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Mechanistic insight into initiation and regioselectivity in the copolymerization of epoxides and anhydrides by Al complexes

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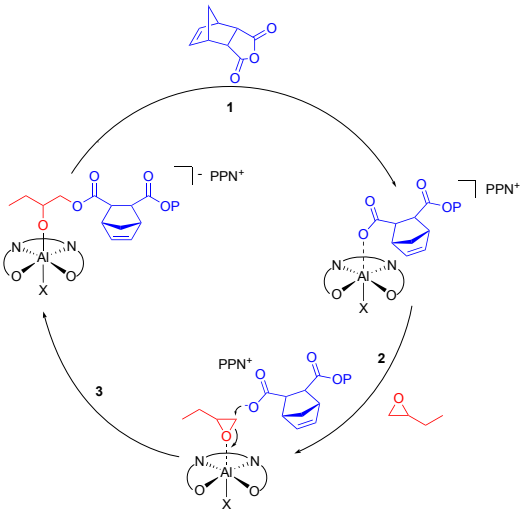
Yanay Popowski,[a] Juan J. Moreno,[c] Asa W. Nichols,[c] Shelby L. Hooe,[c] Caitlin J. Bouchey,[a,b] Nigam P. Rath,[d] Charles W. Machan,[c,*] and William B. Tolman[a,*]

Pentacoordinate Al catalysts comprising bipyridine (bpy) and phenanthroline (phen) backbones were synthesized and their catalytic activity in epoxide/anhydride copolymerization was investigated and compared to ($^{t\text{-Bu}}$salph)AlCl. Stoichiometric reactions of tricyclic anhydrides with Al alkoxide complexes produced ring-opened products that were characterized by NMR spectroscopy, mass spectrometry, and X-ray crystallography, revealing key regio- and stereochemical aspects.

Polyesters prepared from bio-renewable resources are important sustainable substitutes for petroleum-based materials owing to their biodegradability and utility in various applications.[1-5] Ring-opening copolymerization (ROCOP) of epoxides and anhydrides complements other routes (e.g. ring-opening polymerization of cyclic esters) for the synthesis of such sustainable polyesters.[6,7] Among the variety of metal-catalyzed ROCOP processes that have been developed,[6,7] Al complexes of planar N,N'-*o*-phenylenebis[salicylideneimine] (salph) ligands are of special interest because they exhibit the desired combination of catalytic activity and alternating selectivity.[8,9] Mechanistic studies of the (salph)Al system have led to the proposal of a propagation cycle involving alternating incorporation of anhydride and epoxide (Scheme 1, illustrated with carbic anhydride, CPMA, and butylene oxide, BO; X = alkoxide or carboxylate).[10] While supported by kinetic and other evidence, the proposed intermediates shown have not been characterized directly. Such analysis would inform knowledge of the bases for regio- and stereoselectivity in the ring-opening of various substrates,[8,11] including anhydrides, and help future catalyst design. Understanding ligand structural effects on ROCOP activity is also important, with planarity of the ligand framework being apparently necessary to achieve high activity.[6,7]



Scheme 1. Previously proposed catalytic cycle for the copolymerization of butylene oxide (BO) and carbic anhydride (CPMA) comprising three postulated hexacoordinate Al intermediates (X = alkoxide or carboxylate, P = polymer chain, PPN$^+$ = bis(triphenylphosphine)iminium cation).

Herein, we report the synthesis and study of the ROCOP activity of new catalysts with planar and rigid tetradentate bipyridine- and phenanthroline-based ligands as alternatives to salph.[12,13] In addition, we explored stoichiometric ring-opening reactions of anhydrides by Al-alkoxide species supported by salph and the bipyridine-based ligands in order to evaluate step 1 (Scheme 1) in the ROCOP cycle. Key findings include the isolation and structural characterization of the products of ring-opening of several tricyclic anhydrides and the unequivocal determination of regioselectivity in the process.

