3b/6b, and 3c/6c) adopted the same space group and shared nearly identical unit cell dimensions (Tables S1–S4). This similarity is likely a ramification of the two metals sharing a common ionic radius of 78 pm (M^{5+} , coordination number = 6). 36 In all cases, the phenoxyimine ligand is coordinated through the phenolate and the imine nitrogen (*O,N*) to form a six-membered ring. Two ethoxide ligands reside in the equatorial position, *trans* to either the phenolate or the imine, and the other two occupy axial positions. This general solid-state structure is fully consistent with the NMR data discussed previously.

$\text{M}-\text{O}_{\text{alkoxide}}$ bond lengths were similar throughout the 10 complexes, varying by less than 0.1 \AA and ranging from 1.851 to 1.928 \AA , with an average of 1.903 \AA . Generally, $\text{M}-\text{O}_{\text{alkoxide}}$ bonds corresponding to the ethoxide ligand *trans* to the ligand phenolate are shorter on average (1.888 \AA) than their counterparts *trans* to the ligand imine (1.904 \AA). These values are both shorter than the average axial $\text{M}-\text{O}_{\text{alkoxide}}$ bond length (1.911 \AA). Only two Nb and Ta phenoxyimine structures that contain alkoxide ligands have been reported in the literature. 23 These adopt a pseudo-octahedral $\text{M}(\text{L})(\text{OEt})_2(\text{Cl})_2$ configuration, with the chloride ligands occupying axial positions. The two ethoxide ligands reside in the equatorial position and are *trans* to the phenolate and the imine. The shortest of the two $\text{M}-\text{O}_{\text{alkoxide}}$ bonds is the ligand *trans* to the imine in both cases [$\text{Nb} = 1.828(2)\text{ \AA}$, $\text{Ta} = 1.830(5)\text{ \AA}$], while the longer bond is the one *trans* to the phenolate [$\text{Nb} = 1.837(3)\text{ \AA}$, $\text{Ta} = 1.848(5)\text{ \AA}$]. 23 Overall, these bond lengths are considerably shorter than those we report here, most likely due to the difference in axial ligands.

