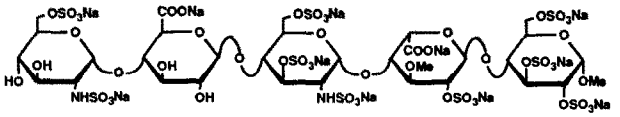
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1992**, 2, 897

BIOLOGICALLY ACTIVE HEPARIN-LIKE FRAGMENTS WITH A "NON-GLYCOSAMINO"GLYCAN STRUCTURE.
Part 1: A PENTASACCHARIDE CONTAINING A 3-O-METHYL IDURONIC ACID UNIT.

G. Jaurand[a], J. Basten[b], I. Lederman[a], C.A.A. van Boeckel[b*] and M. Petitou[a*]
a. Sanofi Recherche-Centre Choay, 9 rue du président Salvador Allende, 94256 Gentilly Cedex (France)
b: Organon International B.V., PO Box 20, 5340 BH Oss (The Netherlands)

Abstract. The following compound has been prepared. It is antithrombotic in animal models.

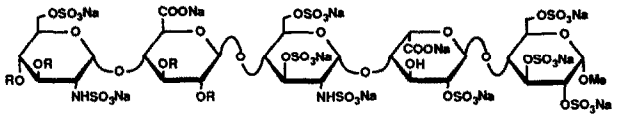


BioMed. Chem. Lett. **1992**, 2, 901

BIOLOGICALLY ACTIVE HEPARIN-LIKE FRAGMENTS WITH A "NON-GLYCOSAMINO"GLYCAN STRUCTURE.
Part 2 : A TETRA-O-METHYLATED PENTASACCHARIDE WITH HIGH AFFINITY FOR ANTITHROMBIN III.

J. Basten[a], G. Jaurand[b], B. Olde-Hanter[a], M. Petitou[b*] and C.A.A. van Boeckel[a*].
a Organon International B.V , PO Box 20, 5340 BH Oss, The Netherlands
b Sanofi Recherche, 9, rue du Président Salvador Allende, 94256 Gentilly, France

Abstract. Methylation keeps this pentasaccharide's biological properties intact.

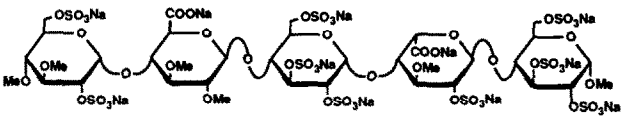


BioMed. Chem. Lett. **1992**, 2, 905

BIOLOGICALLY ACTIVE HEPARIN-LIKE FRAGMENTS WITH A "NON-GLYCOSAMINO"GLYCAN STRUCTURE.
Part 3 : O-ALKYLATED-O-SULPHATED PENTASACCHARIDES.

J. Basten[a], G. Jaurand[b], B. Olde-Hanter[a], P. Duchaussoy[b], M. Petitou[b*] and C.A.A. van Boeckel[a*]
a Organon International B V , PO Box 20 , 5340 BH Oss, The Netherlands
b: Sanofi Recherche; 9, rue du Président Salvador Allende, 94256 Gentilly, France.

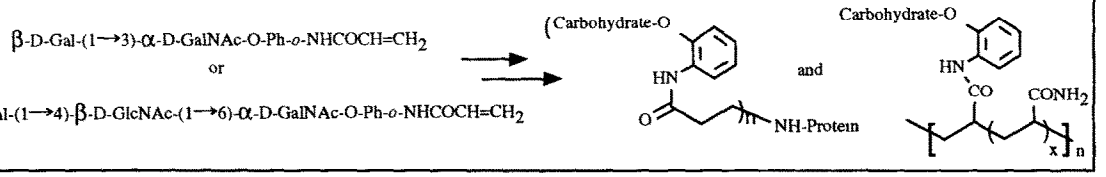
Abstract. This compound has been synthesised. It displays the samebiological properties as heparin fragments.



BioMed. Chem. Lett. **1992**, 2, 911

DIRECT ACCESS TO NEOGLYCOPROTEINS AND GLYCOPOLYMERS FROM SINGLE PRECURSORS. SYNTHESIS OF T- ANTIGEN AND N-ACETYL-LACTOSAMINE-β-D-(1→6)-α-D-GalNAC CONJUGATES.

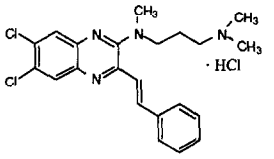
René Roy*, François D. Tropper, Anna Romanowska, *Department of Chemistry, University of Ottawa, Ottawa,ONT., Canada K1N 6N5, and* Rakesh K. Jain, Conrad F. Piskorz, Khushi L. Matta, *Department of Gynecologic Oncology, Roswell Park Cancer Institute, Elm & Carlton Street, Buffalo, N.Y. 14263.*



BioMed. Chem. Lett. **1992**, *2*, 915

CP-99,711 : A Non-Peptide Glucagon Receptor Antagonist

Judith L. Collins, Paul J. Dambek, Steven W. Goldstein, and W. Stephen Faraci*
Central Research Division, Pfizer Inc, Groton, CT 06340



CP-99,711

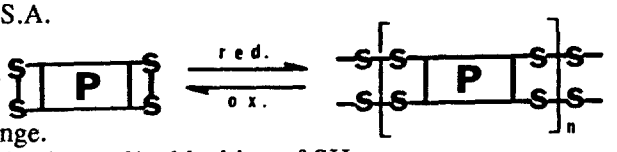
CP-99,711, identified in a screening program, displaces [125I]-glucagon from rat liver receptor. We describe here the synthesis of this compound and its characterization as a functional glucagon antagonist.

THIOL-INDUCED CROSSLINKING OF HUMAN BLOOD PROTEINS: IMPLICATIONS FOR TUMOR IMMUNITY.

BioMed. Chem. Lett. **1992**, *2*, 919

Boguslaw Lipinski* and Laszlo G. Egyud
H.S. Research Laboratory and Albert Szent-Gyorgyi Research Institute, 100 Inman St., Cambridge, MA 02139, U.S.A.

Limited reduction of disulfides in blood proteins causes their intra- to inter-molecular exchange.

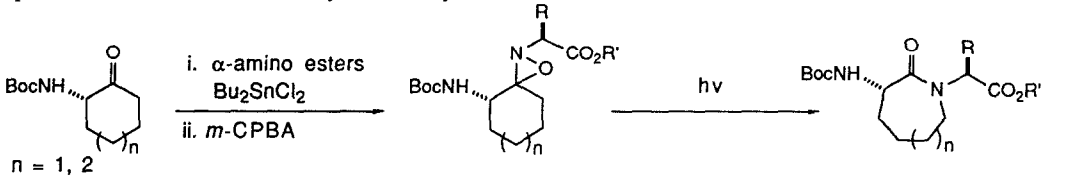


This reaction is inhibited by oxidation and/or blocking of SH groups.

