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Exploration of Cocatalyst Effects on a Bimetallic Cobalt Catalyst System: Enhanced Activity and Enantioselectivity in Epoxide Polymerization

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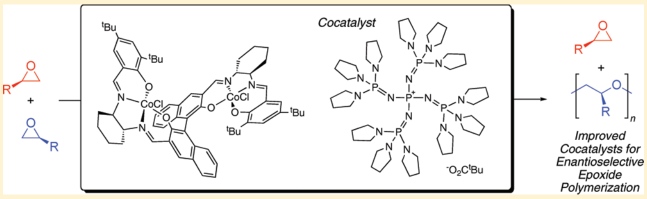
S Supporting Information

ABSTRACT: Organic ionic compounds were synthesized and investigated as cocatalysts with a bimetallic cobalt complex for enantioselective epoxide polymerization. The identities of both the cation and the anion were systematically varied, and the subsequent reactivity was studied. The nature of the ionic cocatalyst dramatically impacted the rate and enantioselectivity of the catalyst system. The ionic cocatalyst $[P(N{=}P(N(CH_2)_4)_3)_4^+][^tBuCO_2^-]$ in combination with a bimetallic cobalt complex produced a catalyst system that exhibited the greatest activity and selectivity for a variety of monosubstituted epoxides.



■ INTRODUCTION

Isotactic polyethers are a potentially important class of materials that are difficult to synthesize from racemic epoxides.[1] Previous catalysts used to synthesize isotactic polyethers suffer from poor activity, low stereoselectivity, or limited substrate scope.[1b,2] In 2008, we reported a bimetallic cobalt complex (**1a**) (Scheme 1) that is active for the enantioselective polymerization of a broad range of racemic monosubstituted epoxides in the presence of the ionic cocatalyst bis(triphenylphosphine)iminium (PPN) acetate ($[Ph_3P{-}N{=}PPh_3^+][MeCO_2^-]$; **2a**) (Scheme 1).[3] This system displays very high enantioselectivities (s-factor = s = k_{fast}/k_{slow}) for the synthesis of isotactic polyethers from racemic epoxides. A related isoselective cobalt complex (**1b**) displays moderate activity and selectivity in combination with **2a**, both of which are improved using bis(triphenylphosphine)iminium pivalate ($[Ph_3P{-}N{=}PPh_3^+][^tBuCO_2^-]$; **2b**) as the cocatalyst.[4]

Complexes **1a** and **1b** show no appreciable polymerization activity in the absence of a cocatalyst. The addition of an ionic cocatalyst results in the formation of a catalytically active system. The exact identity of the catalytically active complex is currently unclear, but we propose that the anion of the cocatalyst binds to cobalt outside the catalyst cleft, activating an interior trans ligand for nucleophilic ring-opening of an epoxide bound to the adjacent cobalt center. We further propose that the bulky pivalate group of **2b** is less likely to enter the bimetallic cleft, consistent with its role as an axial donor and not an initiator (Scheme 2).[4] This postulate is supported by previous reports that cobalt(III) salen complexes for epoxide hydrolysis display dramatic rate differences with various axial donors.[5]

We propose that a suitable cocatalyst should contain an anion that is a good axial donor and also contain a stable cation. PPN is believed to be a noncoordinating and unreactive cation; however, it decomposes in the presence of strong bases such as alkoxides that may be generated during the course of polymerization.[6] Additionally, PPN salts suffer from limited solubility under preferred epoxide polymerization conditions.

The large reactivity and selectivity differences between systems **1b**/**2a** and **1b**/**2b** demonstrate the importance of the cocatalyst for isoselective epoxide polymerization.[4] Cobalt(III) salen epoxide/CO_2 copolymerization systems also show dramatic cocatalyst dependency.[7] On the basis of these prior results, the development of a more soluble and base-stable cocatalyst could improve this bimetallic polymerization system and other related systems.[7] In this paper, we report new polyatomic ionic cocatalysts (Scheme 3) for the enantioselective polymerization of epoxides with **1a**.

