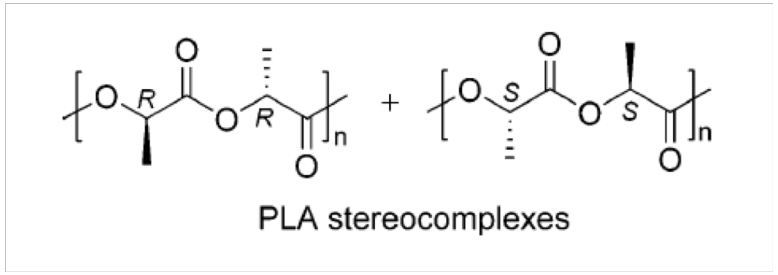
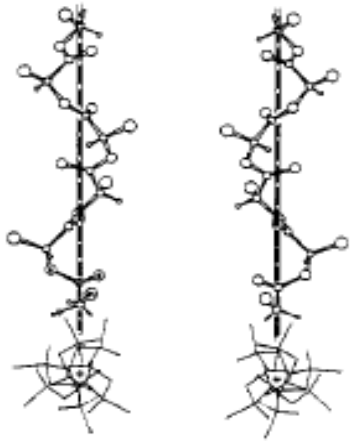
Stereocomplexes of PLA

Structure



PLA stereocomplexes

Extremely interesting BPs (very high Tm ~ 220-230°C)
Excellent thermic and mechanical properties



poly(L-lactide) poly(D-lactide)

Chain models of poly(L-lactide) and poly(D-lactide).

Left-handed
Helicoidal chain

Right-handed
Helicoidal chain

Limitations: no straigthforward synthetic pathways available (Expensive material)

Applications: biomedical devices

*Ikada et al. Macromolecules **1987***

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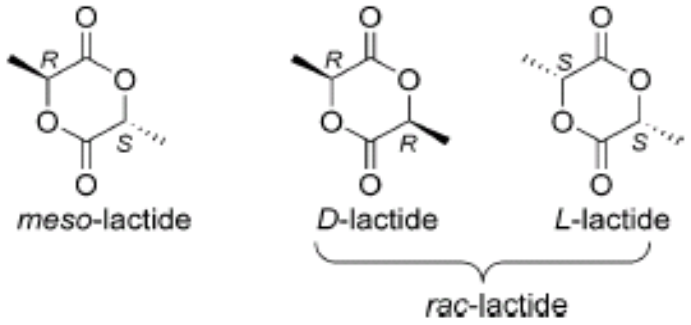
How?

Through polymerization catalysis of lactide with a well-defined catalyst

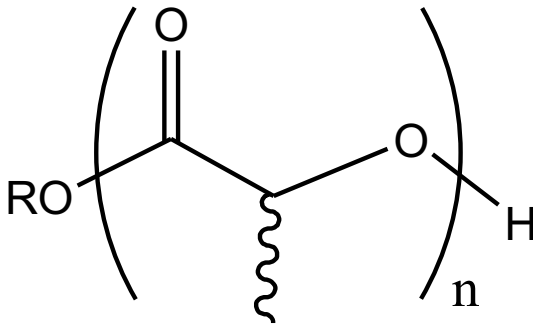
Possibility of a controlled polymerization process affording polymers with well-defined chain length and stereoregularity

Current Approach: Ring-opening polymerization of lactides catalyzed by a well-defined metal complex M-OR



1) M-OR Catalyst

2) Hydrolysis



Dimers of lactic acid

Poly(lactic acid)

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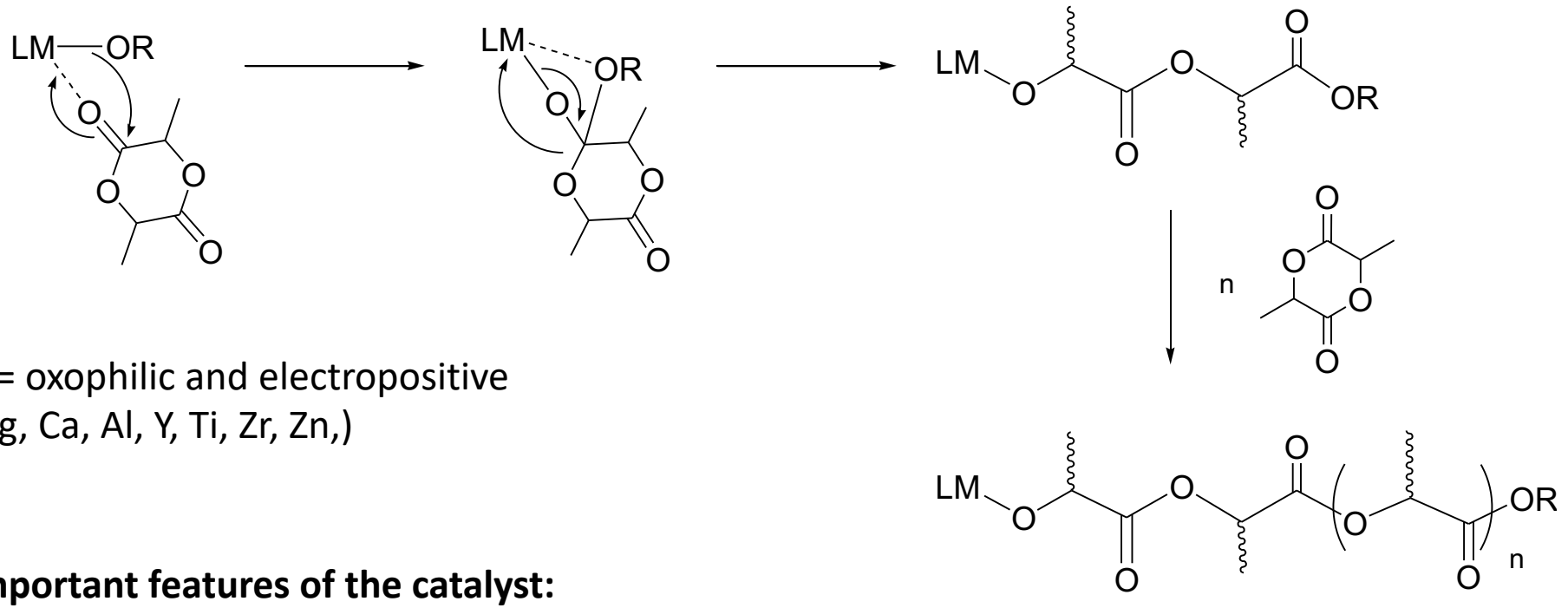
General Mechanism for the Ring-opening Polymerization of Lactides by Metal Alkoxides Complexes



M = oxophilic and electropositive
(Mg, Ca, Al, Y, Ti, Zr, Zn,)

Important features of the catalyst:

- Lewis acidity of M
- Nucleophilicity de RO^-
- Nature of the ligand L

Living polymerization (in the ideal case)

