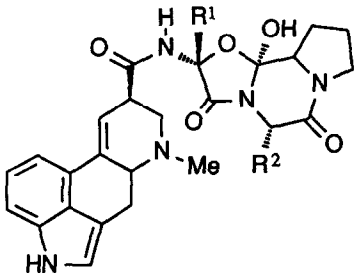
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1992**, *2*, 9

CHOLECYSTOKININ ANALOGUES: THE ERGOPEPTINE ALKALOIDS AS MODELS OF THE ACTIVE CONFORMATION OF CCK

David A. Kendrick*, Hamish Ryder, Graeme Semple and Michael Szelke
Ferring Research Institute, 1 Venture Road, Chilworth Research Centre, Southampton SO1 7NP, U.K.

Ergotamine (R^1 = Me, R^2 = CH_2Ph) was shown to inhibit the binding of radiolabelled CCK to both CCK-A and CCK-B receptors (IC_{50} = 30 μM and 17 μM).

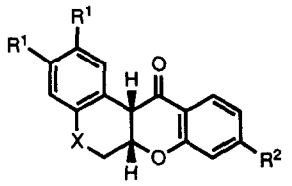


BioMed. Chem. Lett. **1992**, *2*, 13

ROTENOID CORE STRUCTURE: MODIFICATIONS TO DEFINE THE REQUIREMENTS OF THE TOXOPHORE.

Leslie Crombie,[a] Jonathan L. Josephs,[a] Jane Cayley,[b] John Larkin[b] and John B. Weston.[b]
[a] Department of Chemistry, The University of Nottingham, Nottingham, NG7 2RD, UK.
[b]Wellcome Research Laboratories, Ravens Lane, Berkhamsted, Hertfordshire, HP4 2DY, UK

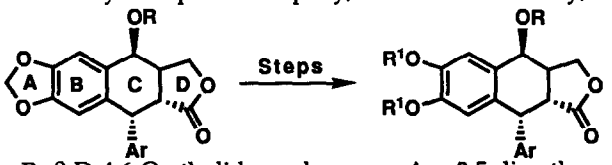
A number of modified analogues of the core rotenoid structure have been made and assayed for their inhibition of NADH dehydrogenase in a blow fly muscle submitochondrial preparation.



BioMed. Chem. Lett. **1992**, *2*, 17

SYNTHESIS AND ANTILEUKEMIC ACTIVITY OF ETOPOSIDE A-RING ANALOGS

J. F. Kadow*, M. M. Tun, A. R. Crosswell, W. C. Rose, D. M. Vyas, and T. W. Doyle.
Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492



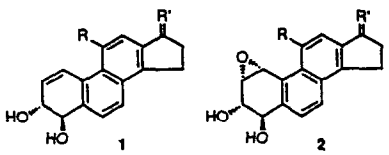
R=ß-D-4,6-O-ethylidene glucose. Ar= 3,5-dimethoxy-4-hydroxy phenyl.

BioMed. Chem. Lett. **1992**, *2*, 23

SYNTHESIS OF BIOLOGICALLY ACTIVE DIHYDRODIOL METABOLITES OF 16,17-DIHYDRO-15*H*-CYCLOPENTA[A]-PHENANTHRENE AND ITS CARCINOGENCIC 11-METHYL AND 17-KETO DERIVATIVES

R.J. Young, C. Cortez, E. Luna, H. Lee, and R.G. Harvey*
Ben May Institute, University of Chicago, Chicago, Illinois 60637

Abstract: Synthesis of the title compounds (**1**), implicated by biological studies as metabolic precursors of the carcinogenic diol epoxide metabolites (**2**), are described.



R = H or CH_3; R' = H_2 or O

BioMed. Chem. Lett. **1992**, *2*, 27

1SYNTHESIS AND BIOLOGICAL ACTIVITY OF C-6 MODIFIED DERIVATIVES OF THE GLUCOSIDASE INHIBITOR 1-DEOXYNOJIRIMYCIN.

