

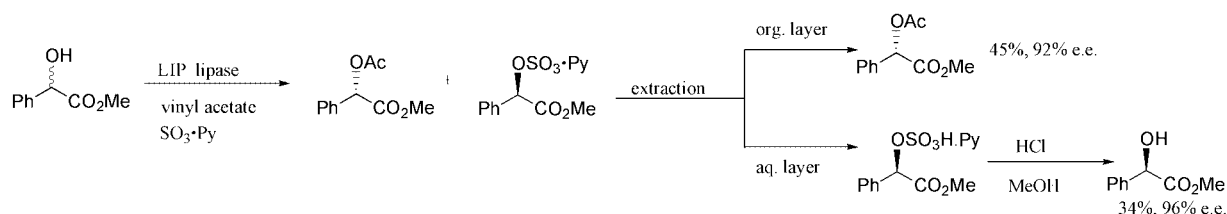
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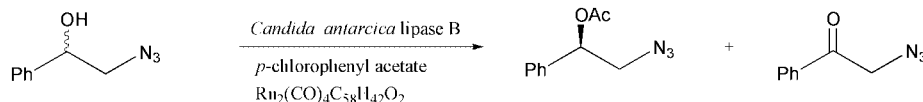
Perkin 1 Abstracts: Biocatalysis in Organic Synthesis aims to cover recent literature concerning the applications of enzymes and micro-organisms as catalysts in organic synthesis. The abstracts will emphasise the key synthetic step(s) that are mediated by the biocatalyst. Emerging technologies for biocatalyst design and optimisation will also be included.

<p>Enantioselective aminolysis of an α-chloroester</p>	<p><i>Lipase</i></p>
	<p>86% yield, 92% e.e.</p>
<p>J. D. Badjic, E. N. Kadnikova and N. M. Kostic, <i>Org. Lett.</i>, 2001, 3, 2025.</p>	
<p>The scope and limitations of the aminolysis were investigated. The silica matrix enhances the enzyme activity and improves the chiral discrimination by lipase.</p>	
<p>Preparation of highly active enzyme-coated micro-crystals</p>	<p><i>Lipase</i></p>
	<p>A rapid, inexpensive method for production of highly active biocatalysts. These water soluble, enzyme coated micro-crystals exhibit high catalytic activity and stability in non-aqueous media.</p>
<p>M. Kreiner, B. D. Moore and M. C. Parker, <i>Chem. Commun.</i>, 2001, 1096.</p>	
<p>Dynamic kinetic resolution of hydroxy acids, diols and aldehydes protected with a bulky group</p>	<p><i>Lipase</i></p>
	<p>Hydroxy acids: R¹ = Me, R² = CO₂Bn, CO₂C₆H₄-OMe, CO₂CH₂C₆H₄-C₆H₅, CO₂tBu Diols: R¹ = Me or Et, R² = OTr, CH₂OTr Hydroxy aldehydes: R¹ = Me, R² = </p>
<p>M.-J. Kim, Y. K. Choi, M. Y. Choi, M. J. Kim and J. Park, <i>J. Org. Chem.</i>, 2001, 66, 4736.</p>	
<p>All dynamic kinetic resolutions investigated resulted in high enantioselectivity (i.e. 91-99% e.e.) and excellent yields (i.e. 90-97% yield).</p>	
<p>Enzymatic acylation of amino groups</p>	<p><i>Lipase</i></p>
	<p>80% yield</p>
<p>I. Lavandera, S. Fernández, M. Ferrero and V. Gotor, <i>J. Org. Chem.</i>, 2001, 66, 4079.</p>	
<p>Diacetylated derivative was detected as a minor product (5% yield). Various other acyl moieties were screened to show the versatility of this enzymatic reaction.</p>	

Resolution of racemic alcohols and esters using lipases and chemical sulfation
Lipase