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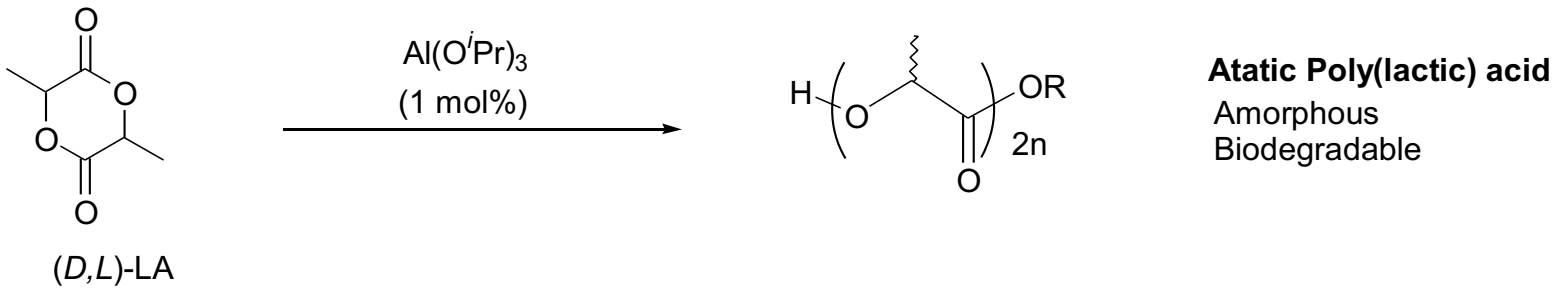
Initial Studies in the 1970's



(*D,L*)-LA

Atatic Poly(lactic) acid
Amorphous
Biodegradable

Positive Aspect:

Living Polymerization (control of the polymer chain length)

Negative Aspect:

No discrimination between the two lactide enantiomers

→ **No stereoregularity in the prepared PLA**

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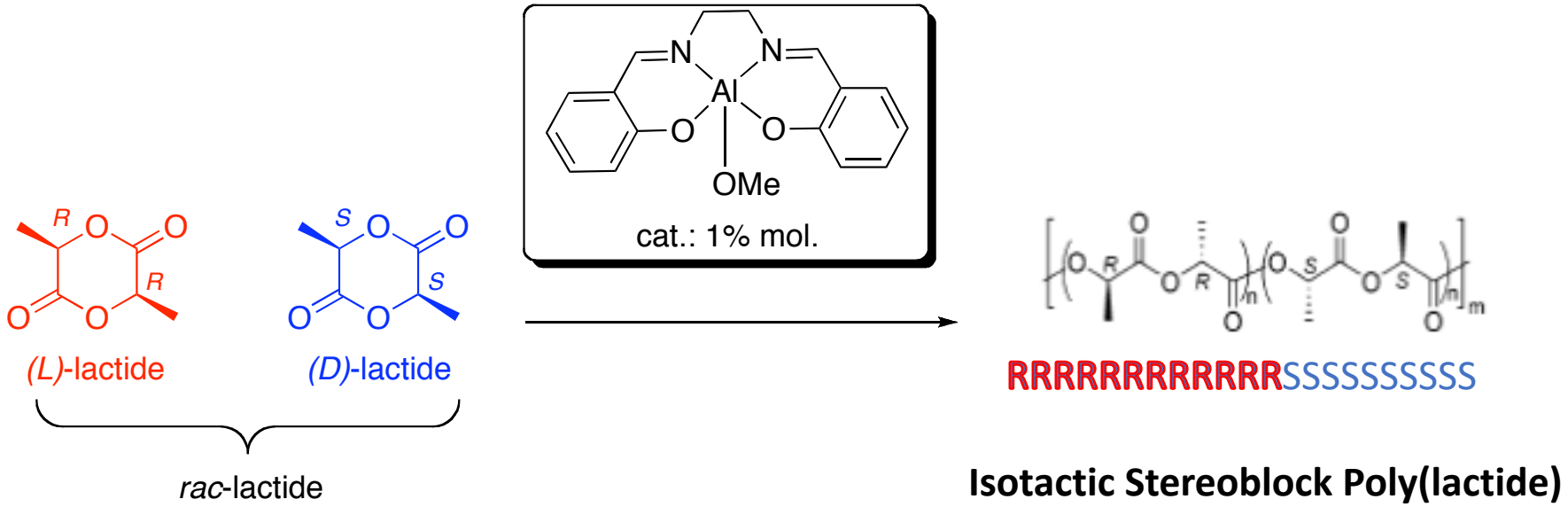
Stereoselective Polymerization of *rac*-lactide: Access to stereoregular PLAs



Isotactic Stereoblock Poly(lactide)

Properties: New material, extremely high melting point (T_m up to 190 °C)
And highly resistant

- Importance of the use of a well-defined and single-site catalyst

Le Borgne, A.; Vincens, V.; Jouglard, M.; Spassky, N. *Makromol. Chem., Macromol. Symp.* ***1993, 73,*** 37.
Nomura, N.; Ishii, R.; Akakura, M.; Aoi, K. *J. Am. Chem. Soc.* **2002, *124, 5938.***

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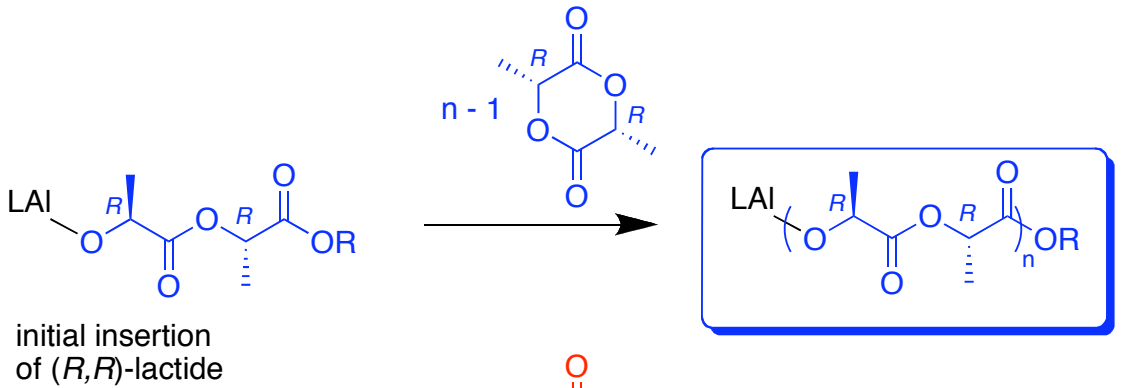
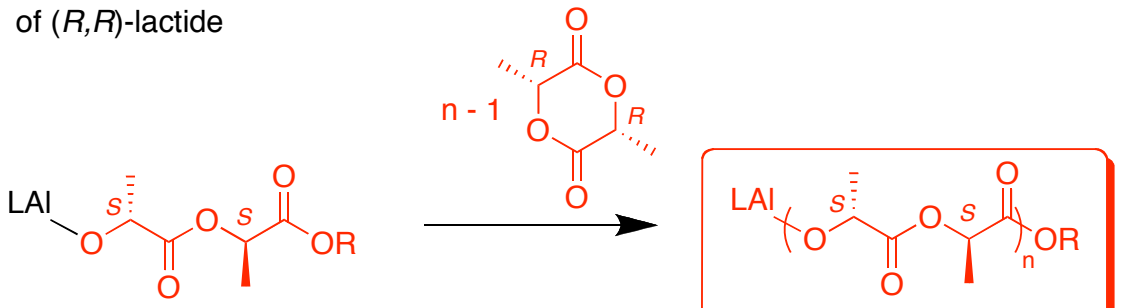
Chain-end Stereocontrol mechanism