A DIVERGENT ROUTE TOWARD LACTAM-BASED DIPEPTIDYL BUILDING BLOCKS

BioMed. Chem. Lett. **1992**, *2*, 925

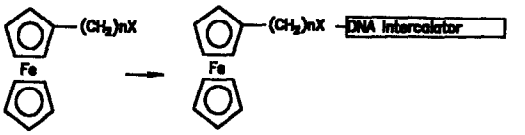
Jeffrey Aubé* and Michael S. Wolfe
Department of Medicinal Chemistry, University of Kansas, Lawrence, KS 66045-2506



BioMed. Chem. Lett. **1992**, *2*, 929

A FERROCENE-INTERCALATOR CONJUGATE WITH A POTENT CYTOTOXICITY

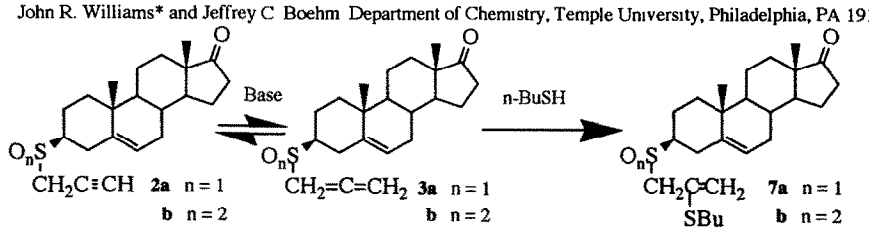
Chi Wi Ong[a]*, Jing Yueh Jeng[a], Shyh Shiann Juang[b], and Chia Fu Chen[c]
a. Department of Chemistry, National Sun Yat-Sen Universty, Kaoshiung, Taiwan; b. The Chia Naan Junior College of Pharmacy, Tainan Hsien, Taiwan; c. Medical Defense College, Triservice Hospital, Taipei, Taiwan.



BioMed. Chem. Lett. **1992**, *2*, 933

The Synthesis and Reativity of β,γ-Acetylenic and Allenic Sulfoxides and Sulfones As Masked Affinity Labels

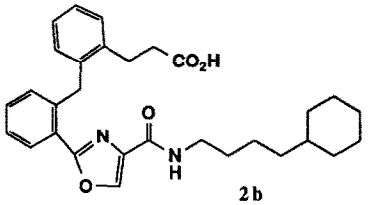
John R. Williams* and Jeffrey C Boehm Department of Chemistry, Temple University, Philadelphia, PA 19122



BioMed. Chem. Lett. **1992**, *2*, 937

INTERPHENYLENE PHENYL OXAZOLES: NOVEL, POTENT THROMBOXANE RECEPTOR ANTAGONISTS. R. N. Misra, H. J. Goldenberg, D. N. Harris, I. M. Michel, M. L. Webb, B. R. Brown*
Bristol-Myers Squibb Pharmaceutical Research Institute, PO Box 4000, Princeton, N. J. 08543-4000

The synthesis and *in vitro* evaluation of a novel series of structurally simple interphenylene phenyl oxazoles is described. The optimal interphenylene substitution pattern and carboxyl side chain length were determined and from this series **2b** has been identified as a potent TxA_2 antagonist (AAIPA I_{50}=31 nM, K_d=19 nM).



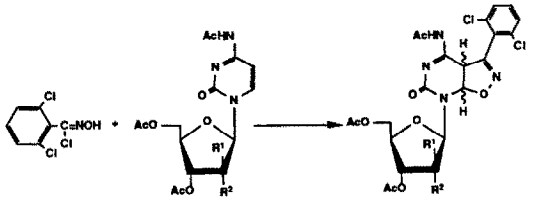
2b

BioMed. Chem. Lett. **1992**, *2*, 941

THE REACTIONS OF 2,6-DICHLOROBENZONITRILE OXIDE WITH THE 5,6-DOUBLE BOND OF CYTOSINE NUCLEOSIDES

Jae Nyoung Kim and Eung K. Ryu*
Korea Research Institute of Chemical Technology,
P. O. Box 9, Daedeog-Danji, Daejeon 305-606, Korea

The reactions of 2,6-dichlorobenzonitrile oxide with some cytosine nucleosides afforded diastereomeric mixtures of [3+2] dipolar cycloaddition products.

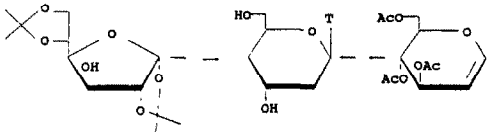


BioMed. Chem. Lett. **1992**, *2*, 945

SYNTHESIS OF 1-(2,4-DIDEOXY-β-D-ERYTHRO-HEXOPYRANOSYL)THYMINE

Koen Augustyns, Arthur Van Aerschot and Piet Herdewijn*
Laboratory of Pharmaceutical Chemistry, Rega Institute, Minderbroedersstraat 10, B-3000 Leuven, Belgium

The title compound was synthesized starting from either 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (12 steps) or from tri-*O*-acetyl-D-glucal (11 steps).

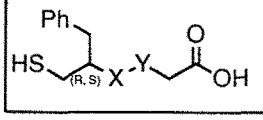


BioMed. Chem. Lett. **1992**, *2*, 949

IMPORTANCE OF THE AMIDE BOND OF THIORPHAN IN THE INHIBITOR-ENKEPHALINASE DOCKING PROCESS DEMONSTRATED WITH SOME THIORPHAN ISOSTERES.

Monteil T.,[a] Kotera M.,[a] Duhamel L.,[a] Duhamel P.,[a] Gros C.,[b] Noel N.,[b] Schwartz J. C.,[b*] and Lecomte J. M. [c]

[a] *UA 464 CNRS et IRCOF, BP 118, 76134 Mont Saint Aignan Cedex, France ;* [b] *UA 109 INSERM, Centre Paul Broca, 2ter rue d'Alésia, 75014 Paris, France ,* [c] *Laboratoire Bioprojet, 30 rue des Francs Bourgeois, 75003 Paris, France*



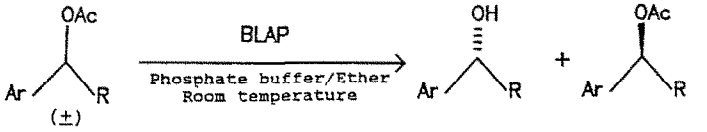
Syntheses and biological activities of four thiorphan isosteres or analogs are described. The central amide linkage is replaced by ketomethylene, aminomethylene, thioamide, and trans-olefinic functionalities.Double chelation mechanism for the inhibitor-enkephalinase docking process is proposed.

BioMed. Chem. Lett. **1992**, *2*, 955

BOVINE LIVER ACETONE POWDER (BLAP): A CRUDE ENZYME FOR SYNTHESIS OF OPTICALLY ACTIVE 1-ARYL-1-ALKANOLS

D.Basavaiah*and S.Bhaskar Raju
School of Chemistry, University of Hyderabad, Hyderabad - 500134, India.

Enantioselective hydrolysis of 1-acetoxy-1-arylalkanes using crude bovine liver acetone powder (BLAP).

