Enzymes in Organic Synthesis
Attractive Properties

Enzymes catalyze a wide variety of organic reactions

- reversibly
- under mild conditions

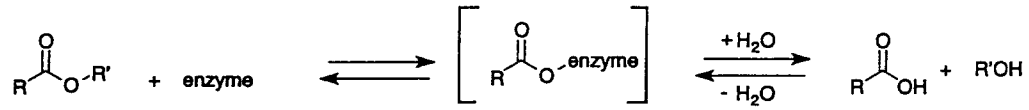
Enzymes are highly -chemoselective
-regioselective
-diastereoselective
-enantioselective catalysts

Enzymes frequently display

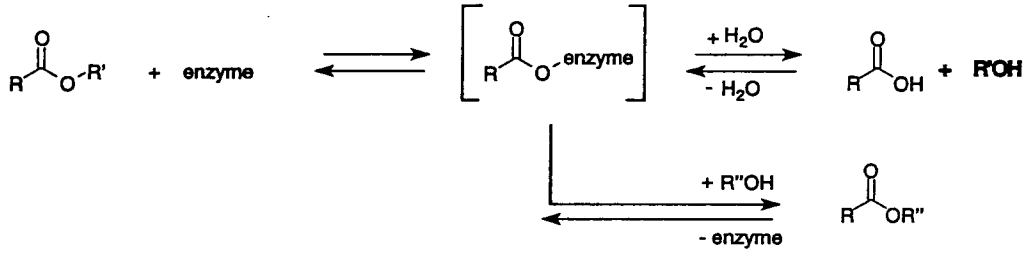
-high substrate specificity
-remarkable broad substrate tolerance
-stability towards
temperature
organic media

Esterhydrolases - Catalytic Transformations

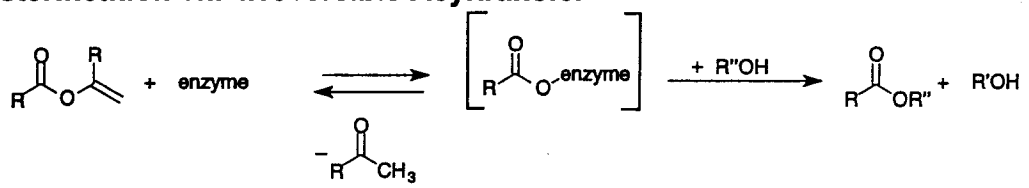
Hydrolysis and Esterification



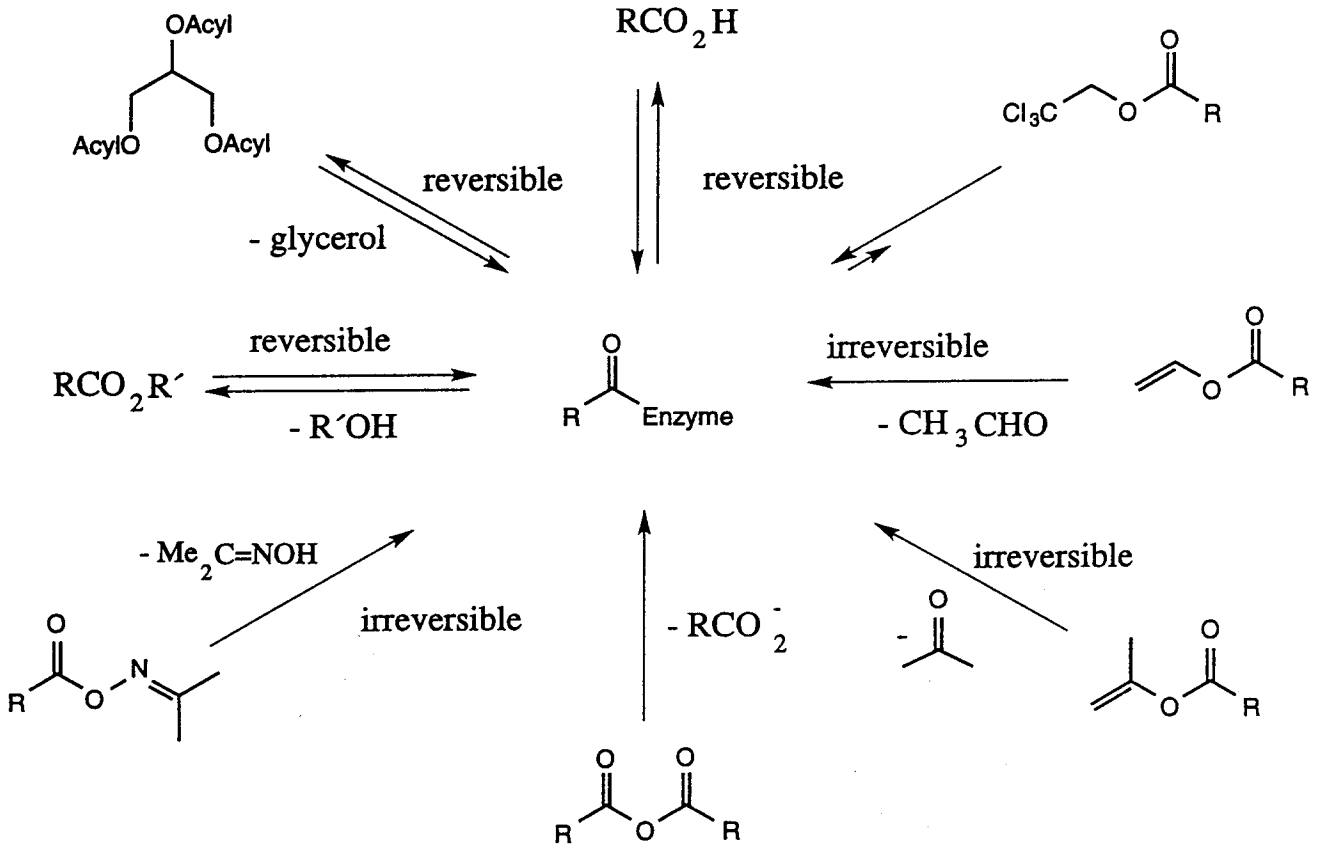
Esterification *via* Reversible Acyltransfer



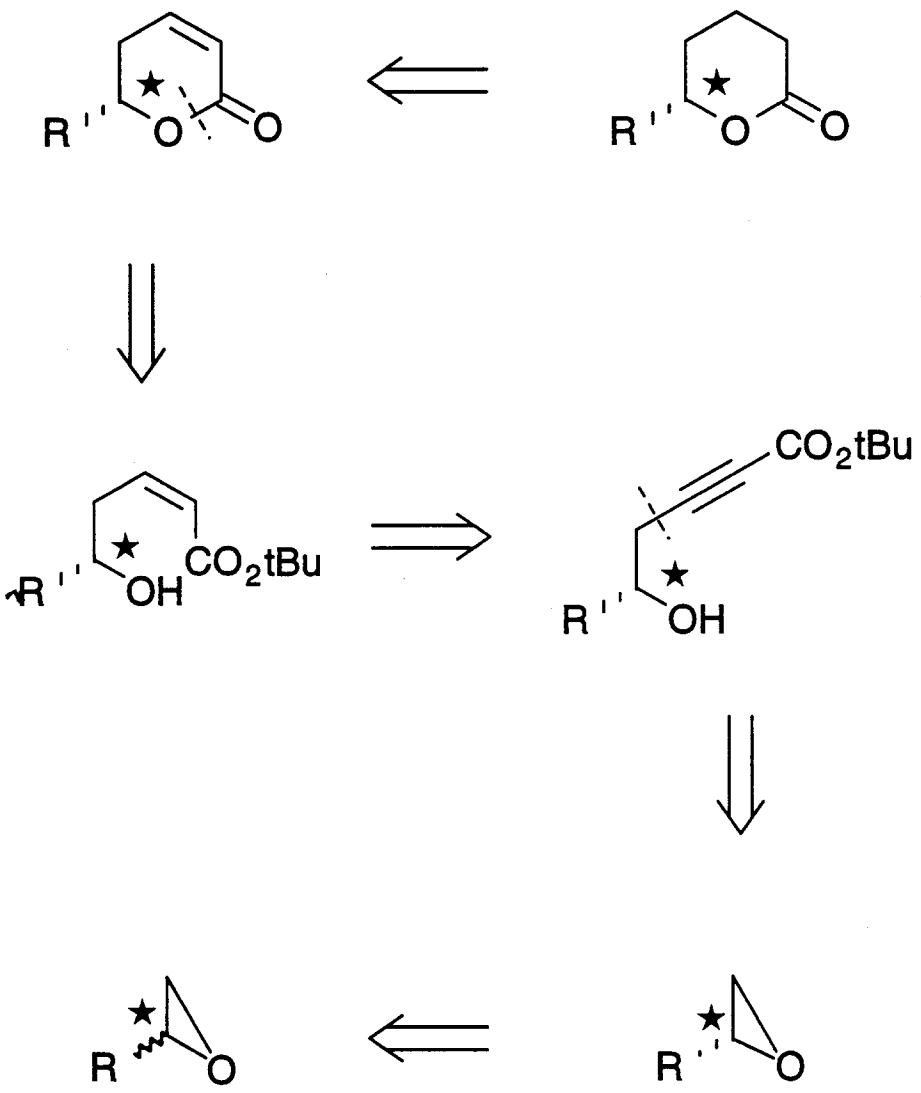
Esterification *via* Irreversible Acyltransfer



