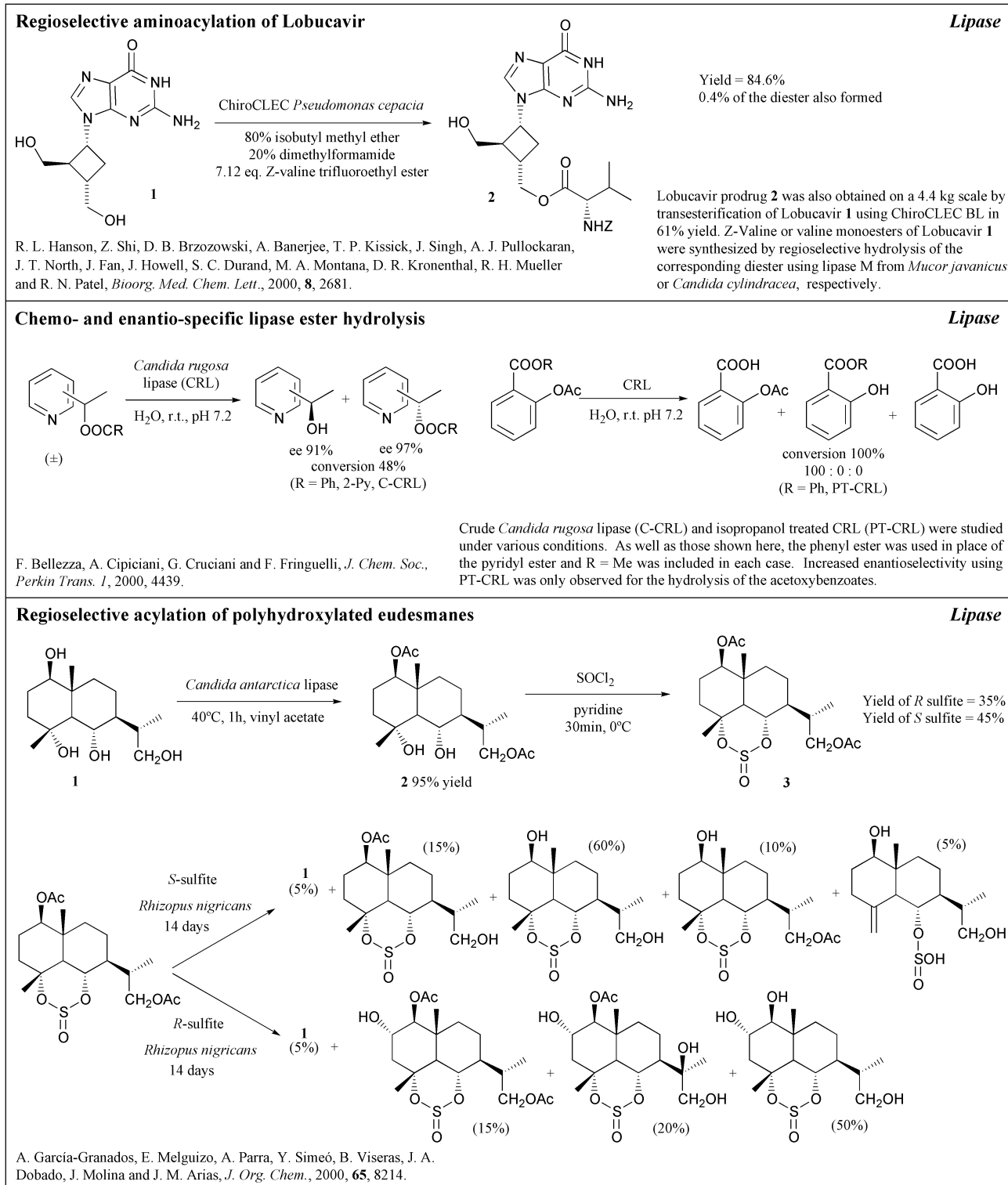


Gideon Grogan,^a Alexis Carstairs,^b Ian Jackson,^b Denise McIntyre,^b Alan Watt,^b Sabine Flitsch^b and Nicholas Turner^b

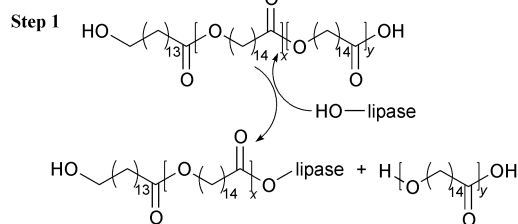
^a Department of Chemistry, University of York, Heslington, York, UK YO10 5DD

^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.

