PERKIN 1 ABSTRACTS

Perkin 1 Abstracts: Biocatalysis in Organic Synthesis

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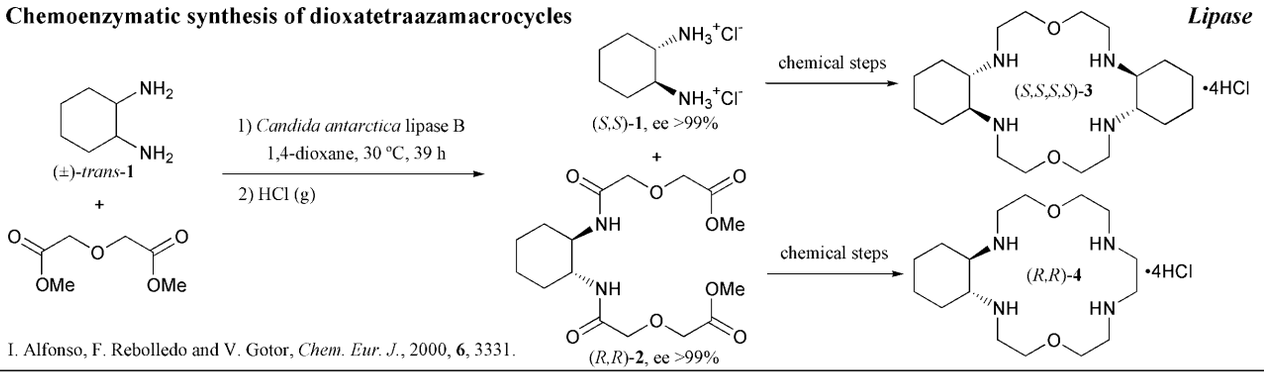
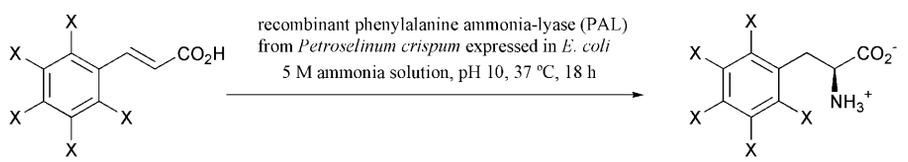
Perkin 1 Abstracts: Biocatalysis in Organic Synthesis aims to cover recent literature concerning the applications of enzymes and micro-organisms as catalysts in organic synthesis. The abstracts will emphasise the key synthetic step(s) that are mediated by the biocatalyst. Emerging technologies for biocatalyst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

Chemoenzymatic synthesis of dioxatetraazamacrocycles — ***Lipase***



I. Alfonso, F. Rebolledo and V. Gotor, *Chem. Eur. J.*, 2000, **6**, 3331.

Synthesis of L-arylalanines — ***Phenylalanine ammonia-lyase***

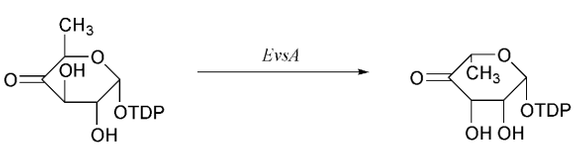


X = H/F, H/Cl.

A. Gloge, J. Zoň, Á. Kövári, L. Poppe and J. Rétey, *Chem. Eur. J.*, 2000, **6**, 3386.

Nine different fluoro- and chloro-phenylalanines were synthesised from their corresponding cinnamic acids. Kinetic measurements and theoretical calculations were used to help elucidate the mechanism.