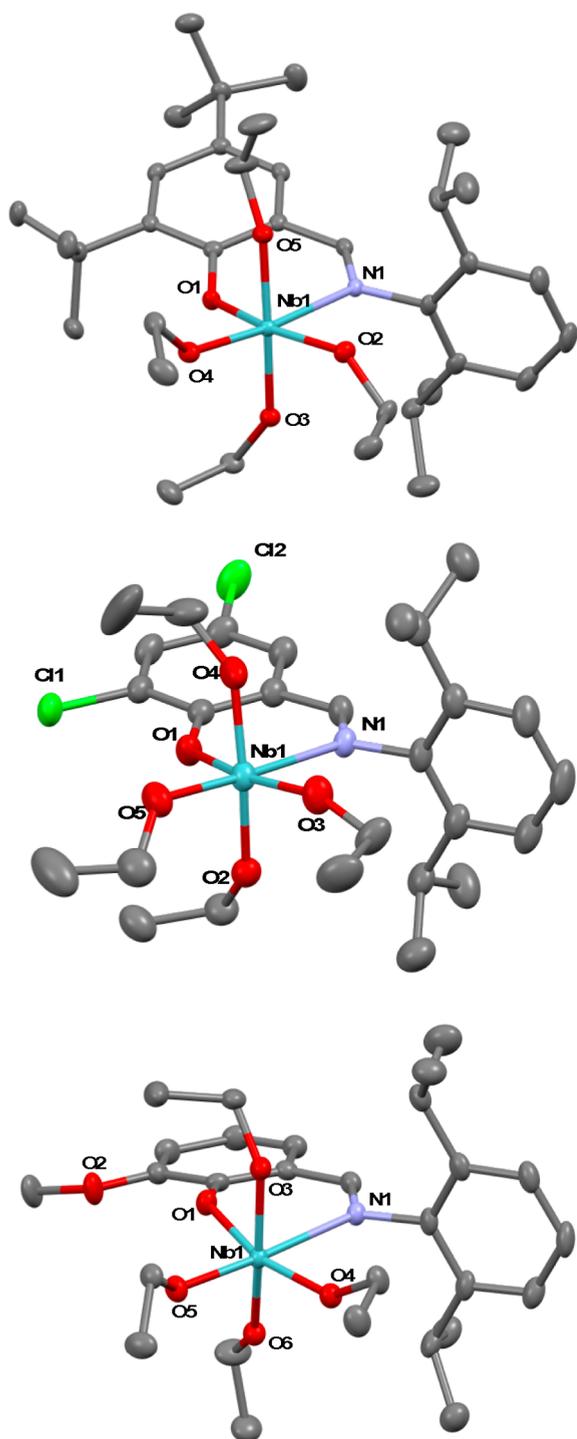


Figure 2. X-ray crystal structures of **1**, **2**, and **3c**. Thermal ellipsoids drawn at 50% probability; hydrogen atoms and disorder are excluded for clarity. Only one of three molecules in the asymmetric unit shown for **3c** (teal: niobium; dark gray: carbon; scarlet: oxygen; blue: nitrogen; green: chlorine).

Titanium metal alkoxides supported by salicylaldehyde-derived phenoxyimine ligands adopt a different coordination chemistry as steric bulk is increased, ultimately leading to reduced reactivity.²⁵ This increase in steric pressure results in failure to coordinate through the imine nitrogen in some cases. In contrast, *o*-vanillin derivatives are able to access *O,O*-coordination through the ligand methoxy group, which is less

sterically encumbered.²⁶ We looked to see if this unique coordination chemistry applied analogously to group V alkoxides by altering the steric bulk on the ligand R_3 position ($R_3 = \text{Ph}$ [**3a**, **6a**] < 2,6-diMePh [**3b**, **6b**] < 2,6-di^{*i*}PrPh [**3c**, **6c**] < 2,4,6-tri^{*t*}BuPh [**3d**, **6d**]). Complexes **3a–c** and **6a–c** were structurally similar in the solid state to those coordinated by alkyl- (**1** and **5**) and halo- (**2** and **6**) phenoxyimines, showing only *O,N*-coordination. Evidently, these ligands do not have sufficient bulk to induce *O,O*-coordination through the methoxy group. Unfortunately, efforts to obtain X-ray quality crystals of the most extreme steric case, **3d** and **6d**, failed after numerous attempts. However, 2,4,6-tri^{*t*}BuPh derivatives have previously been shown to facilitate *O,O*-coordination in group IV complexes,²⁶ as may be the case in **3d** and **6d**. Despite the difficulty in crystallizing the 2,4,6-tri^{*t*}BuPh derivatives, one hydrolysis product, $(L_{3d})_2\text{Nb}_4(\text{OEt})_{10}\text{O}_4$ (**3e**), was successfully isolated and analyzed by SCXRD (Figure 3A). **3e** is a tetrameric cluster best described as a bimetallic dimer. In one bimetallic fragment, Nb(1) is coordinated by the ligand through a five-membered *O,O*—rather than six-membered *O,N*—binding mode due to its steric bulk. Nb(1) is bridged to another Nb(2), containing three terminal ethoxide ligands, by both a shared ethoxide ligand and a bent oxide (Nb–O–Nb = 112°). This bimetallic fragment then forms a dimer with Nb(3) and Nb(4) through linear oxides (Nb–O–Nb = 175°) (Figure 3C).

In addition to the hydrolysis product (**3e**), a doubly substituted side product, $\text{Nb}(L_{3d})_2(\text{OEt})_3$ (**3f**), also selectively crystallized out of a concentrated pentane solution (Figure S71). **3f** again showed one of the *o*-vanillin ligands coordinated through the an *O,O*-bonding mode, while the other was bound only through the phenoxy group. The remaining ethoxide ligands formed a *fac* arrangement around the metal center.