■ EXPERIMENTAL SECTION[8]

Representative Synthesis of Tetrakis[(tri-1-pyrrolidinylphosphoranyliden)amino]phosphonium Acetate (3a). To a solution of tetrakis[(tri-1-pyrrolidinylphosphoranyliden)amino]phosphonium tetrafluoroborate[9] (0.57 g, 0.50 mmol) in 8 mL of methanol was added potassium acetate (59 mg, 0.60 mmol) in 150 μL of water. The resulting suspension was then stirred at 20 °C for 5 min and subsequently filtered. The solution was concentrated under vacuum, leaving a white solid, which was rinsed with water (2 × 20 mL) before being dried overnight under vacuum. A pale blue powder was attained (420 mg, 77%). ^1H NMR (CD_3OD, 600 MHz): δ 3.26−3.18 (m, 48H), 1.84−1.75 (m, 48H), 1.89 (s, 3H). $^{13}C\ \{^1H\}$ NMR (CD_3OD, 150 MHz): δ 180.08, 47.61 (d, J = 5.5 Hz), 27.43 (d, J = 9.0 Hz), 24.24.

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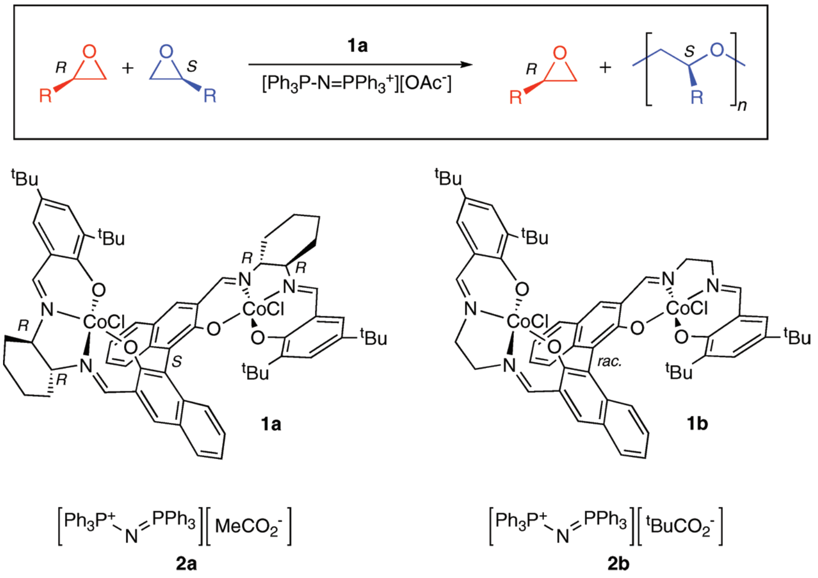
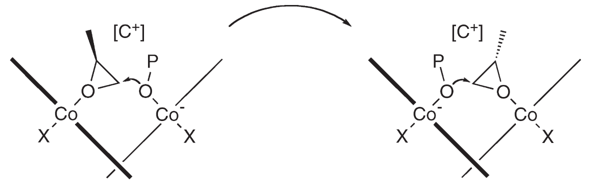
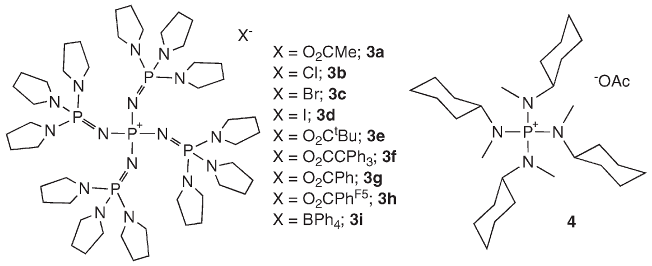
Scheme 1. Bimetallic Complexes for the Synthesis of Isotactic Polyethers



Scheme 2. Proposed Mechanism of Polymerization for 1a and 1b (P = Polymer Chain; X = Chloride or Carboxylate; C^+ = Cocatalyst Cation)



Scheme 3. Phosphazenium (3) and Phosphonium (4) Ionic Organic Cocatalysts for Bimetallic Cobalt Enantioselective Epoxide Polymerization Catalysts



Elemental analysis: Calcd for $C_{50}H_{99}N_{16}O_2P_5$: C, 54.04%; H, 8.98%; N, 20.17%. Found: C, 53.81%; H, 9.18%; N, 20.02%.