initial insertion
of (*R,R*)-lactide

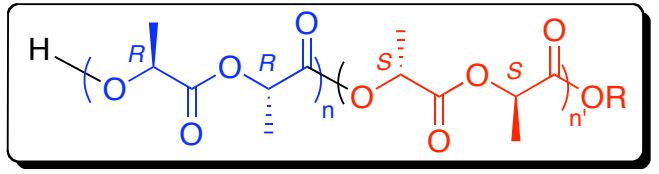


initial insertion
of (*S,S*)-lactide

The last inserted lactide unit stereocontrols the insertion of the subsequent unit

transesterification
hydrolysis

Isotactic Stereoblock PLA



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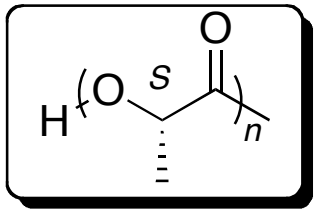
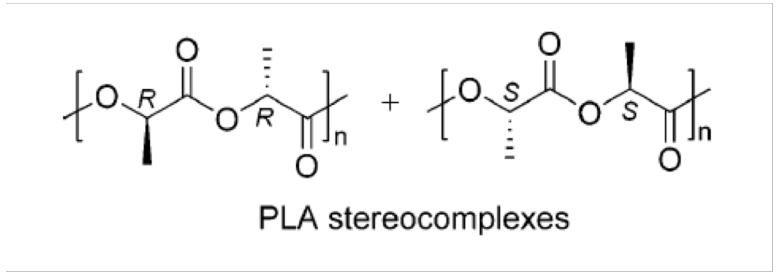
« Stereocomplex Character » in Isotactic poly(lactic acid)



Commercial
Poly(lactic acid)
T_m = 162 °C



Extremely interesting BPs (very high Tm ~230°C)
Excellent mechanical properties

Isotactic Stereoblock Poly(lactic acid) (Tm ~ 190 °C)

Inter-molecular
Chain interactions { RRRRRRRRRRRRSSSSSSSSSSRRRRRRRRRR
SSSSSSSSSSSSSRRRRRRRRRSSSSSSSSSSS }

Intra-molecular
Chain interactions [SSSSSSSSSSSSSSSSSS
RRRRRRRRRRRRRRRRRR]

→ **The « Stereocomplex Character » improves its thermal properties**

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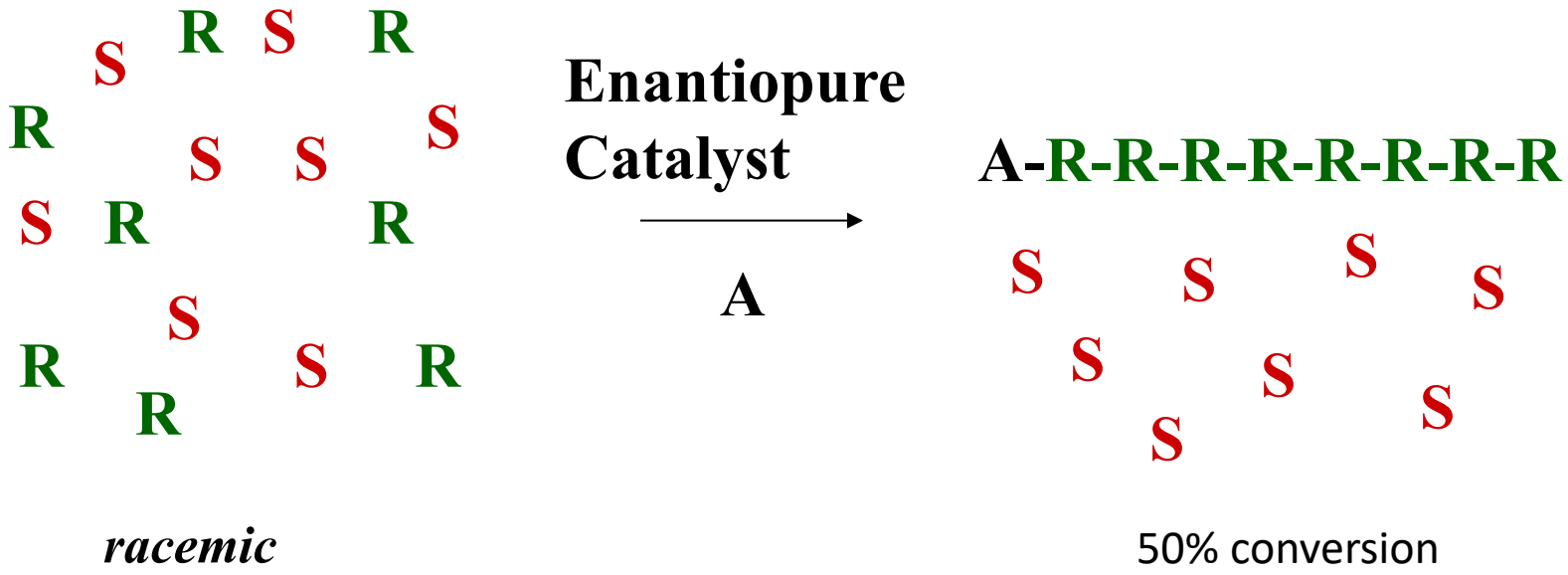
Enantioselective Polymerization

Principle: In an enantioselective polymerization, one enantiomer of a racemic monomer mixture is preferentially polymerized to give an optically active polymer (with a specific chain stereochemistry)



Major advantage: - Obtention of a polymer with a controlled stereochemistry

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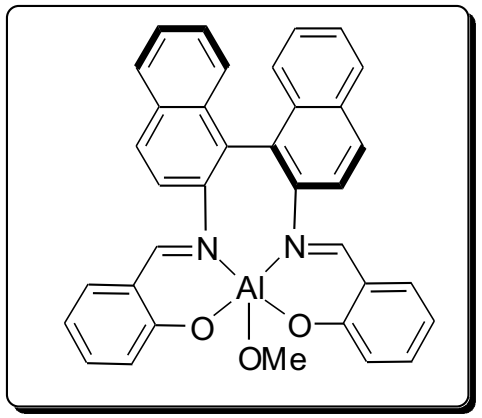
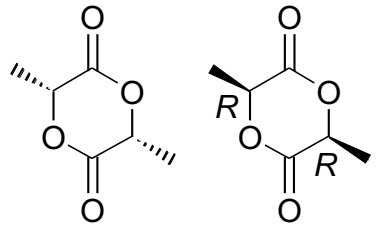
The use of enantiomerically pure Al Complexes: Enantioselective Polymerization of Lactides

- **Interest:** Access to stereoregular PLA polymers



≡ (*R*)-L*Al



(*L*)-LA (*D*)-LA

racemic

(*R*)-L*Al

(*D*)-lactide polymerized preferentially
(optically active isotactic Poly(*D*-lactide)

At 50% conversion, ee (unreacted monomer) = 80% ee

$k_D/k_L = 20$

Spassky *Macromol. Chem. Phys.* **1996**, *197*, 2627.