The ligands $^{t\text{-Bu}}$dhbpyH$_2$[12] and $^{t\text{-Bu}}$dhphenH$_2$ were synthesized via Suzuki-type cross-coupling reactions (see ESI). Metalation of the ligands with Et$_2$AlCl in CH$_2$Cl$_2$ at ambient temperature afforded the complexes ($^{t\text{-Bu}}$dhbpy)AlCl and ($^{t\text{-Bu}}$dhphen)AlCl in quantitative yield (Scheme 2). Alternatively,

[a]*Department of Chemistry, Washington University in St. Louis, Campus Box 1134, 1 Brookings Drive, St. Louis, MO 63130, USA.*
[b]*Department of Chemistry, University of Minnesota, 207 Pleasant St. SE, Minneapolis, MN 55455, USA.*
[c]*Department of Chemistry, University of Virginia, PO Box 400319, Charlottesville, VA 22904-4319, USA.*
[d]Department of Chemistry and Biochemistry and Center for Nanoscience, University of Missouri-St. Louis, One University Boulevard, St. Louis, MO 63121
† Footnotes relating to the title and/or authors should appear here.
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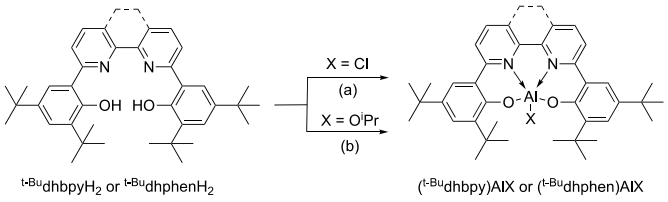
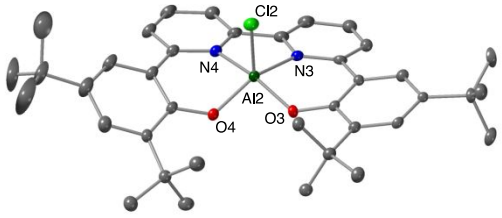
isopropoxo complexes were obtained by treatment of the ligands with $Al(O^iPr)_3$ in toluene at 100 °C. The complexes were characterized by elemental analysis, electrospray ionization high-resolution mass spectrometry (ESI-HRMS) and multinuclear NMR spectroscopy (see ESI; Figures S3-S8). The molecular structure of ($^{t\text{-Bu}}$dhbpy)AlCl (Scheme 2) was confirmed by means of X-Ray crystallography, revealing a square pyramidal geometry with τ_5 values[14] of 0.14 and 0.18 for the two crystallographically distinct molecules in the unit cell. These values are comparable to those reported for closely-related analogues of ($^{t\text{-Bu}}$salph)AlCl (0.15-0.18).[15]



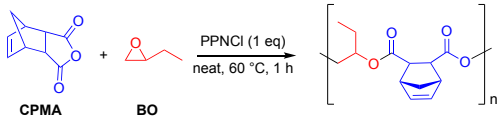
$^{t\text{-Bu}}$dhbpyH$_2$ or $^{t\text{-Bu}}$dhphenH$_2$ ($^{t\text{-Bu}}$dhbpy)AlX or ($^{t\text{-Bu}}$dhphen)AlX



Scheme 2. Synthesis of $^{t\text{-Bu}}$dhbpy and $^{t\text{-Bu}}$dhphen Al complexes (*top*). Conditions: (a) Et_2AlCl, CH_2Cl_2, R.T., 24 h; (b) $Al(O^iPr)_3$, toluene, 100 °C, 24 h; Representation of the X-ray crystal structure of ($^{t\text{-Bu}}$dhbpy)AlCl, (*bottom*), showing non-hydrogen atoms for one of two molecules in the unit cell as 50% ellipsoids. Selected interatomic distances (Å) and angles (deg): Al2-Cl2, 2.174(2); Al2-O3, 1.767(3); Al2-O4, 1.792(3); Al2-N4, 2.020(4); Al2-N3, 2.031(4); O3-Al2-O4, 91.01(14); O3-Al2-N4, 155.4(2); O4-Al2-N4, 87.5(1); O3-Al2-N3, 88.2(1); O4-Al2-N3, 144.6(2); N4-Al2-N3, 79.1(1); O3-Al2-Cl2, 105.9(1); O4-Al2-Cl2, 111.1(1); N4-Al2-Cl2, 97.6(1); N3-Al2-Cl2, 103.1(1).

