GRAPHICAL ABSTRACTS

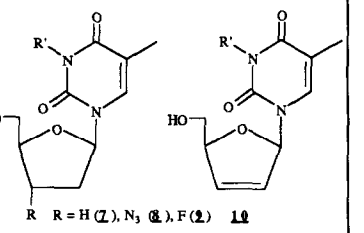
BioMed. Chem. Lett. **1992**, *2*, 1469

PREPARATION AND ANTI-HIV ACTIVITY OF N-3 AMINO SUBSTITUTED THYMIDINE NUCLEOSIDE ANALOGS

M. Maillard[a], J-C Florent[b], M. Lemaître[c], F. Begassat[c], A. Bugnicourt[c], C. Ferrieux[c], C. Rombi[c] E. Pacaud[c], D. Thierry[d], A. Zerial[c], C. Monneret[b], D.S. Grierson[a]

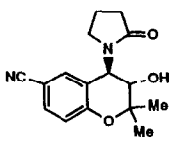
a) ICSN-CNRS, Ave. de la Terrasse, 91198 Gif-sur-Yvette, Fr.; b)Institut Curie, Section de Biologie, 26 rue d'Ulm, Paris 05 Cedex, Fr.; c)Rhône-Poulenc Rorer, 13 Quai Jules Guesde, BP 14, 94403 Vitry-sur-Seine, Fr.; d) SARAM, IPSN, CBN, BP 6, Fontenay-aux Rose, Fr.

The N-3 amino derivatives **7-10** *of ddt, AZT, 3'-Fddt, and D4T were prepared by electrophilic amination of the parent compounds and evaluated for their anti-HIV activity*

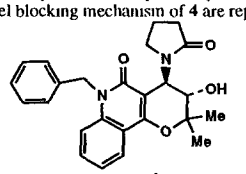


BioMed. Chem. Lett. **1992**, *2*, 1475

THE DISCOVERY OF A NOVEL CALCIUM CHANNEL BLOCKER RELATED TO THE STRUCTURE OF POTASSIUM CHANNEL OPENER CROMAKALIM. Karnail S. Atwal,* John, R. McCullough, Anders Hedberg, Mary L. Conder, Syed Z. Ahmed, Gabriella Cucinotta, and Diane E. Normandin. Bristol-Myers Squibb Pharmaceutical Research Institute, P. O. Box 4000, Princeton, N. J. 08543-4000. During our studies aimed at the identification of novel analogs of the potassium channel opener cromakalim (3), we serendipitously observed pyranoquinoline **4** to possess pure calcium channel blocking activity. The results of the studies conducted to confirm the calcium channel blocking mechanism of **4** are reported in this paper.



Cromakalim (3)



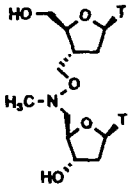
4

BioMed. Chem. Lett. **1992**, *2*, 1479

SYNTHESIS AND INCORPORATION OF METHYLENEOXY(METHYLIMINO) LINKED THYMIDINE DIMER INTO ANTISENSE OLIGONUCLEOSIDES

Françoise Debart, Jean-Jacques Vasseur, Yogesh S. Sanghvi*, and P. Dan Cook
ISIS Pharmaceuticals, 2280 Faraday Avenue, Carlsbad, CA 92008, USA

Abstract: A convenient synthesis of a thymidine (T) nucleoside dimer (T-3'-CH_2-O-NCH_3-5'-T) **12** has been accomplished via a nucleoside coupling reaction. An alternative synthesis of 2',3'-dideoxy-3'-C-hydroxymethylthymidine is described. The new dimer and methodology is useful for the development of backbone modified antisense oligonucleosides.



BioMed. Chem. Lett. **1992**, *2*, 1483

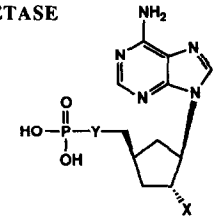
CARBOCYCLIC PHOSPHONATE ANALOGS OF 2',3'-DIDEOXYADENOSINE-5'-MONOPHOSPHATE (ddAMP) AS SUBSTRATES OF 5-PHOSPHORIBOSYL-1-PYROPHOSPHATE (PRPP) SYNTHETASE

Jean-François Navé, Dominique Wolff-Kugel and Serge Halazy
Marion Merrell Dow Research Institute, 16 rue d'Ankara
67009 Strasbourg, France

The title compounds were pyrophosphorylated by *E. coli* 5-phosphoribosyl-1-pyrophosphate (PRPP) synthetase in the presence of PRPP. Structure-activity relationships are discussed.