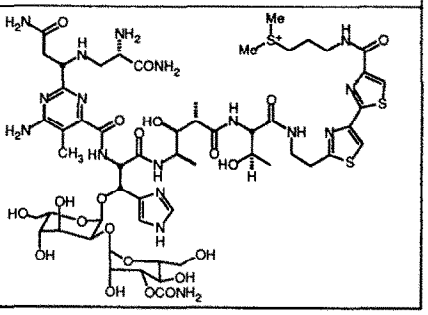


BioMed. Chem. Lett. **1992**, *2*, 959

A SIMPLE METHOD FOR THE PURIFICATION AND ISOLATION OF BLEOMYCIN A_2

Dale L. Boger,* Royce F. Menezes, and Wenjin Yang, *Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, California 92037 USA.*

Abstract. A simple procedure for the direct purification and isolation of bleomycin A_2 from blenoxane is detailed and its use in the preparation and purification of deglycobleomycin A_2 is described.

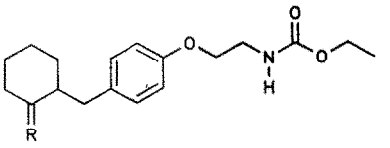


BioMed. Chem. Lett. **1992**, *2*, 963

CARBAMATE SERIES OF JUVENOIDS

Martin Rejzek, Marie Zarevúcká and Zdeněk Wimmer*
Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Flemingovo náměstí 2, 166 10 Prague 6, Czechoslovakia

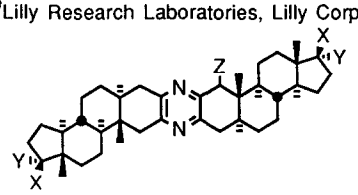
Abstract: A more convenient method for the synthesis of the carbamate series of juvenoids has been described.



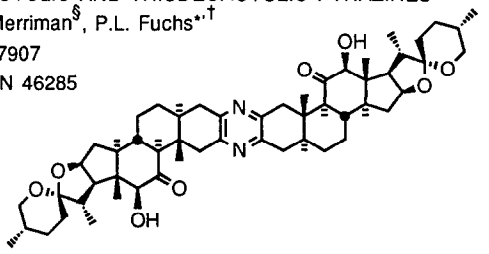
BioMed. Chem. Lett. **1992**, *2*, 967

SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF NONACYCLIC AND TRISDECACYCLIC PYRAZINES RELATED TO CEPHALOSTATIN

Y. Pan[†], L. R. Tanzer[§], R. L. Merriman[§], P.L. Fuchs*[,†]
[†]Department of Chemistry, Purdue University, West Lafayette, IN 47907
[§]Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285



16A X=OH, Y=H, Z=H
16B X=Y=O, Z=H
16C X=C_8H_{17}, Y=H, Z=H
16D X=Y=OCH_2CH_2O, Z=H
18A X=OH, Y=H, Z=N_3

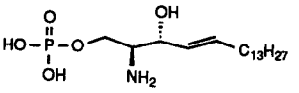


BioMed. Chem. Lett. **1992**, *2*, 973

CHEMICAL SYNTHESIS OF D-ERYTHRO-SPHINGOSINE-1-PHOSPHATE, AND ITS INHIBITORY EFFECT ON CELL MOTILITY

Fuqiang Ruan, Yoshito Sadahira, Sen-itiroh Hakomori, and Yasuyuki Igarashi*. The Biomembrane Institute, Seattle, WA 98119; and Department of Pathobiology, University of Washington, Seattle, WA 98195.

The first chemical synthesis of D-erythro-sphingosine-1-phosphate (which occurs naturally) is described. This compound had an inhibitory effect on motility of mouse melanoma B16/F1 cells in an in vitro assay system.

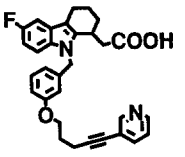


BioMed. Chem. Lett. **1992**, *2*, 979

DISCOVERY OF DUAL ACTIVITY MOLECULES WITH THROMBOXANE ANTAGONIST AND THROMBOXANE SYNTHASE INHIBITORY ACTIVITY

K. Russell*[§], H. Gaskin, R Jessup
Research Department, ICI Pharmaceuticals , Alderley Park, Macclesfield, Cheshire, SK10 4TG, England
[§]Current address, *Medicinal Chemistry Department, ICI Pharmaceuticals Group, ICI Americas Inc., Wilmington, DE 19897*

Abstract: Modification of a known thromboxane antagonist by the incorporation of a tethered pyridine moiety gave a series of dual acting thromboxane antagonist/thromboxane synthase inhibitors e.g. **9**.



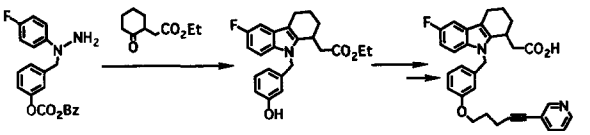
9

BioMed. Chem. Lett. **1992**, *2*, 985

SYNTHESIS OF DUAL ACTIVITY MOLECULES WITH THROMBOXANE ANTAGONIST AND THROMBOXANE SYNTHASE INHIBITORY ACTIVITY

K. Russell*[§], H. Gaskin
Research Department, ICI Pharmaceuticals , Alderley Park, Macclesfield, Cheshire, SK10 4TG, England
[§]Current address, *Medicinal Chemistry Department, ICI Pharmaceuticals Group, ICI Americas Inc., Wilmington, DE 19897*

Abstract: Synthesis of a series dual activity thromboxane antagonist/ thromboxane synthase inhibitors is described.

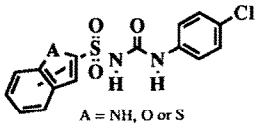


BioMed. Chem. Lett. **1992**, 2, 987

ANTINEOPLASTIC BICYCLICSULFONYLUREAS

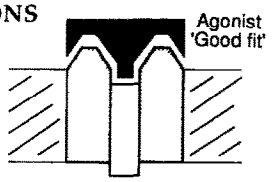
Fariborz Mohamadi*, Michael M. Spees, and Gerald B. Grindey
Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46285

This manuscript summarizes the antitumor properties of 23 bicyclicsulfonylureas (substructure depicted below) against subcutaneously implanted 6C3HED lymphosarcoma in C3H mice.



BioMed. Chem. Lett. **1992**, 2, 993

CONSEQUENCES FOR MOLECULAR RECOGNITION AND LIGAND-RECEPTOR COMPLEMENTARITY OF ENTROPY CHANGES IN PHASE TRANSITIONS



Mark S. Searle & Dudley H. Williams
Cambridge Centre for Molecular recognition, Cambridge CB2 1EW, UK.

Many agonists bind to receptors with large enthalpies of interaction, which we equate a high degree of complementarity. Comparisons are drawn with analogous enthalpy/entropy compensations observed in the fusion of organic crystals.

BioMed. Chem. Lett. **1992**, 2, 997

SOLUTION STABILITY OF IRON-SACCHARIDE COMPLEXES

Chebrolu P. Rao*, K. Geetha and Rajiv P. Bandwar
Dept. of Chemistry, IIT, Powai, Bombay - 400 076, India

Soluble and stable low-molecular weight iron-saccharide complexes exhibiting qualities suitable for dietary supplementation of iron.

