ALIPHATIC POLYESTERS : SYNTHESIS, STRUCTURES, PROPERTIES AND APPLICATIONS

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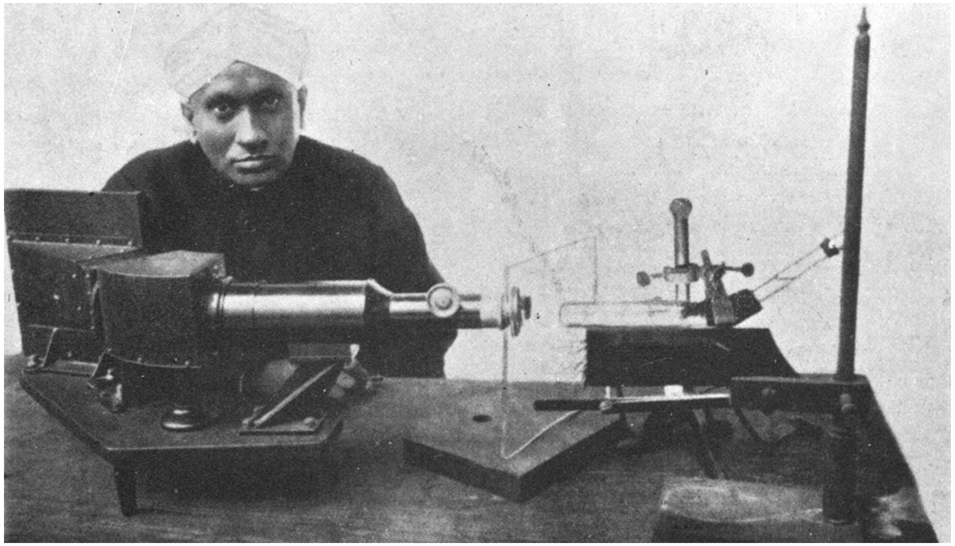
DR. REDDY'S LABORATORIES
HYDERABAD
FEBRUARY 27, 2015

THE RAMAN EFFECT



On February 28, 1928, through his experiments on the scattering of light, Raman discovered a phenomena called Raman Effect

Raman was confident of winning the Nobel Prize in Physics and was disappointed when the Nobel Prize went to Richardson in 1928 and de Broglie in 1929. He was so confident of winning the prize in 1930 that he booked tickets in July, even though the awards were to be announced in November, and would scan each day's newspaper for the announcement, tossing it away if it did not carry the news.

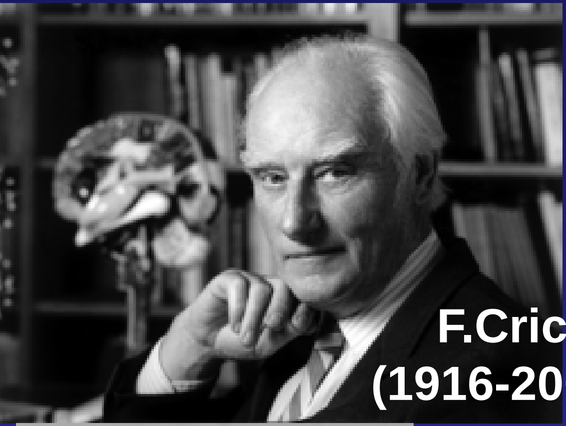
He did eventually win the 1930 Nobel Prize in Physics "for his work on the scattering of light and for the discovery of the effect named after him ''. He was the first Asian and first non-white to get a Nobel Prize in the sciences.

C. V. Raman
1888-1970

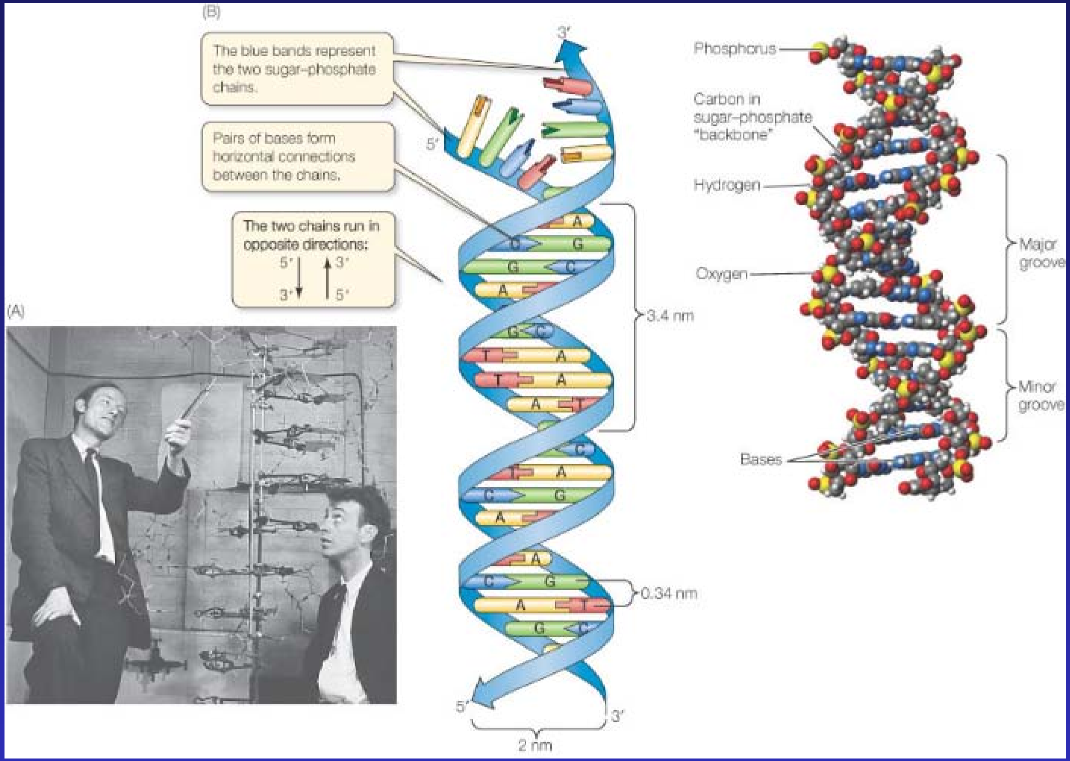
1906 Stood 1st in M.Sc. (did not attend classes!!)
1907 Assistant Auditor General, AG`s Office, Calcutta
1907 Starts research at IACS, part time and publishes the first paper

“Indian mind is not inferior ; what we lack is courage and a spirit of victory. If that indomitable spirit were to arise, nothing can hold us from achieving our rightful destiny”

28 FEBRUARY 1953 : ANOTHER HISTORIC DAY FOR SCIENCE



F.Crick
(1916-2004)



J.D.Watson
(1928-)

“This structure has novel features which are of considerable biological interest“………It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material"

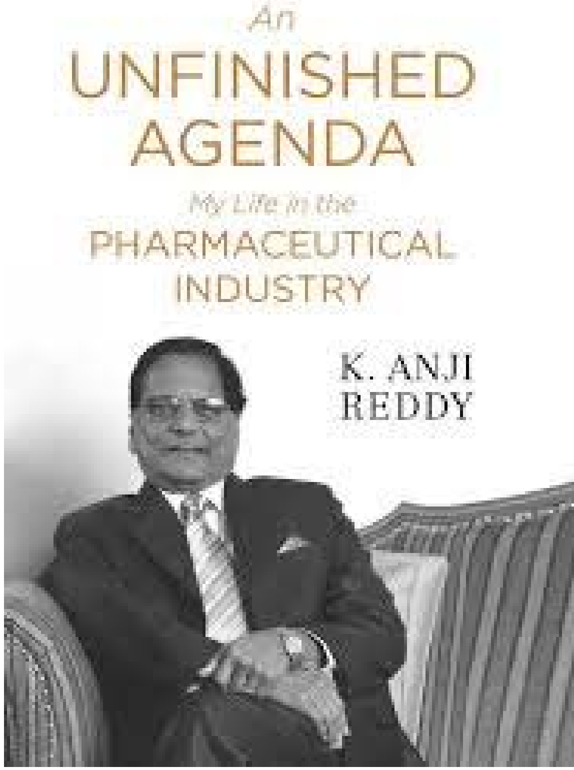
Watson and Crick in Nature, April 25, 1953

“ To bring new molecules to the country at a price the common man can afford”

“ Innovate for the benefit of the poor of India”

1940 - 2013
PhD, Chemical Engineering,
National Chemical Laboratory,
Pune, 1967

“ I strongly believe that drug discovery is a noble, perhaps, even a spiritual pursuit. It is beyond bottom lines and Investor relations. The mission is to improve the quality of life. This requires good science. But for science to be good, it has to result in affordable medicines”



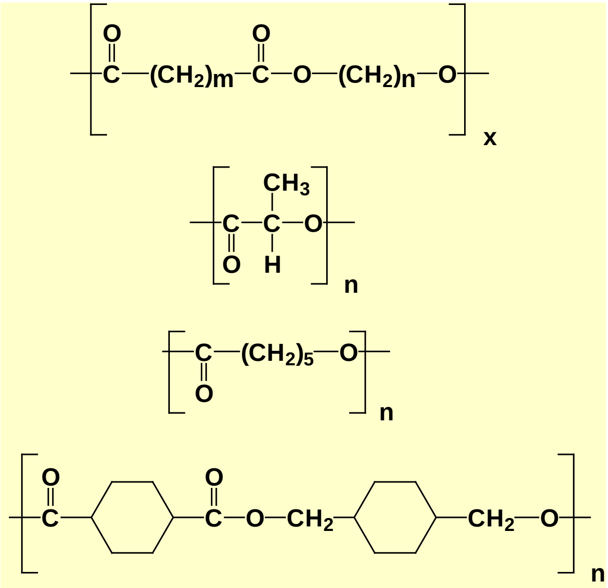
An
UNFINISHED
AGENDA
My Life in the
PHARMACEUTICAL
INDUSTRY
K. ANJI
REDDY

OUTLINE

- Aliphatic Polyesters and Poly(Lactic Acid)s : A brief introduction
- Introduction to Ring Opening Polymerization (ROP)
- Poly(lactic acid) s: Polymer Architectures
- Some examples from current research
    - Telechelic polyesters
    - Non aqueous monomer for PLLA
    - Homo coupling of hetero-telechelics
    - Conformationally constrained monomers
    - Star branched PLLA’s

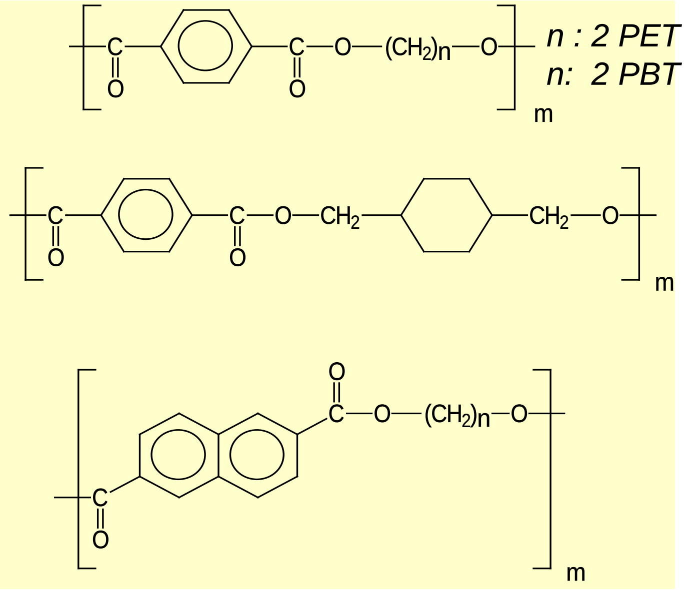
GENERAL CLASSES OF POLYESTERS

Aliphatic polyesters



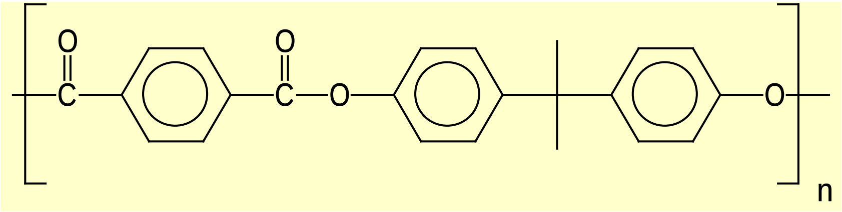
< 200,000 tons per annum !

Aliphatic-Aromatic polyesters



60 million tons per annum;
One third goes for making bottles !

Fully Aromatic polyesters

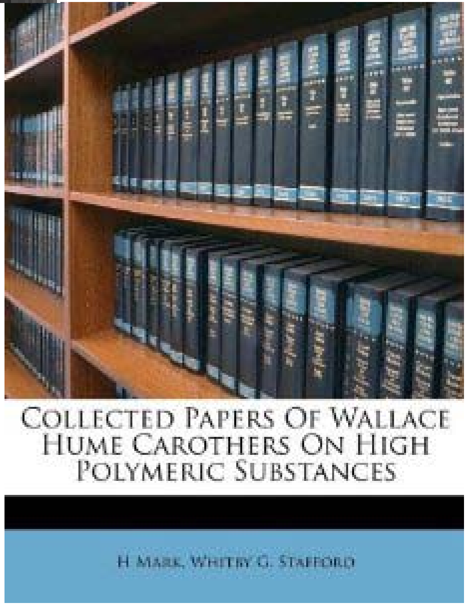


ALIPHATIC POLYESTERS : PIONEERING CHEMISTRY OF WALLACE HUME CAROTHERS

1896-1937

54 papers
400 pages

Enough for one lifetime !



COLLECTED PAPERS OF WALLACE HUME CAROTHERS ON HIGH POLYMERIC SUBSTANCES

H. MARK, WHITBY G. STAFFORD

Published 1940

STUDIES ON POLYMERIZATION AND RING FORMATION

Twenty eight papers from 1929 to 1935

Carothers addressed one important question:

(a) If two bifunctional molecules, e. g., one dibasic acid and one glycol or diamide, react, two possibilities occur. The reaction can result (1) in a chain polymer of lower or higher molecular weight, which still bears either hydroxyl or carboxyl terminal groups or (2) in a smaller or larger ring, which does not contain the reactive group.

Under what conditions does either of these two possibilities take place and what is the molecular weight of the resulting compound?

CAROTHER'S DELINEATION OF POLYMERIZATION OF HYDROXY CARBOXYLIC ACIDS

1 α-hydroxy acetic acid (Glycolic acid) → + Oligomers

2 β-Hydroxy Propionic acid →

3 γ-Hydroxy butyric acid →

4 δ-Hydroxy pentanoic acid → + Oligomers

5 ε-Hydroxy Caproic acid → + Oligomers

→ + Oligomers

Ref. : Carothers, Chem Rev; 8 353 (1931)

IX. Polymerization*

TABLE OF CONTENTS

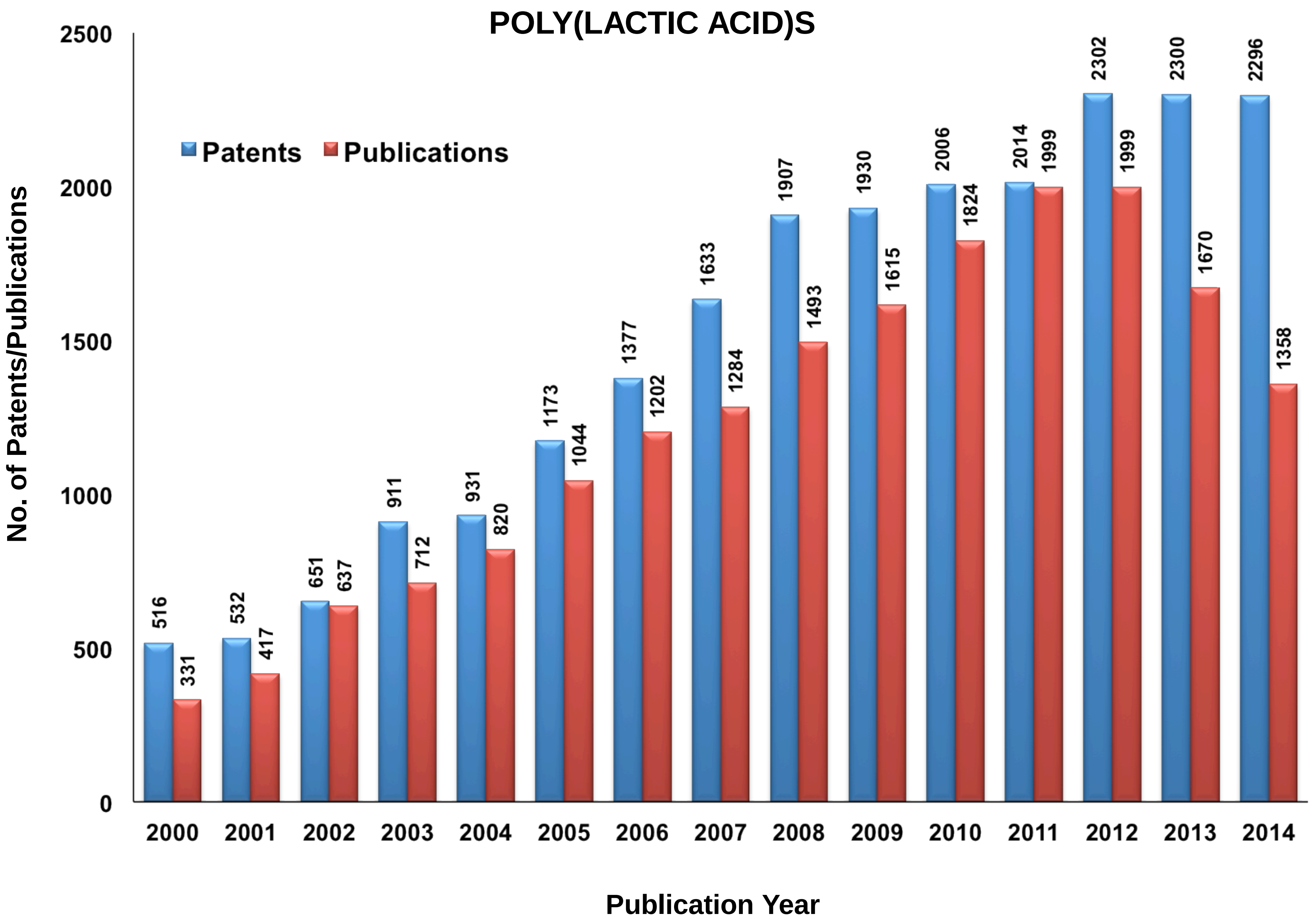
** Wallace H. Carothers; Chemical Reviews 8, 353-426 (1931); Communication No. 55 from the Experimental Station of the E. I. du Pont de Nemours and Company.*
Received March 21, 1931. Published June 1931.