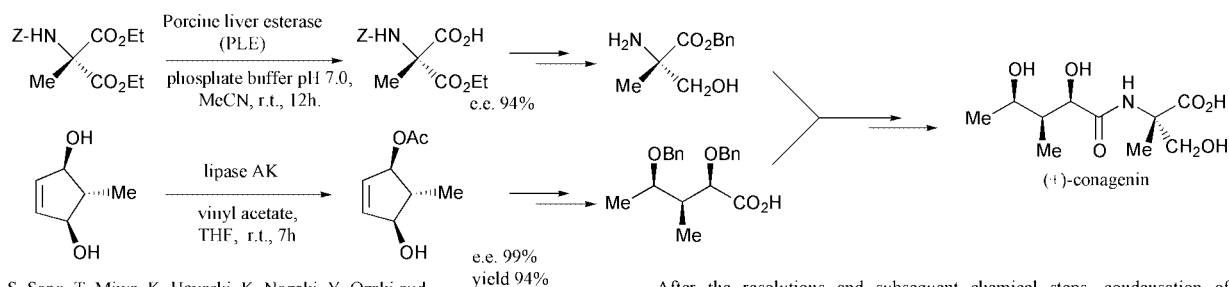
O. Yamano, F. Kikumoto, S. Yamamoto, K. Miwa, M. Kawada, T. Ito, T. Ikemoto, K. Tomimatsu and Y. Mizuno, *Chem. Lett.*, 2000, 448.

Lipase catalysed transformation of racemic alcohols and esters yields mixtures of optically active species. Sulfation by sulfur trioxide pyridine complex enables isolation of optically active esters by extraction rather than column chromatography.

Dynamic kinetic resolution of β -azido alcohols
Lipase


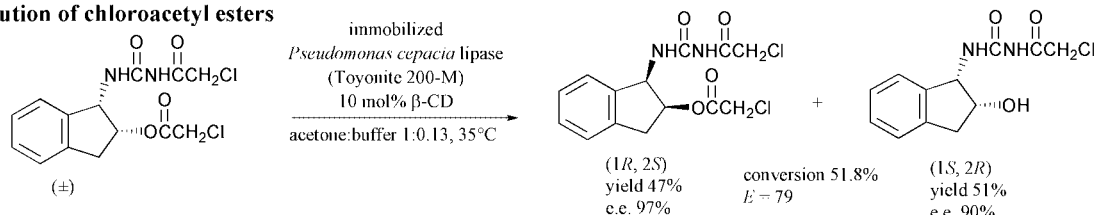
O. Parnies and J. E. Backvall, *J. Org. Chem.*, 2001, 66, 4022.

Vicinal azido acetates were prepared in good yields and with high enantioselectivity using chemoenzymatic dynamic kinetic resolution techniques. These azido acetates may then be transformed to enantiomerically pure β -amino alcohols and aziridines.

Resolution of a diester and a diol for the synthesis of (+)-conagenin
Lipase


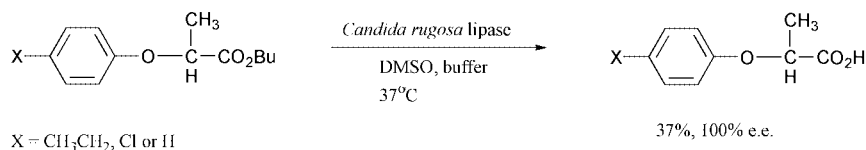
S. Sano, T. Miwa, K. Hayashi, K. Nozaki, Y. Ozaki and Y. Nagao, *Tetrahedron Lett.*, 2001, 42, 4029.

After the resolutions and subsequent chemical steps, condensation of the products, followed by hydrogenolysis gave (+)-conagenin, an immunomodulator.