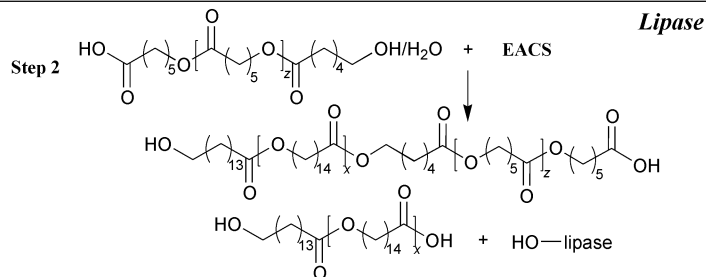


New synthetic routes to copolymers



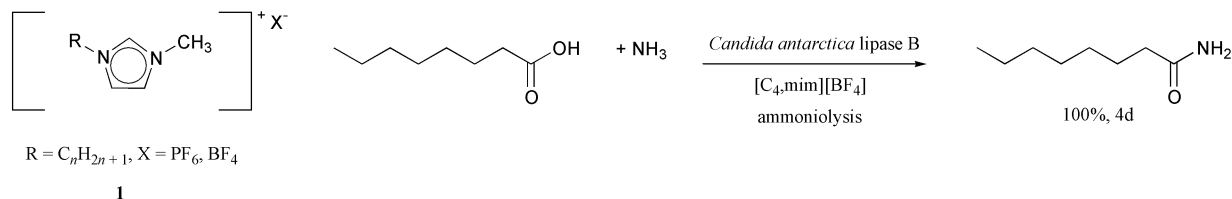
Enzyme Activated Chain Segment (EACS)

A. Kumar and R. A. Gross, *J. Am. Chem. Soc.*, 2000, **122**, 11767.



The mechanism of *Candida antarctica* lipase B-catalysed transesterification of polymer chains is shown. This type of reaction can be used to regulate block lengths along copolymer chains. In fact, this reaction can occur to such a high extent that copolymers with random repeat unit sequence distributions can be formed.

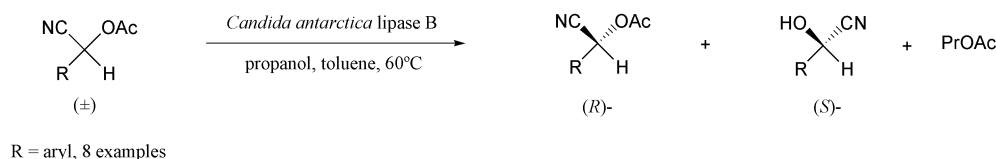
Lipase catalysed reactions in ionic liquids



R. Madeira Lau, F. van Rantwijk, K. R. Seddon and R. A. Sheldon *Org. Lett.*, 2000, **2**, 4189.

The first example of the use of free enzyme in an ionic liquid **1** in the absence of water is reported. Alcoholysis, the transesterification of ethylbutanoate with butyl alcohol, ammoniolysis and perhydrolysis reactions were demonstrated. Reaction rates were comparable with selected reactions in organic media.

