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Effects of Lewis Acidity and Size of Lanthanide Salts for Ring-Opening Copolymerization

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Lanthanide chloride salts, with a cocatalyst, are used as a near "one-size-fits-all" catalyst system to perform the ring-opening copolymerization of diverse epoxides and cyclic anhydrides. Variation of the metal in the lanthanide series leads to subtle changes in selectivity for random, gradient, and block copolymers when monomer mixtures are used.

The ring-opening copolymerization of epoxides and cyclic anhydrides (ROCOP) represents one way to achieve a variety of polyester structures that can hold many different properties (e.g., thermal, tensile, and degradation).[1,2] Catalyst design has played an important role in this field, with simple metal salt and mono- and multinuclear salen complexes proving to maintain control while having a high activity.[1-5] One common theme throughout the literature is that there is no "one-size-fits-all" catalyst system, meaning that there is no catalyst design that is best suited for all monomer pairs tested so far, in terms of rate of polymerization and suppression of side reactions (such as homopolymerization, transesterification, and epimerization). Despite numerous catalyst systems reported, in addition to over 400 epoxide/anhydride pairs available, there is not a clear methodology for what makes a catalyst best for certain monomer pairs.

There are a few examples of trends as the metal ion of an active catalysts is varied. When studying the polymerization of PA (phthalic anhydride)/EGE(ethyl glycidyl ether) with four different alkali metal carboxylate salts, it was found that the larger (i.e., less Lewis acidic) metals led to faster polymerization rates (**Fig. 1a**).[6] This is hypothesized to be due to the larger metals having a weaker Lewis acid/base pair interaction, leaving the alkali metal more available for epoxide activation. However, it isn't known if the trend holds for other monomer pairs.

More active catalysts have been elaborately designed. Williams and coworkers performed a systematic study on bimetallic catalysts for ROCOP to better understand the role of the secondary alkali metal when the primary Lewis acidic center was Al (**Fig. 1b**).[7,8] It was found that the less Lewis acidic metals performed the best with Al, which was hypothesized to stem from weaker interaction with the carboxylate chain end, allowing for a more nucleophilic anion to ring open an epoxide bound to the Al. When the primary metal center is changed from Al to other metal centers, the trend is less clear and there is no apparent reason why certain metals perform better.[9]

One of the most active catalysts reported in the literature includes a cyclopropenium cocatalyst covalently tethered to a salophen ligand, with six metals tested (**Fig. 1c**).[10] Cr(III), Co(III), and Al(III) performed the best (turnover frequencies, TOFs = 111, 376, 93 h^{-1} respectively). However, Cr(III) leads to increased

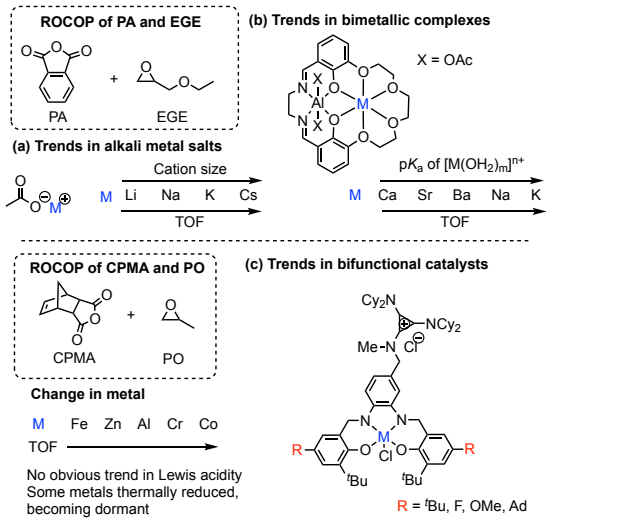

Fig. 1 Comparison of trends metal changes for different catalyst systems for the ROCOP of epoxides and cyclic anhydrides: a) trends in alkali metal salts in metal carboxylate catalysts, b) trends in secondary metal for bimetallic Al/M catalysts, and c) trends in primary metal ion in tethered metal/cyclopropenium catalysts.