Resolution of chloroacetyl esters
Lipase


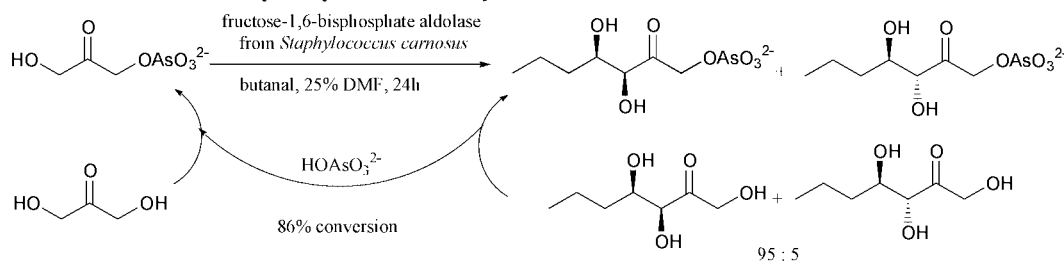
M. Suzuki, C. Nagasawa and T. Sugai, *Tetrahedron*, 2001, 57, 4841.

The hydrolysis has been optimised with respect to ratio of cosolvent:water, enzyme, cosolvent and additive (Triton X-100 and β -cyclodextrin). Choice of substrate was dictated by ease of synthesis. The enriched (1*S*, 2*R*) alcohol was reacylated and hydrolysed with *Pseudomonas* lipase giving the desired alcohol in >99% e.e. The 1*S*, 2*R* alcohol is important in the synthesis of a component of Crixivan[®] and a chiral auxiliary for the asymmetric aldol reaction.

DMSO enhances enantioselectivity in resolution of 2-phenoxypropionic acyl derivatives
Lipase


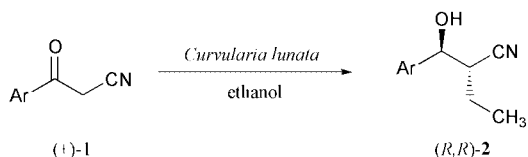
K. Watanabe and S. Ueji, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1386.

The enantioselectivity of the hydrolysis of butyl 2-(4-substituted phenoxy) propionates was increased through the addition of DMSO as a co-solvent.

Enzymatic aldol reactions with dihydroxyacetone in the presence of arsenate
Aldolase


R. Schoevaart, F. van Rantwijk and R. A. Sheldon, *J. Org. Chem.*, 2001, **66**, 4559.

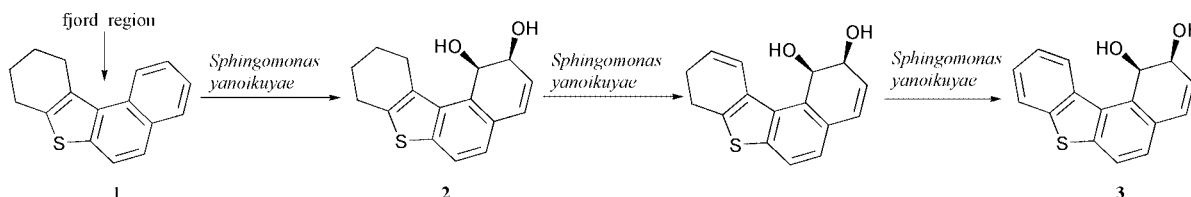
Arsenate acts as a phosphate mimic for the dihydroxyacetone phosphate-dependent aldolase. The use of 25% DMF as cosolvent increased the solubility of the aldehyde, afforded higher reaction rates and increased enzyme stability.

Stereoselective alkylation–reduction of β-ketonitriles
Curvularia lunata


a Ar = Ph-	69%, 96% d.e., 98% e.e.
b Ar = 3-Me-Ph-	42%, 78% d.e., 70% e.e.
c Ar = 4-Me-Ph-	64%, 92% d.e., 83% e.e.
d Ar = 4-MeO-Ph-	58%, 88% d.e., 75% e.e.
e Ar = 2-thienyl	63%, 94% d.e., 93% e.e.
f Ar = 2-furyl	59%, 72% d.e., 87% e.e.