X = H Y = CH_2, CF_2, CH_2O

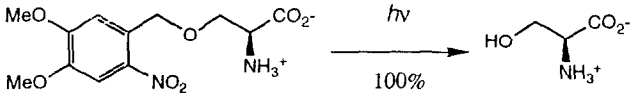
X = OH Y = CH_2



BioMed. Chem. Lett. **1992**, *2*, 1489

SYNTHESIS OF PHOTODEPROTECTABLE SERINE DERIVATIVES. "CAGED SERINE"

Michael C. Pirrung* & David S. Nunn
Department of Chemistry, Duke University
P. M. Gross Chemical Laboratory
Durham, North Carolina 27706 USA

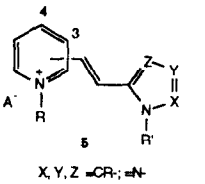


Syntheses of two nitrobenzyl derivatives of L-serine have been developed for use as photodeprotectable enzyme substrates. They are deprotected on irradiation with UV light with sub-10 min half-lifes and provide serine in high yield and without racemization.

BioMed. Chem. Lett. **1992**, *2*, 1493

(*E*)-1-ALKYL-[2-(1*H*-AZOL-2-YL)VINYL]PYRIDINIUM SALTS: THEORETICAL ANALYSIS, SYNTHESIS AND EVALUATION OF THEIR INTERACTION WITH CHOLINE ACETYLTRANSFERASE.

E.Alcalde*, T.Roca, Lab. Química Orgánica, Facultad de Farmacia, E-08028 Barcelona, Spain.
A.Barat, G.Ramirez, Centro de Biología Molecular, CSIC-UAM, E-28049 Madrid, Spain.
P.Goya, A.Martinez, Instituto de Química Medica, CSIC, E-28006 Madrid, Spain.



5

X, Y, Z =CR-; =N-

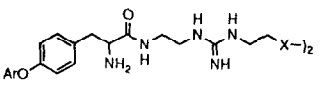
A new type of aza-analogues **NVP+ 5** have been investigated. The evaluation of the ChAT inhibition together with the results of the semiempirical calculations suggest that coplanarity and polarization criteria may not be enough to account for ChAT activity of vinylpyridinium salts and that steric requirements might play a very important role in their interaction with the enzyme.

BioMed. Chem. Lett. **1992**, *2*, 1497

NEUROPEPTIDE Y (NPY) FUNCTIONAL GROUP MIMETICS: DESIGN, SYNTHESIS, AND CHARACTERIZATION AS NPY RECEPTOR ANTAGONISTS

Michael B. Doughty*†, Shao Song Chu†, Gregory A. Misse¶, and Richard Tessel¶
Departments of Medicinal Chemistry† and Pharmacology and Toxiology¶, School of Pharmacy, University of Kansas, Lawrence, KS 66045-2506, U.S.A.

SC3117 (**3**) and SC3199 (**4**) have been designed as neuropeptide Y (NPY) functional group mimetics. Both **3** and **4** displace ^{3}H-NPY from rat brain binding sites, and **4** is a reversible, NPY receptor antagonist in the periphery.



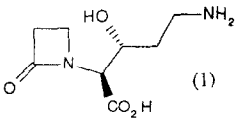
3 (SC3117). X=S; Ar=2,6-dichlorobenzyl
4 (SC3199): X=CH_2, Ar=2,6-dichlorobenzyl

BioMed. Chem. Lett. **1992**, *2*, 1503

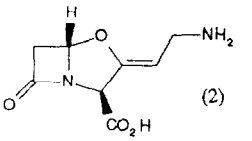
STUDIES ON THE SUBSTRATE SPECIFICITY OF CLAVAMINIC ACID SYNTHASE AND ASSOCIATED ENZYMES

S. W. Elson, K. H. Baggaley, S. Holland, N. H. Nicholson, J. T. Sime* and S. R. Woroniecki.
SmithKline Beecham Pharmaceuticals, Brockham Park, Betchworth, Surrey, RH3 7AJ, UK.

The substrate specificity of the enzyme responsible for the conversion of proclavaminic acid (1) to clavaminic acid (2) has been investigated by the use of structural analogues of (1).