[Fe(III)-saccharide] complex $\xrightarrow{\text{pH 2.5 - 11}}$ stable

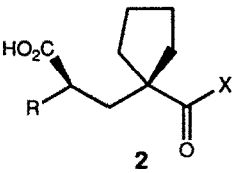
BioMed. Chem. Lett. **1992**, 2, 1003

Studies in ANF Potentiation. Synthesis of Rigid Bicyclic Analogs of Cyclopentyl Glutaryl Derivatives

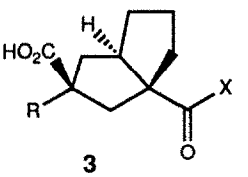
Samuel Chackalamannil*, Yuguang Wang, and Martin F. Haslanger

Schering-Plough Research Institute
60 Orange St., Bloomfield,, New Jersey 07003, U.S.A.

The synthesis of bicyclic NEP inhibitors represented by the structure **3** is presented. Their diminished potency, compared to that of the cycloalkyl glutaryl derivatives **2**, is rationalized on the basis of bioactive conformation.



2



3

BioMed. Chem. Lett. **1992**, *2*, 1007

AN EFFICIENT METHOD FOR CONJUGATION OF THIAMINE TO PROTEINS,

M. Jayamani and Philip S. Low, *Chemistry Department, Purdue University, West Lafayette, Indiana 47907*

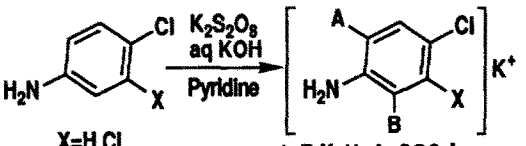
Abstract: New derivatives of thiamine were prepared by reacting succinic, glutaric or maleic anhydride with the hydroxyl group of thiamine. The resulting free carboxyl group was then activated using N, N, N′, N′-tetramethyl-O-(-N-succinimidyl)uronium tetrafluoroborate 3 and conjugated to proteins. Alternatively, proteins were reacted with 2-iminothiolane and the resulting sulfhydryl groups were then added across the double bond of thiamine monomaleiate 2c prepared by the above method.

BioMed. Chem. Lett. **1992**, *2*, 1013

THE SYNTHESIS OF o-AMINOPHENYL SULFATE METABOLITES OF THE ONCOLYTIC SULFONYLUREAS

John E. Toth,* James Ray, and William J. Ehlhardt#
Cancer Research Division and
Department of Drug Metabolism#
Lilly Research Laboratories, Eli Lilly & Company
Lilly Corporate Center, Indianapolis, Indiana, 46285

Abstract. Application of the Boyland-Sims oxidation to 4-chloro- and 3,4-dichloroaniline is reported.



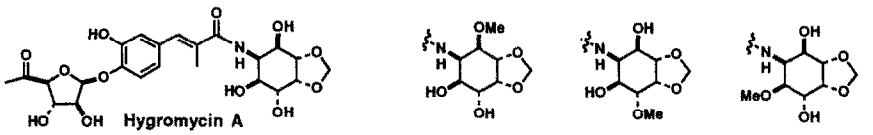
1, B,X=H; A=OSO_3^-
2, X=Cl; B=H; A=OSO_3^-
3, X=Cl; A=H; B=OSO_3^-

BioMed. Chem. Lett. **1992**, *2*, 1015

SEMISYNTHETIC MODIFICATION OF HYGROMYCIN A. 3. SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF AMINOCYCLITOL ANALOGS

Scott J. Hecker,* Susan C. Lilley, Martha L. Minich, and Kim M. Werner, Pfizer Inc, Central Research Division, Groton, CT 06340

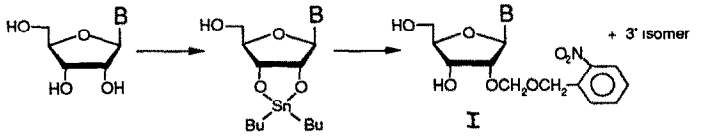
Aminocyclitol analogs of hygromycin A have been prepared, which explore the effects of substitution on each hydroxyl group.



BioMed. Chem. Lett. **1992**, *2*, 1019

RAPID SYNTHESIS OF OLIGORIBONUCLEOTIDES USING 2′-*O*-(*o*-NITROBENZYLOXYMETHYL)-PROTECTED MONOMERS

M. E Schwartz, R R Breaker, G T Asteriadis, J S. deBear and G. R Gough*
Department of Biological Sciences, Purdue University, West Lafayette, Indiana 47907



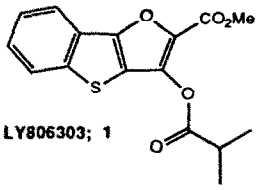
B = uracil-1-yl, adenin-9-yl, or 2-*N*-isobutyrylguanin-9-yl, I (B = cytosin-1-yl) is derived from I (B = uracil-1-yl)

A new, easily introduced protecting group for ribonucleoside 2′ hydroxyls, *o*-nitrobenzyloxymethyl, permits fast, effective solid phase synthesis of RNA.

BioMed. Chem. Lett. **1992**, *2*, 1025

CHARACTERIZATION OF LY806303 AS A POTENT AND SELECTIVE THROMBIN INHIBITOR.

Daniel J. Sall,* Dennis R. Berry, William J. Coffman, Trelia J. Craft, Michael L. Denney, Donetta S. Gifford-Moore, Marcia L. Kellam, and Gerald F. Smith
Lilly Research Laboratory, Eli Lilly and Company, Indianapolis, IN 46285



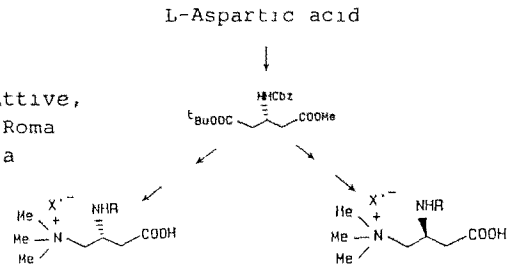
LY806303; 1

Methyl 3-(2-methyl-1-oxopropoxy)[1]benzothieno[3,2-b]furan-2-carboxylate (LY806303; **1**) has been characterized as a novel, potent and selective inhibitor of thrombin.