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homopolymerization of epoxide, and Co(III) undergoes thermal reduction at low catalyst loadings, leading to Al being the optimized catalyst. Thus, both rate and suppression of side reactions are critical values to consider as catalysts are optimized.

There is a need for a catalyst system that can be finely tuned to be efficient and controlled for different monomer pairs without drastic changes in the ligand framework or metal center. This would allow for easy catalyst modification to optimize rate of polymerization for varied monomer pairs without altering preference for undesirable side reactions. Recently, we reported that YCl_3 salts ($YCl_3{\cdot}6H_2O$ and $YCl_3THF_{3.5}$) are excellent catalysts for this polymerization in the presence of bis(triphenylphosphine)iminium chloride ([PPN]Cl) as a cocatalyst.[11] Yttrium is a rare-earth metal and behaves very similarly regarding size and reactivity as the lanthanide series. The lanthanide series offers a unique opportunity to study how systematic changes in size and Lewis acidity of a metal ion affect the rate of polymerization, as the entire series often reacts in similar ways, lowering the likelihood of varied side reactions across metals.[12]

As monomer structures change, the requirements to achieve optimal rates of polymerization must change. In the rate-determining step (RDS) of epoxide ring-opening, as supported for multiple catalysts systems including this system,[13,14] an active metal catalyst must be large and Lewis acidic enough to activate the epoxide, while not too Lewis acidic that it chelates the carboxylate polymer chain end. Herein, simple lanthanide hydrate salts in the presence of a [PPN]Cl cocatalyst are used to understand the optimum size and Lewis acidity of a catalyst for six monomer pairs (**Fig. 2**). The lanthanide salts and monomer pairs were chosen to represent a range of variations in Lewis acidity and monomer structure (see electronic supplementary information (ESI) for more information). Systematic changes in the ionic radii and Lewis acidity of eight rare-earth metals reveal every monomer pair can be optimized to a different set of catalyst parameters. Competition studies with more than one cyclic anhydride are also used to better understand what roles Lewis acidity and coordination environment play in the ring-opening of a cyclic

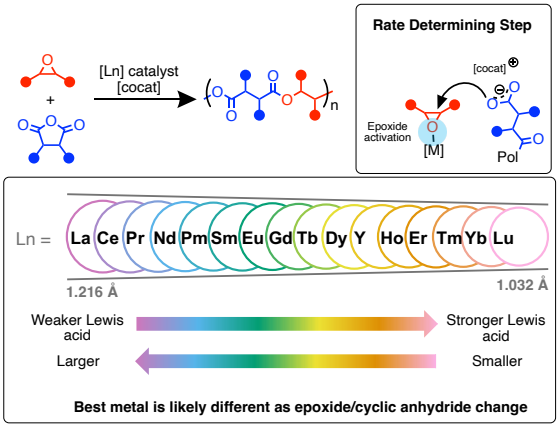

Fig. 2 ROCOP of epoxides and cyclic anhydrides with rare-earth metal salts, in which the metal series presents a spectrum of Lewis acidities and ionic radii that are hypothesized to impact the epoxide ring-opening rate-determining step.

anhydride, a step that does not impact the rate law in the ROCOP of epoxides and cyclic anhydrides. This mechanistic step is very poorly understood, and competition experiments with varied catalysts offer a pathway to better understand this step.

For the ring-opening of an epoxide with a simple rare-earth metal salt in the 3+ oxidation state and a [PPN]Cl cocatalyst, there are four chain ends per metal ion, as there are four anionic chloride initiators that will ring open an epoxide to initiate ROCOP. The active catalyst species could have many combinations of alkoxide and carboxylate chain ends during polymerization (**Fig. S1**). Without a ligand supporting this catalyst, it is difficult to experimentally assess the resting state of the catalyst. For simplicity of discussion, the hypotheses presented herein will represent a metal center as "[M]" and one relevant polymer chain end. While it is expected that carboxylate end groups are bound to the metal, the hypothesized role for the [PPN] cation is to stabilize free carboxylate that has a much better ability to attack the back side of a metal-bound epoxide than a metal-bound carboxylate. Dynamic binding of carboxylate to the metal center could allow the [PPN] cation to accomplish this role more easily, therefore improving polymerization rates for all growing polymers.

