Literature Report III

Asymmetric Alternating Copolymerization of Epoxides and Anhydrides

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Checker: Zhou-Hao Zhu
Date: 2019-8-26

Lu, X.-B. *et al*. *J. Am. Chem. Soc.* **2016**, *138*, 11493.
Lu, X.-B. *et al*. *J. Am. Chem. Soc*. **2019**, *141*, 8937.

Contents

CV of Prof. Xiao-Bing Lu

Xiao-Bing Lu

Background:

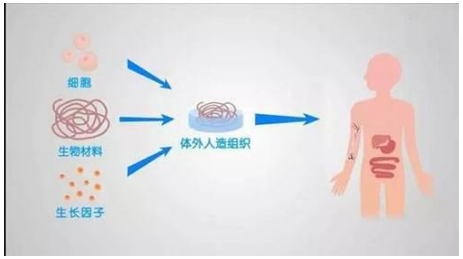
- **1994-1997** M.S., University of Science and Technology of China
- **1998-2002** Ph.D., Dalian University of Technology
- **2005-now** Professor, Dalian University of Technology

Research Interests:

- Stereoregular polymerization
- Asymmetric polymerization

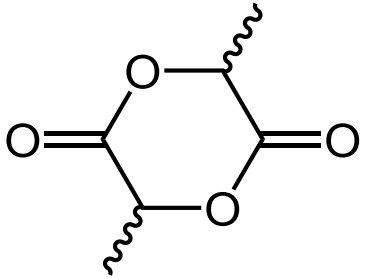
Introduction

Polyester

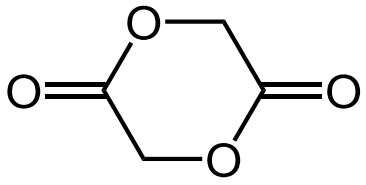


Introduction

1. ring-opening polymerization of cyclic esters



lactide



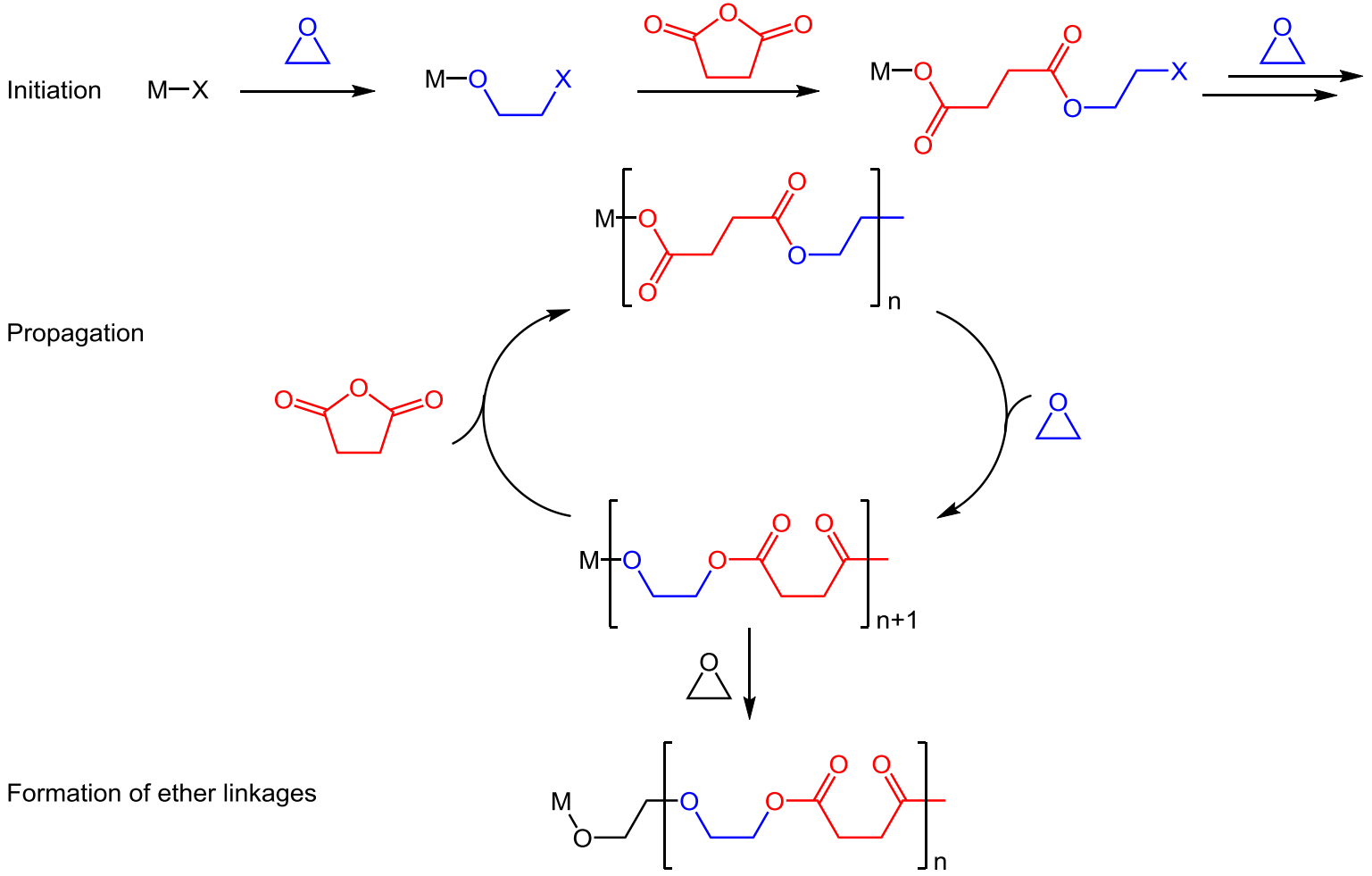
glycolide

2. condensation polymerization of diols with diacids or diesters

high energy cost, high temperature

3. ring-opening copolymerization of epoxides and cyclic anhydrides

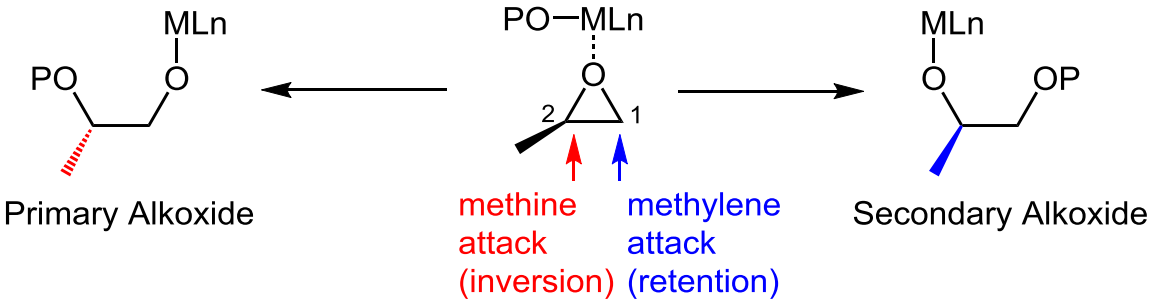
Challenge



Williams, C. K. *et al. Chem. Commun.* **2015**, *51*, 6459.

Challenge

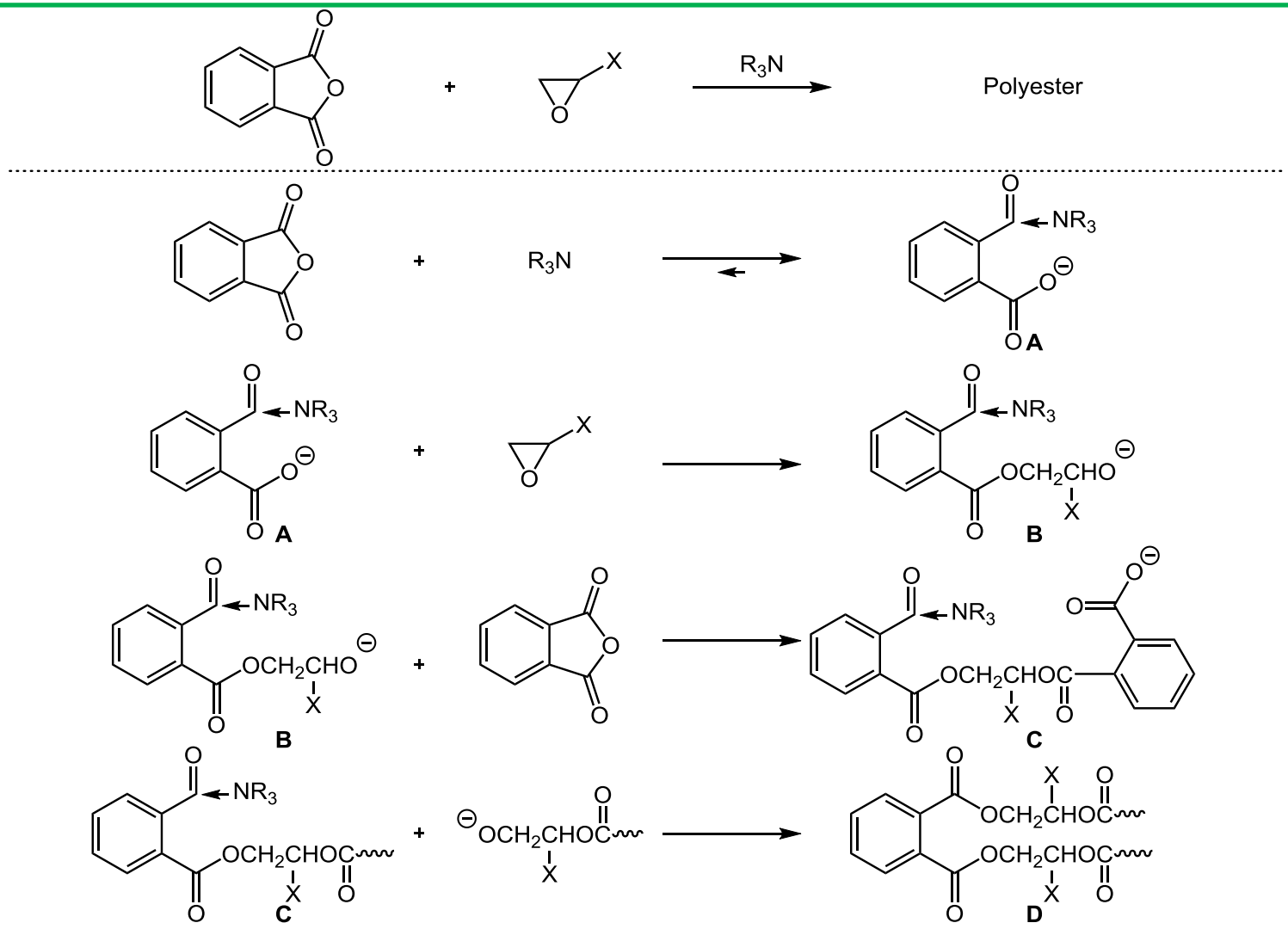
Regio- and Stereochemistry of S_N2-Type Epoxide Ring Opening