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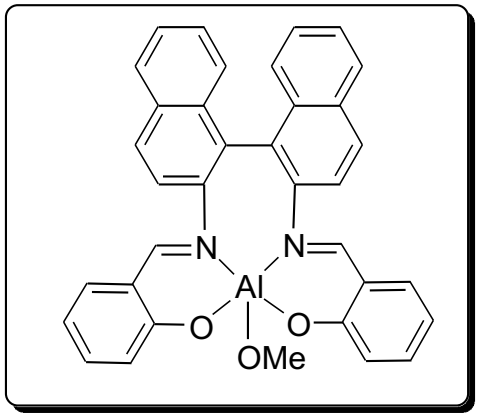
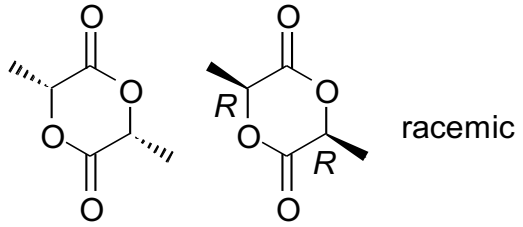
Formation of new materials via the formation of enantiomeric poly(L-LA) and poly(D-LA) block polymers



≡ (*R*)-L*Al, (*S*)-L*Al } racemic



(*L*)-LA (*D*)-LA

(*S*)-L*Al (*R*)-L*Al

Poly(L-lactide) (isotactic) Poly(D-lactide) (isotactic)

Smith et al. *JACS* **2000**, *122*, 1552.

Due to chain transfer during the polymerization process

Isotactic Stereoblock Poly(lactide)

RRRRRRRRRRRSSSSSSSSSSRRRRRRRRRR

Properties: New material, extremely high melting point (T_m = 187 °C)
And highly resistant

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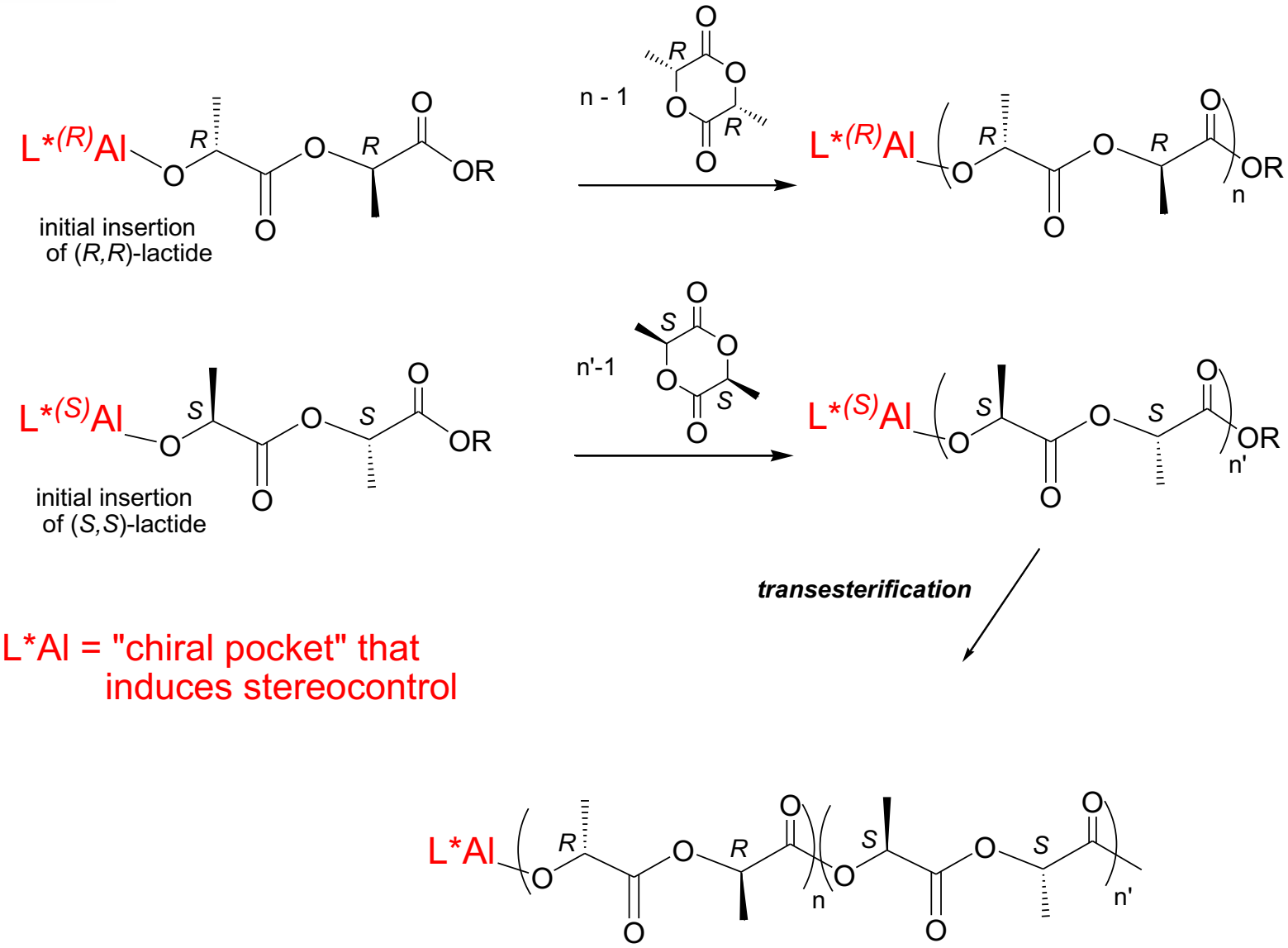
Metal-site Stereocontrol Mechanism



L*Al = "chiral pocket" that induces stereocontrol

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Required Features for Stereoregular PLA: Stereoregularity and Low Cost

Importance of the Metal Catalyst

Activity: Mg, Ca, Y > Zn, Sn > Al > Ti, Zr

Stereoregularity: Al > Zn, Sn, Y > Ti, Zr > Mg, Ca

Toxicity: Sn whereas Zn, Ca, Mg are biocompatible

Cost: Y is an expensive metal

Lactide Monomer

High purity required for high activity (it costs!!!)

