Perkin 1 Abstracts: Biocatalysis in Organic Synthesis

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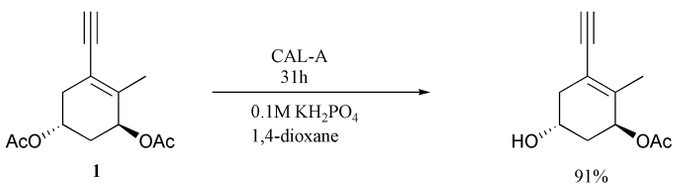
Perkin 1 Abstracts: Biocatalysis in Organic Synthesis aims to cover recent literature concerning the applications of enzymes and micro-organisms as catalysts in organic synthesis. The abstracts will emphasise the key synthetic step(s) that are mediated by the biocatalyst. Emerging technologies for biocatalyst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

Synthesis of precursors of 1α,25-dihydroxyvitamin D_3 ***Lipase***

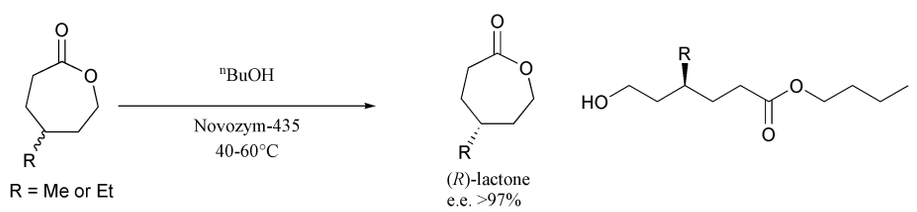


1 91%

V. Gotor-Fernández, M. Ferrero, S. Fernández and V. Gotor, *J. Org. Chem.*, 2002, **67**, 1266.

A series of monoacylated 1α,25-dihydroxyvitamin D_3 A-ring precursors were synthesised using enzymatic hydrolysis. For *trans*-isomers, such as **1**, *Candida antarctica* A lipase hydrolysed the acetate at the C-5 position while *Chromobacterium viscosum* lipase was used to deacetylate at the C-3 position of the respective *cis*-isomers.

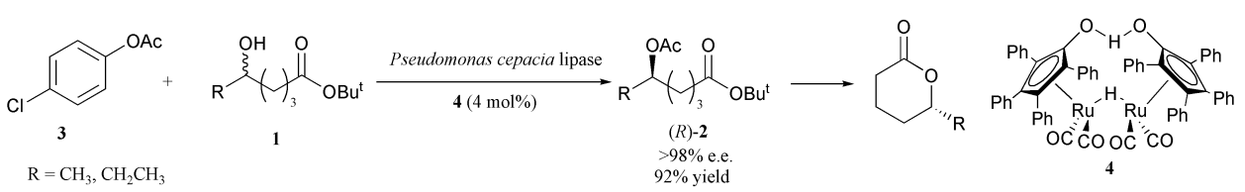
Lipase-catalysed solvent-free kinetic resolution of substituted ε-caprolactones ***Lipase***



L. Kondaveti, T. F. Al-Azemi and K. S. Bisht, *Tetrahedron: Asymmetry*, 2002, **13**, 129.

Lipase-catalysed butanolysis was used in the kinetic resolution of racemic seven-membered ring lactones under solvent free conditions. The lactones studied were substituted at either the 4- or the 6-position.

An efficient synthesis of δ-chiral lactones *via* dynamic kinetic resolution ***Lipase***

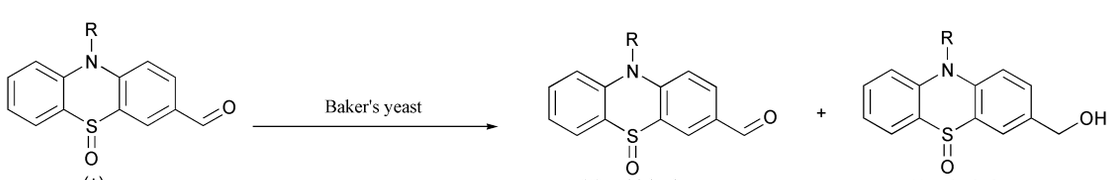


3 **1** **4**

O. Pàmies and J.-E. Bäckvall, *J. Org. Chem.*, 2002, **67**, 1261.

A highly efficient dynamic kinetic resolution of racemic *tert*-butyl δ-hydroxy esters, **1**, *via* lipase catalysed esterification is reported. Enzymatic kinetic resolution was combined with ruthenium catalysed isomerisation resulting in efficient dynamic kinetic resolution.