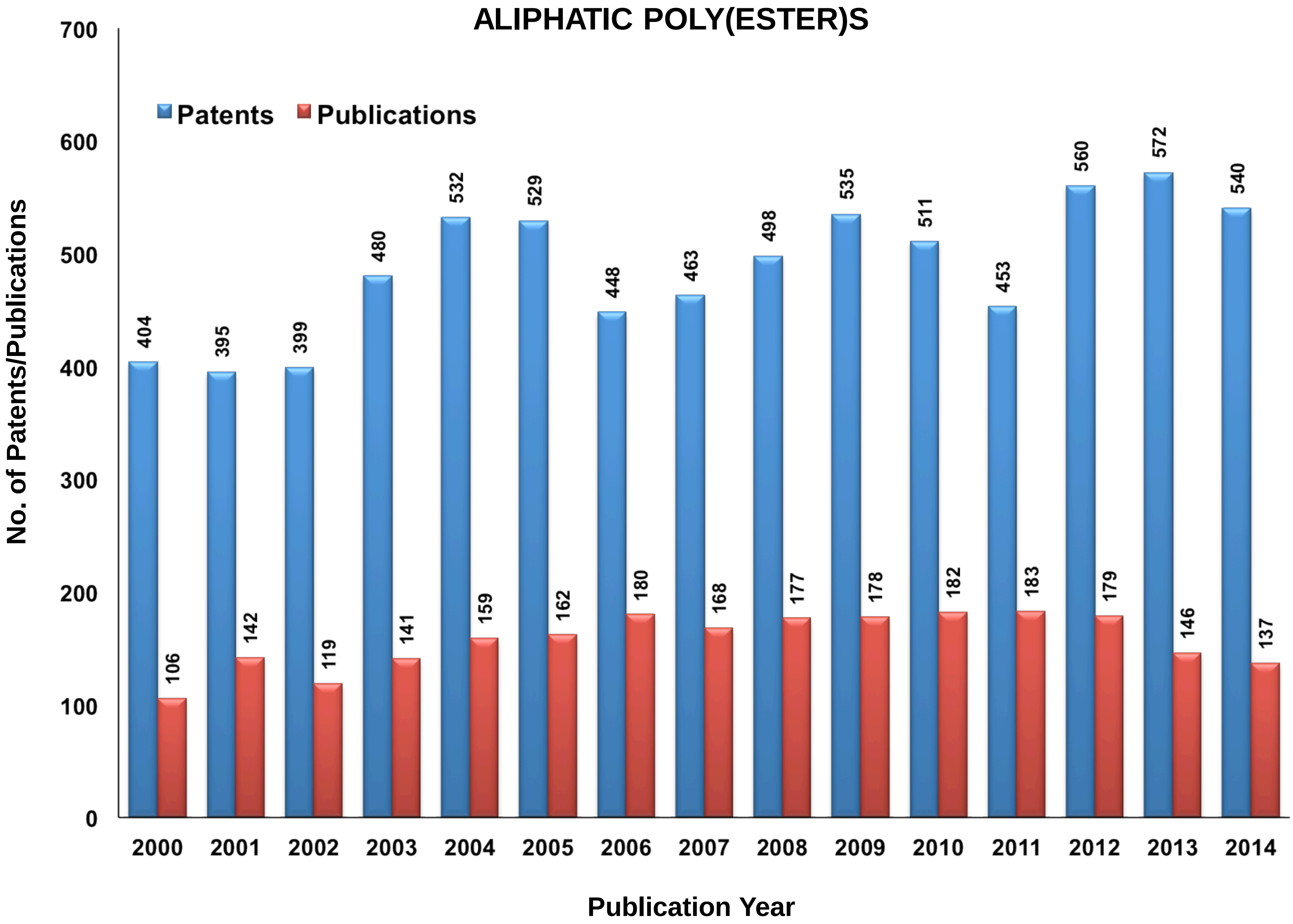
Key questions

- *On what factors do the relative rates k_1 and k_2 depend ?*
- *What is the importance of general acid catalysis in these reactions?*
- *Can larger oligomers undergo thermolysis to large rings?*
- *If ring formation limits chain growth reaction, is there an alternative chemistry to make high molecular weight linear aliphatic polyesters ?*

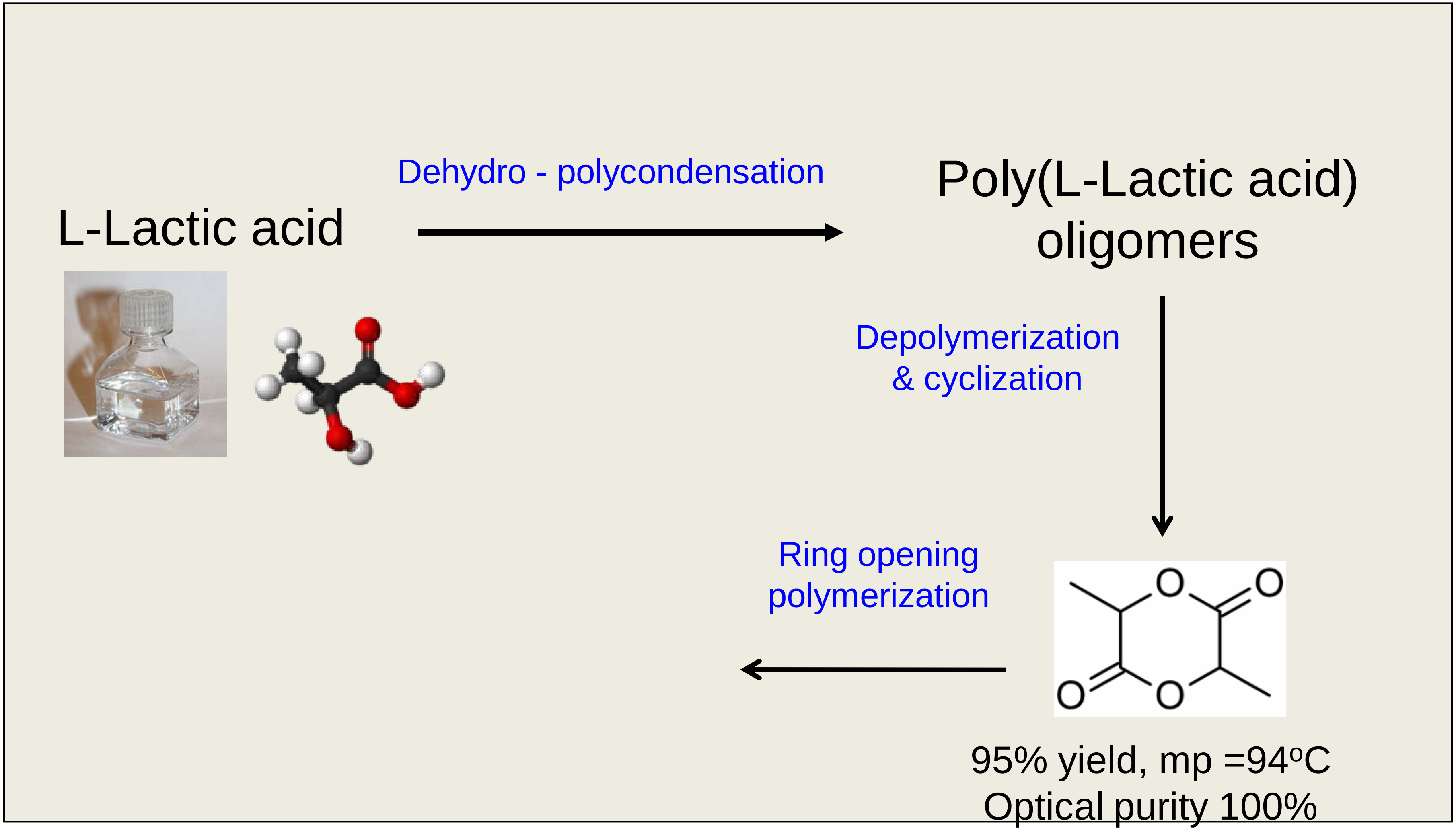
LACTIC ACID AND POLY (LACTIC ACID)S :TIME LINES

1780	Carl Wilhelm Scheele Isolates lactic acid from sour milk
1808	Jacob Berzelius discovers that L-lactate is produced by muscles during exertion
1845	T-J. Pelvaze synthesizes poly(lactic acid) by polymerization of lactic acid
1856	Louis Pasteur discovers lactobacillus and its role in making lactic acid
1895	Boehringer Ingelheim commences commercial production of L(+)-lactic acid
1932	Wallace Carothers develops a method to convert cyclic lactide to the polymer of lactic acid
1954	First patent on PLA issued to DuPont (US Pat.2,668.162)
1972	Poly(lactide-co-glycolide) introduced by Ethicon Inc., as resorbable sutures
2001	First commercial production of cyclic lactide PLLA at Blair, Nebraska by Cargill Inc.


POLY(LACTIC ACID)S
Patents
Publications
No. of Patents/Publications
Publication Year
0
500
1000
1500
2000
2500
2000
516
331
2001
532
417
2002
651
637
2003
911
712
2004
931
820
2005
1173
1044
2006
1377
1202
2007
1633
1284
2008
1907
1493
2009
1930
1615
2010
2006
1824
2011
2014
1999
2012
2302
1999
2013
2300
1670
2014
2296
1358


ALIPHATIC POLY(ESTER)S
Patents
Publications
No. of Patents/Publications
0
100
200
300
400
500
600
700
Publication Year
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
404
106
395
142
399
119
480
141
532
159
529
162
448
180
463
168
498
177
535
178
511
182
453
183
560
179
572
146
540
137

POLY(L+) (LACTIC ACID)S (PLLA) : PREPARATION



L-Lactic acid

Dehydro - polycondensation

Poly(L-Lactic acid) oligomers

Depolymerization & cyclization

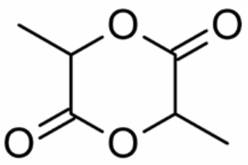
Ring opening polymerization

95% yield, mp =94°C

Optical purity 100%

Properties of L-Lactide

Formula: $C_6H_8O_4$
Chemical Name: 3,6-dimethyl-1,4-dioxane-2,5-dione
Molecular Weight: 144 g/mol
CAS Registry Number: 95-96-5



cyclic di-ester of lactic acid

Attribute	Typical Value	Method
Stereochemistry	L-Lactyl	GC
Color	White	Visual inspection
Purity	≥ 99%	GC
Melting Range (Peak) (^{O}C)	95-98	DSC at 20^{o}C min^{-1}
Specific Gravity: Solid at 25^{o}C	1.36	Pyknometer
Specific Gravity: Liquid at 130^{o}C	1.16	Hydrometer
Specific Heat Capacity: Solid at 25^{o}C (J g^{-1}K^{-1})	1.3	DSC
Specific Heat Capacity: Liquid at 130^{o}C (J g^{-1}K^{-1})	2.2	DSC
Heat of Vaporization (kJ mol^{-1})	~63	-

SUGAR CANE

FERMENTATION OF SUGAR CANE JUICE TO L(+) LA

CRUDE
L(+) LACTIDE
FORMATION

L(+) LACTIDE CRYSTALLIZATION

L(+) LACTIDE CRYSTALS

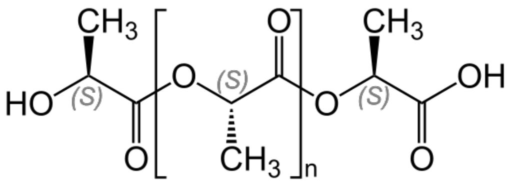
ROP

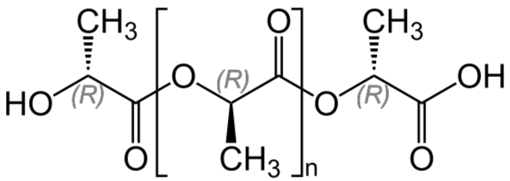
THERMAL AND MECHANICAL PROPERTIES OF PLA

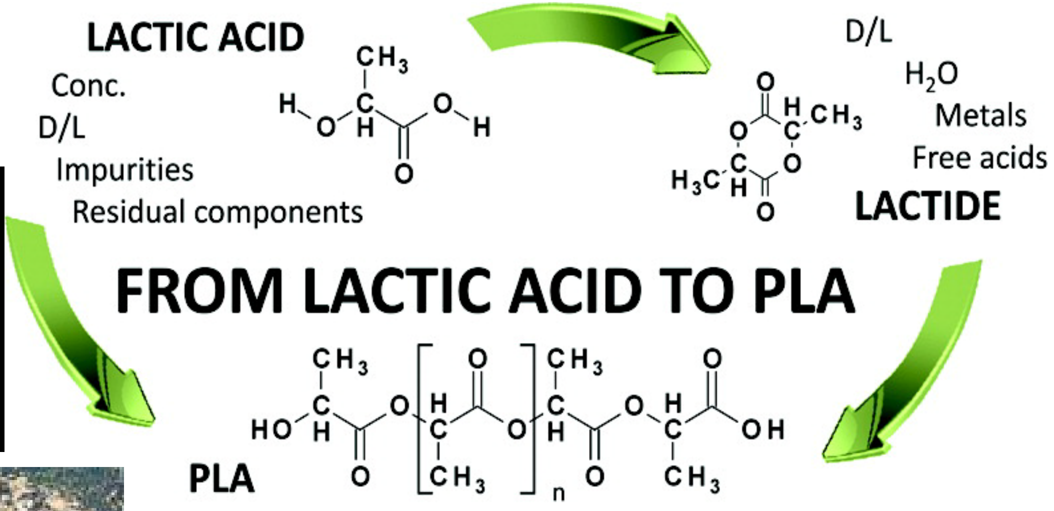
PROPERTY	VALUE
Glass transition temperature (T_g)	50-70 ^oC
Melting temperature(T_m)	170-190^oC
Crystallinity (X_c)	~ 35%
Intrinsic viscosity (η, in chloroform)	3.8-8.2 dL g^{-1}
Tensile strength (film)	28-50 Mpa
Tensile modulus (film)	1200-3000 Mpa
Shear strength	54.5 Mpa
Share modulus	1210-1430 Mpa
Bending strength	132 Mpa
Bending modulus	2800 Mpa
Elongation at break (film)	2.0-6.0%

POLY (LACTIC ACID)S : AN ALIPHATIC POLYESTER FROM THE MOST SIMPLE AB MONOMER

Insoluble in water, moisture and grease resistant
Biodegradable and compostable
Clarity and glossiness similar to PET
Requires 20 to 50% less fossil fuels to produce than PET
CO2 emissions down by 60% (0.75 kg of CO2 per kg vs 3.4 for PET







LACTIC ACID

Conc.
D/L
Impurities
Residual components

D/L
H_2O
Metals
Free acids

LACTIDE

FROM LACTIC ACID TO PLA

PLA

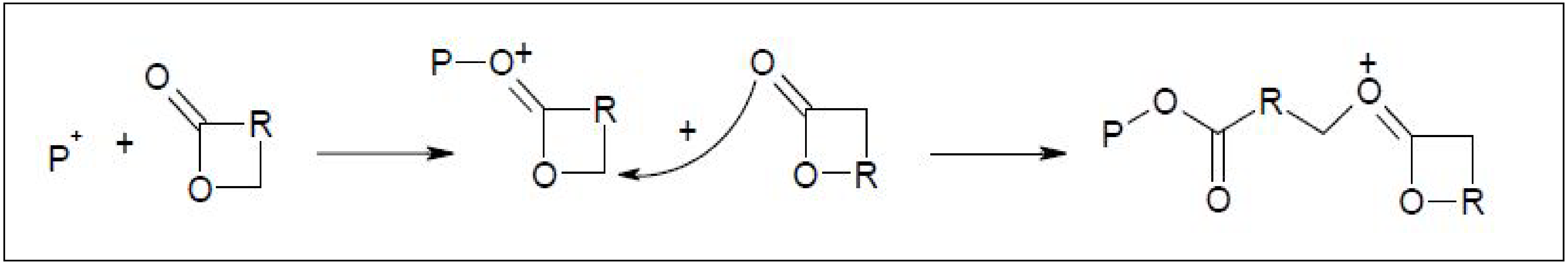
Structure-property relationships
Residual components, degradation products

RING OPENING POLYMERIZATION OF CYCLIC ESTERS

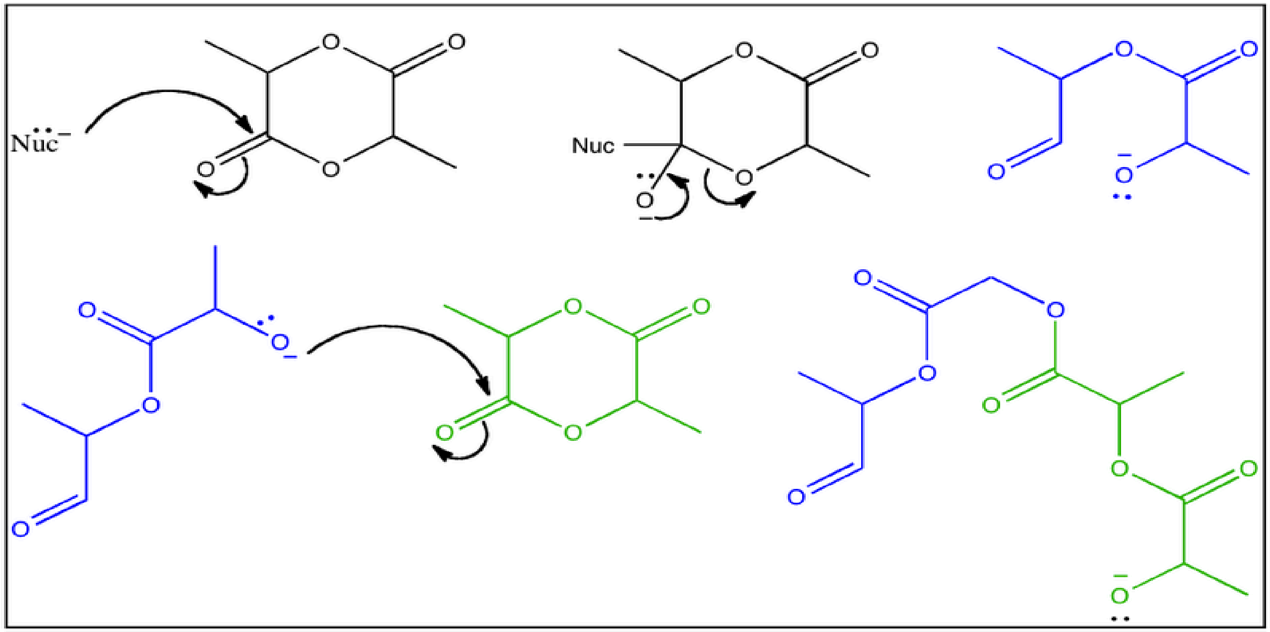
Only practical way to polymerize glycolic or lactic acid
is via their corresponding cyclic esters