OP = polymer chain

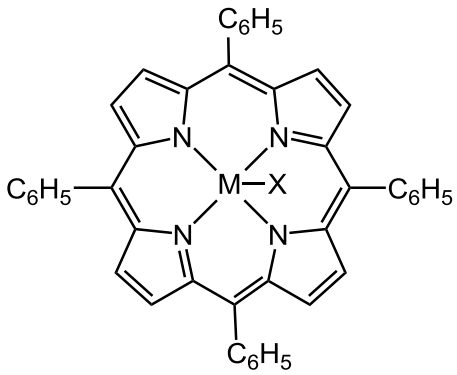
Williams, C. K. *et al. Chem. Commun.* **2015**, *51*, 6459.

Introduction

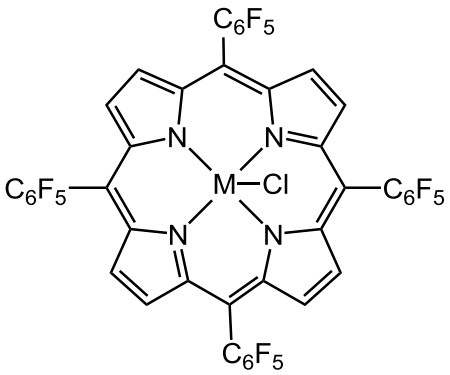


Fischer, R. F. *J. Polym. Sci.* **1960**, *44*, 155.

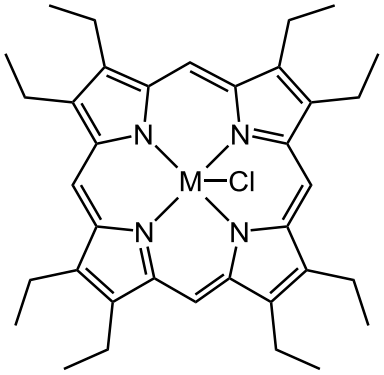
Introduction



M = Al, Cr, Co, Mn
X = Cl, $OCOC(CH_3)_3$



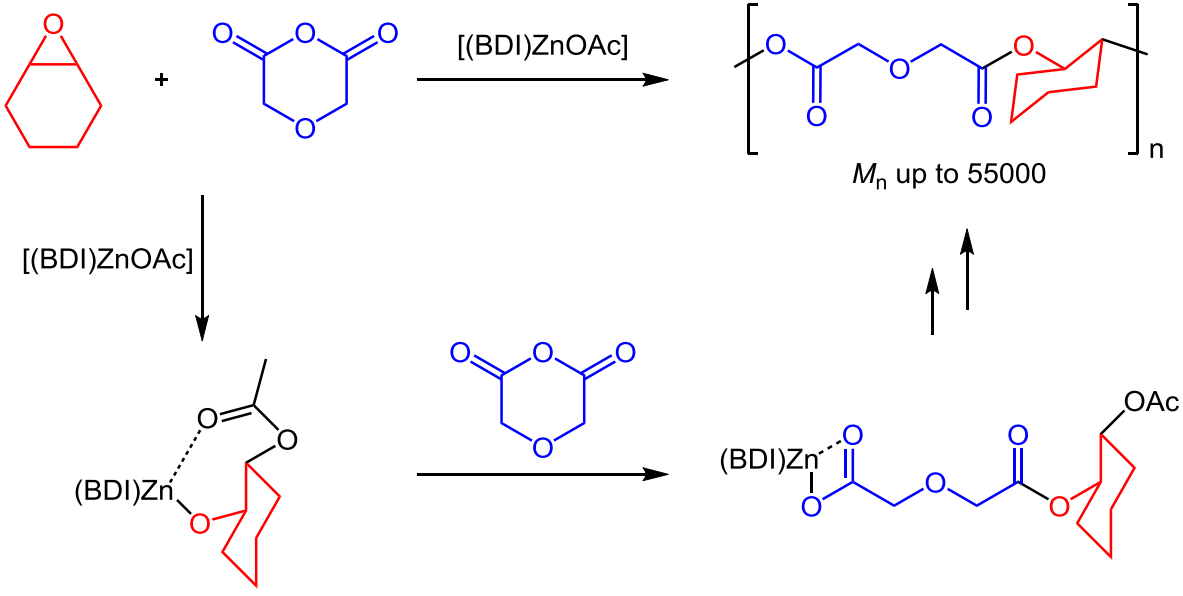
M = Al, Cr, Co



M = Al, Cr, Co

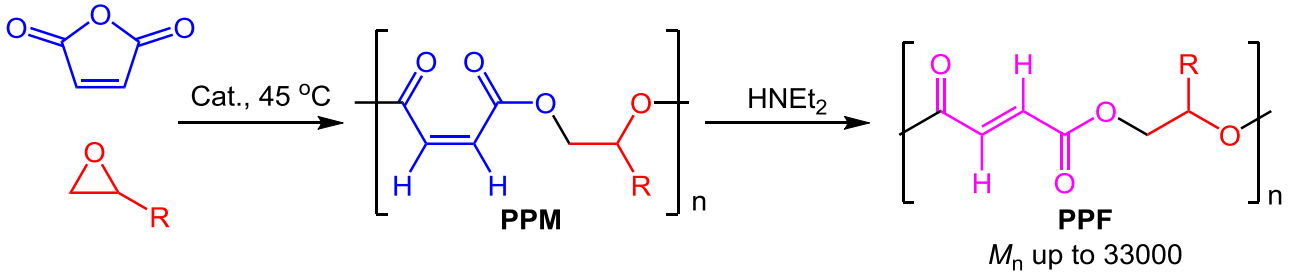
Hamann, K. *et al. Macromol. Chem. Phys*. **1964**, *75*, 211.
Kern, R. J. *et al. J. Am. Chem. Soc.* **1968**, *90*, 2476.
Inoue, S. *et al. J. Am. Chem. Soc.* **1985**, *107*, 1358.
Inoue, S. *et al. Macromolecules* **1985**, *18*, 1049.

Introduction



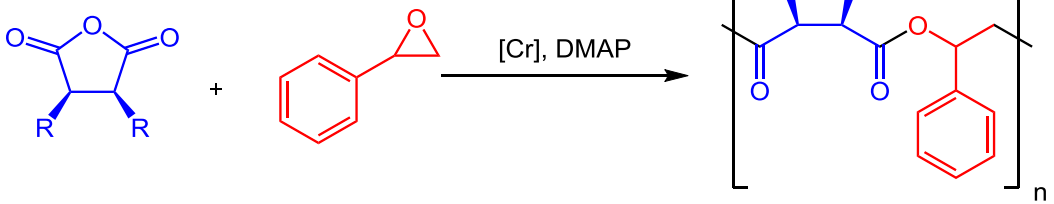
Coates, G. W. *et al*. *J. Am. Chem. Soc.* **2007**, *129*, 11330.

