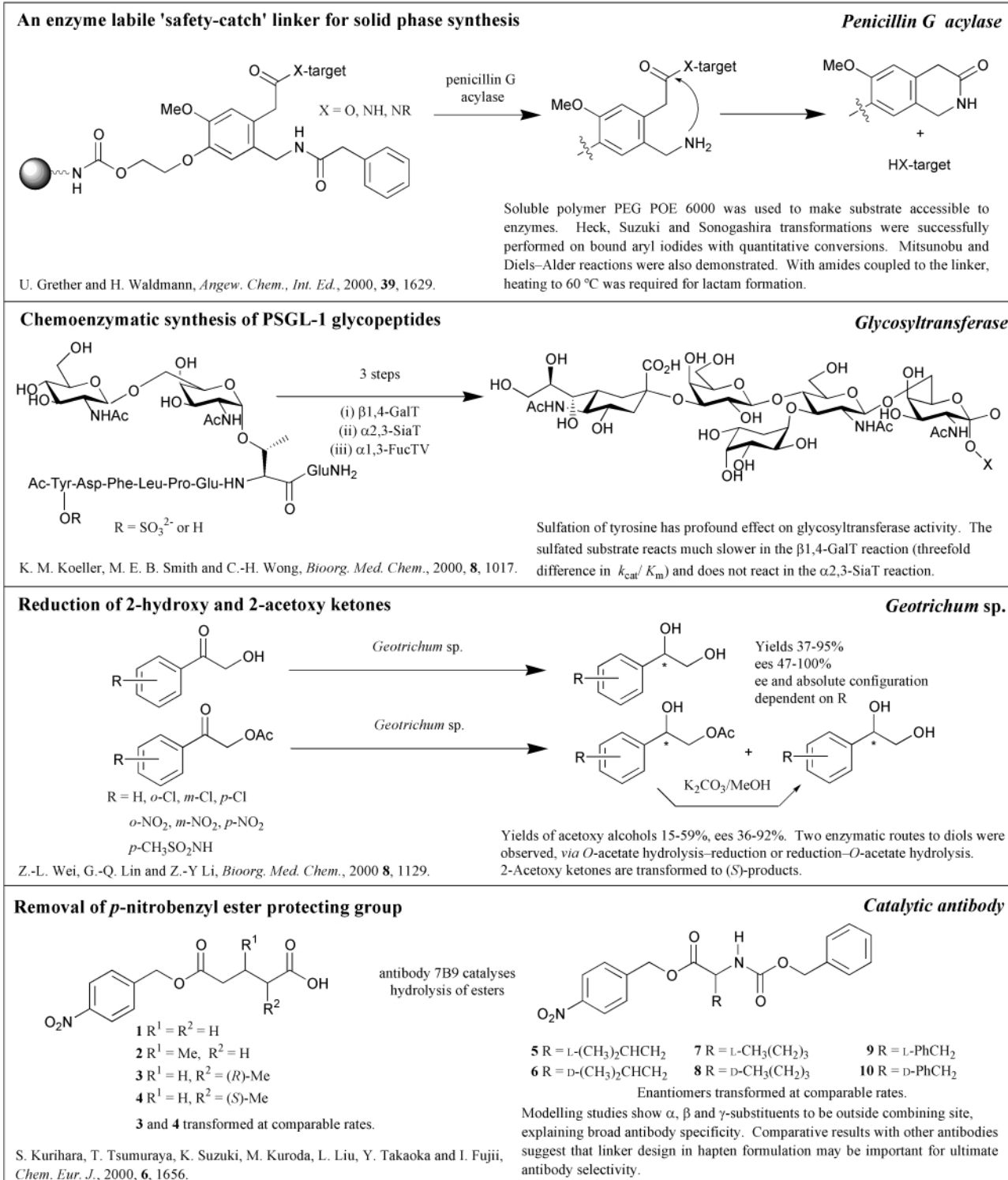


Gideon Grogan, Alexis Carstairs, Ian Jackson, Denise McIntyre, Alan Watt, Sabine Flitsch and Nicholas Turner