(1)



(2)

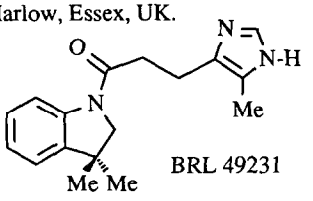
BioMed. Chem. Lett. **1992**, 2, 1509

Indazole and Indoline as Aromatic Bioisosteres in the Imidazole Class of Serotonin 5-HT_3 Receptor Antagonists

J. Bermudez, F.D. King* and G.J. Sanger

*SmithKline Beecham Pharmaceuticals,Coldharbour Road, The Pinnacles, Harlow, Essex, UK.

The synthesis and 5-HT_3 receptor antagonist activity of imidazole derivatives of 3-keto-indazoles, 3,3-dimethylindolin-1-yl (as exemplified by BRL 49231) and o-methoxyphenyl amides is described. Results show that indazole and indoline are effective indole bioisosteres in the imidazole class of 5-HT_3 receptor antagonists.



BRL 49231

BioMed. Chem. Lett. **1992**, 2, 1513

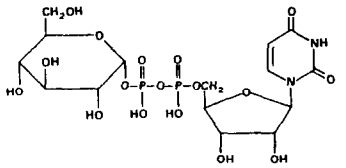
MECHANISTIC STUDIES OF BIOLOGICAL GLYCOSYLATION. DETERMINATION OF THE GLUCOSYLATING REACTIVITY OF URIDINE-5'-DIPHOSPHO-α-D-GLUCOSE (UDPG) AND ASSESSMENT OF THE CATALYTIC POWER OF THE GLYCOSYLTRANSFERASES.

Colin T Bedford,[a,b,*] Alan D Hickman,[b] and Christopher J Logan[b]

[a] School of Biological and Health Sciences, University of Westminster, 115 New Cavendish Street, London WIM 8JS.

[b] Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG

Abstract: Enzymic rate enhancements of the glycosyltransferases are estimated to be in the order of 10^{16}, as revealed by a determination for the first time of the magnitude of the spontaneous glucosylating reactivity (which prevails only at pH 1-3) of the prototypical 'activated' co-substrate of biological glycosylation, UDPG



α-UDPG

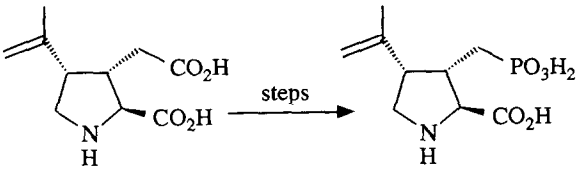
BioMed. Chem. Lett. **1992**, 2, 1519

SYNTHESIS OF THE ω-PHOSPHONIC ACID ANALOGUE OF KAINIC ACID

Ian Jefferies

Central Research Laboratories, Ciba Geigy PLC, Hulley Road, Macclesfield, Cheshire, SK10 2NX.

The ω-phosphonic acid analogue of kainic acid was synthesised from the naturally occurring carboxylic acid in nine steps and 6% overall yield.



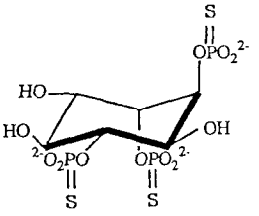
BioMed. Chem. Lett. **1992**, 2, 1523

SYNTHESIS OF L-*CHIRO*-INOSITOL 1,4,6-TRISPHOSPHOROTHIOATE, A POTENT AND SELECTIVE INHIBITOR OF *MYO*-INOSITOL 1,4,5-TRISPHOSPHATE 5-PHOSPHATASE

C Liu[1], S T Safrany[2], S R Nahorski[2] and B V L Potter[1]*

[1]School of Pharmacy and Pharmacology and Institute for Life Sciences, University of Bath, Claverton Down, Bath BA2 7AY, UK. [2]Department of Pharmacology and Therapeutics, University of Leicester, Leicester LE1 9NH, UK.

L-*chiro*-inositol 1,4,6-trisphosphorothioate is the most potent and selective inhibitor of Ins(1,4,5)P_3 5-phosphatase yet synthesized.