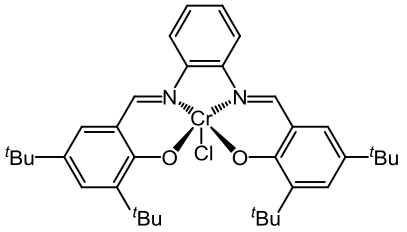
Introduction

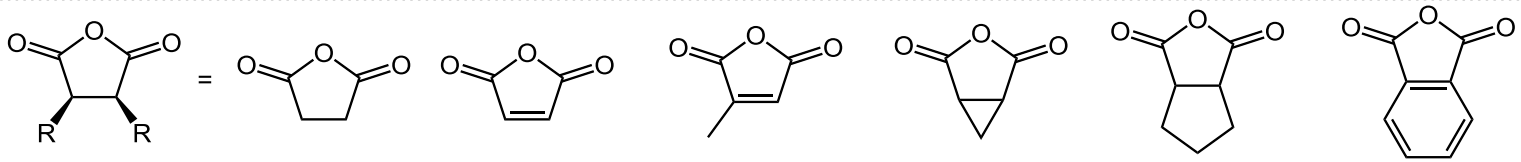


Coates, G. W. *et al*. *J. Am. Chem. Soc.* **2011**, *133*, 10724.

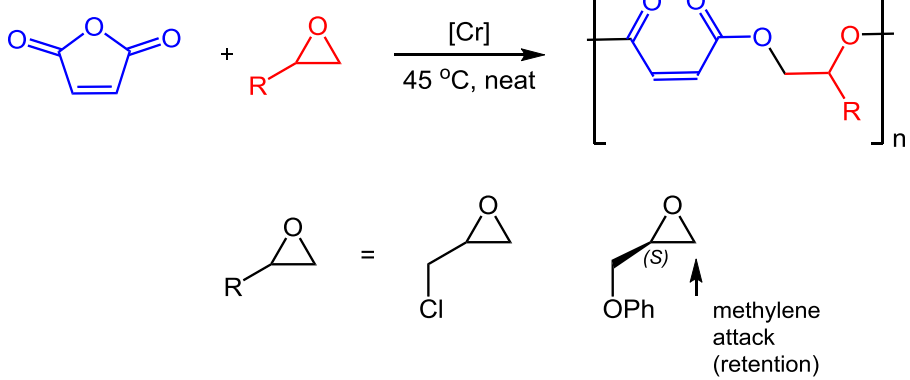
Introduction

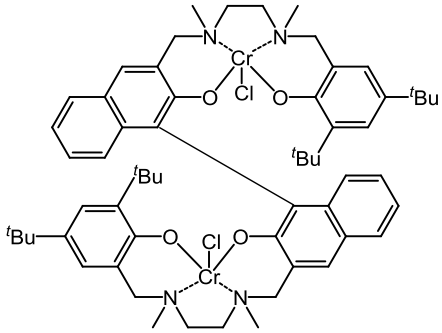






Duchateau, R. *et al. Polym. Chem.* **2012**, *3*, 1308.

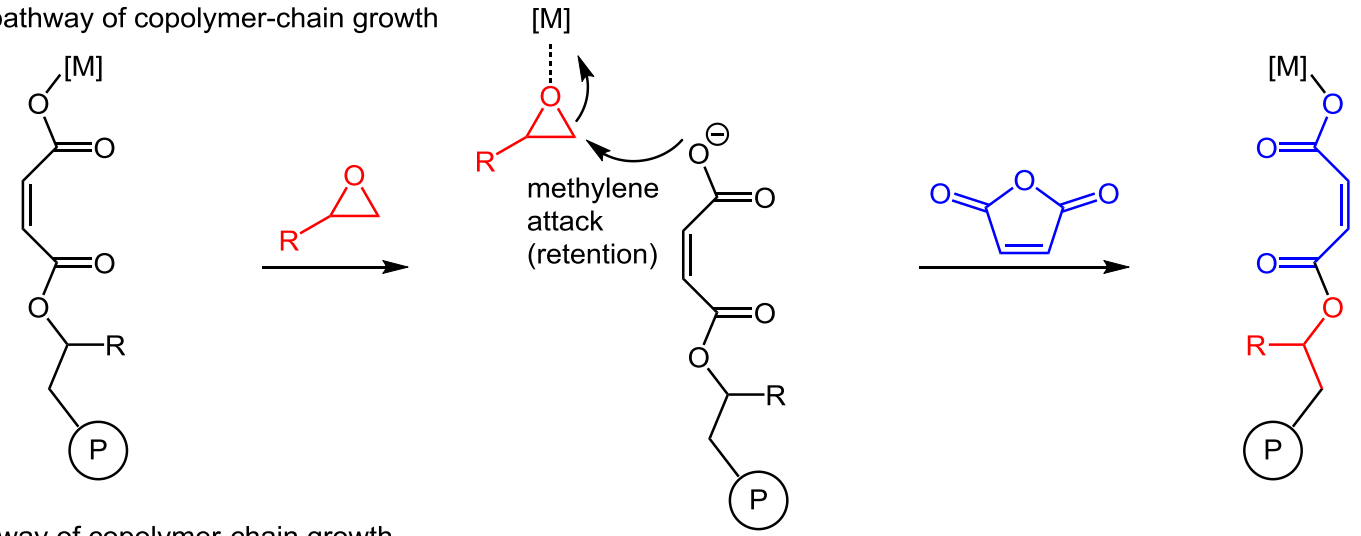




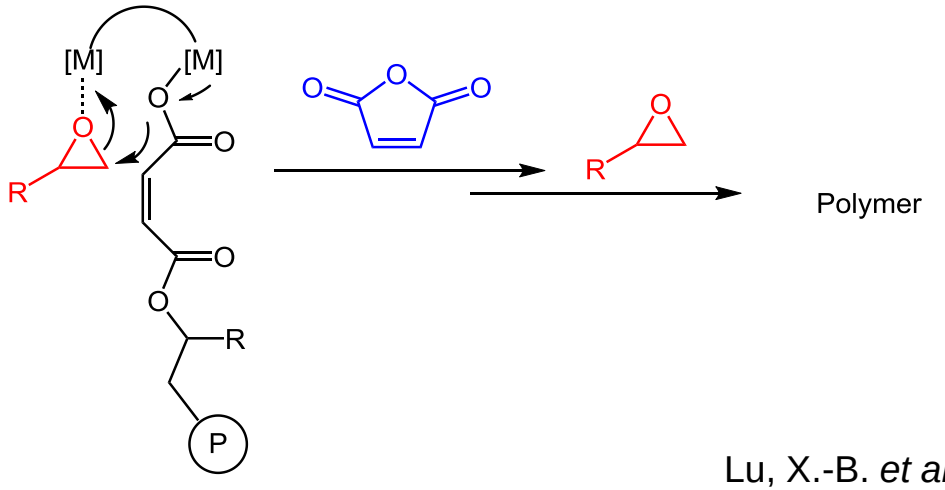
Lu, X.-B. *et al. Polym. Chem.* **2013**, *4*, 1439.

Introduction

Monometallic pathway of copolymer-chain growth

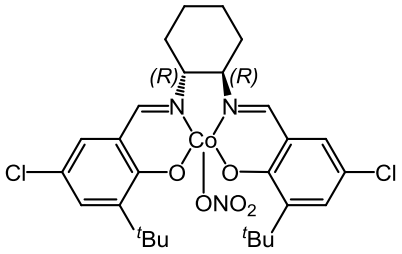


Bimetallic pathway of copolymer-chain growth

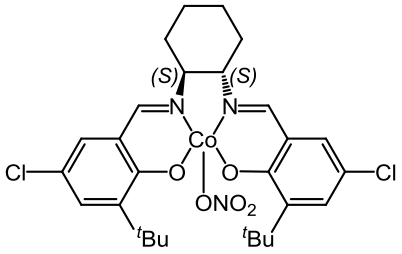


Lu, X.-B. *et al. Polym. Chem.* **2013**, *4*, 1439.

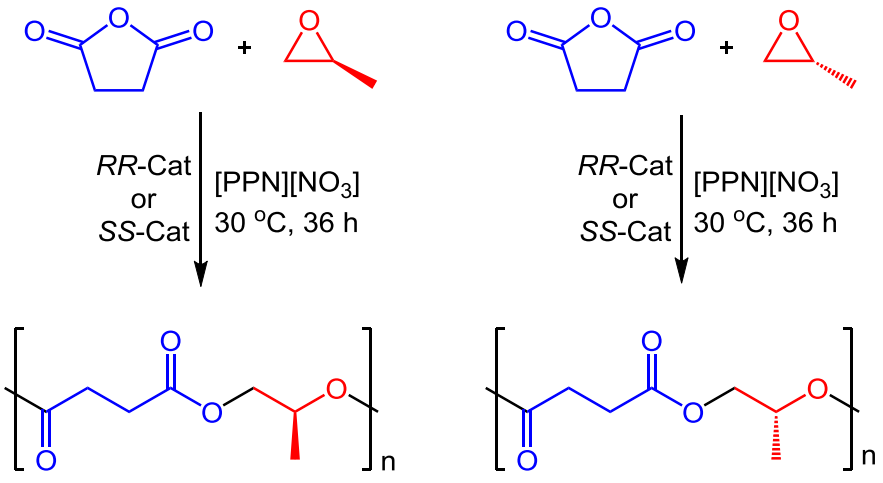
Introduction



(*R,R*)-(Cl-salcy)$CoNO_3$ (*RR*-Cat)



(*S,S*)-(Cl-salcy)$CoNO_3$ (*SS*-Cat)

