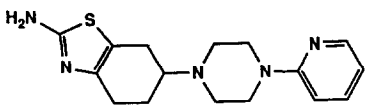
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1991**, *1*, 189

NOVEL 4,5,6,7-TETRAHYDROBENZOTHIAZOLE DOPAMINE AGONISTS DISPLAY VERY LOW STEREOSELECTIVITY IN THEIR INTERACTION WITH DOPAMINE RECEPTORS.

J. Jaen,[+]* B. Caprathe,[+] L. Wise,[+] S. Smith,[+] T. Pugsley,[#] T. Heffner,[#] and L. Meltzer.[#]
Depts. of Chemistry[+] and Pharmacology,[#] Parke-Davis Pharm. Res., Ann Arbor, Michigan 48105.

The synthesis, resolution, and central dopamine (DA) agonist activity of **7** are described. Both enantiomers are equipotent DA agonists.



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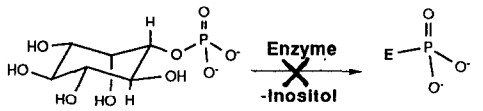
BioMed. Chem. Lett. **1991**, *1*, 193

Inositol Dependent Phosphate-Oxygen Ligand Exchange Catalysed by Inositol Monophosphatase.

Graham R. Baker and David Gani*
Chemistry Department, The Purdie Building, The University, St. Andrews, Fife. KY16 9ST. U.K.

Inositol monophosphatase is unable to catalyse the exchange of ^{18}O-label from ^{18}O-water into inorganic phosphate in the absence of inositol indicating that, unlike for other phosphatases, free phosphorylated enzyme (E-P) does not form during ester hydrolysis.

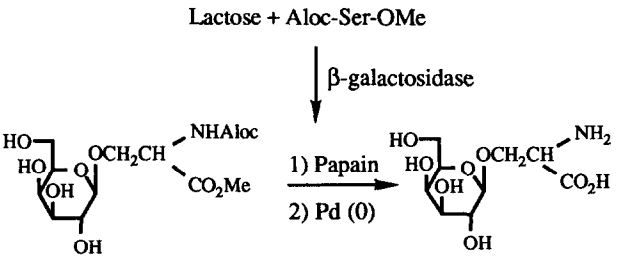


BioMed. Chem. Lett. **1991**, *1*, 197

STEREOSPECIFIC CHEMOENZYMATIC SYNTHESIS OF GALACTOPYRANOSYL-L SERINE

Danièle Cantacuzène, Sandra Attal and Sylvie Bay
Unité de Chimie Organique, UA CNRS 487, Département de Biochimie et Génétique Moléculaire, Institut Pasteur, 28 rue du Dr Roux 75724 Paris (France)

Transgalactosidation from lactose to Aloc-Ser-OMe is catalyzed by β-galactosidase. The protective groups of the serine residue are cleaved in mild conditions with papain catalyzed hydrolysis of the ester group and Pd(0) hydrostannolytic cleavage of the amino group.

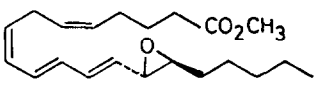


BioMed. Chem. Lett. **1991**, *1*, 201

ENANTIOSPECIFIC SYNTHESIS OF 14S,15S LEUKOTRIENE A_4 METHYL ESTER

A V Rama Rao*, A V Purandare and A K Singh
Indian Institute of Chemical Technology, Hyderabad 500 007, India

A practical enantiospecific synthesis of methyl 14S,15S-oxido-5Z,8Z,10E,12E-eicosatetraenoate (14S,15S LTA_4 methyl ester) from D-glucose as chiral precursor has been described.



BioMed. Chem. Lett. **1991**, *1*, 205

FKBP, THOUGHT TO BE IDENTICAL TO PKCI-2, DOES NOT INHIBIT PROTEIN KINASE C

Mark W. Albers,[a] Jun Liu,[a] Sandra E. Wilkinson,[b] Julie Wadsworth,[b]
Dolores Perez-Sala,[c] Robert R. Rando,[c] John S. Nixon,[b] and Stuart L. Schreiber[a],*
[a] Department of Chemistry, Harvard University, Cambridge, MA 02138; [b] Research Centre, Roche Products, Ltd., Welwyn Garden City, Hertsfield, England; [c] Deparument of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115.

The FK506 and rapamycin binding protein (FKBP), recently shown to be identical to PKCI-2, and its ligands FK506 and rapamycin either acting alone or complexed to FKBP do not inhibit the kinase activity of isolated protein kinase C or protein kinase C-mediated events in cells.