Synthesis of optically active sulfoxides by yeast catalysed reductions ***Baker's yeast***



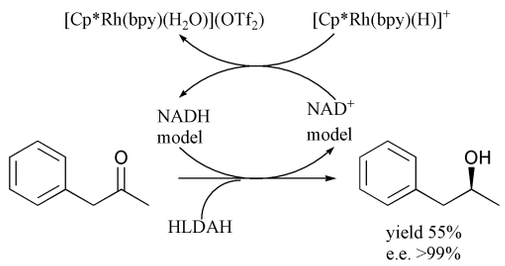
R = CH_3, C_2H_5, C_3H_7, C_4H_9, *iso*-C_4H_9, *iso*-C_5H_{11}, C_5H_{11}, C_7H_{15}

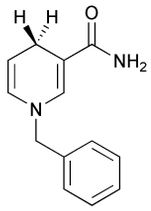
M. Tosa, C. Paizs, C. Majdik, L. Novák, P. Kolonits, F.-D. Irimie and L. Poppe, *Tetrahedron: Asymmetry* 2002, **13**, 211.

A series of racemic 10-alkyl-3-formyl-10*H*-phenothiazine-5-oxides were subjected to biotransformation with baker's yeast resulting in optically active aldehydes and alcohols in moderate enantiomeric excesses. A novel NMR method using enantiopure dibenzoyl tartaric acid as a chiral additive was developed for determination of the enantiomeric composition of the optically active products.

Biomimetic NAD^+ models

Dehydrogenase





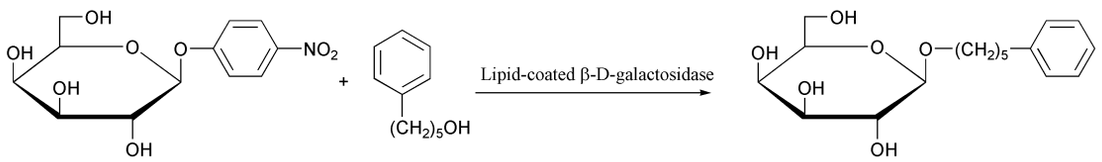
1 1-benzyl-1,4-dihydronicotinamide NADH model

The NADH model **1** was prepared and found to be effective in the reduction of ketones. The analogue was recognised by the HLDAH cofactor binding site. 5 Ketones including camphor were converted using this system, with yields and e.e.'s similar to those observed using NAD^+. The transition metal hydrides were formed *in situ* using sodium formate.

H.C. Lo and R. H. Fish, *Angew. Chem., Int. Ed.*, 2002, **41**, 478.

Reversible control of enzymatic transglycosylation in supercritical fluoroform

Glycosidase

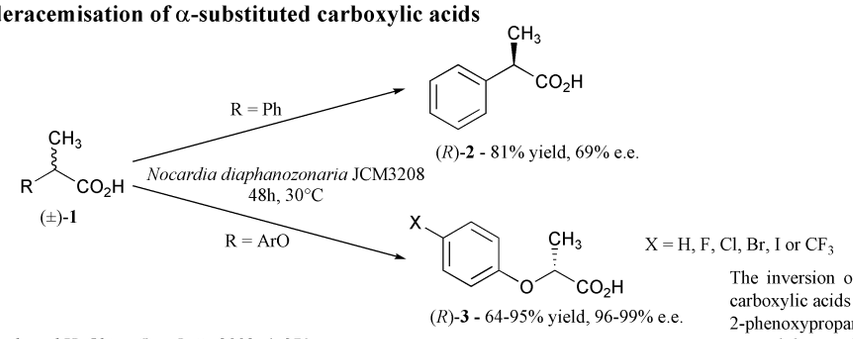


The rate of transgalactosylation by lipid-coated β-D-galactosidase in supercritical fluoroform can be reversibily controlled by changing temperature or pressure without damage to the enzyme.

T. Mori, M. Li, A. Kobayashi and Y. Okahata, *J. Am. Chem. Soc.*, 2002, **124**, 1188.

Microbial deracemisation of α-substituted carboxylic acids

Microbe

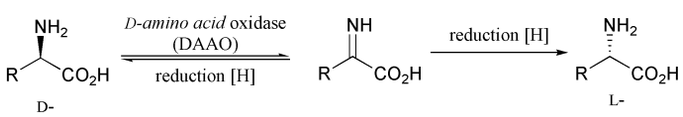


The inversion of chirality of various α-substituted carboxylic acids such as 2-phenylpropanoic acid and 2-phenoxypropanoic acid derivatives is reported, *via* a novel deracemization reaction.