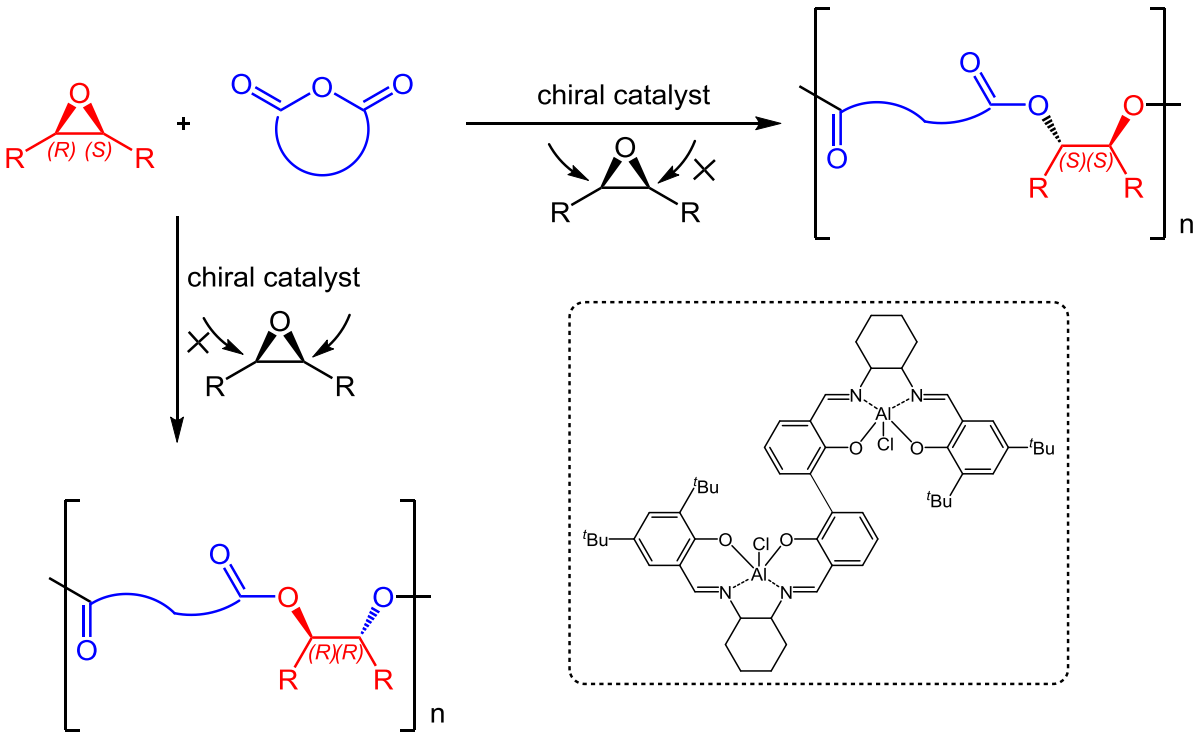


poly((*S*)-propylene succinate)
SS-Cat: 86% H-T linkages
RR-Cat: 97% H-T linkages

poly((*R*)-propylene succinate)
RR-Cat: 86% H-T linkages
SS-Cat: 96% H-T linkages

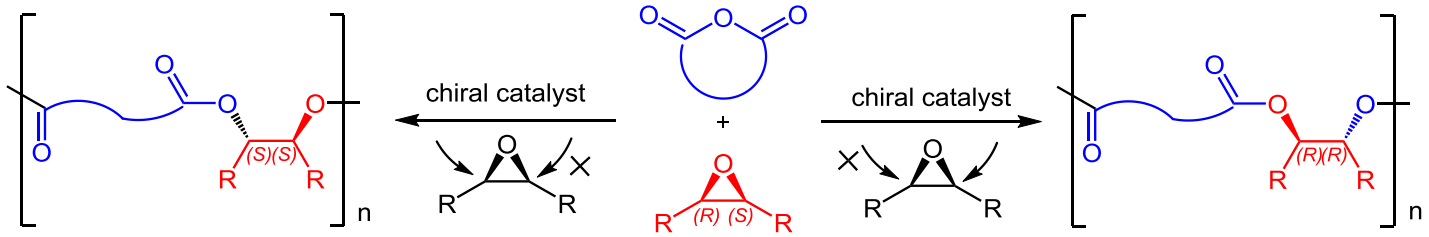
Coates, G. W. *et al*. *J. Am. Chem. Soc.* **2014**, *136*, 15897.

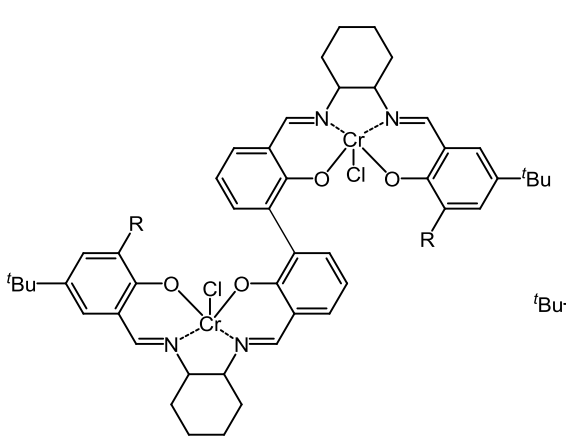
Polymerization of *Meso*-epoxides and Anhydrides



Lu, X.-B. *et al*. *J. Am. Chem. Soc.* **2016**, *138*, 11493.

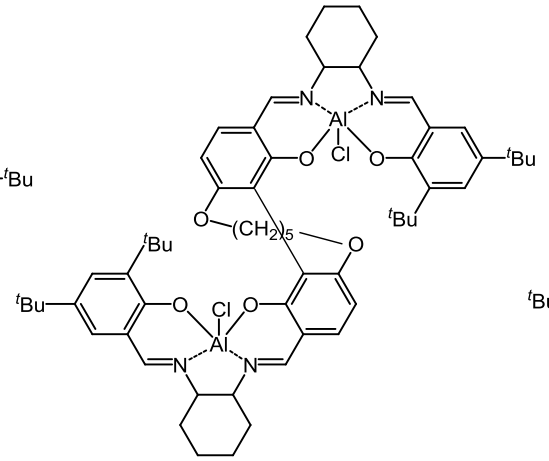
Catalyst Screening





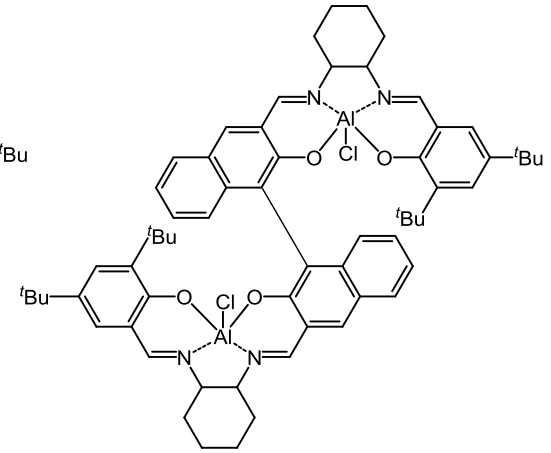
1: M = Co
1a: R = CH_3;
1b: R = ^{t}Bu

2: M = Cr
2a: R = CH_3;
2b: R = ^{t}Bu



3: M = Al
3a: R = CH_3;
3b: R = ^{t}Bu;
3c: R = TMS

4



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Catalyst Screening

Entry[a]	Catalyst	t [h]	T [°C]	*Conv* [%]	TOF [h^{-1}]	Ester [%]	M_n [kg/mol]	PDI	Ee [%]
1	(*R*,*R*,*R*,*R*)-**1a**	0.5	50	60	300	>99	6.4	1.22	0
2	(*R*,*R*,*R*,*R*)-**1b**	0.3	50	64	539	>99	7.3	1.19	5 (*R*,*R*)
3	(*R*,*R*,*R*,*R*)-**2a**	2	50	58	73	>99	4.7	1.23	0
4	(*R*,*R*,*R*,*R*)-**2b**	1	50	78	196	>99	6.2	1.20	7 (*R*,*R*)
5	(*R*,*R*,*R*,*R*)-**3a**	6	50	63	26	42	5.9	8.16	11 (*R*,*R*)
6	(*R*,*R*,*R*,*R*)-**3b**	0.3	50	90	750	>99	9.8	1.14	71 (*R*,*R*)
7	(*R*,*R*,*R*,*R*)-**3c**	5.3	50	99	47	>99	3.9	1.10	21 (*R*,*R*)
8[b]	(*R*,*R*,*R*,*R*)-**3b**	0.1	50	0	0	0	8.4	6.65	
9	(*R*,*R*,*R*,*R*)-**3b**	2.5	25	98	98	>99	6.6	1.11	85 (*R*,*R*)