BioMed. Chem. Lett. **1992**, *2*, 1529

HIV AND REVERSE TRANSCRIPTASE INHIBITION BY TANNINS

Robert E Kilkuskie, [a, e] Yoshiki Kashiwada, [b] Gen-ichiro Nonaka,[c] Itsuo Nishioka,[c] Anne J Bodner, [a] Yung-Chi Cheng,[d] and Kuo-Hsiung Lee [b]*

[a] *Cambridge Biotech Corporation, 1600 East Gude Drive, Rockville, Maryland 20850*

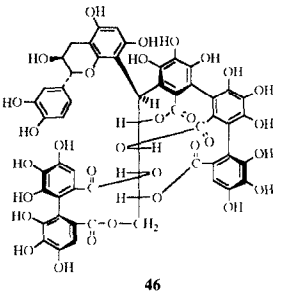
[b] *Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, North Carolina 27599*

[c] *Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan*

[d] *Department of Pharmacology, Yale University, School of Medicine, New Haven, Connecticut 06510*

[e] *Present address Hybridon, Inc., Worcester, MA 01605*

Further evaluation of tannins as anti-HIV agents indicates that these compounds inhibited HIV replication only slightly in the absence of toxicity (therapeutic index ≤ 5). In addition, no correlation was found between inhibition of reverse transcriptase and of HIV in cell culture



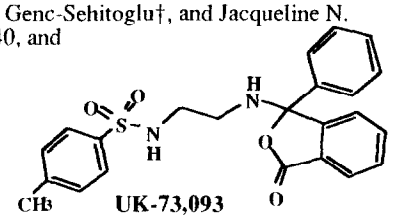
46

BioMed. Chem. Lett. **1992**, *2*, 1535

UK-73,093 : A NON-PEPTIDE NEUROTENSIN RECEPTOR ANTAGONIST,

R Michael Snider*, Dennis A Pereira, Kelly P. Longo, Ralph E. Davidson, Fredric J. Vinick, Kirsti Laitinen†, Ece Genc-Sehitoglu†, and Jacqueline N. Crawley†, Central Research Division, Pfizer Inc, Groton, CT 06340, and †National Institute of Mental Health, Bethesda MD 20892

Abstract: The synthesis and biological activity of a non-peptide neurotensin receptor antagonist is reported (*in vitro* EC50 = 4 μM).



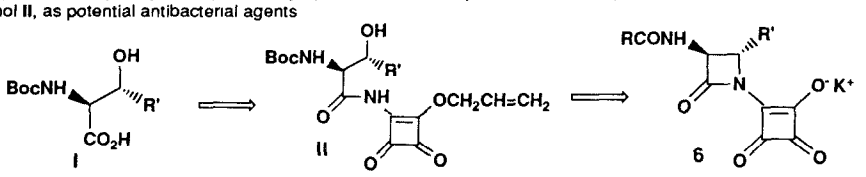
UK-73,093

BioMed. Chem. Lett. **1992**, *2*, 1541

SYNTHESIS OF α-(S)-ACYLAMINO-N-(HYDROXYDIOXOCYCLOBUTENYL)-β-LACTAMS AS POTENTIAL ANTIBIOTICS

Y. Ueda*, A. Mikkilineni and R.A. Partyka
Bristol-Myers Squibb Company, Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492-7660 USA

α-(S)-Acylamino-N-(hydroxydioxocyclobutenyl)-β-lactams **6** were synthesized from (L)-N-^{t}Boc-serine or threonine **I** via alcohol **II**, as potential antibacterial agents

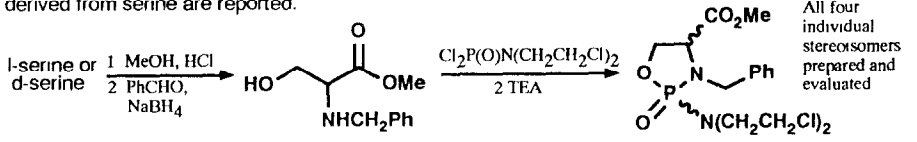


BioMed. Chem. Lett. **1992**, *2*, 1547

SYNTHESIS OF CHIRAL PHOSPHORUS MUSTARDS DERIVED FROM SERINE

John A. Jackson, Jeffrey A. Frick and Charles M. Thompson*
Dept. of Chemistry, Loyola University of Chicago, Chicago, IL 60626

The synthesis and biological evaluation of chiral, diastereomeric phosphorus mustards derived from serine are reported.



