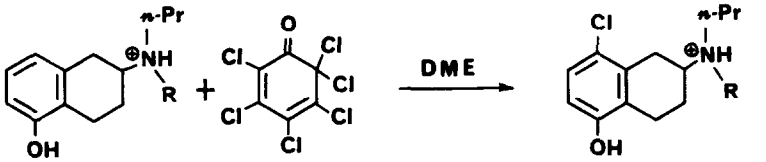
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1992**, 2, 115

A SIMPLE, UNEXPECTED REGIOSELECTIVE CHLORINATION OF A SERIES OF 5-OH-2-(ALKYLAMINO)TETRALINS: POTENTIAL DOPAMINERGIC AGENTS

Durk Dijkstra and Cor J. Grol, University Centre for Pharmacy, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands

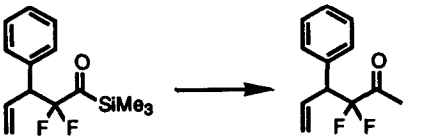


BioMed. Chem. Lett. **1992**, 2, 119

SYNTHESIS OF α,α-DIFLUOROKETONES: NOVEL SYNTHESIS OF α,α-DIFLUOROKETONES FROM α,α-DIFLUOROACYLSILANES

Peter A. McCarthy*, Lewin T. Wint and Christina L. Diaz
Department of Medicinal Chemistry, Central Research Pfizer, Inc., Eastern Point Road, Groton, Connecticut 06340

Abstract: **α,α-Difluoroketones, targets of interest as potential transition state mimics and enzyme inhibitors, have been synthesized from the corresponding α,α-difluoroacylsilanes by treatment with diazoalkanes.**

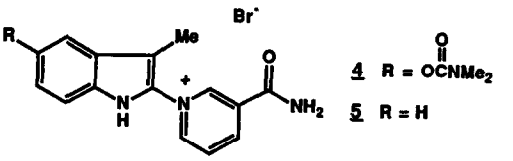


BioMed. Chem. Lett. **1992**, 2, 123

SYNTHESIS OF 1-(2-INDOLYL)PYRIDINIUM SALTS: A PRODRUG APPROACH TO ACETYLCHOLINESTERASE INHIBITION,

Jeffrey J. Ares,* Steven M. Ronkin, and Lane J. Wallace
Department of Chemistry, Worcester Polytechnic Institute, Worcester, MA 01609 and Division of Pharmacology, College of Pharmacy, The Ohio State University, Columbus, Ohio 43210

1-(2-Indolyl)pyridinium bromide 4 and related pyridinium salt 5 have been synthesized as part of a prodrug strategy for acetylcholinesterase inhibition.



BioMed. Chem. Lett. **1992**, 2, 127

THE SYNTHESIS AND EVALUATION OF DIACYLGLYCEROL ANALOGUES AS POTENTIAL SECOND-MESSENGER ANTAGONISTS

J.C. Briggs, A.P. Dawson, I. Gibson, A.H. Haines,* J. Hook, A. Lloyd, S. Meiners, and R.J.K. Taylor*
University of East Anglia, Norwich, NR4 7TJ, U.K.

Structural analogues of diacylglycerol have been synthesized in an attempt to discover antagonists of protein kinase C with the aim of developing new agents for preventing cell proliferation.

BioMed. Chem. Lett. **1992**, *2*, 131

THE SYNTHESIS OF CONFORMATIONALLY RESTRICTED DIACYL GLYCEROL ANALOGUES

J.C. Briggs, A.P. Dawson, I. Gibson, A.H. Haines,* and R.J.K. Taylor*
University of East Anglia, Norwich, NR4 7TJ, U.K.

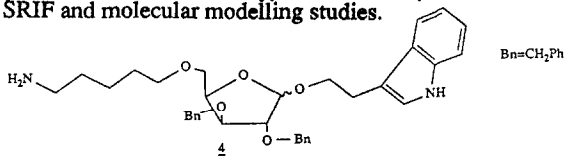
A series of conformationally restricted diacylglycerol analogues have been prepared in homochiral form as potential protein kinase C antagonists. D-Ribonolactone and D- and L-2-deoxyribose were used as starting materials.

BioMed. Chem. Lett. **1992**, *2*, 135

DESIGN,SYNTHESIS,AND BINDING AFFINITY OF A NONPEPTIDE MIMIC OF SOMATOSTATIN

C.Papageorgiou*,R.Haltiner, C.Bruns and T.J.Petcher, Sandoz Pharma Ltd., Preclinical Research, CH-4002 Basel, Switzerland

Abstract: The tetrasubstituted xylose derivative 4 (Ic_{50}=23μM) was synthesised as SRIF mimetic, based on conformational analysis of SRIF and molecular modelling studies.