BioMed. Chem. Lett. **1992**, *2*, 1029

A STEREOSELECTIVE SYNTHESIS OF BOTH ENANTIOMERS OF EMERIAMINE FROM A SINGLE PRECURSOR: L-ASPARTIC ACID

D. Misiti[a*], M. Santaniello[b], G. Zappia[a]
a) Dip. Studi Chim. Tecnol. Sost. Biolog. Attive, Univ. "La Sapienza", P.le A. Moro 5, 00185 Roma
b) Lab. Ricerca Chim., Sigma Tau S.p.A., Via Pontina km 30.400, 00040 Pomezia (Italy)

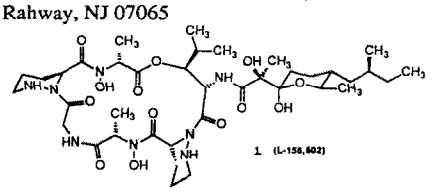


BioMed. Chem. Lett. **1992**, *2*, 1033

THE INHIBITION OF C5a RECEPTOR BINDING BY ANALOGS OF L-156,602, A NOVEL CYCLIC HEXADEPSIPEPTIDE ANTIBIOTIC

P. L. Durette, I. E. Kopka, T. J. Lanza J. L. Goulet, J. F. Kinneary, C. G. Caldwell, M. L. Hammond, S. S. Bondy, R. A. Zambias, J. Boger, T. Rollins, S. Siciliano, D. N. Cianciarulo, S. V. Kobayashi, M. S. Springer, W. K. Hagmann*, Merck Research Laboratories, Rahway, NJ 07065

The cyclic hexadepsipeptide antibiotic L-156,602 (**1**) was found to be an inhibitor of anaphylatoxin C5a binding to its receptor. The effects of chemical modification of the structure of **1** on C5a receptor inhibition and nonspecific actions are reported.



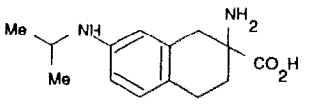
1 (L-156,602)

BioMed. Chem. Lett. **1992**, *2*, 1039

7-AMINOALKYL-2-AMINO-1,2,3,4-TETRAHYDRO-2-NAPHTHOIC ACIDS AS INHIBITORS OF TRYPTOPHAN UPTAKE

Clive V. Denyer[a*], Susan J. Turner-Brown[a], Richard G Knowles[b], and John Dawson[b]
Wellcome Research Laboratories, Langley Court, Beckenham, Kent, BR3 3BS, UK

The synthesis and biological activity of the title compounds is described.



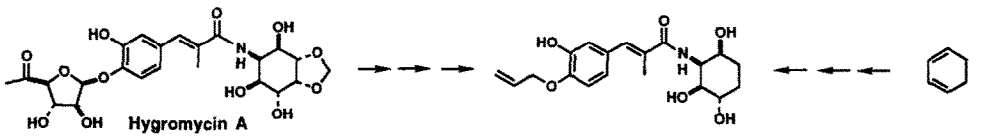
has K_i 0.8μM in W_1D_r cells

BioMed. Chem. Lett. **1992**, 2, 1043

HYGROMYCIN A: PREPARATION OF AMINOCYCLITOL ANALOGS DEFINING THE MINIMUM FUNCTIONALITY REQUIRED FOR BIOLOGICAL ACTIVITY.

Scott J. Hecker,* Susan C. Lilley, and Kim M. Werner, Pfizer Inc, Central Research Division, Groton, CT 06340

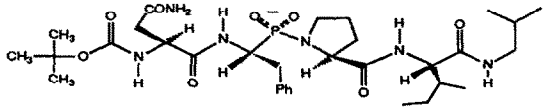
Aminocyclitol analogs of hygromycin A lacking the methylenedioxy ring have been prepared both in racemic and homochiral form.



BioMed. Chem. Lett. **1992**, 2, 1047

Synthesis of Stereochemically Defined Phosphonamidate-Containing Peptides: Inhibitors for the HIV-1 Proteinase

Nicholas P. Camp, Paul C. D. Hawkins, Peter B. Hitchcock[†] and David Gani*, *Chemistry Department, The Purdie Building, The University, St. Andrews, Fife, KY16 9ST, U.K. and* [†]*School of Chemistry and Molecular Sciences, University of Sussex, Brighton, BN1 9QJ, U.K.*



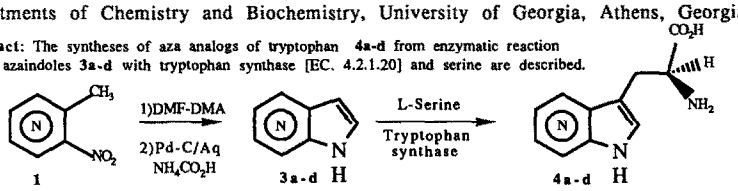
The above compound and its methyl phosphonamide ester derivatives are inhibitors of the HIV-1 proteinase.

BioMed. Chem. Lett. **1992**, 2, 1053

ENZYMATIC SYNTHESIS OF AZA-L-TRYPTOPHANS: The Preparation of 5- and 6-aza-L-tryptophan

Milton J. Sloan and Robert S. Phillips*
Departments of Chemistry and Biochemistry, University of Georgia, Athens, Georgia 30602.

Abstract: The syntheses of aza analogs of tryptophan **4a-d** from enzymatic reaction of the azaindoles **3a-d** with tryptophan synthase [EC. 4.2.1.20] and serine are described.

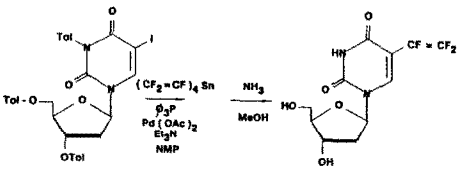


BioMed. Chem. Lett. **1992**, 2, 1057

SYNTHESIS AND ANTI-HERPES ACTIVITY OF 5-TRIFLUOROVINYL-2'-DEOXYURIDINE.

Herdewijn P.*, Kerremans, L., Snoeck, R., Van Aerschot, A., Esmans, E. and De Clercq, E.
Laboratory of Pharmaceutical Chemistry, Rega Institute, Minderbroedersstraat 10, B-3000 Leuven, Belgium

The title compound was synthesized from IdUrd and tetrakis(perfluorovinyl)tin. 5-Trifluorovinyl-2'-deoxyuridine inhibits the HSV-1-induced cytopathogenicity by 50% at 0.05 μg/mL.

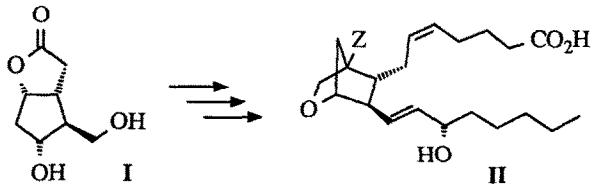


BioMed. Chem. Lett. **1992**, *2*, 1063

SYNTHESES OF NEW TXA_2/PGH_2-RECEPTOR ANTAGONISTS AND THEIR BIOLOGICAL PROPERTIES

P. Deicke and U. Klar
Research Laboratories of Schering AG,
Müllerstr. 170-178, W-1000 Berlin 65, FRG

The syntheses of new types of TXA_2/PGH_2-receptor antagonists are described and their structure activity relationships are discussed.