General Procedure for the Polymerization of Racemic Propylene Oxide (PO). In a drybox under nitrogen atmosphere, **1a** (4.0 mg, 3.5 μmol) and cocatalyst **3a** (3.9 mg, 3.5 μmol) were added to a reactor vial containing a stir bar and 12 mL of dimethoxyethane (DME). The vial was sealed with a Teflon-lined septum cap and removed from the drybox. The vial was cooled in an ice bath, and PO (0.828 g, 14.3 mmol) was added via syringe. The polymerization was kept at 0 °C during the course of the reaction. After 30 s all volatiles were quickly removed under vacuum. The product was dried overnight. Conversion was determined by polymer mass (0.380 g, 45.9%). The recovered substrate was determined by chiral gas chromatography to be (*R*)-propylene oxide. The conditions for separation were as follows: flow, 1.4 mL/min; velocity, 34 cm/s; pressure, 7 psi; isothermal at 40 °C. A concentrated sample of polymer (50 mg in 0.7 mL of $CDCl_3$) was analyzed using ^{13}C NMR spectroscopy to determine polymer tacticity. ^1H NMR ($CDCl_3$, 600 MHz): δ 3.56−3.49 (m, 2H), 3.39 (m, 1H), 1.11 (d, $J = 5.5$ Hz, 3H). ^{13}C {^1H} NMR ($CDCl_3$, 150 MHz): δ 75.70, 73.61, 17.64. M_n = 157 kg/mol, M_w/M_n = 1.9, M_n^{theo} = 107 kg/mol.

RESULTS AND DISCUSSION

We first explored the effects of various cocatalyst cations on the polymerization of PO with **1a** while maintaining acetate as the anion (Table 1). After a solvent screen, the polar aprotic solvent DME was chosen to increase the solubility of these ionic cocatalysts while maintaining high activity. Given our mechanistic proposal of an anionic active species, we used 1 equiv of cocatalyst relative to **1a**.[4] The enantiomeric purity of polymer repeat units (ee_P) was calculated using equation 1 from the *mm*-triad content of the polymer [*mm*], which was determined using ^{13}C NMR spectroscopy.[3a]

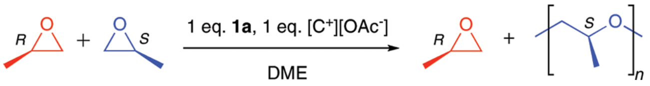
$$ee_P = (2[mm] + [mr] + [rm] - 1)^{1/2} \qquad (1)$$

The *s*-factors for the polymerizations were calculated using eq 2,[10] which is only applicable when monomer conversions (*c*) are less than 50%.[3a]

$$s = s\text{-factor} = ln[1 - c(1 + ee_P)]/ln[1 - c(1 - ee_P)] \qquad (2)$$

Alkali metal salts (lithium, sodium, and potassium acetate) showed essentially no activity in 24 h (entries 1−3), while tetrabutylammonium acetate gave moderate activity and low tacticity (entry 4). We hypothesize that the base instability of tetrabutylammonium acetate accounts for its poor performance.[9] Thus, we decided to explore cations that have been reported to be base stable, such as phosphoniums and phosphazeniums (Scheme 3).[9] Phosphonium ($(R_2N)_4P^+$) and phosphazenium

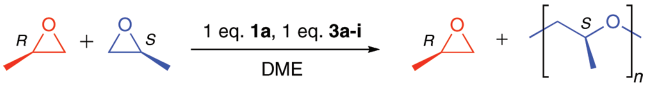
Table 1. Screening of Acetate-Based Cocatalysts for the Polymerization of PO with 1a: Effect of Cation[a]



entry	cocatalyst	time (min)	T_{rxn} (°C)	[PO] (M)	conv (%)[b]	M_n (kg/mol)[c]	M_w/M_n[c]	[*mm*] (%)[d]
1	Li[OAc]	1440	20	2	<1.0			
2	Na[OAc]	1440	20	2	<1.0			
3	K[OAc]	1440	20	2	<1.0			
4	$[(Bu)_4N][OAc]$	1440	20	2	10.2	22	2.2	82.0
5	**2a**	30	0	1	43.5	126	2.6	89.7
6	**3a**	0.5	0	1	45.9	157	1.9	97.1
7	**4**	180	0	2	37.3	25	2.0	88.6

[a] General conditions: [**1a**]:[cocatalyst] = 1:1, [**1a**]:[PO] = 1:4000 in DME. [b] Determined by gravimetric analysis of the polymer. [c] Determined by gel-permeation chromatography calibrated with polystyrene standards in 1,2,4-$Cl_3C_6H_3$ at 140 °C. [d] Isotactic *mm* triad content determined by ^{13}C NMR spectroscopy.