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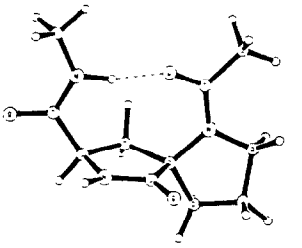
BioMed. Chem. Lett. **1992**, *2*, 141

DESIGN OF A NATURAL *cis* PEPTIDE BOND MOTIF TO FORM TYPE VI β-TURN MIMETIC

P.K.C.Paul*, P.A.Burney, M.M.Campbell and D.J.Osguthorpe

Molecular Graphics Unit, University of Bath, Claverton Down, Bath, BA2 7AY, U.K.

The design of a type VI β-turn mimetic is presented from conformational analysis and molecular dynamics simulations. In the designed structure, which is a spiro compound, three out of a possible four angles defining the β-turn are constrained by local cyclisations.

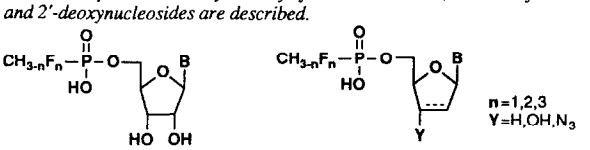


BioMed. Chem. Lett. **1992**, *2*, 145

SYNTHESIS OF ACID STABLE 5'-O-FLUOROMETHYL PHOSPHONATES OF NUCLEOSIDES. EVALUATION AS INHIBITORS OF REVERSE TRANSCRIPTASE.

Patrick J. Casara,*[a] Karin C. Jund,[a]Annie Clauss,[a] Jean-François Navé,[a] and Ronald D. Snyder.
[a]Marion Merrell Dow Research Institute,16, rue d'Ankara, 67009 Strasbourg (France)

The synthesis and the reverse transcriptase inhibitory activity of new 5'-O-mono-,di- and trifluoromethylphosphonate derivatives of nucleosides and 2'-deoxynucleosides are described.



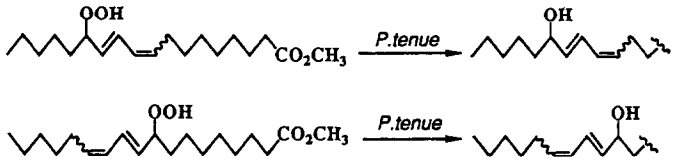
BioMed. Chem. Lett. **1992**, *2*, 149

BIOREDUCTION OF HYDROPEROXY FATTY ACID BY CYANOBACTERIUM, *PHORMIDIUM TENUE*

N. Murakami[a], T. Morimoto[a], H. Shirahashi[a], T. Ueda[a], S. Nagai[a], J. Sakakibara[a], and N. Yamada[b]

[a]Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

[b]Aichi Prefectural Institute of Public Helth, Nagare, Tuji-machi, Kita-ku, Nagoya 462, Japan

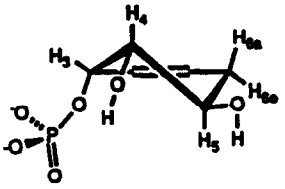


BioMed. Chem. Lett. **1992**, *2*, 151

EPSP Synthase Inhibitor Design I. Conformations of Enzyme Bound Shikimate-3-Phosphate and 5-Enolpyruvoylshikimate-3-Phosphate Using TRNOE

Gregory C. Leo, Stephen Castellino, R. Douglas Sammons, and James A. Sikorski*
New Products Division, Monsanto Agricultural Company
A Unit of Monsanto Company, 800 North Lindbergh Blvd.
St. Louis, MO 63167

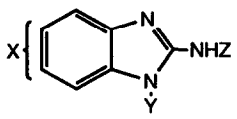
The conformations of S3P, 1 and EPSP, 2 bound to *E. Coli* EPSP synthase have been determined using 2D transfer NOE experiments.



BioMed. Chem. Lett. **1992**, *2*, 155

PREPARATION OF FUNCTIONALIZED DERIVATIVES OF BENZIMIDAZOLE: ALBENDAZOLE AND ITS SULFOXIDE AND SULFONE

Michael E. Mount, Brian J. Evans, S. Janaki, Department of Veterinary Pharmacology and Toxicology, School of Veterinary Medicine, and W. Kenneth Musker*, Department of Chemistry, University of California, Davis, CA 95616.