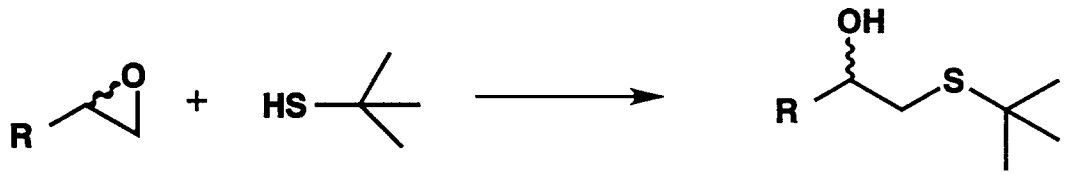
Lipase catalyzed esterifications - Acyldonors

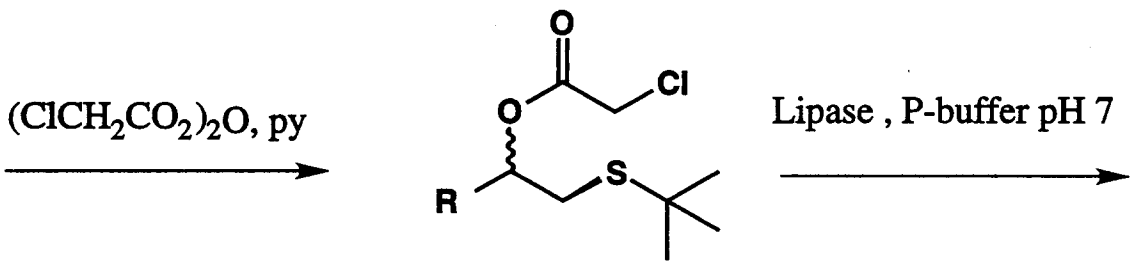


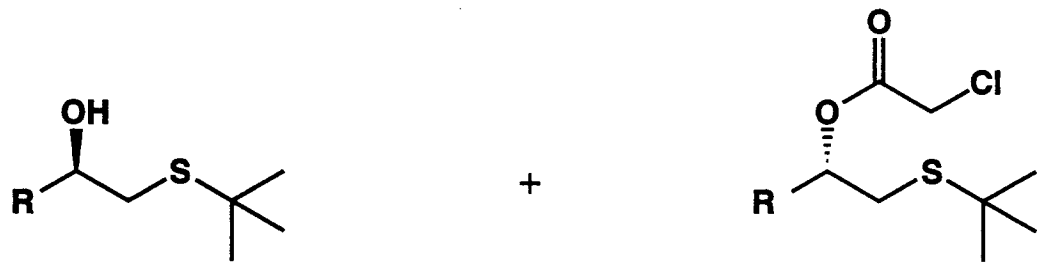
Enantiomerically pure δ-lactones
Retrosynthetic analysis



Synthesis of enantiomerically pure oxiranes





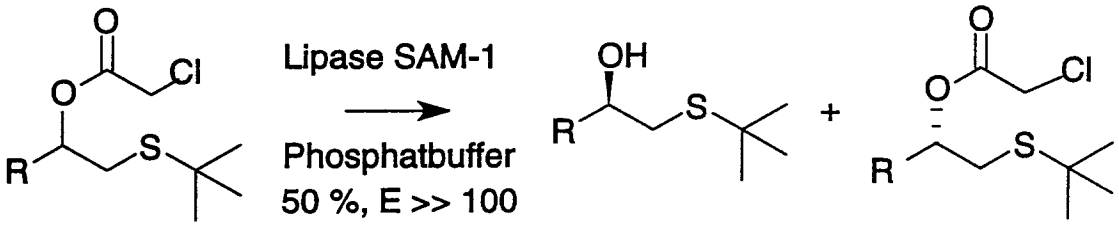


(1) $Me_3O^+ BF_4^-$
(2) OH^-

Separation by distillation

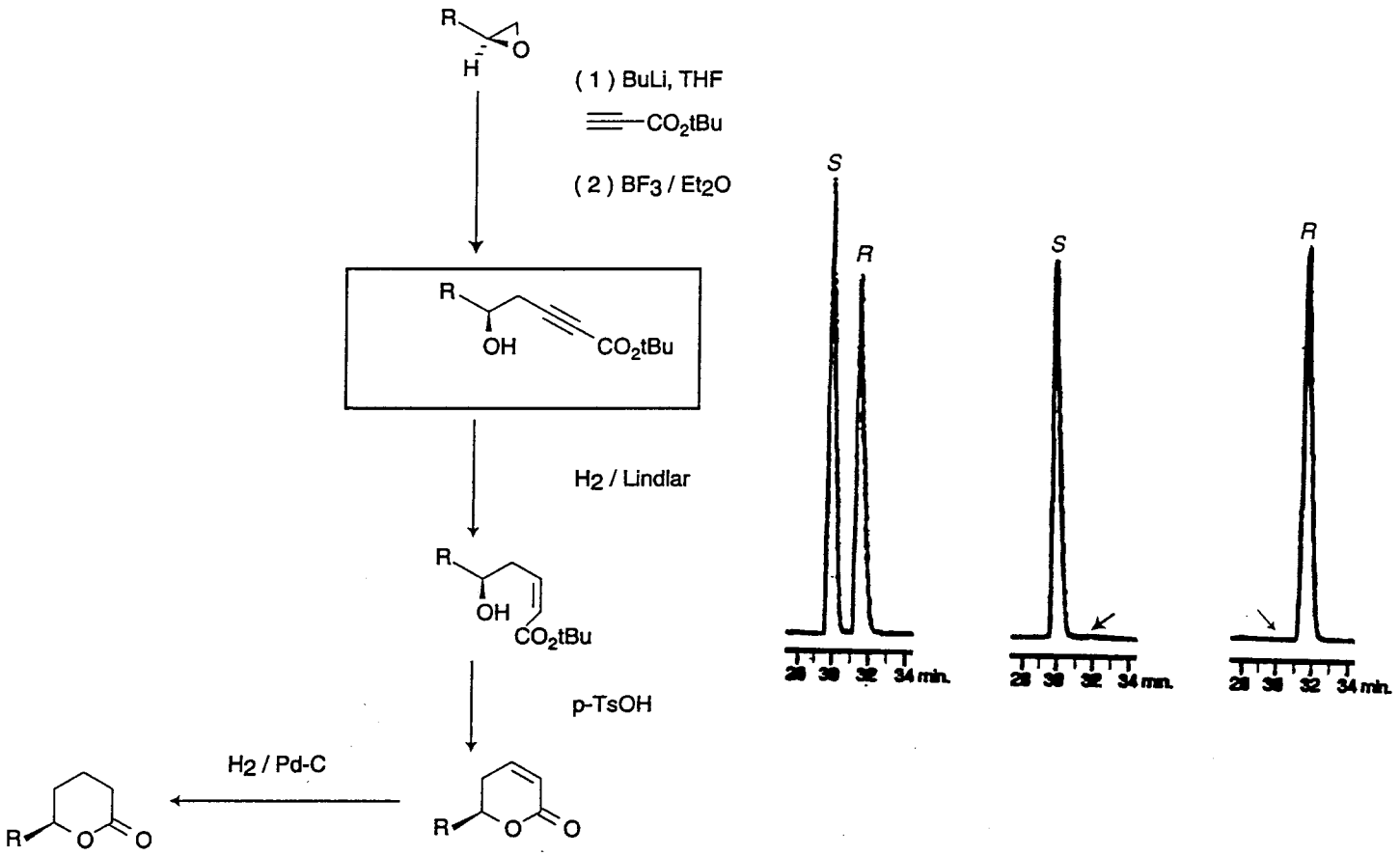
(1) K_2CO_3 / MeOH
(1) Me_3O^+ / BF_4^-
(1) OH

