#### **GRAPHICAL ABSTRACTS**

BioMed. Chem. 1994, 2, 371

## Glyoxylic Acid Production Using Immobilized Glycolate Oxidase and Catalase

John E. Seip, Susan K. Fager, John E. Gavagan,
David L. Anton, and Robert Di Cosimo\*
CR&D Dept., E. I. du Pont de Nemours & Co.,
Experimental Station, PO Box 80328, Wilmington, DE 19880-0328

A variety of enzyme immobilization methods have been examined for the preparation of a catalyst for the oxidation of glycolic acid to glycoylic acid in 99 % yield.

BioMed. Chem. 1994, 2, 379

## INACTIVATION OF D-3-HYDROXYBUTYRATE DEHYDROGENASE BY FUMAROYL BIS(METHYL PHOSPHATE, Ronald Kiuger\* and

Stephen Bearne, Department of Chemistry, University of Toronto, Toronto, Canada M5S

1A1

**Abstract:** Fumaroyl bis(methyl phosphate) inactivates D-3-hydroxybutyrate dehydrogenase while cross-linking the two subunits of the enzyme.

Enzyme-Catalysed Kinetic Resolution of 4-endo-Hydroxy-2-oxabicyclo[3.3.0]-oct-7-ene-3-one and Employment of the

BioMed. Chem. 1994, 2, 387

Pure Enantiomers for the Synthesis of Anti-viral and Hypocholestemic Agents.

R. A. MacKeith, R. McCague, H. F. Olivo, S. M. Roberts, S. J. C. Taylor and H. Xiong aDepartment of Chemistry, Exeter University, Exeter, Devon EX4 4QD, U.K. bResearch Division, Chiroscience Ltd, Science Park, Cambridge CB4 4WE, U.K.

Reduction of Bicyclo[3.3.1]nonane-2,8,-diones with Baker's Yeast

BioMed. Chem. 1994, 2, 395

Kenji Mori,\*a Shuichi Takayama\* and Masaru Kidob\* aDepartment of Agricultural Chemistry, The University of Tokyo, Yayoi 1-1-1,Bunkyo-ku, Tokyo 113, Japan bAnalytical Chemistry Laboratory, 2nd Tokushima Institute of New Drug Research, Otsuka Pharmaceutical Co., Ltd., Kawauchi, Tokushima 771-01, Japan

Reduction of bicyclo[3.3.1]nonane-2,8-dione(1) and its homologues 2 and 3 with baker's yeast affords (1R, 5S, 8S)-8-hydroxybicyclo[3.3.1]nonan-2-one (4) and its homologues 5 and 6.

baker's yeast O i OH

I R=H

4 R = H

2 R = Me

5 R = Me

3 R = CH<sub>2</sub>CH=CH<sub>2</sub>

6 R = CH<sub>2</sub>CH=CH<sub>2</sub>

#### BioMed. Chem. 1994, 2, 403

BioMed. Chem. 1994, 2, 411

# Large Scale Preparation of Chiral Building Blocks for P<sub>3</sub> Site of Renin Inhibitors

S. Doswald, H. Esterman, E. Kupfer, H. Stadler, W. Walther, T. Weisbrod, B. Wirz\*, W. Wostl Pharma Research, New Technologies, \*Dept. of Microbiology or \*Physics; Pharma Operations, Manufacturing, \*bChemical Production or \*Process Development; \*Pharma Research, Cardiovascular Diseases; F. Hoffman-La Roche Ltd, 4002 Basel, Switzerland

# AMINOTRANSFERASE CATALYSIS APPLIED TO THE SYNTHESIS OF A PAF ANTAGONIST

David L. Coffen, Masami Okabe, Ruen Chu Sun, Seoju Lee and George W. J. Matcham, Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ 07110 Celgene Corporation, Warren, NJ 07059

L-CARNITINE VIA ENZYME-CATALYZED OXIDATIVE KINETIC RESOLUTION. Dennis Ditullio, David Anderson, Ching-Shih Chen, and Charles J. Sih\* School of Pharmacy, University of Wisconsin, Madison, WI 53706 U.S.A.

L-Carnitine of high optical purity was prepared via kinetic resolution using a mutant strain of *Acinetobacter calcoaceticus* ATCC 39647. This organism preferentially metabolized the D-enantiomer of the racemate to furnish L-carnitine. Recovery of L-carnitine was 93%, providing a total weight yield of 46.5% in 92% enantiomeric excess. The mode of degradation of carnitine was shown to proceed via a monooxygenase-catalyzed oxidative cleavage resulting in the formation of trimethylamine and malic acid.