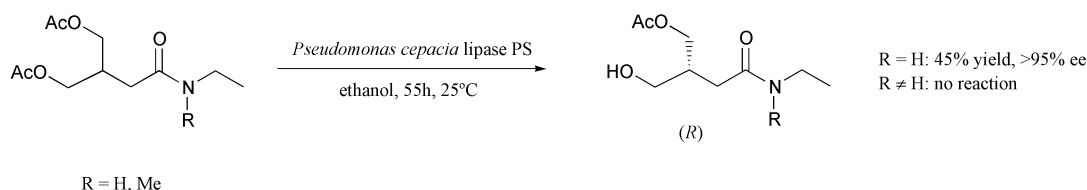
Lipase catalysed synthesis of cyanohydrins



U. Hanefeld, Y. Li, R. A. Sheldon and T. Maschmeyer, *Synlett*, 2000, 1775.

The resolution of a series of aryl cyanohydrins was accomplished using CAL-B in propanol–toluene mixture. A substrate concentration of 0.1 M was used and 100 mg enzyme/mmol substrate. *E* values of up to 360 were obtained.

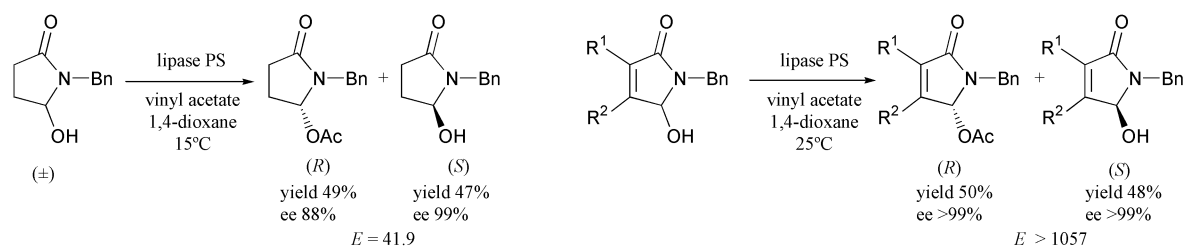
Desymmetrization of prochiral propane-1,3-diols and their diacetates



K. Takabe, Y. Iida, H. Hiyoshi, M. Ono, Y. Hirose, Y. Fukui, H. Yoda and N. Mase, *Tetrahedron: Asymmetry*, 2000, **11**, 4825.

The esterification of the propanediol was also studied, and it was found that when R = H the reaction proceeded with excellent enantioselectivity for the *pro-S* hydroxy, but with ~20–40% production of the diacetate. When R ≠ H the *pro-R* hydroxy is preferentially acylated with good to excellent enantioselectivity, and only trace amount of diacetate produced.

Resolution of a hydroxypyrrolidinone and hydroxydihydropyrrolones

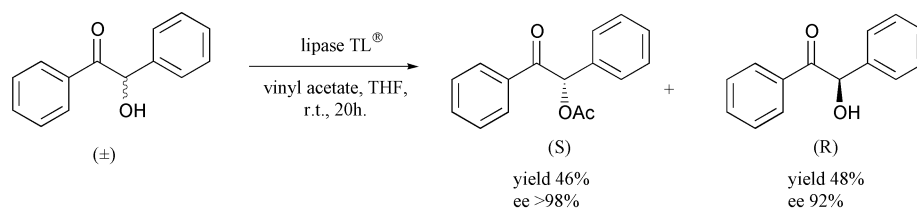


K. Takabe, M. Suzuki, T. Nishi, M. Hiyoshi, Y. Takamori, H. Yoda and N. Mase, *Tetrahedron Lett.*, 2000, **41**, 9859.

In both cases the corresponding hydrolysis was found to be less effective. Example shows yields *etc.* for R¹ = R² = H. Other R groups, alternatives to the benzyl group and Novozyme SP435 were also tested for suitability.

Lipase mediated kinetic resolution of (\pm)-benzoin

Lipase

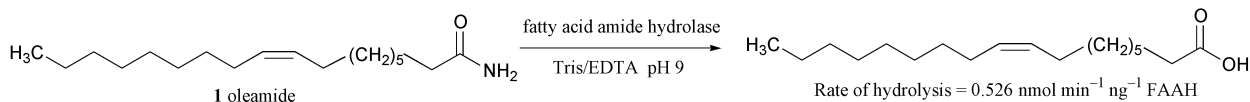


Y. Aoyagi, N. Agata, N. Shibata, M. Horiguchi and R. M. Williams, *Tetrahedron Lett.*, 2000, **41**, 10159.

The resolution was studied using 11 different lipases. Lipase TL[®] was found to be most effective, and solvent and acetate donor were optimised for this reaction. Results appear to be similar using recycled enzyme.