RING OPENING POLYMERIZATION: TYPES

- Cationic Ring Opening Polymerization

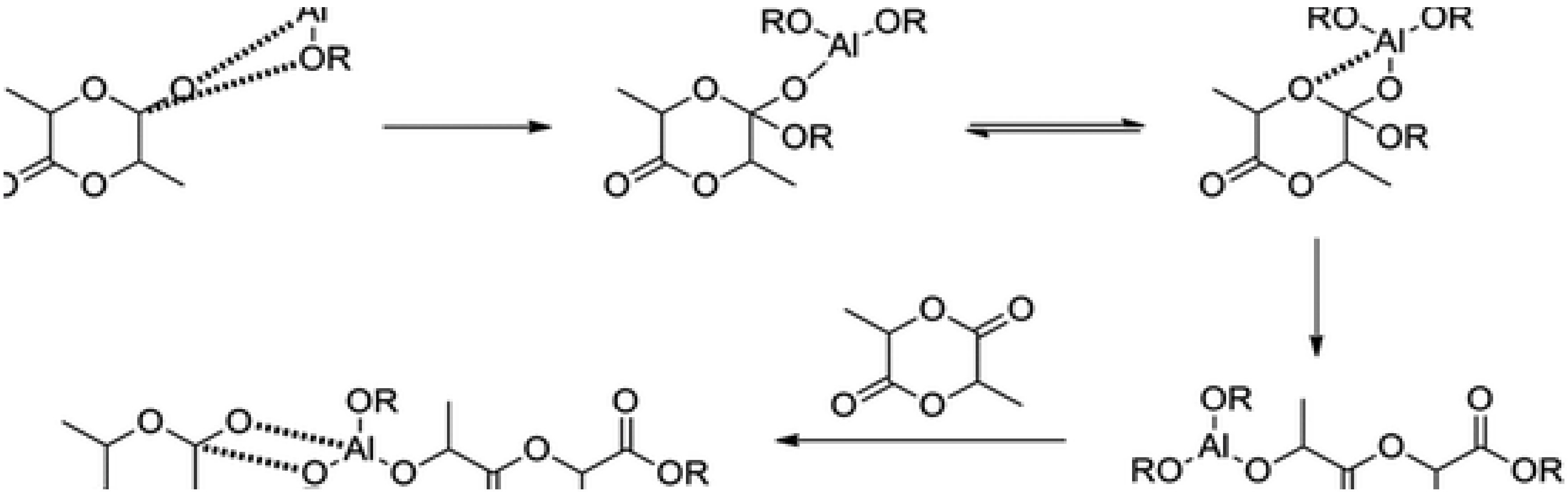


- Anionic Ring Opening Polymerization

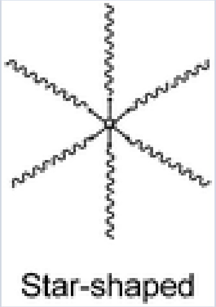
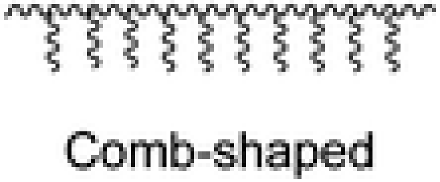
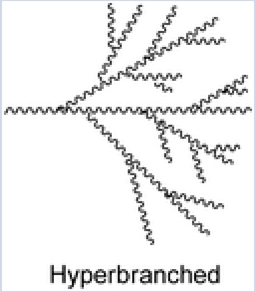


RING OPENING POLYMERIZATION: TYPES

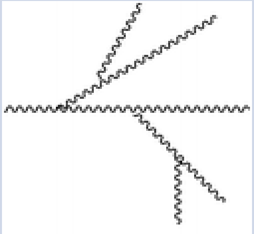
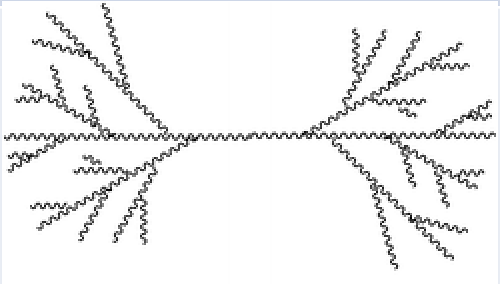
- Coordination Insertion Ring Opening Polymerization



STRUCTURE-PROPERTY EFFECT OF THE DIFFERENT PLA ARCHITECTURES COMPARED TO THE LINEAR HOMOPOLYMER

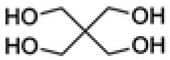
Structure	Properties
 Star-shaped	Lowe dilute solution viscosity More prominent shear-thinning behavior Higher storage and loss moduli Lower (T_g) (T_m) and crystallinity
 Comb-shaped	Higher degradability Lower (T_g) (T_m) and crystallinity Increased hydrophilicity Lower intrinsic viscosity Better histocompatibility
 Hyperbranched	Lower (T_g) (T_m) and melting enthalpy ΔH_m Higher thermal stability

STRUCTURE-PROPERTY EFFECT OF THE DIFFERENT PLA ARCHITECTURES COMPARED TO THE LINEAR HOMOPOLYMER

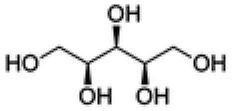
Structure	Properties
 Long-chain branched	Lower crystallinity Lower contraction factor Lower intrinsic viscosity
 Dumbbell-shaped	Lower (T_g) (T_m) (T_d) Lower crystallinity Decreased hydrophobicity

SOME CORES FOR BRANCHING

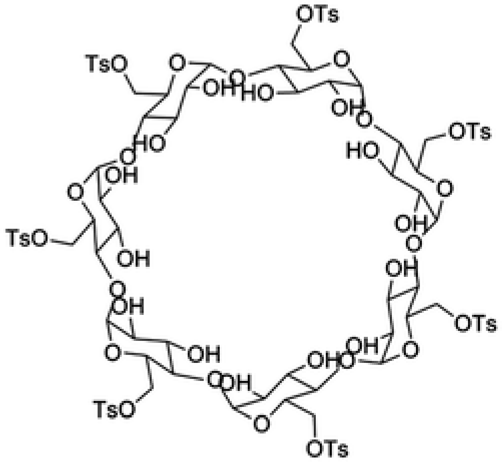
glycerol



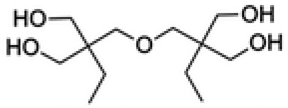
pentaerythritol



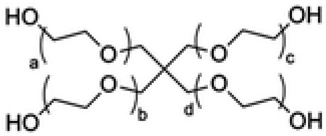
xylitol



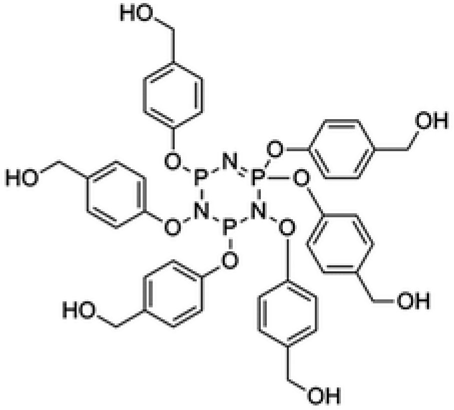
tosylated β-cyclodextrin



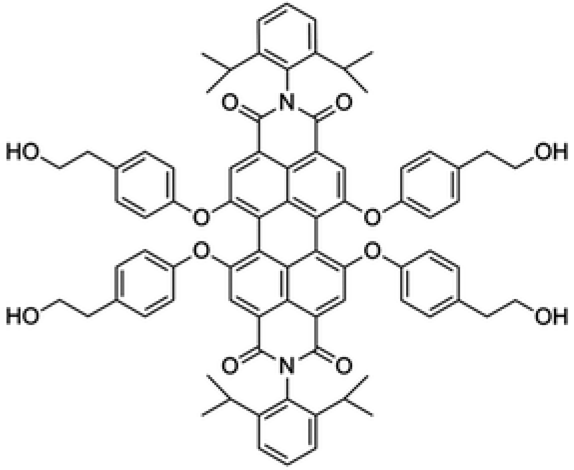
di(trimethylolpropane)