D. Kato, S. Mitsuda and H. Ohta, *Org. Lett.*, 2002, **4**, 371.

Deracemisation and stereoinversion of α-amino acids

Oxidase

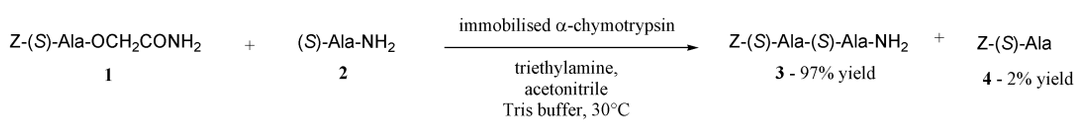


Initial deracemisation of racemic amino acids used proline as the substrate and sodium cyanoborohydride as the reducing agent, with yields and e.e.'s of >90%. A range of substrates with side-chains containing aromatic, thiol, alkyl or cyclic groups were tested, using sodium borohydride in place of sodium cyanoborohydride. Yields ranged from 75 to 90% and e.e.'s were >98%.

T. M. Beard and N. J. Turner, *Chem. Commun.*, 2002, 246.

Superiority of the carbamoylmethyl ester as an acyl donor for amide-bond formation

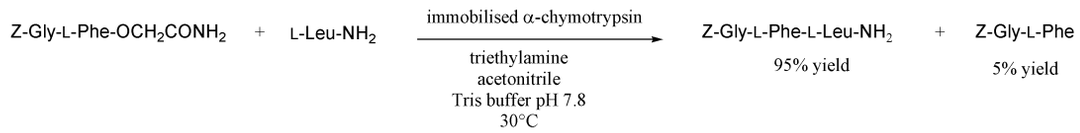
Protease



The effectiveness of carbamoylmethyl ester in the α-chymotrypsin catalysed couplings of **1** with different amino acid amides is reported. This approach was applied to the incorporation of halogenophenylalanines into peptides and to the enantioselective acylation of chiral amines with an *N*-protected amino acid ester as an acyl donor.

T. Miyazawa, E. Ensatsu, N. Yabuuchi, R. Yanagihara and T. Yamada, *J. Chem. Soc., Perkin Trans. 1*, 2002, 390.

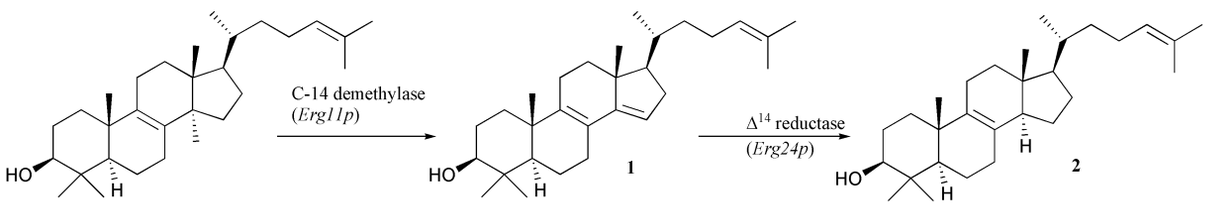
α-Chymotrypsin-catalysed segment condensations using carbamoylmethyl esters as acyl donors in organic media *Protease*



T. Miyazawa, E. Ensatsu, M. Hiramatsu, R. Yanagihara and T. Yamada, *J. Chem. Soc., Perkin Trans. 1*, 2002, 396.

The scope and limitations of using carbamoylmethylesters as acyl donors for the α-chymotrypsin-catalysed segment condensations is demonstrated in several model systems carried out in organic media with low water content.

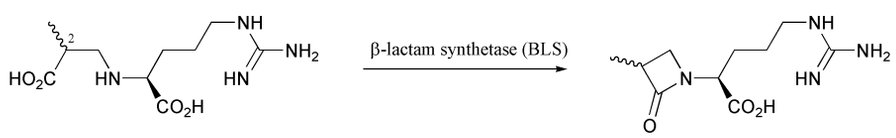
Production of sterols from metabolically engineered yeast *Saccharomyces cerevisiae*



R. Xu, W. K. Wilson and S. P. T. Matsuda, *J. Am. Chem. Soc.*, 2002, **124**, 918.

The use of metabolic engineering to produce significant amounts of sterols, which would otherwise be difficult to obtain, is reported. A number of stable yeast mutants were constructed in which the desired sterols FF-MAS, **1**, and T-MAS, **2**, were formed without further metabolism to normal yeast sterols.

Formation of an unnatural β-lactam *Synthetase*



M. C. Sleeman, C. H. MacKinnon, K. S. Hewitson and C. J. Schofield, *Bioorg. Med. Chem. Lett*., 2002, **12,** 597.

Using the 2-methylated unnatural substrate shown here, BLS was able to catalyse the conversion to 2-methyl deoxyguanidinoproclavaminic acid. It was found that both C-2 epimers were suitable substrates for BLS.