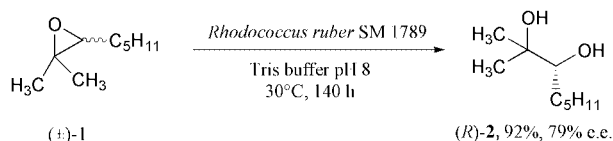
J. R. Delhi and V. Gotor, *Tetrahedron: Asymmetry*, 2001, **12**, 1485.

Variation of the alcohol resulted in lower yields and stereoselectivities. Simple aliphatic β-ketonitriles were not accepted as substrates in this reaction.

Dihydroxylation of fjord region polycyclic arenes
Dioxygenase


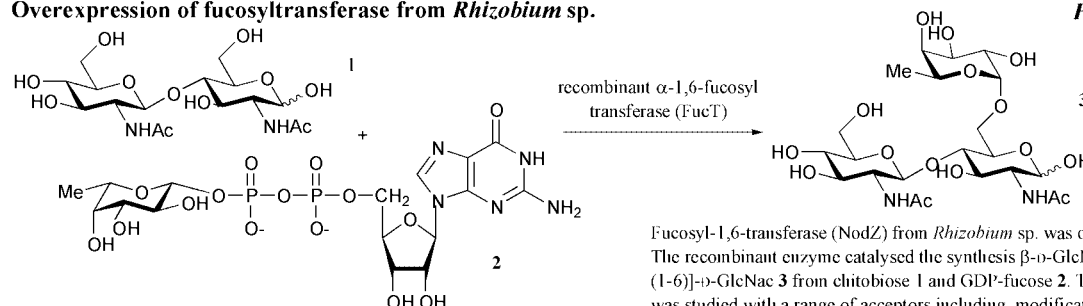
D. R. Boyd, N. D. Sharma, J. S. Harrison, M. A. Kennedy, C. C. R. Allen and D. T. Gibson, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1264.

Exclusive oxidations of the fjord region of tetracyclic arenes and tetracyclic-tetrahydroarenes was observed using *S. Yanoikuyae*. Bacterial dioxygenase catalysed oxidation of 1 yielded 2 and a subsequent bis-desaturation step yielded 3.

Asymmetric and enantioconvergent hydrolysis of trisubstituted oxiranes
Epoxide hydrolase


