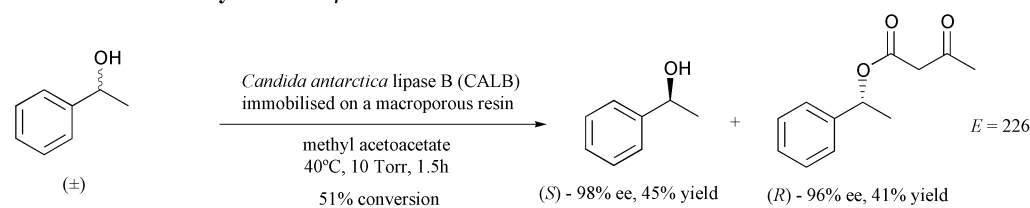
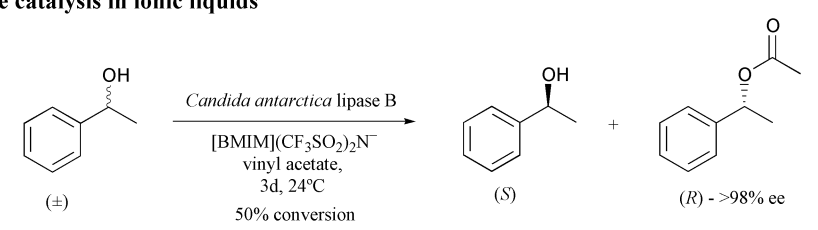
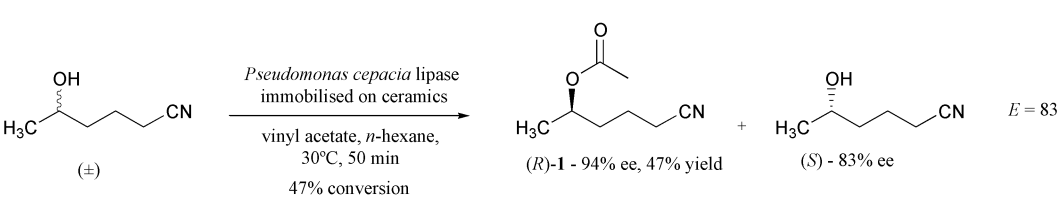
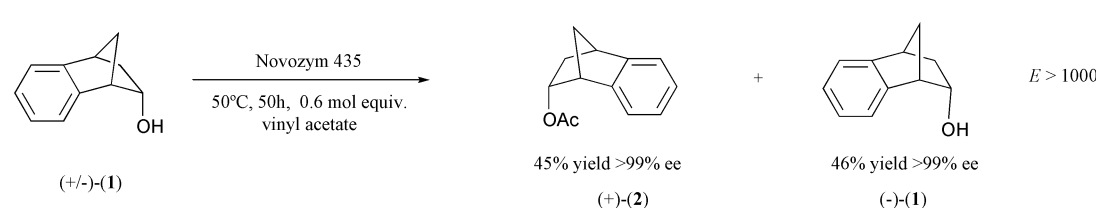


Gideon Grogan,<sup>a</sup> Alexis Carstairs,<sup>b</sup> Ian Jackson,<sup>b</sup> Denise McIntyre,<sup>b</sup> Alan Watt,<sup>b</sup> Sabine Flitsch<sup>b</sup> and Nicholas Turner<sup>b</sup>

<sup>a</sup> Department of Chemistry, University of York, Heslington, York, UK YO10 5DD

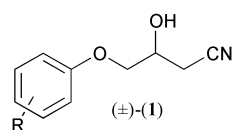
<sup>b</sup> Department of Chemistry, The University of Edinburgh, King's Buildings, West Mains Road, Edinburgh, UK EH9 3JJ

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.

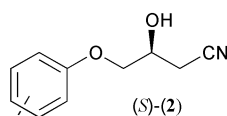
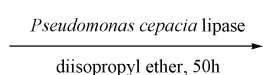
<p><b>Chemo- and stereoselective synthesis of <math>\beta</math>-keto esters</b></p>  <p>A. Córdova and K. D. Janda, <i>J. Org. Chem.</i>, 2001, <b>66</b>, 1906.</p>	<p><b>Lipase</b></p> <p>This method provides a simple route to optically active <math>\beta</math>-keto esters that are useful building blocks for natural product synthesis.</p>
<p><b>Enzyme catalysis in ionic liquids</b></p>  <p>S. Schöfer, N. Kaftzik, P. Wasserscheid and U. Kragl, <i>Chem. Commun.</i>, 2001, 425.</p>	<p><b>Lipase</b></p> <p>Nine lipases and two esterases were screened for activity in ten different ionic liquids. The lipases showed, in some cases, improved enantioselectivity in pure ionic liquids, however there was no activity observed for the two pig liver esterases.</p>
<p><b>Chemoenzymatic synthesis of (2R)-2-hydroxyundecan-6-one</b></p>  <p>E. Ljuboviae and V. Sunjiae, <i>Synthesis</i>, 2001, <b>3</b>, 423.</p>	<p><b>Lipase</b></p> <p>Several lipases were screened for activity. Substrate (R)-1 is the key intermediate in the synthesis of the title compound.</p>
<p><b>Resolution of racemic <i>endo</i>-benzonorbornenol</b></p>  <p>F. Fernández, X. García-Mera and J. E. Rodríguez-Borges, <i>Tetrahedron: Asymmetry</i>, 2001, <b>12</b>, 365.</p>	<p><b>Lipase</b></p> <p>A range of reaction conditions were investigated with yields of <b>2</b> in the range 36 to 49% and ee &gt;99%.</p>