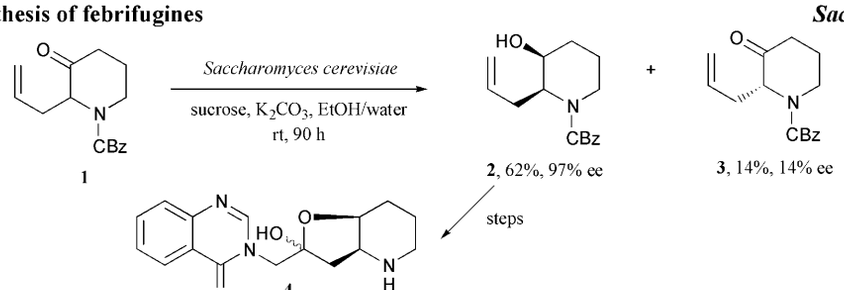
Epimerisation of TDP-4-keto-6-deoxyglucose — ***Sugar epimerase***



A sugar epimerase (encoded by the gene *EvsA*) that catalyses the first step in TDP-4-*epi*-vancosamine biosynthesis from TDP-4-keto-deoxyglucose has been characterised. Exchange experiments in D_2O followed by derivatisation and GCMS analysis reveal deuterium incorporation at both positions 3 and 5 of the sugar. The enzymatic reaction is a preliminary step in the biosynthesis of vancomycin and chloroeremomycin.

P. N. Kirkpatrick, W. Scaife, T. M. Hallis, H.-w. Liu, J. B. Spencer and D. H. Williams, *Chem. Commun.*, 2000, 1565.

Asymmetric synthesis of febrifugines — ***Saccharomyces cerevisiae***

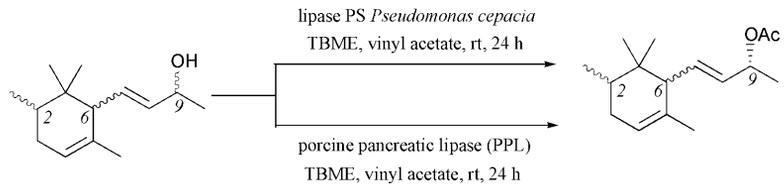


Y. Takeuchi, K. Azuma, K. Takakura, H. Abe and T. Harayama, *Chem. Commun.*, 2000, 1643.

Reduction of ketone **1**, under dynamic conditions was achieved using *Saccharomyces cerevisiae* in an ethanol/ K_2CO_3 mixture. **2** serves as a synthon for isofebrifugine **4**.

Acetylation of racemic *cis*- and *trans*-α-irols

Lipase

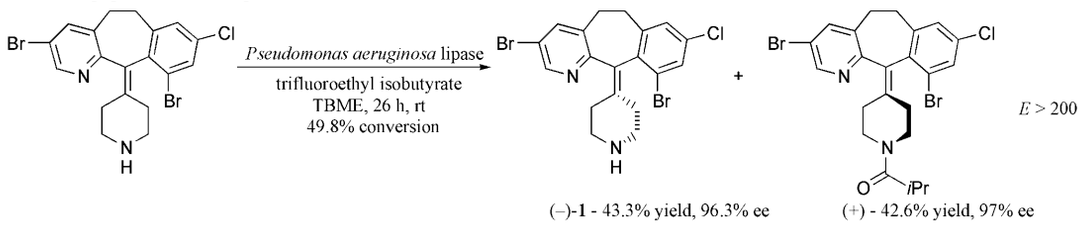


Both lipases exhibited excellent enantioselectivity at the 9-position (99% ee), however only PPL showed diastereoselectivity with a 2:1 *cis:trans* ratio and diastereomeric enrichment of 78%. The major product of the PPL catalysed reaction was the precursor to (–)-*cis*-(α)-irone, a highly precious substance in the flavour industry.