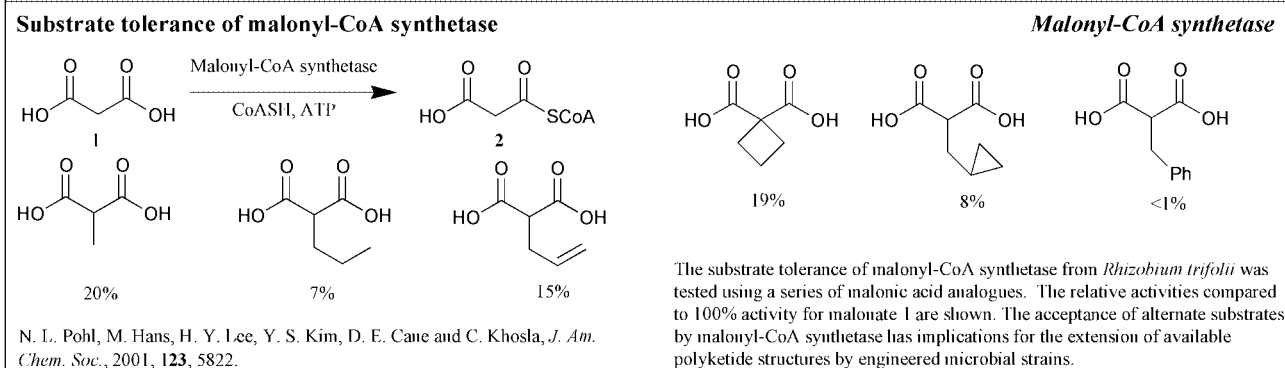
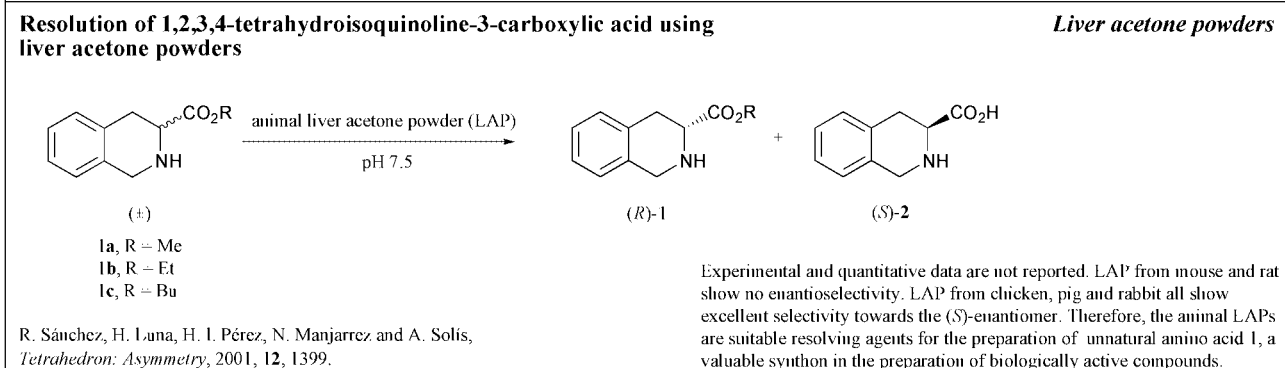
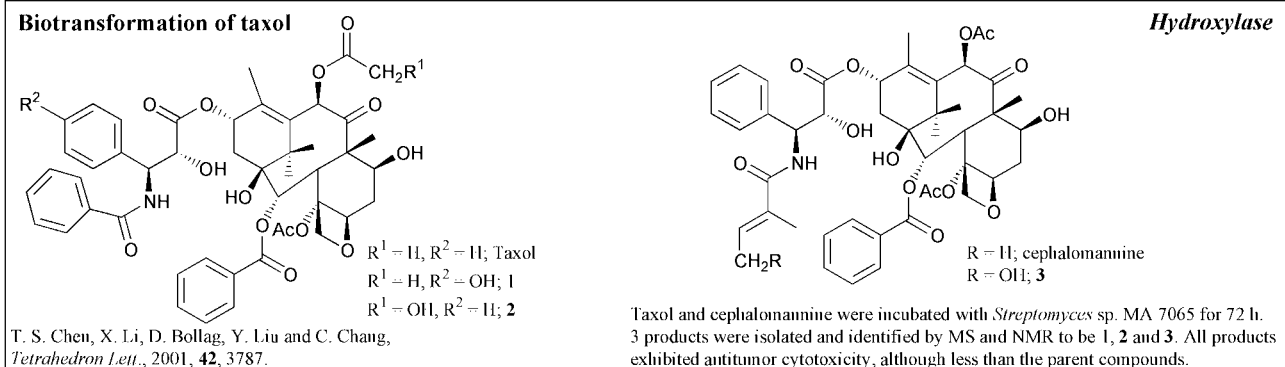
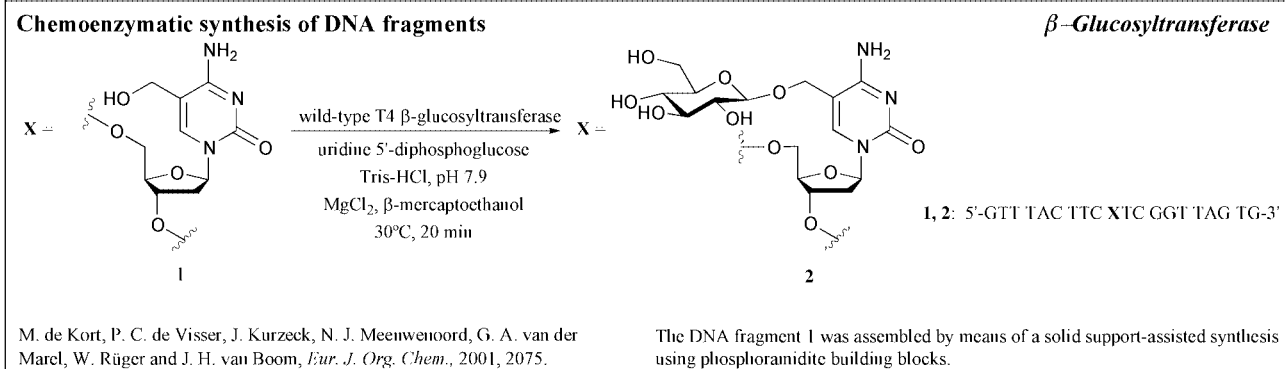