pentaerythritol ethoxylate

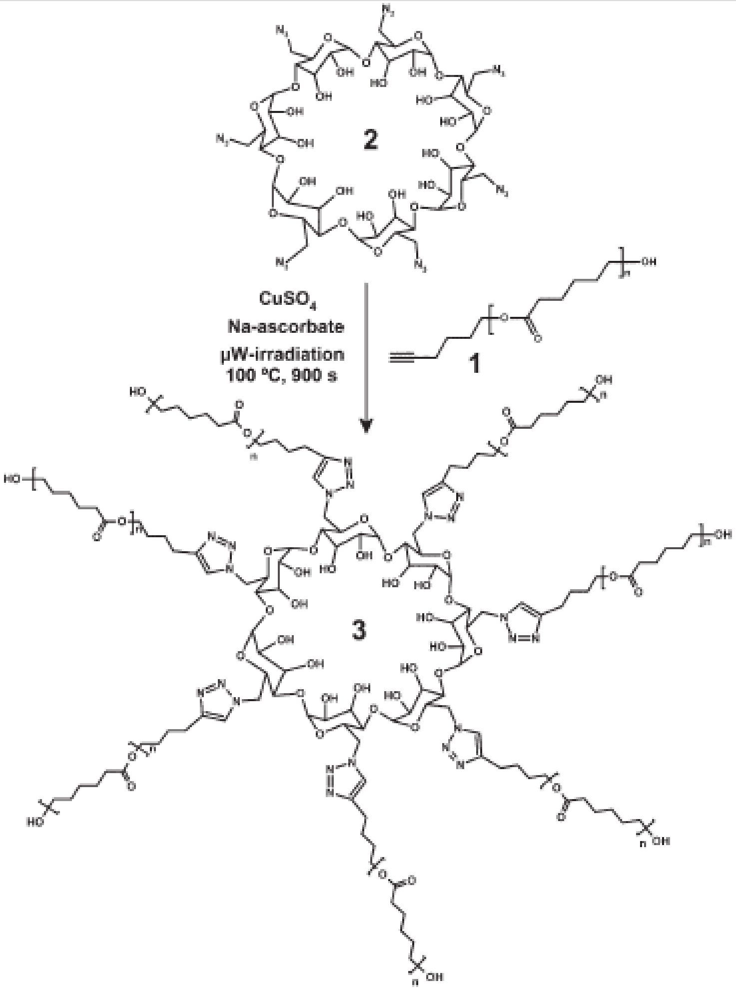


Hexakis[p-(hydroxymethyl)phenoxy]cyclotriphosphazene

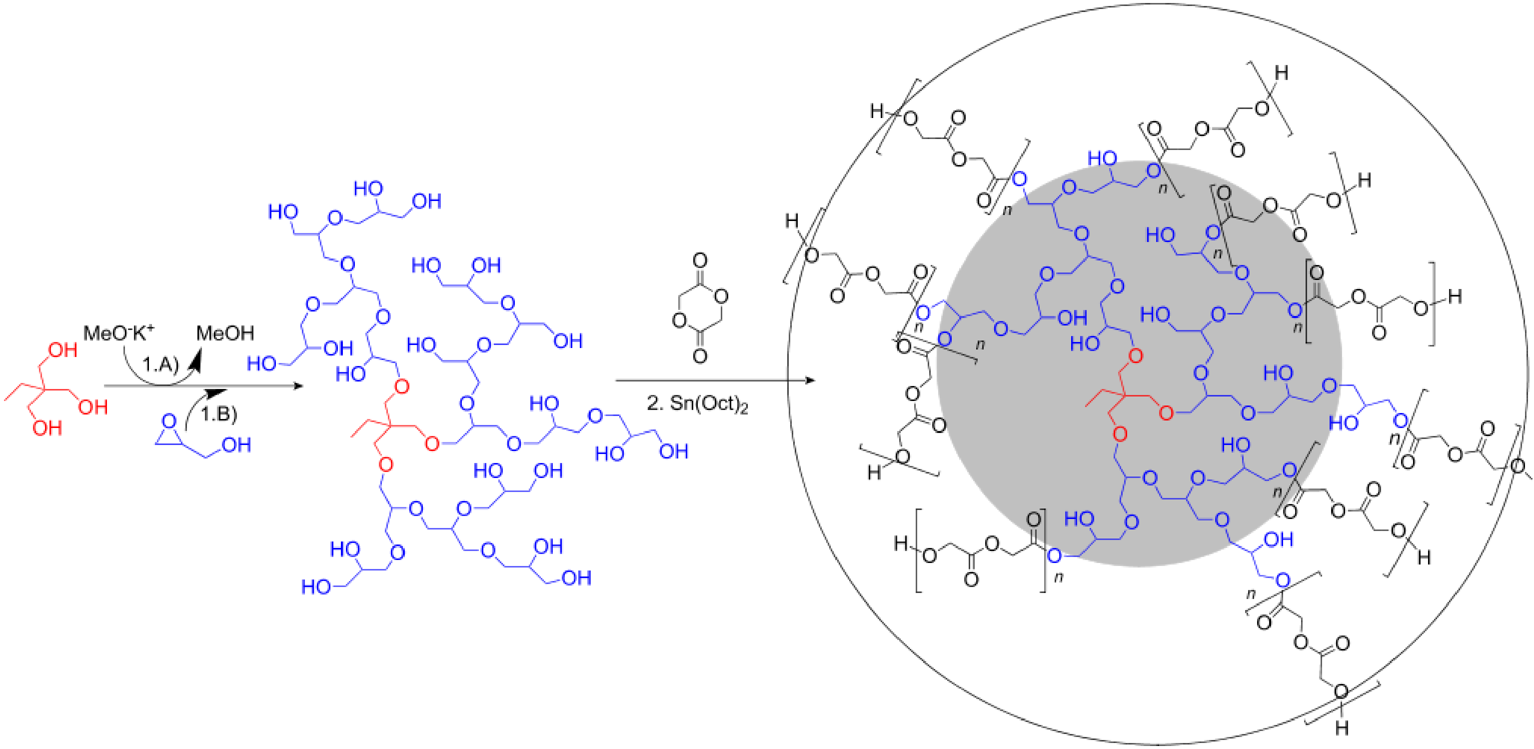


tetrahydroxyperylene

CYCLODEXTRIN AS CORE

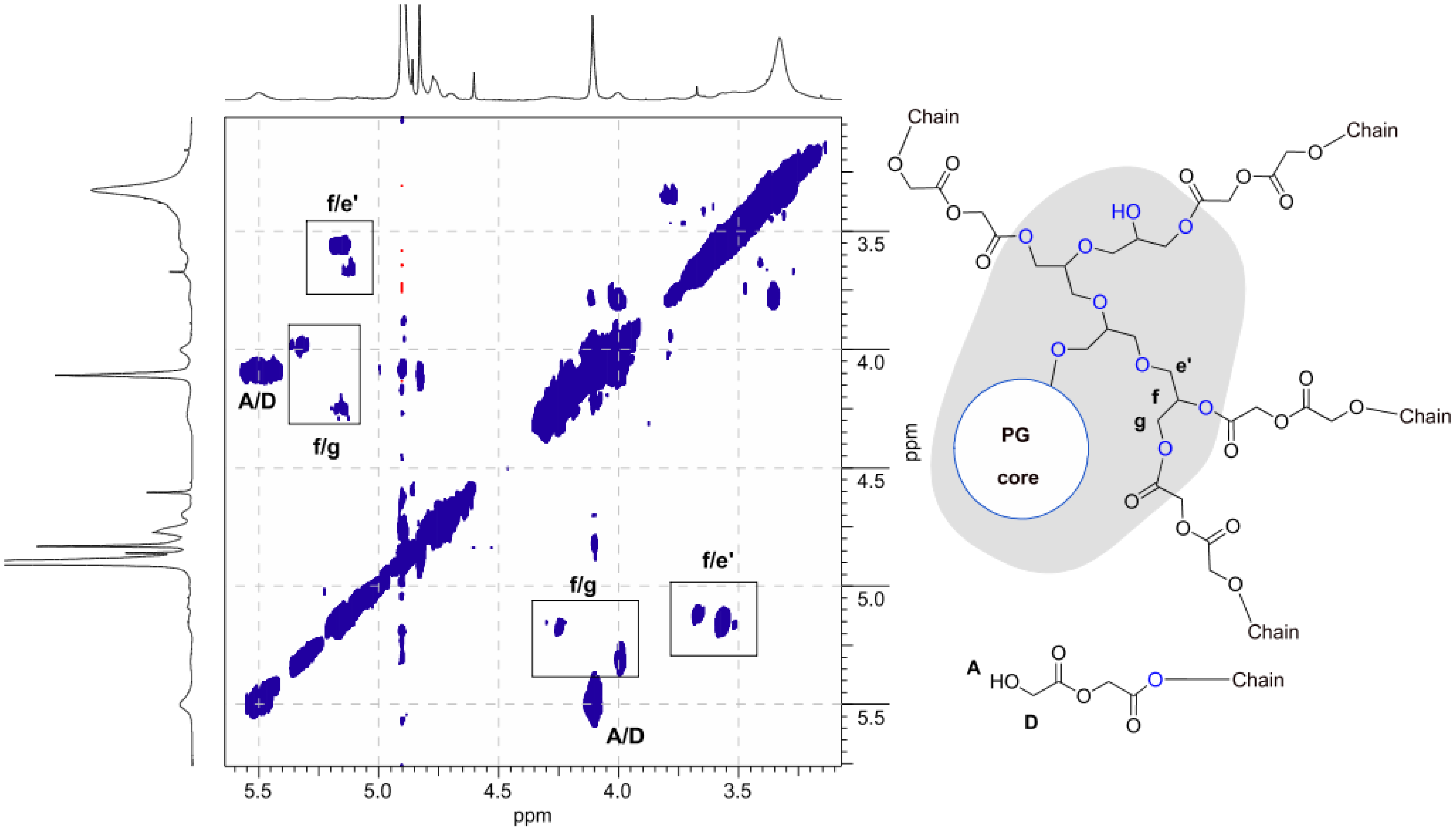


BRANCHED POLY (GLYCOLIC ACID)S



Frey et al , Beilstein J. Org. Chem., 2010

BRANCHED PLGA: STRUCTURE BY COSY



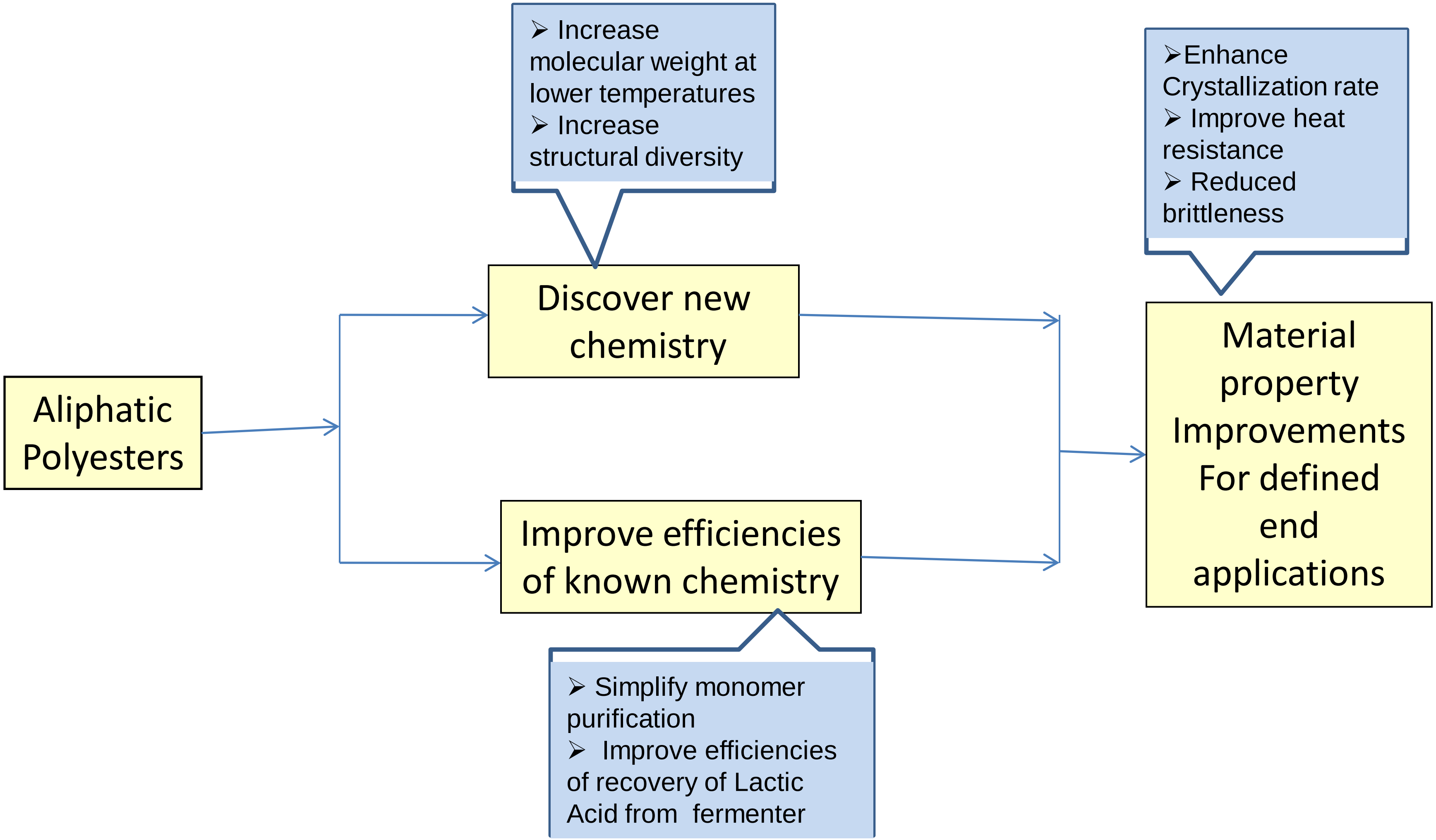
SUSTAINABLE POLYMERS FROM BIO-DERIVED AND BIO-RENEWABLE RESOURCES

Objectives

Expand the chemistry toolbox with new methods and techniques for next generation products

Materials Platform

Aliphatic Polyesters



- Increase molecular weight at lower temperatures
- Increase structural diversity

- Enhance Crystallization rate
- Improve heat resistance
- Reduced brittleness

Aliphatic Polyesters

Discover new chemistry

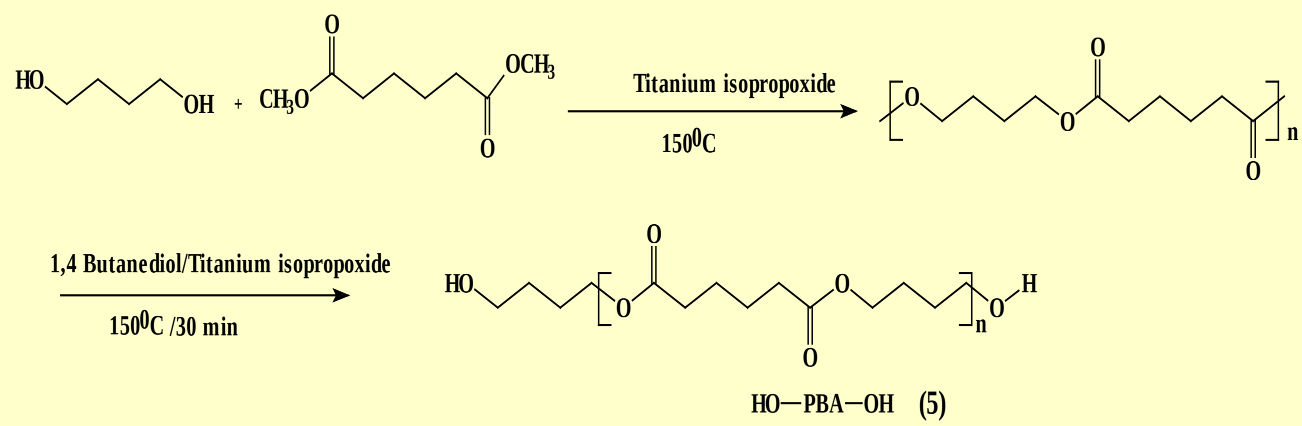
Improve efficiencies of known chemistry

Material property Improvements For defined end applications

- Simplify monomer purification
- Improve efficiencies of recovery of Lactic Acid from fermenter

SYNTHESIS OF TELECHELIC POLYESTERS

Telechelic PBA was prepared by polycondensation of dimethyl adipate and 1,4- butanediol (BD) followed by glycolysis with BD



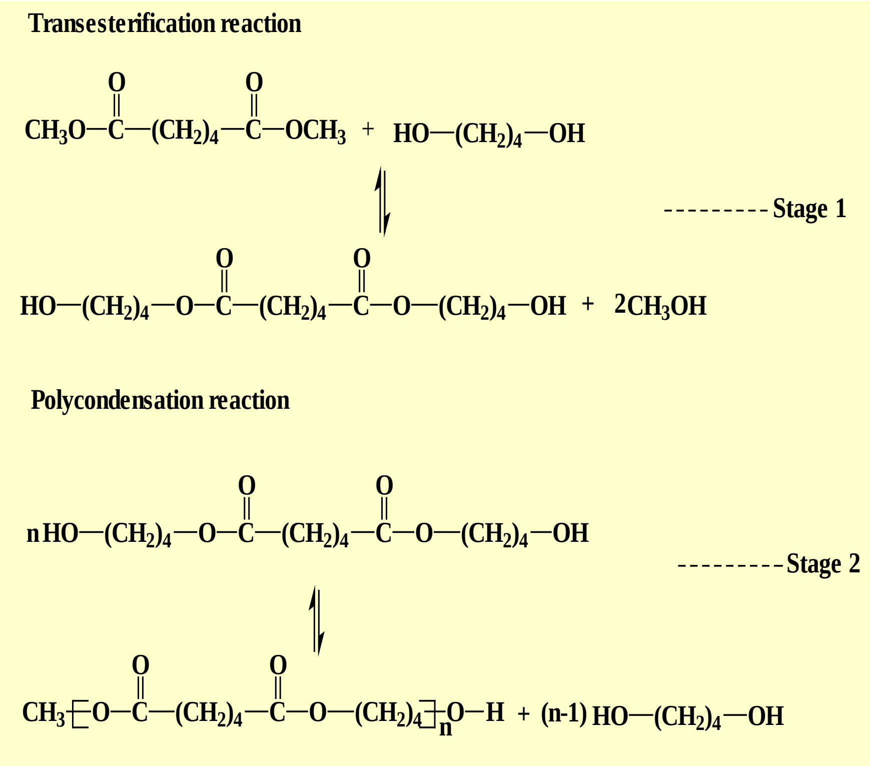
Sivaram and Neeta, unpublished results

η_{inh} in chloroform at 25^{0}C (dL/g)	M_n (VPO)	M_n (^{31}P NMR)	M_n (GPC)	M_w (GPC)	M_w/M_n	T_m (^{0}C)
0.211	**2700**	**2430**	**7600**	**11,930**	**1.57**	**55**

Concentration of hydroxyl end groups as determined by ^{31}P NMR was found to be 8.232 x 10^{-4} and the number average functionality was 0.9

Hydroxyl telechelics were found to be thermally stable up to 200^{0}C by TGA.

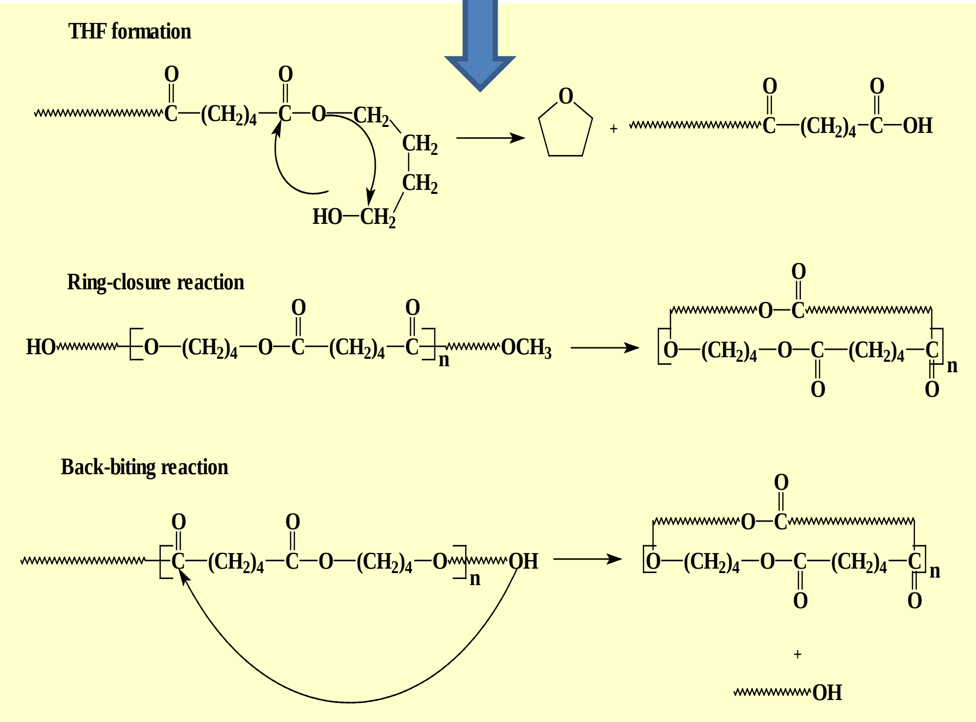
SYNTHESIS OF PBA BY POLYCONDENSATION OF DIMETHYL ADIPATE (DMA) AND 1,4-BUTANEDIOL (BD)



$$CH_3O-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-OCH_3 + HO-(CH_2)_4-OH \rightleftharpoons HO-(CH_2)_4-O-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-O-(CH_2)_4-OH + 2CH_3OH$$

$$n\,HO-(CH_2)_4-O-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-O-(CH_2)_4-OH \rightleftharpoons CH_3\left[O-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-O-(CH_2)_4\right]_n O-H + (n-1)\,HO-(CH_2)_4-OH$$

All these reactions result in loss of end groups needed for chain growth reaction



EFFECT OF REACTION TEMPERATURE ON POLYCONDENSATION REACTION

No.	Temp. (^0C)	Conv.[a] (%mol)	Conv.[b] (%)	Yield [c] (% wt.)	THF [d] (%mol)	M_n[e] (VPO)	M_w/M_n[e]	T_m[e] (^0C)	T_c[e] (^0C)
1	125	88	95	27	3.0	3980	1.6	58	22
2	150	92	97	75	3.7	7060	1.5	60	25
3	180	94	98	85	3.7	9010	1.5	61	20
4	200	95	97	86	4.4	7720	1.6	60	21
5	220	93	98	86	3.8	8120	1.6	61	21

a : conversions based on moles of methanol formed as determined by GC

b : % conversion calculated using the Carothers equation $X_n = 1/1-p$

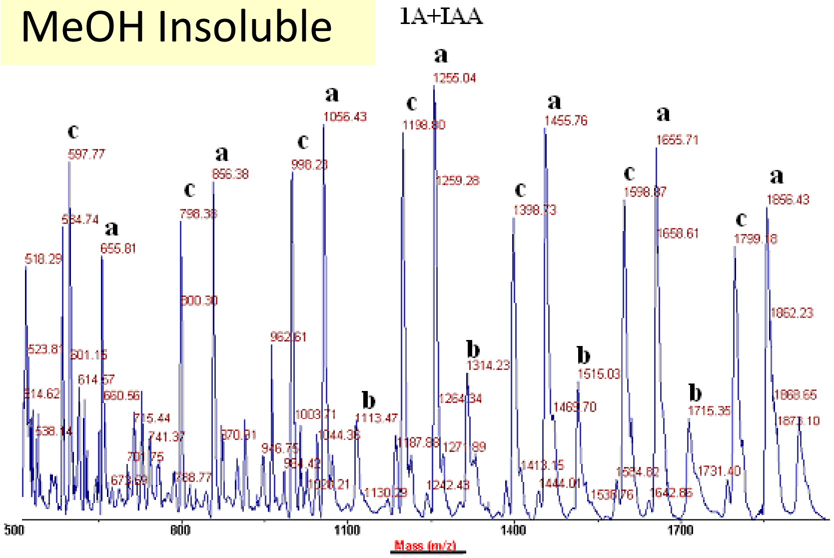
c: yield of methanol insoluble fraction calculated based on the total weight of polymer obtained

d :THF calculated based on moles of BD from GC; e- M_n , M_w/M_n , T_m & T_c of methanol insoluble fraction

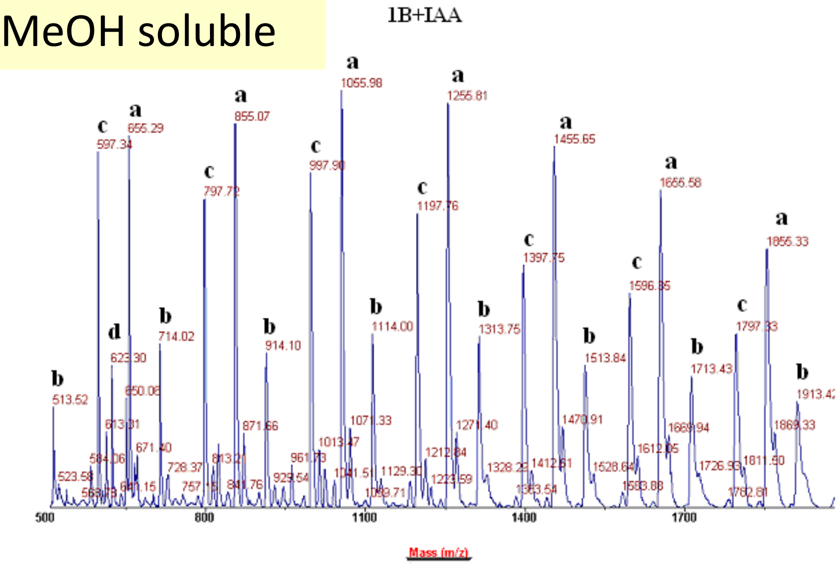
Neeta Kulkarni, PhD Thesis, 2007

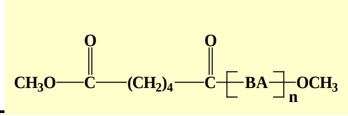
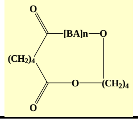
MALDI-TOF MS of PBA, 125^{0}C