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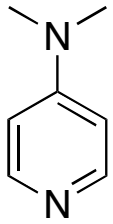
Latest Developments: Organocatalytic Polymerization of Lactides

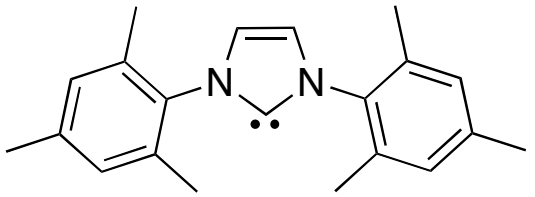
Interest: - use of metal-free catalysts (because of toxicity problems)
- no need to remove metal traces prior to polymer processing (costly)

Approach: - use of very nucleophilic organic species to ring-open lactide
- the ring-opened species ring-opens another lactide unit and so on….

Most efficient Nucleophiles to date:



dimethylamino-
-pyridine (DMAP)

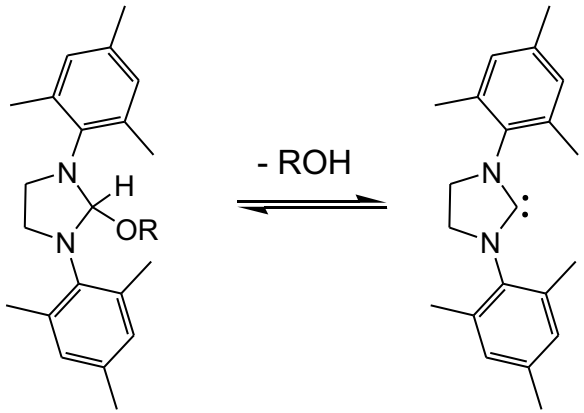


N-heterocyclic carbenes
(highly nucleophilic)

Metal-free Lactide Polymerization: Organocatalysis

Atactic PLA

entry	cat.	M/cat.[a]	conv[b]	DP[c]	PDI[d]
1	**2** (OMe)	100	89	89	1.18
2	**3** (OEt)	100	94	94	1.28
3	**5** (OPyr)	100	99	99	1.27
4	**6** (ODEG)	100	98	98	1.34
5	**7** (OEGO)	100	84	84	1.21
6	**8** (triol)	157	99	156	1.16
7	**1** (SIMes)[e]	100	87	87	1.30



Waymouth, Hedrick et al. *JACS* **2005**, *127*, 9079.

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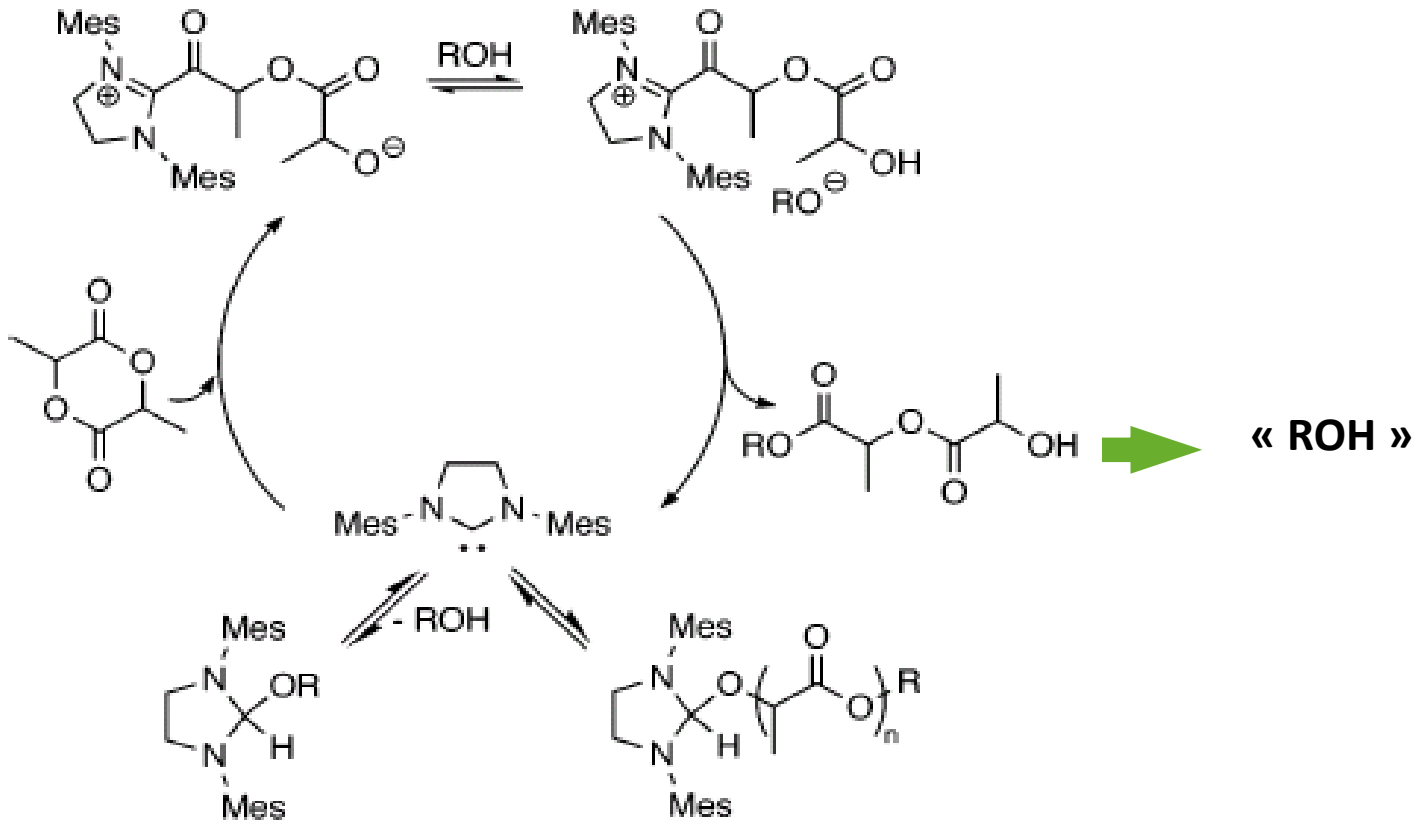
Mechanism



« ROH »