#### BioMed. Chem. 1994, 2, 415

## A KINETIC STUDY AND APPLICATION OF A NOVEL CARBONYL REDUCTASE ISOLATED FROM RHODOCOCCUS ERYTHROPOLIS

Thomas Zelinski and Maria-Regina Kula Institut für Enzymtechnologie der Heinrich-Heine-Universität Düsseldorf, KFA Jülich, PO Box 2050, 52404 Jülich, FRG

Summary: A NADH-dependent Carbonyl Reductase which reduce a broad range of carbonyl compounds to (S)-hydroxy compounds. Application of the enzyme in preparative synthesis of 3-hydroxyacid esters.

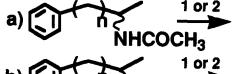
BioMed. Chem. 1994, 2, 421

BioMed. Chem. 1994, 2, 429

### Enzymatic asymmetric synthesis of $\alpha$ -methyl arylalkylamines and α-methyl arylalkylalcohols by arylalkyl acylamidases.

Jun Ogawa, Sakayu Shimizu and Hideaki Yamada,

Department of Agricultural Chemistry, Kyoto University, Sakyo-ku, Kyoto 606, Japan



1) Pseudomonas putida Sc2 AKU 881 n = 295% e.e. for (F)\*

99% e.e. for (5) \*\* n = 1,

2) Cellulomonas fimi AKU 671

n = 0, 99% e.e. for (5) \*

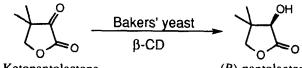
n = 2. 99% e.e. for (S) \*

94% e.e. for (S) \*\*

#### EFFECT OF CYCLODEXTRIN ON IMPROVEMENT OF ENANTIOSELECTIVITY IN THE REDUCTION OF KETO-PANTOLACTONE WITH BAKERS' YEAST

BioMed. Chem. 1994, 2, 433

Kaoru Nakamura, Shin-ichi Kondo, Atsuyoshi Ohno\* Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan



Addition of \( \beta\)-cyclodextrin improves enantioselectivity in the reduction of ketopantolactone mediated by bakers' yeast.

Ketopantolactone

(R)-pantolactone

#### CHEMICAL AND ENZYME-CATALYSED SYNTHESIS OF QUINOLINE HYDRATES.

R.Agarwal, D.R.Boyd, N.D.Sharma, R.A.S.McMordie, and H.P.Porter,

School of Chemistry, The Queen's University of Belfast, Belfast BT95AG, UK.

B.van Ommen, and P.J. van Bladeren,

Department of Biological Toxicology, TNO Toxicology and Nutrition Institute, P.O.Box360, 3700 AJ Zeist, The Netherlands.

Four arene hydrates of quinoline have been synthesised by chemical and enzyme-catalysed (fungal and animal) methods.

#### BioMed. Chem. 1994, 2, 439

#### Microbial Hydrolysis of Glutatonitrile Derivatives with Brevibacterium Sp R312

A. Kerridge, J. S. Parratt, S. M. Roberts, F. Thiel, N. J. Turner

and A. J. Willetts

<sup>a</sup>Department of Biological Sciences, University of Exeter, Exeter, Devon EX4 4QG, U.K. bDepartment of Chemistry, University of Exeter, Exeter, Devon EX4 4QD, U.K. CZentrum für Selektive Organische Synthese, Rudower Chaussee 5, D-12484-Berlin-Adlershof, Germany

The mechanism of conversion of dinitriles (A) into cyanoacids (B) using Brevibacterium R312 is discussed.

#### BioMed. Chem. 1994, 2, 447

(A)

**(B)** 

### CHARACTERIZATION OF A CATALYTIC ANTIBODY FOR

BioMed. Chem. 1994, 2, 457

STEREOSELECTIVE ESTER HYDROLYSIS

-A CATALYTIC RESIDUE AND MODE OF PRODUCT INHIBITION-

Takuji Nakatani<sup>1</sup>, Jun Hiratake<sup>1</sup>, Akihiro Shinzaki<sup>2</sup>, Ritsuko Umeshita<sup>1</sup>, Tadao Suzuki<sup>2</sup>, Hiroshi Nakajima<sup>2</sup>, and Junichi Oda<sup>1, •</sup> <sup>1</sup>Institute for Chemical Research, Kyoto University <sup>2</sup>Biochemistry Department, R&D Center, Unitika, Ltd. Uji, Kyoto 611, Japan

An esterolytic antibody was generated and characterized in terms of kinetic behavior, stereoselectivity, catalytic residue, and product inhibition. A keyrole of a catalytic Arg in product inhibition is noted.