J. Aleu, B. Bergamo, E. Brenna, C. Fuganti and S. Serra, *Eur. J. Org. Chem.*, 2000, 3031.

Resolution of piperidine atropisomers

Lipase

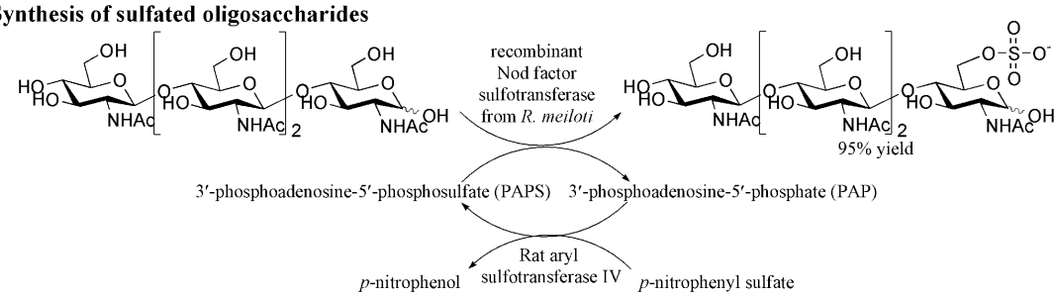


The resolution was optimised in terms of acylating agent, solvent and moisture content. (–)- **1** was racemised and recycled through further resolutions to increase the yield of the desired (+)-enantiomer, which is an intermediate in the synthesis of a farnesyl protein transferase inhibitor, SCH66336.

B. Morgan, A. Zaks, D. R. Dodds, J. Liu, R. Jain, S. Megati, F. G. Njoroge and V. M. Girijavallabhan, *J. Org. Chem.*, 2000, **65**, 5451.

Synthesis of sulfated oligosaccharides

Sulfotransferase

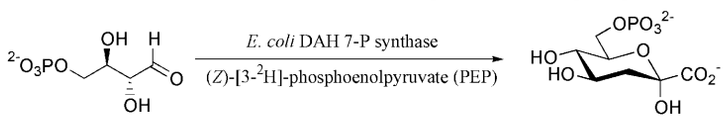


Several enzymatic methods were tested for the regeneration of PAPS. The oligosaccharide sulfates obtained were further glycosylated using glycosyltransferases.

M. D. Burkart, M. Izumi, E. Chapman, C.-H. Lin and C.-H. Wong, *J. Org. Chem.*, 2000, **65**, 5565.

Synthesis of labelled 3-deoxy-D-*arabino*-heptulosonate 7-phosphate (DAH 7-P)

Synthase



erythrose 4-phosphate (E 4-P)

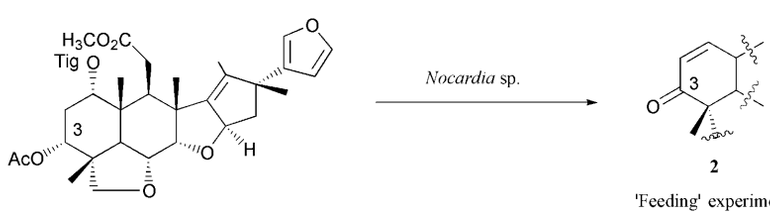
(3*S*)-[3-^{2}H]-DAH 7-P

Condensation of (E 4-P) with (*E*)-[3-^{2}H]-PEP affords the complementary (3*R*)-[3-^{2}H]-DAH 7-P isomer. Five other phosphorylated monosaccharide analogues were separately condensed with (*Z*)- and (*E*)-[3-^{2}H]-PEP to investigate the stereochemistry of DAH 7-P synthase. The results were in agreement with the observed facial selectivity of DAH 7-P synthase for E 4-P providing evidence that DAH 7-P synthase catalyses the *SI* face addition of the C3 of PEP to the *RE* face of C1 of the phosphorylated monosaccharides tested.

A. K. Sundaram and R. W. Woodard, *J. Org. Chem.*, 2000, **65**, 5891.

Biotransformations of salannin

Nocardia sp.