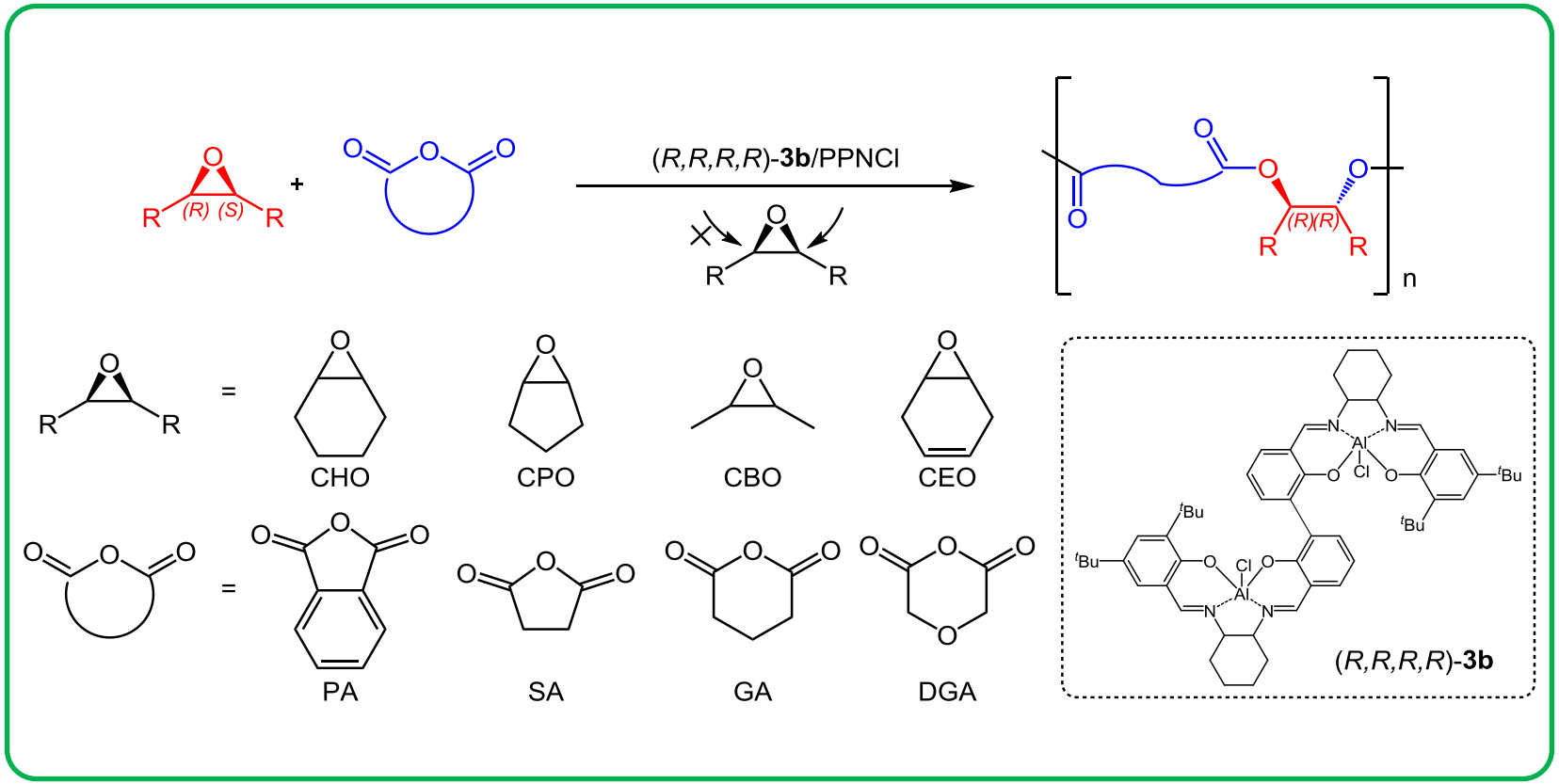
[a] Conditions: The reaction was performed in neat CHO (5.0 mL, 50 mmol) in a 20 mL autoclave, CHO/PA/Catalyst/PPNCl = 1000/250/1/2, molar ratio, except for entries 8 and 12. [b] In the absence of PPNCl. [c] CHO/PA/Catalyst/PPNCl = 1000/500/1/2, molar ratio. [d] The reaction was carried out in toluene solution CHO/toluene = 1:2 (volume ratio). [e] Equimolecular.

Catalyst Screening

Entry[a]	Catalyst	t [h]	T [°C]	*Conv* [%]	TOF [h^{-1}]	Ester [%]	M_n [kg/mol]	PDI	Ee [%]
10	(*R*,*R*,*R*,*R*)-**3b**	24	0	96	10	>99	9.5	1.09	87 (*R*,*R*)
11	(*R*,*R*,*R*,*R*)-**3b**	36	-10	99	7	>99	9.0	1.12	91 (*R*,*R*)
12[c]	(*R*,*R*,*R*,*R*)-**3b**	1	50	98	490	>99	10.6	1.13	70 (*R*,*R*)
13[d]	(*R*,*R*,*R*,*R*)-**3b**	24	0	96	10	>99	9.5	1.12	91 (*R*,*R*)
14[d]	(*S*,*S*,*S*,*S*)-**3b**	24	0	97	10	>99	9.0	1.12	91 (*S*,*S*)
15	(*R*,*R*,*R*,*R*,*R*)-**4**	2.5	25	44	44	>99	8.7	1.14	90 (*R*,*R*)
16	(*R*,*R*,*S*,*R*,*R*)-**4**	48	25	58	3	>99	4.7	1.23	27 (*R*,*R*)
17[e]	(*R*,*R*,*R*,*R*,*R*)-**4** /(*R*,*R*,*S*,*R*,*R*)-**4**	6	25	63	26	>99	9.8	1.19	83 (*R*,*R*)
18	(*S*,*S*,*S*,*S*,*S*)-**5**	18	25	99	14	>99	7.8	1.11	81 (*S*,*S*)

[a] Conditions: The reaction was performed in neat CHO (5.0 mL, 50 mmol) in a 20 mL autoclave, CHO/PA/Catalyst/PPNCl = 1000/250/1/2, molar ratio, except for entries 8 and 12. [b] In the absence of PPNCl. [c] CHO/PA/Catalyst/PPNCl = 1000/500/1/2, molar ratio. [d] The reaction was carried out in toluene solution CHO/toluene = 1:2 (volume ratio). [e] Equimolecular.

Substrate Scope

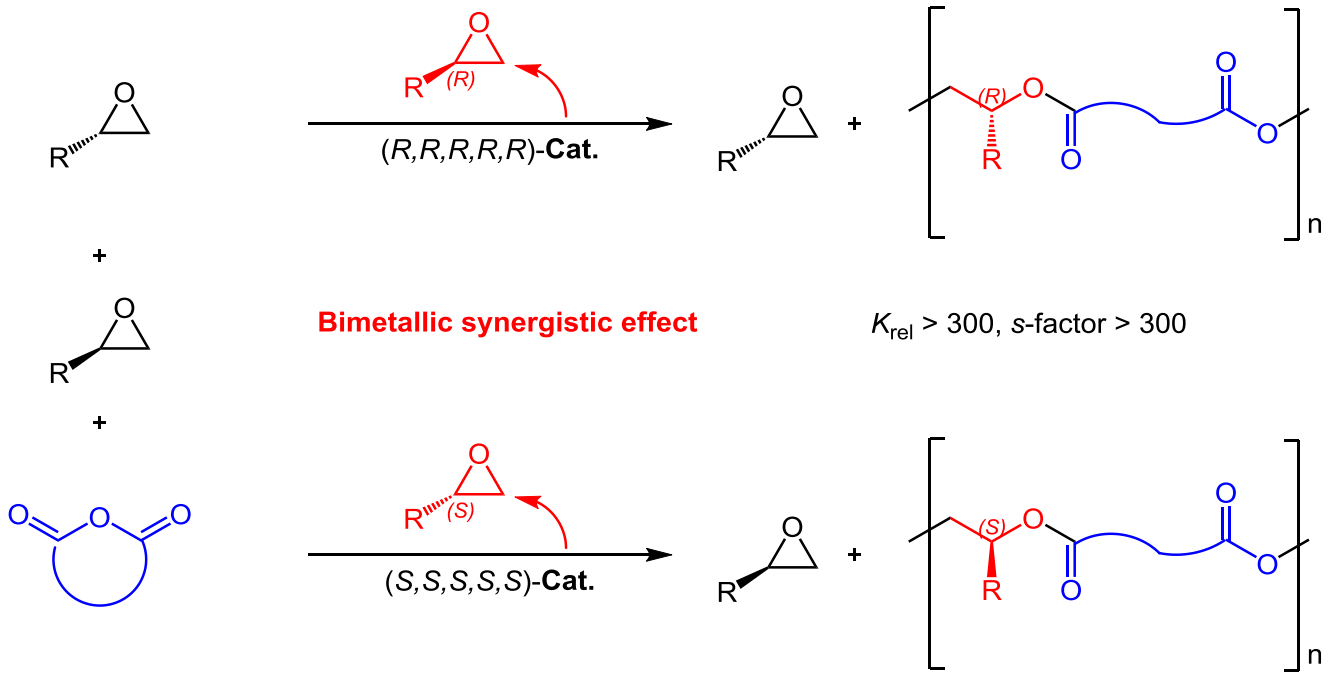


Substrate Scope

Entry[a]	Reactants	t [h]	T [°C]	TOF [h^{-1}]	Ester [%]	M_n [kg/mol]	PDI	Ee [%][b]
1	CHO/SA	36	25	2	>99	2.3	1.15	61 (*R,R*)
2	CHO/GA	36	25	3	>99	3.9	1.34	60 (*R,R*)
3	CHO/DGA	36	25	7	47	0.5	1.45	15 (*R,R*)
4	CPO/PA	32	25	4	>99	3.3	1.38	65 (*R,R*)
5[c]	CPO/PA	50	25	2	>99	6.1	1.24	67 (*R,R*)
6	CBO/PA	30	25	4	>99	10.1	1.18	75 (*R,R*)
7[c]	CBO/PA	13	25	10	>99	4.8	1.10	85 (*R,R*)
8	CEO/PA	48	0	2	>99	4.0	1.10	81 (*R,R*)
9[c]	CEO/PA	48	0	3	>99	5.0	1.13	90 (*R,R*)

[a] Conditions: The reaction was performed in neat *meso*-epoxide (5.0 mL, 50 mmol) in a 20 mL autoclave, *meso*-epoxide/anhydride/(*R,R,R,R*)-**3b**/PPNCl = 1000/250/1/2, molar ratio, except for entries 5, 7 and 9. [b] Measured by hydrolyzing the polymer and analyzing the resulting diol by chiral GC, and the (*R,R*)-diol is the major enantiomer. [c] Epoxide/anhydride/Catalyst/PPNCl = 250/250/1/2, molar ratio; epoxide/toluene =1:2 (volume ratio).

