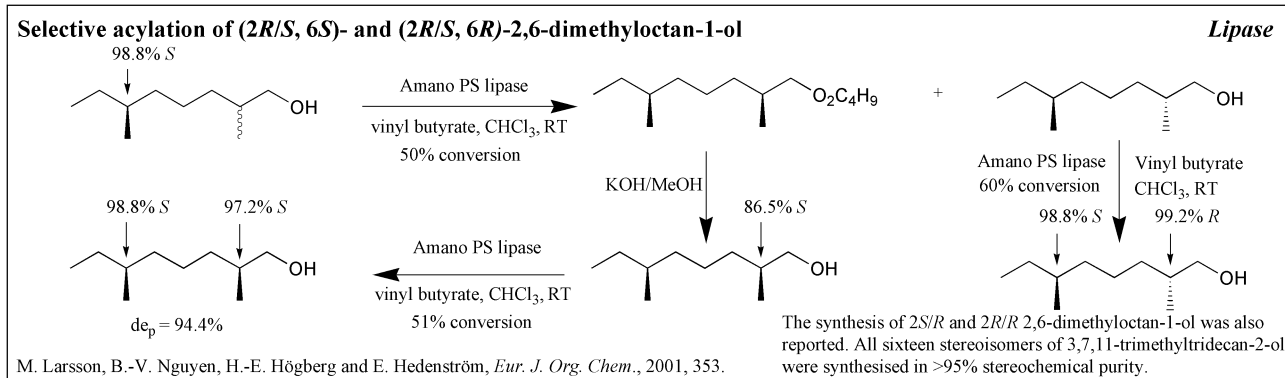


Gideon Grogan,^a Alexis Carstairs,^b Ian Jackson,^b Denise McIntyre,^b Alan Watt,^b Sabine Flitsch^b and Nicholas Turner^b

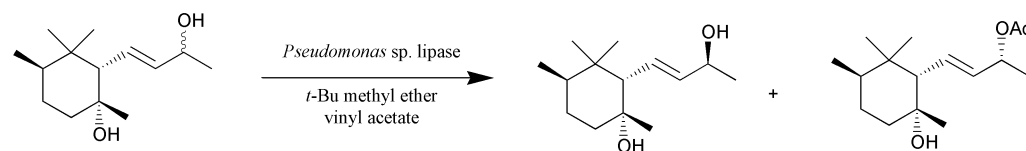
^a Department of Chemistry, University of York, Heslington, York, UK YO10 5DD

^b 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.



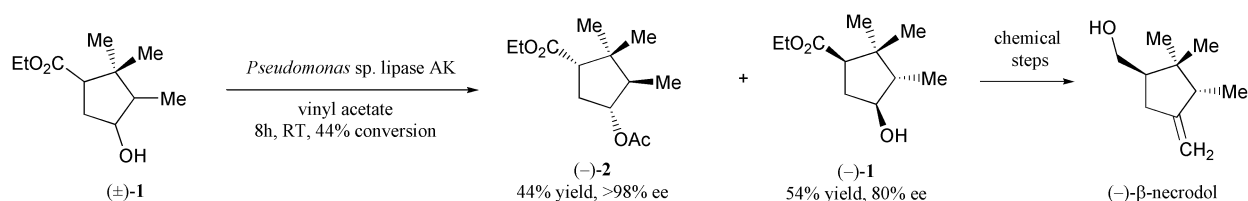
Preparation of irone terpenoids



E. Brenna, M. Delmonte, C. Fuganti and S. Serra, *Helv. Chim. Acta*, 2001, **84**, 69.

An extensive study of the biotransformation of irone terpenoid acetates was presented. Experiments directed toward producing (+)- and (-)-β-irone from Irone Alpha revealed *Pseudomonas* sp. lipase to be the enzyme of choice for the type of resolutions shown.

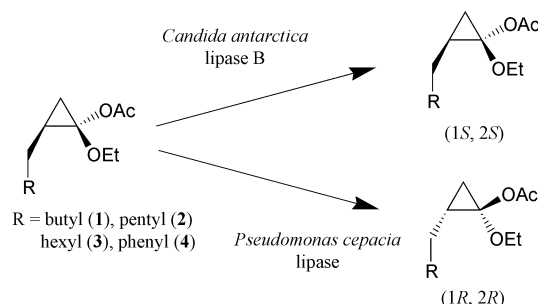
Enzyme-assisted enantioselective synthesis of (-)-β-necrodiol



J.-M. Galano, G. Audran, L. Mikolajczyk and H. Monti, *J. Org. Chem.*, 2001, **66**, 323.

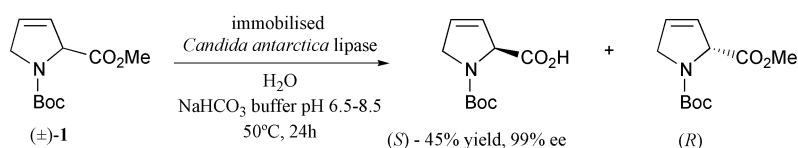
Lipase resolution allows access to the thermodynamically unfavourable *trans*-1,3-cyclopentane stereochemistry. Repeat enzymatic transesterification of (-)-1 led to an increase in ee to >98% with an overall yield of 45%.