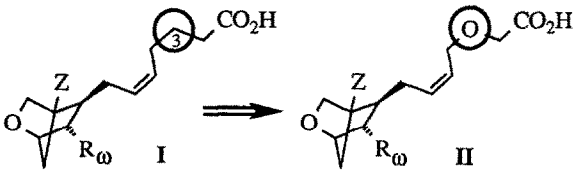


BioMed. Chem. Lett. **1992**, *2*, 1069

SYNTHESES OF NEW METABOLICALLY STABILISED TXA_2/PGH_2-RECEPTOR ANTAGONISTS AND THEIR BIOLOGICAL PROPERTIES

P. Deicke and U. Klar
Research Laboratories of Schering AG,
Müllerstr. 170-178, W-1000 Berlin 65, FRG

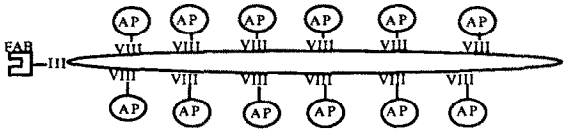
The syntheses of metabolically stabilized TXA_2/PGH_2-receptor antagonists of type II are described and the influence of this structural modification on receptor binding and antiaggregatory activity is discussed.



BioMed. Chem. Lett. **1992**, *2*, 1073

PHOPHABS: ANTIBODY-PHAGE-ALKALINE PHOSPHATASE CONJUGATES FOR ONE STEP ELISA'S WITHOUT IMMUNIZATION

James Light and Richard A. Lerner,* The Scripps Research Institute, La Jolla, CA 92037



Fab=antibody fragment, AP=alkaline phosphatase, III,VIII phage coat proteins

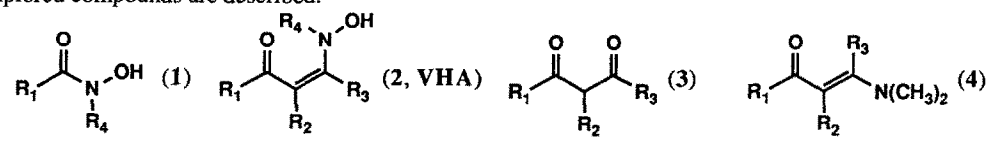
PhoPhabs have been created by incorporating alkaline phosphatase and antibody Fab's from combinatorial libraries on a filamentous phage framework. These PhoPhabs are antigen specific and can replace antibodies and eliminate the need for immunizations in ELISA (enzyme linked immunoassay) methods.

BioMed. Chem. Lett. **1992**, *2*, 1079

Vinylogous Hydroxamic Acids: 5-Lipoxygenase Inhibitors.

Stephen W. Wright,* Donald J. Pinto, Susan R. Sherk, Alicia M. Green,
Ronald L. Magolda. The Du Pont Merck Pharmaceutical Company, Wilmington, Delaware 19880.

Summary: The title compounds (**2**), vinylogs of hydroxamic acids (**1**), are inhibitors of 5-lipoxygenase. The syntheses of **2** from **3** and **4**, and the preliminary *in vitro* biological activities and SAR of these relatively unexplored compounds are described.

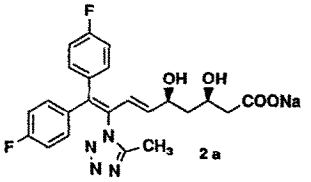


BioMed. Chem. Lett. **1992**, *2*, 1085

SYNTHESIS OF TETRAZOL-1-YL ANALOGS OF HMGCOA REDUCTASE INHIBITORS BMS180431 (FORMERLY BMY21950)

S. Y. Sit*, Rex A. Parker and J. J. Wright, Bristol-Myers Squibb Pharmaceutical Research Institute
5 Research Parkway, Wallingford, CT 06492-7660

Abstract : A series of tetrazol-1-yl analogs were prepared and compared with the corresponding parent tetrazol-5-yl HMGCO-A reductase inhibitors. The weaker enzyme inhibitory activity of **2a** may be attributed to the shorter distance between the heterocycle and the backbone of the molecule. The corresponding unsubstituted parent compound becomes the most active in this series.



2a

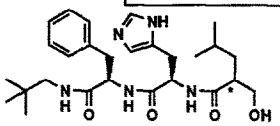
BioMed. Chem. Lett. **1992**, *2*, 1089

Retro-Inverso Tripeptide Renin Inhibitors

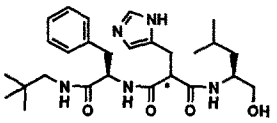
Dinesh V. Patel* and Denis E. Ryono

Bristol-Myers Squibb Pharmaceutical Research Institute
P.O. Box 4000, Princeton, NJ 08543-4000

Application of the retro-inverso peptide backbone modification concept to the tripeptide alcohol renin inhibitor Boc-Phe-His-Leucinol **1** (I_{50} = 16 uM) is described. While the diastereomeric mixture of partial retro analogs **3ab** was substantially less active (I_{50} = 1200 uM), the complete retro-inverso modification was well tolerated, as evidenced by the equipotency of **2b** (I_{50} = 20 uM) to parent compound **1**.



2 (*a,b)



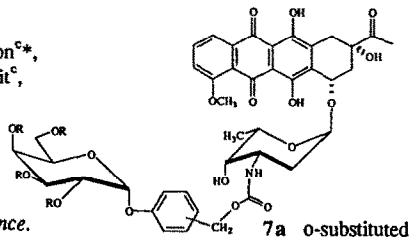
3 (*ab)

BioMed. Chem. Lett. **1992**, *2*, 1093

SYNTHESIS OF NOVEL TARGETED PRO-PRODRUGS OF ANTHRACYCLINES POTENTIALLY ACTIVATED BY A MONOCLONAL ANTIBODY GALACTOSIDASE CONJUGATE

S. Andrianomenjanahary[a], X. Dong[b], J.-C. Florent[b], G. Gaudel[b], J.-P. Gesson[c]*, J.-C. Jacquesy[c], M. Koch[a]*, S. Michel[a], M. Mondon[c], C. Monneret[b]*, P. Petit[c], B. Renoux[c], F. Tillequin[a].

[a]*Laboratoire de Pharmacognosie, Faculté des Sciences Pharmaceutiques, 4 avenue de l'Observatoire, 75006 Paris, France.*
[b]*Laboratoire de Chimie, Section de Biologie, Institut Curie, 26 rue d'Ulm, 75005 Paris, France*
[c]*Laboratoire de Chimie XII, 40 avenue du recteur Pineau, 86022 Poitiers, France.*



7a o-substituted
7b p-substituted

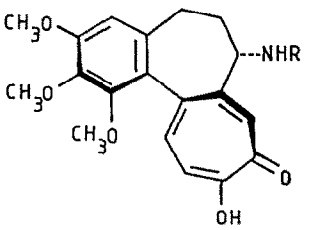
Glycoconjugates **7a** and **7b** have been prepared as pro-prodrugs of daunorubicin.