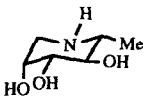
A. Berger, K. Dax, G. Gradnig, V. Grassberger, A. E. Stütz*, and M. Ungerank
Institut für Organische Chemie der Technischen Universität Graz, Stremayrgasse 16, A-8010 Graz, Austria
G. Legler
Institut für Biochemie der Universität Köln, Zülpicherstrasse 47, D-5000 Köln, Germany
E. Bause
Institut für Physiologische Chemie der Universität Bonn, Nußallee 11, D-5300 Bonn, Germany

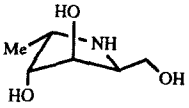
The enzyme inhibitory activities of two novel C-6 modified 1-deoxynojirimycin derivatives were tested against a set of α- and β-glucosidases. One of them, *(6S)*-6-*C*-ethyl-1-deoxynojirimycin, exhibited improved inhibitory activity against α-glucosidases from yeast and rice compared to 1-deoxynojirimycin and castanospermine.

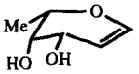
BioMed. Chem. Lett. **1992**, *2*, 33

Azasugar and Glycal Inhibitors of α-L-Fucosidase

David P. Dumas,[†] Tetsuya Kajimoto,[†] Kevin K.-C. Liu, [†] Chi-Huey Wong, [†*] David B. Berkowitz,[§] Samuel J. Danishefsky[§]
[†]Department of Chemistry, The Scripps Research Institute, 10666 N. Torrey Pines Road, La Jolla, CA 92037
[§]Department of Chemistry, Yale University, New Haven, CT 06511





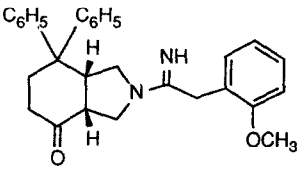


BioMed. Chem. Lett. **1992**, *2*, 37

SYNTHESIS OF RP-67,580, A NEW POTENT NONPEPTIDE SUBSTANCE P ANTAGONIST

Jean-François Peyronel, Alain Truchon, Claude Moutonnier and Claude Garret*
Medicinal Chemistry Department, Rhône-Poulenc-Rorer Central Research
Centre de Recherches de Vitry-Alfortville, 13 Quai Jules Guesde, BP 14
94403 VITRY sur SEINE, FRANCE.

The synthesis of RP-67580, a new non peptide substance P antagonist, is described with the resolution of intermediate diphenyl-7,7 perhydroisoindol-4-one. The key step in the preparation of this new ring system is an azomethine ylid 1,3-dipolar cycloaddition to 4,4-diphenyl-cyclohex-2-enone.



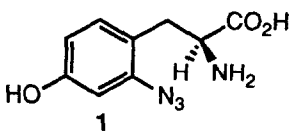
RP-67,580

BioMed. Chem. Lett. **1992**, *2*, 41

AN ENZYMATIC SYNTHESIS OF 2-AZIDO-L-TYROSINE

D. Hebel, D. C. Furlano, R. S. Phillips,# S. Koushik,# C. R. Creveling and K. L. Kirk*
Laboratory of Bioorganic Chemistry National Institute of Diabetes and Digestive and Kidney Diseases, National Institutesof Health, Bethesda MD 20892 and #Department of Chemistry, University of Georgia, Athens, GA 30602

The tyrosine-phenol lyase-catalyzed synthesis and preliminary biological evaluation of 3-azido-L-tyrosine (**1**) are described.



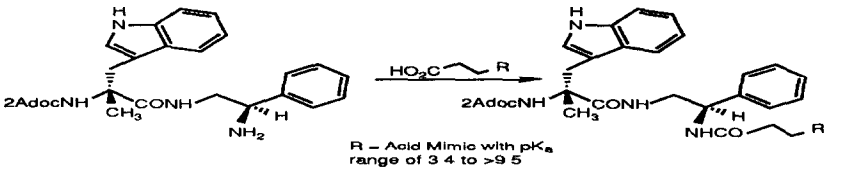
1

BioMed. Chem. Lett. **1992**, *2*, 45

THE SYNTHESIS AND CCK RECEPTOR AFFINITIES OF SELECTED CARBOXYLIC ACID MIMICS OF CI-988 - A POTENT AND SELECTIVE CCK-B ANTAGONIST

Martin J. Drysdale *, Martyn C. Pritchard and David C. Horwell

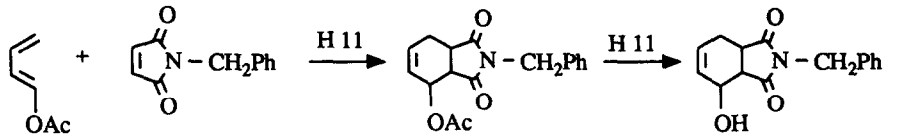
Parke Davis Neuroscience Research Centre, Addenbrookes Hospital Site, Hills Rd., Cambridge, CB2 2QB,U.K.