These results, taken together, show that *o*-vanillin-derived phenoxyimines are capable of accessing both *O,N*- and *O,O*-binding modes, depending on steric bulk in systems other than titanium,²⁶ though, byproducts, resulting from hydrolysis (**3e**) or over substitution (**3f**), may be produced.

Ring-Opening Polymerization. The catalysts **1–3c** and **4–6c** were each tested for ROP activity with two monomers, ϵ -caprolactone (CL) and *rac*-lactide (LA). The polymerization reactions were run under solventless conditions in a nitrogen glovebox at 140 °C. At the end of the reaction, one aliquot was taken for NMR analysis to assess monomer conversion, and a second was removed for analysis by gel permeation chromatography (GPC) to determine M_n and polymer dispersity (\mathcal{D}).

The reaction of CL with all 10 catalysts, **1–3c** and **4–6c**, went to full conversion (>90%, when stirring was impeded) within 1–3 h and showed $M_n(\text{GPC})$ values corresponding to four growing polymer chains (~2500–3500 g/mol) initiated by the four ethoxide ligands. Dispersity values varied from well controlled, 1.19, to poorly controlled, 2.10, depending on the choice of metal and ligand (Table 1). To benchmark the catalyst family, $\text{Nb}(\text{OEt})_5$ and $\text{Ta}(\text{OEt})_5$ were studied under the same conditions. $\text{Nb}(\text{OEt})_5$ reached full conversion in 15 min, faster than any other catalyst tested, but suffered from poor control ($\mathcal{D} = 2.15$). $\text{Ta}(\text{OEt})_5$ likewise showed poor control ($\mathcal{D} = 2.39$) and took longer to reach full conversion, 1 h, than $\text{Nb}(\text{OEt})_5$. For the Nb catalysts **1–3c**, the addition of a phenoxyimine ligand universally slows down polymerization relative to the parent homoleptic alkoxide—based on polymer

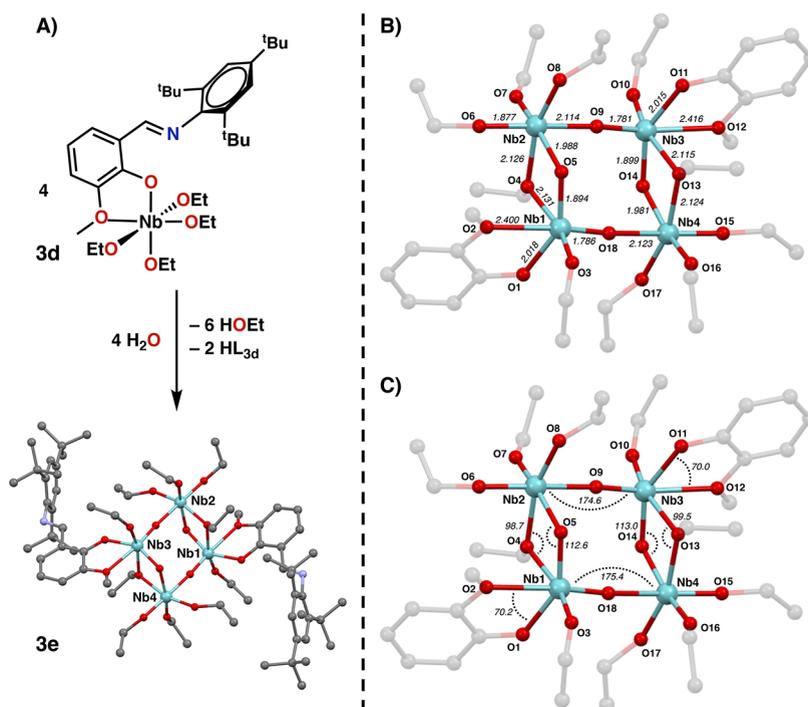


Figure 3. (A) Proposed conversion of 3d to 3e through hydrolysis by adventitious water. Crystal structure of the 3e core is shown in a ball-and-stick format with disorder and hydrogen atoms omitted for clarity. (B) Selected Nb–O bond distances (Å). (C) bond angles (°) of the metal core.