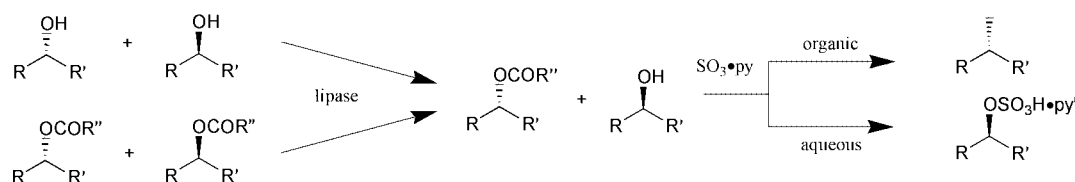
Department of Chemistry, The University of Edinburgh, King's Buildings, West Mains Road, Edinburgh, UK EH9 3JJ

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.



Resolution of alcohols *via* lipase catalysed transformation and sulfation

Lipase

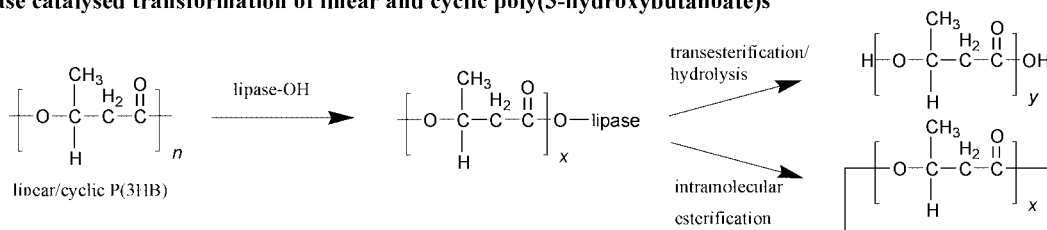


T. Yamano, F. Kikumoto, S. Yamamoto, K. Miwa, M. Kawada, T. Ito, T. Ikemoto, K. Tomimatsu and Y. Mizuno, *Chem. Lett.*, 2000, 448.

A method for the large scale isolation of enantiopure alcohols or esters is presented, using sulfur trioxide-pyridine for alcohol complexation and solvation in the aqueous phase. Six lipases were used successfully. Six structural examples are given. 1-(*R*)-Phenylethanol was isolated in 42% yield with 99% ee.

Lipase catalysed transformation of linear and cyclic poly(3-hydroxybutanoate)s

Lipase

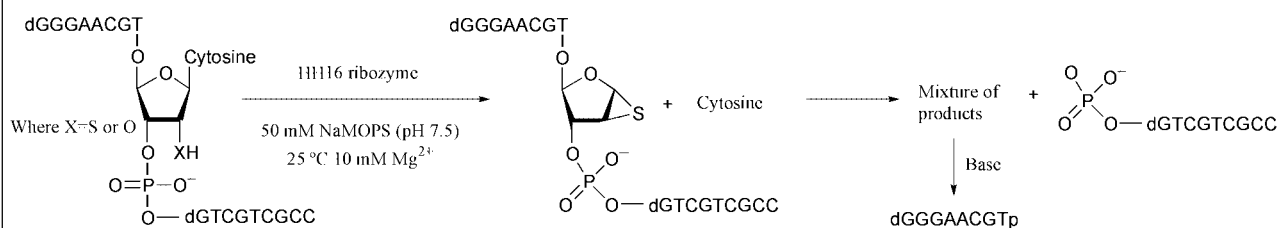


Y. Osanai, K. Toshima and S. Matsumura, *Chem. Lett.*, 2000, 576.

Linear and cyclic P(3HB) polymer species were subjected to hydrolysis, transesterification and intramolecular esterification by lipase. Two series of polymers of linear and cyclic structures were observed, having variable molecular weights of higher and lower mass than that of the substrate.