Enzymatic resolution of β-hydroxythioethers

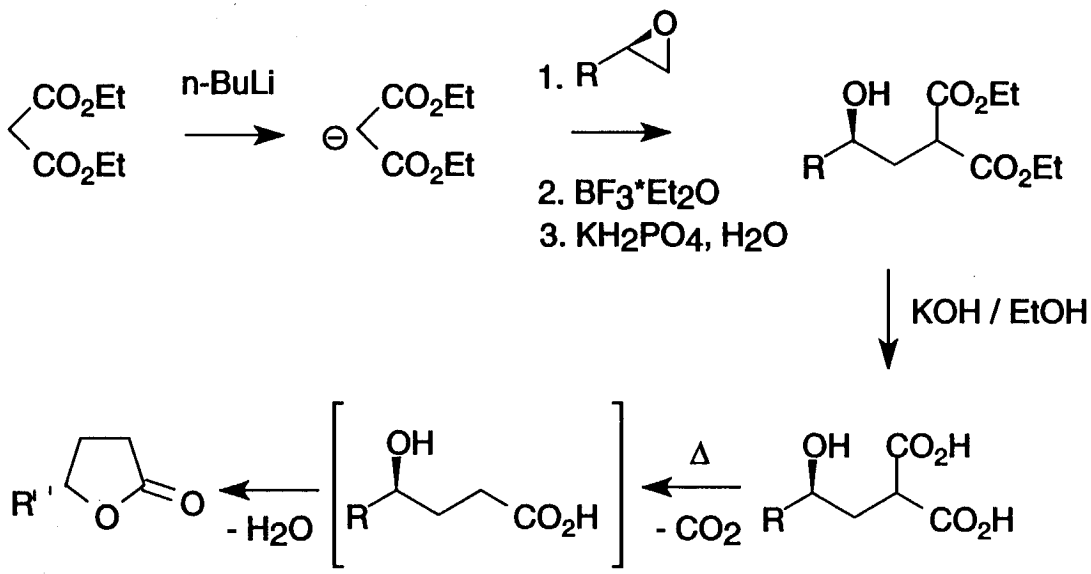


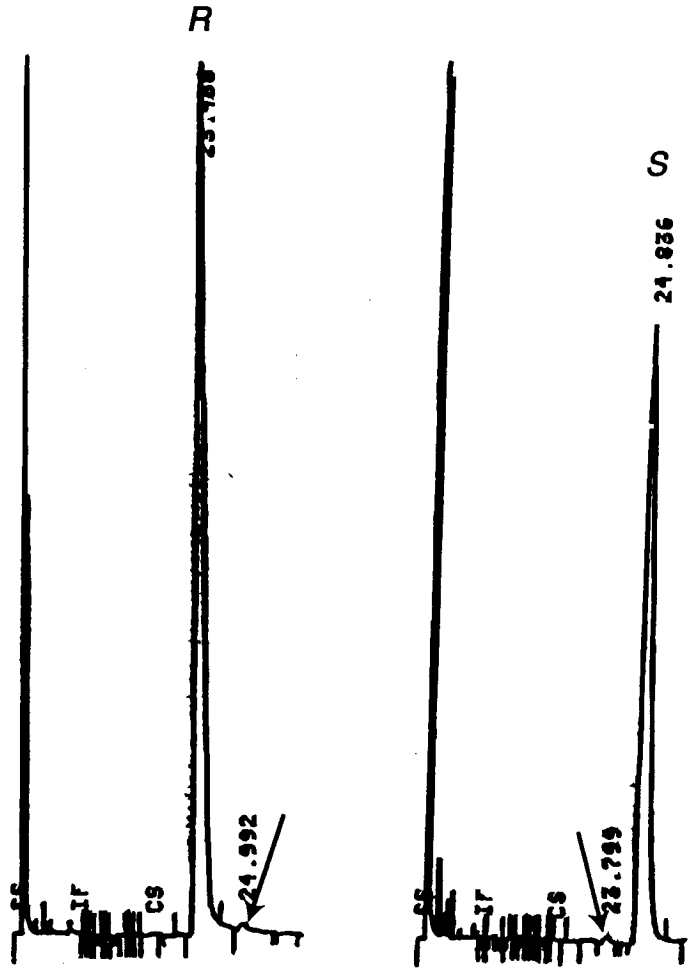
$R = CH_3 - C_{10}H_{21}$

Synthesis of δ-lactones



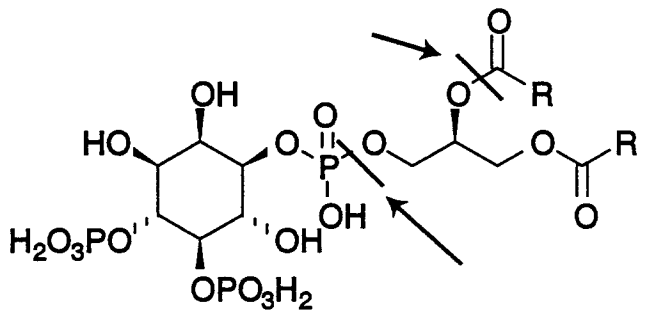
Synthesis of enantiomerically pure γ-lactones



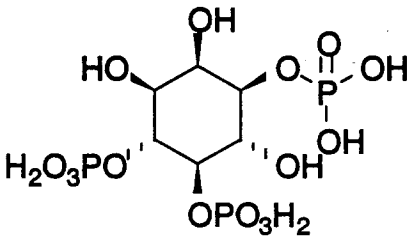


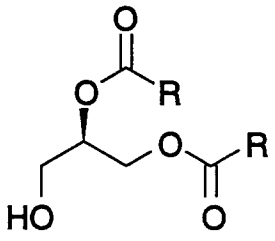
Lipodex E, 135 °C, 1.0 bar He

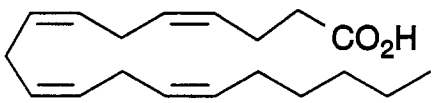
The phosphatidylinositol pathway
(Retro) - synthetic approaches

