

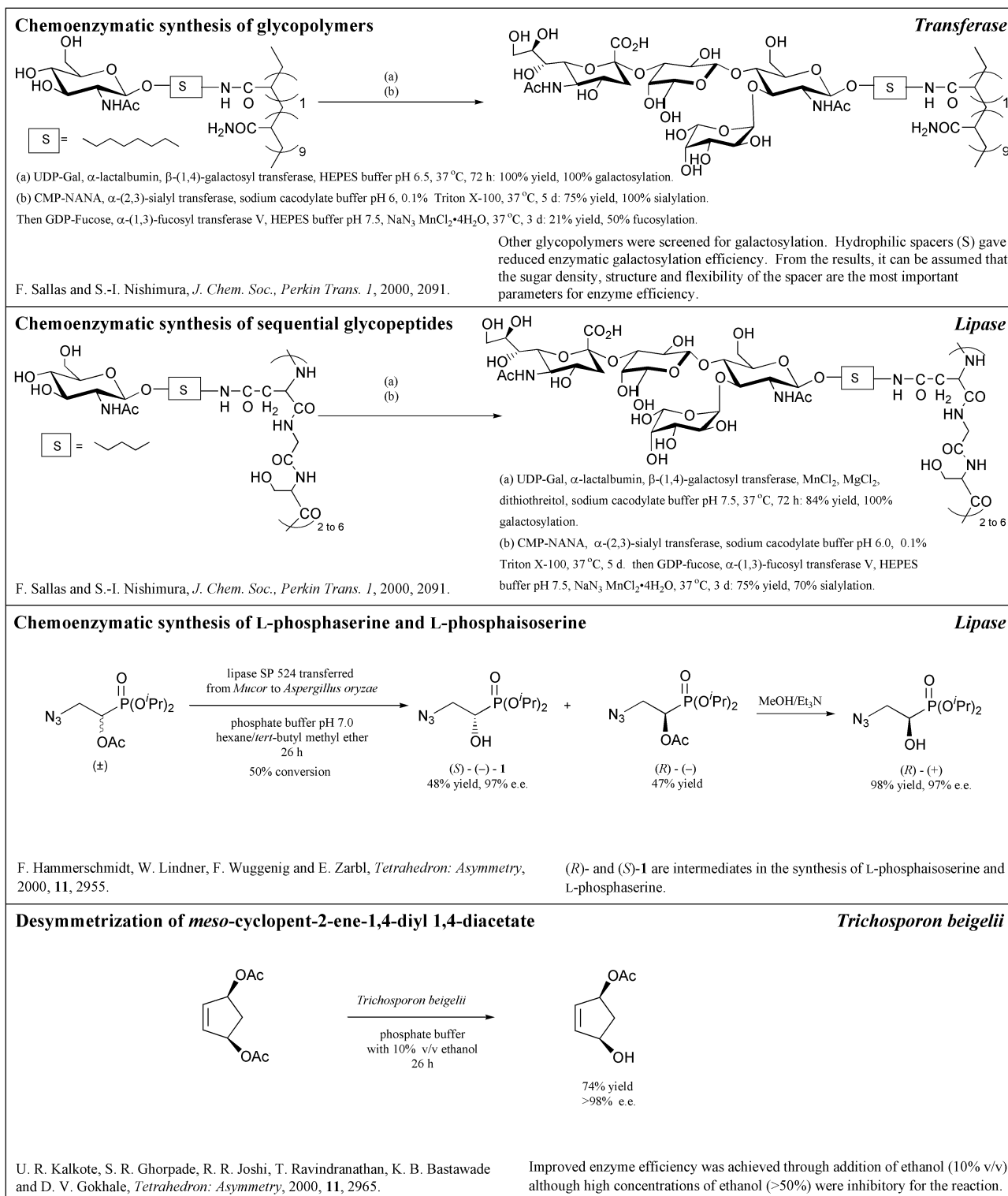
Perkin 1 Abstracts: Biocatalysis in Organic Synthesis