Fatty acid amide hydrolase substrate specificity

Hydrolase

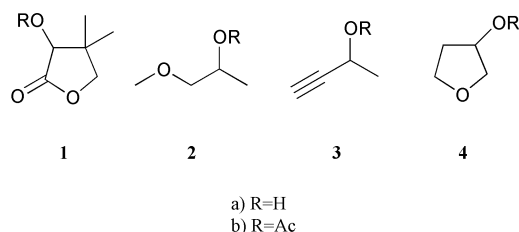


D. L. Boger, R. A. Fecik, J. E. Patterson, H. Miyauchi, M. P. Patricelli and B. F. Cravatt, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 2613.

The rates of hydrolysis of several fatty acid amides by recombinant rat fatty acid amide hydrolase (FAAH) were determined and reported relative to 1. Fatty acid primary amides containing *cis* double bonds are among the best substrates for FAAH and are hydrolysed faster than the corresponding ethanolamides. Saturation of the fatty acid amide reduces the rate of hydrolysis incrementally with increases in the degree of saturation. Incorporation of *Z* unsaturation at or near the amide bond increases the rate of hydrolysis more effectively than at more distal sites. Introduction of *E* unsaturation diminishes the rate of hydrolysis more effectively than removal of the double bond. The introduction of a methyl group or heteroatom α to the carbonyl decreases the rate of hydrolysis by FAAH.

Rapid screening of hydrolases for the enantioselective conversion of "difficult-to-resolve" substrates

Hydrolase



Four difficult to resolve compounds were chosen as models for the screening programme.

First round. 110 commercial enzymes were screened for hydrolytic activity. Compounds **1b-4b** were incubated at 37 °C for 3 hours with Bromothymol Blue as pH indicator. A colour change from blue to yellow indicated activity.

Second round. 20 enzymes exhibited hydrolytic activity.

Small scale reactions were performed and analysed by chiral GC for enantioselectivity.

1b - four enzymes with *E* > 100, **2b** - two enzymes with *E* > 100, **3b** - one enzyme with *E* = 75.

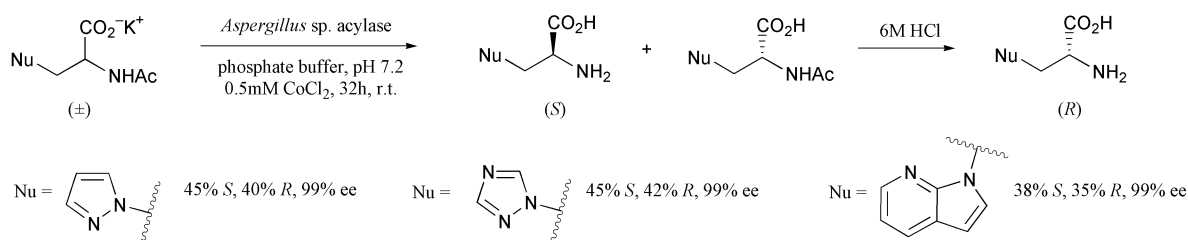
Third round. 6 enzymes with high enantioselectivity selected for preparative reaction.

M. Baumann, B. H. Hauer and U. T. Bornscheuer, *Tetrahedron: Asymmetry*, 2000, **11**, 4781.

Enzymes showing high selectivity were found for the resolution of compounds **1-3**, however compound **4** remains difficult to resolve.