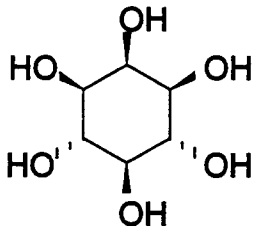


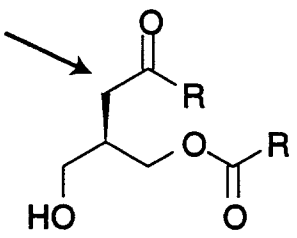
PLC PLA$_2$

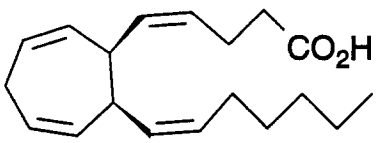




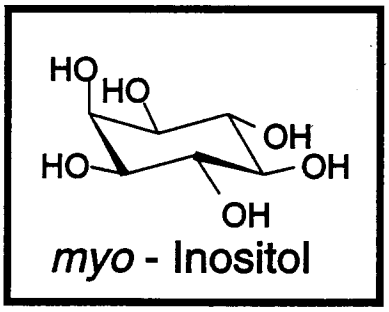


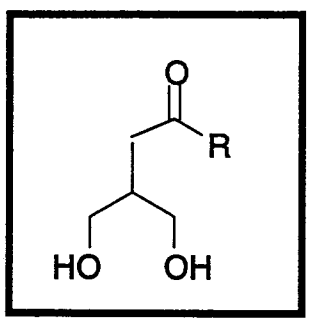


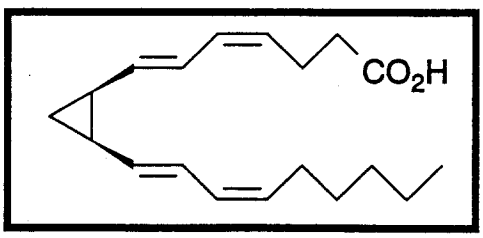




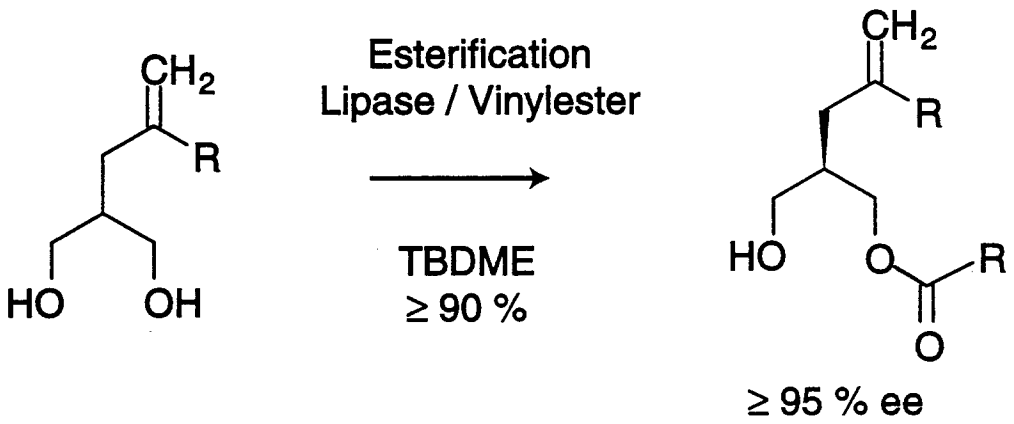
III





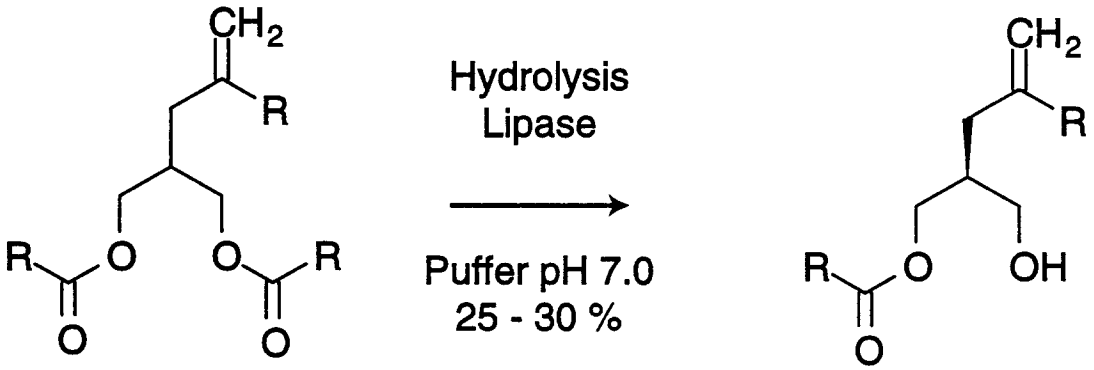


C - Analogous glycerides



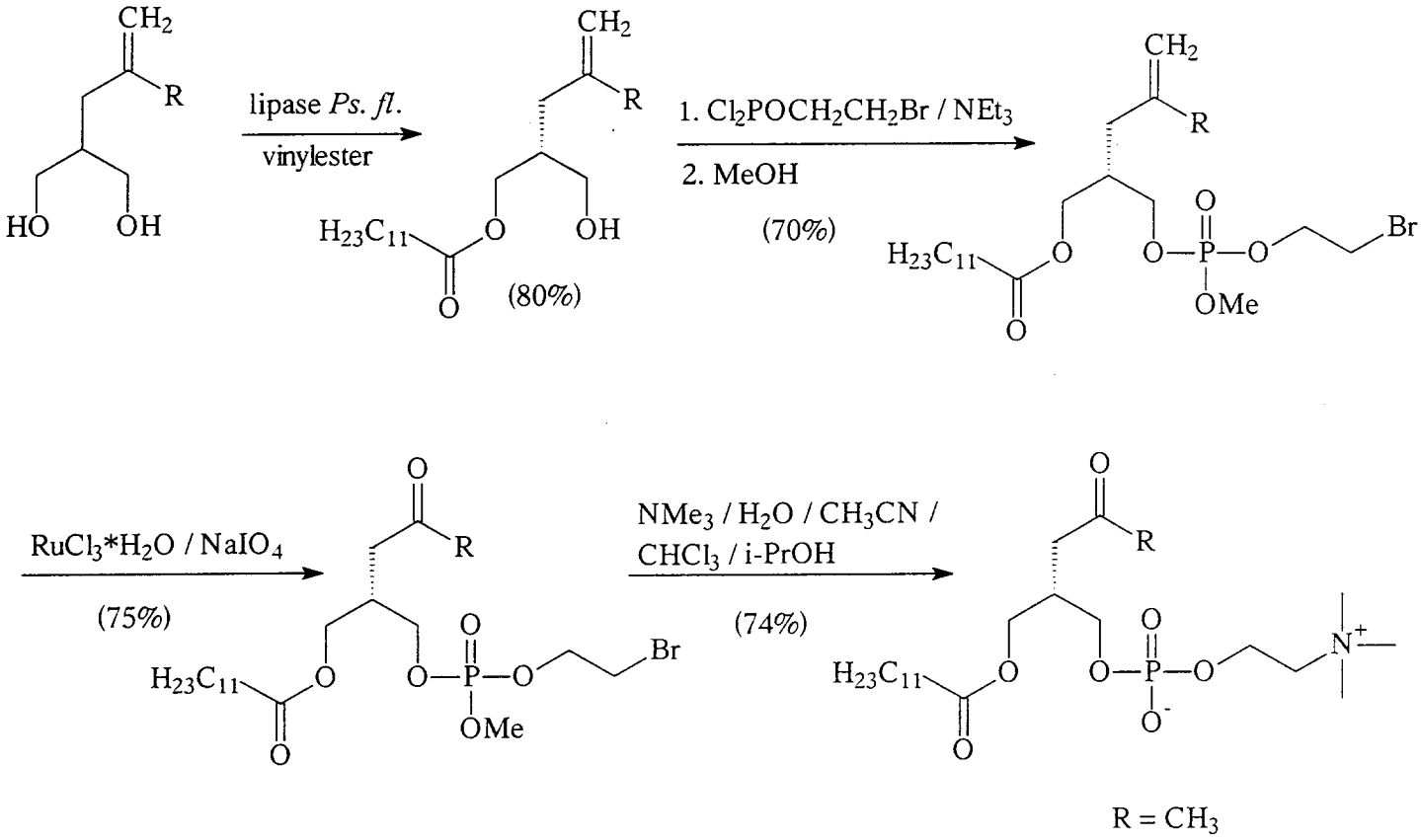
≥ 95 % ee

R = CH_3 - C_{18}

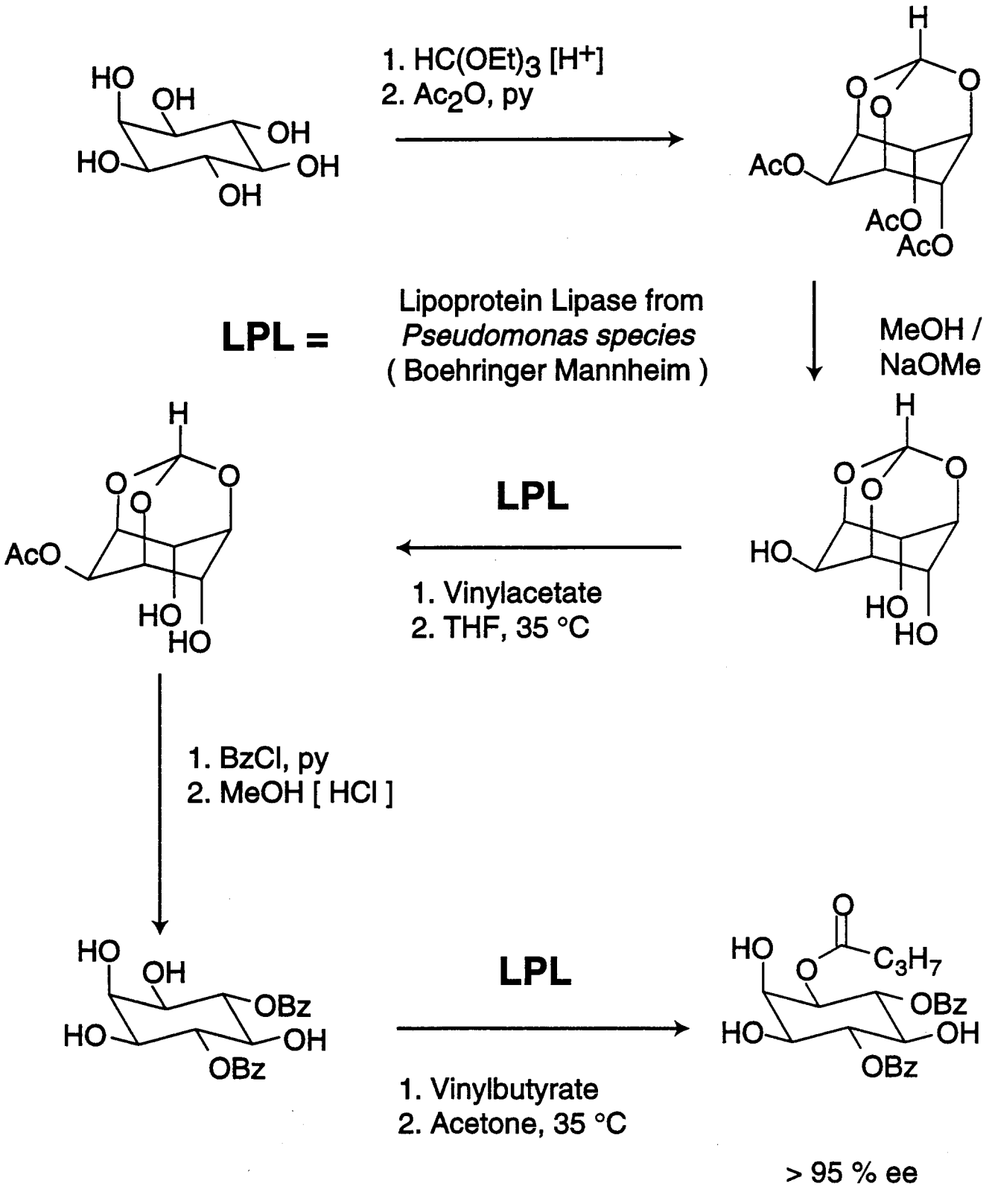


≥ 95 % ee