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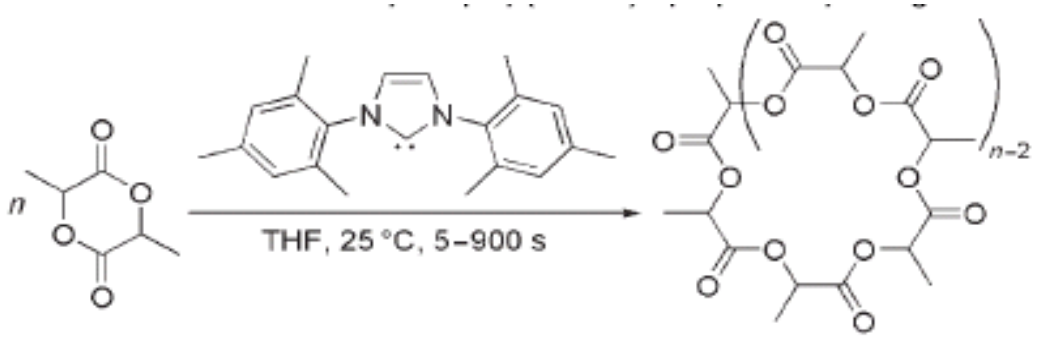
Access to unprecedented Cyclic PLA materials



Entry	t [s]	M/I[a]	Conv. [%][b]	M_n [kDa][c]	PDI[d]
1	30	100	75	15 (8.4)	1.16
2	10	100	35	7.3 (4.2)	1.15
3	60	200	73	18 (11)	1.17
4	20	200	32	9.9 (5.8)	1.28
5	900	200	92	26 (15)	1.35
6[e]	120	100	90	22[f]	1.27

Cyclic PLAs are more **thermally** stable linear PLAs

Waymouth, Hedrick et al. *Angew. Chem. Int. Ed.* **2007**, *46*, 2627

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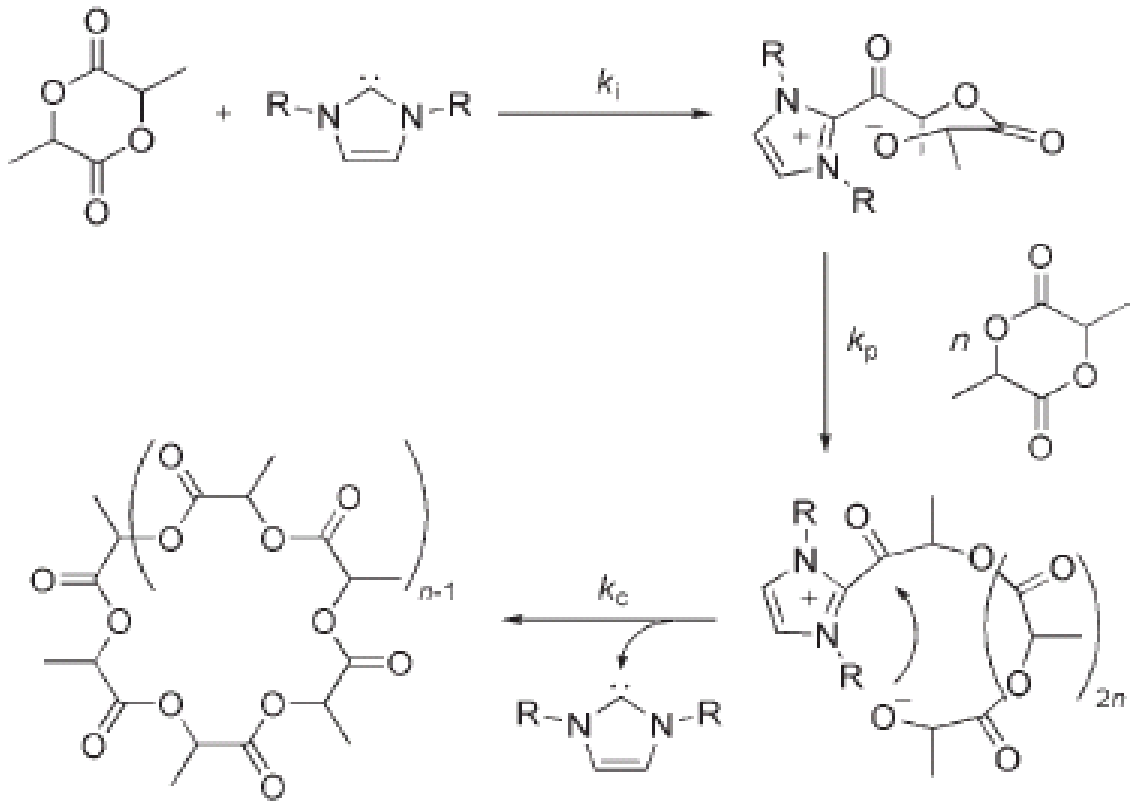
Mechanism



Scheme 2. Proposed mechanism for NHC-mediated zwitterionic polymerization of lactide.

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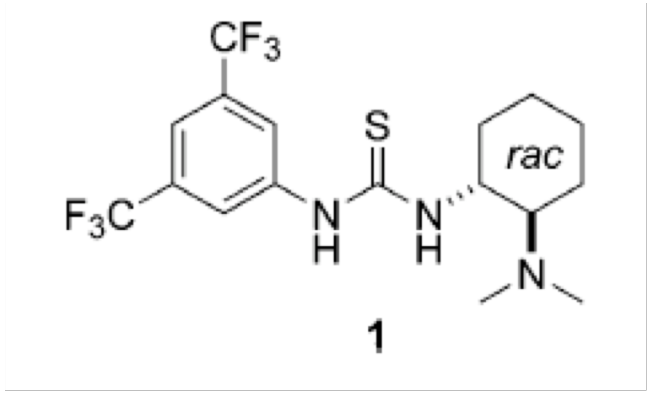
Organocatalysis: ROP of lactide thanks to supramolecular recognition

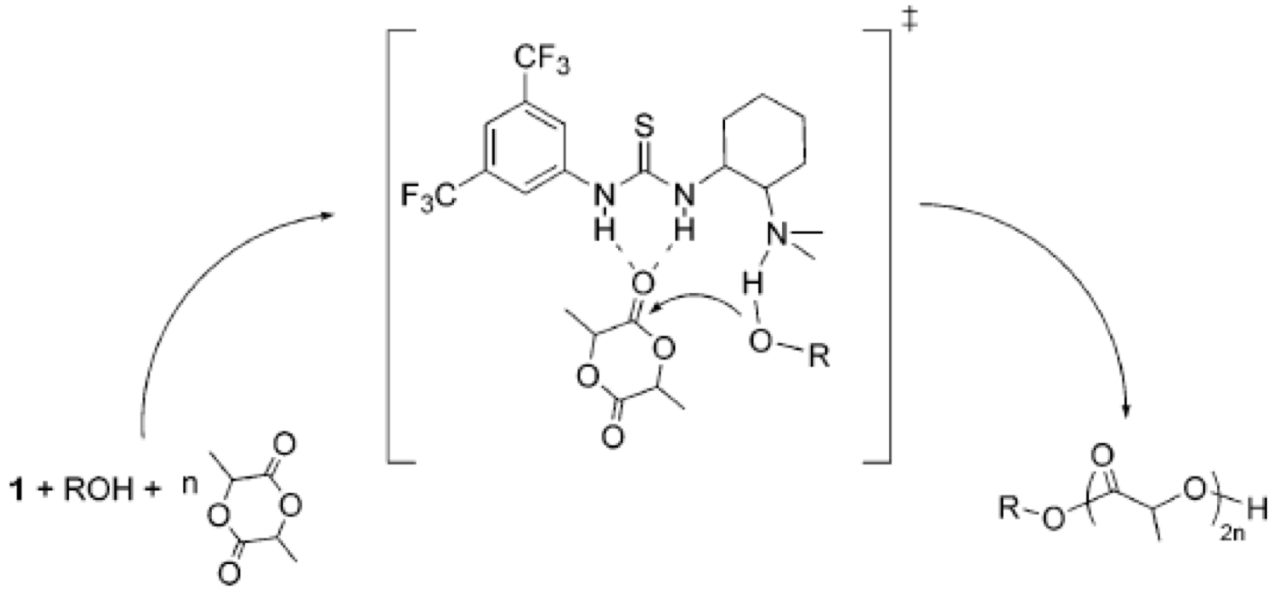
Waymouth et al. *J. Am. Chem. Soc*. **2005**