dispersity; however, the control of polymerization was enhanced. 3a was found to reach full conversion in 1 h, faster than the other four Nb catalysts, while catalyst 2 showed the greatest degree of polymerization control, $\bar{D} = 1.27$. Ta-based catalysts 4–6c performed similarly to their Nb counterparts and shared the same general trends. Catalyst 6a reached 95% conversion in 1 h while sacrificing some polymerization control, $\bar{D} = 1.94$. Conversely, though 5 was slower, it achieved excellent control, $\bar{D} = 1.19$.

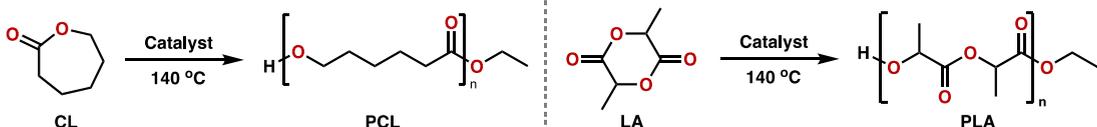
The polymerization of LA was slower than that of CL. In general, all catalysts went to >90% conversion in 4–7 h, in some cases faster than their parent homoleptic alkoxide. Like the CL results, $M_n(\text{GPC})$ values correspond to four growing polymer chains with moderate polymerization control (1.41–1.86). The ligand trends seen in CL did not generally correspond to LA. However, all catalysts showed better polymerization control when coordinated by the phenoxyimine ligand. In the case of the Nb catalysts, 3b appeared to be the fastest of the group, reaching 94% conversion in 4 h, while the lowest polymer dispersity resulted from catalyst 1. Similarly, for the Ta catalysts, 6b reached 94% conversion in 4 h, and all five catalysts produced polymers with similar dispersities, 1.52–1.70.

The data suggest that the choice of ligand, rather than the metal, plays a critical role in catalysis, particularly when polymerizing CL. This result is perhaps not surprising given the isostructural nature of the two sets of catalysts. Ligand trends with respect to CL seem to be more dramatic than with LA. The time required to achieve high conversion appears to be increased by decreasing steric bulk on the ligand imine (3a > 3b > 3c), but this change has little effect on catalyst control. Optimal polymer control, based on dispersity, came from the catalysts 2 and 5, which bear electron-withdrawing chloride ligands, while control was generally poor with catalysts 1 and 4, which are supported by *tert*-butyl substituents. Indeed, the

breadth of dispersities found in the family, 1.19–2.10, suggests that the fine tuning of electronic and steric factors is critical for limiting transesterification and maximizing polymerization control. The ligand set, L₂ (Scheme 1), appears to limit transesterification of the growing polymer chain, likely by balancing these factors. This result is particularly striking given the reaction conditions, as we would expect a high degree of transesterification while growing four chains simultaneously, at high temperatures, under solventless conditions. Ligand trends were less pronounced for the polymerization of LA, though performance was increased relative to the homoleptic alkoxides. This may be due to a difference in the catalyst resting state between growing PCL and PLA chains, as the most recently inserted monomer in PLA is capable of chelating back onto the metal through the proximal carbonyl functionality.^{12,37,38} Further mechanistic studies are underway in our lab to better understand the nature of these intermediates and why transesterification is suppressed in some cases and uncontrolled in others.