The catalytic activity of the Al complexes of $^{t\text{-Bu}}$dhbpy, $^{t\text{-Bu}}$dhphen, and the $^{t\text{-Bu}}$salph control for the ROCOP of CPMA and BO was investigated under previously optimized reaction conditions[10] for the same time period (1 h, 60 °C, 1:5 anhydride/epoxide ratio, 0.5-1% mol catalyst/PPNCl co-catalyst; Table 1). Overall, conversion percentages observed for the complexes of $^{t\text{-Bu}}$dhbpy and $^{t\text{-Bu}}$dhphen were comparable to that of ($^{t\text{-Bu}}$salph)AlCl. The presence of co-catalyst PPNCl is critical, as reflected by complete suppression of polymerization in its absence (entries 4 and 6). Allowing the polymerizations catalyzed by ($^{t\text{-Bu}}$dhbpy)AlCl to proceed after complete conversion of CPMA (24 h at 60 °C) showed transesterification and epimerization side reactions, similar to what is known for ($^{t\text{-Bu}}$salph)AlCl.[16] We conclude from the similar ROCOP behaviour that the $^{t\text{-Bu}}$dhbpy and $^{t\text{-Bu}}$dhphen ligands confer similar structural constraints and Lewis acidity to their Al complexes as salph.[8,9]

Table 1. Data for the ROCOP of CPMA and BO by the indicated complexes.

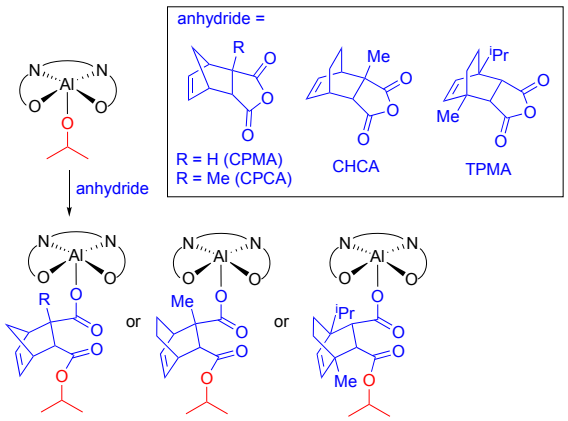


CPMA BO

Entry	Catalyst	CPMA eq.	Conv. (%)[a]
1	($^{t\text{-Bu}}$dhbpy)AlCl	100	49-69
2	($^{t\text{-Bu}}$dhbpy)AlCl	200	15
3	($^{t\text{-Bu}}$dhbpy)AlO^iPr	200	36
4[b]	($^{t\text{-Bu}}$dhbpy)AlCl	100	<1
5	($^{t\text{-Bu}}$dhphen)AlCl	100	67
6[b]	($^{t\text{-Bu}}$dhphen)AlCl	100	<1
7	($^{t\text{-Bu}}$salph)AlCl	100	61-77
8	($^{t\text{-Bu}}$salph)AlCl	200	37-46

[a] Determined by ^{1}H NMR spectroscopy; 1 h, 60 °C, 1:5 anhydride/epoxide ratio, 0.5-1% mol catalyst/PPNCl; [b] Without co-catalyst.

With similar catalytic ROCOP activity verified for the $^{t\text{-Bu}}$dhbpy, $^{t\text{-Bu}}$dhphen, and $^{t\text{-Bu}}$salph complexes, we turned to stoichiometric reactions of their corresponding (L)AlO^iPr compounds with anhydrides in order to evaluate the specific anhydride ring-opening step, an approach recently used to understand initiation stereocontrol in the ring-opening polymerization of *rac*-lactide.[17] Previous work had indicated no reaction upon treatment of ($^{t\text{-Bu}}$salph)AlO^iPr with CPMA at 50 °C for 1 h.[10] Upon further study, we found that this reaction, as well as the one with ($^{t\text{-Bu}}$dhbpy)AlO^iPr, performed at 60 °C (40 mM) led to the slow formation (44% conversion after 22 h, 74% after 48 h for the $^{t\text{-Bu}}$dhbpy catalyst) of new peaks in ^{1}H NMR spectra that we attribute to the ring-opened product (Scheme 3). Illustrative data and assignments for formation of ($^{t\text{-Bu}}$dhbpy)Al(oCPMA-O^{i}Pr) are shown in Figure 1 (full spectra shown in Figures S9, S10, S20-S21).



Scheme 3. Reactions of (L)Al(O^iPr) with anhydrides (L = $^{t\text{-Bu}}$dhbpy with CPMA; L = $^{t\text{-Bu}}$salph with CPMA, CPCA, CHCA, and TPMA).