Resolution of cyclopropanone hemiacetals

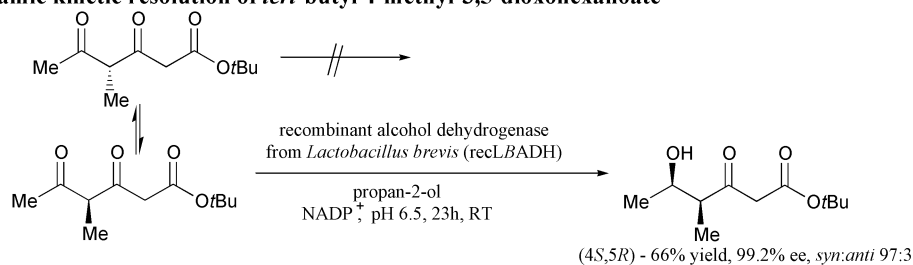


B. Westermann and B. Krebs, *Org. Lett.*, 2001, **3**, 189.

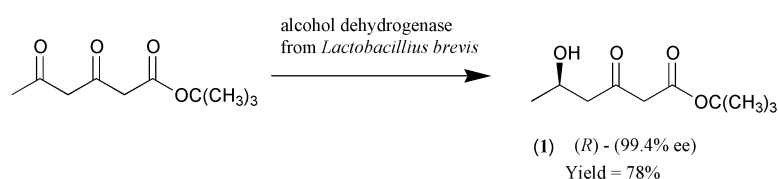
Enantiodivergent resolutions of cyclopropanone acetals **1-4**, of *trans*-configuration, were performed using two different lipases. Products in yields of up to 98% and optical purities up to >99% ee were obtained. *cis*-Configured substrates were not transformed.

Synthesis of (S)-1-Boc-2,5-dihydro-1H-pyrrole-2-carboxylic acid
Lipase

 R. Stürmer, B. Schäfer, V. Wolfart, H. Stahr, U. Kazmaier and G. Helmchen, *Synthesis*, 2001, 46.

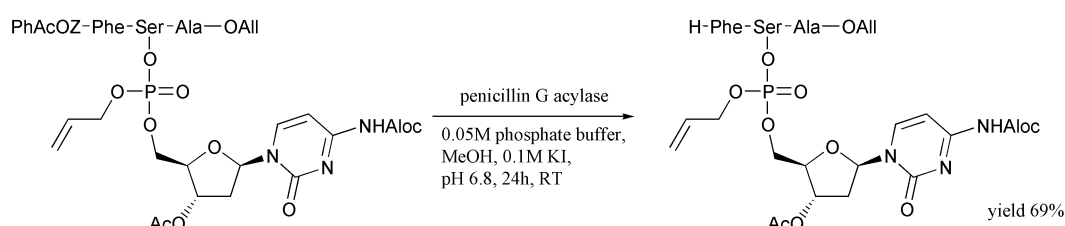
 Racemic **1** was obtained from the protected diallylamine derivative *via* ring-closing metathesis followed by alkoxy-carbonylation using an alkyl carbonate (69% yield).

Dynamic kinetic resolution of *tert*-butyl 4-methyl-3,5-dioxohexanoate
Alcohol dehydrogenase

 A. Ji, M. Wolberg, W. Hummel, C. Wandrey and M. Müller, *Chem. Commun.*, 2001, 57.

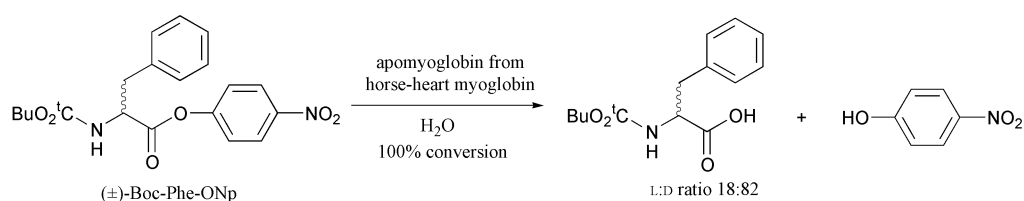
A new enzymatic method for the dynamic kinetic resolution of a racemic, 2-methyl substituted, unsymmetrical 1,3-diketone to give an enantiomerically pure compound is reported.

Regio- and enantioselective reduction of *tert*-butyl 3,5-dioxohexanoate
Alcohol dehydrogenase

 D. Drochner and M. Müller, *Eur. J. Org. Chem.*, 2001, 211.

 (*R*)-*semi*-Vioxanthin was synthesized in five steps from **1**. The synthesis of (*S*)-*semi*-Vioxanthin was also described.