Based on the M_n data and the narrow to moderate dispersities of the catalyst family, it is most likely that polymerization proceeds through the well-known coordination-insertion mechanism (Scheme 2).¹⁷ Previous reports of Nb- and Ta-supported phenoxyimines and aminophenols invoke this mechanism of ROP as well but suggest that the ligand itself initiates polymerization, rather than attendant ethoxide ligands.^{23,39} Interestingly, the most closely related complexes to those we report (Table 1, entries 27 and 28) show remarkable polymerization control despite this.²³ By contrast, in our system, we see two pieces of evidence that suggest that ethoxide initiates polymerization (as is the case with group IV catalysts^{26,40}). In all instances, the GPC M_n corresponds closely to a theoretical M_n calculated for four ethoxide initiators (Table 1), strongly implying that each ethoxide ligand, rather than the Schiff-base ligand itself, is

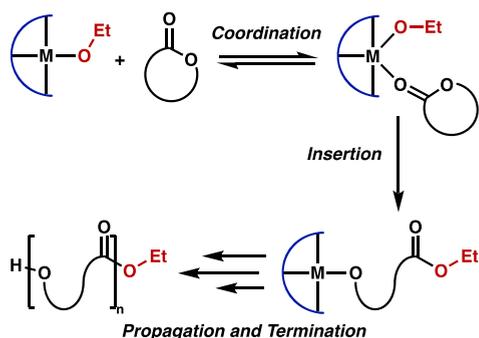
Table 1. Polymerization Results



entry	catalyst ^a	monomer	time (h)	monomer conversion (%) ^b	M_n , calc (g/mol) ^c	M_n , GPC (g/mol) ^d	\bar{D}
1	Nb(OEt) ₅	CL	0.25	99	2260	2850	2.15
2	1	CL	3	99	2820	3480	1.91
3	2	CL	3	98	2800	3170	1.27
4	3a	CL	1	97	2770	3100	1.64
5	3b	CL	2	93	2650	2720	1.58
6	3c	CL	3	99	2820	3360	1.75
7	Ta(OEt) ₅	CL	1	99	2260	2560	2.39
8	4	CL	3	94	2680	3250	2.10
9	5	CL	3	95	2710	3310	1.19
11	6a	CL	1	95	2710	2710	1.94
11	6b	CL	1.5	99	2820	3330	1.42
12	6c	CL	3	99	2820	3080	1.69
13	Nb(OEt) ₅	LA	6	97	2800	2370	2.00
14	1	LA	6	93	3260	2970	1.41
15	2	LA	5	93	3350	3420	1.58
16	3a	LA	7	94	3390	2770	1.58
17	3b	LA	6	94	3390	2740	1.86
18	3c	LA	5	93	3260	2970	1.63
19	Ta(OEt) ₅	LA	6	97	2720	2380	1.70
20	4	LA	6	93	3260	3190	1.61
21	5	LA	5	93	3350	3260	1.54
22	6a	LA	6	94	3390	2720	1.52
23	6b	LA	6	95	3420	3390	1.67
24	6c	LA	5	93	3351	3210	1.59
25 ^{e(20)}	[(L')Ta(OEt) ₂]	LA	24	0			
27 ^{f(23)}	[(L'')Ta(OEt) ₂ (Cl) ₂]	LA	0.667	99	29170	31250	1.02
28 ^{g(23)}	[(L'')Ta(OEt) ₂ (Cl) ₂]	CL	0.867	98	23170	24580	1.05
29 ^{h(26)}	[(L''')Ti(O ⁱ Pr) ₂]	CL	0.10	90	10300	12100	1.63

^aReaction conditions: 140 °C; neat; monomer/catalyst, 100:1. ^bDetermined by ¹H NMR analysis of the crude reaction mixture through integration of the CL/PCL methylene protons (4.22/4.05 ppm) or LA/PLA methine protons (5.04/5.16 ppm). ^cCalculated as M_n , calc = $[MW_{\text{monomer}} \times (\text{monomer loading})]/(\# \text{ of initiators}) \times (\% \text{ conversion}/100)$; ($MW_{\text{CL}} = 114.14 \text{ g/mol}$, $MW_{\text{LA}} = 144.13 \text{ g/mol}$). ^d M_n , GPC was determined using poly(styrene) standards as a calibration and corrected by a factor of PCL = 0.56, PLA = 0.58.⁴¹ ^eReaction conditions: 130 °C, neat; LA/Catalyst = 300:1, L': tris(2-oxy-3,5-dimethylbenzyl)amine. ^fReaction conditions: 130 °C, neat; LA/catalyst = 200:1 L'': $R^1 = R^2 = \text{'Bu}$, $R^3 = (4\text{-OMe})\text{C}_6\text{H}_4$. ^gReaction conditions: 80 °C, neat; CL/catalyst = 200:1 L'': $R^1 = R^2 = \text{'Bu}$, $R^3 = (4\text{-OMe})\text{C}_6\text{H}_4$. ^hReaction conditions: 140 °C, neat; CL/catalyst = 200:1 L''': $R^1 = \text{OMe}$, $R^2 = \text{H}$, $R^3 = 2,6\text{-di}^i\text{PrPh}$.