### Resolution of $\beta$ -hydroxy nitriles

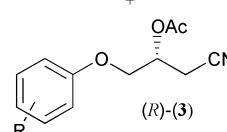
Lipase



R = H, 2-CH<sub>3</sub>, 4-CH<sub>3</sub>, 4-Cl, 4-Br,  
2,3-(CH=CH-CH=CH)- or 3,4-(CH=CH-CH=CH)-



When R = 4-CH<sub>3</sub> Yield = 46% ee = 91.8%



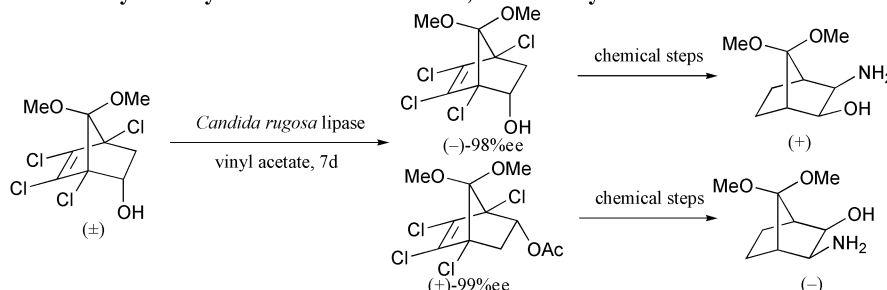
When R = 4-CH<sub>3</sub> Yield = 45% ee = >99%

Several 4-aryloxy-3-hydroxybutanenitriles were resolved with yields of **2** in the range 41 to 62% and ee in the range 35 to 93.8% and yields of **3** in the range 34 to 55% and ee in the range 88.7 to >99%.

A. Kamal and G. B. R. Khanna, *Tetrahedron: Asymmetry*, 2001, **12**, 405.

### Chemoenzymatic synthesis of 3-*exo*-amino-7,7-dimethoxynorbornan-2-*exo*-ols

Lipase

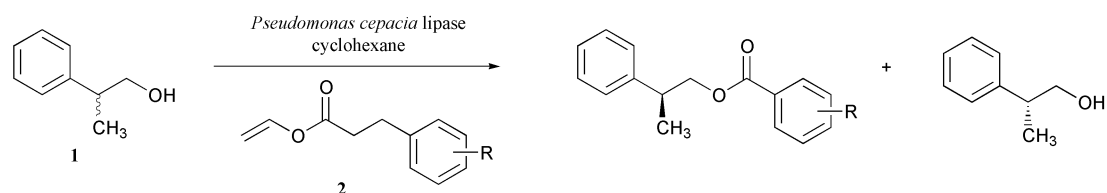


A. A. M. Lapis, O. C. Kreutz, A. R. Pohlmann and V. E. U. Costa,  
*Tetrahedron: Asymmetry*, 2001, **12**, 557.

Enantiopure starting material was obtained by an enzyme catalysed acylation.