MeOH Insoluble



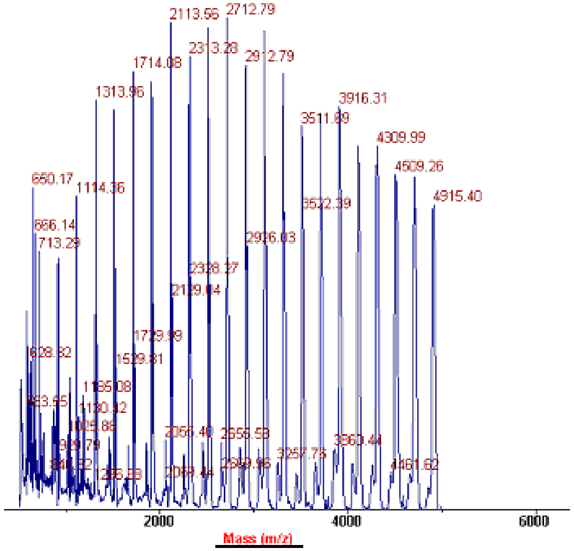
MeOH soluble

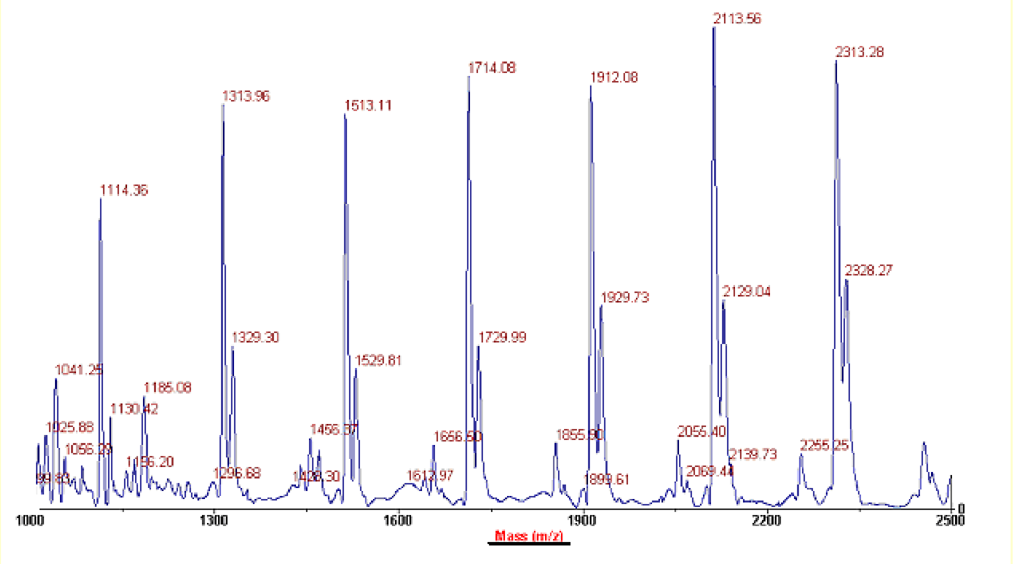


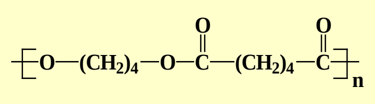
Peak	End group	Structure
a	hydroxy-ester	$H\text{-}[BA]_n\text{-}OCH_3$
b	hydroxy-hydroxy	$H\text{-}[BA]_n\text{-}O\text{-}(CH_2)_4\text{-}OH$
c	ester-ester	 $CH_3O\text{-}C(=O)\text{-}(CH_2)_4\text{-}C(=O)\text{-}[BA]_n\text{-}OCH_3$
d	No end group	
e	carboxy –hydroxy	$H\text{-}[BA]_n\text{-}OH$

- **MALDI-ToF MS analysis shows formation of varying amounts of cyclic oligomers and carboxylic end groups which result in loss of end groups and thereby limiting further step growth polymerization**
- **Cyclics of DP : 2 were detected even at 125^{0}C whereas cyclics of DP 2 to 12 were detected at 180-220^{0}C**
- **Structure of the oligomers changes from linear oligomers with hydroxy-ester end groups to cyclics with no end groups**

END GROUP ANALYSIS OF PBA TELECHELIC BY MALDI-TOF MS

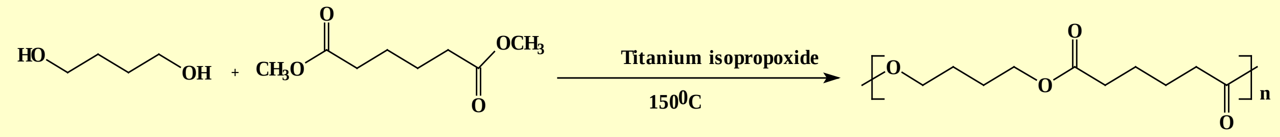


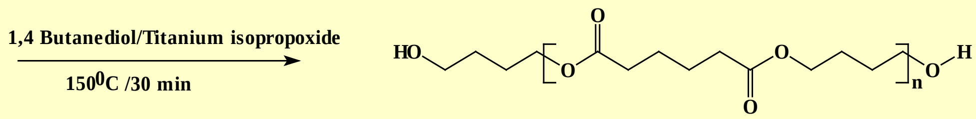


Repeat unit structure	Sum of end groups (observed)	Structure of end groups	Series
 $\left[O-(CH_2)_4-O-\overset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}\right]_n$	89-91	$H-[BA]_n-O-(CH_2)_4-OH$	1114,1314,1513,…Na^+ adduct
	89-91	$H-[BA]_n-O-(CH_2)_4-OH$	1130,1329,1530,…K^+ adduct
	33-34	$H-[BA]_n-OCH_3$	1056,1456,1656,…Na^+ adduct

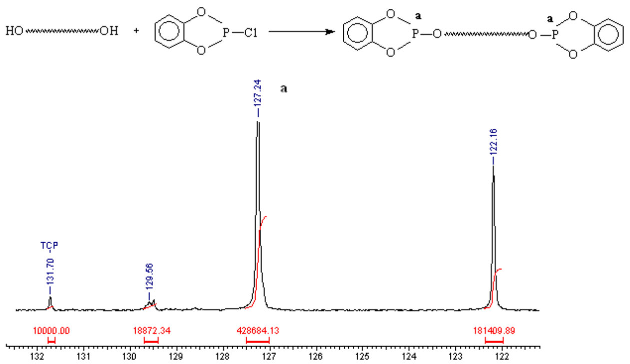
Poly(butylene adipate) oligomers contain mainly chains with hydroxyl end groups along with small amounts of hydroxy ester end groups

SYNTHESIS AND CHARACTERIZATION OF HYDROXYL TERMINATED POLY(BUTYLENE ADIPATE)





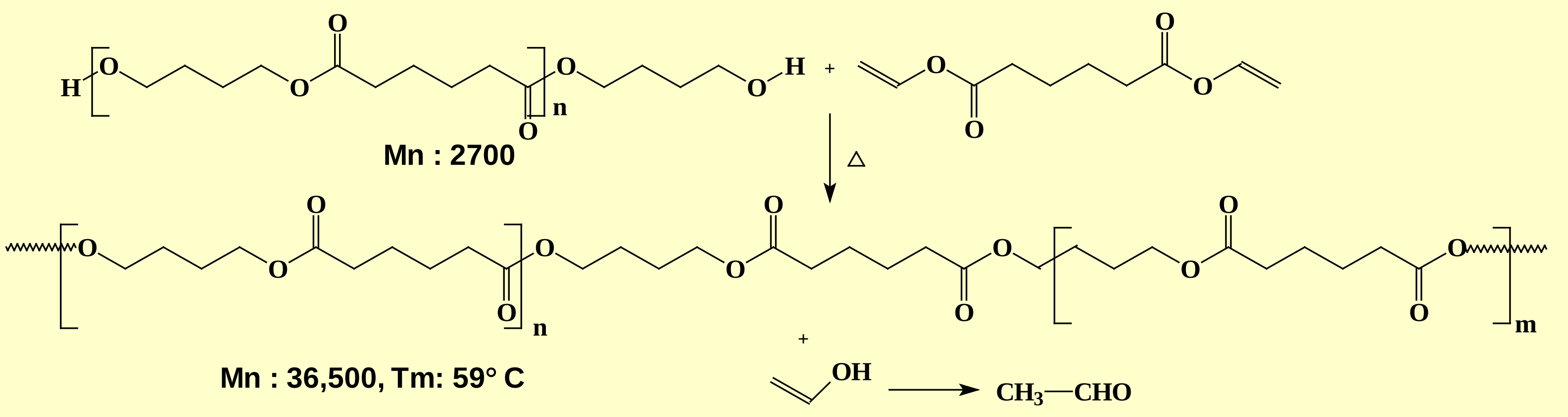
HO—PBA—OH (5)



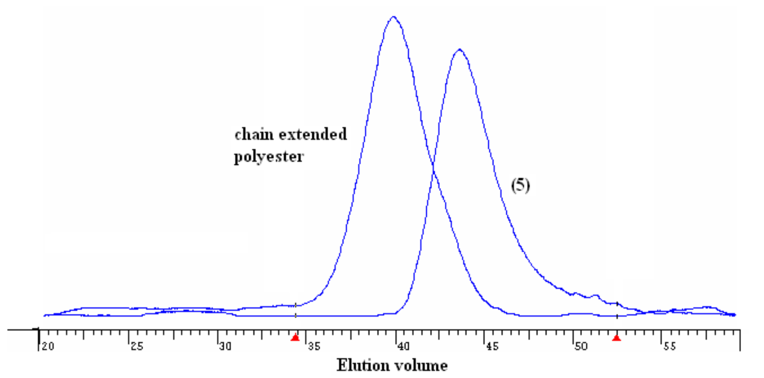
η_{inh} in chloroform at 25^0C (dL/g)	M_n (VPO)	M_n (^{31}P NMR)	M_n (GPC)	M_w (GPC)	M_w/M_n	T_m (^0C)
0.211	2700	2430	7600	11,900	1.57	55

- ***Concentration of hydroxyl end groups as determined by ^{31}P NMR was found to be 8.232 x 10^{-4} mol / g, corresponding to 1.9 hydroxyl groups per molecule***
- ***The telechelic oligomer was found to be thermally stable up to 200^0C by TGA.***

CHAIN EXTENSION WITH DIVINYL ADIPATE : FIRST EXAMPLE OF IRREVERSIBLE POLYCONDENSATION



The reaction by product cannot react with the growing polymer chain !



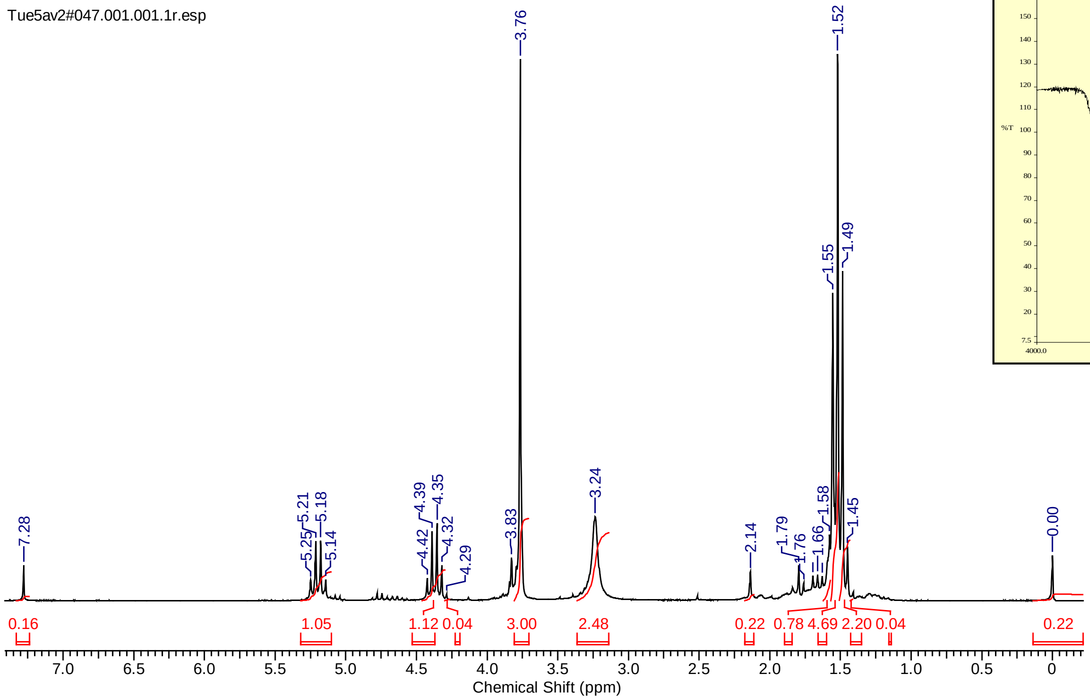
GPC of telechelic and the polyester chain extended with divinyl adipate (DVA)

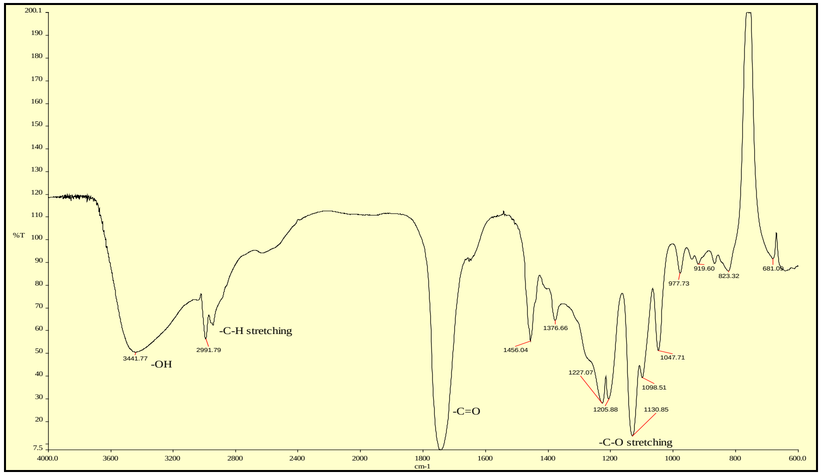
SYNTHESIS OF A LINEAR DIMER FROM L(+)-LACTIC ACID AND METHYL-L-LACTATE

60 %

- bp : 107 ^{0}C at 5 mm
- Can be purified by distillation

1 M solution in methylene chloride obtained by L-L extraction





GENERAL ACID CATALYZED SELF POLYMERIZATION OF LACTIC ACID

General Acid Catalysis

- Commercial 90 % lactic acid in water contains : HL = 60 % HL2+ oligomers = 27 % and LL = 13 %
- Pka : 3.86; ! stronger than acetic acid due to intramolecular hydrogen bond
- Purification by crystallization possible only via lactide; however processes for purification expensive.
- Lactide has a mp 96 ^{0}C and sublimes
- Difficult to copolymerize Lactide by any other mechanism except ROP
- Methyl Lactate is a volatile liquid with a bp of 144 ^{0}C

Need

An AB monomer, which has a bp above 250 ^{0}C, high vapor pressure, easily purified, hydrophobic , preferably a methyl ester

TRANS-ESTERIFICATION OF LINEAR DIMER

- ➢ No free acidity; general acid catalysed self oligomerization not possible
- ➢ Shelf stable
- ➢ Simple purification by distillation

Negligible Cyclization !

Titanium Isopropoxide
Two stage
polymerization
150-190 ^{0}C

Nevare and sivaram, research in progress

SYNTHESIS OF HIGH MOLECULAR WEIGHT LINEAR ALIPHATIC POLYESTERS

Problem

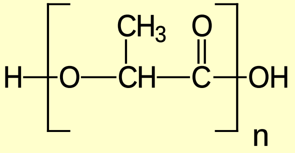
Beyond 150 C , aliphatic polyester forming polycondensation reactions result in variable quantities of macrocycles; hence high molecular weight polymers cannot be realized. Alternative chemistries are needed

- Coupling of preformed oligomer chains with suitably disposed end groups at temperatures less than 150C
- Converting a reversible chain growth reaction into an irreversible reaction; avoid removal of volatile by products from a melt to drive conversion
- Use of conformationally constrained cyclo-aliphatic diacid or diol monomers

DIRECT CATALYTIC POLYCONDENSATION OF L(+)- LACTIC ACID

solvent	Temp. C	Conv.,%	Lactide,%	Mn,VPO	Mw/Mn
Xylene	143	96	Nil	800	2.0
Mesitylene	165	76	27	1800	4.0
Decalin	190	82	15	5500	4.7

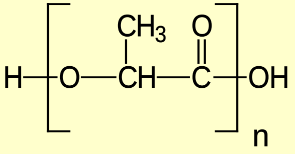
< 150°C



$H-\left[O-\overset{CH_3}{\overset{|}{CH}}-\overset{O}{\overset{\|}{C}}\right]_n-OH$

n = 5 - 24

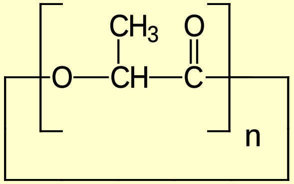
150 - 190 °C



$H-\left[O-\overset{CH_3}{\overset{|}{CH}}-\overset{O}{\overset{\|}{C}}\right]_n-OH$

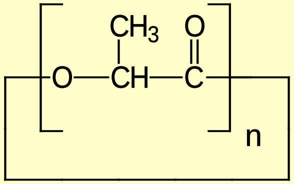
n = 14 - 30

+



$\left[O-\overset{CH_3}{\overset{|}{CH}}-\overset{O}{\overset{\|}{C}}\right]_n$

> 190°C



$\left[O-\overset{CH_3}{\overset{|}{CH}}-\overset{O}{\overset{\|}{C}}\right]_n$

n = 13 - 40

Oligomer structures established by 13 C NMR and MALDI TOF MS

Mixtures of linear and cyclics

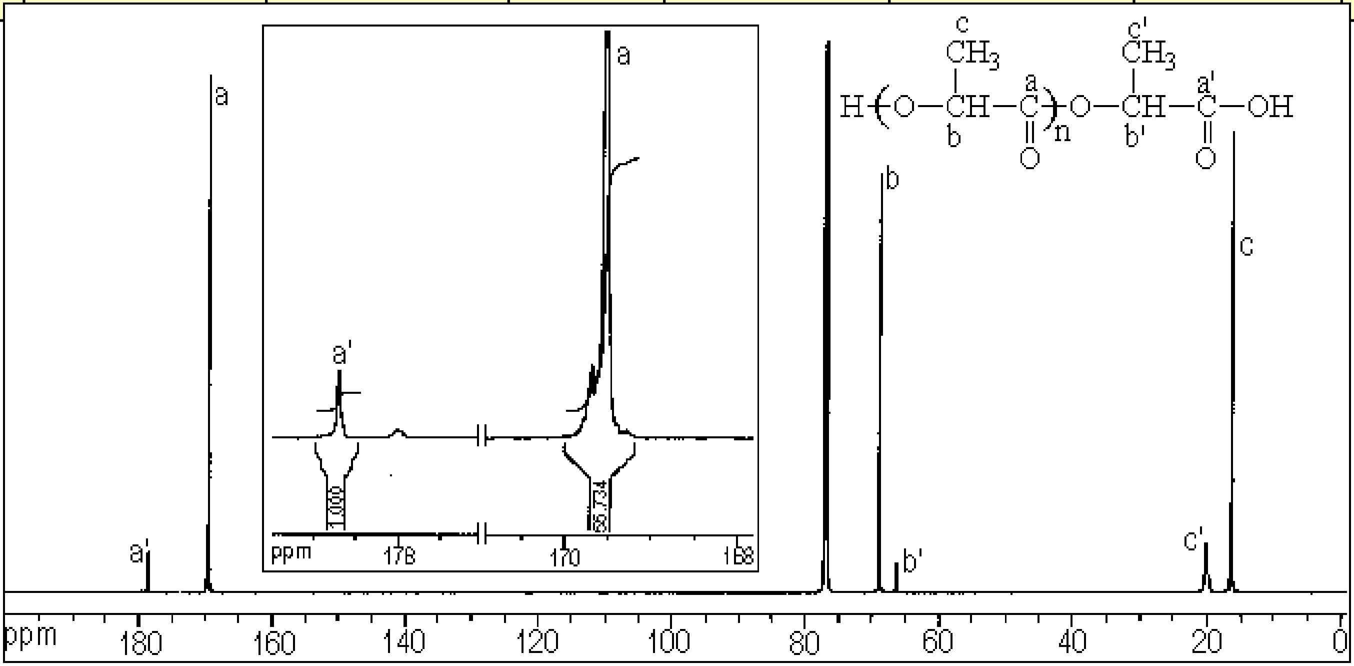
Exclusively cyclics !