Carba-analogues of Phospholipids - Modification of the *sn* - 2 Position

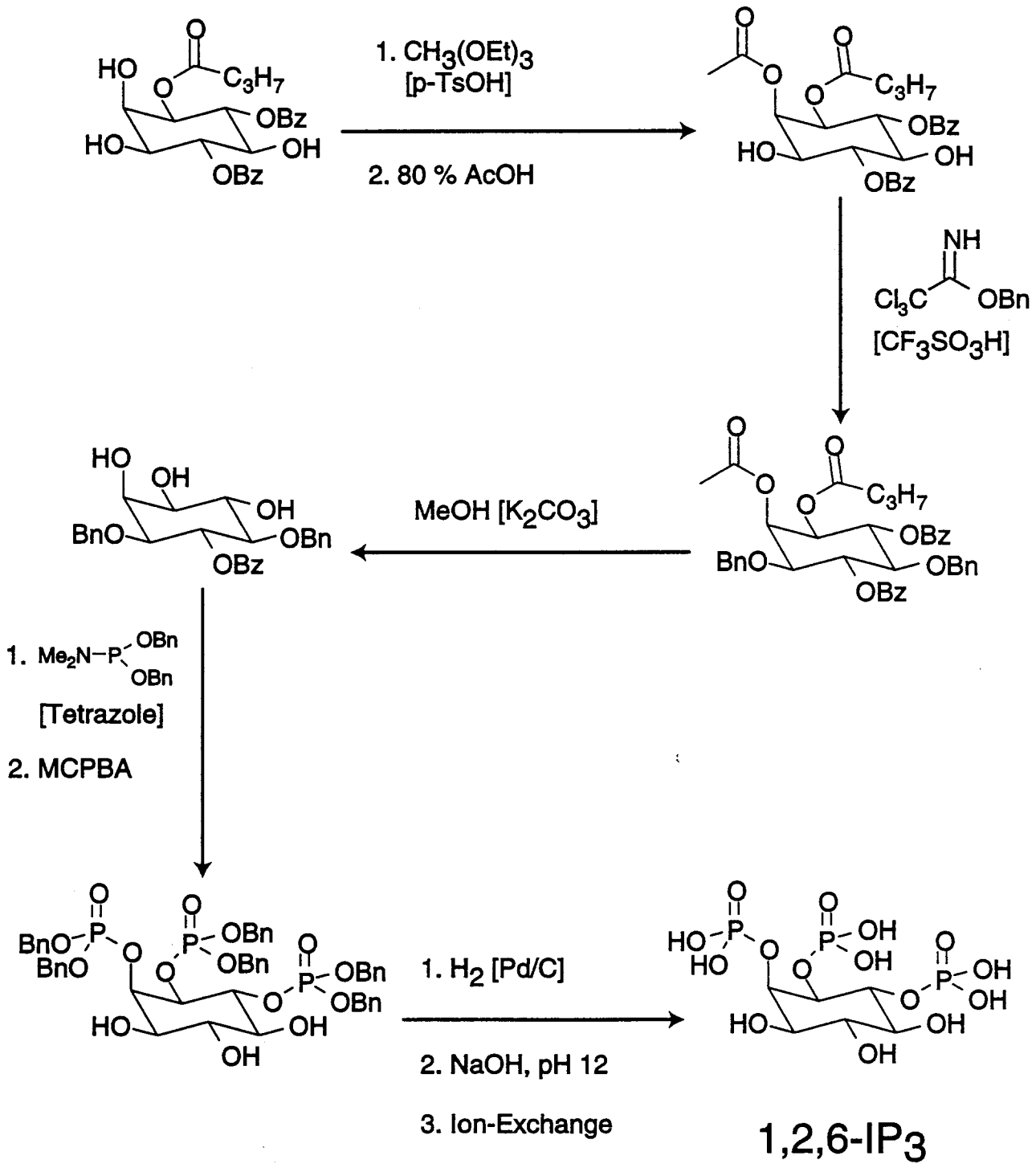


LPL Assisted Synthesis of Enantiomerically Pure 1D-1-*O*-Butyryl-4,6-*O*-Dibenzoyl-*myo*-Inositol

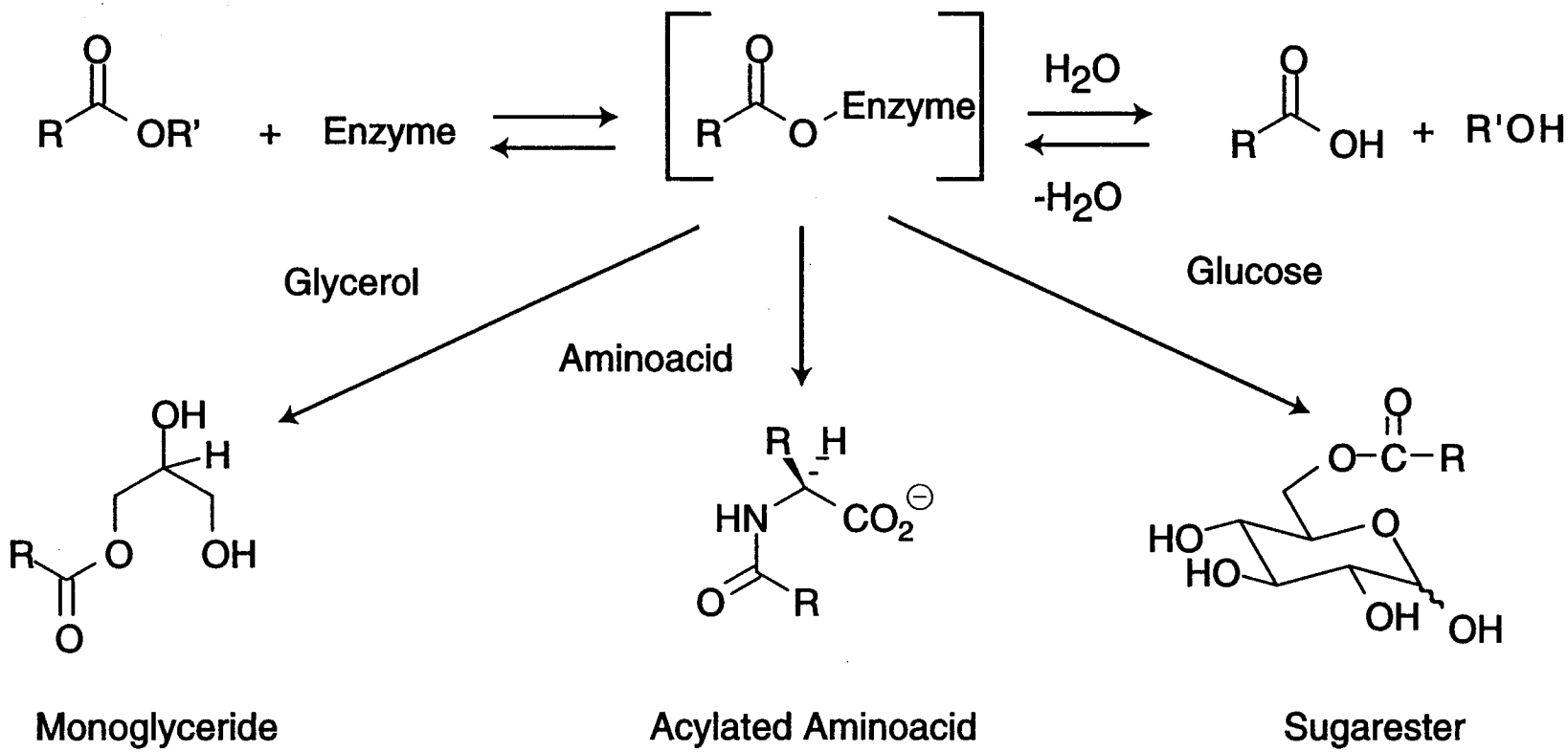


> 95 % ee

Synthesis of D-*myo*-Inositol-1,2,6-trisphosphate



Enzymatic acyltransfer

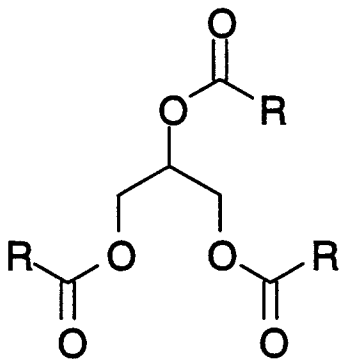


Monoglyceride

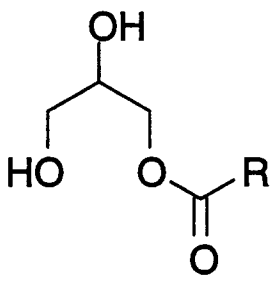
Acylated Aminoacid

Sugarester

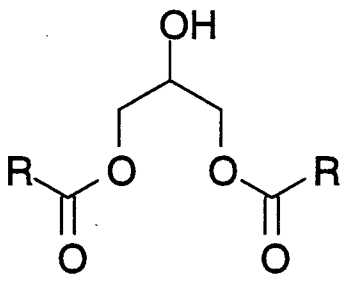
Isomerically pure mono- and diacylglycerides possible routes