Deglycosylation of 2'-mercaptoctidine

Hammerhead Ribozyme

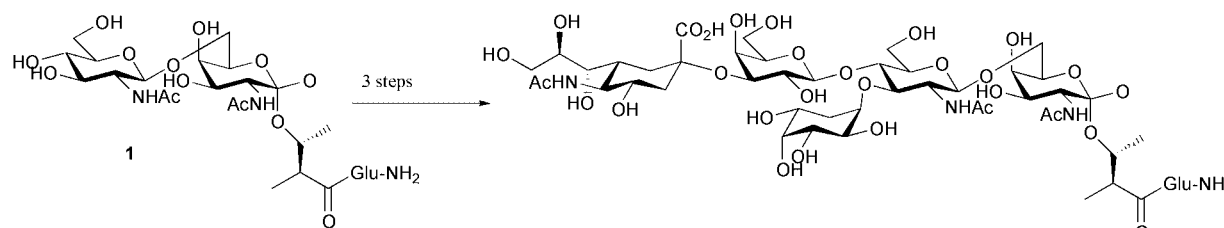


M. L. Hamm, J. P. Schwans and J. A. Piccirilli, *J. Am. Chem. Soc.*, 2000, **122**, 4223.

When X = O the 1H116 ribozyme catalyses a phosphotransesterification reaction.

Chemoenzymatic synthesis of a PSGL-1 N-terminal glycopeptide

Glycosyltransferase

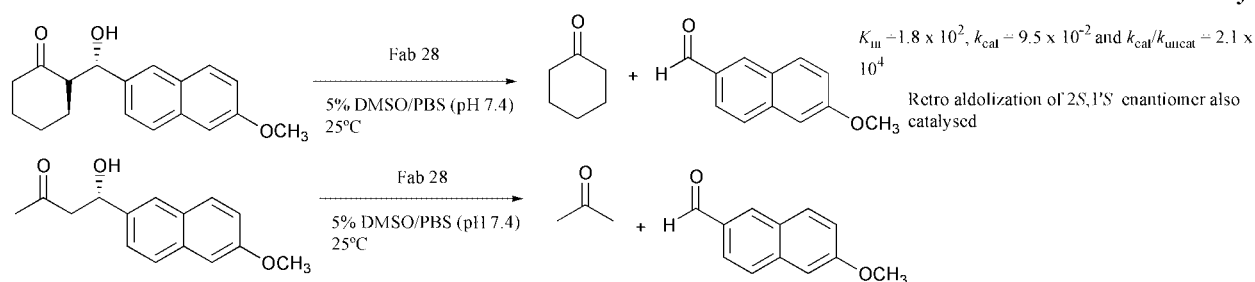


K. M. Koeller, M. E. B. Smith, R.-F. Huang and C.-H. Wong, *J. Am. Chem. Soc.*, 2000, **122**, 4241.

Glycoconjugate 1 was constructed using Fmoc-based SPPS and transformed using β -1,4-galactosyltransferase, α -2,3-sialyltransferase and α -1,3-fucosyltransferase-V. The yields of each glycosyltransferase step were improved by the addition of a protease inhibitor cocktail.

Reconstructed aldolase antibodies

Aldolase antibody

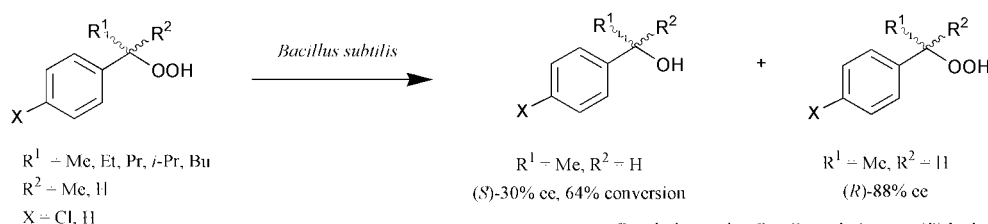


F. Tanaka, R. A. Lerner and C. F. Barbas III, *J. Am. Chem. Soc.*, 2000, **122**, 4835.

Gene shuffling was used to reconstruct aldolase antibodies while retaining the catalytic residues, mechanism and enantioselectivity of the parental antibodies.