Shyamroy, Garnaik and Sivaram, J. Polymer Science: Part A: Polymer Chemistry, 43,2164 (2005)

TELECHELIC ALIPHATIC POLYESTERS

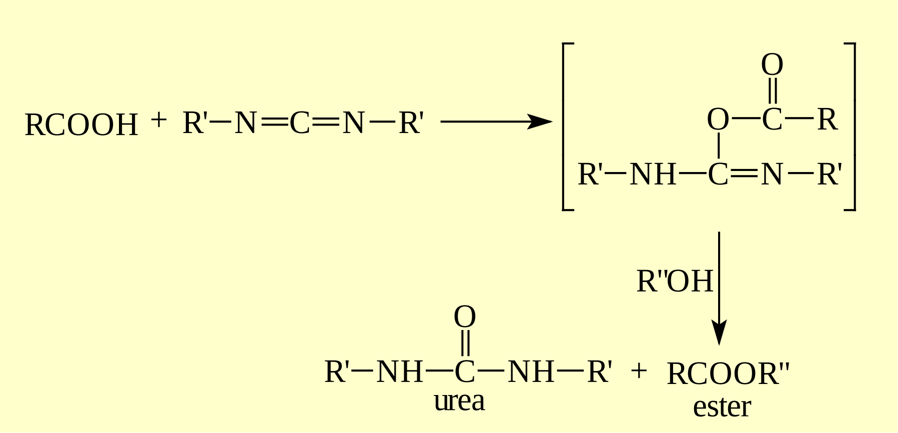
Number average molecular weights of the PLA oligomers synthesized by ROP of L-lactide with water as co-initiator and $Sn(Oct)_2$ as initiator.

PLA sample	[Lactide]/ $[Sn(Oct)_2]$	[Lactide]/ $[H_2O]$	Conv. (%)	$DP_{n, Calc}$	$DP_{n, NMR}$	$M_{n, NMR}$	$M_{n, VPO}$
3.1	200	32	86	55	60	4320	4400
3.2	400	45	87	79	77	5540	5690



13C-NMR spectrum of PLLA oligomer synthesized by ROP . Inset showing ester and carboxylic acid carbonyl region

HOMO COUPLING OF POLY(ACTIC ACID)S OLIGOMERS ACTIVATED POLYCONDENSATION

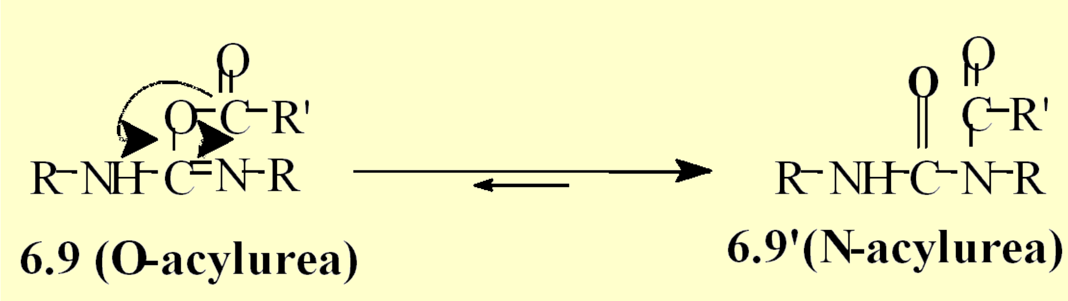


$$RCOOH + R'-N=C=N-R' \longrightarrow \left[R'-NH-\overset{\overset{\displaystyle O-\overset{\overset{\displaystyle O}{\|}}{C}-R}{|}}{C}=N-R' \right] \xrightarrow{R''OH} \underset{\text{urea}}{R'-NH-\overset{\overset{\displaystyle O}{\|}}{C}-NH-R'} + \underset{\text{ester}}{RCOOR''}$$

Mn increases from 15,000 to 50,000 !

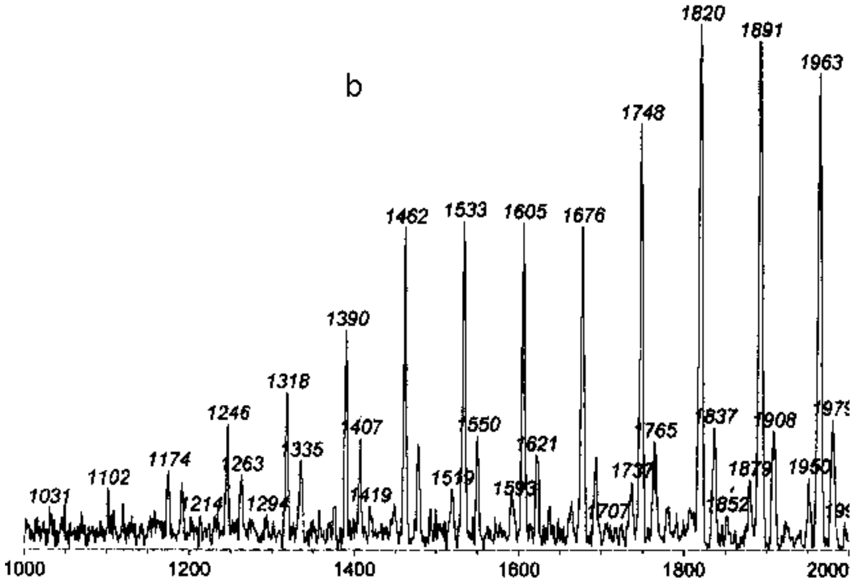
Shyamroy, Garnaik and Sivaram, Polymer Bulletin , 2015

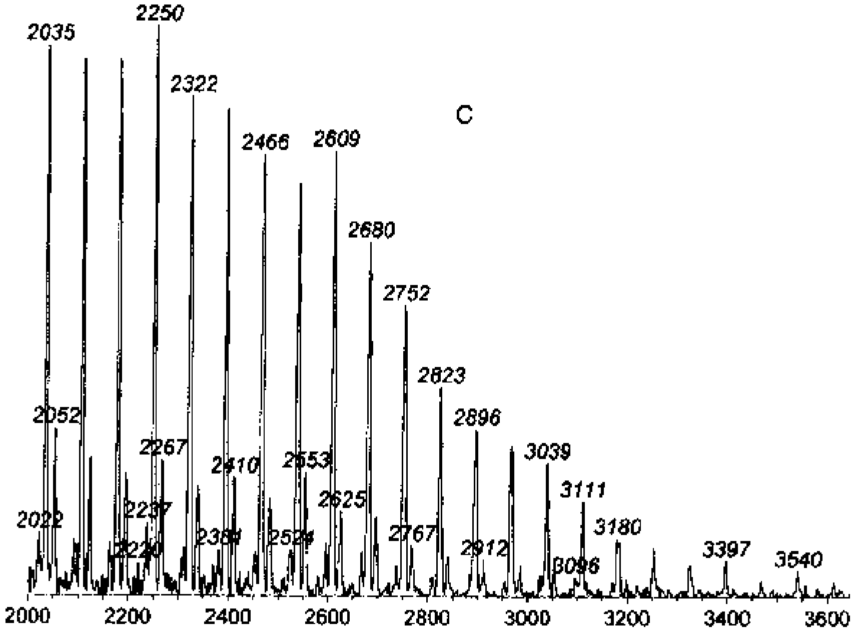
CHAIN TERMINATION VIA N-ACYL UREA FORMATION



6.9 (O-acylurea)

6.9'(N-acylurea)





M = $(CH_3)_2$CH-NH-CO-N(CH$(CH_3)_2$)-(CO-CH(CH_3)-O)$_n$-H-----Na^+

= 72n + 143 + 23

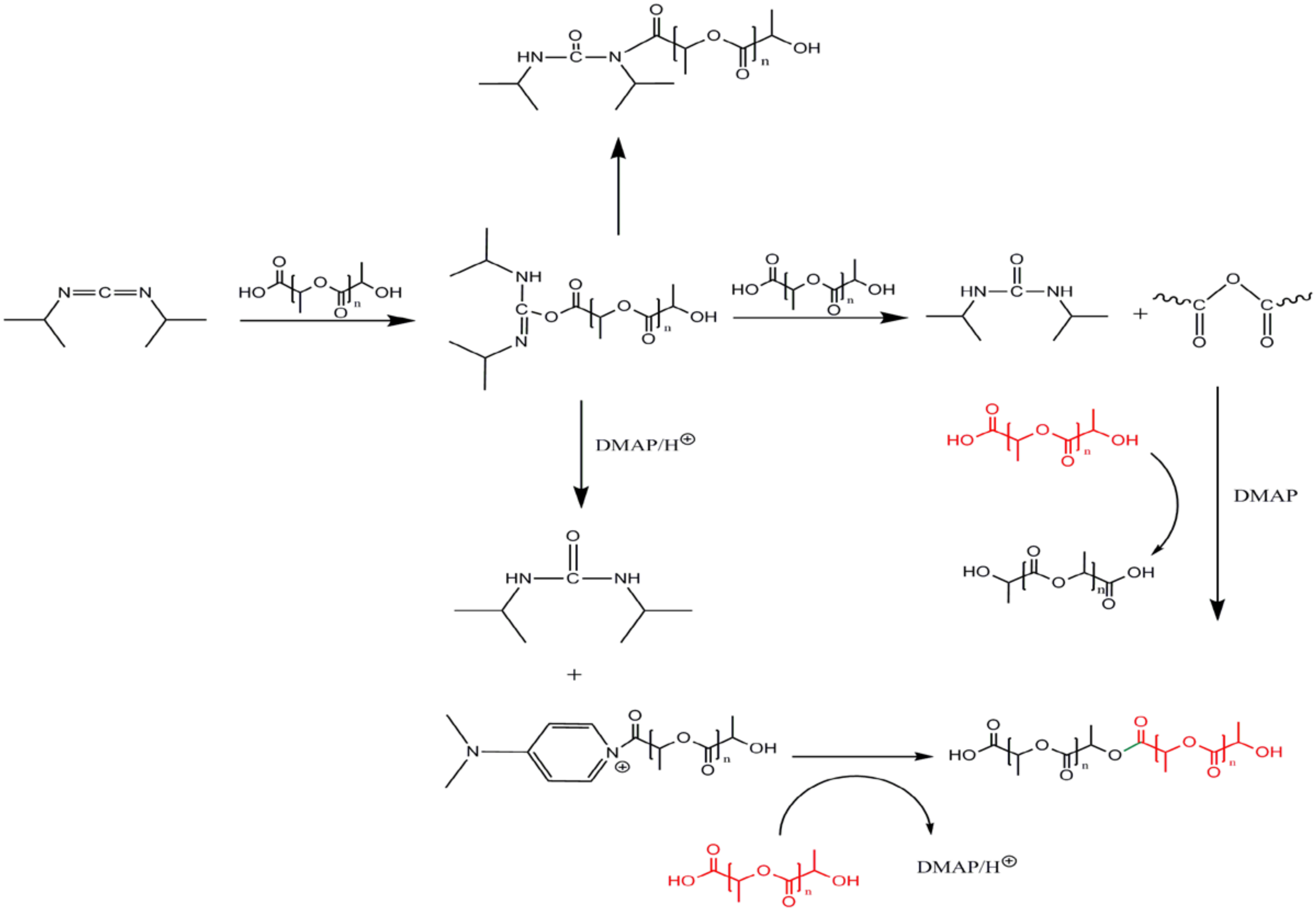
Also 72n + 143 + 39 found (K^+)

M = $(CH_3)_2N$-$C_5H_{10}NH^+$ $^-$O-(CO-CH-(CH_3)-O)$_n$-H-----Na^+

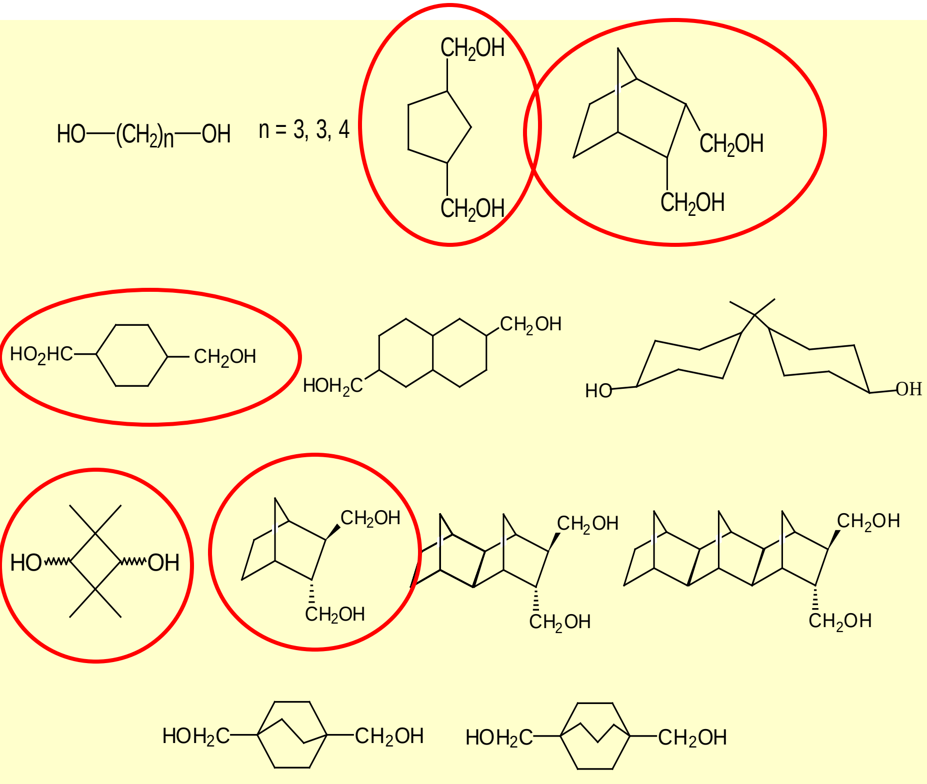
= 72n + 51 + 23

Also 72n + 51 + 39 found (K^+)

CHAIN EXTENSION BY COUPLING OF HETEROTELECHELICS

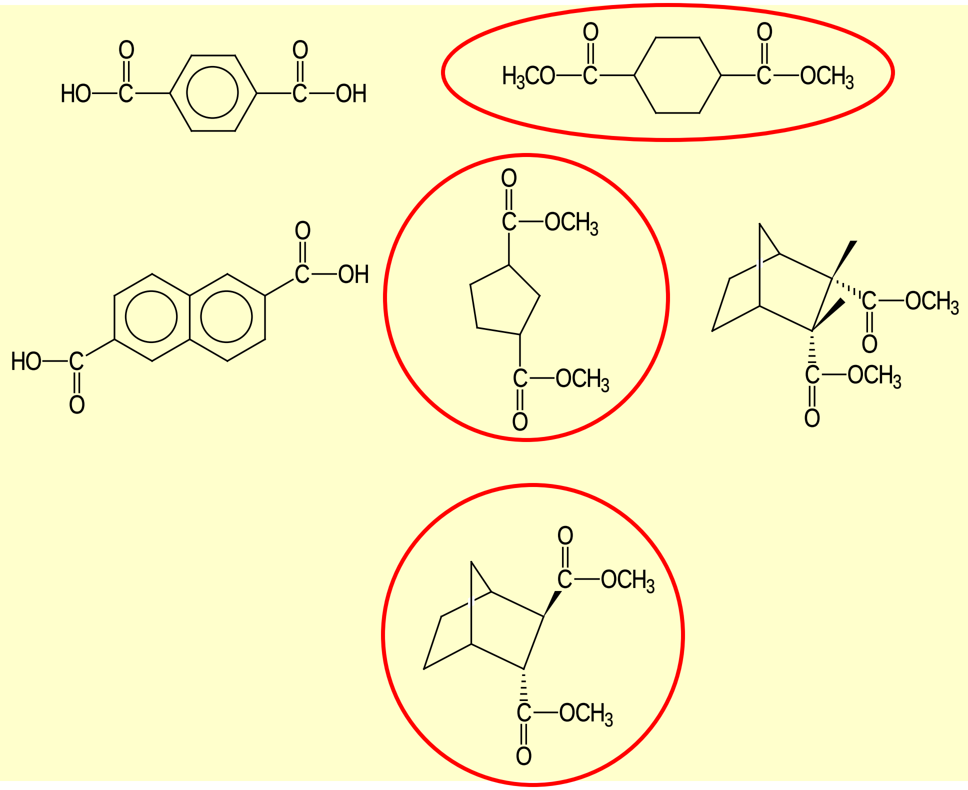


ALIPHATIC POLYESTERS BASED ON CONFORMATIONALLY CONSTRAINED MONOMERS

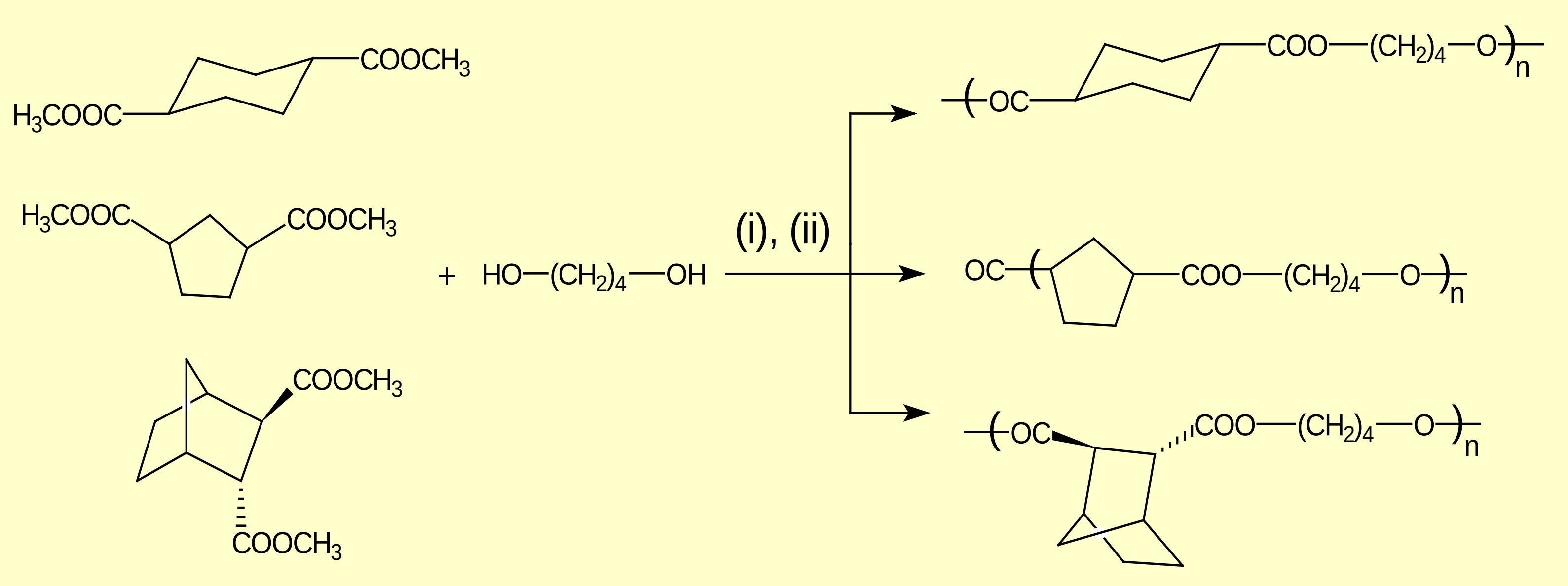


DIOLS

DIACIDS



ALIPHATIC POLYESTERS: SYNTHESIS



Catalyst : Titanium Isopropoxide

(i) Transesterification 180-230°C/6-10h
(ii) Polycondensation 210-260°C/10-12 h/0.02 mbar

