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

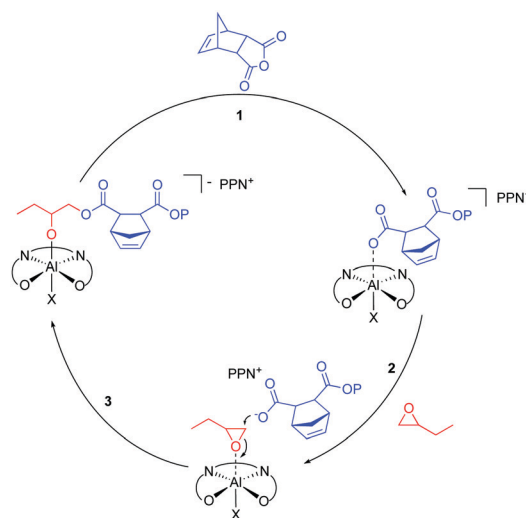
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Pentacoordinate Al catalysts comprising bipyridine (bpy) and phenanthroline (phen) backbones were synthesized and their catalytic activity in epoxide/anhydride copolymerization was investigated and compared to (^t-Bu₃salph)AlCl. Stoichiometric reactions 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 also is important, with planarity of the ligand framework being apparently necessary to achieve high activity.^{6,7}

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.



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).

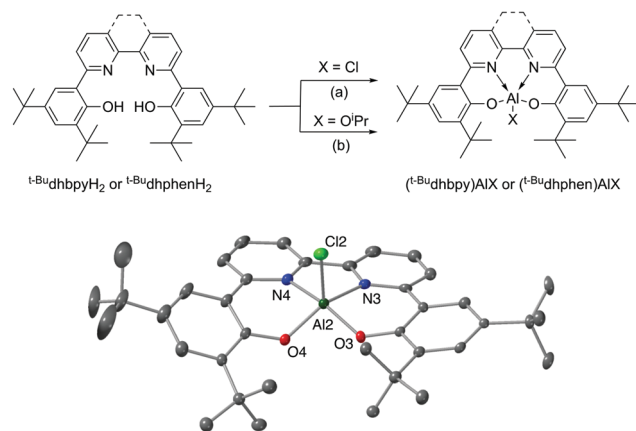
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Scheme 2 Synthesis of $t\text{-Bu}_{\text{dhbpy}}$ and $t\text{-Bu}_{\text{dhphen}}$ Al complexes (top). Conditions: (a) Et_2AlCl , CH_2Cl_2 , R.T., 24 h; (b) $\text{Al}(\text{O}^i\text{Pr})_3$, toluene, 100°C , 24 h; Representation of the X-ray crystal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

The ligands $t\text{-Bu}_{\text{dhbpy}}\text{H}_2$ ¹² and $t\text{-Bu}_{\text{dhphen}}\text{H}_2$ were synthesized *via* Suzuki-type cross-coupling reactions (see ESI†). Metalation of the ligands with Et_2AlCl in CH_2Cl_2 at ambient temperature afforded the complexes $(t\text{-Bu}_{\text{dhbpy}})\text{AlCl}$ and $(t\text{-Bu}_{\text{dhphen}})\text{AlCl}$ in quantitative yield (Scheme 2). Alternatively, isopropoxo complexes were obtained by treatment of the ligands with $\text{Al}(\text{O}^i\text{Pr})_3$ 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†; Fig. S3–S8). The molecular structure of $(t\text{-Bu}_{\text{dhbpy}})\text{AlCl}$ (Scheme 2) was confirmed by means of X-ray crystallography, revealing a square pyramidal geometry with τ_5 values¹⁴ 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 $(t\text{-Bu}_{\text{salph}})\text{AlCl}$ (0.15–0.18).¹⁵