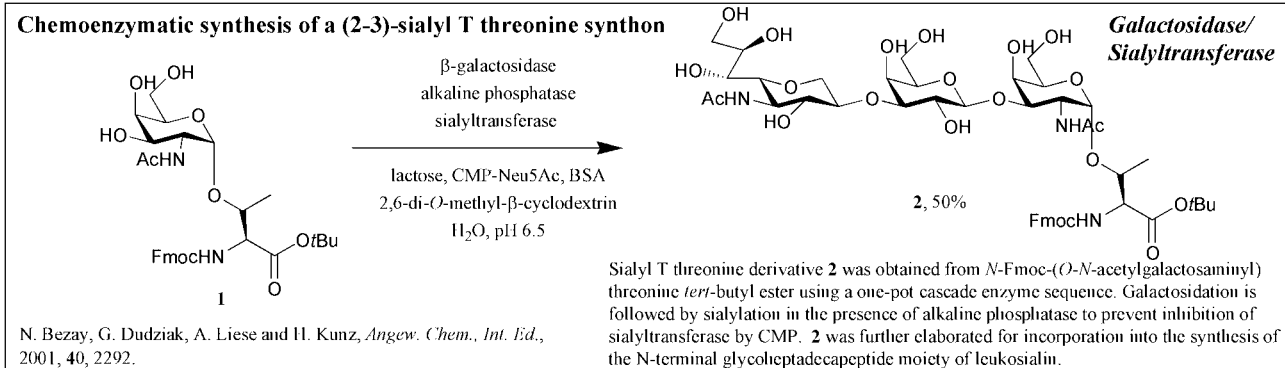
A. Steinreiber, S. F. Mayer, R. Saf and K. Faber, *Tetrahedron: Asymmetry*, 2001, **12**, 1519.