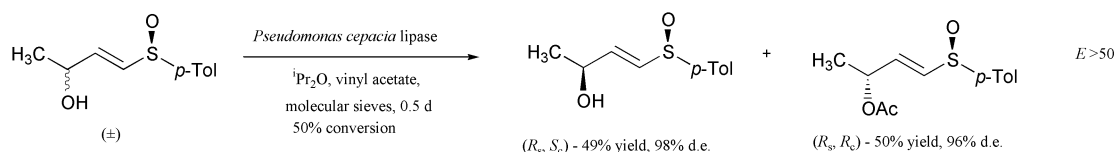
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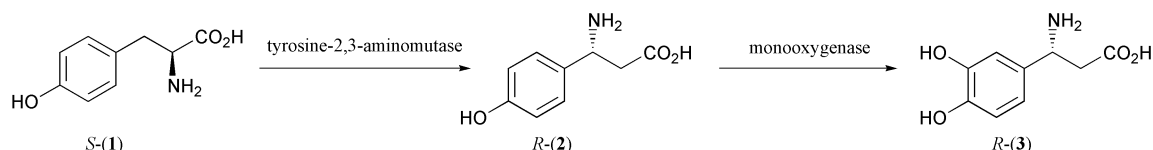
Perkin 1 Abstracts: Biocatalysis in Organic Synthesis aims to cover recent literature concerning the applications of enzymes and micro-organisms as catalysts in organic synthesis. The abstracts will emphasise the key synthetic step(s) that are mediated by the biocatalyst. Emerging technologies for biocatalyst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



Resolution of (*E*)- γ -hydroxy- α,β -unsaturated *p*-tolylsulfoxides
Lipase


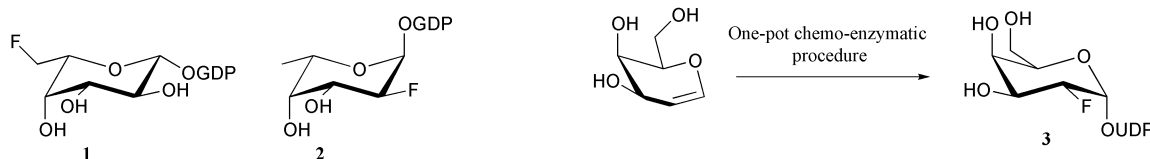
V. G. de la Rosa, M. Ordóñez and J. M. Llera, *Tetrahedron: Asymmetry*, 2000, **11**, 2991.

Various γ -analogues (^tPr, ^tBu, Pent, Et) were screened to study the reactivity and diastereoselectivity of the enzymatic reaction.

Discovery of a novel tyrosine-2,3-aminomutase
2,3-Aminomutase


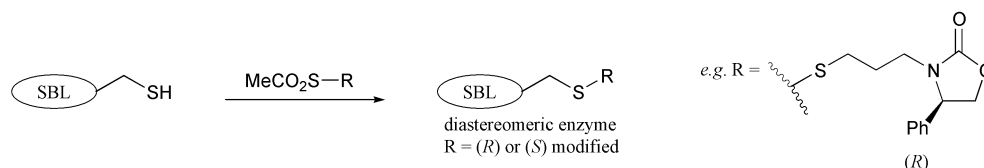
P. Spittler, M. Rùth, F. von Nussbaum and W. Steglich, *Angew. Chem., Int. Ed.*, 2000, **39**, 2754.

Labelling studies were used to determine the biosynthetic pathway of the mushroom *Cortinarius violaceus*. Tyrosine-2,3-aminomutase was identified which is the first aminomutase to be detected in fungus. Additional labelling studies confirmed that β -tyrosine (2) was not formed through an addition-elimination mechanism.

Synthesis of fluorinated sugar nucleotides and their use as mechanistic probes
Glycosyltransferase


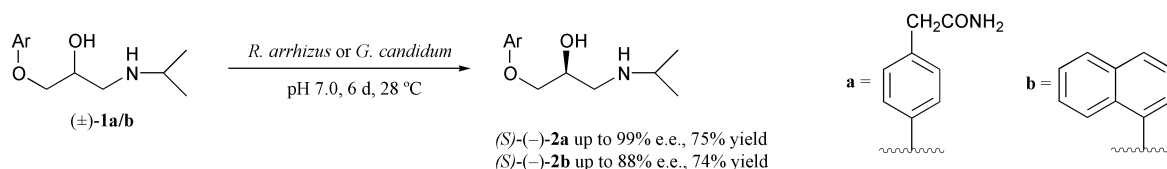
M. D. Burkart, S. P. Vincent, A. Düffels, B. W. Murray, S. V. Ley and C.-H. Wong, *Bioorg. Med. Chem.*, 2000, **8**, 1937.