BioMed. Chem. Lett. **1992**, *2*, 49

AN ANTIBODY WITH DUAL CATALYTIC ACTIVITY Colin J. Suckling* M. Catriona Tedford, Laura M. Bence, June I. Irvine and William H. Stimson, Departments of Pure and Applied Chemistry and Immunology, University of Strathclyde, Glasgow, Scotland

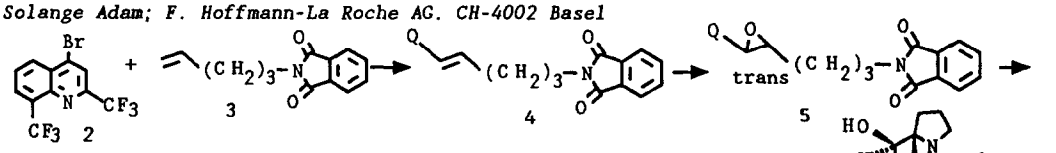
Abstract: An antibody raised to a product analogue for a Diels Alder reaction has been found to catalyse sequentially the planned electrocyclic reaction and a subsequent hydrolysis.



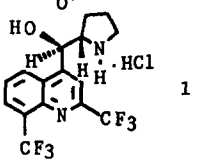
BioMed. Chem. Lett. **1992**, *2*, 53

NOR-MEFLOQUINE: STEREOSPECIFIC SYNTHESIS AND BIOLOGICAL PROPERTIES

Solange Adam; F. Hoffmann-La Roche AG. CH-4002 Basel



Nor-mefloquine 1 has been synthesised in a stereospecific way resting on the E geometry of the key-step olefin 4 obtained via the Heck's palladium catalysed vinylic substitution reaction

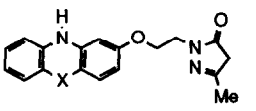


1

BioMed. Chem. Lett. **1992**, *2*, 59

Phenothiazine and Phenoxazine Derivatives of Nafazatrom. In Vitro Evaluation as 5-Lipoxygenase and Iron-Dependent Lipid Peroxidation Inhibitors. Melvin J. Yu,* Jefferson R. McCowan, Barbara Bertsch, Peter P.K. Ho, Lee A. Phebus, Kenneth J. Ruterbories, Terry D. Lindstrom, Jeffrey K. Smallwood and Paul J. Simpson, *Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285*

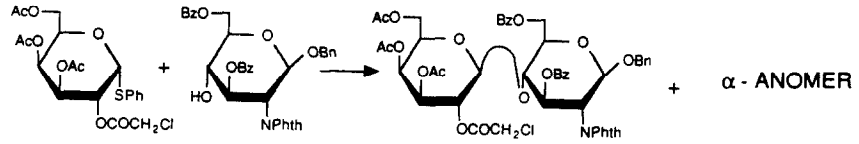
The titled compounds were evaluated as free radical scavengers and as *in vitro* inhibitors of 5-lipoxygenase and iron-dependent lipid peroxidation.



X = O, S

BioMed. Chem. Lett. **1992**, *2*, 63

SYNTHESIS OF 2'-O-SUBSTITUTED β-D-Gal-(1→4)-β-D-GlcNAc-1-O-Bn AS SPECIFIC ACCEPTORS FOR α-L-(1→3) FUCOSYLTRANSFERASES, R. K. Jain, R. D. Locke, E. V. Chandrasekaran and K. L. Matta, Dept. of Gynecologic Oncology, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, NY 14263

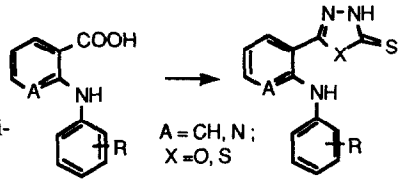


BioMed. Chem. Lett. **1992**, *2*, 69

CONVERSION OF NSAIDS INTO BALANCED DUAL INHIBITORS OF CYCLOOXYGENASE AND 5-LIPOXYGENASE

Diane H. Boschelli*#, David T. Connor#, Milton Hoefle#, Dirk A. Bornemeier% and Richard D. Dyer% Departments of Chemistry# and Biochemistry%, Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company, 2800 Plymouth Rd., Ann Arbor, MI 48105

Replacing the carboxylic acid group of several fenamates with 1,3,4-oxadiazole-2-thiones and1,3,4-thiadiazole-2-thiones converted selective cyclooxygenase (CO) inhibitors into inhibitors of both CO and 5-lipoxygenase.