Streptomyces lavendulae was also found to enantioselectively hydrolyse the trisubstituted oxirane 1. The stereochemical pathways of the biolhydrolyses are discussed.

Overexpression of fucosyltransferase from Rhizobium sp.
Fucosyltransferase


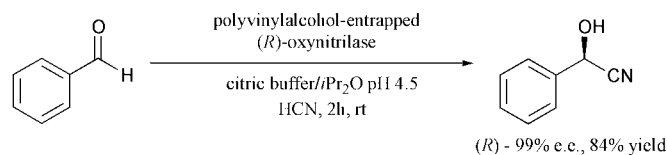
A. Bastida, A. Fernández-Mayoralas, R. Gómez Arrayás, F. Tradier, J. C. Carretero and E. García-Jimceda, *Chem. Eur. J.*, 2001, **7**, 2390.

Fucosyl-1,6-transferase (NodZ) from *Rhizobium* sp. was overexpressed in *E. coli*. The recombinant enzyme catalysed the synthesis β-D-GlcNAc-(1-4)-α-L-Fuc-(1-6)-D-GlcNAc 3 from chitobiose 1 and GDP-fucose 2. The specificity of NodZ was studied with a range of acceptors including modifications to the GlcNAc structure. The enzyme was shown to be inhibited by a series of polyhydroxylated indolizidine derivatives related to castanospermine.



Asymmetric synthesis of an (*R*)-cyanohydrin

Oxynitrilase

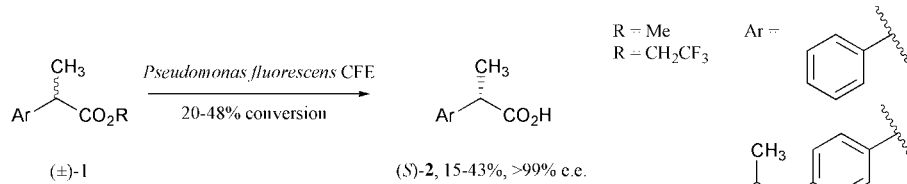


H. Gröger, E. Capan, A. Barthuber and K.-D. Vorlop, *Org. Lett.*, 2001, 3, 1969.

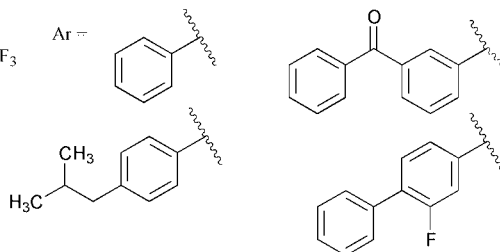
These immobilised biocatalysts show no catalyst leaching and can be recycled 20x.

Preparation of enantiomerically pure 2-arylpropanoic acids

Pseudomonas fluorescens



R = Me
R = CH₂CF₃

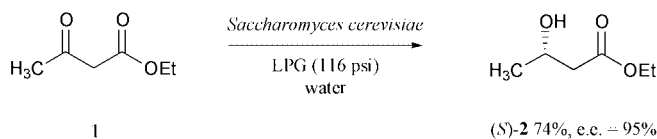


At 100% conversion racemic **2** is obtained. The rate of reaction and enantioselectivity is dependent on the size of the aryl group. A bulky group decreases reaction rate but increases selectivity.

I. Kumar, K. Manju and R. S. Jolly, *Tetrahedron: Asymmetry*, 2001, 12, 1431.

Liquefied petroleum gas (LPG) as a solvent for reduction by yeasts

Saccharomyces cerevisiae



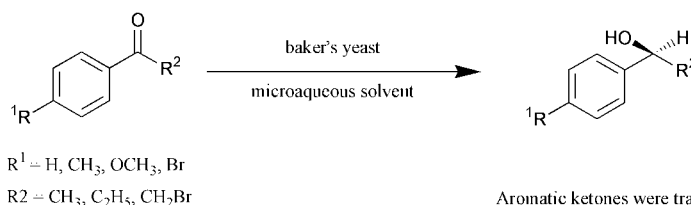
LPG = 98% propane, 1.8% butane, 0.15% propylene and 0.06% other hydrocarbons

M. K. Johns, A. J. Smallridge and M. A. Trehwella, *Tetrahedron Lett.*, 2001, 42, 4261.

LPG offers a more environmentally friendly alternative to organic solvents. The reaction in LPG compares favourably to the same reaction carried out in petroleum ether: 69% yield, 99% e.e. However, a higher yeast to substrate ratio is required.