Table 2. Screening of Phosphazenium-Based Cocatalysts for the Polymerization of PO with 1a: Effect of Anion[a]



entry	cocatalyst	X	time (min)	conv (%)[b]	M_n (kg/mol)[c]	M_w/M_n[c]	[*mm*] (%)[d]	*s*-factor
1	**3a**	O_2CMe	0.50	45.9	157	1.9	97.1	>300
2	**3b**[e]	Cl	10	48.6	36	2.4	94.7	>200
3	**3c**	Br	1440	<1.0				
4	**3d**	I	1440	<1.0				
5	**3e**	O_2C^tBu	0.25	49.3	157	1.9	95.8	>300
6	**3f**[f]	O_2CCPh_3	1440	25.2	42	1.8	91.7	50[g]
7	**3g**	O_2CPh	4	49.9	94	2.1	96.5	>300
8	**3h**[f]	$O_2CPh\text{-}F_5$	1440	34.3	114	3.1	88.2	40[g]
9	**3i**	BPh_4	1440	<1.0				

[a] General conditions: [**1a**]:[cocatalyst] = 1:1, [**1a**]:[PO] = 1:4000, T_{rxn} = 0 °C, [PO] = 1 M in DME. [b] Determined by gravimetric analysis of the polymer. [c] Determined by gel-permeation chromatography calibrated with polystyrene standards in 1,2,4-$Cl_3C_6H_3$ at 140 °C. [d] Isotactic *mm* triad content determined by ^{13}C NMR spectroscopy. [e] [**1a**]:[PO] = 1:1000. [f] T_{rxn} = 20 °C. [g] The *s*-factor was calculated from *mm* content of crude polymer, which contains trace atactic PPO.[15]

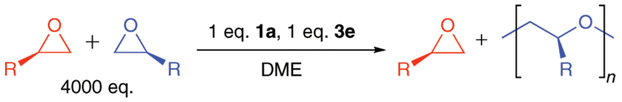
$(((R_2N)_3P{=}N)_4P^+)$ salts, as well as phosphazenes $((NR_2)_3P{=}NR)$, are used as initiators for anionic epoxide polymerizations.[11] Phosphazenium salts have applications as cocatalysts for controlled radical polymerizations[12] and catalysts for epoxide ring-opening reactions.[13]

Phosphonium salt **4** showed good activity and moderate stereoselectivity but was less active than **2a** (entries 5 and 7).[14] Phosphazenium cocatalyst **3a** displayed the highest rate and a selectivity that is above the maximum measurable by ^{13}C NMR (*s* > 300)[3] for polymerization of PO (entry 6). In summary, acetate cocatalysts with large charge-delocalized cations such as **3a** show the highest rates and selectivities. We propose that this is due to a combination of increased stability of the solvent-separated ion pair and inability of the large cation to enter and block the catalyst cleft.

A variety of phosphazenium salts with different anions were synthesized by salt metathesis of tetrakis[(tri-1-pyrrolidinylphosphoranyliden)amino]phosphonium tetrafluoroborate with the appropriate potassium salt in aqueous methanol. These compounds are easily dried and are not hygroscopic. These phosphazenium salts were then screened as cocatalysts with **1a** (Table 2). Cocatalyst **3b** showed good activity and selectivity, while PPNCl displayed no activity, demonstrating the utility of phosphazenium cocatalysts (entry 2). Other halides such as bromide (**3c**) and iodide (**3d**) showed no activity (entries 3 and 4). The bulky pivalate cocatalyst (**3e**) displayed the highest initial rate (TOF ∼ 8000/min) and selectivity (*s* > 300, entry 5). Further increasing the steric bulk of the anion to triphenyl acetate (**3f**) led to a decrease in activity and selectivity (entry 6).[15] The benzoate cocatalyst (**3g**) showed good activity and high selectivity (entry 7); however, the more electron-deficient pentafluorobenzoate (**3h**) showed dramatically decreased performance (entry 8).[15] The noncoordinating anion tetraphenyl borate (**3i**) showed no activity. These results suggest that the most active and selective cocatalysts contain anions that are strong donors with moderate steric bulk (entry 9).