Chemoenzymatic synthesis of β -heterocyclic amino acid derivatives

Acylase

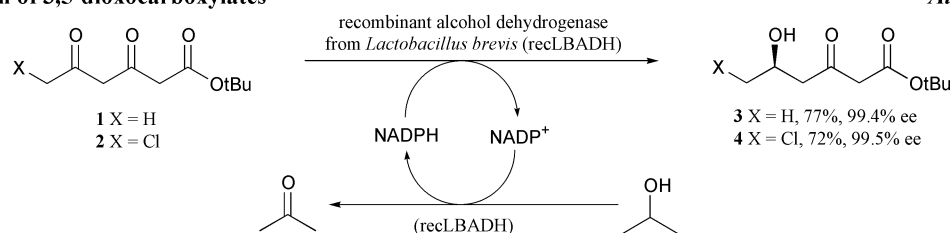


V. Rolland-Fulcrand, N. Haroune, M.-L. Roumestant and J. Martinez, *Tetrahedron: Asymmetry*, 2000, **11**, 4719.

An efficient route to both enantiomers of a series of enantiomerically pure unnatural amino acids.

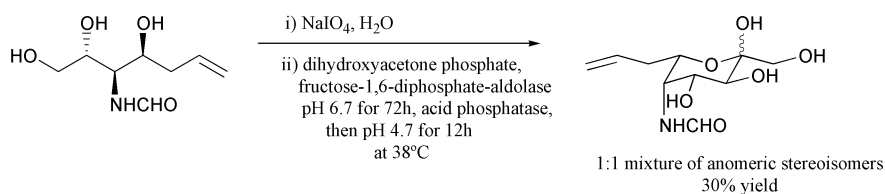
Reduction of 3,5-dioxocarboxylates

Alcohol dehydrogenase

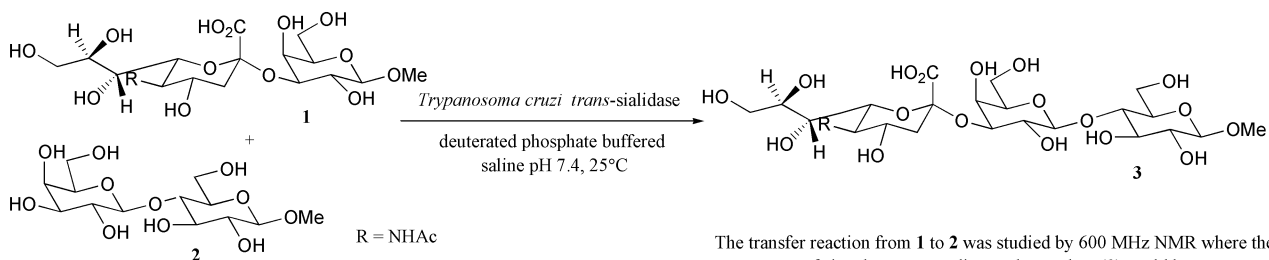


M. Wolberg, W. Hummel, C. Wandrey and M. Müller, *Angew. Chem., Int. Ed.*, 2000, **39**, 4306.

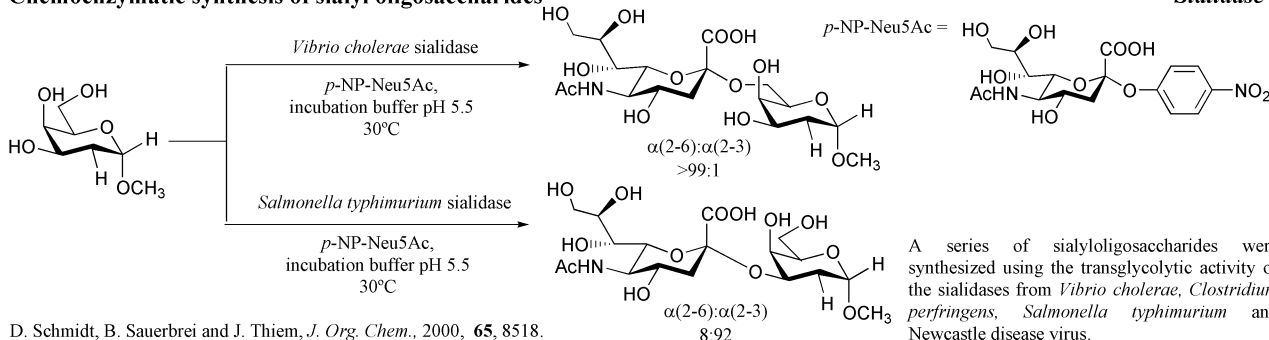
Recombinant LBADH expressed in *E. coli* was used to catalyse the regio- and enantioselective reduction of ketones **1** and **2** on 75 g scale using 1 mole% NADP as reducing equivalent. Compound **4** serves as a synthon for the mevinic acid type HMG CoA reductase inhibitors.