### The effect of acyl donor structure on transesterification

Lipase

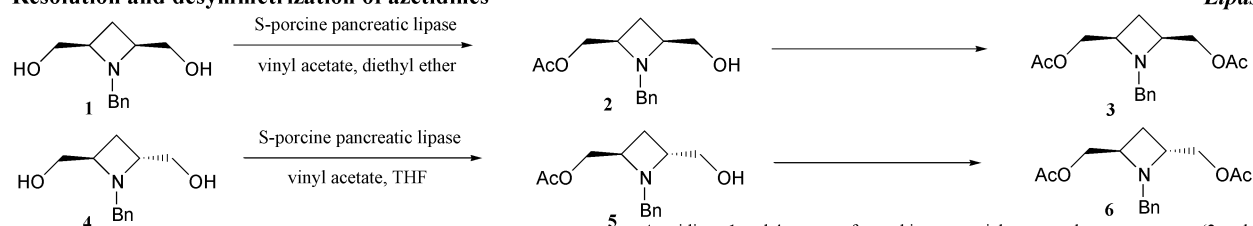


M. Kawasaki, M. Goto, S. Kawabata and T. Kometani, *Tetrahedron: Asymmetry*  
2001, **12**, 585.

The effect of the structure of various vinyl esters as acyl donors in the transesterification of 2-phenylpropan-1-ol **1** was investigated. When the acyl donor was vinyl acetate,  $E = 5$ . The  $E$  value was improved when aromatic vinyl esters of type **2** were employed. For R = H,  $E = 32$ ; for R = *p*-I,  $E = 116$ ; for R = *p*-CF<sub>3</sub>,  $E = 138$ . *ortho* and *meta* derivatives were also assessed.

### Resolution and desymmetrization of azetidines

Lipase

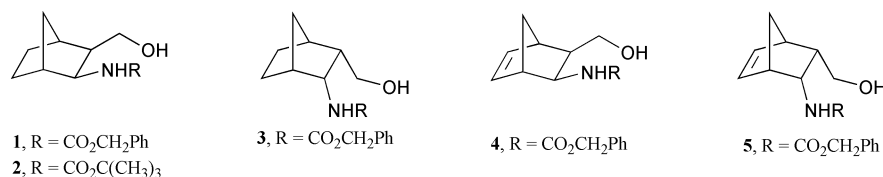


G. Guanti and R. Riva, *Tetrahedron: Asymmetry*, 2001, **12**, 605.

Azetidines **1** and **4** are transformed in sequential steps to the mono acetate (**2** and **5**) and diacetate (**3** and **6**) derivatives. *Meso* azetidine **1** was transformed to the monoacetate **2** with >99.5% ee when the ratio of **2** to **3** was 1:1. Resolution of racemic azetidine **4** of C<sub>2</sub> symmetry resulted in a 50:19:31 mixture of **4:5:6** with enantiomeric excesses of 86%, 62% and 99% respectively.

### Resolution of bicyclic amino alcohols

Lipase

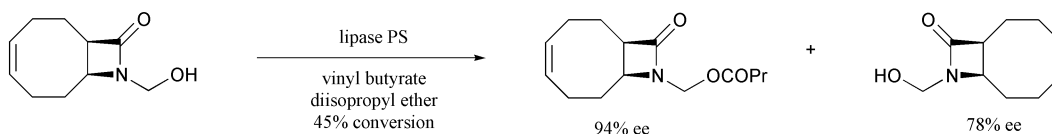


J. Kámán, J. Van der Eycken, A. Péter and F. Fülöp, *Tetrahedron: Asymmetry*,  
2001, **12**, 625.

The resolution of bicyclic amino alcohols **1-5** was studied using seven enzymes operating under conditions of various temperatures, solvents and acyl donors. For compound **2**, Novozym 435 used with vinyl butyrate as acyl donor in diethyl ether at room temperature was resolved with an  $E$  value of 127.

### Resolution of anatoxin synthons

*Lipase*

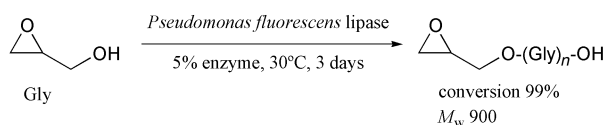


A series of enzyme systems were screened for the resolution of **1**. The effect of solvent, enzyme and acyl donor were assessed. The best result employed vinyl butyrate as donor in diisopropyl ether using lipase PS. Addition of triethylamine gave no further improvement in *E* value. When the temperature was dropped to  $-15^{\circ}\text{C}$ , the resolution proceeded with an improved *E* value of 102.