We applied the optimized catalytic system **1a**/**3e** to the polymerization of several other monosubstituted epoxides. This system (**1a**/**3e**) displayed significantly higher activity with epoxides than our previously reported system (**1a**/**2a**),[3] as shown in Table 3.[16] It is notable that the selectivities calculated for all

Table 3. Enantioselective Polymerization of Epoxides with Optimized Catalyst System **1a**/**3e**[a]



entry	R	[epoxide] (M)	time (min)	conv (%)[b]	M_n (kg/mol)[c]	M_w/M_n[c]	[*mm*] (%)[d]	*s*-factor	*s*-factor (**1a**/**2a**)[3]
1	−Bu	2.0	1	49.1	140	2.1	98.9	>300	>300
2	$-CH_2OPh$	0.5	0.25	49.2	100	2.2	96.9	>300	70
3	$-CH{=}CH_2$	2.0	0.25	49.8	97[f]	2.9[f]	87.6	70	20
4	−Ph	2.0	4	47.8[e]	77	5.3	98.5	>300	70
5	$-CF_3$	2.0	30	49.3	140[g]	1.8[g]	99.3	>300	>300

[a] General conditions: [**1a**]:[**3e**] = 1:1, T_{rxn} = 0 °C, [**1a**]:[epoxide] = 1:4000 in DME. [b] Determined by gravimetric analysis of the polymer. [c] Determined by gel-permeation chromatography calibrated with polystyrene standards in 1,2,4-$Cl_3C_6H_3$ at 140 °C. [d] Isotactic *mm* triad content determined by ^{13}C NMR spectroscopy. [e] Conversion determined by ^1H NMR spectroscopy. [f] Determined by gel-permeation chromatography at 40 °C in chloroform, calibrated with polystyrene standards. [g] Determined by gel-permeation chromatography at 33 °C in *N*,*N*-dimethylformamide, calibrated with polystyrene standards.

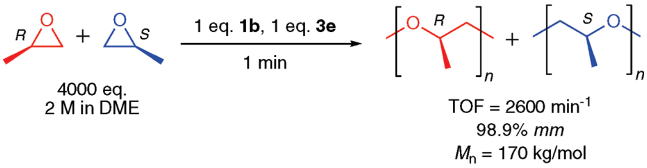


Figure 1. Isoselective polymerization of PO using system **1b**/**3e**.

polymerizations other than butadiene monoepoxide are greater than we can accurately measure by ^{13}C NMR spectroscopy (s > 300). Butadiene monoepoxide was previously polymerized with system **1a**/**2a** and displayed an *s*-factor of 20,[3] while system **1a**/**3e** polymerized butadiene monoepoxide with an average TOF of 8000 min^{-1} and a synthetically more useful *s*-factor of 70.

Cocatalyst **3e** also showed improved reactivity compared to **2b** in isoselective polymerizations of PO with racemic complex **1b**. System **1b**/**2b** had an initial TOF of 440 min^{-1} and produced polymer with *mm* = 97%,[4] while **1b**/**3e** showed improved activity and high isoselectivity (initial TOF = 2600 min^{-1}, *mm* = 98.9%) for PO polymerization (Figure 1). Despite the improved performance of **3e**, these systems did not show living polymerization behavior ($M_w/M_n \sim 2$). We are actively investigating the mechanism of these systems to determine the origin of the large rate and selectivity increases from **3e**.

CONCLUSIONS

A wide range of cocatalysts was screened with **1a** for the enantioselective polymerization of propylene oxide. Variation of both the cation and anion of the cocatalyst dramatically affected the reactivity and stereoselectivity of the catalyst system, and the bulky, base stable phosphazenium pivalate cocatalyst (**3e**) was found to give the highest activities and selectivities. This system showed improved polymerization performance for a number of epoxides, allowing for facile access to enantiopure as well as racemic isotactic polyethers.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures for cocatalyst syntheses and epoxide polymerizations. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) We previously reported higher activities and *s*-factors for PO when [**1a**]:[**2a**] = 1:2; this is consistent with the poor solubility of **2a** necessitating an excess to form the active species (see ref 3a).

(15) Systems **1a**/**3g** and **1a**/**3i** were found to create small (<10% by mass) amounts of acetone-soluble, low tacticity impurities. Complexes **3g** and **3i** showed no activity for polymerization of PO without **1a** in dme.

(16) All entries in Table 3 display high conversion of the desired enantiomer and high *mm* values. The high activity of system **1a**/**3e** makes it difficult to stop these reactions at low conversions, thus increasing the errors associated with measuring conversions and subsequent *s*-factors. See: Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307–1315.