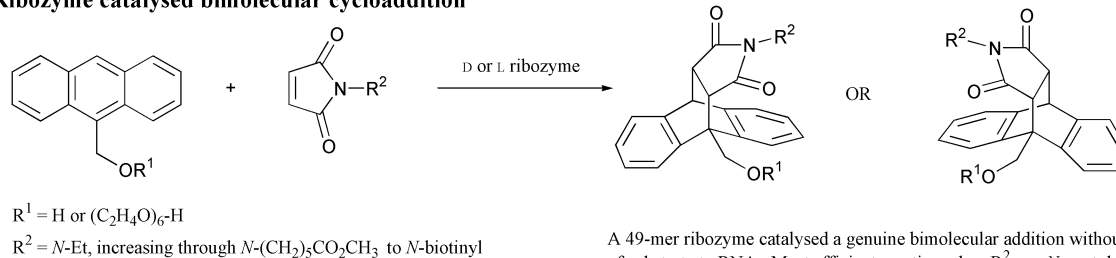
Chemoenzymatic synthesis of 3-epiaustraline and australine
Aldolase

 A. Romero and C.-H. Wong, *J. Org. Chem.*, 2000, **65**, 8264.

 Ozonolysis of the product followed by bis-reductive amination using H₂ with a Pd/C catalyst produced 3-epiaustraline (70% yield). When bis-reductive amination was carried out with NaCNBH₃, australine was produced in 52% yield.

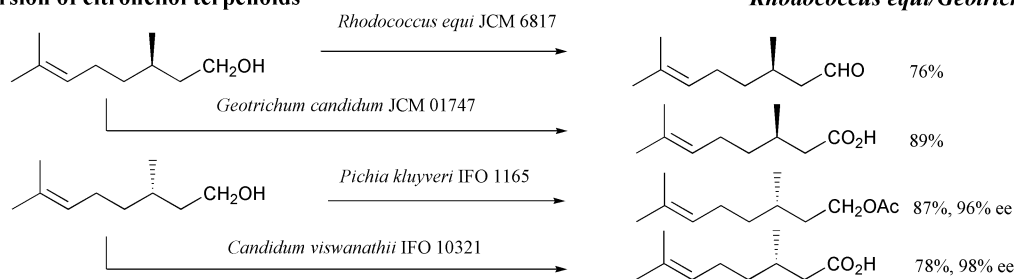
¹H NMR investigation of sialic acid transfer by the trans-sialidase from *Trypanosoma cruzi*
trans-Sialidase

 J. C. Wilson, M. J. Kiefel, S. Albouz-Abo and M. von Itzstein, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 2791.

 The transfer reaction from **1** to **2** was studied by 600 MHz NMR where the appearance of signals corresponding to the product (**3**) could be distinguished. The transfer reaction from α(2,3)-sialylactose to *N*-acetylactosamine was also studied.