The catalytic activity of the Al complexes of $t\text{-Bu}_{\text{dhbpy}}$, $t\text{-Bu}_{\text{dhphen}}$, and the $t\text{-Bu}_{\text{salph}}$ control for the ROCOP of CPMA and BO was investigated under previously optimized reaction conditions¹⁰ 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 $t\text{-Bu}_{\text{dhbpy}}$ and $t\text{-Bu}_{\text{dhphen}}$ were comparable to that of $(t\text{-Bu}_{\text{salph}})\text{AlCl}$. 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 $(t\text{-Bu}_{\text{dhbpy}})\text{AlCl}$ to proceed after complete conversion of CPMA (24 h at 60°C) showed transesterification and epimerization side reactions, similar to what is known for $(t\text{-Bu}_{\text{salph}})\text{AlCl}$.¹⁶ We conclude from the similar ROCOP behaviour that the $t\text{-Bu}_{\text{dhbpy}}$ and $t\text{-Bu}_{\text{dhphen}}$ ligands confer similar structural constraints and Lewis acidity to their Al complexes as *salph*.^{8,9}

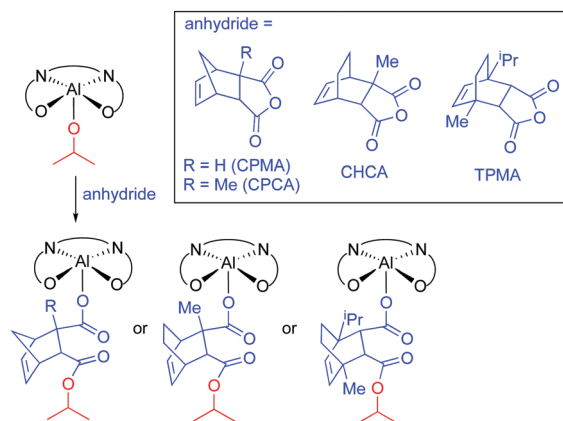
Table 1 Data for the ROCOP of CPMA and BO by the indicated complexes

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

^a Determined by ^1H 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 $t\text{-Bu}_{\text{dhbpy}}$, $t\text{-Bu}_{\text{dhphen}}$, and $t\text{-Bu}_{\text{salph}}$ complexes, we turned to stoichiometric reactions of their corresponding $(\text{L})\text{AlO}^i\text{Pr}$ 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 $(t\text{-Bu}_{\text{salph}})\text{AlO}^i\text{Pr}$ with CPMA at 50°C for 1 h.¹⁰ Upon further study, we found that this reaction, as well as the one with $(t\text{-Bu}_{\text{dhbpy}})\text{AlO}^i\text{Pr}$, performed at 60°C (40 mM) led to the slow formation (44% conversion after 22 h, 74% after 48 h for the $t\text{-Bu}_{\text{dhbpy}}$ catalyst) of new peaks in ^1H NMR spectra that we attribute to the ring-opened product (Scheme 3). Illustrative data and assignments for formation of $(t\text{-Bu}_{\text{dhbpy}})\text{Al}(\text{oCPMA}-\text{O}^i\text{Pr})$ are shown in Fig. 1 (full spectra shown in Fig. S9, S10, S20 and S21, ESI†).

Similar reactions of $(t\text{-Bu}_{\text{salph}})\text{AlO}^i\text{Pr}$ 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, ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR data,



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

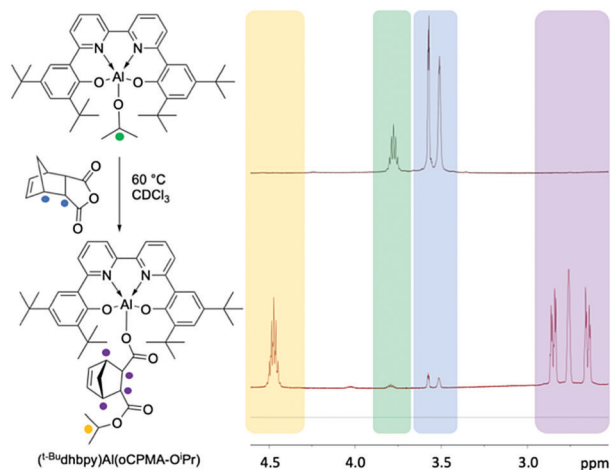


Fig. 1 Selected ^1H NMR signal assignments in the reaction mixture of $(t\text{-Bu})_2\text{dhbpy})\text{Al}(\text{O}^i\text{Pr})_3$ and CPMA at R.T. (top) and after 22 h at 60 $^\circ\text{C}$ (bottom), for the product $(t\text{-Bu})_2\text{dhbpy})\text{Al}(\text{oCPMA-O}^i\text{Pr})$.