Polymerization of *Racemic* Epoxides and Anhydrides



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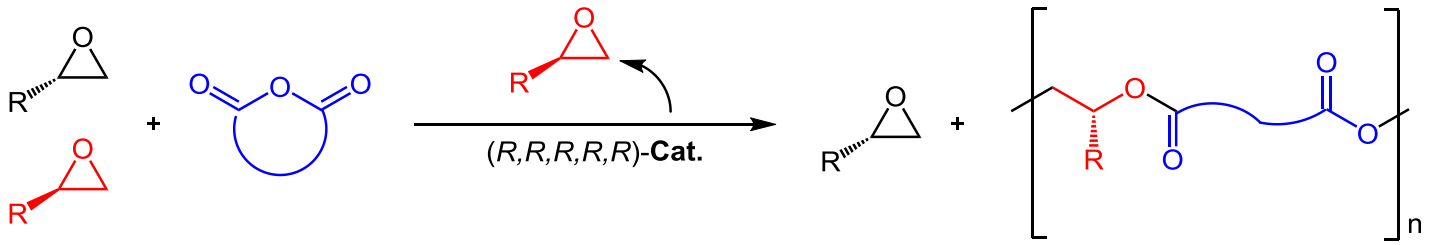
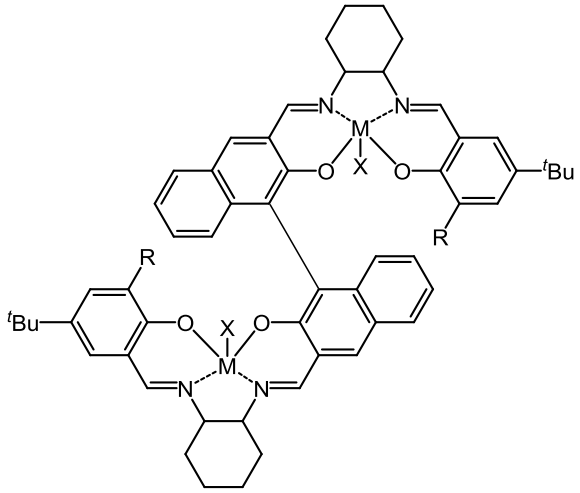
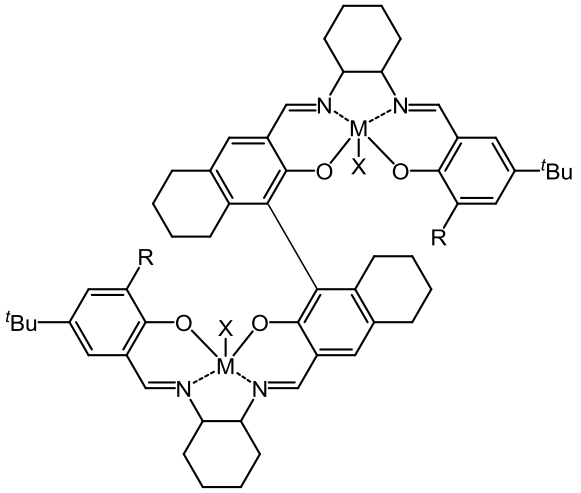
Catalyst Screening







1: M = Co(III), X = DNP
1a: R = ^{t}Bu;
1b: R = CH_3

2: M = Al(III), X = Cl
2a: R = ^{t}Bu;
2b: R = CH_3;
2c: R = ^{i}Pr

3: M = Co(III), X = DNP
R = ^{t}Bu

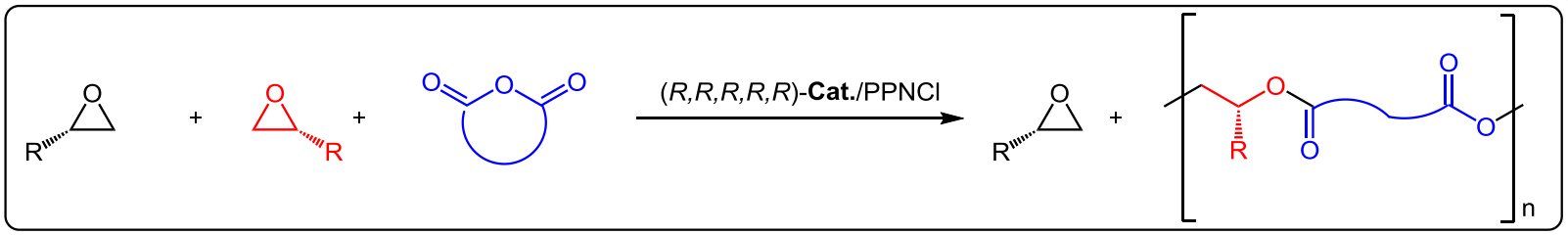
4: M = Al(III), X = Cl
4a: R = ^{t}Bu;
4b: R = ^{i}Pr

