Perkin 1 Abstracts: Biocatalysis in Organic Synthesis

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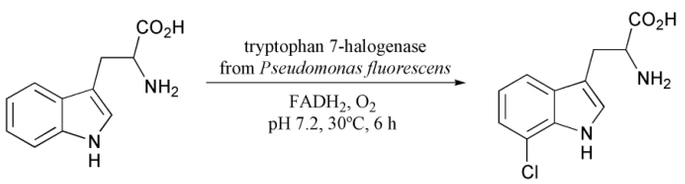
Perkin 1 Abstracts: Biocatalysis in Organic Synthesis aims to cover recent literature concerning the applications of enzymes and micro-organisms as catalysts in organic synthesis. The abstracts will emphasise the key synthetic step(s) that are mediated by the biocatalyst. Emerging technologies for biocatalyst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

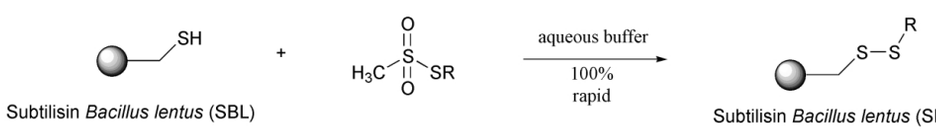
Purification of tryptophan 7-halogenase ***Tryptophan 7-halogenase***



S. Keller, T. Wage, K. Hohaus, M. Hölzer, E. Eichhorn and K.-H. van Pée, *Angew. Chem., Int. Ed.*, 2000, **39**, 2300.

The enzyme tryptophan 7-halogenase was purified from *Pseudomonas fluorescens*. During purification it was discovered that a second protein was necessary for activity. This was identified as a flavin reductase and is required to reduce FAD to $FADH_2$, with the help of NADH. A mechanism is also postulated to explain the regiospecific halogenation.

Site-selective protein glycosylation ***Protease***



Subtilisin *Bacillus lentus* (SBL)

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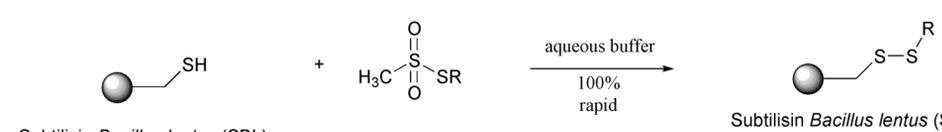
R = D-glucose (α,β), D-galactose (α,β), D-mannose (α,β), lactose all acetylated and deprotected

B. G. Davis, R. C. Lloyd and J. B. Jones, *Bioorg. Med. Chem.*, 2000, **8**, 1527.

Site-selective glycosylation was achieved by site-directed mutagenesis at re-selected positions, followed by reaction of the thiol residue with glycomethanethiosulfonates. Effects of glycosylation on amidase activity was assessed by measuring the k_{cat} and K_M values for the reaction with succinyl-AAPF-*p*-nitroanilide. A precise set of structure-activity relationships was generated, the first example of such data.

Site-selective protein glycosylation ***Protease***



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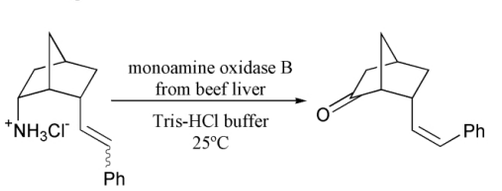
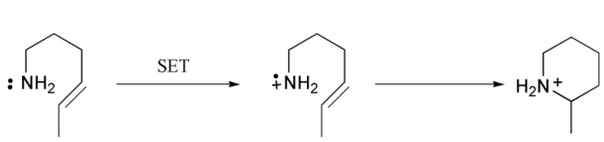
R. C. Lloyd, B. G. Davis and J. B. Jones, *Bioorg. Med. Chem.*, 2000, **8**, 1537.

The effects of site-selective glycosylation on the esterase activity of subtilisin *Bacillus lentus* were studied. It was found that glycosylations at key positions can increase esterase activity up to 8-fold. The ratio of esterase to amidase activity was also studied, and it was found that the ratio could be enhanced up to 17-fold. This enhancement will be advantageous in peptide synthesis where a high esterase to amidase ratio is desirable.

Probing the mechanism of monoamine oxidase ***Monoamine oxidase***



E and *Z* *Z*



(1)

X. Wang and R. B. Silverman, *Bioorg. Med. Chem.*, 2000, **8**, 1645.

Both the *E* and *Z* isomer are inhibitors of monoamine oxidase B, but only the *Z* isomer shows any conversion to the ketone. The experiment was designed to trap the proposed aminium radical cation intermediate **(1)**, formed by an initial single electron transfer. A number of explanations were put forward to account for the fact that no cyclised product was observed.