Use of a thiourea-amine
Bifunctional catalyst such as **1**



1

Scheme 2. Polymerization of Lactide by **1**



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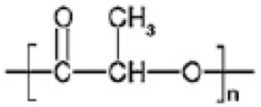
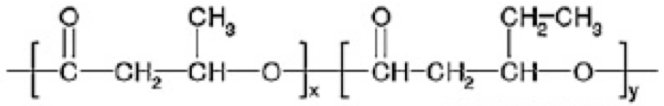
Overview of Agro-resources based Polyesters

Agro-resources based polyesters:

	Trade Name	Company
Poly(lactic acid) (PLA) 	Natureworks	Cargill (USA)
	Lacty	Shimadzu (Japan)
	Lacea	Mitsui Chemicals (Japan)
	Heplon	Chronopol (USA)
	CPLA	Dainippon Ink Chem. (Japan)
	PLA	Galactic/Total (Belgium)
	Eco Plastic	Toyota (Japan)
	Treofan	Treofan (Netherland)
	PDLA	Purac (Netherland)
	Ecoloju	Mitsubishi (Japan)
	Biomer L	Biomer (Germany)
Polyhydroxyalkanoate (PHA) 		
(PHBV, PHB)	Biopol	Monsanto (USA)*
(PHBV, PHB)	Mirel	Metabolix/ADM (USA)
(PHB, PHBV)	Biocycle	PHB Industrial (Brazil)
(PHB, PHBV)	Biomer P	Biomer (Germany)
(PHB, PHBV)	Enmat	Tianan (China)
(PHBHx, PHBO, PHBOd)	Nodax	Procter & Gamble (USA)*

From: *P. Bordes et al. / Progress in Polymer Science 34 (2009) 125–155*

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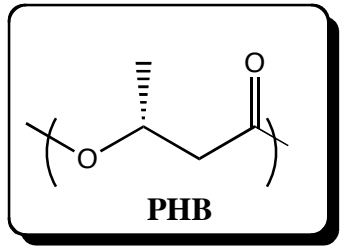
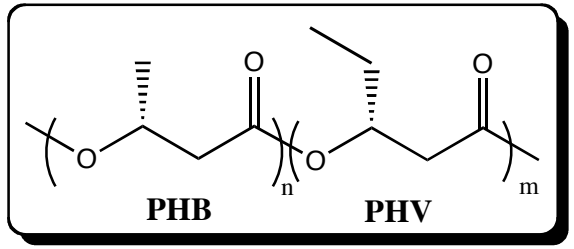
Poly(hydroalkanoates) : PHAs

PHAs are naturally produced by micro-organisms from various carbon sources (typically from the sugar family)

- Some micro-organisms may accumulate PHA
  From 30% to 80 % of cellular dry weight
- Depending on the carbon source, different monomers and thus Polymers may be obtained.
- Polyhydrobutyrate (PHB) is the main polymer of this family





(Biopol, Monsanto, 20% HV)

Major problem: the extraction and recovery steps are expensive

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Historical Background on PHB

- First observed in bacteria by Lemoigne et al. in the 1920s

Optically active macromolecules (PHBs) used as a « carbon reserves » by bacteria

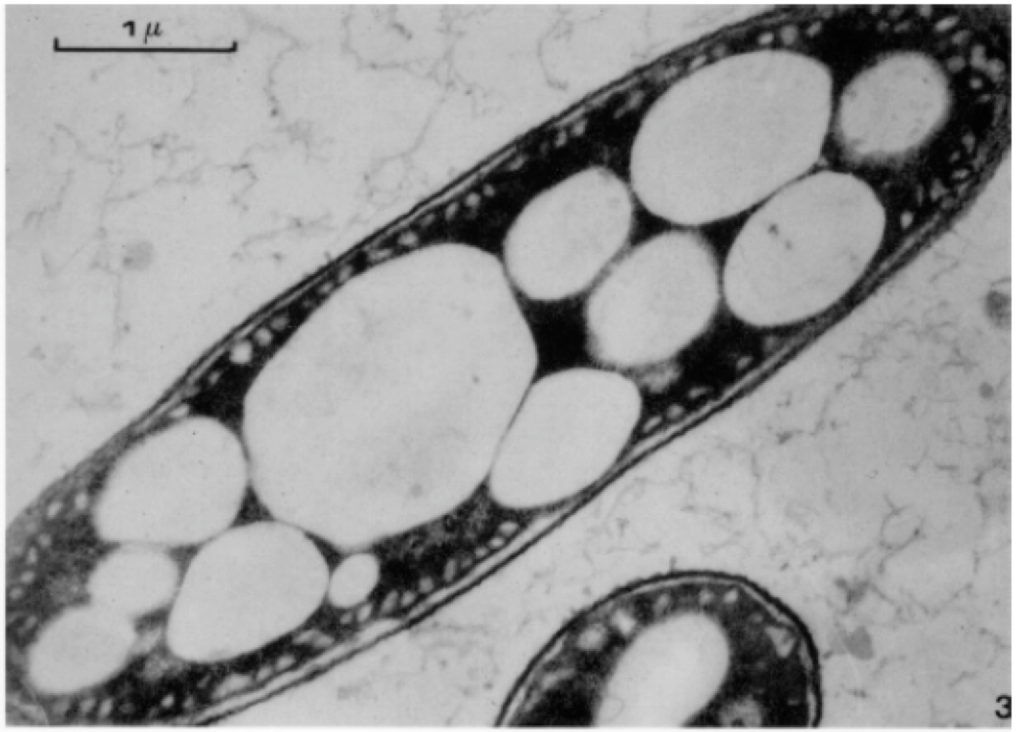

Figure 2. Transmission electron micrograph of ultrathin section of *Azotobacter chroococcum* cell treated with phenylacetic acid. From