Three fluorinated sugars (1-3) were synthesised. A one-pot procedure for the synthesis of the UDP-2-deoxy-2-fluoro galactose (3) which utilised galactokinase, acetate kinase, then galactose-1-phosphate uridylyltransferase, pyrophosphorylase and pyrophosphatase was reported. These compounds were used to investigate the mechanism of action of fucosyltransferases, sialyltransferase and galactosyltransferase.

Chemical modification of Subtilisin *Bacillus lentus* (SBL)
Hydrolase


M. Dickman and J. B. Jones, *Bioorg. Med. Chem.*, 2000, **8**, 1957.

Subtilisin *Bacillus lentus* cysteine mutants were subjected to chemical modification. The effectiveness of the resulting modified mutants as amidases and esterases was investigated. Various R groups were examined as chiral modifiers. The most remarkable change in the enzyme activity was observed for the R group shown, modifying the N62C mutant *e.g.* esterase activity was 5.4 fold better than the wild type.

Preparation of (*S*)-Atenolol and (*S*)-Propranolol
Rhizopus arrhizus* / *Geotrichum candidum


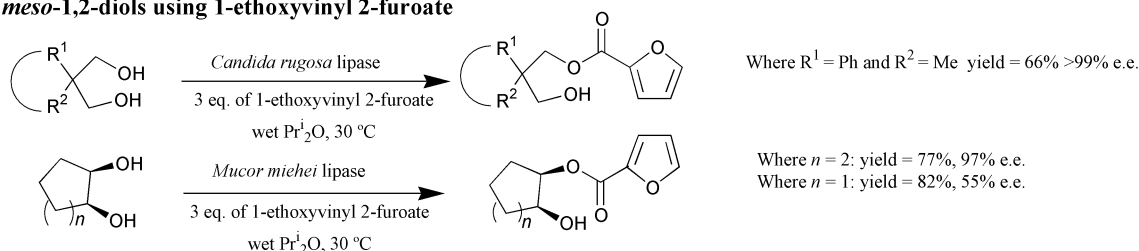
S. V. Damle, P. N. Patil and M. M. Salunkhe, *Bioorg. Med. Chem.*, 2000, **8**, 2067.

Novel preparation of (*S*)-Atenolol (2a) and (*S*)-Propranolol (2b) using the fungi *Rhizopus arrhizus* and *Geotrichum candidum*. The advantage over previous synthesis is the simplicity of the reaction. The organisms also metabolise the (*R*)-acetates but with lower enantioselectivity.

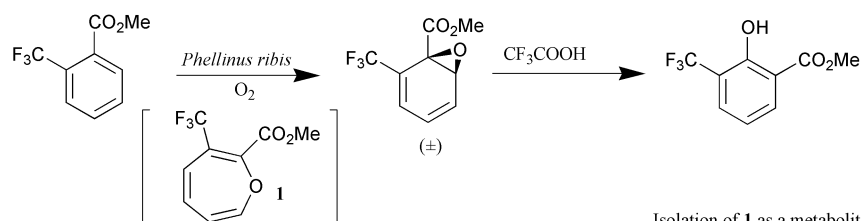
Alcohol dehydrogenase is active in supercritical carbon dioxide
Dehydrogenase

 T. Matsuda, T. Harada and K. Nakamura, *Chem. Commun.*, 2000, 1367.

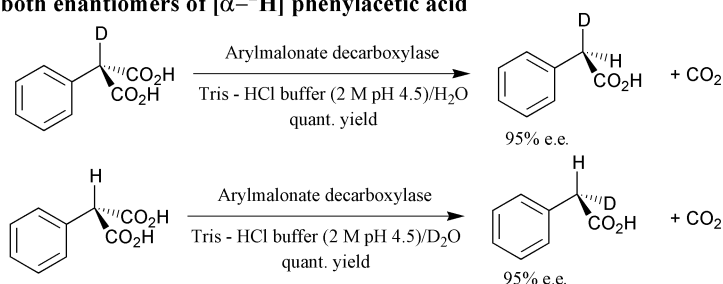
 Various ketones were studied giving yields in the range 11 to 96% and e.e. from 96 to >99%. The effect of fluorine substitution at the *ortho*, *para* and α position was also studied. Substitution *ortho* and α increased the yield while *para* substitution led to decreased yields.