Kinetic resolution of racemic hydroperoxides

Bacillus subtilis/
Aspergillus niger

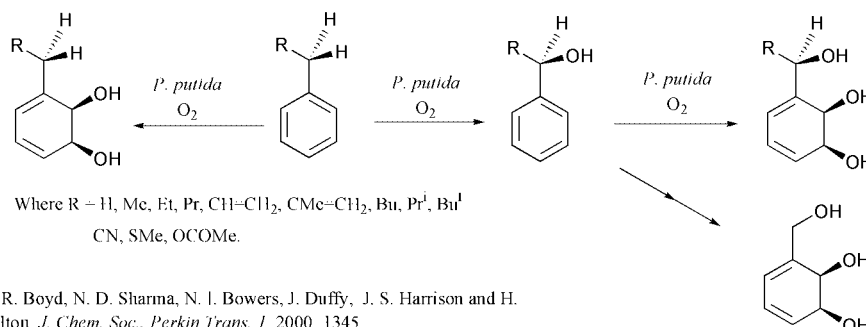


W. Adam, Z. Lukacs, C. R. Saha-Möllner and P. Schreiber, *J. Am. Chem. Soc.*, 2000, 122, 4887.

Resolutions using *Bacillus subtilis* gave (*R*)-hydroperoxides with ees of 16-99% depending on extent of conversion. Reactions were less enantioselective when R^1 was larger or $X = \text{Cl}$. *A. niger* gave (*S*)-hydroperoxides with poorer enantioselectivities in general.

Di- and tri-hydroxylation of monosubstituted benzenes

Dioxygenase

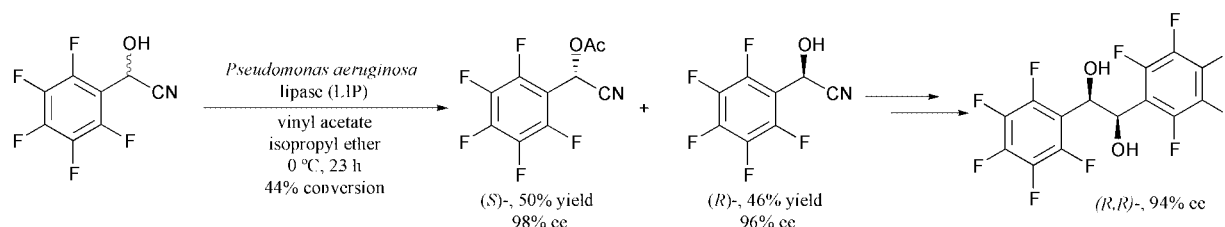


D. R. Boyd, N. D. Sharma, N. I. Bowers, J. Duffy, J. S. Harrison and H. Dalton, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1345.

Transformations carried out using mutant strain (UV4) of *Pseudomonas putida*. The (*1S,2R*) *cis*-dihydrodiols were formed in yields ranging from 9-60% and typical ees of >98% were obtained. Dioxygenase catalysed oxidation of benzene rings can result in either benzylic mono hydroxylation or *cis*-dihydroxylation depending on the size and nature of the benzylic substituent. In some cases the formation of benzylic alcohol metabolites, followed by spontaneous decomposition to benzaldehyde and oxidation to the *cis*-dihydrodiol of benzyl alcohol has been observed.

Synthesis of perfluoro-1,2-diols

Lipase

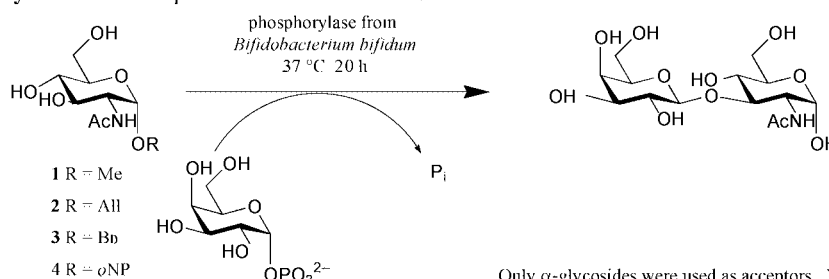


T. Sakai, Y. Miki, M. Tsuboi, H. Takeuchi, T. Ema, K. Uneyama and M. Utaka, *J. Org. Chem.*, 2000, 65, 2740.

The (*S*)-acetate was chemically hydrolysed and then used to synthesise the (*S,S*)-antipode in 91% ee. Crystallisation improved the ee of both compounds to >99%.