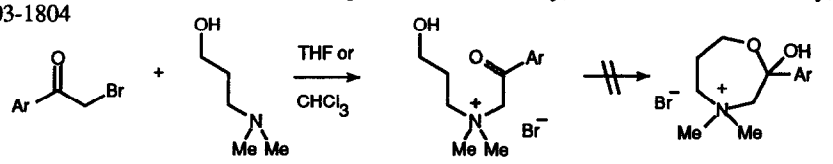


X = H, SC_3H_7	Y = CH_2COOH	Z = CO_2CH_3
X = H, $S(O)_{n=0,1,2}C_3H_7$	Y = H	Z = $CO(CH_2)_2CO_2H$
X = HS, $S(O)_{n=0,1,2}(CH_2)_2CO_2H$	Y = H	Z = CO_2CH_3

BioMed. Chem. Lett. **1992**, *2*, 157

THE STRUCTURE OF THE PRODUCTS WHEN α-BROMOACETOARENONES REACT WITH 3-(*N*,*N*-DIMETHYLAMINO)PROPAN-1-OL.

J. Gabriel Garcia, Frank R. Fronczek, and Richard D. Gandour*, Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803-1804

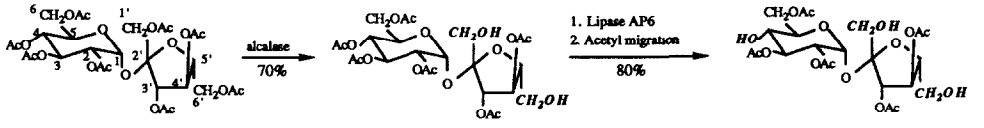


Summary: The title reaction yields the hydroxy ketone and not the seven-membered ring hemiketal.

BioMed. Chem. Lett. **1992**, *2*, 161

PREPARATION OF 2,3,6,3',4'-PENTA-*O*-ACETYL SUCROSE, THE PRECURSOR OF SUCRALOSE, BY ENZYMATIC MEHTODS

Geok-Toh Ong, Shih-Hsiung Wu* and Kung-Tsung Wang
Institute of Biological Chemistry, Academia Sinica and
Institute of Biochemical Sciences, National Taiwan University, Taipei, Taiwan

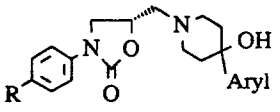


BioMed. Chem. Lett. **1992**, *2*, 165

(5S)-3-ARYL-5-(1-PIPERIDINYLMETHYL)-2-OXAZOLIDINONES, A NEW CLASS OF POTENTIAL NEUROLEPTICS WITH A HIGH AFFINITY FOR SIGMA RECEPTORS

H.Prücher, R.Gottschlich*, A.Haase#, M.Stohrer#, and C.Seyfried#*
**Medicinal Chemistry Research Department, #Biological Research Department,*
E.Merck, D 6100 Darmstadt, Federal Republic of Germany

The synthesis of 3,5-substituted 2-oxazolidinones, potential novel neuroleptic agents, is described. Like other"atypic" neuroleptics these compounds show high affinity for the σ-(SKF 10047)-receptor. Structur-activity relationships are discussed.

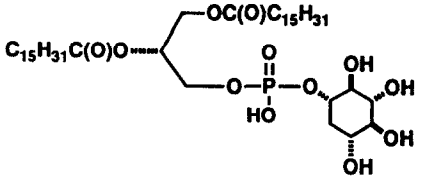


BioMed. Chem. Lett. **1992**, *2*, 171

SYNTHESIS AND ENZYMATIC PROPERTIES OF A DEOXY ANALOG OF PHOSPHATIDYLINOSITOL

Steven P. Seitz*[a], Robert F. Kaltenbach III[a], Remko H. Vreekamp[a], Joseph C. Calabrese[b], and Frank W. Perrella[a]
[a]Du Pont Merck Pharmaceutical Company [b]E. I. Du Pont de Nemours
Central Research and Development Department
Wilmington, Delaware 19880

The preparation of an analog of phosphatidylinositol that is deoxygenated on the 2 position of the inositol ring is described. The compound was evaluated as a substrate and inhibitor of a phospholipase C isolated from a human melanoma cell line.