Enzyme labile protecting group for nucleopeptide synthesis
Acylase

 D. A. Jeyaraj and H. Waldmann, *Tetrahedron Lett.*, 2001, 42, 835.

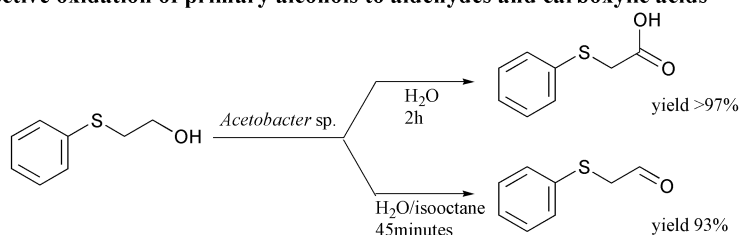
The effectiveness of the phenylacetoxycarbonyl (PhAcOZ) group as a protecting group in the synthesis of nucleopeptides was demonstrated. Other nucleotriptides (Val/Pro in place of Phe) were also studied in the same way. Subsequent peptide chain elongation and repetition of the enzymatic cleavage gave the corresponding nucleopeptide in ~40% yield.

Enantioselective hydrolysis of amino acid esters
Apomyoglobin

 K. Tomisaka, Y. Ishida, K. Konishi and T. Aida, *Chem. Commun.*, 2001, 133.

 Some unreacted Boc-Phe-ONp (99%) was also obtained which was predominantly the *D*-isomer. This shows that apoglobin mediated hydrolysis enables kinetic resolution of racemic Boc-Phe-ONp.

Selective oxidation of primary alcohols to aldehydes and carboxylic acids

Acetic acid bacteria

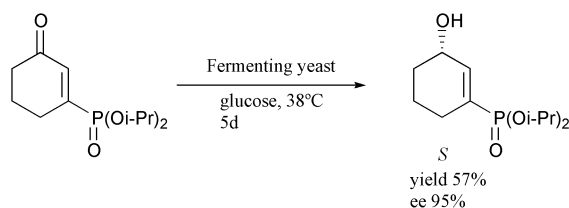


Using a 2 liquid phase system instead of water alone allowed accumulation of the aldehyde. 9 alcohols were tested, in both solvent systems and also with *Gluconobacter asaii*. Treatment of racemic 2-phenylpropan-1-ol with *Acetobacter* sp. gave the (S) alcohol in 95% ee at 40% conversion.

R. Gandolfi, N. Ferrara and F. Molinari, *Tetrahedron Lett.*, 2001, **42**, 513.

Enantioselective reduction of cyclic enones

Baker's yeast

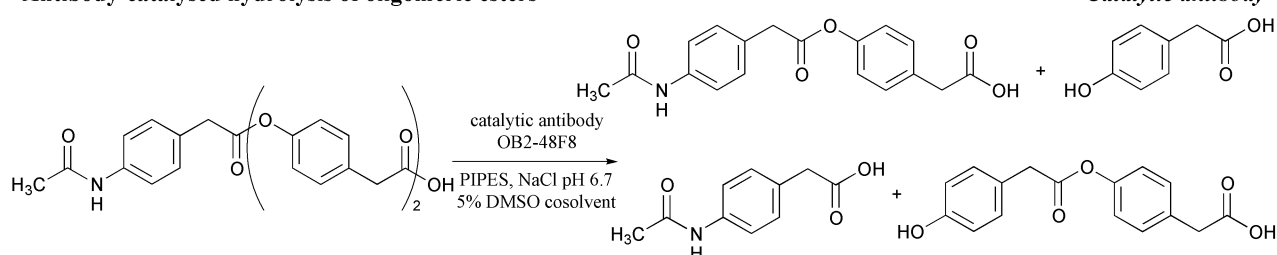


5 and 7 membered rings were also tested but found to be lower yielding and with poorer ee's. Reduction in steric bulk of the phosphorus alkyl groups, use of organic solvent and changing of various other conditions resulted in lower yields or ee's

M. Attolini, F. Bouguir, G. Iacazio, G. Peiffer and M. Maffei, *Tetrahedron*, 2001, **57**, 537.

Antibody-catalysed hydrolysis of oligomeric esters

Catalytic antibody

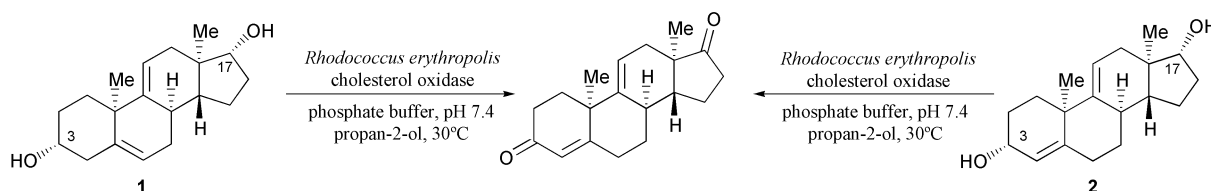


O. Brümmer, T. Z. Hoffman, D.-W. Chen and K. D. Janda, *Chem. Commun.*, 2001, 19.

A catalytic antibody has been discovered that degrades oligomeric esters. These findings are important as only enzymes were previously thought to degrade oligo materials.