Sandhya, Ramesh and Sivaram, Macromolecules, , 2007

STRUCTURE –PROPERTY RELATIONSHIPS IN ALIPHATIC POLYESTERS

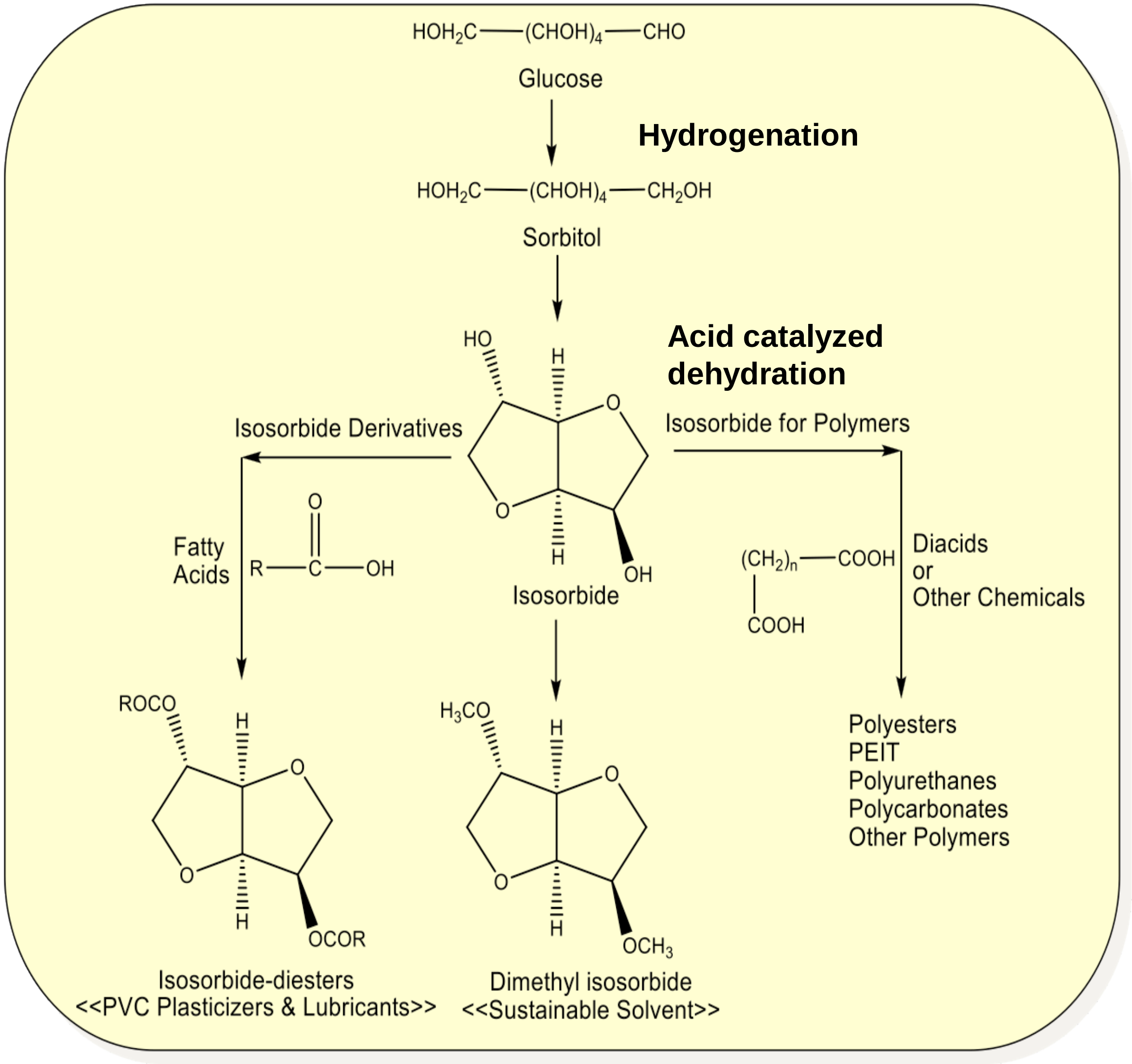
ee: ae	*Mn*	*Tm,* ºC	*Tg,* ºC	*IDT,* ºC
100	20,000	163	31	403
70:30	16,500	56	-10	400

cis: trans	*Mn*	*Tm,* ºC	*Tg,* ºC	*IDT,* ºC
100	57,000	-	-44	400
50:50	36,000	-	-15	408

cis: trans	*Mn*	*Tm,* ºC	*Tg,* ºC	*IDT,* ºC
100	36,000	-	-24	500

	Mn	*Tm,* ºC	*Tg,* ºC	*IDT,* ºC
exo-endo	37,000	-	-56	480

ISOSORBIDE: A BIO DERIVED RENEWABLE MONOMER



$HOH_2C—(CHOH)_4—CHO$

Glucose

Hydrogenation

$HOH_2C—(CHOH)_4—CH_2OH$

Sorbitol

Acid catalyzed dehydration

Isosorbide

Isosorbide Derivatives

Fatty Acids

$R—C(=O)—OH$

Isosorbide for Polymers

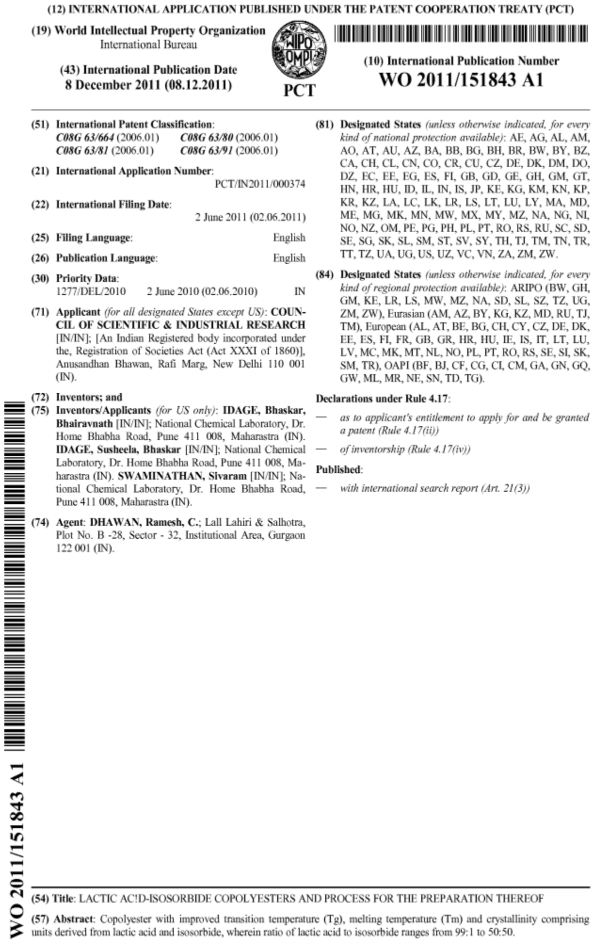
$(CH_2)_n(COOH)_2$

Diacids or Other Chemicals

Isosorbide-diesters
<<PVC Plasticizers & Lubricants>>

Dimethyl isosorbide
<<Sustainable Solvent>>

Polyesters
PEIT
Polyurethanes
Polycarbonates
Other Polymers



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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PCT

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C08G 63/664 (2006.01) ***C08G 63/80*** (2006.01)
C08G 63/81 (2006.01) ***C08G 63/91*** (2006.01)

(21) International Application Number:
PCT/IN2011/000374

(22) International Filing Date:
2 June 2011 (02.06.2011)

(25) Filing Language: English

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(30) Priority Data:
1277/DEL/2010 2 June 2010 (02.06.2010) IN

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(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **IDAGE, Bhaskar, Bhairavnath** [IN/IN]; National Chemical Laboratory, Dr. Home Bhabha Road, Pune 411 008, Maharastra (IN). **IDAGE, Susheela, Bhaskar** [IN/IN]; National Chemical Laboratory, Dr. Home Bhabha Road, Pune 411 008, Maharastra (IN). **SWAMINATHAN, Sivaram** [IN/IN]; National Chemical Laboratory, Dr. Home Bhabha Road, Pune 411 008, Maharastra (IN).

(74) Agent: **DHAWAN, Ramesh, C.**; Lall Lahiri & Salhotra, Plot No. B -28, Sector - 32, Institutional Area, Gurgaon 122 001 (IN).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *of inventorship (Rule 4.17(iv))*

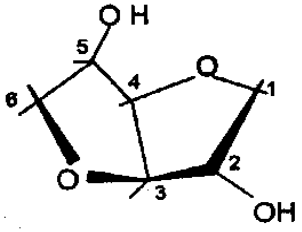
Published:
— *with international search report (Art. 21(3))*

WO 2011/151843 A1

(54) Title: LACTIC AC!D-ISOSORBIDE COPOLYESTERS AND PROCESS FOR THE PREPARATION THEREOF

(57) Abstract: Copolyester with improved transition temperature (Tg), melting temperature (Tm) and crystallinity comprising units derived from lactic acid and isosorbide, wherein ratio of lactic acid to isosorbide ranges from 99:1 to 50:50.

L(+) LA- ISOSORBIDE COPOLYMER : SYNTHESIS



ROP

Mn : 80,000

Melt or Solution
70 to 150 °C

Mn : 39,000

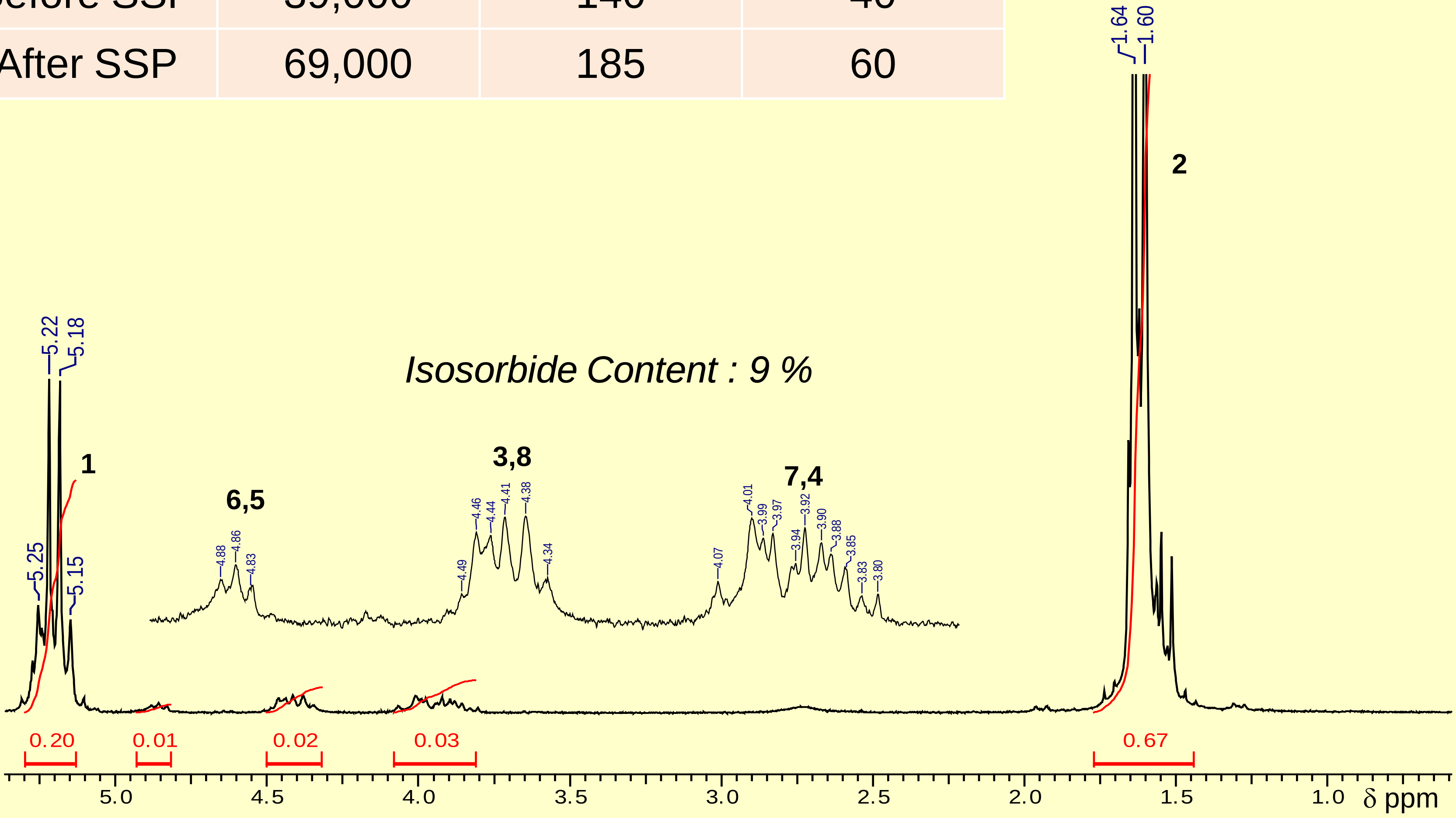
Solid State Polymerization (SSP)
150 °C, 2- 4 h

Mn : 69,000

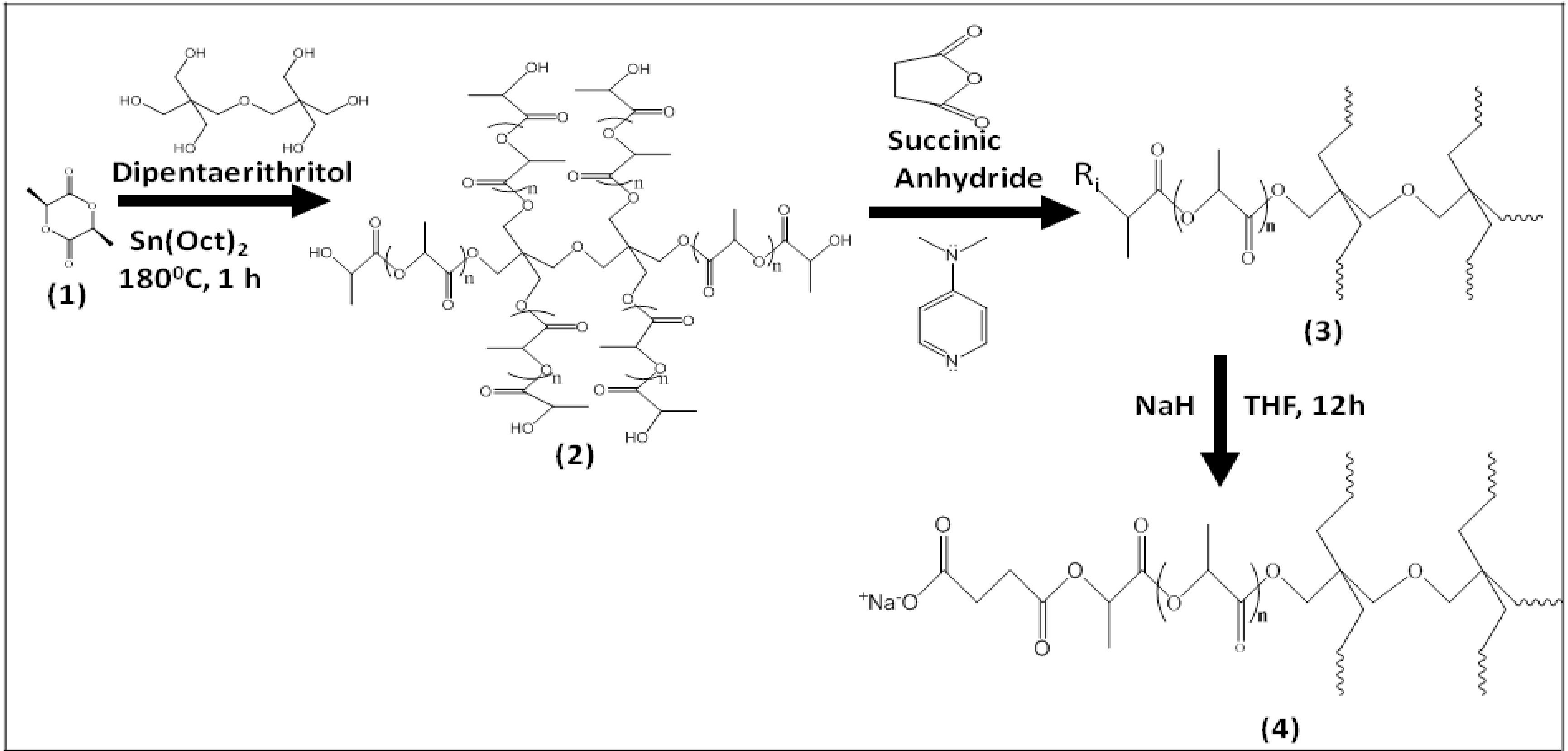
B. B. Idage, S.B. Idage and Sivaram, WO 151843, 2012 (June 2, 2011)