E. Forró, J. Árva and F. Fülöp, *Tetrahedron: Asymmetry*, 2001, **12**, 643.

### Enzyme-catalysed polymerisation of glycidol

*Lipase/Epoxide hydrolase*

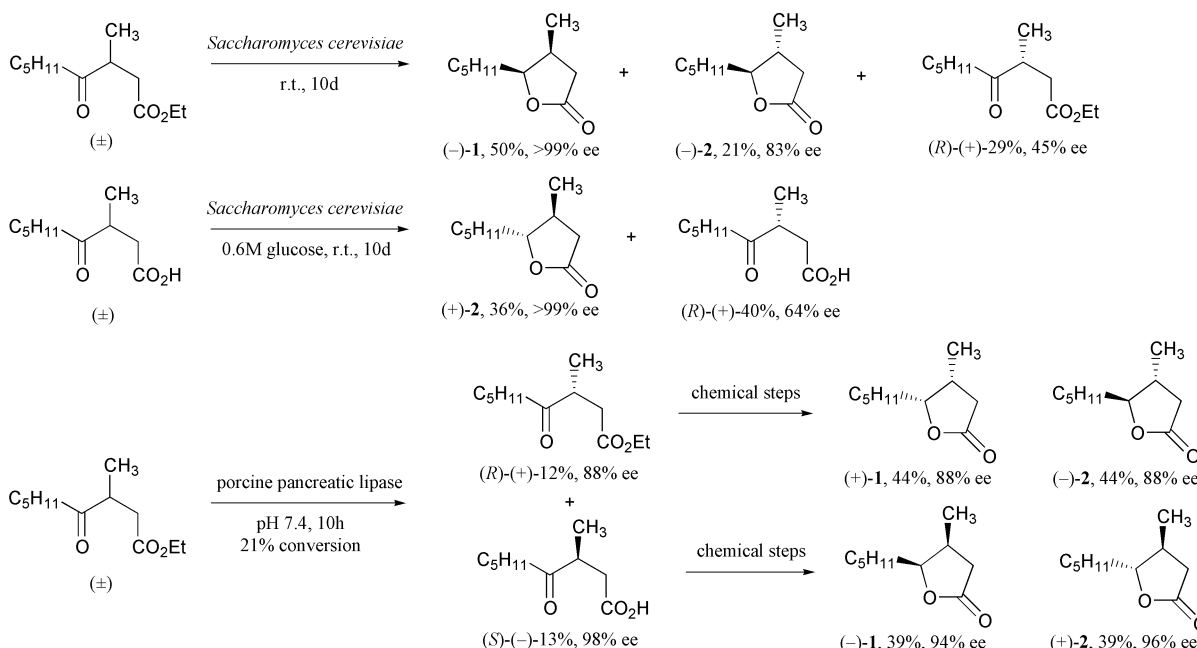


Various other lipases and *Rhodococcus* sp. NCIMB 11216 were also tested. Neither hydrolysis nor polymerisation were observed without enzyme. The enzyme appeared to be capable of facilitating an intermolecular reaction between polymer chains.

Y. Soeda, K. Toshima and S. Matsumura, *Chem. Lett.*, 2001, 76.

### Chemoenzymatic syntheses of all stereoisomers of cognac lactones

*Saccharomyces cerevisiae*/Lipase

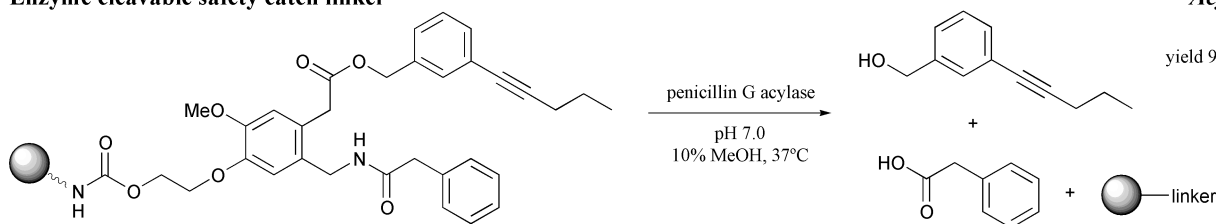


F. Benedetti, C. Forzato, P. Nitti, G. Pitacco, E. Valentin and M. Vicario, *Tetrahedron: Asymmetry*, 2001, **12**, 505.

Reductive or hydrolytic enzymes were used in the enantiodifferentiating step in the synthesis of both enantiomers of the diastereomeric cognac lactones **1** and **2**.

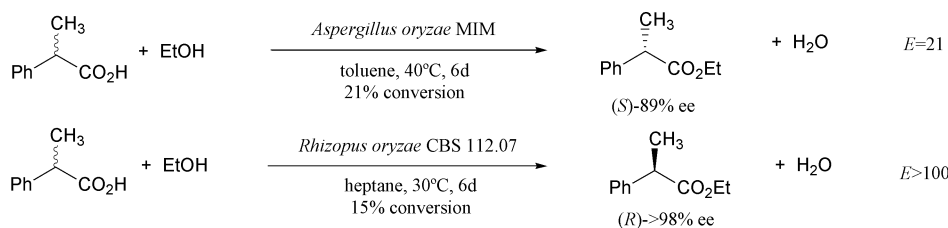
### Enzyme cleavable safety catch linker