Using baker's yeast in organic solvents

Saccharomyces cerevisiae

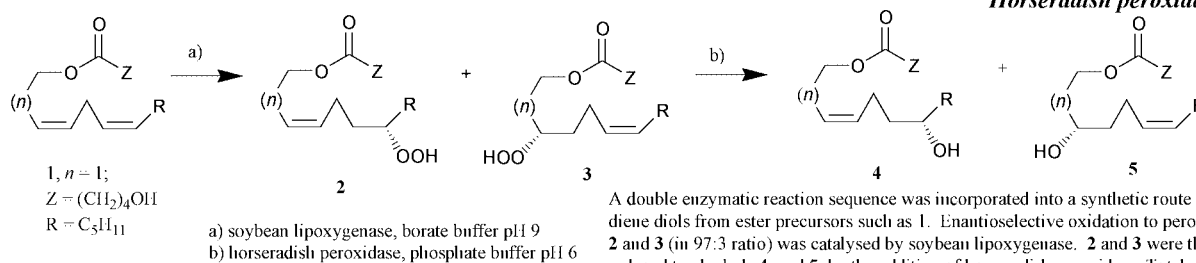


Aromatic ketones were transformed to corresponding alcohols in a range of organic solvents using 2% water as co-solvent. The yeast was more active in non-polar solvents such as petroleum ether (62% conversion of acetophenone; 90% e.e.), but was also active in THF (50% conversion of acetophenone; 85% e.e.). Alcoholic products of (*S*) were obtained predominantly.

X. Liu, T.-S. Zlm, P.-D Sun and J.-H. Xu, *Synth. Commun.*, 2001, 31, 1521.

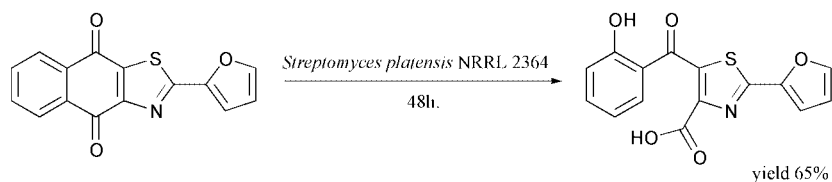
Asymmetric oxidation/reductions by lipoygenase/peroxidase

Soybean lipoygenase/Horseradish peroxidase



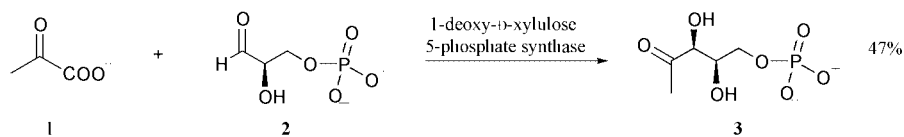
A double enzymatic reaction sequence was incorporated into a synthetic route to diene diols from ester precursors such as **1**. Enantioselective oxidation to peroxides **2** and **3** (in 97:3 ratio) was catalysed by soybean lipoygenase. **2** and **3** were then reduced to alcohols **4** and **5** by the addition of horseradish peroxidase. Total yields for the two steps of 50-60% and enantiomeric excesses of >98% were reported. **5** and **6** were saponified with base to yield the diene diol products.

J. S. Yadav, S. Nanda and A. B. Rao, *Synlett*, 2001, 787.

Oxidative ring cleavage of some heterocyclic quinones*Streptomyces platensis* NRRL 2364

L. Le Texier, S. Roy, C. Fosse, M. Neuwels and R. Azerad,
Tetrahedron Lett., 2001, **42**, 4135.

Of 8 substrates tested, only 4 were metabolised with yields from 30-65%. The expected lactone Baeyer–Villiger product was not observed in any of the products.

Enzyme assisted preparation of isotopically labeled 1-deoxy-D-xylulose 5-phosphate*Synthase*

S. Hecht, K. Kis, W. Eisenreich, S. Amslinger, J. Wümgintaweekul, S. Herz, F. Rohdich and A. Bacher, *J. Org. Chem.*, 2001, **66**, 3948.

The synthase was used to prepare ^{13}C or ^{14}C labeled isotopomers of **3** by condensation of appropriately isotope-labeled pyruvate **1** with glyceraldehyde 3-phosphate **2** in a one pot reaction.