Enantioselective desymmetrization of prochiral 2,2-disubstituted propane-1,3-diols and meso-1,2-diols using 1-ethoxyvinyl 2-furoate
Lipase

 S. Akai, T. Naka, T. Fujita, Y. Takebe and Y. Kita, *Chem. Commun.*, 2000, 1461.

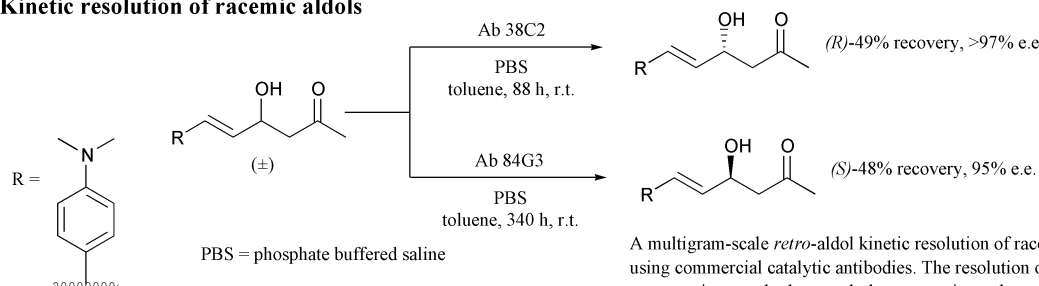
Several other examples are given for congested diols (yields range from 35 to 93%, 61 to 92% e.e.) An improvement in optical purity was observed by prolonging the reaction time and hydrolysing any diester formed.

Isolation of stable benzene oxide and evidence for an NIH shift of the carboxymethoxy group during hydroxylation of methyl benzoates
Phellinus ribis

 D. R. Boyd, J. T. G. Hamilton, N. D. Sharma, J. S. Harrison, W. C. McRoberts and D. B. Harper, *Chem. Commun.*, 2000, 1481.

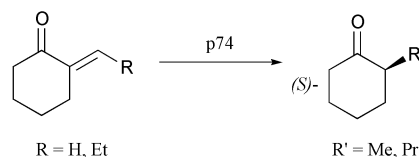
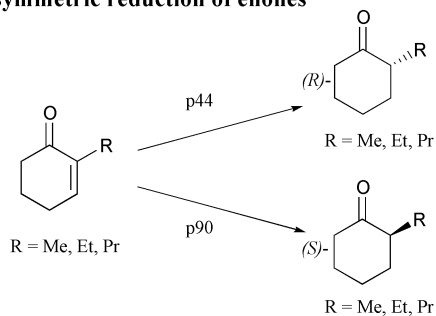
 Isolation of **1** as a metabolite provides evidence that *o*-hydroxylation of methyl benzoates proceeds *via* benzene oxide intermediates. This is the first report of a hydrogen atom migration from the hydroxylation site and its retention at an adjacent carbon atom ('NIH shift').

Synthesis of both enantiomers of [α -²H] phenylacetic acid
Decarboxylase

 K. Matoishi, S. Hanzawa, H. Kakidani, M. Suzuki, T. Sugai and H. Ohta, *Chem. Commun.*, 2000, 1519.

 Arylmalonate decarboxylase (EC. 4. 1. 1. 76) was obtained by overexpression in *E. coli* JM 109.

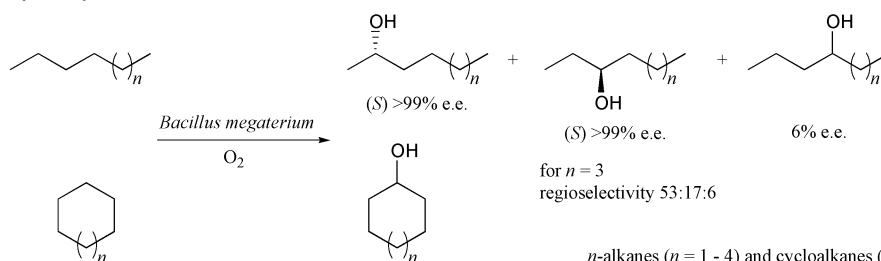
Kinetic resolution of racemic aldols
Aldolase antibodies