Enzymatic synthesis of Gal-β-1-3GlcNAc derivatives

Phosphorylase

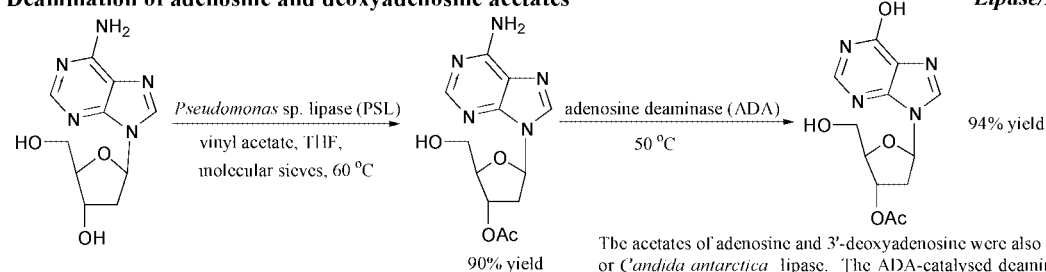


E. Farkas, J. Thiem, F. Krzewinski and S. Bouquetlet, *Synlett*, 2000, 728.

Only α -glycosides were used as acceptors. Yields of 14-30% could be improved if 1.2 molar equivalents acceptor used instead of 1. No reaction was observed with substrate 4.

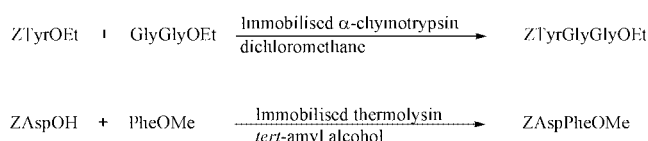
Deamination of adenosine and deoxyadenosine acetates

Lipase/Adenosine deaminase



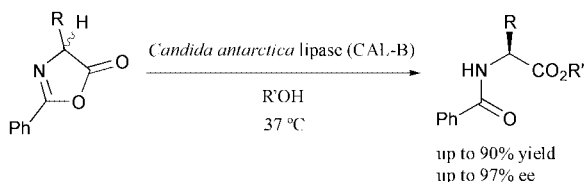
P. Ciuffreda, S. Casati and E. Santaniello, *Tetrahedron*, 2000, 56, 3239.

The acetates of adenosine and 3'-deoxyadenosine were also prepared using either PSL or *Candida antarctica* lipase. The ADA-catalysed deamination of each acetate was carried out. Only acetates with free 5'-hydroxy groups react to afford the corresponding inosine acetates confirming that the 5'-hydroxy group plays a crucial role at the ADA active site.

Zeolite immobilised enzymes in peptide synthesis
Protease


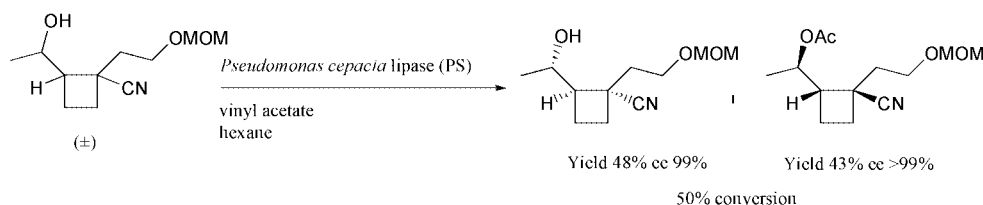
The effectiveness of α -chymotrypsin and thermolysin immobilised on a range of zeolites has been investigated. The reusability, effect of changing reaction time and percentage of water in the solvent were studied.

G.-W. Xing, X.-W. Li, G.-L. Tian and Y.-H. Ye, *Tetrahedron*, 2000, **56**, 3517.

Dynamic kinetic resolution: synthesis of optically active α -amino acid derivatives
Lipase


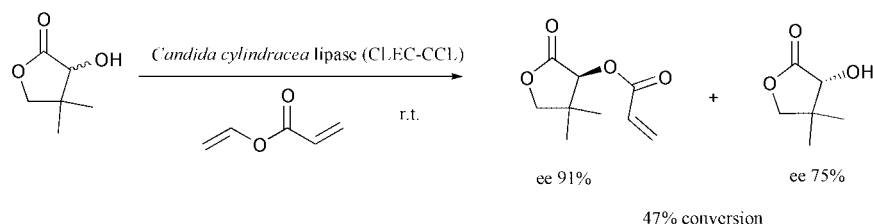
CAL-B has been shown to be effective in catalysing the synthesis of optically active α -amino acid derivatives. Yields and ees vary according to solvent, R, R' and presence of organic base.