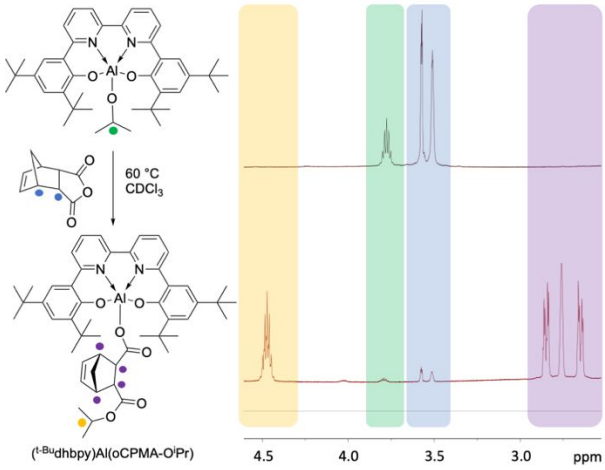


Figure 1. Selected ^{1}H NMR signal assignments in the reaction mixture of ($^{t\text{-Bu}}$dhbpy)AlO^{i}Pr and CPMA at R.T. (*top*) and after 22 h at 60 °C (*bottom*), for the product ($^{t\text{-Bu}}$dhbpy)Al(oCPMA-O^{i}Pr).

Similar reactions of ($^{t\text{-Bu}}$salph)AlO^{i}Pr with the substituted anhydrides CPCA, CHCA, and TPMA also led to the corresponding ring-opened products (Scheme 3), but excess anhydride was necessary in order to obtain reasonable conversions (see ESI). Importantly, ^{1}H and ^{13}C{^{1}H} NMR data, including 2-dimensional heteronuclear correlation experiments (HSQC, HMBC) for these products indicated high regioselectivity (>90%) in the ring-opening step to give the products shown in Scheme 3, with only trace amounts of other unquantifiable species apparent in the baseline (Figures S11-S19). The major products are derived from the attack of the isopropoxide at the least hindered carbonyl of the anhydride in the ring-opening of CPCA, CHCA, and TPMA. Finally, experiments whereby ($^{t\text{-Bu}}$salph)Al(oCPMA) was heated at 80 °C in $CDCl_3$ with CPCA either in the presence or absence of PPNCl showed no conversion to ($^{t\text{-Bu}}$salph)Al(oCPCA) after 24 h, suggesting that under these conditions the ring-opening reaction is not reversible.

The structural assignments for the ring opened products were corroborated by ESI-HRMS, as well as by X-ray crystallography. Suitable single crystals were isolated from the crude product solutions by layering with pentane and storing at -30 °C for the reactions of CPMA with ($^{t\text{-Bu}}$dhbpy)AlO^{i}Pr (Figure 3a), CPCA with ($^{t\text{-Bu}}$salph)AlO^{i}OPr (Figure 3b),[18] and CHCA with ($^{t\text{-Bu}}$salph)AlO^{i}Pr (Figure S26).[18] While the quality of the data does not permit detailed evaluation of bond distances and angles due to issues with extent of diffraction, disorder, and/or twinning, the structures show the ring-opened product bound to the metal center *via* the carboxylate with the isopropoxide initiator bound to the distal carbonyl. The Al centers in all three examples adopt distorted square pyramidal geometries (approximate τ_5 values of 0.18, 0.04, and 0.001, respectively).[14] The structures of the products of reactions with CPCA (Figure 3b) and CHCA (Figure S26) unambiguously show that the nucleophilic attack of the alkoxide occurs at the less sterically-hindered carbonyl of the anhydride, consistent with the regioselectivity indicated by NMR spectroscopy. Retention of stereochemistry is indicated by observation of a cis-(*endo*, *endo*) configuration in the ring-opened products, in agreement with the findings from stoichiometric[19] and polymerization experiments.[11]

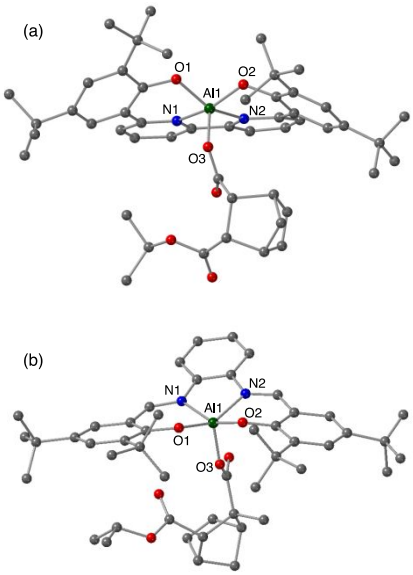


Figure 2. Representation of the X-ray crystal structures of (a) ($^{t\text{-Bu}}$dhbpy)Al(oCPMA-O^{i}Pr) and (b) ($^{t\text{-Bu}}$salph)Al(oCPCA-O^{i}Pr), showing all non-hydrogen atoms as isotropic spheres (Al and ligand donor atoms labelled).