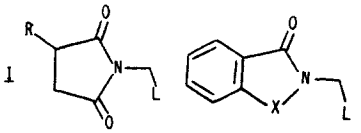


BioMed. Chem. Lett. **1992**, *2*, 175

POTENTIAL MECHANISM-BASED INHIBITORS OF PROTEOLYTIC ENZYMES

William C. Groutas*, Michael J. Brubaker, Radhika Venkataraman, Jeffrey Epp, Nadene Houser-Archield, Lee S. Chong, and Jerald J. McClenahan
Department of Chemistry, Wichita State University, Wichita, Kansas, 67208

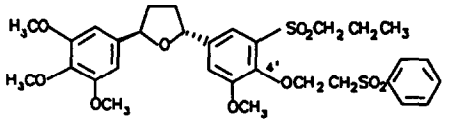
The design, synthesis, and inhibitory activity toward human neutrophile elastase, of a series of potential mechanism-based inhibitors (I-III) is described.



BioMed. Chem. Lett. **1992**, *2*, 181

SYNTHESIS AND BIOLOGICAL ACTIVITY OF THE PLATELET-ACTIVATING FACTOR ANTAGONIST (±)-*trans*-2-(3-METHOXY-4-PHENYLSULFONYLETHOXY-5-*n*-PROPYLSULFONYLPHENYL)-5-(3,4,5-TRIMETHOXYPHENYL) TETRAHYDROFURAN (L-671,284) AND ITS ANALOGS. **Robert L. Bugianesi,* Mitree M. Ponpipom, William H. Parsons, San-Bao Hwang, Thomas W. Doebber, My-Hanh Lam, Margaret S. Wu, Alfred W. Alberts and John C. Chabala.** *Merck Sharp and Dohme Research Laboratories, Rahway, New Jersey 07065 (U.S.A.)*

(±)-*trans*-2-(3-Methoxy-4-phenylsulphonylethoxy-5-*n*-propylsulfonylphenyl)tetrahydrofuran (**L-671,284**) is a highly potent, selective, competitive PAF-receptor antagonist with a K_i of 1 0 n*M* for inhibition of binding of [^{3}H]C_{18}-PAF to human platelets and exhibits little or no gender differences in bioactivities in rats. Several 4' positional analogs of **L-671,284** have been synthesized and evaluated *in vitro*.



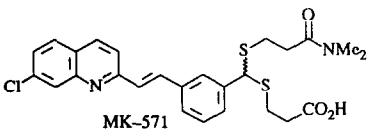
L-671,284

BioMed. Chem. Lett. **1992**, *2*, 185

THE STRUCTURE OF MK-571 (FORM I) AT 170 K AND CONFORMATIONAL ANALYSIS BY MOLECULAR MODELING

Joseph G. Stowell, Pascal H. Toma, and Stephen R. Byrn*
Department of Medicinal Chemistry and Pharmacognosy,
Purdue University, West Lafayette, IN 47907-1333

Crystal structure, molecular modeling, conformational studies, and energy minimizations of a potent leukotriene D4 receptor antagonist, MK-571, (±)-(E)-3-[[[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl][[3-(di-methylamino)-3-oxopropyl]thio]methyl]thio]propanoic acid.

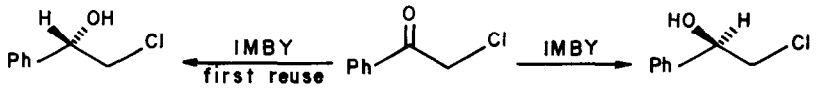


MK-571

BioMed. Chem. Lett. **1992**, *2*, 191

REDUCTION OF PHENYLKETONES BY IMMOBILIZED BAKER'S YEAST

Ana E.P.M. Sorrilha, M. Marques, I. Joekes,
Paulo J.S. Moran* and J. Augusto R. Rodrigues*
Universidade Estadual de Campinas, Instituto de Química
13081 Campinas, Brazil



Baker's yeast immobilized on chrysotile and montmorillonite stereoselectively reduced phenylketones to the corresponding alcohols.

BioMed. Chem. Lett. **1992**, *2*, 197

Enzymatic Synthesis and Properties of Uridine-5'-*O*-(2-thiodiphosphoglucuronate)

Martin M. Klinger* and Dennis J. McCarthy Biochemistry Research Department, Southern Research Institute 2000 Ninth Avenue S., Birmingham AL 35255-5305, USA.

Abstract: Uridine-5'-*O*-(2-thiodiphosphoglucuronate) (UDP(βS)-GA) was synthesized from UDP(βS)-glucose and NAD^+ in a reaction catalyzed by UDP-glucose dehydrogenase. UDP(βS)-GA was not a substrate for the *p*-nitrophenol glucuronosyltransferase of rat liver but was a better inhibitor of nucleotide phosphodiesterase than the natural compound.