Unusual oxidation by cholesterol oxidase

Cholesterol oxidase

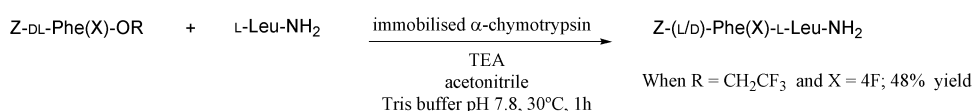


D. Kitamoto, S. Dieth, A. Burger, D. Tritsch and J.-F. Biellmann, *Tetrahedron Lett.*, 2001, **42**, 505.

The two unnatural enantiomers 1 and 2 were oxidised with similar kinetic parameters to that of the corresponding natural steroids. Interestingly both the C-3 and C-17 positions were oxidised in the unnatural compounds whereas only C-3 is oxidised in the natural steroid.

α -Chymotrypsin-catalysed peptide synthesis

α -Chymotrypsin

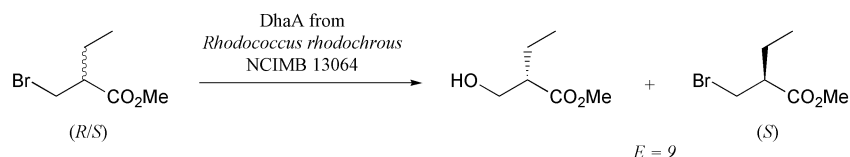


T. Miyazawa, S. Nakajo, M. Nishikawa, K. Hamahara, K. Imagawa, E. Ensatsu, R. Yanagihara and T. Yamada, *J. Chem. Soc., Perkin Trans. 1*, 2001, 82.

When R = Me and X = bulky substituent (e.g. *o*-Cl or *o*-Br), peptide yields were very low. The yields were greatly improved by the use of trifluoroethyl esters in acetonitrile with low water content.

The enantioselectivity of haloalkane dehalogenases

Dehalogenase

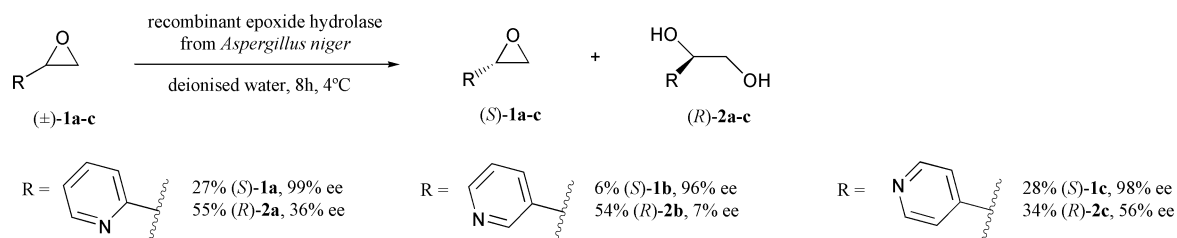


Other chiral haloalkanes (including some dihaloalkanes), some *meso* haloalkanes and the enzyme DhIA, from *Xanthobacter autotrophicus* GJ10 were also tested. Changes in the ester or ethyl substituent at the chiral center resulted in poorer *E* values. Resolution of the *meso* compounds (e.g. tribromopropane) gave ee's as high as 47%.

R. J. Pieters, J. H. L. Spelberg, R. M. Kellogg and D. B. Janssen, *Tetrahedron Lett.*, 2001, **42**, 469.

Green chemistry preparation of enantiopure pyridyloxiranes

Epoxide hydrolase

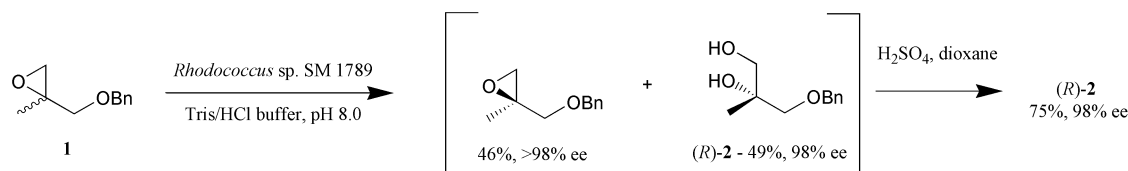


Y. Genzel, A. Archelas, Q. B. Broxterman, B. Schulze and R. Furstoss, *J. Org. Chem.*, 2001, **66**, 538.

A new "green" route to nearly enantiopure epoxides previously inaccessible by conventional chemical methods.