Scheme 2. Generic Coordination-Insertion Mechanism for Ring-Opening Polymerization



active in polymerization. Furthermore, upon purification and ¹H NMR analysis of representative PCL and PLA samples, the polymer end group was found to be ethoxide (Figures S77 and S78).

Catalysts 1–3c and 4–6c were an improvement when compared to a previous study of (EtO)₂Ta[tris(2-oxy-3,5-dimethylbenzyl)amine], which showed no polymerization of LA (Table 1, entry 25). It was suggested in this work that the catalyst's positive charge density was insufficient upon expanding its coordination environment, thus limiting its ability to bind the monomer.²⁰ It would appear that catalysts 1–3c and 4–6c do not suffer from this limitation, as they all successfully polymerized both LA and CL; however, this may ultimately play a role in future optimization of the catalytic system. When compared to more widely studied titanium phenoxyimines under similar conditions (Table 1, entry 26), catalysts 1–3c and 4–6c proved to be slower, but in some cases more controlled.²⁶

Copolymerization Studies. That the catalyst family successfully polymerizes both CL and LA under solventless conditions suggests that the catalysts may also be capable of producing copolymers of the two. To our knowledge, there are no reports in the literature of poly(caprolactone-co-lactide) produced from group V alkoxide catalysts, so it is unknown if

they could behave, for example, like some magnesium catalysts that enchain only one monomer before terminating^{37,42} or like titanium catalysts that enchain both.⁴⁰

Copolymerization activity was tested with **5**, the catalyst that shows the most polymerization control, in an effort to limit transesterification as much as possible. The reaction was run at 140 °C under solventless conditions with a CL/LA/**5** loading of 100:100:1. Stirring was impeded due to increased viscosity after 5.5 h, at which point an aliquot was taken to determine conversion by NMR and M_n by GPC. NMR analysis of the LA methine region (5.04–5.16 ppm) and the CL methylene region (4.05–4.25 ppm) shows a LA conversion of 93% and a CL conversion of 92%. The GPC was monomodal, with an uncorrected M_n of 9500 g mol⁻¹ and a relatively high dispersity of 2.0. Following purification, the ¹H NMR spectrum shows two signals in the CL methylene region, a triplet at 4.04 ppm corresponding to CL–CL linkages and a multiplet at 4.11 ppm corresponding to CL–LA linkages. This result is expected for random copolymers of CL and LA⁴³ (Figure S79). The random nature of the polymer is further supported by ¹³C{¹H} NMR, which shows many signals in the carbonyl region ranging from 169 to 174 ppm, rather than just the two carbonyl signals expected from a block copolymer^{4,43–45} (Figure S79).

It is clear from these results that LA–CL copolymers can indeed be generated with the catalyst family; however, the broad dispersity and the random nature of the polymer architecture indicate that transesterification plays a significant role. Suppression of transesterification will be crucial for obtaining block copolymers,⁴⁵ which suggests that further exploration of Nb and Ta catalysts with other ligand architectures is warranted.