S. A. Brown, M.-C. Parker and N. J. Tumer, *Tetrahedron: Asymmetry*, 2000, **11**, 1687.

Preparation of optically active cyclobutane derivatives
Lipase


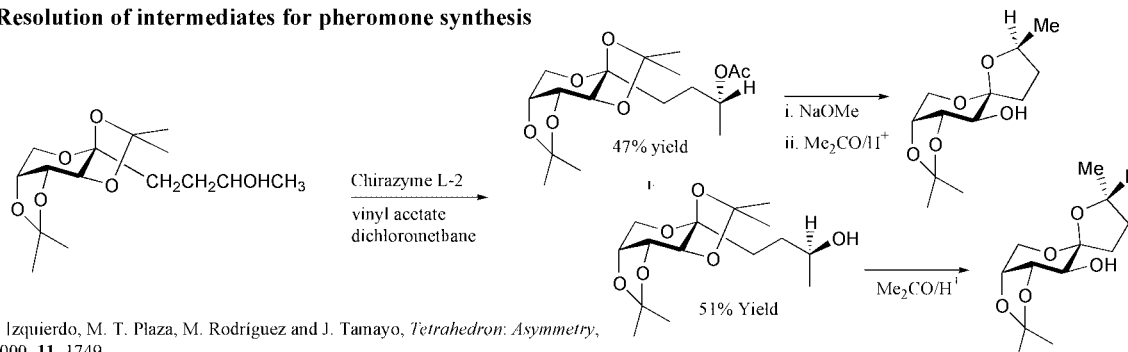
A chiral intermediate for the synthesis of grandisol and oleander scale pheromone has been prepared by transesterification in the presence of Lipase PS or *Pseudomonas fluorescens* lipase.

I. Petschen, M. P. Bosch and A. Guerrero, *Tetrahedron: Asymmetry*, 2000, **11**, 1691.

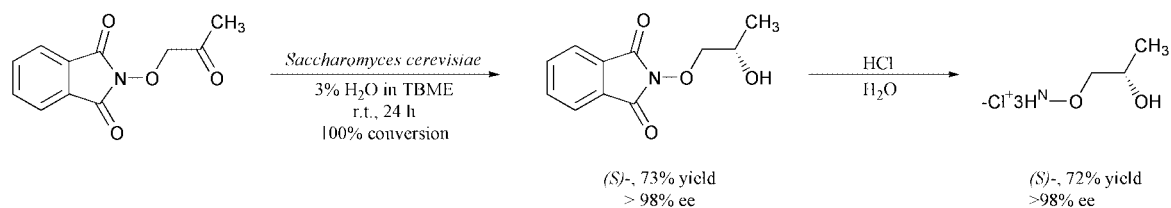
Highly enantioselective synthesis of pantolactone acrylate
Lipase


Lipase catalysed resolution of pantolactone has been investigated. Conversion and ees depend on solvent, reaction time and concentration of acyl donor and enzyme (CLEC-CCl).

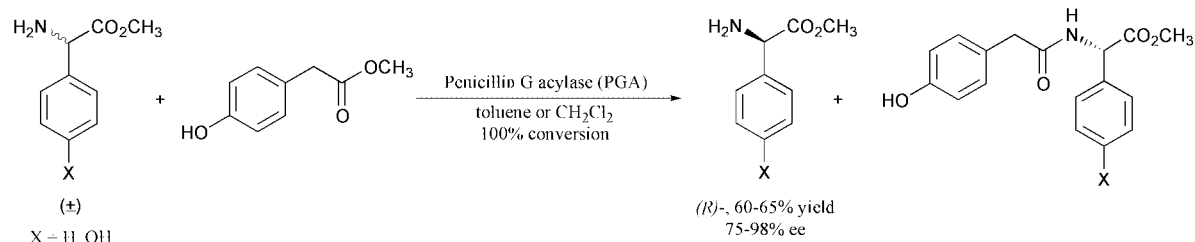
I. Haughton, J. M. J. Williams and J. A. Zimmermann, *Tetrahedron: Asymmetry*, 2000, **11**, 1697.