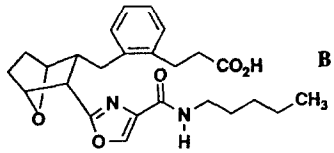


BioMed. Chem. Lett. **1992**, *2*, 73

THROMBOXANE RECEPTOR ANTAGONIST BMS-180291: A NEW PRE-CLINICAL LEAD

Raj N. Misra,* B. R. Brown, P. M. Sher, M. M. Patel, S. E. Hall, W.-C. Han, J. C. Barrish, D. M. Floyd, P. W. Sprague, R. A. Morrison, R. E. Ridgewell, R. E. White, G. C. DiDonato, D. N. Harris, A. Hedberg, W. A. Schumacher, M. L. Webb and M. L. Ogletree
Bristol-Myers Squibb Pharmaceutical Research Institute, PO Box 4000, Princeton, NJ 08543-4000

The synthesis and initial pharmacological evaluation of TxA_2 receptor antagonist BMS-180291 is described. BMS-180291 is an orally bioavailable, potent, selective antagonist with a long duration of action that has been selected for further development.



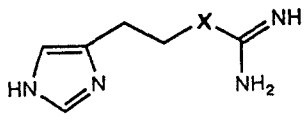
BMS-180291

BioMed. Chem. Lett. **1992**, *2*, 77

TWO NOVEL, POTENT AND SELECTIVE HISTAMINE H_3 RECEPTOR AGONISTS

William Howson*, Michael E. Parsons, Pravin Raval, and George T.G. Swayne
SmithKline Beecham Pharmaceuticals, The Frythe, Welwyn, Herts AL6 9AR

Abstract: 5-[2-(4-(5)-imidazoyl)ethyl]isothiourea X = S and 4-(4-(5)-imidazoyl)-butyramidine X = CH_2 were shown to be potent H_3 agonists on the guinea pig ileum with very little activity on H_1 and H_2 preparations.

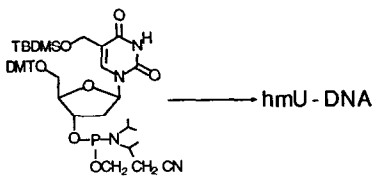


BioMed. Chem. Lett. **1992**, *2*, 79

Solid Phase Synthesis Of 5-Hydroxymethyluracil Containing DNA

Maria R. Conte[a], Aldo Galeone[a], Daina Avizonis[b], Victor L.Hsu[b], Luciano Mayol[a]* and David R. Kearns[b]*

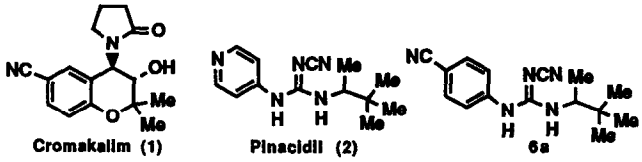
a) Dipartimento di Chimica delle Sostanze Naturali, Università di Napoli Federico II
via Domenico Montesano 49, I-80131 Napoli, Italy
b) Department of Chemistry, University of California
San Diego, La Jolla, California 92093



The suitably protected nucleotide has been prepared and used for the automated synthesis of hmU containing DNA.

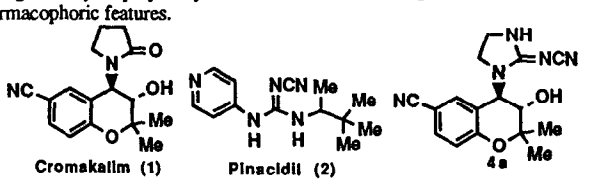
BioMed. Chem. Lett. **1992**, *2*, 83

Aryl Cyanoguanidine Potassium Channel Openers. Karnail S. Atwal* Suzanne Moreland, John R. McCullough, Brian C. O'Reilly, Syed Z. Ahmed and Diane E. Normandin, Bristol-Myers Squibb Pharmaceutical Research Institute, P. O. Box 4000, Princeton, N. J. 08543-4000. To investigate whether potassium channel openers cromakalim (1) and pinacidil (2) share common pharmacophoric features, the combination compound **6a** was prepared and evaluated for biological activity. The potent vasorelaxant/antihypertensive activity displayed by **6a** and some of its analogs suggest cromakalim (1) and pinacidil (2) may share common pharmacophoric features.