1 salannin

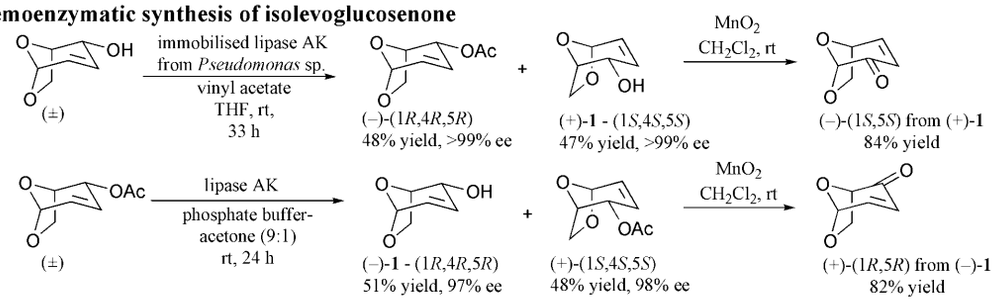
2

'Feeding' experiments with postulated intermediates confirmed that **1** is converted into **2** *via* deacetylation and oxidation at C-3 followed by OTig removal and dehydration. THF derivatives were also accepted as substrates, as were lactonic analogues. In an extensive study, a variety of oxidations and deacetylations were observed with metabolite analogues depending on the structure of the biotransformation substrate.

K. Madhava Madyastha and K. Venkatakrishnan, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3055.

Chemoenzymatic synthesis of isolevoglucosenone

Lipase

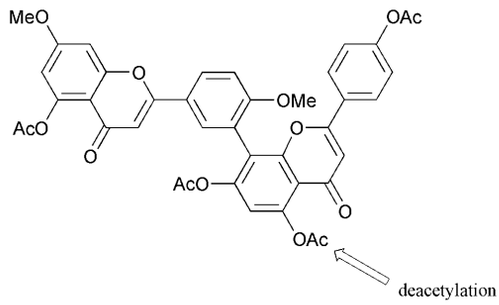


K. Kodota, A. S. ElAzab, T. Taniguchi and K. Ogasawara, *Synthesis*, 2000, **10**, 1372.

An efficient route to enantiopure isolevoglucosenone in both enantiomeric forms is reported.

Regioselective deacetylation of ginkgetin derivatives

Lipase

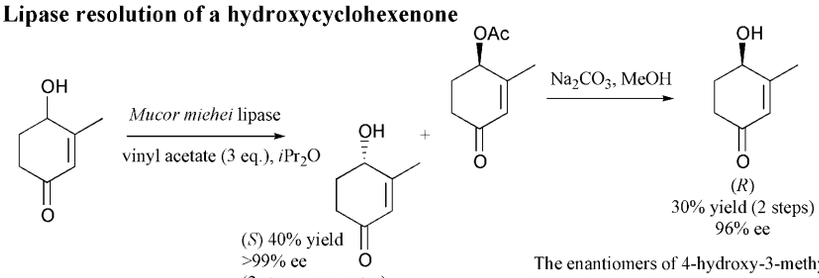


B. Das, A. Kashinatham and B. Venkataiah, *Synth. Commun.* 2000, **30**, 3765.

The tetraacetyl ginkgetin illustrated was deacetylated specifically at the position shown by Amano PS lipase in THF/water. 5',7",4"'-triacetylginkgetin was isolated in 64% yield.

Lipase resolution of a hydroxycyclohexenone

Lipase

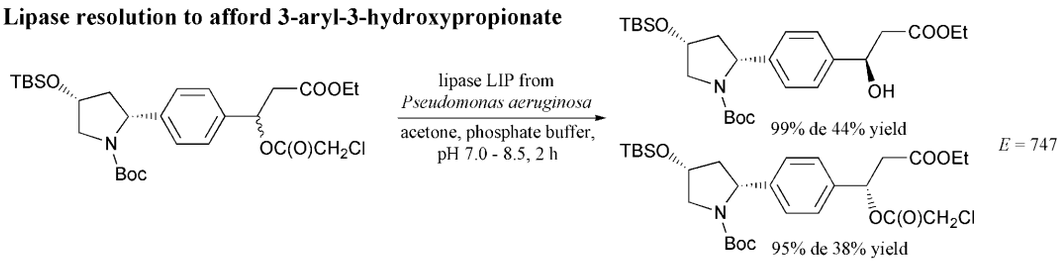


The enantiomers of 4-hydroxy-3-methylcyclohex-2-en-1-one were separated by lipase resolution. Initial reaction for 48 h gave the (*S*) alcohol (66% ee), which after separation and further reaction with the lipase for 7 days, resulted in an ee of >99%. The (*R*) acetate was hydrolysed by chemical means, and both enantiomers were used to synthesise the corresponding karahana lactone and karahana ether.