Resolution of intermediates for pheromone synthesis
Lipase


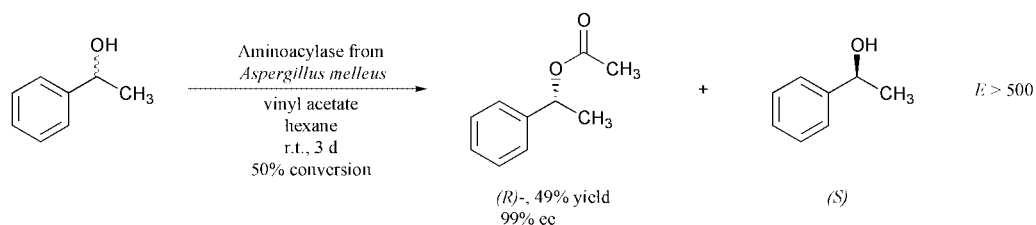
I. Izquierdo, M. T. Plaza, M. Rodríguez and J. Tamayo, *Tetrahedron: Asymmetry*, 2000, **11**, 1749.

Reduction of oxyaminoketones
Saccharomyces cerevisiae

 E. Buchalska, I. Madura, K. Okrasa, J. Plenkiewicz and J. Zachara, *Tetrahedron: Asymmetry*, 2000, 11, 1781.

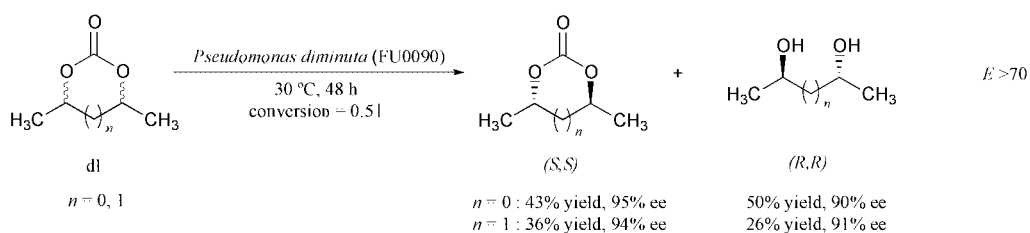
First report of the preparation of optically active oxyamino alcohols. The stereochemistry of the product was confirmed by X-ray crystallography.

Resolution of phenylglycine in organic solvents
Acylase

 A. Basso, P. Braiņa, L. De Martin, C. Ebert, L. Gardossi and P. Linda, *Tetrahedron: Asymmetry*, 2000, 11, 1789.

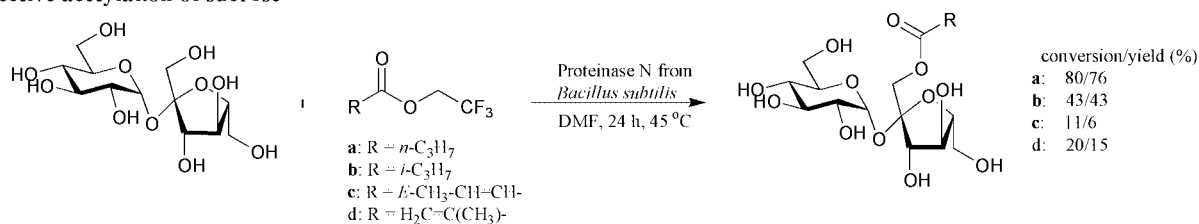
 Enantioselectivity of PGA in organic solvents is demonstrated. The stereochemistry of the products was confirmed by electrospray mass spectrometry and kinetic studies. *t*-enantiomer of the methyl ester of phenylglycine reacts 18 times faster than the *D*-enantiomer.

Resolution of secondary alcohols
Aminoacylase

 M. Bakker, A. S. Spruijt, F. van Rantwijk and R. A. Sheldon, *Tetrahedron: Asymmetry*, 2000, 11, 1801.

The transesterification of secondary alcohols by an aminoacylase was studied and shown to proceed with higher productivity than the corresponding lipase reaction. A variety of secondary alcohols were investigated and the reaction rates and stereochemical results rationalised in terms of the active site. Yields ranged from 22-47%.