Hydrolysis of 2,2-substituted epoxides

Epoxide hydrolase

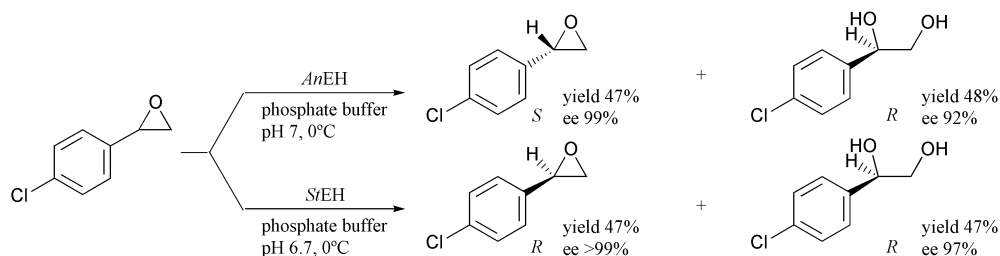


A. Steinreiber, H. Hellström, S. F. Mayer, R. V. A. Orru and K. Faber, *Synlett*, 2001, 111.

Rhodococcus sp. SM 1789 was shown to be the catalyst of choice for the preparative hydrolysis of **1**. Nucleophilic attack occurs at the least hindered carbon atom. Hence the addition of acid to the resolved mixture yields *R*-2 in 75% yield with 98% ee.

Epoxide resolution

Epoxide hydrolase

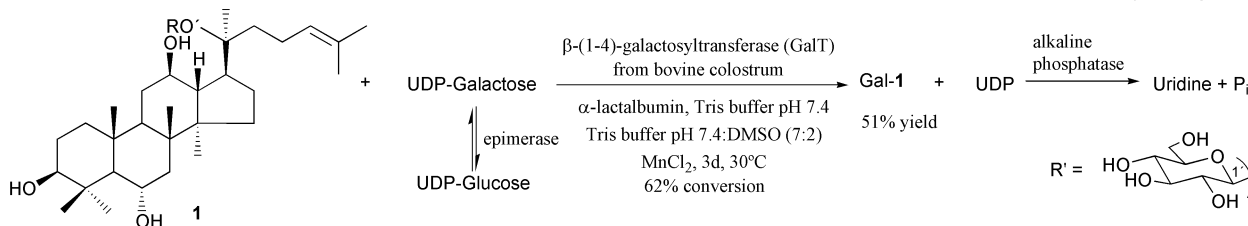


K. M. Manoj, A. Archelas, J. Baratti and R. Furstoss, *Tetrahedron*, 2001, **57**, 695.

The most effective epoxide hydrolases were found to be AnEH from *Aspergillus niger* and StEH from *Solanum tuberosum* L. It was possible to exploit the complementary nature of these EHS by subjecting the products of the reaction with StEH to AnEH, giving the *R* diol in 93% yield and 96% ee.

Regioselective enzymatic glycosylation of natural polyhydroxylated compounds

Galactosyltransferase

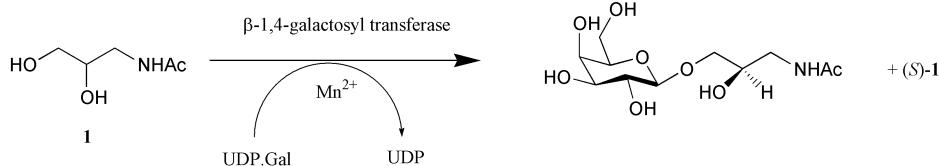


B. Danieli, L. Falcone, D. Monti, S. Riva, S. Gebhardt and M. Schubert-Zsilavecz, *J. Org. Chem.*, 2001, **66**, 262.

The enzyme showed the well-known specificity for the C-4-OH of the sugar substrate. These results confirm that glycosylations catalysed by β -(1,4)-GalT are not restricted to simple sugars, but can be applied to more complex saccharides provided that a nonsubstituted glucopyranosyl moiety is present in the molecule.

Galactosyl transferase reaction with an acyclic acceptor substrate

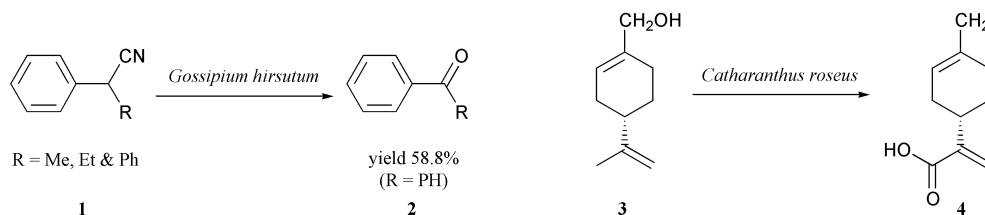
Galactosyl transferase



The first bovine β -1,4-galactosyl transferase reaction with an acyclic acceptor, 3-acetamidopropane-1,2-diol, is reported. The reaction is enantioselective, accepting only the (*R*)- substrate, and proceeds with 25% yield on preparative scale. Glycerol is not a substrate, suggesting a crucial role for the amine group in substrate binding.