Fig. 3 shows the comparison for the TOF of each metal salt for each monomer pair. A comparison of net impact referenced to the slowest rare-earth metal for each monomer pair can be found in **Fig. S4.** As seen in **Fig. 3b**, the BO/CPMA monomer pair displays a trend where the largest and least Lewis acidic rare-earth metal has the highest TOF of all catalysts tested. For example, $LaCl_3{\cdot}7H_2O$ has a TOF 30-35% greater than the smaller metals such as $GdCl_3{\cdot}7H_2O$ and $TmCl_3{\cdot}6H_2O$ when polymerizing BO/CPMA. The TOF steadily decreases, with smaller metals showing a lower TOF. One hypothesis of why the larger lanthanide salts perform better with CPMA as the cyclic anhydride is because the polymer chain end (e.g., carboxylate) is bulky, leading to a higher kinetic preference of epoxide coordination to (and activation by) the larger metals than the smaller ones due to the bigger coordination sphere of the former (**Fig. S3**). That is, a bulky carboxylate polymer chain end kinetically inhibits coordination of epoxide to the smaller metals for activation due to steric repulsion within their smaller coordination sphere. For the CHO/CPMA monomer pair, the trends are often within error of each other, generally revealing the CHO epoxide to have less variation with metal ion size than BO.

When GA is the cyclic anhydride, the opposite trend is observed, in which smaller lanthanide salts have higher TOFs for both epoxides (**Fig. 3c**). For example, when polymerizing CHO/GA, $YCl_3{\cdot}6H_2O$ has a TOF 80% greater than $LaCl_3{\cdot}7H_2O$. This can be reasoned as epoxide ring opening is the RDS, therefore a more Lewis acidic metal activates the epoxide more. Compared to polymerization with GA instead of CPMA, the anionic chain end is less sterically encumbering, and therefore epoxide coordination is efficient for all lanthanide salts (**Fig. S3**). If the polymer chain end can still easily bind to the metal, it would be expected to be more difficult for PPN to stabilize a "free" carboxylate nucleophile, and therefore lower the TOF. Since the smaller metals are faster when GA is the anhydride, the rate

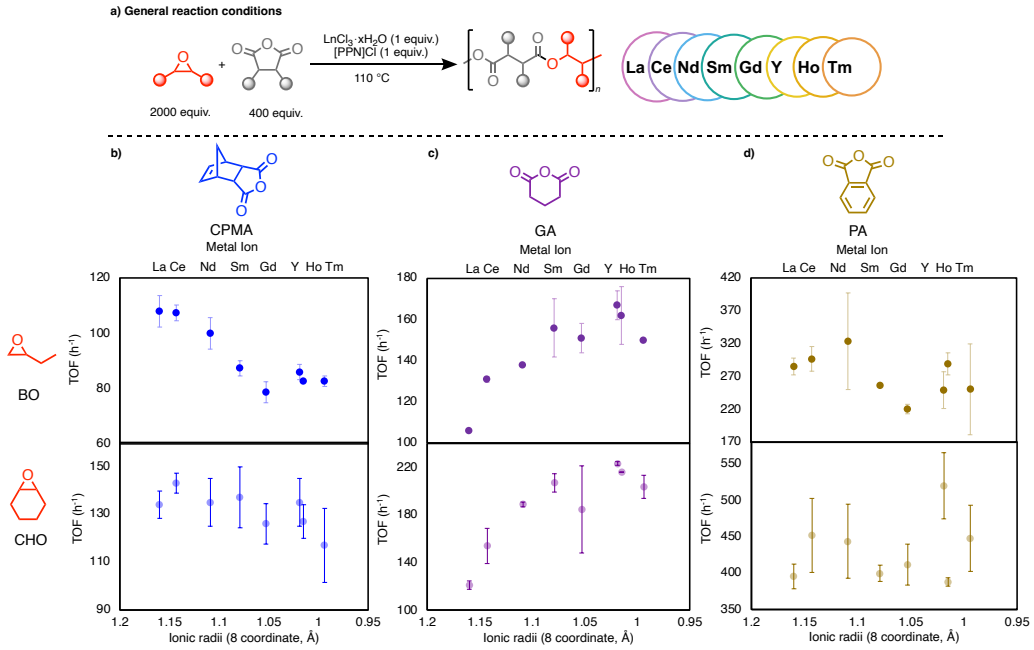

Fig. 3 Differences in catalytic activity between $LnCl_3{\cdot}XH_2O$ (X= 6, 7) salts for chosen monomer pairs. Error bars represent one standard deviation, calculated from duplicate measurements.

gained from epoxide activation must be greater than the rate lost for having a less nucleophilic carboxylate chain end.