EtO 
$$N-R$$
  $\frac{\text{antibody}}{-\text{EtOH}}$   $\frac{\text{antibody}}{-\text{EtOH}}$   $\frac{\text{N-R}}{\text{H}}$   $\frac{\text{HO}}{\text{Hapten}}$   $\frac{\text{N-R}}{\text{H}}$   $\frac{\text{R} = (CH_2)_5CO_2H}{\text{H}}$ 

### **Effect of Conformation of the Substrate on Enzymatic** Decarboxylation of α-Arylmalonic Acid

BioMed. Chem. 1994, 2, 469

Kenji MIYAMOTO, Hiromichi OHTA.

Department of Chemistry, Keio University, 3-14-1, Hiyoshi, Kohokuku, Yokohama 223, Japan Yoshihiro OSAMURA,

Department of Chemistry, Rikkyo University, 3-34-1, Nishiikebukuro, Toshimaku Tokyo 171, Japan

Syn-periplanar conformation of 1 is proposed to be essential to smooth enzymatic decarboxylation of 1 to afford chiral monocarboxylic acid 2.

BioMed. Chem. 1994, 2, 477

#### ACETYLESTERASE FROM ORANGE PEEL AS BIOCATALYST FOR THE CHEMO- AND REGIOSELECTIVE **DEPROTECTION OF CARBOHYDRATES**

Herbert Waldmann\* and Axel Heuser

Universität Karlsruhe, Institut f. Organ. Chemie, Richard-Willstätter-Allee 2, D-76128 Karlsruhe

### P. Mirabilis Dehydrogenates Aldonates and Aldarates with an (R)-

BioMed. Chem. 1994, 2, 483

Configured α-Carbon Atom to the Corresponding 2-Oxocarboxylates

C. Schinschel and H. Simon, Institute of Organic Chemistry, Technische Universität München, D-85747 Garching

### CHEMOENZYMATIC ACCESS TO ENANTIOMERIC BICYCLO[2.2.1]HEPTAN-2,5-DIONES

BioMed. Chem. 1994, 2, 493

Alexandra Weissfloch and Robert Azerad\*, Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, URA 400 CNRS, Université René Descartes, 45 rue des Saints-Pères, 75270-Paris Cedex 06, France.

(1R,4R) : 96% e.e. (1S,4S) : 99% e.e.

### Enhanced Stereoselectivity in Pig Liver Esterase Catalysed Diester Hydrolysis. The Role of a Competitive Nucleophile

BioMed. Chem. 1994, 2, 501

Anders Mattson, John Boutelje, Ingeborg Csöregh, Mats Hjalmarsson, Ulla Jacobsson, Mariane Lindbäck, Torbjörn Norin, Peter Szmulika and Karl Hultb\*

<sup>a</sup>Department of Chemistry, Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm, Sweden <sup>b</sup>Department of Biochemistry and Biotechnology, Royal Institute of Technology, S-100 44 Stockholm, Sweden <sup>c</sup>Department of Structural Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm, Sweden

The increased enantioselectivity of pig liver esterase catalysed hydrolysis of cis-N-benzyl-2,5-bis(methoxycarbonyl)-pyrrolidine,performed in media buffered with tris-(hydroxymethyl)

Heo The-buffer Meo PLE HO Ph HO Ph OMe

aminomethane (Tris), was explained by the preference of Tris to react faster with one of the diastereomeric acyl enzymes over the other. An acid-amide product was isolated, and NMR-studies revealed the presence of an ester-amide intermediate.

### DO CARBOHYDRATES PLAY A ROLE IN THE LIGNIN PEROXIDASE CYCLE?

redex catalysis in the endergonic region of the driving force Hans E. Schoemaker<sup>1,4</sup>, Taina K. Lundell<sup>2</sup>, René Floris<sup>3</sup>, Tuomo Glumoff<sup>4</sup>, Kaspar H. Winterhalter<sup>5</sup> and Klaus Piontek<sup>5</sup>

<sup>1</sup>DSM Research, Bio-organic chemistry section, P.O. Box 18, 6160 MD Geleen, The Netherlands; <sup>2</sup>University of Helsinki, Finland;

<sup>3</sup>University of Amsterdam, The Netherlands;

University of Turku, Finland; SETH, Zürich, Switzerland;

Abstract: The redox cycle of lignin peroxidase is described in terms of Marcus theory of electron transfer. The oxidation of veratryl alcohol occurs in the endergonic region of the driving force, still the reduction of LiP Compound I is irreversible. A reversible reaction of the incipient veratryl alcohol radical cation with a glucose residue located at the entrance of the active site channel is postulated.