Y. Nishida, H. Tamakoshi, K. Kobayashi and J. Thiem, *Org. Lett.*, 2001, 2, 1.

Hydroxylation of some benzyl cyanides and monoterpenes

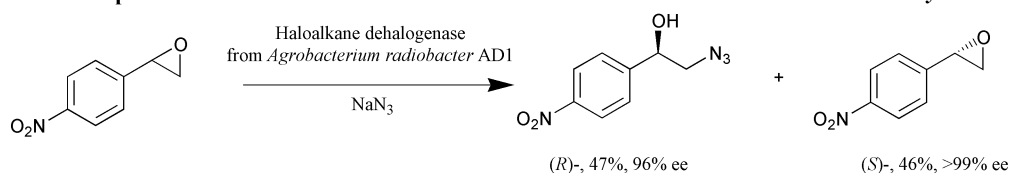
Gossipium hirsutum & *Catharanthus roseus*

H. Hamada, T. Tanaka, T. Furuya, H. Takahata and H. Nemoto, *Tetrahedron Lett.*, 2001, 42, 909.

The biotransformation of some benzyl cyanides was studied. In addition to those shown, 1-(4-methoxybenzo)cyclobutenecarbonitrile was converted to the corresponding ketone. Hydroxylation of the allylic positions of some monoterpenes was also studied. The biotransformation was successful for both 4*S*-(-)-perillyl alcohol (3) and 3*S*-(-)-citronellol.

Azidolysis of aromatic epoxides

Haloalkane dehalogenase

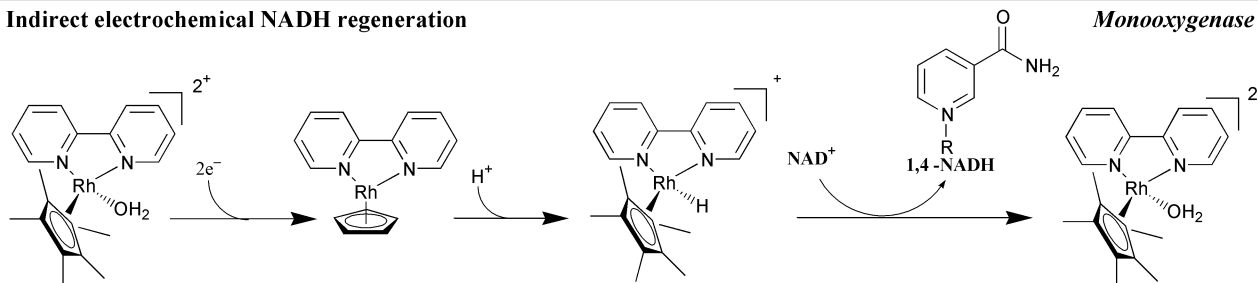


J. H. Lutje Spelberg, J. E. T. van Hylckama Vlieg, L. Tang, D. B. Janssen and R. M. Kellogg, *Org. Lett.*, 2001, 3, 41.

The enzymatic resolution of racemic 1 was described using haloalkane dehalogenase from *Agrobacterium radiobacter* AD1. Addition of azide occurs almost exclusively at the β -position, in contrast to the non-enzyme catalysed process. Evolution of side products was minimised by slow addition of azide.

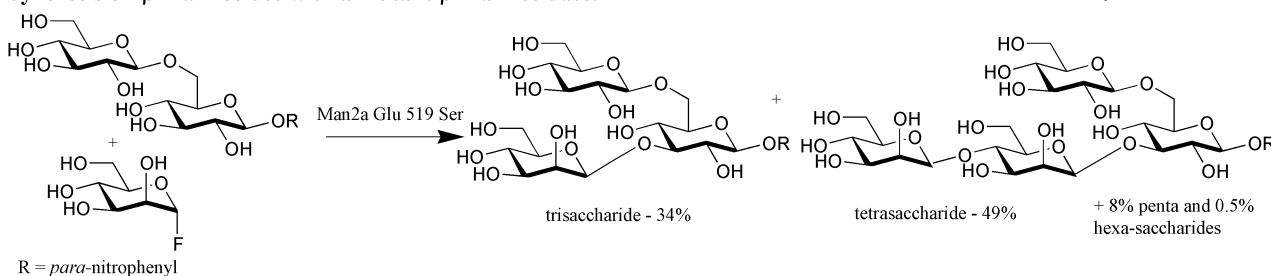
Indirect electrochemical NADH regeneration

Monooxygenase



F. Hollmann, A. Schmid and E. Steckhan, *Angew. Chem., Int. Ed.*, 2001, 40, 169.

Indirect electrochemical regeneration of NADH was employed with isolated 2-hydroxybiphenyl-3-monooxygenase from *P. azelaica*. A productivity rate of 204 mg $L^{-1}h^{-1}$ was reported.