CONCLUSIONS

A series of Nb and Ta phenoxyimine catalysts were synthesized and characterized for the ROP of CL and LA. The structure of 10 catalysts tested for polymerization showed a pseudo-octahedral geometry with the phenoxyimine ligand bound through *O,N*-coordination; however, upon increasing the steric bulk of *o*-vanillin-derived ligands, the evidence suggests that *O,O*-coordination is preferred. Alteration of the coordinating ligand was found to affect both the time required to reach high polymer conversion and the polymer dispersity. Nb and Ta catalysts chelated by the same ligand were found to be isostructural with little difference between the polymerization properties, indicating that the ligand, rather than the metal, is key to their performance. Random poly(caprolactone-*co*-lactide) was successfully obtained from catalyst **5**, which shows that group V complexes of this kind are capable of enchainning both CL and LA in a single reaction pot; however, block copolymers were unable to be obtained due to transesterification. These results suggest that group V catalysts merit additional attention as initiators for ROP of cyclic esters. Further exploration into the catalyst design and mechanistic details of these systems is currently underway in our group.

General Experimental Procedures. A detailed account of the experimental procedures, including general considerations, adapted ligand synthesis, analytical details, and full NMR assignments, can be found in the Supporting Information. Some general and analytical procedures in our lab have been described previously.⁴⁰

General Catalyst Synthesis. The desired amounts of ligand (HL₁–HL_{3c}) and metal ethoxide [Nb(OEt)₅ or

Ta(OEt)₅] were weighed into oven-dried vials in a nitrogen glovebox. Each compound was then dissolved in anhydrous toluene and mixed. The yellow mixture was allowed to stir for 16 h. Solvent was then removed under high vacuum followed by addition of pentane. Subsequent removal of the pentane under vacuum yielded either a yellow powder or a thick gel. Catalysts could be recrystallized at –35 °C from either THF or pentane.

General PCL and PLA Polymerization Procedure. In a nitrogen glovebox, the desired catalyst was weighed into an oven-dried glass vial followed by addition of the appropriate amount of monomer to produce a 100:1 monomer-to-catalyst ratio. The reaction was then heated to 140 °C until stirring was impeded and conversion was over 90% as determined by NMR. Crude aliquots of the reaction were removed for ¹H NMR, to determine monomer conversion, and GPC, to determine M_n and PDI.

General Copolymerization Procedure. In a nitrogen glovebox, the desired catalyst was weighed in an oven-dried glass vial followed by addition of the appropriate amount of each monomer to produce a 100:100:1 CL/LA/catalyst ratio. The reaction was then heated to 140 °C until stirring was impeded and conversion was over 90%, as determined by NMR. Crude aliquots of the reaction were removed for ¹H NMR, to determine monomer conversion, and GPC, to determine M_n and PDI.

Polymer Purification. Representative samples of PCL, PLA, and poly(caprolactone-*co*-lactide) were purified by dissolving the crude polymer in dichloromethane followed by precipitation in either petroleum ether (PCL) or cold methanol (PLA and copolymer). The resulting material was filtered and dried. This procedure was repeated once more to yield the purified polymer in each case.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.2c02880>.

Detailed experimental procedures, 1D and 2D NMR spectra, X-ray structures, SCXRD data, and NMR of selected polymers (CIF)

¹H NMR spectrum of HL₁, HL₂, HL_{3a}, HL_{3b}, HL_{3c}, and HL_{3d} in CDCl₃; ¹H NMR, COSY ¹H NMR, HSQC, HMBC, and ¹³C{¹H} NMR spectra of **1**, **2**, **3a**, **3b**, **3c**, **3d**, **4**, **5**, **6a**, **6b**, and **6c** in CDCl₃; X-ray crystal structure of **1**, **2**, **3a**, **3b**, **3c**, **3e**, **3f**, **4**, **5**, **6a**, **6b**, and **6c**; selected regions of ¹H NMR of purified PCL in CDCl₃ from **2** and PLA from **5**; selected regions of ¹H and ¹³C{¹H} NMR in CDCl₃ for purified poly(lactide-*co*-caprolactone) from **5**; and crystallographic details (PDF)

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Notes

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