Further insight into anhydride ring opening was provided by kinetics studies of the reactions of ($^{t\text{-Bu}}$salph)AlO^{i}Pr (~0.05 M) with CPMA (~0.05-1 M) in 1,2-dichloroethane (10% d_4) at 80 °C (monitored by ^{1}H NMR; see ESI for details). Pseudo first-order rate constants (k_{obs}) determined from linear plots of ln[complex] vs. time (Table S3) ranged between 1-6 x 10^{-5} s^{-1}. These k_{obs} values increase linearly as a function of $[CPMA]_0$ between 1-15 eq., consistent with a second-order rate law with $k \sim 1 \times 10^{-4}$ $M^{-1}s^{-1}$, but the k_{obs} values at $[CPMA]_0$ between 15-40 eq. were roughly constant (Figure S24). These latter results, indicative of saturation, suggest a pre-equilibrium binding of substrate prior to ring-opening.

In conclusion, we have presented a new class of pentacoordinated Al catalysts supported by $^{t\text{-Bu}}$dhbpy and $^{t\text{-Bu}}$dhphen for epoxide/anhydride ROCOP that exhibit comparable catalytic activity to the well-established complexes supported by salph.[8,9] Initiation studies of both 5-coordinate systems revealed that ring-opening of the anhydride is feasible without the presence of a co-catalyst under polymerization conditions (60 °C, 40 mM anhydride), indicating possible alternative initiation and propagation pathways relative to previously suggested mechanisms that invoked the need for an additional ligand and/or additive.[10] With the isolation and characterization of the initiation reaction products resulting from the ring-opening of anhydrides by Al-alkoxides, key regio- and stereochemical aspects were unequivocally defined, providing important knowledge relevant to the anhydride/epoxide copolymerization mechanism.

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Conflicts of interest

There are no conflicts to declare.

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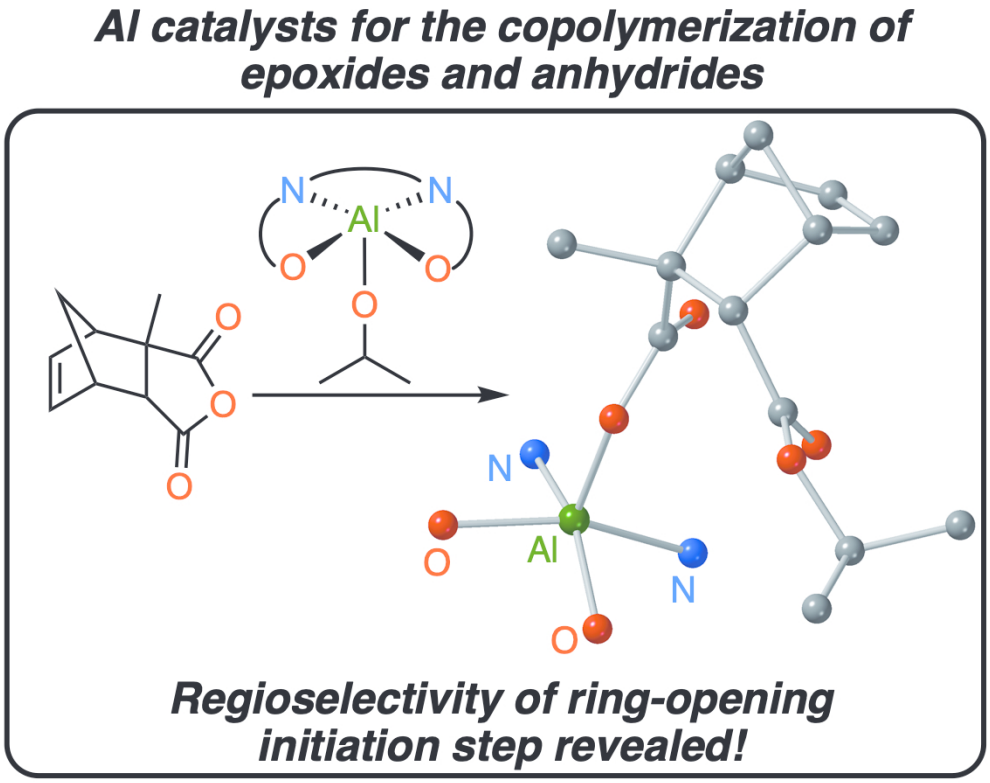

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