Selective hydrolysis
Selective glycerolysis

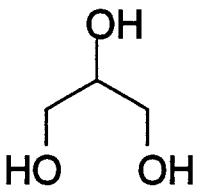


1(3)-Monoacylglycerols

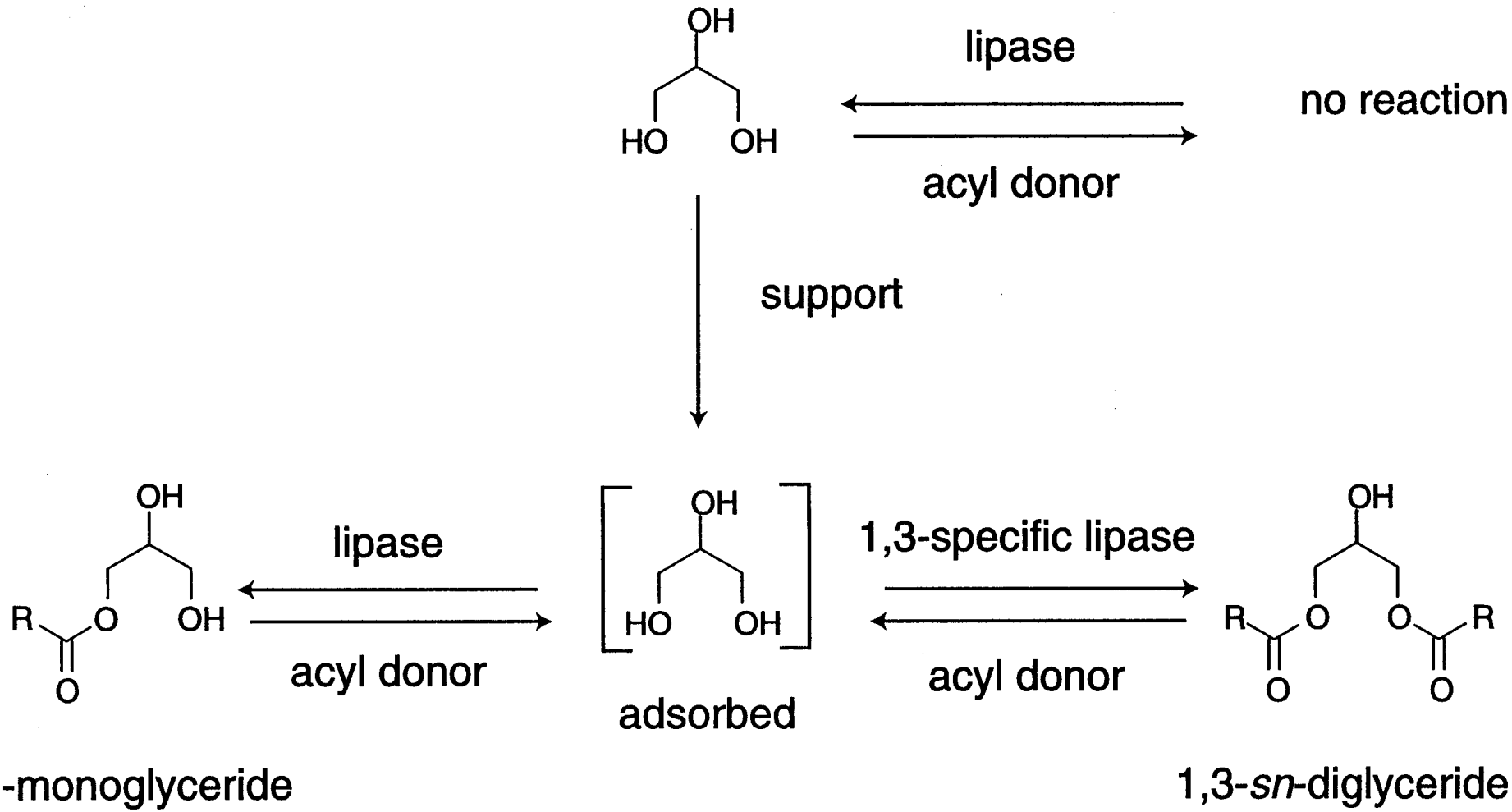


1,3-Diacylglycerols

Selective esterification

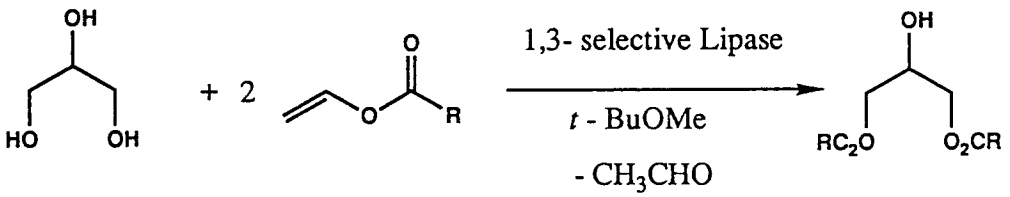


Enzymatic esterification of glycerol in organic media



Regioisomerically Pure 1,3-sn-Diglycerides

Irreversible Acyltransfer

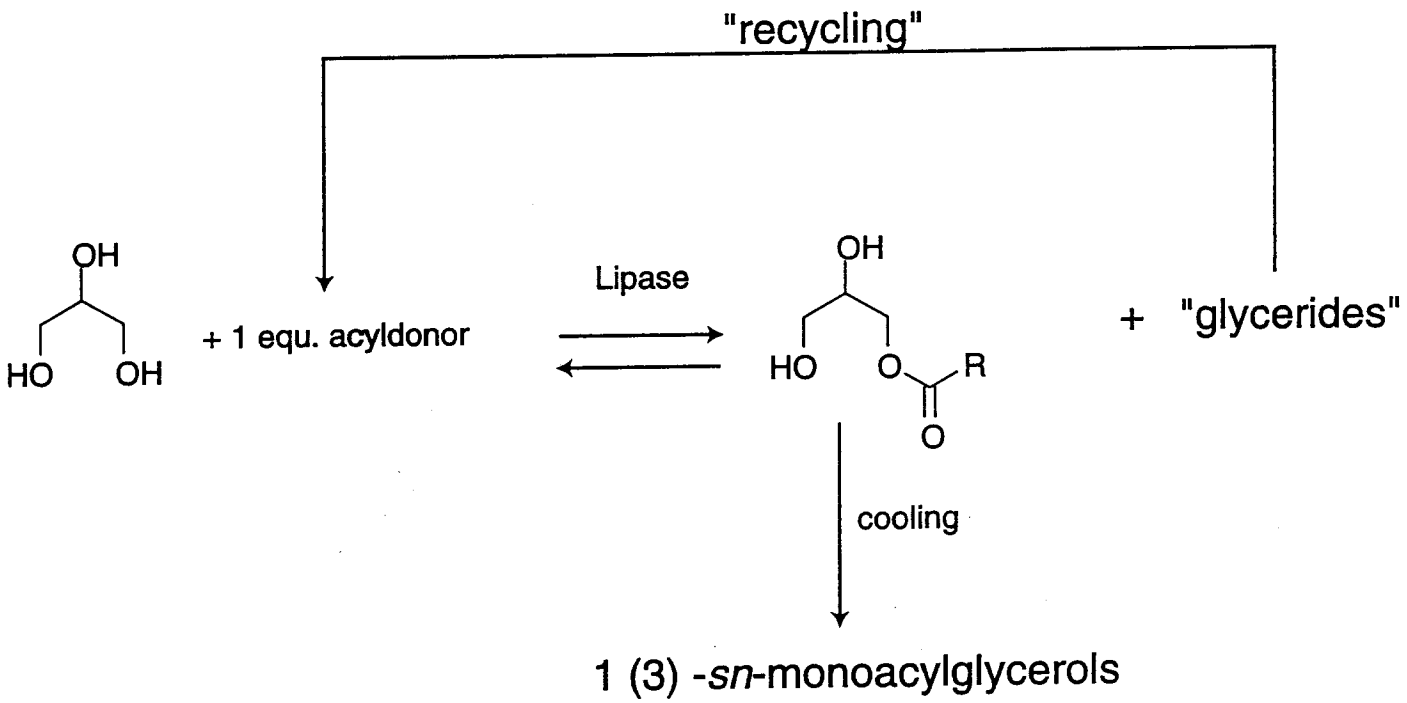


$R = C_{11}H_{23}$

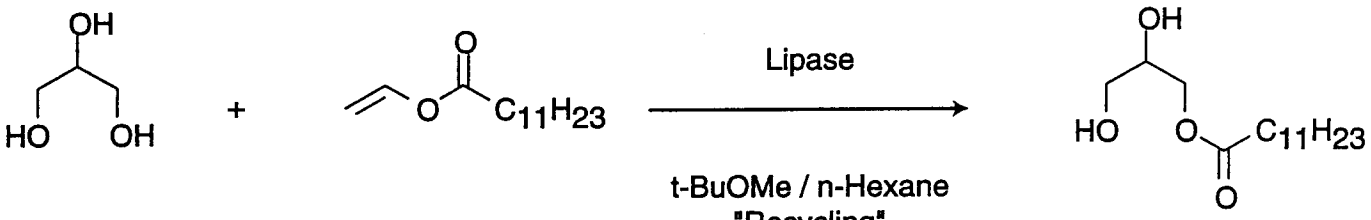
$= C_{15}H_{31}$

Yield > 90 %
Isomeric purity ≥99.5 %

Regioisomerically pure 1 (3) - *sn* - monoglycerides Synthetic process

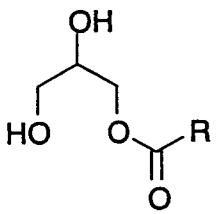


Regiosiomerically pure 1 (3) - *sn* - monoglycerides
Irreversible acyltransfer



Yield 90 %
Isomeric Purity ≥ 97 %
(crude product)