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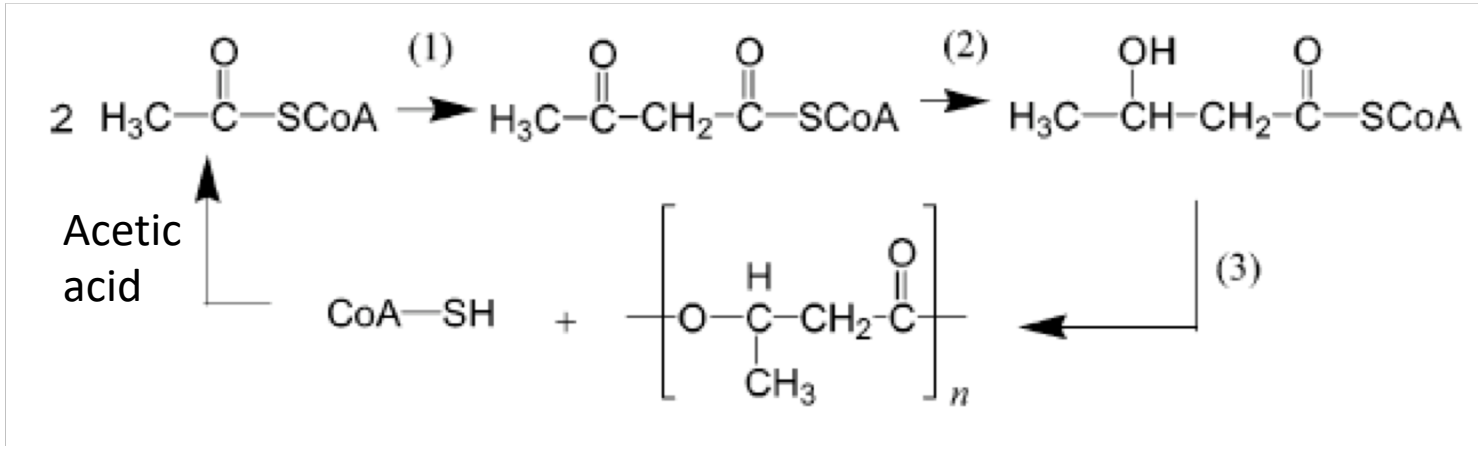
Biosynthesis of PHB



Implicated enzymes:

(1) ketothiolase: dimerizes acetyl-CoA

(2) reductase: hydrogenation to (R)-3-hydroxy-butyryl-CoA

(3) Synthase (or polymerase): polymerisation: access to PHB

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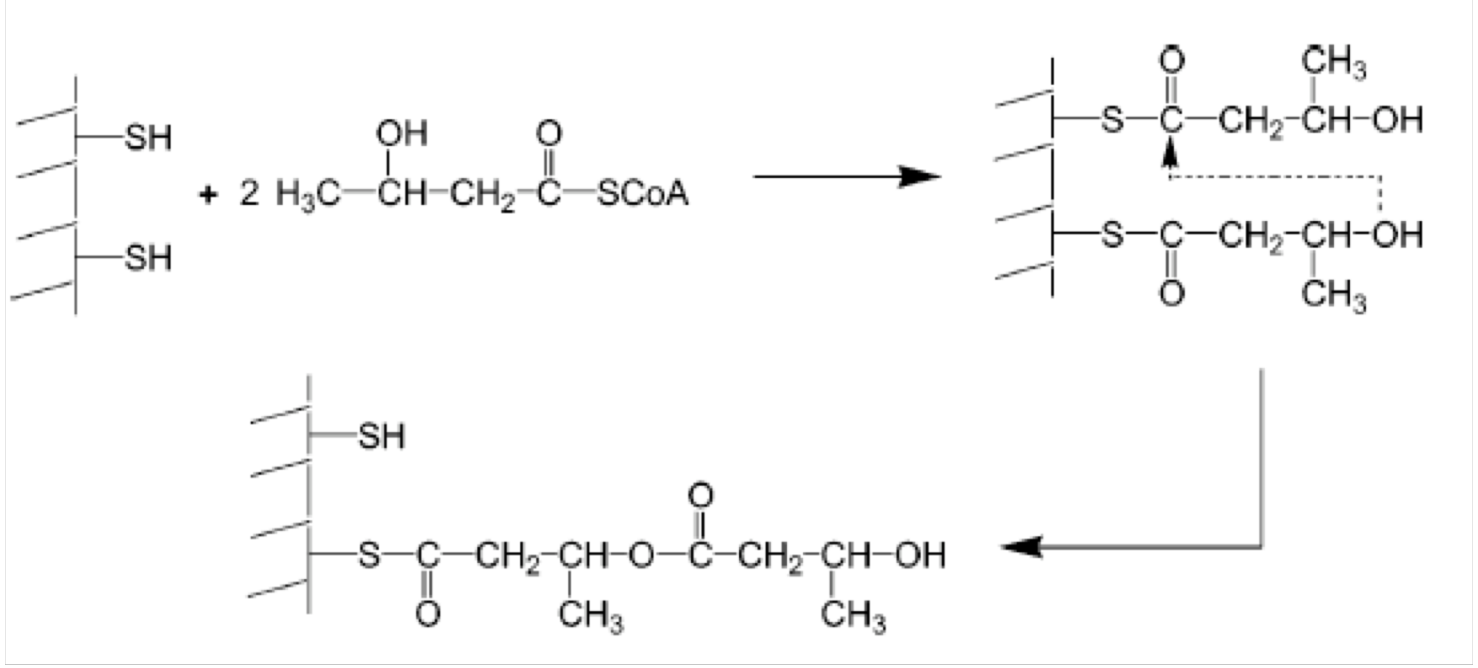
Polymerisation initiation and propagation



Two thiol groups within the polymerase enzyme are believed to be involved in the initiation and propagation polymerisation process.

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Polyhydroxybutyrate: PHB

PHB is a highly crystalline biodegradable and biocompatible polymer (Tg = 5 °C, Tm = 153°C)

	PLA Dow–Cargill (NatureWorks)	PHBV Monsanto (Biopol D400G – HV= 7 mol%)
Density	1.25	1.25
Melting point (°C)[a]	152	153
Glass transition (°C)[a]	58	5
Crystallinity[b] (in %)	0–1	51
Modulus (MPa) (NFT 51-035)	2050	900
Elongation at break (%) (NFT 51-035)	9	15
Tensile stress at break or max. (MPa) (NFT 51-035)	–	–
Biodegradation[c] (mineralization in %)	100	100
Water permeability WVTR at 25 °C ($g/m^2/day$)	172	21
Surface tension (γ) (mN/m)	50	–
γ_d (dispersive component)	37	–
γ_p (polar component)	13	–

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Molecular Structure of Coenzyme A