J.-M. Galano, G. Audran and H. Monti, *Tetrahedron*, 2000, **56**, 7477.

Lipase resolution to afford 3-aryl-3-hydroxypropionate

Lipase

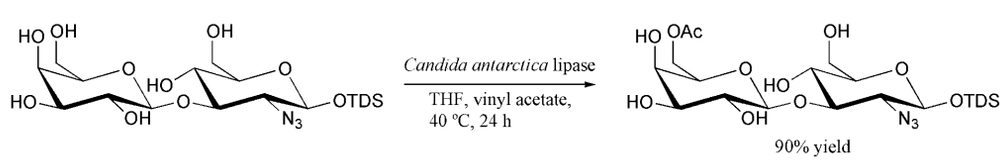


Y. Sugimoto, H. Imamura, A. Shimizu, M. Nakano, S. Nakajima, S. Abe, K. Yamada and H. Morishima, *Tetrahedron: Asymmetry*, 2000, **11**, 3609.

The resolution was attempted with various enzymes at different pH's, giving the (*R*) alcohol. Best results were observed for lipase LIP at pH 7.0 - 8.5. The (*S*) alcohol was obtained by chemical hydrolysis. The alcohol was used in the synthesis of a novel carbapenem.

Selective lipase acylation of some azido disaccharides

Lipase

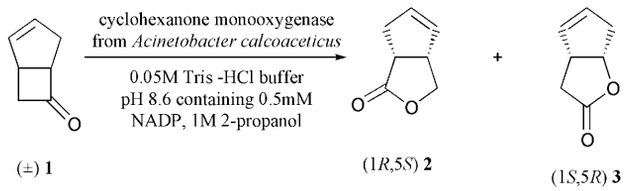


B. La Ferla, L. Lay, G. Russo and L. Panza, *Tetrahedron: Asymmetry*, 2000, **11**, 3647.

Selective protection of the disaccharides using lipase from *Candida antarctica* was achieved. The effect of changing solvent and temperature resulted in different regioselectivity. This was exploited to form different disaccharide building blocks. The disaccharide with (1-4) connectivity was subjected to similar conditions and also found to acylate at the 6′ position

Enantioselectivity of cyclohexanone monooxygenase from *Acinetobactor calcoaceticus*

Monooxygenase



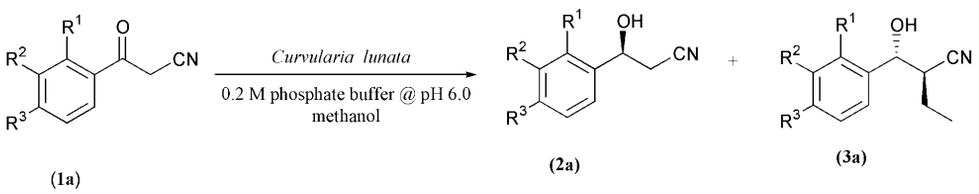
At 4.6 mM of **1** ee of **2** ≥ 98% and ee of **3** ≥ 98% after complete conversion of substrate into products

The ee values of lactone **3**, but not lactone **2**, were found to be dependent on the degree of conversion and substrate concentration. The results were rationalized using a model which hypothesizes the binding of a second substrate molecule to an enzyme site distinct from the catalytic site.

F. Zambianchi, P. Pasta, G. Ottolina, G. Carrea, S. Colonna, N. Gaggero and J. M. Ward, *Tetrahedron: Asymmetry*, 2000, **11**, 3653.