 J. M. Turner, T. Bui, R. A. Lerner, C. F. Barbas III and B. List, *Chem. Eur. J.*, 2000, 6, 2772.

 A multigram-scale *retro*-aldol kinetic resolution of racemic aldols was developed using commercial catalytic antibodies. The resolution offers a number of advantages over previous methods, namely lower reaction volumes, the ability to recycle the catalyst and mild reaction conditions. The scope of the reaction was examined and other racemic aldols were resolved with yields of 44-50% and e.e.'s of 97-99%.

Asymmetric reduction of enones
Nicotiana tabacum


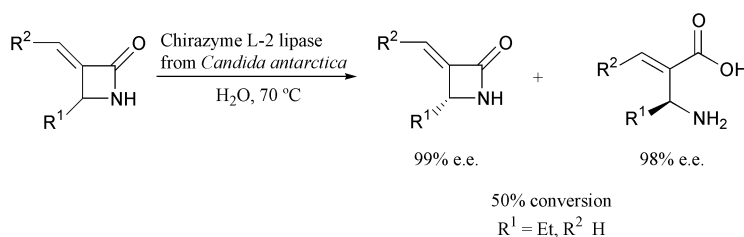
Three enone reductases, p44, p74 and p90, isolated from *Nicotiana tabacum*, were used to asymmetrically reduce the C-C double bond of enones. Complementary reactivity was observed, with both *endo*- and *exo*-cyclic double bonds being reduced in moderate to high e.e. (75-99%) and yield (35-99%).

T. Hirata, K. Shimoda and T. Gondai, *Chem. Lett.*, 2000, 850.

Asymmetric hydroxylation of unactivated alkanes
Monoxygenase


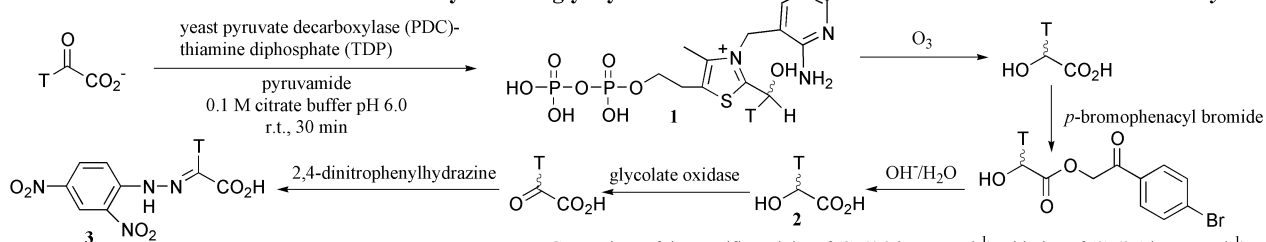
W. Adam, Z. Lukacs, C. R. Saha-Möller, B. Weckerle and P. Schreier, *Eur. J. Org. Chem.*, 2000, 2923.

n-alkanes ($n = 1 - 4$) and cycloalkanes ($n = 1$ and 3) were subjected to biohydroxylation by *B. megaterium*. Overoxidation to the corresponding ketone was observed to increase with n , and more markedly for the cyclic systems.

Lipase resolution of α -methylene β -lactams
Lipase


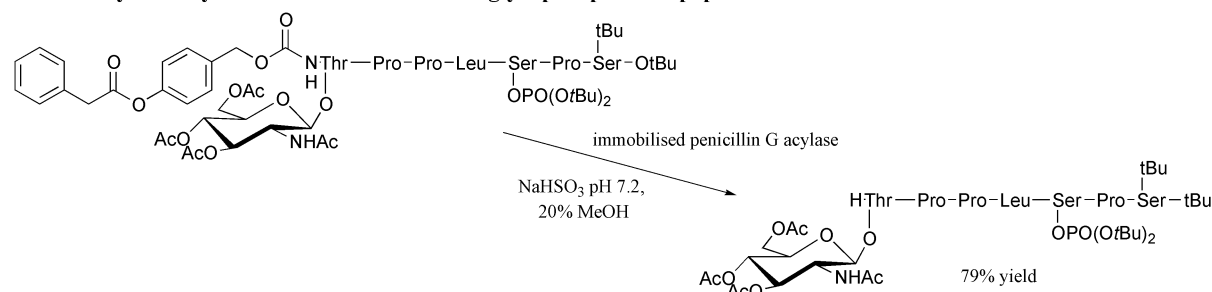
W. Adam, P. Groer, H.-U. Humpf and C.R. Saha-Möller, *J. Org. Chem.*, 2000, 65, 4919.