BioMed. Chem. Lett. **1992**, *2*, 87

BENZOPYRANYL-CYANOGUANIDINE POTASSIUM CHANNEL OPENERS. Karnail S. Atwal,* Suzanne Moreland, John R. McCullough, Syed Z. Ahmed and Diane E. Normandin. Bristol-Myers Squibb Pharmaceutical Research Institute, P. O. Box 4000, Princeton, N. J. 08543-4000. To investigate whether potassium channel openers cromakalim (1) and pinacidil (2) share common pharmacophoric features, the cyanoguanidine analog **4a** of cromakalim (1) was prepared and evaluated for biological activity. The potent vasorelaxing activity displayed by **4a** and some of its analogs support the hypothesis that cromakalim (1) and pinacidil (2) share common pharmacophoric features.

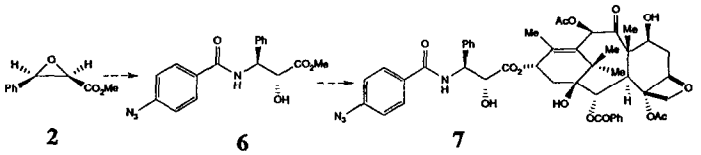


BioMed. Chem. Lett. **1992**, *2*, 91

Synthesis of a Photoreactive Taxol Side Chain

Arindam Chatterjee,[a] John S. Williamson,[a] Jordan K. Zjawiony,[b] John R. Peterson[b]*
[a] Department of Medicinal Chemistry, [b] Department of Pharmacognosy and the Research Institute of Pharmaceutical Sciences, School of Pharmacy, The University of Mississippi, University, Mississippi 38677, USA

Abstract: In an effort to synthesize a photoreactive taxol derivative (**7**), the side chain, (2*R*,3*S*)-(-)-N-(4' -azido-benzoyl-3-phenylisoserine methyl ester (**6**), was prepared in four steps from (2*R*,3*R*)-(+)-methyl 3-phenylglycidate (**2**).

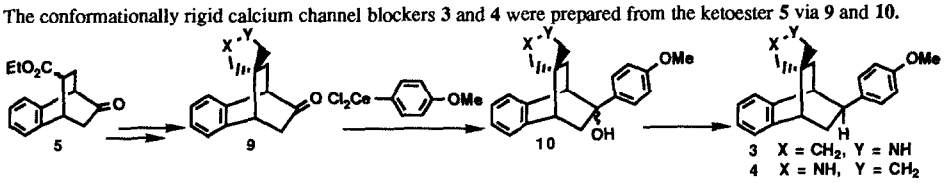


BioMed. Chem. Lett. **1992**, *2*, 95

THE SYNTHESIS OF A CONFORMATIONALLY RIGID CALCIUM CHANNEL BLOCKER

Joel C. Barrish*, Steven H. Spergel, Suzanne Moreland, and S. Anders Hedberg
Chemistry Division, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, New Jersey 08543-4000

The conformationally rigid calcium channel blockers **3** and **4** were prepared from the ketoester **5** via **9** and **10**.

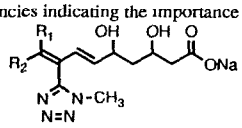


BioMed. Chem. Lett. **1992**, *2*, 99

HMG-CoA REDUCTASE INHIBITORS 4. TETRAZOLE SERIES: CONFORMATIONAL CONSTRAINTS AND STRUCTURAL REQUIREMENTS AT THE HYDROPHOBIC DOMAIN.

N. Balasubramanian*, Peter J. Brown, Rex A. Parker, and J.J. Wright Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492.

Structural modification at C9 and introduction of conformational constraints at C8-C9 resulted in a drop in inhibitory potencies indicating the importance of specificity requirements at the hydrophobic region.



$R_1 = R_2$ = 4-fuorophenyl : BMY 21950
R_1 = H; R_2 = 4-fuorophenyl
R_2 = H; R_1 = 4-fuorophenyl
R_1 and R_2 are linked
R_2 and tetrazole are linked; R_1 =H