Enantio- and chemoselective bioreduction of β-keto nitriles by *Curvularia lunata*

Curvularia lunata



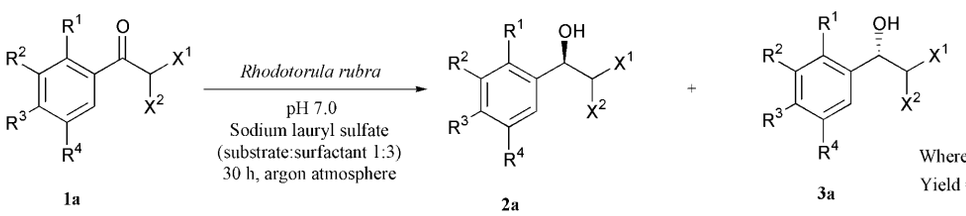
Where R^1=R^3=H, R^2=Cl.
Yield **2a** = 57% ee = 97%

The use of methanol as co-solvent eliminates the formation of **3a.** A range of aromatic β−keto nitriles were reduced with yields in the range 41-77% and ee in the range 40-98%.

J. R. Dehli and V. Gotor, *Tetrahedron: Asymmetry*, 2000, **11**, 3693.

Microbial reduction of ω- bromoacetophenones in the presence of surfactants

Rhodotorula rubra



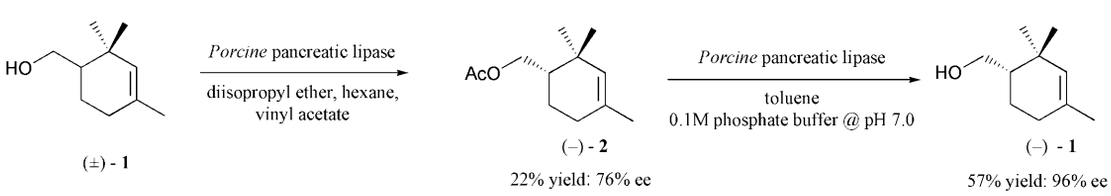
Where X^1=R^1=R^2=R^3=R^4=H, X^2=Br
Yield = 90% ee of **2a** = 95%

Other ω-bromoacetophenone derivatives were reduced to (*R*)-(−)-2-bromo-1-arylethanols with yields in the range 69-90% and ee in the range 89-95%.

A. Goswami, R. L. Bezbaruah, J. Goswami, N. Borthakur, D. Dey and A. K. Hazarika, *Tetrahedron: Asymmetry*, 2000, **11**, 3701.

Resolution of (±)-2,2,4-trimethyl-3-cyclohexene-1-methanol

Lipase

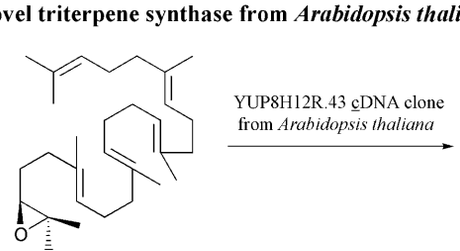


Chemical resolution of (±)-2,2,4-trimethyl-3-cyclohexene-1-carboxylic acid also yielded compound **1**. The synthesis of both enantiomers of *cis*-α-irone and *cis*-γ-irone was achieved in 5 and 9 steps respectively from compound **1**.

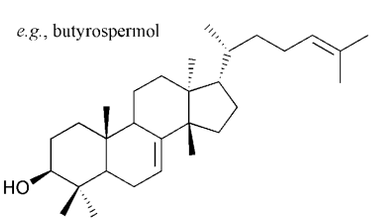
T. Inoue, H. Kiyota and T. Oritani, *Tetrahedron: Asymmetry*, 2000, **11**, 3807.

A novel triterpene synthase from *Arabidopsis thaliana*

Triterpene synthase



9 triterpenes:
butyrospermol
tirucalla-7,21-diene-3β-ol
lupeol
bauerenol
β-amyrin
multiflorenol
taxasterol
ψ-taraxasterol
α-amyrin



A novel triterpene synthase homologue (YUP8H12R.43 from *Arabidopsis thaliana*) was identified. It was found to produce 9 triterpenes. Studies were carried out in order to identify key sections which caused the broad specificity.

T. Kushiro, M. Shibuya, K. Masuda and Y. Ebizuka, *Tetrahedron Lett.*, 2000, **41**, 7705.