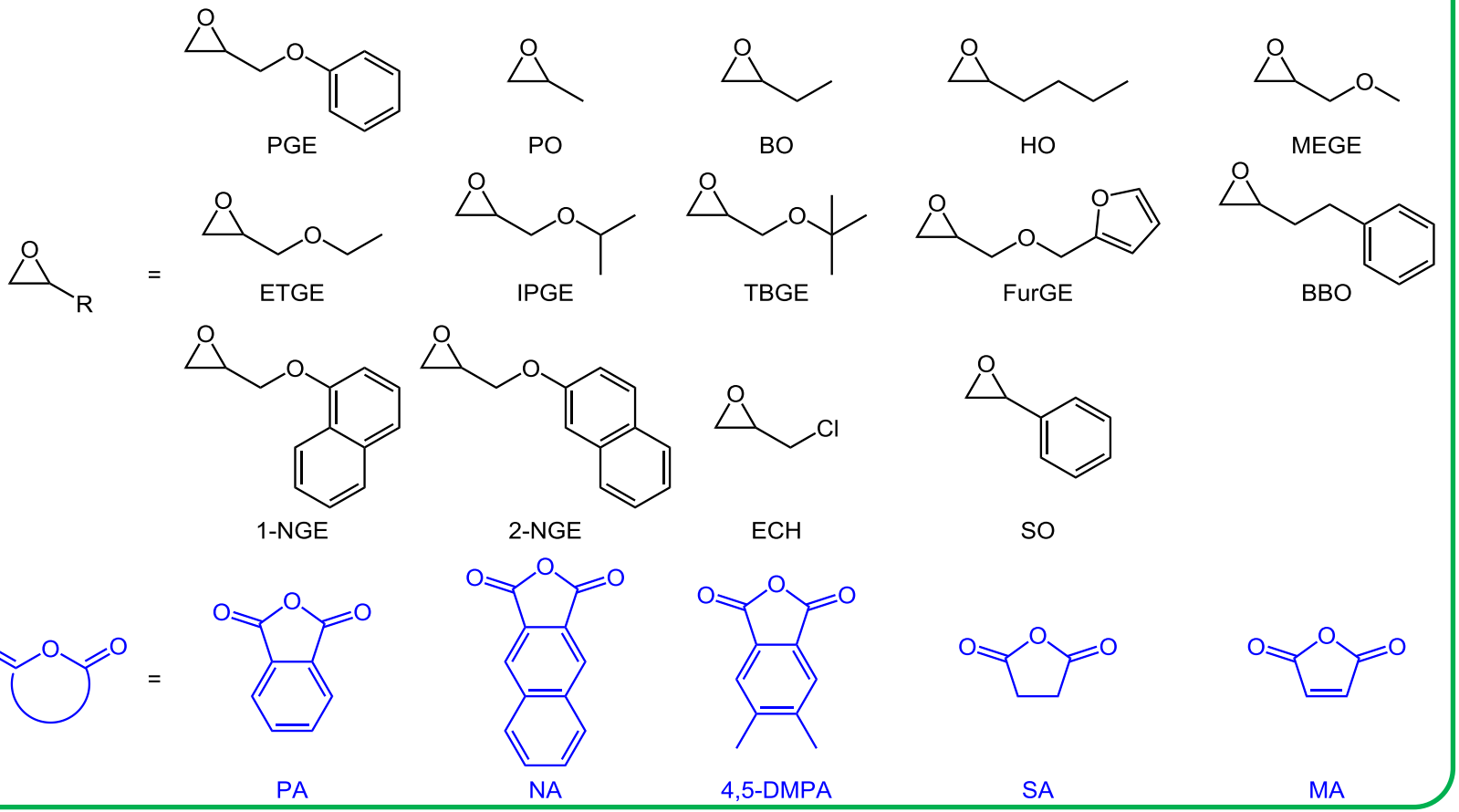
Catalyst Screening

Entry[a]	Catalyst	*Conv* [%][b]	M_n [kDa]	PDI	$Ee_{(epo)}$ [%][c]	K_{rel}[d]	$Ee_{(poly)}$ [%][e]	*s*-factor[f]
1	(*R*,*R*,*R*,*R*,*R*)-**1a**				Polyether			
2	(*R*,*R*,*R*,*R*,*R*)-**1b**				Polyether			
3	(*R*,*R*,*R*,*R*,*R*)-**2a**	49	43.3	1.13	92 (*R*)	152	96 (*S*)	163
4	(*R*,*R*,*R*,*R*,*R*)-**2b**	27	20.3	1.13	34 (*R*)	33	89 (*S*)	24
5	(*R*,*R*,*R*,*R*,*R*)-**2c**	33	34.3	1.23	45 (*R*)	35	91 (*S*)	33
6[g]	(*R*,*R*,*R*,*R*,*R*)-**2a**	40	43.1	1.16	67 (*R*)	>300	99 (*S*)	>300
7[g]	(*S*,*S*,*S*,*S*,*S*)-**2a**	43	46.2	1.21	75 (*S*)	>300	99 (*R*)	>300
8	(*R*,*R*,*S*,*R*,*R*)-**2a**	45	41.2	1.15	61 (*S*)	13	70 (*R*)	10
9	(*R*,*R*,*R*,*R*,*R*)-**3**	42	39.3	1.17	15 (*R*)	2	11 (*S*)	1
10	(*R*,*R*,*R*,*R*,*R*)-**4a**	40	39.8	1.23	58 (*R*)	26	85 (*S*)	22
11	(*R*,*R*,*R*,*R*,*R*)-**4b**	45	40.3	1.19	63 (*R*)	15	73 (*S*)	12

[a] Conditions: The reactions were performed under the following conditions: PGE/PA/Catalyst/PPNX/toluene molar ratio = 1000/500/1/2/500. [b] Calculated using ^{1}H NMR spectroscopy, based on the epoxide. [c] Measured by analyzing the resulting mixture via HPLC. [d] Calculated using $K_{rel} = \ln[(1-c)(1-ee_{(epo)})]/\ln[(1-c)(1+ee_{(epo)})]$, where c is the conversion of epoxides. [e] Measured by hydrolyzing the polymer and analyzing the resulting diol via HPLC. [f] Calculated using *s*-factor = $\ln[1-c(1+ee_{(poly)})]/\ln[1-c(1-ee_{(poly)})]$, where c is the conversion of epoxides. [g] 0 °C.

Substrate Scope





Substrate Scope

Entry[a]	Reactants	*Conv* [%]	M_n [kDa]	PDI	$Ee_{(epo)}$ [%]	K_{rel}	$Ee_{(poly)}$ [%]	*s*-factor
1[f]	PGE/PA	40	43.1	1.16	67 (*R*)	>300	99 (*S*)	>300
2[bf]	PO/PA	43	4.5	1.08	72 (*S*)	93	95 (*R*)	84
3	PO/PA	47	9.7	1.19	82 (*S*)	65	91 (*R*)	53
4[bf]	BO/PA	40	5.1	1.12	63 (*S*)	67	94 (*R*)	62
5	BO/PA	48	10.1	1.22	84 (*S*)	56	90 (*R*)	49
6	HO/PA	43	52.2	1.09	72 (*S*)	93	95 (*R*)	83
7	MEGE/PA	47	11.5	1.21	89 (*R*)	>300	99 (*S*)	>300
8	ETGE/PA	46	13.5	1.19	86 (*R*)	>300	99 (*S*)	>300
9	IPGE/PA	49	34.5	1.16	96 (*R*)	>300	99 (*S*)	>300

[a] Conditions: The reactions were performed under the following conditions: epoxide/anhydride/complex-**2a**/PPNCl/toluene molar ratio = 1000/500/1/2/500, except for entries 2, 4 and 21−26. [b] The reactions were performed under the following conditions: epoxide/PA/complex-**2a**/PPNCl/toluene molar ratio = 200/100/1/2/100. [c] The reactions were performed under the following conditions: epoxide/anhydride/complex-**3**/PPNDNP/toluene molar ratio = 400/200/1/2/200. [d] The reactions were performed under the following conditions: PO/MA/complex-**3**/PPNDNP/toluene molar ratio = 50/25/1/2/50. [e] Not detected. [f] 0 °C.

Substrate Scope

Entry[a]	Reactants	*Conv* [%]	M_n [kDa]	PDI	$Ee_{(epo)}$ [%]	K_{rel}	$Ee_{(poly)}$ [%]	*s*-factor
10	TBGE/PA	47	43.4	1.17	89 (*R*)	>300	99 (*S*)	>300
11	FurGE/PA	49	52.9	1.21	95 (*R*)	>300	99 (*S*)	>300
12	1-NGE/PA	43	57.8	1.25	75 (*R*)	>300	99 (*S*)	>300
13	2-NGE/PA	47	55.3	1.28	88 (*R*)	>300	99 (*S*)	>300
14	BBO/PA	48	46.7	1.14	91 (*S*)	>300	99 (*R*)	>300
15[f]	ECH/PA	43	26.8	1.24	- [e]	-	63 (*R*)	7
16	SO/PA	49	18.3	1.18	86 (*S*)	50	82 (*R*)	24
17	PGE/NA	47	61.4	1.17	85 (*R*)	128	95 (*S*)	104
18[f]	PGE/4,5-DMPA	45	59.2	1.11	77 (*R*)	77	93 (*S*)	63

[a] Conditions: The reactions were performed under the following conditions: epoxide/anhydride/complex-**2a**/PPNCl/toluene molar ratio = 1000/500/1/2/500, except for entries 2, 4 and 21−26. [b] The reactions were performed under the following conditions: epoxide/PA/complex-**2a**/PPNCl/toluene molar ratio = 200/100/1/2/100. [c] The reactions were performed under the following conditions: epoxide/anhydride/complex-**3**/PPNDNP/toluene molar ratio = 400/200/1/2/200. [d] The reactions were performed under the following conditions: PO/MA/complex-**3**/PPNDNP/toluene molar ratio = 50/25/1/2/50. [e] Not detected. [f] 0 °C.

Substrate Scope

Entry[a]	Reactants	*Conv* [%]	M_n [kDa]	PDI	$Ee_{(epo)}$ [%]	K_{rel}	$Ee_{(poly)}$ [%]	*s*-factor
19	PGE/MA	41	35.4	1.27	40 (*R*)	5	45 (*S*)	4
20	PGE/SA	39	30.6	1.25	27 (*R*)	3	25 (*S*)	2
21[c]	PGE/MA	42	9.2	1.22	67 (*R*)	52	93 (*S*)	56
22[df]	PO/MA	43	1.8	1.23	75 (*S*)	>300	99 (*R*)	>300
23[c]	1-NGE/MA	39	10.4	1.25	64 (*R*)	>300	>99 (*S*)	>300
24[cf]	2-NGE/MA	33	11.3	1.24	49 (*R*)	>300	>99 (*S*)	>300
25[c]	1-NGE/SA	42	13.6	1.23	64 (*R*)	31	88 (*S*)	30
26[c]	2-NGE/SA	45	12.8	1.29	81 (*R*)	>300	99 (*S*)	>300

[a] Conditions: The reactions were performed under the following conditions: epoxide/anhydride/complex-**2a**/PPNCl/toluene molar ratio = 1000/500/1/2/500, except for entries 2, 4 and 21−26. [b] The reactions were performed under the following conditions: epoxide/PA/complex-**2a**/PPNCl/toluene molar ratio = 200/100/1/2/100. [c] The reactions were performed under the following conditions: epoxide/anhydride/complex-**3**/PPNDNP/toluene molar ratio = 400/200/1/2/200. [d] The reactions were performed under the following conditions: PO/MA/complex-**3**/PPNDNP/toluene molar ratio = 50/25/1/2/50. [e] Not detected. [f] 0 °C.