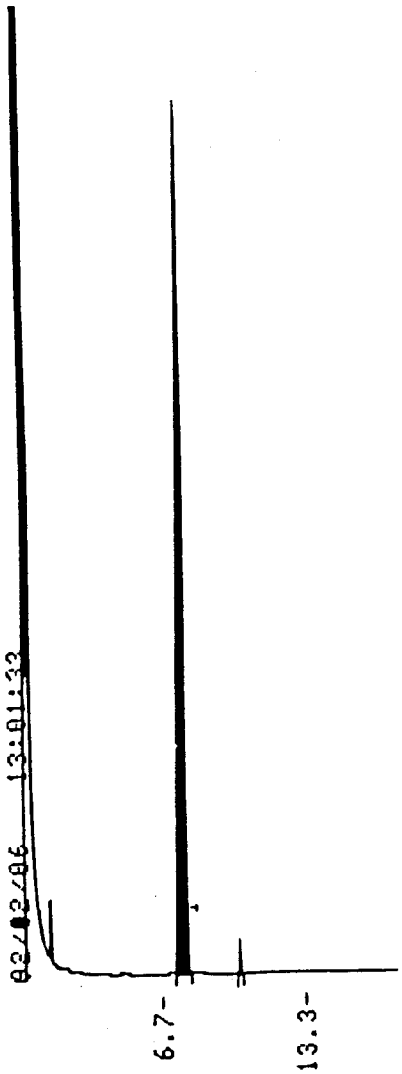
1- Monopentadecanoin



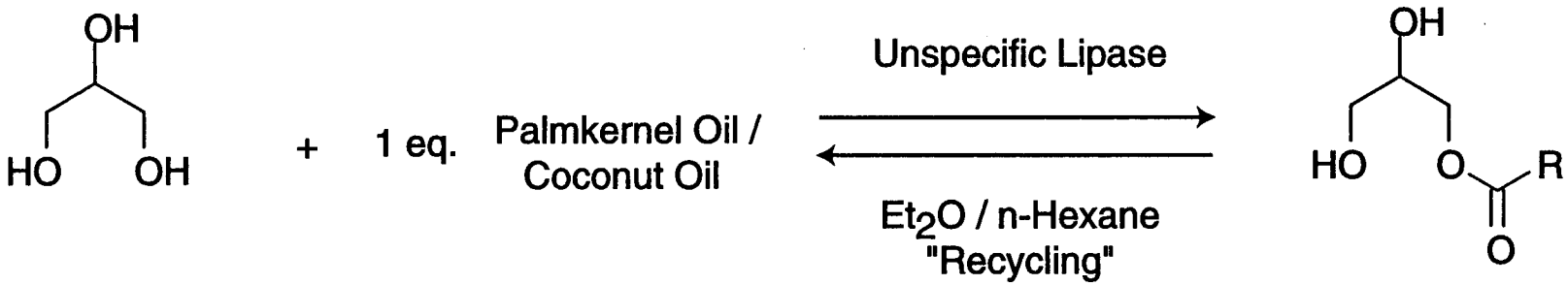
M.W. : 316,4 g/mol

MP. : 69° - 71°C

colorless, odorless

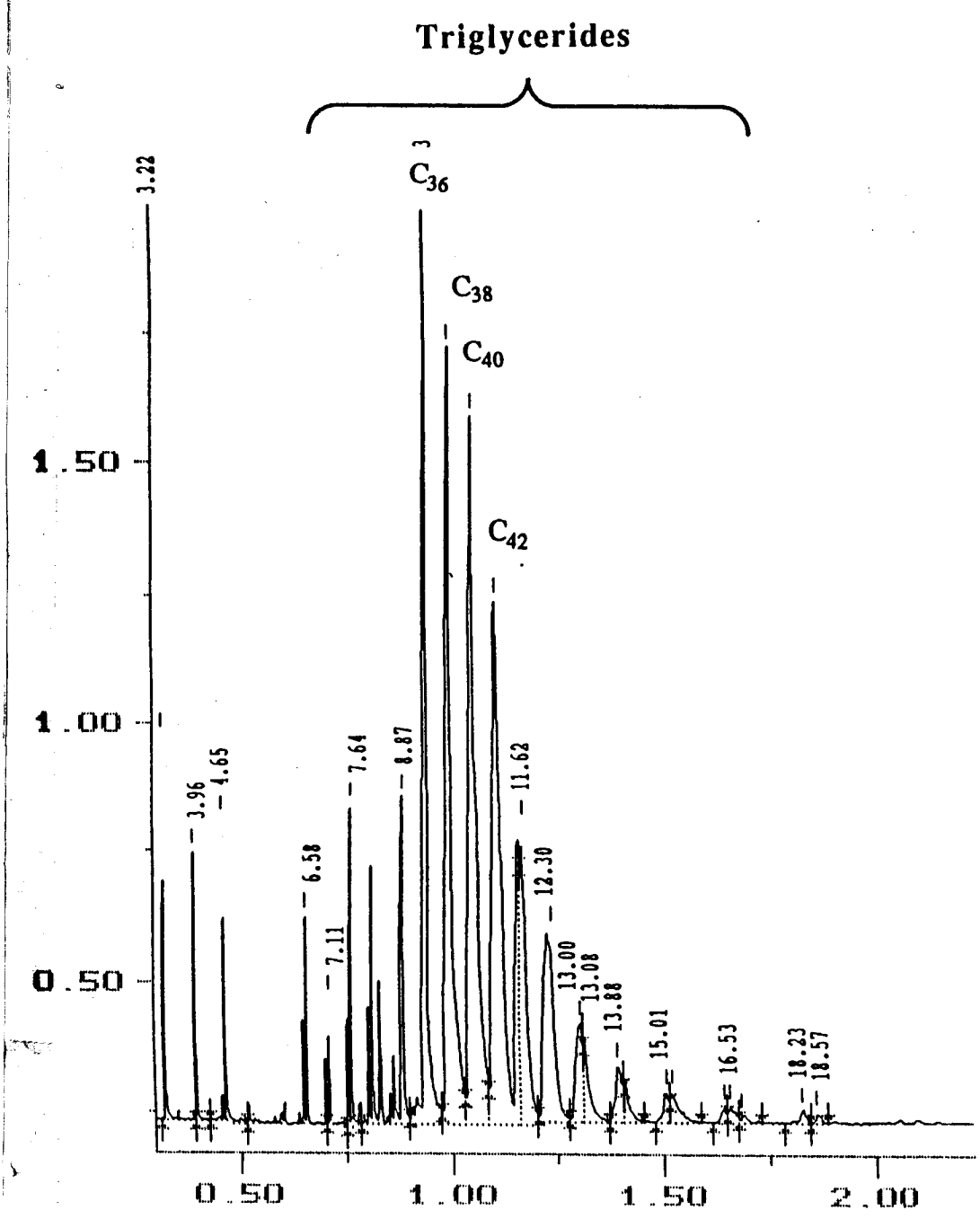


Natural monoglycerides from native oils

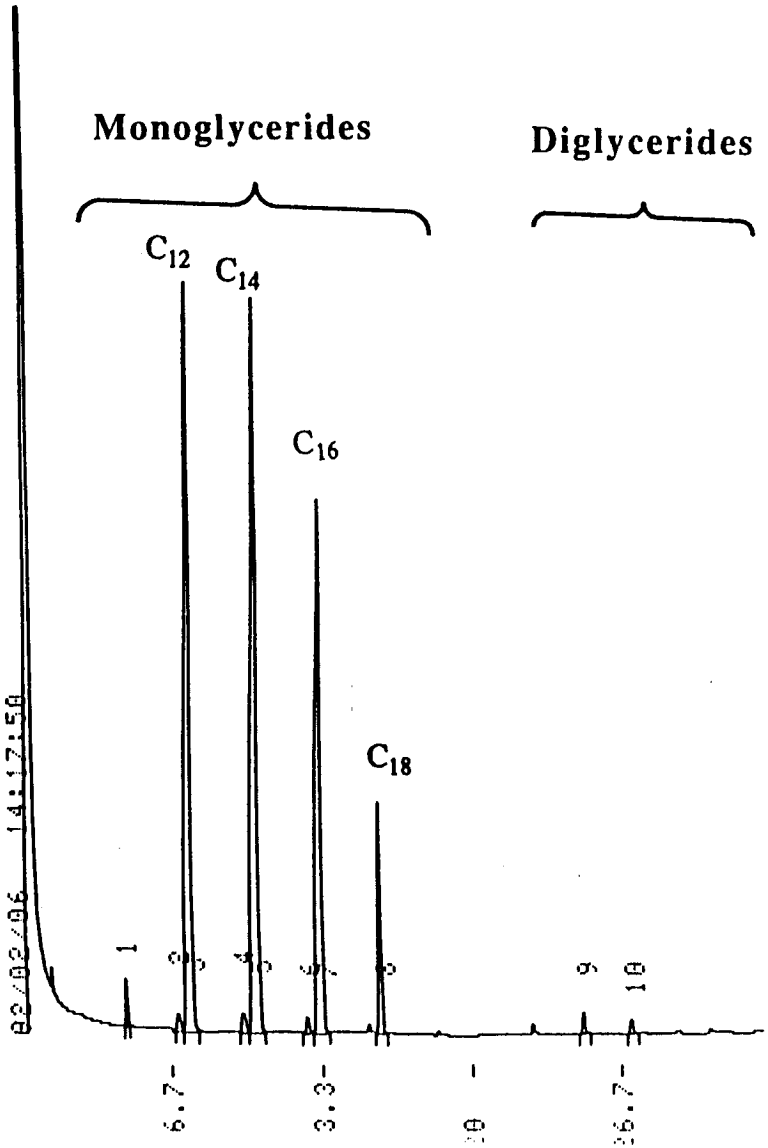


Yield > 75 %
Purity > 95 %

Cocoanutoil



" Cocoanut - monoglyceride "



Biotechnological Routes to Regioisomerically Pure Mono-Diglycerides

Advantages

Starting Materials: Natural Fats and Oils

Natural biocatalysts : Immobilized and Recycled

Non-toxic solvents : Recycled

Reaction conditons : mild, neutral pH

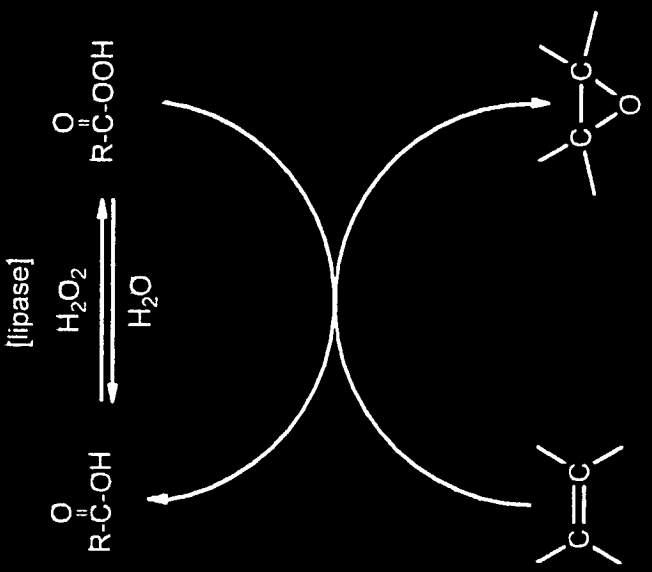
Energyconsumption : Low , Room Temperature or slightly above