The β -lactams were resolved using lipase L-2. Three substrates, with variations in R^1 and R^2 were tested. Other enzymes tested were found to be less effective.

Stereochemical elucidation of the decarboxylation of glyoxylic acid
Decarboxylase


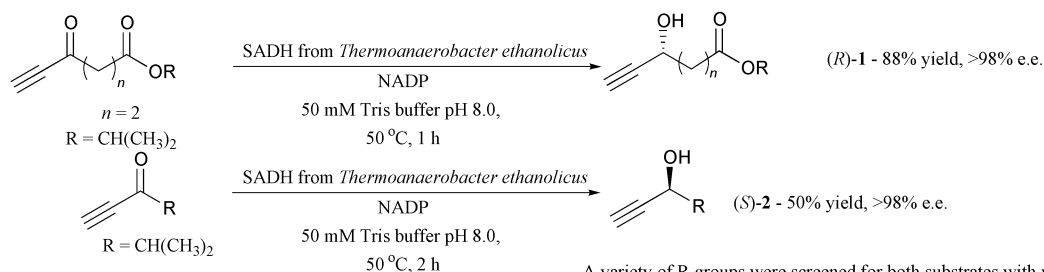
H. Vegad, M. Lobell, S. Bornemann and D. H. G. Crout, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2317.

Comparison of the specific activity of (2) ($4.2 \text{ kBq mmol}^{-1}$) with that of (3) ($2.1 \text{ kBq mmol}^{-1}$) indicated that half of the tritium label had been lost from (2) and it was concluded that (1) was pyruvate decarboxylase.

Chemoenzymatic synthesis of a biotin-labelled glycoposphonapeptide
Acylyase


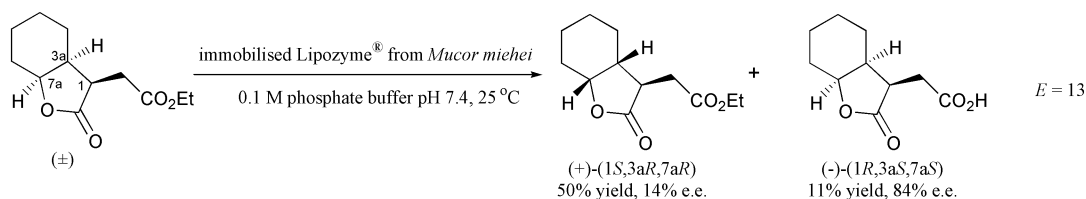
T. Kappes-Roth and H. Waldmann, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2579.

Intermediate in the synthesis of a glycoposphonapeptide of the c-Myc oncoprotein.

Asymmetric reduction of ethynyl ketones and ethynylketoesters
Secondary alcohol dehydrogenase (SADH)


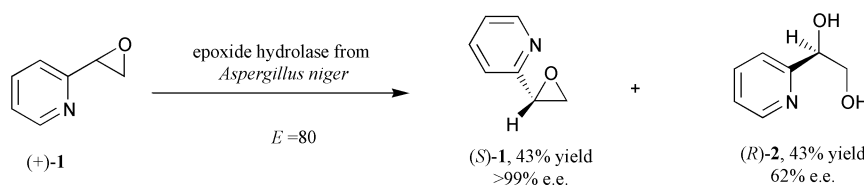
A variety of R groups were screened for both substrates with varying success. Larger ethynyl ketones **2** (e.g. R = CH₂CH(CH₃)₂) were reduced to afford the complementary (R)-alcohols.