When PA is the cyclic anhydride used with either BO or CHO, there is no obvious trend in catalyst activity related to size and Lewis acidity (**Fig. 3d**). For BO/PA, Gd is the slowest catalyst, with La, Ce, and Nd performing the fastest. However, Ho performed just as well as La, despite being a much smaller lanthanide. When CHO/PA is polymerized, all metals are inefficient compared to Y. This absence of a trend could be attributed to the observation that [PPN]Cl in the absence of a metal salt catalyst is itself very efficient at polymerizing BO/PA and CHO/PA. Alternatively, perhaps the two factors impacting CPMA and GA polymerization activity are both important for polymerizations with PA, leaving no net trend.

Reactions of each monomer pair were further run to 90->99% conversion using three select metals that gave the fastest, slowest, and most moderate rates. The resulting purified polymers revealed all monomer pairs are polymerized with excellent control ($Đ$ < 1.3) regardless of the metal catalyst used (**Table S7**). Side reactions are also suppressed throughout polymerization, with polyether and epimerization possible at cyclic anhydride consumption. These results indicate that the lanthanide series, for this catalyst system, can be altered without concern for changes in side reactions and control.

These results highlight that the ultimate catalyst needs for a given monomer pair may not be the same as another, and it is important to identify key differences between monomers. In the case of comparing BO/GA and BO/CPMA monomer pairs, the trend was completely opposite, with small and larger metals in the lanthanide series preferred, respectively. While the RDS of ROCOP is accepted to be epoxide opening, these results indicate that the anhydride structure can have a strong impact on TOF and catalytic trends, since the carboxylate nucleophile depends on the anhydride structure. In this case, a balance needs to be struck between space for epoxide binding and Lewis acidity for epoxide activation.

We also strove to investigate how these subtle catalyst system variations would affect the synthesis of complex polymer morphologies. When one epoxide and two or more cyclic anhydrides are used, block, gradient, and random copolymers can be achieved. The key difference in these variable copolymer sequences lies in the ring-opening of cyclic anhydride, which is not included in the rate law of ROCOP polymerization. There have been two catalyst systems that make direct comparisons of reactivity ratios for cyclic anhydride ring-opening: cesium carboxylates and $YCl_3{\cdot}6H_2O$/[PPN]Cl.[4,6,14] For both catalyst systems, a general reactivity preference trend can be identified in the following order: diglycolic anhydride (DGA) > PA > SA > GA > CPMA. For the $YCl_3{\cdot}6H_2O$/[PPN]Cl system, when using cyclic anhydrides next to each other in this series, gradient copolymers are typically obtained, otherwise more block-like copolymers are obtained, while the Cs system shows a much bigger preference for block copolymers. To understand the influence of the metal ion on these different sequence preferences, studies were performed with $LaCl_3{\cdot}7H_2O$ to better understand if the trend in reactivity holds.

Fig. 4 highlights competition experiments performed between CHO and two cyclic anhydrides next to each other on the reactivity series, in which the impact of changing Y to La can be directly compared. The reactivity trend described above holds for the cases studied with La. When CHO/DGA/PA is polymerized in the presence of $YCl_3{\cdot}6H_2O$/[PPN]Cl, a block-like copolymer is observed with just a 33.5% tapered region, with DGA being consumed more quickly.[14] With $LaCl_3{\cdot}7H_2O$/[PPN]Cl, there is a significant change to form a more gradient-like polymer with a much larger tapered region (70%). The difference between Cs and Y is much larger than the difference between Y and La, allowing for more subtle tunability. When