Selectivities : High

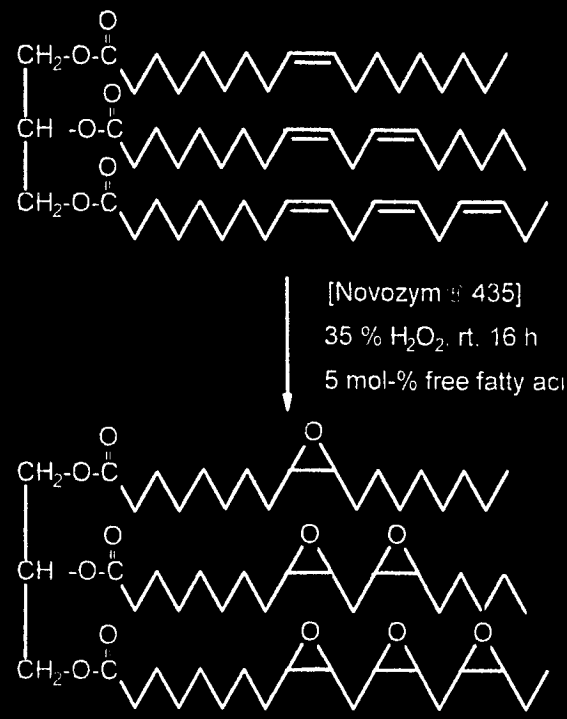
Products: Natural

Properties : Pure Isomers, Colorless, Odorless

Chemo-enzymatic Epoxidation - Reaction Principle -



Chemo-enzymatic "Self-"Epoxidation of Plant Oils



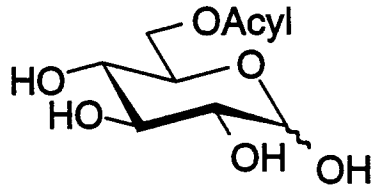
plant oil	rapeseed	sunflower	soybean	linseed	75 % sunflower + 25 % linseed
conversion of C=C	99 %	88 %	99 %	98 %	40 %
yield of epoxide	91 %	88 %	97 %	89 %	99 %
oxirane-oxygen	5.3	6.3	7.1	9.9	3.8

M. Rüsch gen. Klaas and S. Warwel
J. Am. Oil Chem. Soc. 73, 1453 (1996)

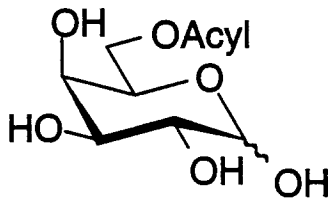
Target Molecules

Sugar Esters

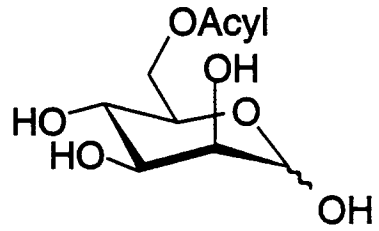
Acyl = C_8 - C_{22}



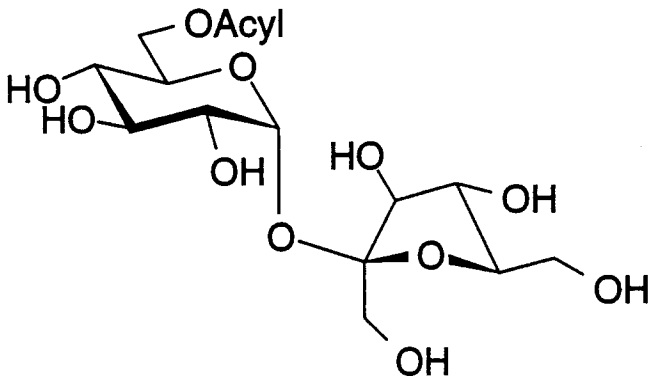
6-*O*-acyl-D-glucose



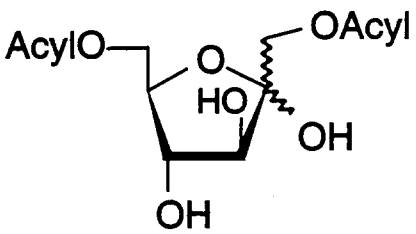
6-*O*-acyl-D-galactose



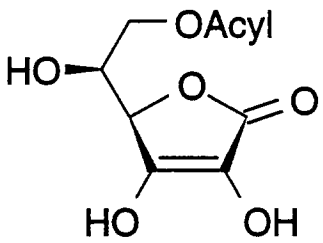
6-*O*-acyl-D-mannose



acylated sucrose

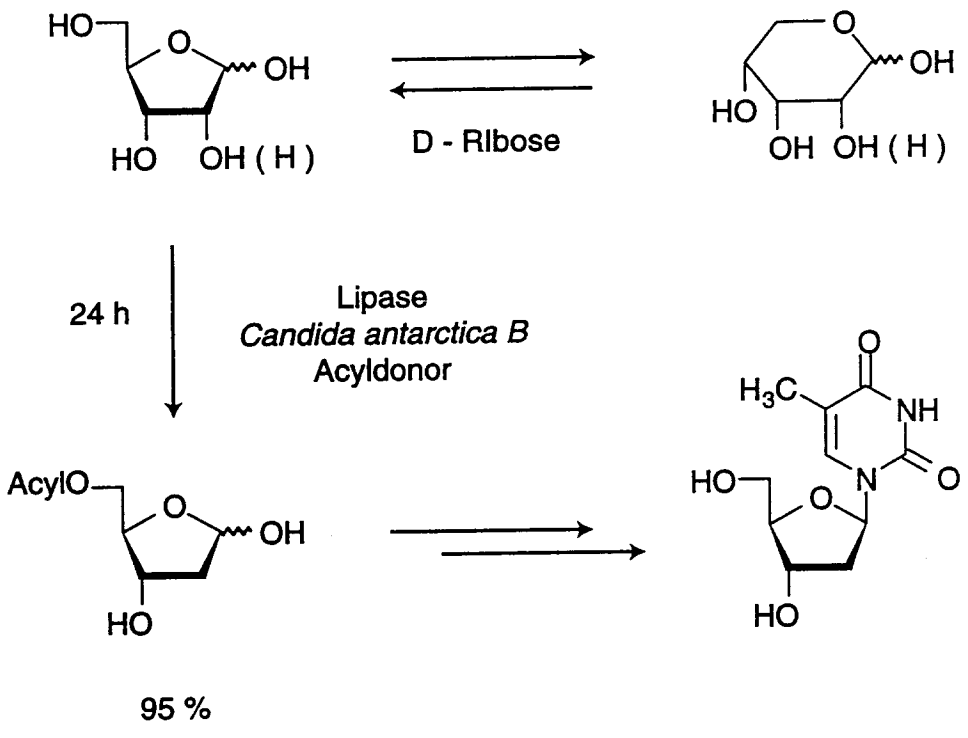


acylated D-fructose



6-*O*-acyl-L-ascorbic acid

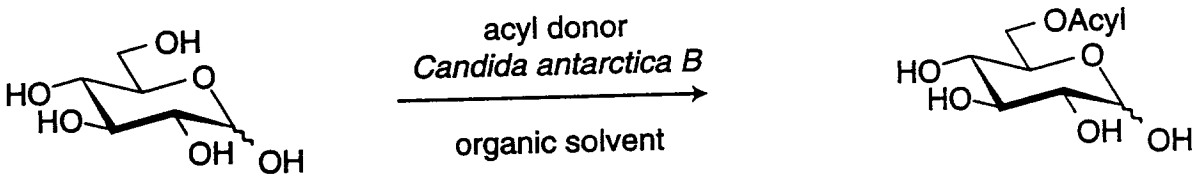
Selective Esterification of D-Ribose



95 %

A.K. Prasad, M. D. Sørensen, V.S. Parmar, J . Wengel, *Tetrahedron Lett.* **36** (1995) 6163

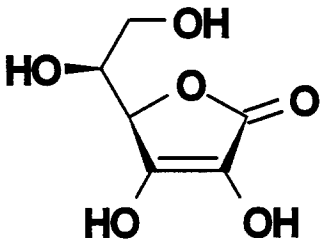
Glucose Esters

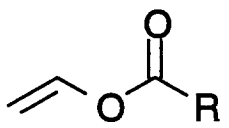


fatty acids from C_8 - C_{22}

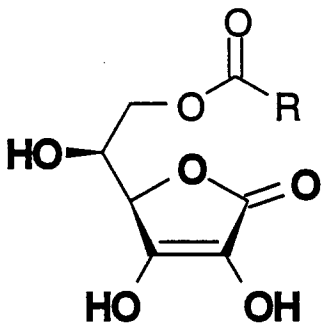
87 %

Acylation of other compounds

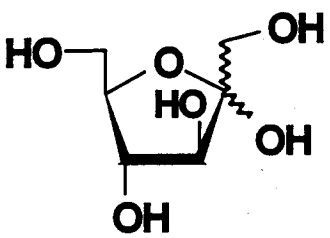




Candida antarctica B
Novozym SP 435
THF, 50 °C, 72 h



78 %



Candida antarctica B
Novozym SP 435

THF, 50 °C, 24

unidentified mixture of acylated molecules

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