C. Heiss and R. S. Phillips, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2821.

Resolution of (1*R*^{*},3*aS*^{*},7*aS*^{*})-hexahydro-2-oxobenzofuran-3-ylacetic acid ethyl ester
Lipase


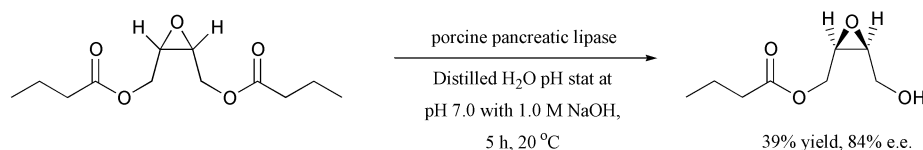
At higher conversion values (64%) the (+)-ester was obtained in 30% yield with 98% e.e. Other lipases were screened. Horse liver acetone powder (HLAP) showed enantiocomplementary activity with respect to Lipozyme[®].

S. Drioli, F. Felluga, C. Forzato, G. Pitacco and E. Valentin, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2839.

Preparation of enantiopure (S)-2-pyridyloxirane
Epoxide hydrolase


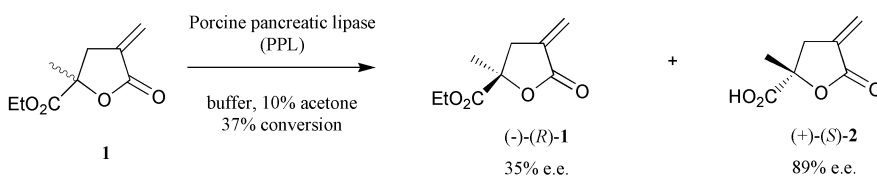
(S)-Pyridyloxirane **1** was resolved using *Aspergillus niger* epoxide hydrolase (AnEH). Enzymatic attack occurs almost exclusively at the β-carbon of each enantiomer of the substrate, resulting in retention of configuration in the diol product.

Y. Genzel, A. Archelas, Q. B. Broxterman, B. Schulze and R. Furstoss, *Tetrahedron: Asymmetry*, 2000, **11**, 3041.

Optimisation of lipase-catalysed hydrolysis of meso-oxiranedimethanol
Lipase


J. D. Moseley and J. Staunton, *Tetrahedron: Asymmetry*, 2000, **11**, 3197.

The butyrate ester was tested against a range of lipases (yields range from 13 to 39%, 6 to 84% e.e.) and optimisation of physical parameters was reported.

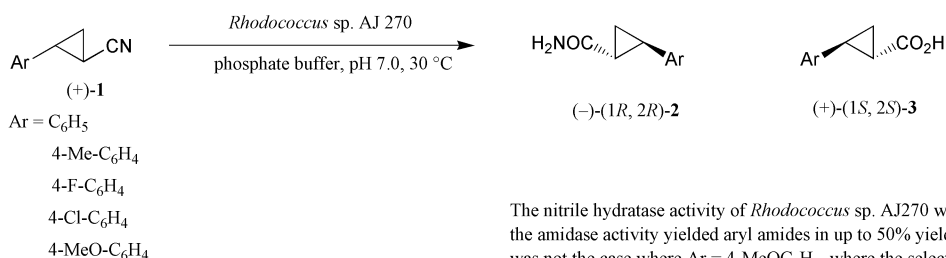
Resolution of an α-methylene-γ-lactonic ester
Lipase


G. Pitacco, A. Sessanta o Santi and E. Valentin, *Tetrahedron: Asymmetry*, 2000, **11**, 3263.

The enantiocomplementary resolution to the one illustrated was performed using *Candida rugosa* lipase to yield (-)-(R)-2 with 82% e.e. Sequential resolutions of optically active acids yielded e.e.s of 97% and 99% for (-)-(S)-2 and (-)-(R)-2 respectively.

Synthesis of chiral cyclopropanes

Rhodococcus sp.

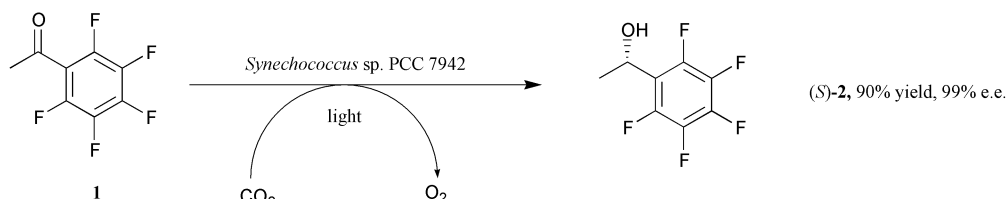


M.-X. Wang and G.-Q. Feng, *Tetrahedron Lett.*, 2000, **41**, 6501.