*Acylase*



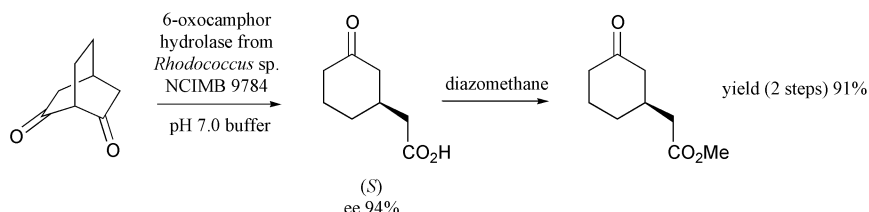
The enzyme cleavage was found to be effective using the soluble polymer POE 6000. The linker was used in palladium chemistry *e.g.* Heck, Suzuki and Sonogashira (shown) reactions, Mitsunobu reaction and some cycloadditions. Furthermore, compounds coupled as amides were also cleaved effectively at  $60^{\circ}\text{C}$ .

U. Grether and H. Waldmann, *Chem. Eur. J.*, 2001, **7**, 959.

**Resolution of (RS)-2-phenylpropanoic acid****Esterase**

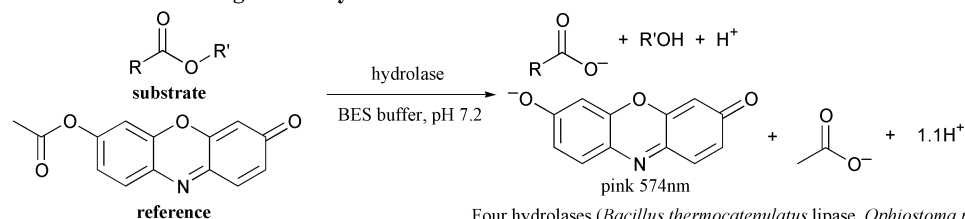
R. Gandolfi, R. Gualandris, C. Zanchi and F. Molinari, *Tetrahedron: Asymmetry*, 2001, 12, 501.

Systematic study of the esterification of 2-phenylpropanoic acid by the two enzymes was undertaken, examining different alcohols, solvents and temperatures. The enantioselectivity of *R. oryzae* was dependant on the alcohol, whereas *A. oryzae* always yielded the *S*-enantiomer for the alcohols studied.

**Retro-Claisen desymmetrization of some cyclic  $\beta$ -diketones****Hydrolase**

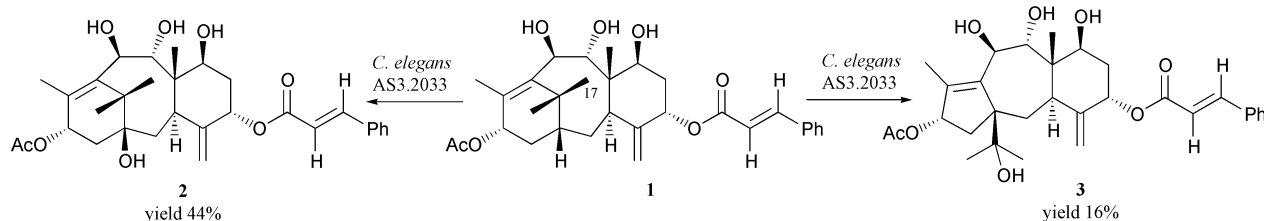
G. Grogan, J. Graf, A. Jones, S. Parsons, N. J. Turner and S. L. Flitsch, *Angew. Chem., Int. Ed.*, 2001, 40, 1111.

Hydrolysis of the corresponding methylene bridged species also gave the *(S)* product, with a poorer ee (84%). A variety of other  $\beta$ -diketones were tested. Acyclic diketones and simple monocyclic diketones were not substrates and other  $\alpha,\alpha$ -disubstituted cyclohexane diones were hydrolysed non-enantioselectively.

**Colorimetric screening of new hydrolases****Hydrolase**

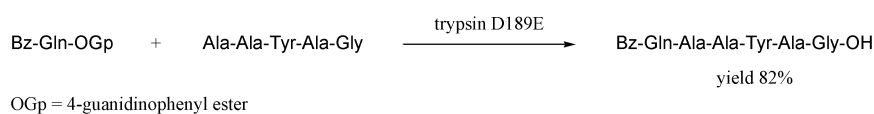
A. M. F. Liu, N. A. Somers, R. J. Kazlauskas, T. S. Brush, F. Zocher, M. M. Enzelberger, U. T. Bornscheuer, G. P. Horsman, A. Mezzetti, C. Schmidt-Dannert and R. D. Schmid, *Tetrahedron: Asymmetry*, 2001, 12, 545.