#### BioMed. Chem. 1994, 2, 509

BioMed. Chem. 1994, 2, 521

# TWISTED $\alpha\textsc{-}KETO$ AMIDES AS TRANSITION-STATE ANALOGUES FOR ACYL-TRANSFER REACTIONS: SYNTHESIS OF THE IMMUNOCONJUGATES

Jari Yli-Kauhaluoma\* and Kim Janda\* #On leave from Technical Research Centre of Finland, Chemical Laboratory, Biologinkuja 7, FIN-02150 Espoo, Finland \*The Scripps Research Institute, Departments of Molecular Biology and Chemistry, 10666 North Torrey Pines Road, La Jolla, CA 92037

Two  $\alpha\text{-keto}$  amides 1 and 2 were employed as antigens to elicit antibodies for acyl-transfer reactions. The rationale for their design, synthesis, and immunization protocols will be discussed.

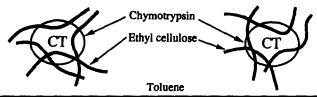
### SYNTHETIC POLYMERS AS SOLUBILIZING VEHICLES FOR ENZYMES IN WATER-POOR MEDIA.

BioMed. Chem. 1994, 2, 529

Patrick Adlercreutz, Bo Mattiasson, Marina Otamiri

Department of Biotechnology, Chemical Center, Lund University, Lund, Sweden

Non-covalent enzyme-polymer complexes were formed by freeze-drying aqueous solutions of enzymes and polymers. Complex formation made it possible to solubilize the enzymes in organic solvents and thereby act as catalysts for the conversion of hydrophobic compounds.



Stereoselective Epoxidation of 2,2-Dimethyl-

2H-1-benzopyran-6-carbonitrile

Ramesh Patel\*, Amit Banerjee, Brian Davis, Jeffrey Howell,

Clyde McNamee, David Brzozowaski, Jeffrey North,

David Kronenthal and Laszlo Szarka

Department of Microbial Technology, Bristol-Myers Squibb Pharmaceutical Research Institute, P.O. Box 191, New Brunswick, NJ 08903

Mortierella ramanniana SC 13840 and Corynebacterium sp.SC 13876 were used to prepare (3S,4S-cis)-3,4-Dihydro-2,2-dimethyl-2H oxireno [c] [1] benzopyran-6-carbonitrile and (3S,4R)-3,4-dihydro-3,4-dihydroxy-2,2-dimethyl-2H-1-benzopyran-6-carbonitrile

BioMed. Chem. 1994, 2, 535

CH<sub>3</sub> MICROBIAL NC CH<sub>3</sub> CH<sub>4</sub> OH

BioMed. Chem. 1994, 2, 543

NC CH<sub>3</sub>

Oxidative Coupling of Mithramycin and Hydroquinone Catalyzed by Copper Oxidases and Benzoquinone. Implications for the Mechanism of Action of Aureolic Acid Antibiotics.

I. O. Anyanwutaku, R. J. Petroski and J. P. N. Rosazza

Division of Medicinal and Natural Products Chemistry, and Center for Biocatalysis and Bioprocessing, University of Iowa, College of Pharmacy, Iowa City, IA 52242, U.S.A.

Epoxidation of Stryrene and Substituted Styrenes by Whole Cells of Mycobacterium sp M156

Stuart R. Rigby, <sup>1</sup> Collette S. Matthews<sup>2</sup> and David J. Leak<sup>2</sup> <sup>1</sup>ZENECA Bio Products, P.O. Box 2, Belasis Avenue, Billingham, Cleveland, TS23 1YN, U.K.

<sup>2</sup>Centre for Biotechnology, Department of Biochemistry, Imperial College of Science Technology and Medicine, London SW7 2AZ, U.K.

Propene grown Mycobacterium sp M156 catalyses the stereospecific conversion of styrene and ring mono-substituted styrenes to their epoxides in high enantiomeric excess, at rates comparable to that of the natural substrate, propene. Substituents closer to the site of epoxidation reduce the rate of reaction.

BioMed. Chem. 1994, 2, 553

R<sub>1</sub> M156, O<sub>2</sub> H"" R<sub>1</sub> R<sub>2</sub>

 $R_1 = F$ ;  $R_2 = F$ , CI,  $CH_3$ ;  $R_3 = F$ , CI,  $CH_3$