BioMed. Chem. Lett. **1992**, *2*, 1097

INHIBITION OF THE YEAST ALCOHOLDEHYDROGENASE BY Cu(II)-COMPLEXES OF COLCHICEINE AND N-DEACETYLCOLCHICEINE

J. Ulrichová[1], D. Valterová[1], F. Březina[2], V. Šimánek[1,*]
[1]Institute of Medical Chemistry, [2]Institute of Inorganic and Physical Chemistry, Palacký University, 77 515 Olomouc, Czechoslovakia

The Cu(II)-complexes of colchiceine and N-deacetylcolchiceine were prepared. They have been shown to be potent inhibitors of the yeast alcoholdehydrogenase. The results indicate the formation of a ternary enzyme-Cu(II)-alkaloid complex.

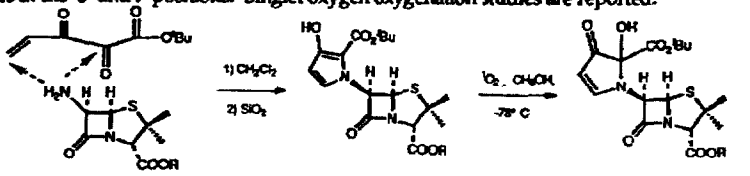


BioMed. Chem. Lett. **1992**, *2*, 1101

PYRROLE DERIVATIVES OF 6-APA AND 7-ACA. OXYGENATION BY SINGLET OXYGEN.

Harry H. Wasserman* and Chuansheng Niu, Department of Chemistry, Yale University, New Haven, CT 06511 USA

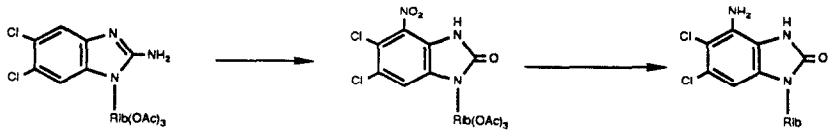
Abstract: The primary amino groups of 6-APA and 7ACA esters react with a vinyl tricarbonyl derivative to form substituted pyrroles at the 6- and 7-positions. Singlet oxygen oxygenation studies are reported.



BioMed. Chem. Lett. **1992**, *2*, 1105

BENZIMIDAZOLE RIBONUCLEOSIDES: OBSERVATION OF AN UNEXPECTED NITRATION WHEN PERFORMING NON-AQUEOUS DIAZOTIZATIONS WITH *t*-BUTYL NITRITE.

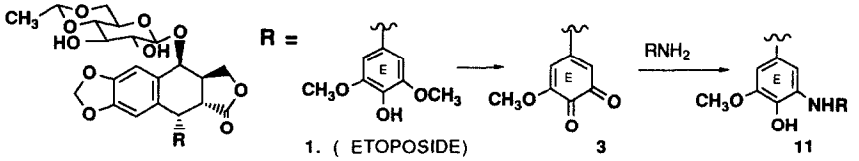
Rodrigo V. Devivar, John C. Drach, and Leroy B. Townsend*. Department of Medicinal Chemistry, College of Pharmacy, Department of Biologic and Materials Sciences, School of Dentistry, and the Department of Chemistry, College of Literature, Science and Arts, the University of Michigan, Ann Arbor, MI 48109-1065.



BioMed. Chem. Lett. **1992**, *2*, 1111

ETOPOSIDE(VP16): CHEMICAL REACTIVITY OF ETOPOSIDE-ORTHO QUINONE WITH AMINES AND THIOLS.

Dolatrai M. Vyas*, John F. Kadow, Karen L. LeBoulluec, Mark G. Saulnier and Terrence. W. Doyle. Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492-7660.

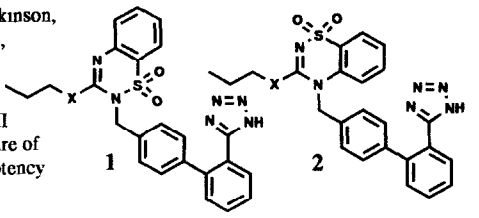


BioMed. Chem. Lett. **1992**, *2*, 1115

BENZOTHIADIAZINE DIOXIDES: A NEW CLASS OF POTENT ANGIOTENSIN-II (AT_1) RECEPTOR ANTAGONISTS.

Harold N. Weller*, Arthur V. Miller, Robert V. Moquin, Kenneth E. J. Dickinson, S. Anders Hedberg, Suzanne Moreland, Robert B. Cohen, Carol L. Delaney, Stephen Skwish, and Sharon Williams. The Bristol-Myers Squibb Pharmaceutical Research Institute, P.O. Box 4000, Princeton, NJ 08543.

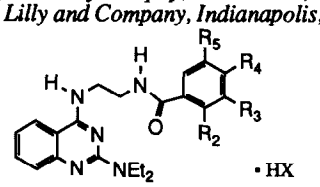
Benzothiadiazine dioxides, exemplified by **1** and **2**, are potent angioentsin-II receptor antagonists. Stability of the compounds is dependent upon the nature of the substituent at position 3 of the benzothiadiazine ring (e.g., X), while potency is dependent upon the nature of substitution on the benzo fused ring.



BioMed. Chem. Lett. **1992**, *2*, 1121

STRUCTURALLY NOVEL ANTIARRHYTHMIC / ANTIOXIDANT QUINAZOLINES. Melvin J. Yu,* Jefferson R. McCowan, Richard D. Towner, Peter P.K. Ho, Lee A. Phebus, Kenneth J. Ruterbories, Terry D. Lindstrom, Robert Boyd, William T. Jackson, Phillip J. Ertel, Mitchell I. Steinberg, Anthony Murphy, Alan Breau, G. Donald Pollock and Richard A. Hahn. *Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285*

In vitro and *in vivo* evaluation of quinazolines **1** - **12** is reported:

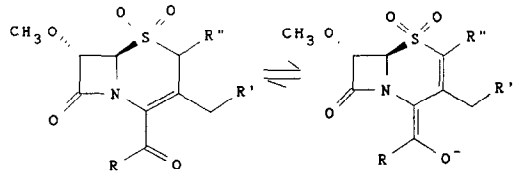


BioMed. Chem. Lett. **1992**, *2*, 1127

CEPHEM SULFONES AS INACTIVATORS OF HUMAN LEUKOCYTE ELASTASE. II. KETO–ENOL TAUTOMERISM IN CEPHEM–4–KETONES.

M. Alpegiani, P. Bissolino, D. Borghi, R. Corigli, S. Del Nero, E. Perrone, G. Razzano, and V. Rizzo*
Farmitalia Carlo Erba R&D, 20014 Nerviano (MI), Italy

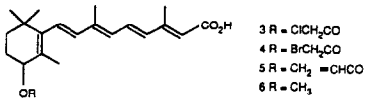
Keto–enol tautomerism has been investigated in cephem–4–ketones, a new class of human leukocyte elastase inhibitors. Potent kinetic efficiency in enzyme inhibition was found compatible with ionization of the compounds as enolates, which confers aqueos solubility and improved hydrolytic stability at physiological pH.