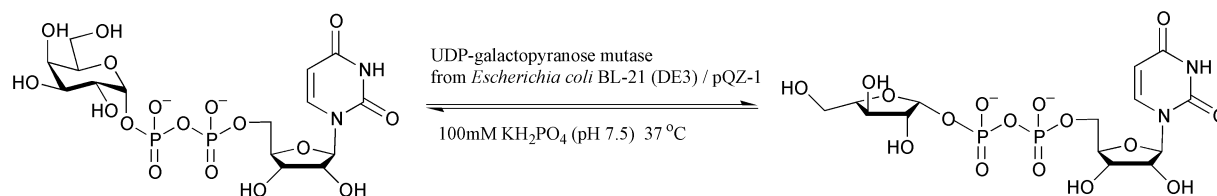
Synthesis of β -mannosides with a mutant β -mannosidase. β -Mannosidase

O. Nashiru, D. L. Zechel, D. Stoll, T. Mohammadzadeh, R. A. J. Warren and S. G. Withers, *Angew. Chem., Int. Ed.*, 2001, 40, 417.

Several other acceptor sugars were studied with yields of oligosaccharides in the range 70 - 99%. The ability of fluoride ions to rescue glycosidic bond cleaving activity was also reported.

Turnover of UDP-β-L-arabinofuranose to UDP-β-L-arabinopyranose by UDP-galactopyranose mutase

Mutase

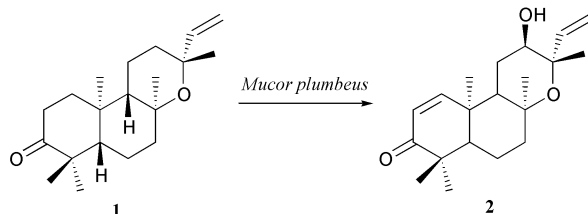


Q. Zhang and H.-w. Liu, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 145.

The synthesis of uridine-5'-diphospho-β-L-arabinofuranose was described.

Biotransformation of ribenone

Mucor plumbeus

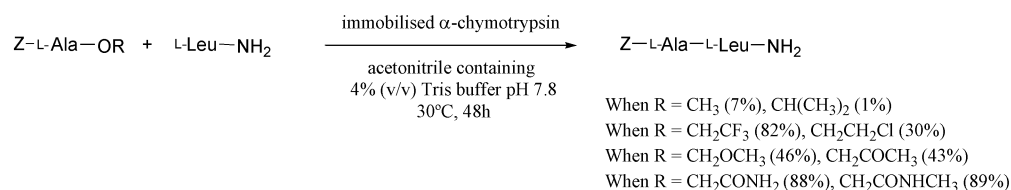


B. M. Fraga, M. G. Hernández, P. González, M. López and S. Suárez, *Tetrahedron*, 2001, **57**, 761.

The scheme shows an example **2** of the products of the biotransformation of ribenone **1** by *M. plumbeus*. Other products included hydroxylations at other sites around the ring system and epoxides.

Broadening of the substrate tolerance of α-chymotrypsin

Protease

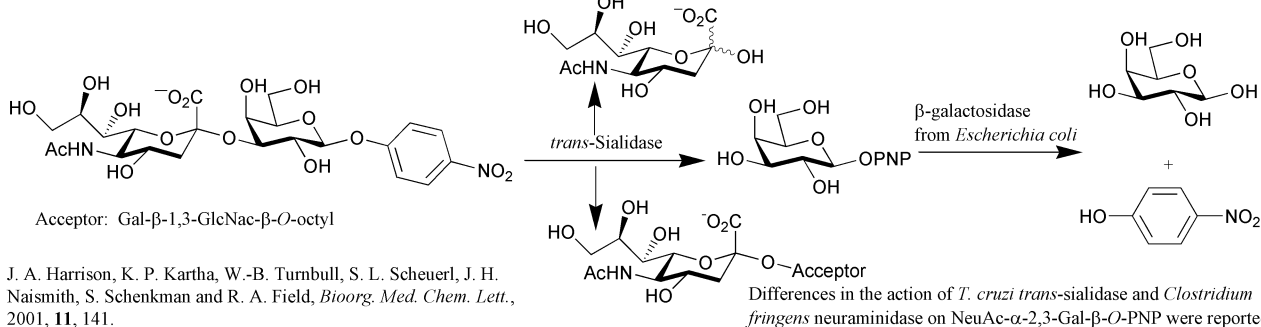


T. Miyazawa, K. Tanaka, E. Ensatsu, R. Yanagihara and T. Yamada, *J. Chem. Soc., Perkin Trans. 1*, 2001, 87.

The broadening of the protease's substrate tolerance was achieved by switching the acyl donor from the conventional methyl ester to the carbamoylmethyl ester.