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 (Fig. S11–S19, ESI †). 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 $(t\text{-Bu})_2\text{salph})\text{Al}(\text{oCPMA})$ was heated at 80 $^\circ\text{C}$ in CDCl_3 with CPCA either in the presence or absence of PPNCl showed no conversion to $(t\text{-Bu})_2\text{salph})\text{Al}(\text{oCPCA})$ 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 $-30\text{ }^\circ\text{C}$ for the reactions of CPMA with $(t\text{-Bu})_2\text{dhbpy})\text{Al}(\text{O}^i\text{Pr})_3$ (Fig. 2a), CPCA with $(t\text{-Bu})_2\text{salph})\text{Al}(\text{O}^i\text{Pr})_3$ (Fig. 2b),¹⁸ and CHCA with $(t\text{-Bu})_2\text{salph})\text{Al}(\text{O}^i\text{Pr})_3$ (Fig. S26, ESI †).¹⁷ 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 (Fig. 2b) and CHCA (Fig. S26, ESI †) 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 stoichiometric¹⁹ and polymerization experiments.¹¹

Further insight into anhydride ring opening was provided by kinetics studies of the reactions of $(t\text{-Bu})_2\text{salph})\text{Al}(\text{O}^i\text{Pr})_3$ ($\sim 0.05\text{ M}$)

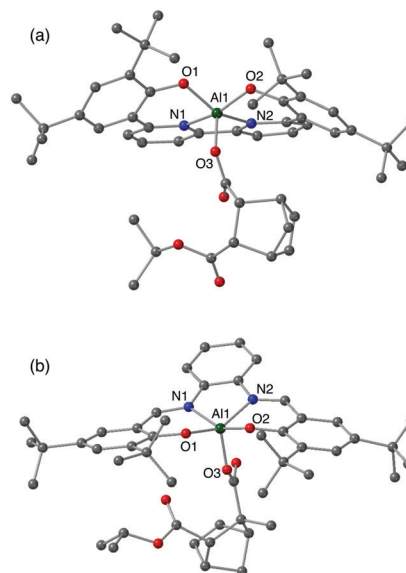


Fig. 2 Ball-and-stick representation of the X-ray crystal structures of (a) $(t\text{-Bu})_2\text{dhbpy})\text{Al}(\text{oCPMA-O}^i\text{Pr})$ and (b) $(t\text{-Bu})_2\text{salph})\text{Al}(\text{oCPCA-O}^i\text{Pr})$, showing all non-hydrogen atoms as isotropic spheres (Al and ligand donor atoms labelled).

with CPMA ($\sim 0.05\text{--}1\text{ M}$) in 1,2-dichloroethane (10% d_4) at 80 $^\circ\text{C}$ (monitored by ^1H NMR; see ESI † for details). Pseudo first-order rate constants (k_{obs}) determined from linear plots of $\ln[\text{complex}]$ vs. time (Table S3, ESI †) ranged between $1\text{--}6 \times 10^{-5}\text{ s}^{-1}$. These k_{obs} values increase linearly as a function of $[\text{CPMA}]_0$ between 1–15 eq., consistent with a second-order rate law with $k \sim 1 \times 10^{-4}\text{ M}^{-1}\text{ s}^{-1}$, but the k_{obs} values at $[\text{CPMA}]_0$ between 15–40 eq. were roughly constant (Fig. S24, ESI †). 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 $^\circ\text{C}$, 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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