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SYNTHESIS AND EVALUATION OF NEW PROTEIN-TYROSINE KINASE INHIBITORS. PART 1. PYRIDINE-CONTAINING STILBENES AND AMIDES.

Mark Cushman, Dhanapalan Nagarathnam, D. Gopal, and Robert L. Geahlen
Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana 47907 USA

A series of pyridine-containing stilbenes (Ar-CH=CH-Ar', E isomers), dihydrostilbenes (Ar-CH_2-CH_2-Ar'), amides (ArCONHAr') and amines (ArCH_2NHAr') based on the structure of piceatannol, a naturally occurring protein-tyrosine kinase inhibitor, has been prepared and tested for inhibition of p56^{lck}. The most potent of these compounds is a competitive inhibitor of p56^{lck} with respect to ATP.

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SYNTHESIS AND EVALUATION OF NEW PROTEIN-TYROSINE KINASE INHIBITORS. PART 2. PHENYLHYDRAZONES.

Mark Cushman, Dhanapalan Nagarathnam, D. Gopal, and Robert L. Geahlen
Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana 47907 USA

A series of 33 phenylhydrazone derivatives (Ar-CH=N-NH-Ar') of polyhydroxylated benzaldehydes has been prepared and tested for inhibition of the protein-tyrosine kinase p56^{lck}. The most potent of these compounds was a competitive inhibitor of p56^{lck} with respect to a tyrosine-containing peptide substrate and was similar in potency to piceatannol, a naturally occurring protein-tyrosine kinase inhibitor.

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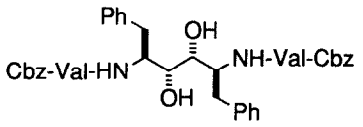
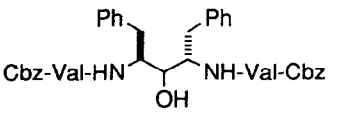
SYNTHESIS OF C_2-SYMMETRIC AND PSEUDO-SYMMETRIC HIV-1 PROTEASE INHIBITORS FROM D-MANNITOL AND D-ARABITOL

Balan Chenera, Jeffrey C. Boehm, and Geoffrey B. Dreyer*, Department of Medicinal Chemistry, SmithKline Beecham Pharmaceuticals, 709 Swedeland Road, PO Box 1539, King of Prussia, PA 19406, USA

Abstract. Facile stereocontrolled syntheses of potent C_2-symmetric and pseudo-C_2-symmetric HIV-1 protease inhibitors are described, employing a unified synthetic route from carbohydrate precursors.

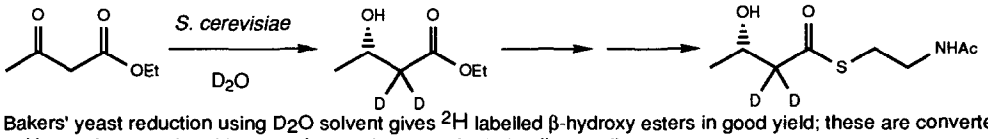




BioMed. Chem. Lett. **1991**, *1*, 223

THE SYNTHESIS OF ISOTOPICALLY LABELLED N-ACETYLCYSTEAMINE THIOESTERS UTILISING A BAKERS' YEAST REDUCTION IN D_2O

M.P. Dillon, M.A. Hayes, T.J. Simpson* and J.B. Sweeney.
School of Chemistry, University of Bristol, Cantocks Close, Bristol, BS8 1TS, U.K.

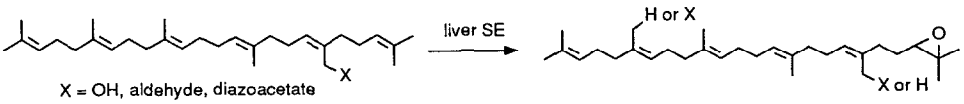


Bakers' yeast reduction using D_2O solvent gives ^2H labelled β-hydroxy esters in good yield; these are converted to N-acetylcysteamine thioesters for use in biosynthetic feeding studies.

BioMed. Chem. Lett. **1991**, *1*, 227

26-HYDROXYSQUALENE AND DERIVATIVES: SUBSTRATES AND INHIBITORS FOR SQUALENE EPOXIDASE.

Mei Bai, Xiao-yi Xiao, and Glenn D. Prestwich*, Department of Chemistry, State University of New York, Stony Brook, New York 11794-3400.



26-Hydroxysqualene and derivatives were competitive inhibitors (K_I for 26-HS = 4 μM) of partially purified pig liver SE. [^{3}H]26-HS was converted to a 3:1 mixture of two regioisomeric 2,3-epoxides.