Four hydrolases (*Bacillus thermocatemulatus* lipase, *Ophiostoma piliferum* lipase, *Pseudomonas fluorescens* esterase and *Streptomyces diastatochromogenes* esterase) were screened against 29 commercially available esters and 23 chiral esters using the QuickE method shown. The QuickE method is much quicker than traditional methods (1 day vs. 1 month), however the limitation is that the reference ester must react slower than the substrate to obtain a true measure of enantioselectivity. A summary of the substrates for each enzyme is given, with some indications of their possible uses in organic chemistry.

**Biotransformation of a taxadiene derivative****Hydroxylase**

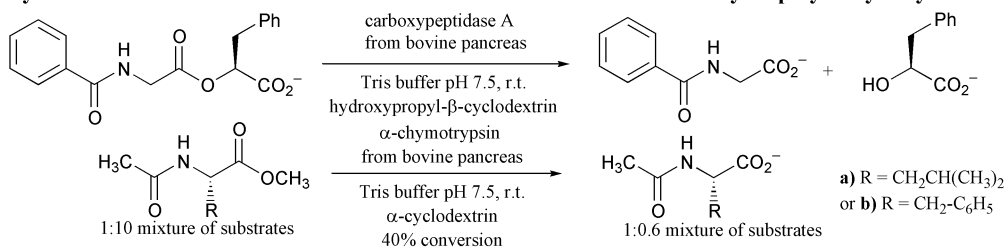
D.-A. Sun, F. Sauriol, O. Mamer and L. O. Zamir, *Bioorg. Med. Chem.*, 2001, 9, 793.

The taxadiene (1) was subjected to transformation by *Cunninghamella elegans* AS3.2033 and ATCC 20230. In addition to the 2 examples shown, products included hydroxylation at other positions (e.g. C-17) and isomerisation of the cinnamoyl group. The equivalent acetylated species was unchanged after incubation.

**Enzyme coupling of peptides with a trypsin mutant****Protease**

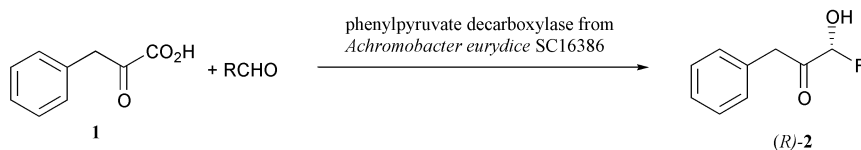
S. Xu, K. Rall and F. Bordusa, *J. Org. Chem.*, 2001, 66, 1627.

Using a mutant of trypsin in which Asp 189 was replaced by Glu, enzyme catalysed peptide coupling was studied. Compared to the *wild type* -trypsin, the yields of hexapeptides were higher, since proteolytic cleavage is much reduced in the mutant trypsin. Coupling with pentapeptides, varying in the position 3 amino acid, and variations in the acyl donor amino acid were investigated. It was observed in each case that the pentapeptides containing Phe or Tyr at the 3 position gave higher yields compared to those containing Lys or Arg, since the latter were more susceptible to cleavage.

**Cyclodextrins to limit substrate inhibition and alter substrate selectivity displayed by enzymes**
**Peptidase/Hydrolase**


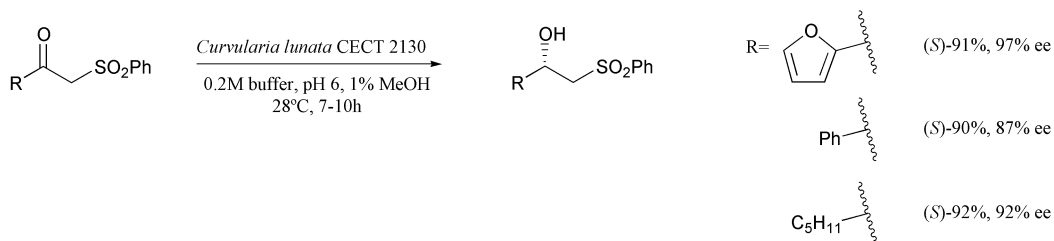
C. J. Easton, J. B. Harper, S. J. Head, K. Lee and S. F. Lincoln, *J. Chem. Soc., Perkin Trans. 1*, 2001, 584.

Hydroxypropyl- $\beta$ -cyclodextrin was found to increase the concentration of the substrate at which the maximum rate of reaction is observed, by more than an order of magnitude. An increase in substrate selectivity was observed in  $\alpha$ -chymotrypsin catalysis of methyl esters a) and b) upon addition of cyclodextrin.