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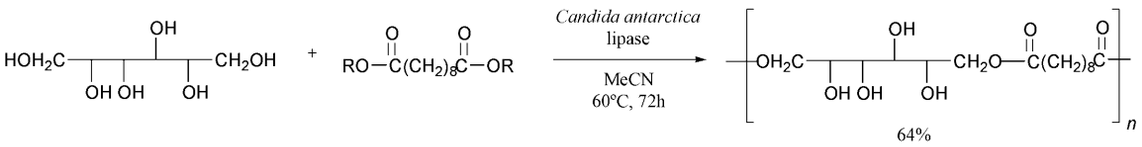
Regioselective polymerisation of sorbitol and divinyl sebacate

Lipase

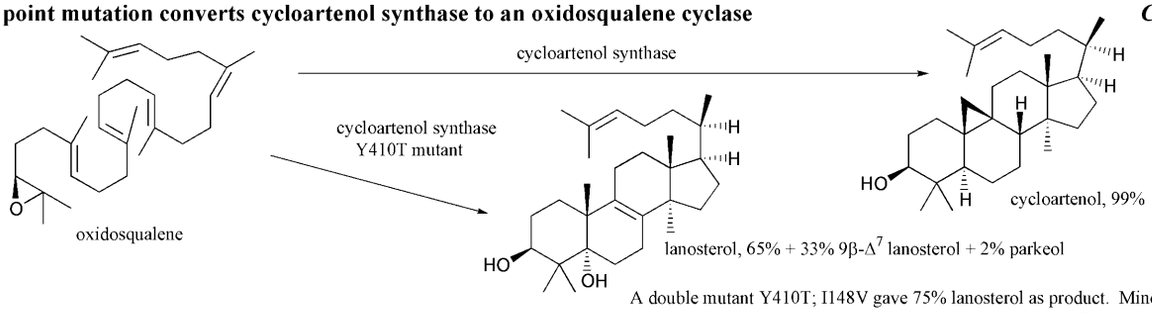


Polymer consisted exclusively of the acylated unit of sorbitol at 1- and 6-positions, indicating perfect control of regioselectivity. Temperature had a marked effect on size and yield of polymer obtained.

H. Uyama, E. Klegraf, S. Wada and S. Kobayashi, *Chem. Lett.*, 2000, 800.

A point mutation converts cycloartenol synthase to an oxidosqualene cyclase

Cyclase

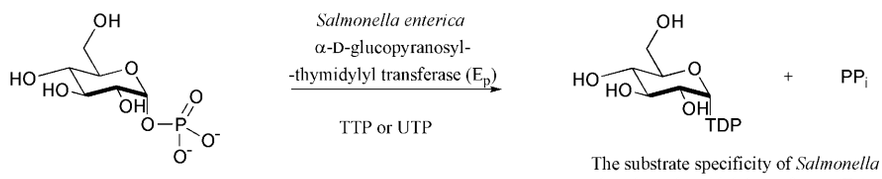


A double mutant Y410T; I148V gave 75% lanosterol as product. Minor mutations can have significant effects on product structure. Tyr 140 is evidently important for cyclopropane synthesis.

J. B. R. Herrera, W. K. Wilson and S. P. Matsuda, *J. Am. Chem. Soc.*, 2000, **122**, 6765.

Synthesis of UDP and TDP nucleotide sugars

Nucleotidylyl transferase

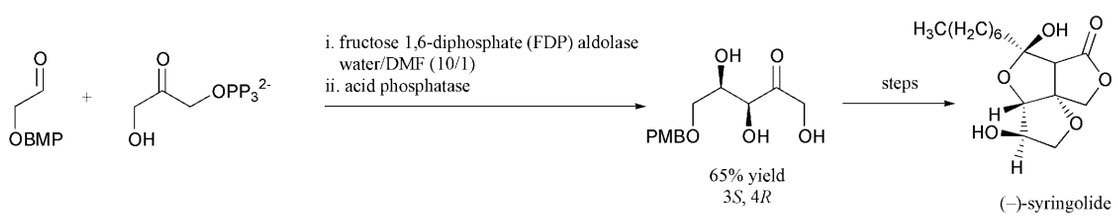


The substrate specificity of *Salmonella enterica* α-D-glucopyranosyl phosphate thymidylyltransferase (E_p) was reevaluated. Twelve glycosyl phosphates were tested as substrates. Eight were successfully transformed with TTP and six with UTP as nucleotide triphosphate. E_p prefers pyranosyl phosphates which exist as $^4C_1$ conformers. A C-2 hydroxy is critical for activity.