BioMed. Chem. Lett. **1992**, *2*, 1133

4-OXYGENATED RETINOIDS: UNEXPECTED CHEMOPREVENTIVE POTENTIAL FOR ANALOGUES ORIGINALLY SYNTHESIZED AS AFFINITY LABELS, Robert W. Curley, Jr.* and Dean L. Carson, *Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, Ohio 43210.*

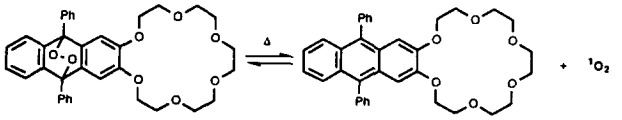
Abstract: The synthesis and alkylating activity of **3** - **5** is reported. The skin cancer preventive potential of **5** and **6** is also disclosed.



BioMed. Chem. Lett. **1992**, *2*, 1137

SYNTHESIS AND KINETIC STUDIES OF A NOVEL SINGLET OXYGEN DONOR WITH ACCEPTOR-BINDING CAPABILITY. Harry H. Wasserman,* Ta Yen Ching, Bruce H. Lipshutz, Haruo Matsuyama, Frank E. Scully, Jr. and Peng Wang, Department of Chemistry, Yale University, New Haven, CT 06511 USA

A singlet oxygen donor has been prepared in which an 18-crown-6 ether residue is attached to the 2,3-position of a 9,10-diphenylanthracene peroxide. Kinetic and preliminary donor-acceptor recognition studies are reported.



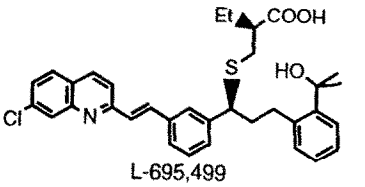
BioMed. Chem. Lett. **1992**, *2*, 1141

THE DISCOVERY OF A NEW STRUCTURAL CLASS OF POTENT ORALLY ACTIVE LEUKOTRIENE D_4 ANTAGONISTS

M Labelle, P Prasit, M. Belley, M. Blouin, E. Champion, L Charette, J.G. DeLuca, C. Dufresne, R. Frenette, J.Y. Gauthier, E Grimm, S.J. Grossman, D. Guay, E.G. Herold, T.R. Jones, C.K Lau, Y. Leblanc, S Léger, A. Lord, M McAuliffe, C. McFarlane, P. Masson, K.M Metters, N Ouimet, D.H. Patrick, H. Perrier, H. Piechuta, P Roy, H Williams, Z Wang, Y B. Xiang, R J Zamboni, A W. Ford-Hutchinson and R N. Young

Merck Frosst Centre for Therapeutic Research, P O Box 1005, Pointe Claire-Dorval, Québec, Canada H9R 4P8

The discovery of the potent and orally active leukotriene D_4 antagonist L-695,499 is reported.



L-695,499

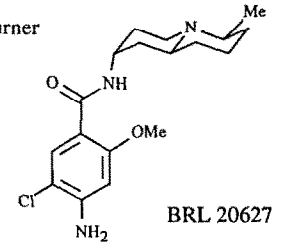
BioMed. Chem. Lett. **1992**, *2*, 1147

Substituted Benzamides with Conformationally Restricted Side Chains. 3. Azabicyclo[x.y.0] Derivatives as Gastric Prokinetic Agents.

M.S. Hadley, F.D. King*, B. McRitchie, D.M. Smith and D.H. Turner

SmithKline Beecham Pharmaceuticals, The Pinnacles, Harlow, Essex CM19 5AD, UK

The effect of alteration of ring size, introduction of alternative substituents and insertion of an exocyclic methylene group on the gastric prokinetic and dopamine antagonist antagonist activity of azabicyclic benzamides related to the serotonin 5-HT_4 receptor agonist, BRL 20627, is described



BRL 20627

BioMed. Chem. Lett. **1992**, *2*, 1153

THE USE OF SYNTHETIC PHOSPHOPEPTIDES FOR EPITOPE MAPPING OF THE α_{S1}-CASEIN PHOSPHOPEPTIDE SEGMENT 59-79.

John W. Perich and Eric C. Reynolds*

Biochemistry and Molecular Biology Unit, School of Dental Science, University of Melbourne, 711 Elizabeth St., Melbourne 3000, Victoria, Australia.

Gln-Met-Glu-Ala-Glu-Ser(*P*)-Ile-Ser(*P*)-Ser(*P*)-Ser(*P*)-Glu-Glu-Ile-Val-Pro-Asn-Ser(*P*)-Val-Glu-Gln-Arg

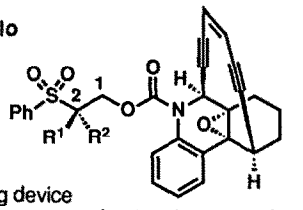
By the use of synthetic Ser(*P*)-containing peptides, both the -Ser(*P*)-Ser(*P*)-Ser(*P*)- and -Ile-Val-Pro-Asn-Ser(*P*)-Val-Glu-Glu- sequences were found to be antigenic determinants of α_{S1}-casein 59-79. A change of the Ser(*P*)-residue to Ser in the latter sequence resulted in a complete loss of recognition of the Ser-containing peptide by the anti-α_{S1}-casein polyclonal antibody.

BioMed. Chem. Lett. **1992**, *2*, 1155

ON THE MECHANISM OF ACTIVATION OF DESIGNED ENEDIYNES WITH SELECTIVE CYTOTOXICITY

K. C. Nicolaou*, W.-M. Dai, S.-C. Tsay, and W. Wrasidlo

Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, CA, 92037 and Department of Chemistry, University of California, San Diego, La Jolla, CA, 92093



3: $R^1 = R^2 = H$
4: $R^1 = H$, $R^2 = Me$
5: $R^1 = Me$, $R^2 = H$
6: $R^1 = R^2 = Me$

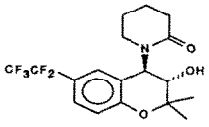
Enediynes **4-6** with substituents at the C2 position of the triggering device were synthesized and their DNA-cleaving activity and cytotoxicity were examined and compared to those of **3**. The results strongly suggusted a β-elimination reaction as the first step for the activation of these cytotoxic agents.

BioMed. Chem. Lett. **1992**, *2*, 1161

SYNTHESIS OF BRL 55834 - A NOVEL, POTENT AIRWAYS SELECTIVE POTASSIUM CHANNEL ACTIVATOR

D.R.Buckle*, D.S. Eggleston+, I.L. Pinto, D.G. Smith and J.M. Tedder.
SmithKline Beecham Pharmaceuticals, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey, KT18 5XQ, UK. + SmithKline Beecham Pharmaceuticals, Physical and Structural Chemistry Department, PO Box 1539, King of Prussia, Pennsylvania, 19406-0939, USA.

A facile synthesis of the potassium channel activator BRL 55834 is described and its 3S,4R stereochemistry deduced from single crystal X-ray analysis.



BRL 55834

BioMed. Chem. Lett. **1992**, *2*, 1165

QSAR OF HIV INHIBITORS

Corwin Hansch* and Litai Zhang
Department of Chemistry, Pomona College, Claremont, CA 91711

Quantitative structure-activity relationships (QSAR) have been derived for the analogues of compounds on the right protecting cells against HIV.