**Asymmetric acyloin condensations**
**Phenylpyruvate decarboxylase**


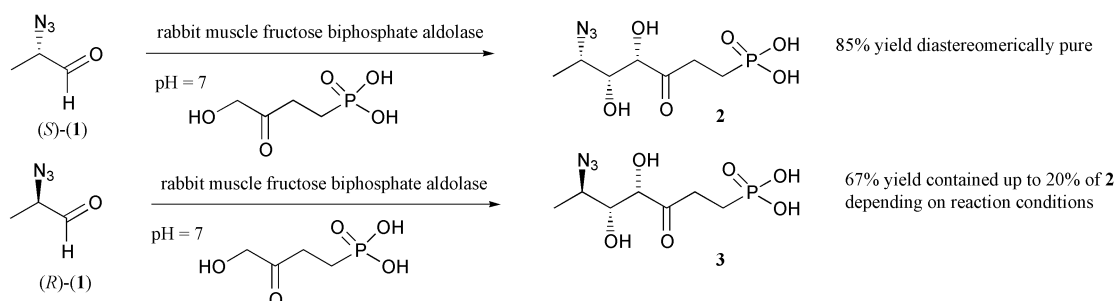
Z. Guo, A. Goswami, V. B. Nanduri and R. N. Patel, *Tetrahedron: Asymmetry*, 2000, 12, 571.

Phenylpyruvate decarboxylase was purified 332-fold from *Achromobacter eurydice* SC16386 in six steps. The pure enzyme catalysed the condensation of 1 with acetaldehyde to give condensation product 2 in 91% yield with 85% ee. The activity was investigated further using immobilised enzyme. As the aldehyde chain length increased, activity decreased. There was minimal activity with aromatic aldehydes. Indole pyruvic acid was reported to be a substrate.

**Enantioselective reduction of  $\beta$ -ketosulfones**
**Dehydrogenase**


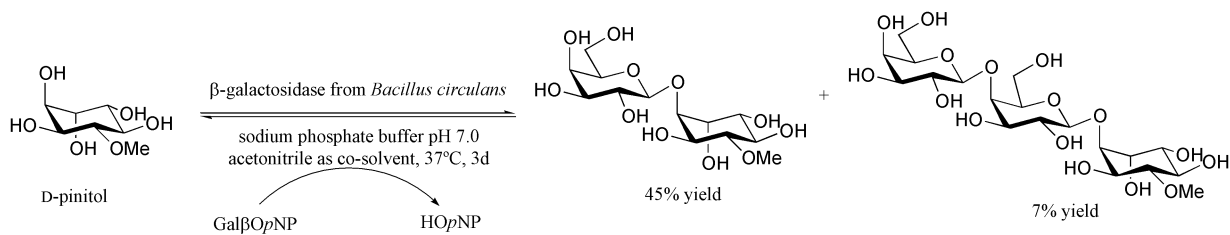
V. Gotor, F. Rebolledo and R. Liz, *Tetrahedron: Asymmetry*, 2001, 12, 513.

Substrate concentration can be increased from 1 mg ml<sup>-1</sup> to 2.8 mg ml<sup>-1</sup> but a longer reaction time is required. The cells can be reused without loss of activity.

**Chemical-enzymatic synthesis of azasugar phosphonic acids**
**Aldolase**


M. Schuster, W.-F. He and S. Blechert, *Tetrahedron Lett.*, 2001, 42, 2289.

2 and 3 were converted to azasugar phosphonates in 1 step.

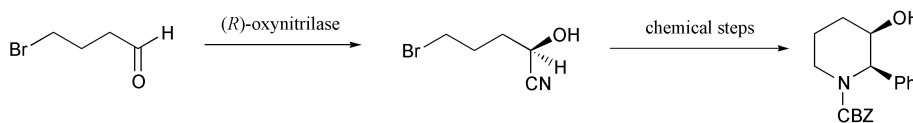
**Enzymatic synthesis of galactosylated 1D-*chiro*-inositol and 1D-pinitol derivatives**
 **$\beta$ -Galactosidase**


J. Hart, A. Falshaw, E. Farkas and J. Thiem, *Synlett*, 2001, 3, 329.

Galactosylations were also carried out using 1D-*chiro*-inositol as acceptor (43% yield of monogalactosylated inositol). This is the first report of enzymatic glycosylation of *chiro*-inositol and its derivatives.