Activity of *Trypanosoma cruzi* trans-sialidase towards NeuAc-α-2,3-Gal-β-O-PNP

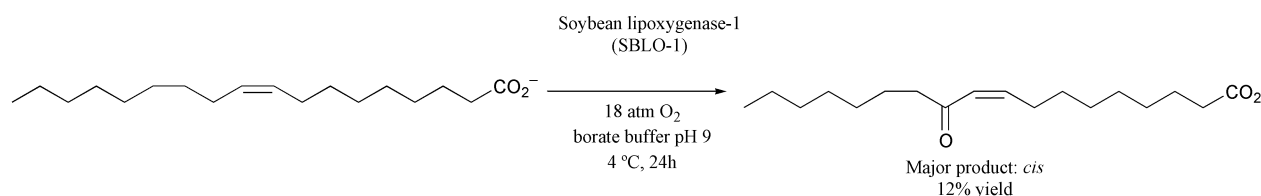
trans-Sialidase



J. A. Harrison, K. P. Kartha, W.-B. Turnbull, S. L. Scheuerl, J. H. Naismith, S. Schenkman and R. A. Field, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 141.

Enzyme-mediated oxygenation of monounsaturated fatty acids

Soybean lipoxygenase

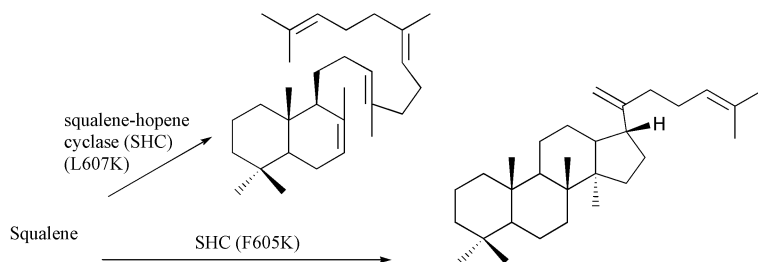


C. H. Clapp, S. E. Senchak, T. J. Stover, T. C. Potter, P. M. Findeis and M. J. Novak, *J. Am. Chem. Soc.*, 2001, **123**, 747.

The minor product was the corresponding *trans* enone. It was observed that the purified *cis* enone, isomerises to the *trans* enone which suggests that perhaps all of the *trans* enone detected arose from isomerization of the initially formed *cis* isomer. These findings represent the first example of SBLO-mediated functionalization of unactivated monounsaturated fatty acids.

Studies of squalene-hopene cyclase mutagenesis

Squalene-hopene cyclase

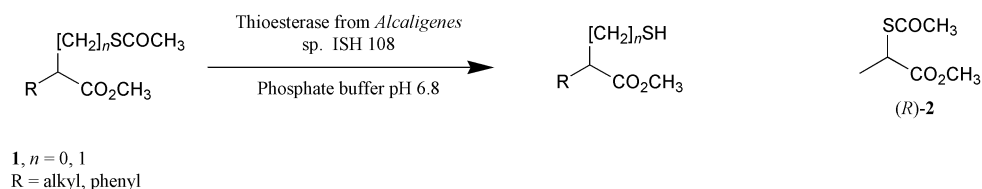


S. Schmitz, C. Füll, T. Glaser, K. Albert and K. Poralla, *Tetrahedron Lett.*, 2001, **42**, 883.

2 Mutants of squalene-hopene cyclase were studied. Mechanistic justification for the products observed was proposed.

Hydrolysis of *S*-acyl sulfanylalkanoates

Thioesterase

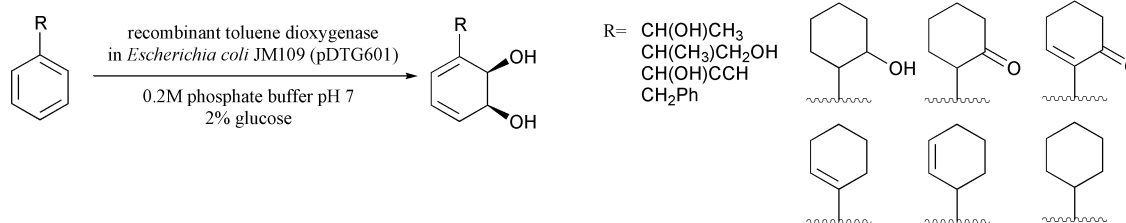


I. Kumar and R. S. Jolly, *Org. Lett.*, 2001, **3**, 283.

A thioesterase was purified from *Alcaligenes* sp. ISH 108 which catalyses the chemoselective hydrolysis of *S*-acyl sulfanylalkanoates. No activity was observed toward carboxylate esters. Yields of up to 97% were obtained. No stereoselectivity was observed, but the hydrolysis of (*R*)-2 was performed with high yield and no racemisation.

Substrate specificity study of toluene dioxygenase

Toluene dioxygenase



V. P. Bui, T. V. Hansen, Y. Stenstrom, T. Hudlicky and D. W. Ribbons, *New J. Chem.*, 2001, **25**, 116.

The activity of toluene dioxygenase towards substituted arenes containing remote chiral centers was examined. The absolute stereochemistry was determined, and no evidence of kinetic resolution was observed. Some metabolites may prove useful synthons in morphine synthesis.