J. Jiang, J. B. Biggins and J. S. Thorson, *J. Am. Chem. Soc.*, 2000, **122**, 6803.

Fructose 1,6-diphosphatase aldolase catalysed condensation

Aldolase

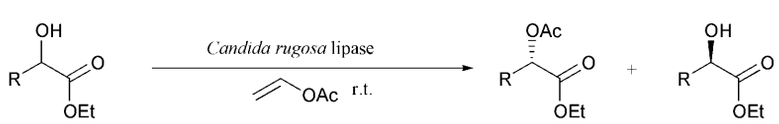


The ketotriol was obtained *via* a FDP aldolase catalysed reaction, and subsequently used as an intermediate for the synthesis of (–)-syringolide.

R. Chênevert and M. Dasser, *J. Org. Chem.*, 2000, **65**, 4529.

Resolution of α-hydroxy esters

Lipase



41% yield, 99% ee
45% conversion.
R = 2-hydroxy-5-tert-butylphenyl

A selection of aromatic α-hydroxy esters were subjected to lipase resolution. Resolution was also effective using *Pseudomonas cepacia* lipase (lipase PS).

W. Zhang and P. G. Wang, *J. Org. Chem.*, 2000, **65**, 4732.

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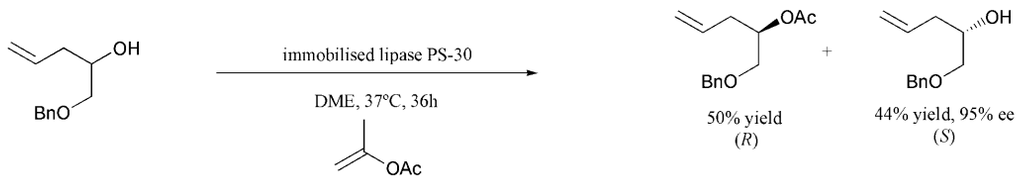
Lipase resolution of a homoallylic alcohol

Lipase

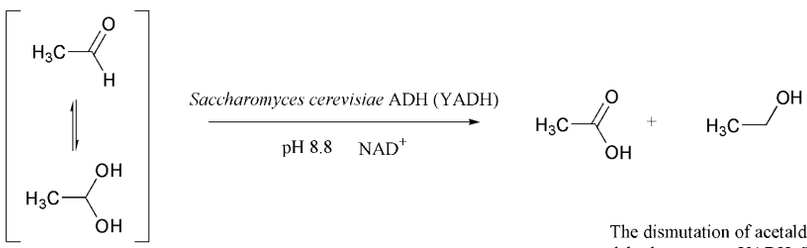


A. K. Ghosh and H. Lei, *J. Org. Chem.*, 2000, **65**, 4779.

The (*R*) acetate was converted to the *(S)*-alcohol in 3 steps with 79% overall yield and 97% ee. Subsequent steps gave a building block for the synthesis of (+)-compactin and (+)-mevinolin.

Dismutation of aldehydes catalysed by alcohol dehydrogenases

Alcohol dehydrogenase

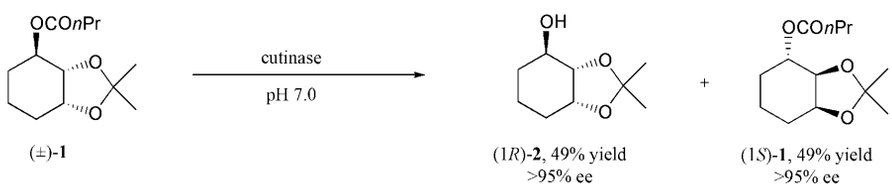


K. Velonia and I. Smonou, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2283.

The dismutation of acetaldehyde was studied for three alcohol dehydrogenases: YADH, *Thermoanaerobium brockii* ADH and *Moraxella* sp. TAE123 ADH, using NMR spectroscopy. The dismutations of propionaldehyde and benzaldehyde were also studied

Resolution of a cyclohexanetriol precursor

Cutinase

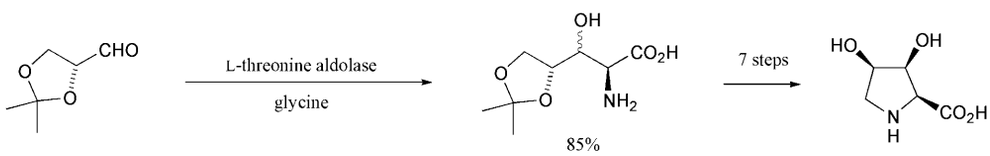


I. Hubrecht, E. Van der Eycken and J. Van der Eycken, *Synlett*, 2000, 971.

Recombinant cutinase from *Fusarium solani pisi* was employed. Enantiopure **2** was used as a synthon for two carbasugars; 6a-carba-α- and 6a-carba-β-D-fructopyranose.