### Chemoenzymatic synthesis of 2,3-disubstituted piperidines

*Oxynitriase*

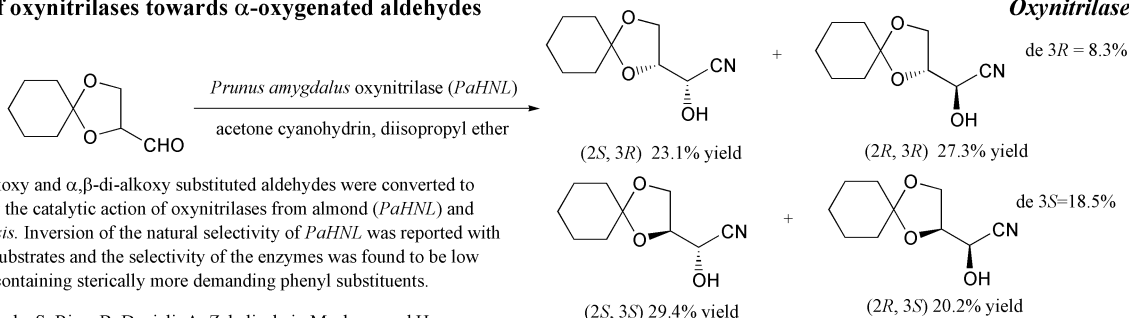


M. I. Monterde, R. Brieva and V. Gotor, *Tetrahedron: Asymmetry*, 2001, 12, 525.

An oxynitriase catalysed transcyanation yields a suitable optically active starting material for the synthesis of 2,3-disubstituted piperidines.

### Selectivity of oxynitriases towards $\alpha$ -oxygenated aldehydes

*Oxynitriase*

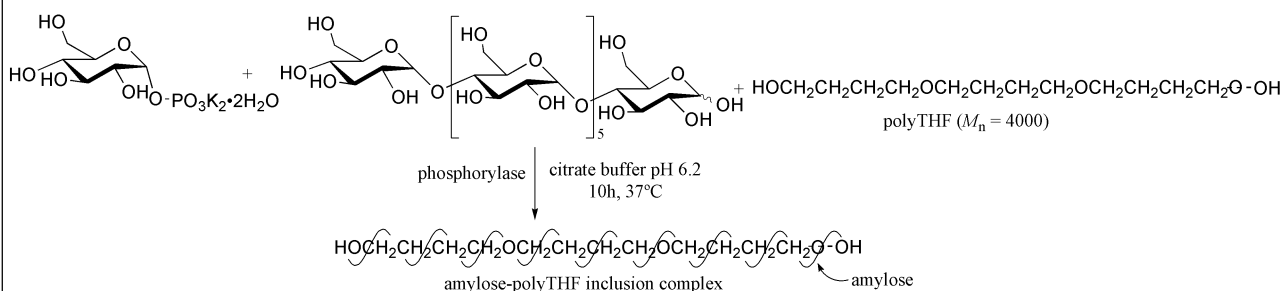


A range of  $\alpha$ -alkoxy and  $\alpha,\beta$ -di-alkoxy substituted aldehydes were converted to cyanohydrins by the catalytic action of oxynitriases from almond (*PaHNL*) and *Hevea brasiliensis*. Inversion of the natural selectivity of *PaHNL* was reported with dioxolane type substrates and the selectivity of the enzymes was found to be low with aldehydes containing sterically more demanding phenyl substituents.

P. Bianchi, G. Roda, S. Riva, B. Danieli, A. Zabelinskaja-Mackova and H. Griengl, *Tetrahedron*, 2001, 57, 2213.

### Synthesis of an amylose-polymer inclusion complex by enzymatic polymerisation

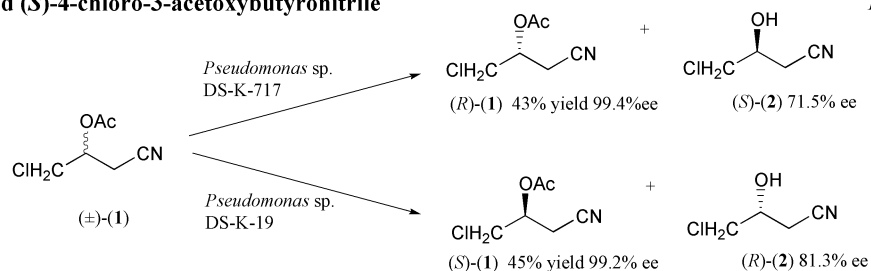
*Phosphorylase*



J. Kadokawa, Y. Kaneko, H. Tagaya and K. Chiba, *Chem. Commun.*, 2001, 449. Provides a new method for the preparation of polymer-polymer inclusion complexes.

### Preparation of (*R*) and (*S*)-4-chloro-3-acetoxybutyronitrile

*Pseudomonas sp.*



H. Idogaki, N. Kasai, M. Takeuchi, M. Hatada and T. Suzuki, *Tetrahedron: Asymmetry*, 2001, 12, 369.

The hydrolytic activity of DS-K-19 was increased 20-fold, compared to the additive free medium, by addition of 0.2% v/v 4-chloro-3-acetoxybutyronitrile.