Polymerization of *Racemic* Epoxides and Anhydrides

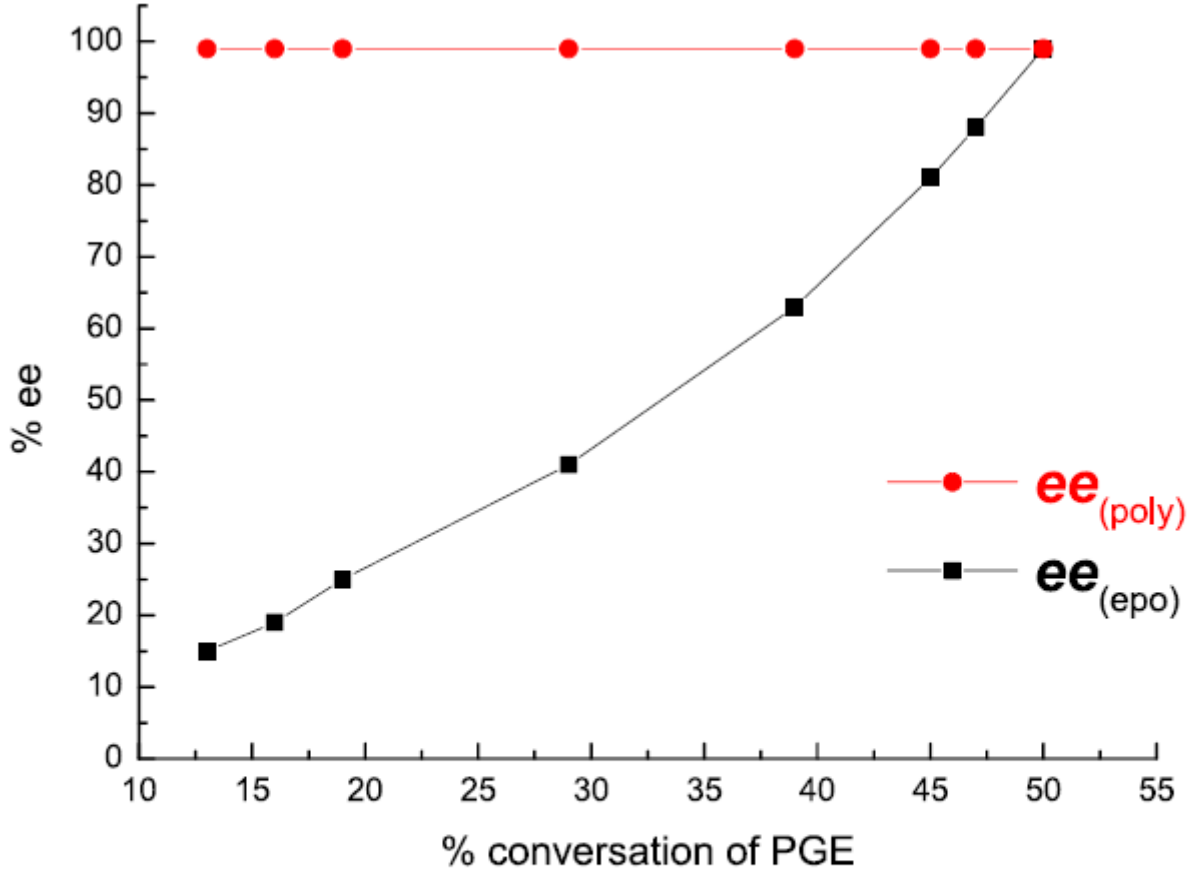
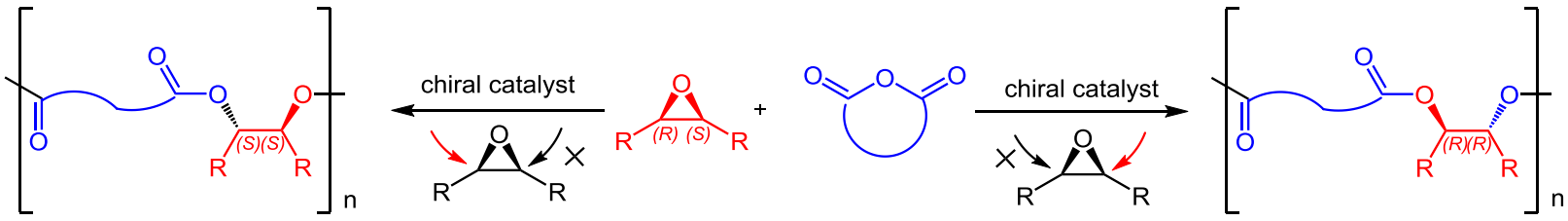
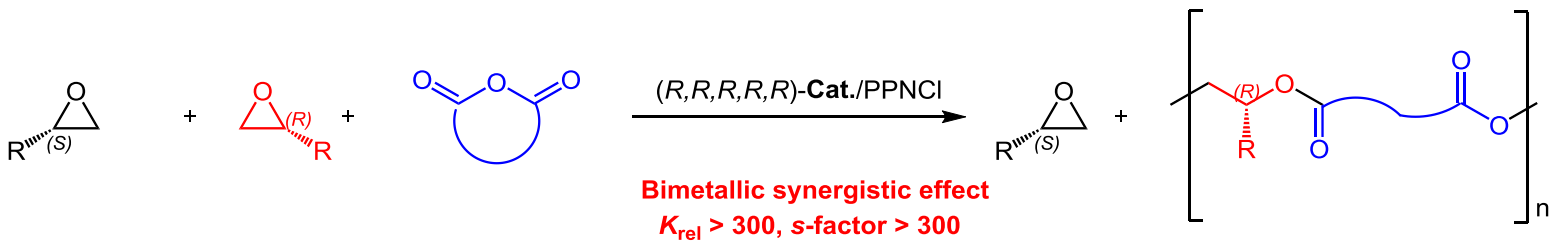


Figure 1. The *ee* values of unreacted PGE and resulting polyesters at various conversions of PGE for enantioselective resolution copolymerization of *racemic* PGE and PA mediated by (*R,R,R,R,R*)-**2a**/PPNCl at 0 °C.

Summary



Lu, X.-B. *et al*. *J. Am. Chem. Soc.* **2016**, *138*, 11493.



Lu, X.-B. *et al*. *J. Am. Chem. Soc.* **2019**, *141*, 8937.

The First Paragraph

Kinetic resolution of *racemic* substrates by chiral catalysts or reagents that mediate the selective reaction of one enantiomer is a powerful strategy for the preparation of enantiopure compounds. A representative example is the hydrolytic kinetic resolution of *racemic* terminal epoxides catalyzed by chiral salen-Co(III) complexes, a general and effective method for producing highly enantioenriched epoxides, which has found widespread applications in both academic and industrial fields. When such a powerful strategy is applied to the enantioselective resolution copolymerization of *racemates* with other substrates, optically active polymers with main-chain chirality can be produced, owing to the configurational retention of one enantiomer of the *racemates* incorporated into the copolymer. This process affords two desirable products, an enantiopure stereoregular copolymer and the unreacted enantiomer. Employing this strategy, several groups independently reported the kinetic resolution copolymerization of *racemic* propylene oxide and CO_2 using binary or bifunctional catalyst systems based on chiral salen-Co(III)X.

The First Paragraph

Although the resultant copolymers have a completely alternating structure and more than 95% head-to-tail linkages, the kinetic resolution coefficients (K_{rel}) are less than 10. The highest K_{rel} of 24.3 was obtained for the multichiral (*S*,*S*,*S*)-Co(III) catalyst containing a (1*S*,2*S*)-1,2-diaminocyclohexane backbone and (*S*)-configured 2′-isopropyloxy-1,10-binaphthyl, for which the resulting poly(propylene carbonate)s were highly regioregular with >99% head-to-tail linkages for the selective copolymerization of CO_2 with the (*R*)-epoxide over the (*S*)-enantiomer. A great significant improvement in the kinetic resolution of epoxides by homopolymerization was achieved by using a chiral bimetallic cobalt complex with a binaphthol linker. The catalyst system was highly active for the polymerization of aliphatic terminal epoxides and exhibited selectivity factors (*s*-factors) in the range from 60 to 370, affording the corresponding polyethers with >99% isotactic [*mm*] content.

The Last Paragraph

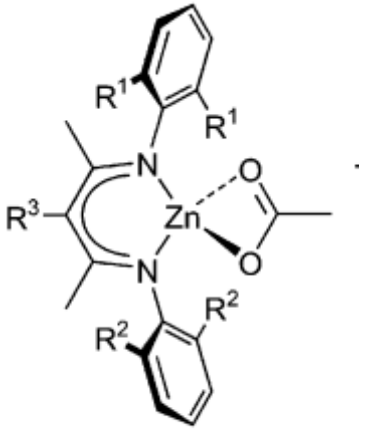
In summary, herein we report the first highly enantioselective resolution copolymerization of *racemic* epoxides with anhydrides, mediated by enantiopure bimetallic complexes in conjunction with a nucleophilic cocatalyst. The catalyst systems based on the enantiopure binaphthol-linked bimetallic Al(III) complex (*R*,*R*,*R*,*R*,*R*)-**2a** or hydrogenated binaphthol-linked Co(III) complex (*R*,*R*,*R*,*R*,*R*)-**3** exhibit unprecedented levels of enantioselectivity, affording the unreacted epoxides in high enantiopurity, and the highly isotactic copolymers with a perfectly alternating structure and narrow molecular weight distribution. Various *racemic* terminal epoxides and anhydrides were tested, and most of these copolymerization systems exhibited both high K_{rel}s and *s*-factors of more than 300.

The Last Paragraph

The extraordinary level of enantioselection in the enantioselective resolution copolymerization outlined above renders this approach extremely attractive for the practical synthesis of a wide range of chiral polyesters, which are mostly semicrystalline materials with melting temperatures between 77 and 160 ^{o}C. Further investigation should focus on understanding the mechanism of this enantioselective copolymerization and developing novel stereoselective resolution copolymerizations of *racemic* epoxides with other nucleophilic reagents.

Thanks
for your attention

Catalyst



[(BDI)ZnOAc]