Chemoenzymatic synthesis of sialyl oligosaccharides
Sialidase

 D. Schmidt, B. Sauerbrei and J. Thiem, *J. Org. Chem.*, 2000, **65**, 8518.

Ribozyme catalysed bimolecular cycloaddition
Ribozyme

 B. Seelig, S. Keiper, F. Stuhlmann and A. Jäschke, *Angew. Chem., Int. Ed.*, 2000, **39**, 4576.

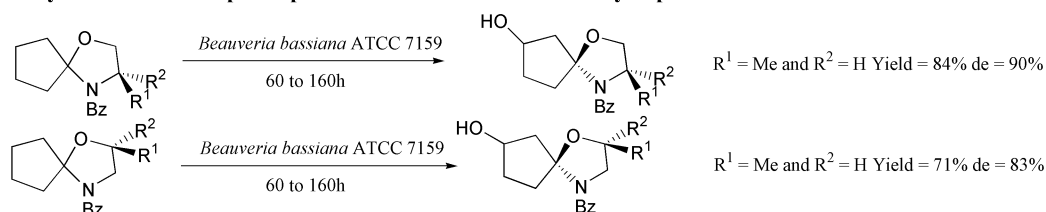
 A 49-mer ribozyme catalysed a genuine bimolecular addition without the conjugation of substrate to RNA. Most efficient reaction when R² was *N*-pentylmaleimide. *K*_M = 370 μm (diene), 8 mM (dienophile). *k*_{cat} = 21 min⁻¹. For R² = *N*-(CH₂)₅CO₂CH₃, a ratio of products corresponding to 90% ee was observed. A 'mirror image' ribozyme of l-nucleotides gave a product of opposite and equal optical purity.

Bioconversion of citronellol terpenoids
***Rhodococcus equi*/Geotrichum candidum**

 S. Oda, T. Sugai and H. Ohta, *Bull. Chem. Soc. Jpn.*, 2000, **73**, 2819.

The reactions were carried out in an 'interface bioreactor'. This consisted of the substrate in organic phase, swirled over a pre-grown microbial culture on an agar plate.

Hydroxylation of enantiopure spirooxazolidines derived from cyclopentanone

Beauveria bassiana

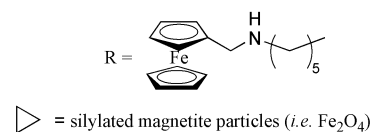
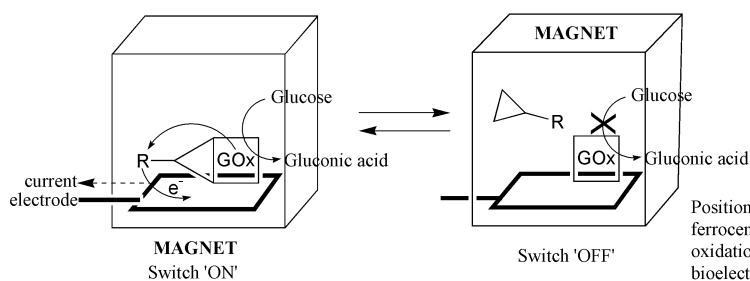


A. de Raadt, B. Fetz, H. Griengl, M. F. Klingler, I. Kopper, B. Krenn, D. F. Münzer, R. G. Ott, P. Plachota, H. J. Weber, G. Braunegg, W. Mosler and R. Saf, *Eur. J. Org. Chem.*, 2000, 3835.

A range of substrates were hydroxylated with yields in the range 0 to 84% and de in the range 17 to 90%. In substrates where C2 has the *S* configuration or C3 the *R* configuration the hydroxylated products are afforded in higher yield and superior diastereomeric excess than the respective enantiomers. Where R^1 or R^2 is a branched alkyl chain the configuration of the hydroxylated carbon can be controlled.

Magneto-switchable bioelectrocatalysis

Oxidase

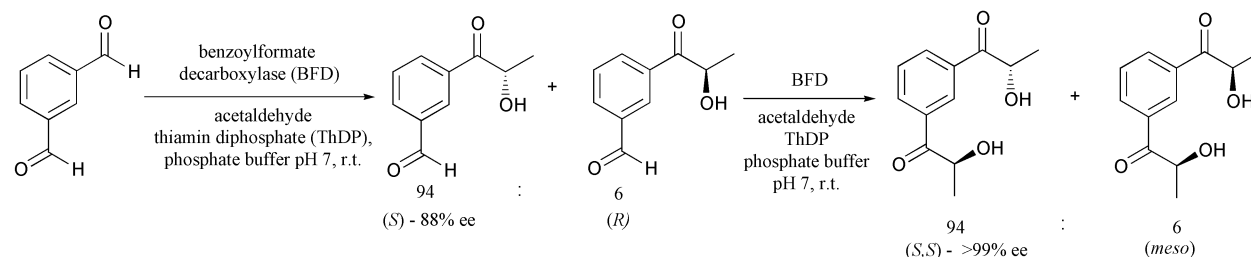


Positioning of a magnet below the electrode attracts the ferrocene-functionalised magnetite particles to the electrode. This enables oxidation of the ferrocene unit which subsequently activates the bioelectrocatalysed oxidation of glucose by glucose oxidase (GOx). Positioning of the magnet above the cell removes the magnetic particles from the electrode and this switches off the oxidation of glucose.