^{1}H NMR SPECTRA OF PLA-ISOSORBIDE COPOLYMER IN CDCL3

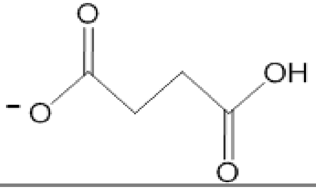
	Mn	Tm, ˚C	Tg, ˚C
Before SSP	39,000	140	40
After SSP	69,000	185	60



Isosorbide Content : 9 %



R$_i$ = I, II Where
I = -OH
II =

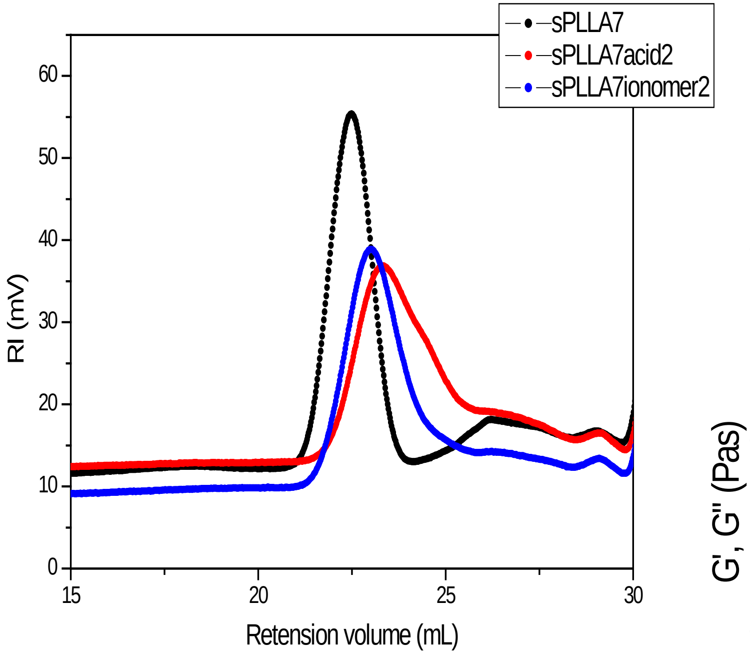


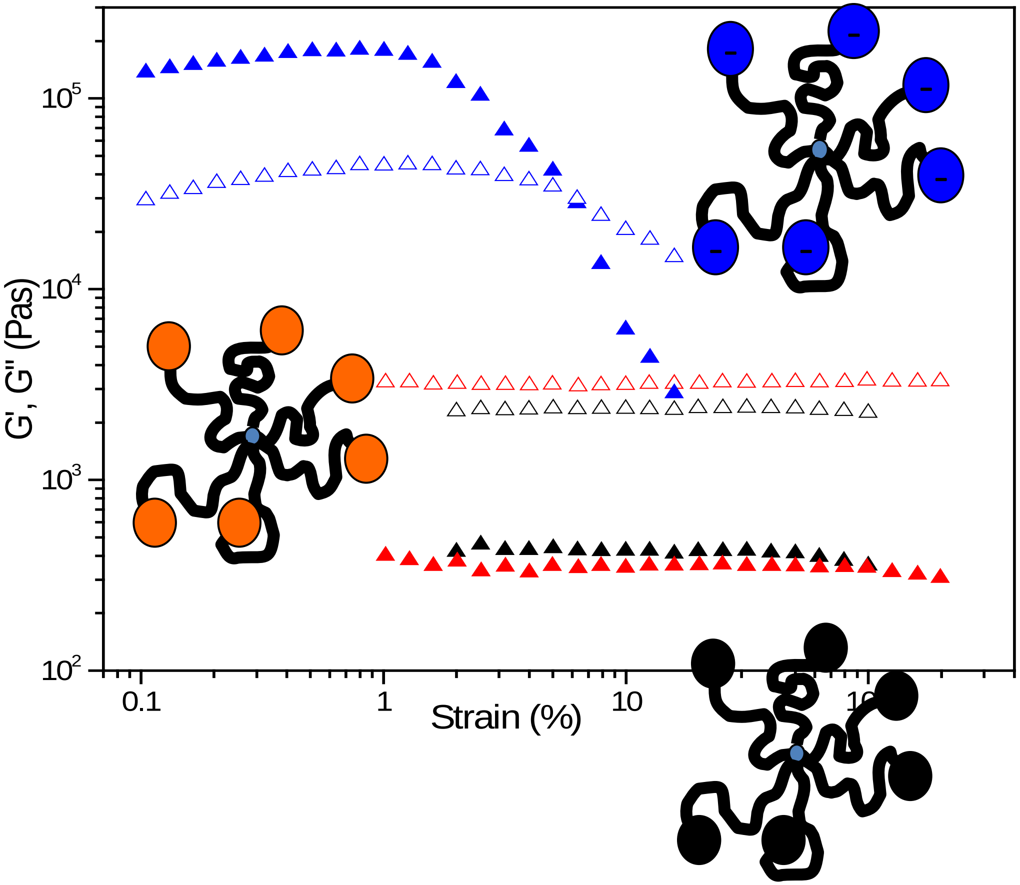
Structure of star PLA acid = **(3)** **(R$_1$)$_x$** **(R$_2$)$_{6-x}$**
Structure **(3a)** when x= 4
(3b) when x= 3
(3c) when x= 2
(3d) when x= 1

(4a-d) are ionomers
Of corresponding star
PLA acid **(3a-d)**

Synthesis of six arm star PLA **(2)** by ring opening polymerization of L-lactide **(1)** in presence of Dipentaerithritol; six arm star PLA acid **(3)** by acidification of hydroxyl end functional groups of star PLA **(2)**; six arm star PLA ionomer **(4)** by neutralization of star PLA acid **(3)** in presence of sodium hydride.

MOLECULAR WEIGHT DISTRIBUTION, STORAGE MODULUS AND COMPLEX VISCOSITY OF STAR BRANCHED PLLA IONOMERS



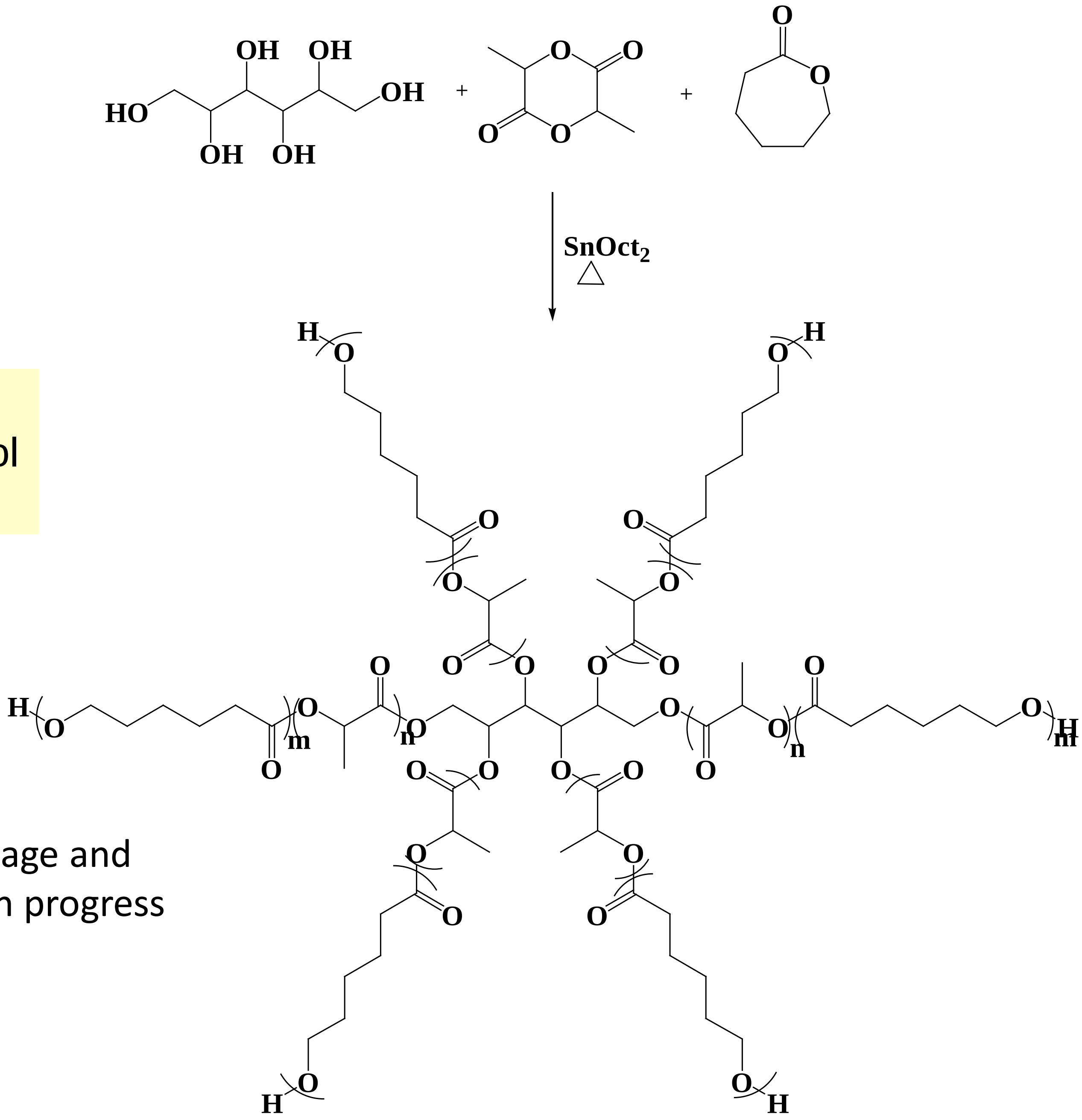


● $-CO_2^-$ Na

● $-CO_2H$

● -OH

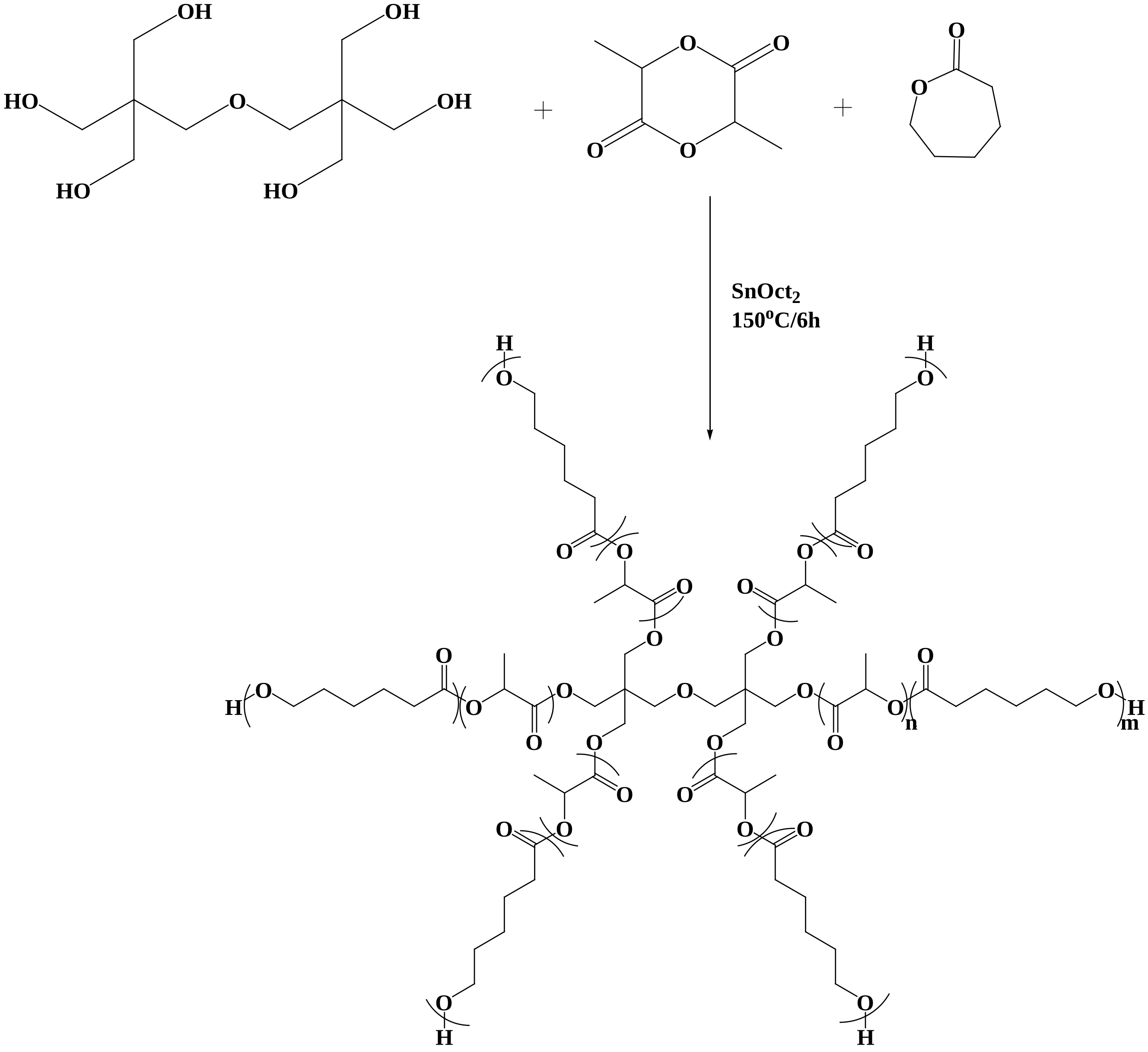
Amruta, Sivaram, Rajamohanan and Lele, J. Polymer Science, Chemistry, 2015, submitted



Synthesis of Star PLCL (60:40) sorbitol copolymer

Megha, Idage, Idage and Sivaram, research in progress

Synthesis of Star PLCL (60:40) dipentaerythritol copolymer

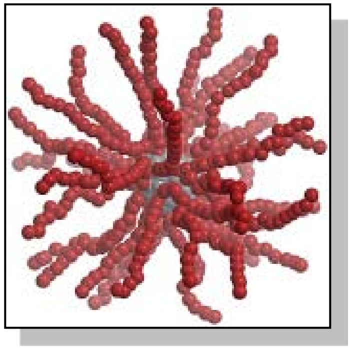


Synthesis of PLA-PEL Star Polymers

L-lactide

Pentaerythritol (PEL)

PLA-PEL Star Polymer

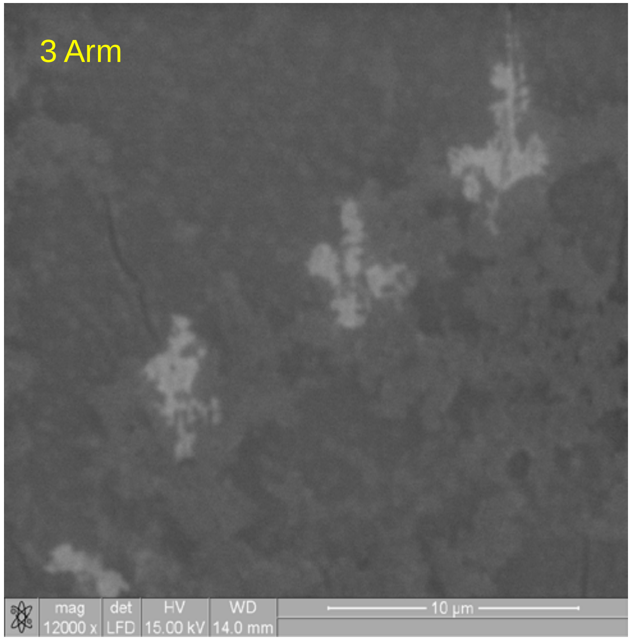


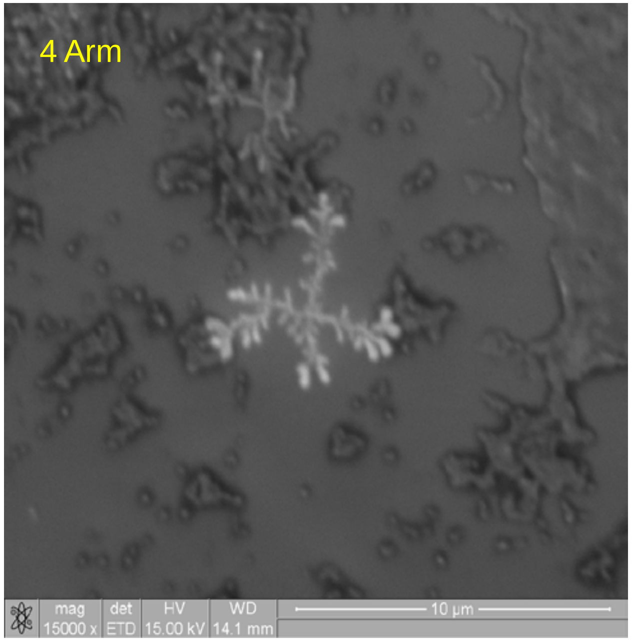
PLA-DITMP

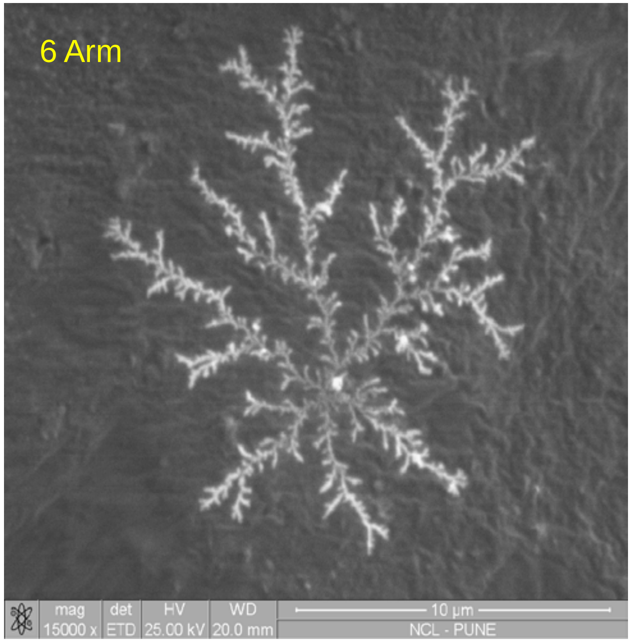
PLA-TMP

PLA-DPEL

Scanning Electron Microscopy







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