Hydrolysis of cyclic carbonates
Pseudomonas diminuta

 K. Matsumoto, Y. Sato, M. Shimojo and M. Hatanaka, *Tetrahedron: Asymmetry*, 2000, 11, 1965.

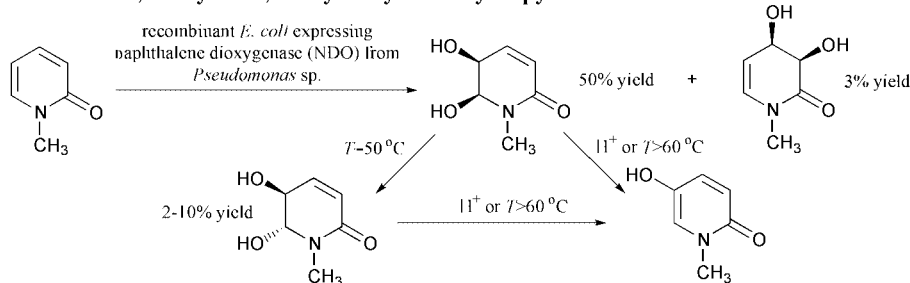
 When $n = 0$, THF is added to inhibit side-reactions caused by oxido-reductases present in the organism.

Selective acetylation of sucrose
Protease

 P. Potier, A. Bouchu, G. Descotes and Y. Queneau, *Tetrahedron Lett.*, 2000, 41, 3597.

Faster reactions were obtained with up to 7% (vol.) of water in DMF. A slurry of the enzyme with a minimum volume of aqueous dimethyl sulfoxide could also be used offering an alternative solvent.

Synthesis of *cis*-5,6-dihydro-5,6-dihydroxy-1-methyl-2-pyridone

Dioxygenase

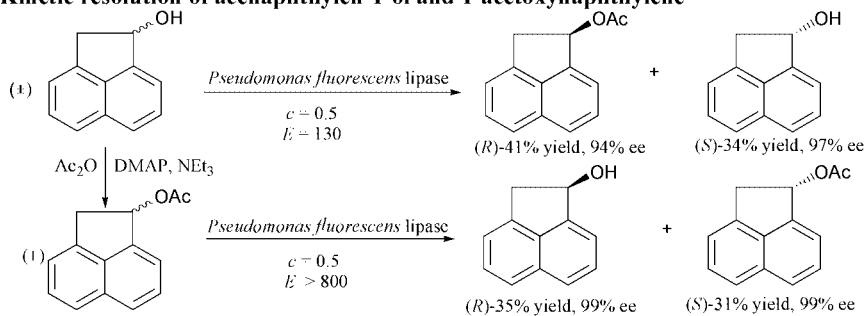


L. Modyanova and R. Azerad, *Tetrahedron Lett.*, 2000, 41, 3865.

First example of NDO catalysed *cis*-dihydroxylation of a monoheterocyclic nitrogen compound.

Kinetic resolution of acenaphthen-1-ol and 1-acetoxynaphthylene

Lipase

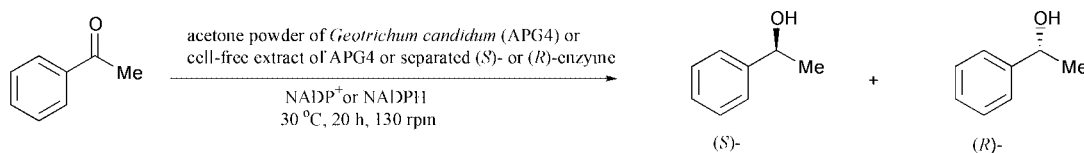


L. Arbi-Zouineche and J.-C. Fiaud, *Tetrahedron Lett.*, 2000, 41, 4085.

Flexible analogues 1-(1-naphthyl)ethyl acetate and 1-(1-naphthyl)ethanol were inactive under the same reaction conditions. Rabbit gastric lipase gave poor enantioselectivities for all substrates.

Asymmetric reduction of acetophenone

Geotrichum candidum



T. Matsuda, T. Harada, N. Nakajima and K. Nakamura, *Tetrahedron Lett.*, 2000, 41, 4135.

The mechanism of improved asymmetric reduction with APG4 was elucidated by using the cell-free extract of APG4 in the presence and absence of cyclopentanol with either NADP⁺ or NADPH as cofactor. Only the (*S*)-enzyme but not the (*R*)-enzyme can use cyclopentanol for recycling of NADPH which explains the high stereoselectivity of the APG4 system.