R. Hirsch, E. Katz and I. Willner, *J. Am. Chem. Soc.*, 2000, 122, 12053.

Enzymatic carbonylation of isophthalaldehyde and acetaldehyde

Decarboxylase

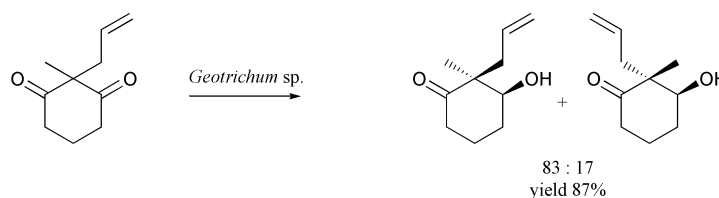


T. Dünwald and M. Müller, *J. Org. Chem.*, 2000, 65, 8608.

The synthesis of these chiral bis(α -hydroxy ketones) allows the formation of new multidentate ligands for asymmetric transition metal catalysis.

Asymmetric reduction of a diketone

Reductase

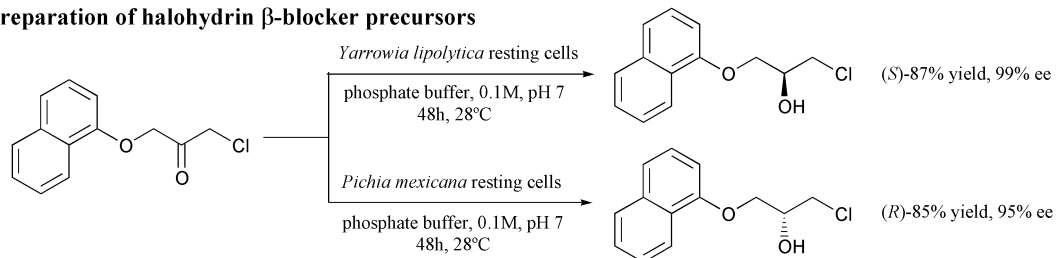


Z.-L. Wei, Z.-Y. Li and G.-Q. Lin, *Synthesis*, 2000, 1673.

The reduction was also attempted using baker's yeast, but lower yield and ee resulted. After conversion to the corresponding acetals, the two diastereomers could be separated by chromatography.

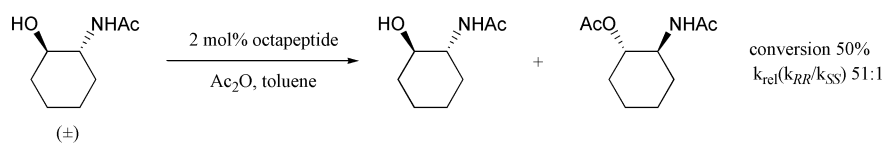
Preparation of halohydrin β -blocker precursors

Reductase



F. Martínez, C. Del Campo, J. V. Sinisterra and E. F. Llana, *Tetrahedron: Asymmetry*, 2000, 11, 4651.

A number of other organisms were investigated for the reduction of haloketones without success. Enzymatic reduction of the halohydrins is shown to be more efficient than chemical reduction (36% yield, 16% ee). Access to both enantiomeric series of the adrenergic β -blockers is achieved.



E. R. Jarvo, M. M. Vasbinder and S. J. Miller, *Tetrahedron*, 2000, **56**, 9773.

5 octapeptides containing a key π -(Me)-histidine (Pmh) in different positions along the chain were synthesised, then used in the resolution of *trans*-1,2-hydroxyacetimides (5, 6 and 7 membered rings). In some instances the *S,S* isomer was preferentially acylated.