The nitrile hydratase activity of *Rhodococcus* sp. AJ270 was not stereoselective, but the amidase activity yielded aryl amides in up to 50% yield with >99% e.e. This was not the case where Ar = 4-MeOC₆H₄, where the selectivity was poor. Carboxylic acids were obtained in yields of up to 53% with e.e.s of up to 71%.

Asymmetric reduction of ketones by a cyanobacterium

Synechococcus sp.

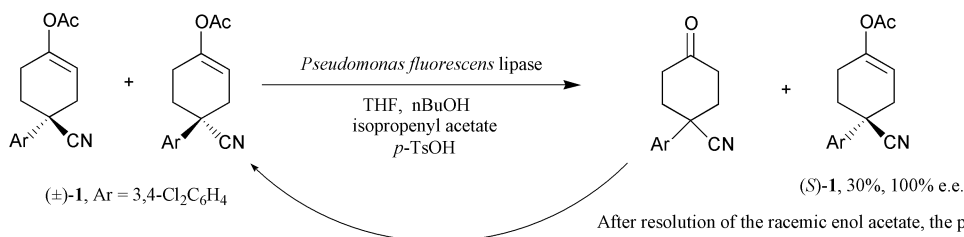


K. Nakamura, R. Yamanaka, K. Tohi and H. Hamada, *Tetrahedron Lett.*, 2000, **41**, 6799.

Synechococcus is a phototrophic cyanobacterium, which requires light and carbon dioxide to grow and perform transformations. In addition to the pentafluoroacetophenone **1** shown, a series of *o*-, *m*-, and *p*-substituted acetophenones are also accepted as substrate, where the substituent is F, Cl, Me and OMe. E.e.s of alcohols obtained were in the range 96-100%.

Resolution of an enol acetate

Lipase

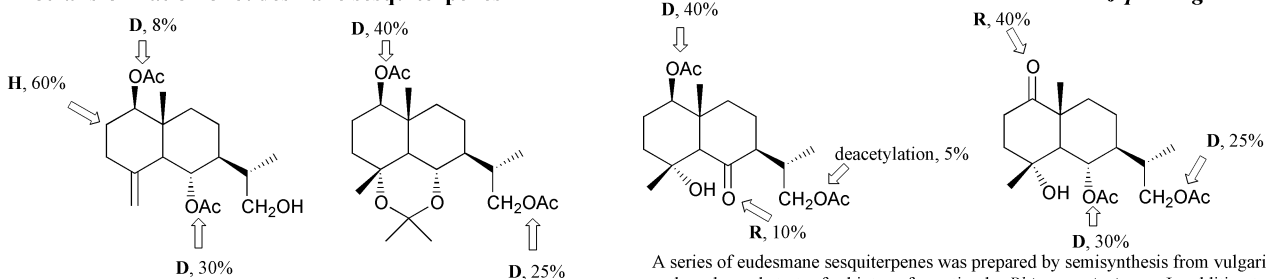


A. J. Carnell, M. L. Escudero Hernandez, A. Pettman and J. F. Bickley, *Tetrahedron Lett.*, 2000, **41**, 6929.

After resolution of the racemic enol acetate, the product ketone is recycled. After 68% conversion to ketone, enol acetate in 30% yield with 100% e.e. was recovered. This synthon was then used in a synthesis of a non-peptide tachykinin NK-2 antagonist.

Biotransformation of eudesmane sesquiterpenes

Rhizopus nigricans



A. Garcia-Granados, E. Melguizo, A. Parra, F.L. Pérez, Y. Simeó, B. Viseras and J. M. Arias, *Tetrahedron*, 2000, **56**, 6517.

A series of eudesmane sesquiterpenes was prepared by semisynthesis from vulgarin and used as substrates for biotransformation by *Rhizopus nigricans*. In addition to regioselective deacetylation (D), hydroxylations (H) and reductions (R) were observed, yielding a series of hydroxyselinane derivatives.