Synthesis of 3,4-dihydroxyprolines

Aldolase

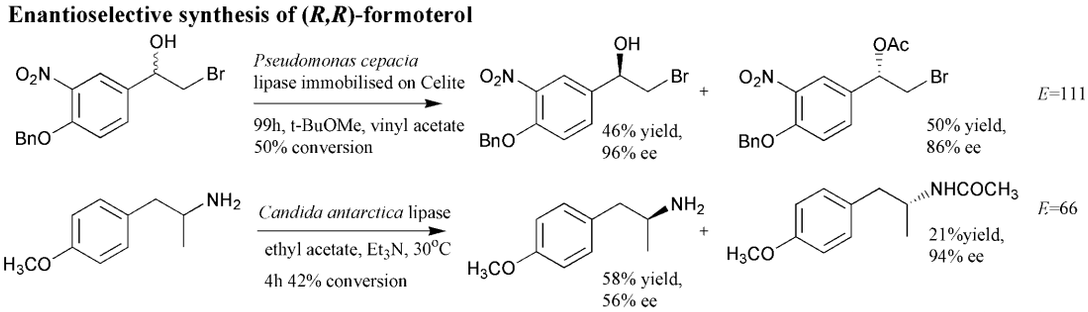


M. Fujii, T. Miura, T. Kajimoto and Y. Ida, *Synlett*, 2000, 1046.

L-threonine aldolase was obtained from *Candida humicola* AKU 4586. The stereochemistry of the α-position was deduced to be L, as it was accepted as a substrate for L-amino acid oxidase (LAAO) but not D-amino acid oxidase (DAAO).

Enantioselective synthesis of (*R,R*)-formoterol

Lipase



F. Campos, M. P. Bosch and A. Guerrero, *Tetrahedron: Asymmetry*, 2000, **11**, 2705.

The unreacted (*R*) alcohol was cyclised to the required epoxide and coupled to the (*R*) amine to give (*R,R*)-formoterol.

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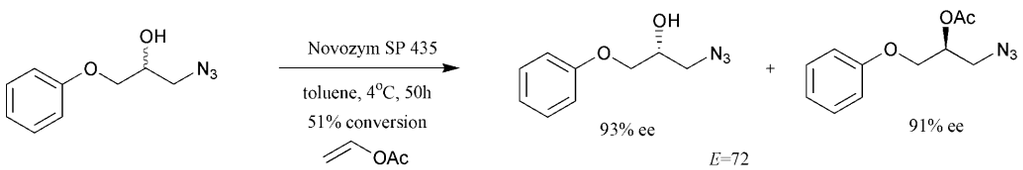
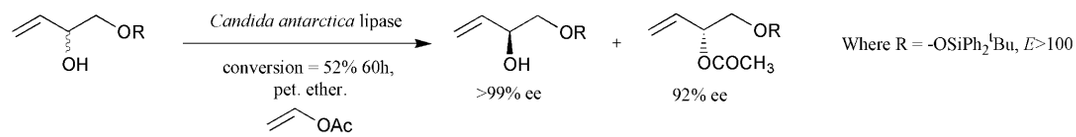
Resolution of 1-azido-3-aryloxypropan-2-ols by enantioselective acetylation ***Lipase***



B. K. Pchelka, A. Loupy, J. Plenkiewicz and L. Blanco, *Tetrahedron*: *Asymmetry*, 2000, **11**, 2719.

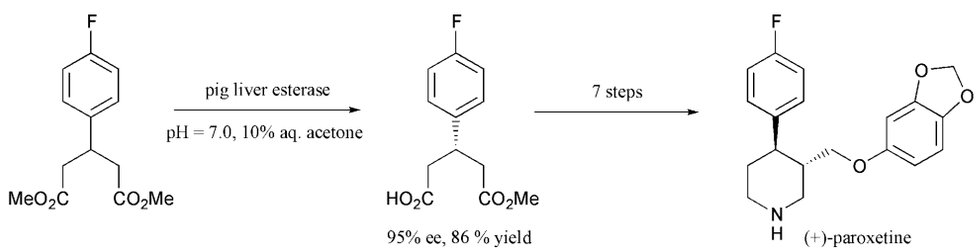
The effects of aromatic substituents, acyl donor, lipase, solvent, temperature and presence of additives were also studied. *E* values from 56 to 72 were reported.

Chemoenzymatic synthesis of the stereoisomers of a β-adrenergic receptor antagonist ***Lipase***



C. Dallanoce, M. De Amici, G. Carrea, F. Secundo, S. Castellano and C. De Micheli, *Tetrahedron*: *Asymmetry*, 2000, **11**, 2741.

Asymmetric synthesis of (–)-paroxetine ***Esterase***



M. S. Yu, I. Lantos, Z.-Q. Peng, J. Yu. and T. Cacchio, *Tetrahedron Lett*., 2000, **41**, 5647.

Pig liver esterase was used to desymmetrise the substituted dimethyl glutarate and hence provide a key building block for (–)-paroxetine.

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