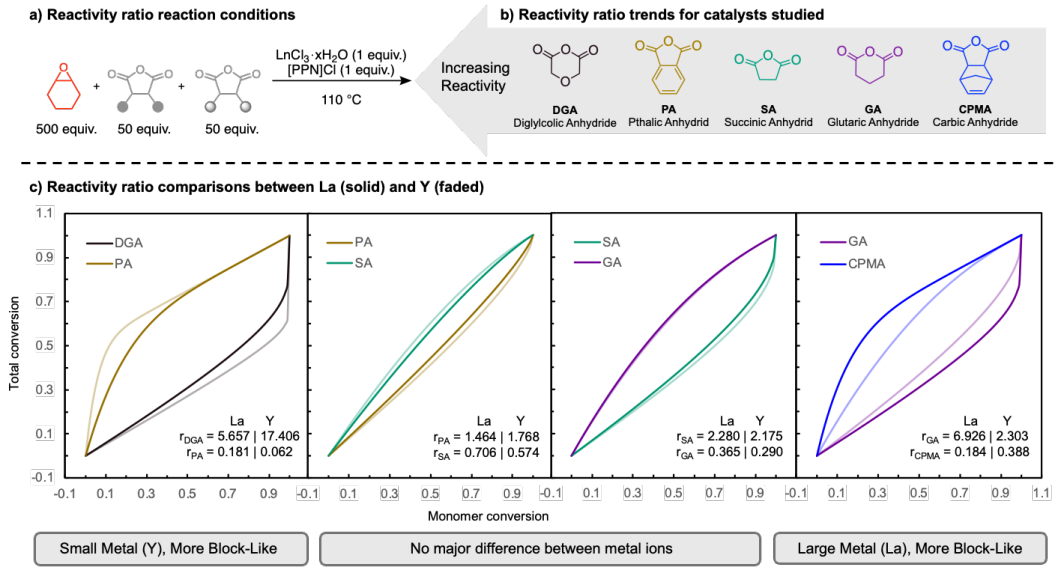

Fig. 4 a) Competition studies of reactions with CHO and two cyclic anhydrides in the presence of $YCl_3·6H_2O$ and $LaCl_3·7H_2O$ pre-catalysts with [PPN]Cl at 110 °C. (b) Reactivity trends for cyclic anhydrides studied. (c) Reactivity ratios and plots with Y (faded lines) and La (dark lines).

CHO/PA/SA and CHO/SA/GA monomers are polymerized, the differences between the Y and La catalyst systems show no large differences. Interestingly, when CHO/GA/CPMA is polymerized, the $LaCl_3·7H_2O$/[PPN]Cl catalyst system shows a more gradient-like preference, with just a 61.5% tapered region, while $YCl_3·6H_2O$/[PPN]Cl shows a more random-like preference with an 89% tapered region.

These results provide clear evidence that changes within the rare-earth metal series can allow for fine-tuning of the ROCOP sequence control, allowing for a wide diversity of polyester structures accessible through this method with a very simple catalyst change. Currently, the smaller, more Lewis acidic metal shows more preference for block-copolymers for the most reactive cyclic anhydrides, while the larger, less Lewis acidic metal shows more preference for block-copolymers for the least reactive cyclic anhydrides.

We have identified that simple chloride salts of the rare-earth metal series are active and controlled for the ROCOP of epoxides and cyclic anhydrides. It was hypothesized that simple changes within the rare-earth metal series would allow for the optimization of polymerization rate for a wide range of monomer pairs without sacrificing polymerization control. Indeed, some monomer pairs preferred a larger metal, some preferred a medium to small-sized metal, and some showed no preference at all. This allows for a simple, near one-size-fits-all salt catalyst system for a larger scope of monomer pairs. Additionally, reactivity ratios for reactions with one epoxide and two cyclic anhydrides reveal that the metal ion in the rare-earth metal series can subtly influence the preference for block-like or gradient-like copolymers. These studies identify new potential to achieve a wide range of polyester structures with the same catalyst system.

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Conflicts of interest

There are no conflicts to declare.

Data availability

Experimental information and data, including methods, materials, NMR data, and GPC data are within the SI.

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Data Availability

The data supporting this article have been included as part of the Supplementary Information