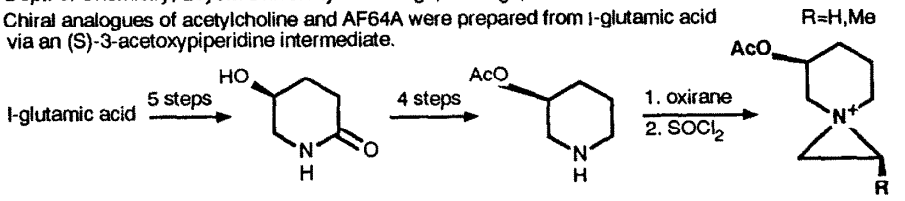
All four individual stereoisomers prepared and evaluated

BioMed. Chem. Lett. **1992**, 2, 1551

CHIRAL, PIPERIDINE-BASED ANALOGUES OF AF64A AND ACETYLCHOLINE

Nam Huh and Charles M. Thompson*
Dept. of Chemistry, Loyola University of Chicago, Chicago, IL 60626

Chiral analogues of acetylcholine and AF64A were prepared from l-glutamic acid via an (S)-3-acetoxypiperidine intermediate.

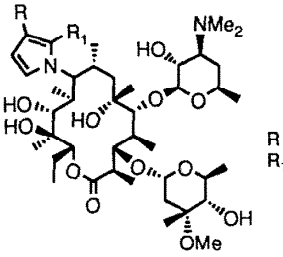


BioMed. Chem. Lett. **1992**, 2, 1555

SYNTHESIS AND ACTIVITIES OF 9-PYRROLO-9-DEOXOERYTHROMYCIN A ANALOGS

K.. Shankaran* and Timothy A. Blizzard
Merck Research Laboratories, R50G-231
P.O. Box 2000, Rahway, NJ 07065

Preparation and biological evaluation of novel 9-pyrrolo-9-deoxoerythromycin A analogs are described.



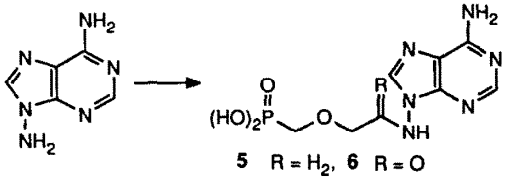
R = H, CHO, OH
R_1 = H, $CO_2{}^tBu$

BioMed. Chem. Lett. **1992**, 2, 1559

SYNTHESIS OF 9-[2-(PHOSPHONOMETHOXY)ETHYLAMINO]ADENINE AND 9-[(PHOSPHONOMETHOXY)ACETAMIDO]ADENINE, ANALOGUES OF A POTENT ANTI-HIV ACYCLONUCLEOTIDE

Michael R. Harnden and Richard L. Jarvest*
SmithKline Beecham Pharmaceuticals, Great Burgh,
Yew Tree Bottom Road, Epsom, Surrey KT18 5XQ, U.K.

Analogues of the potent anti-HIV acyclonucleotide BRL 47923 have been synthesised where the oxygen attached to N-9 has been replaced by an amino (**5**) or amido (**6**) nitrogen. Compounds **5** and **6** were prepared from 9-aminoadenine.



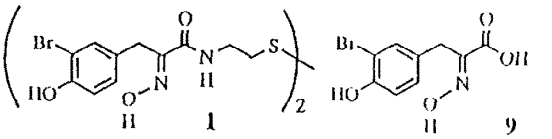
5 R = H_2, **6** R = O

BioMed. Chem. Lett. **1992**, 2, 1561

A CONVENIENT SYNTHESIS OF A BROMOTYROSINE DERIVED METABOLITE, PSAMMAPLIN A, FROM *PSAMMAPLYSILLA SP.*

Osamu Hoshino,* Masatoshi Murakata, and Kohei Yamada
Faculty of Pharmaceutical Sciences, Science University of Tokyo,
12, Ichigaya Funagawara-machi, Shinjuku-ku, Tokyo 162, Japan

Psammaplin A **1**, which is a bromotyrosine dimer containing oxime and disulfide moieties, was synthesized by direct coupling of phenolic oxime-acid **9** with free cystamine using a mixture of DDC and N-hydroxy-phthalimide in the presence of Et_3N



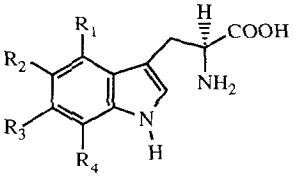
1 **9**

BioMed. Chem. Lett. **1992**, *2*, 1563

ENZYMATIC SYNTHESIS OF CHLORO-L-TRYPTOPHANS

Minsu Lee and Robert S. Phillips*
Departments of Chemistry and Biochemistry, University of Georgia, Athens, GA 30602

4-, 5-, 6- And 7-chloro-L-tryptophan **1a-d** were prepared from the corresponding chloroindoles by reaction with L-serine using tryptophan synthase.



1a: R_1=Cl, R_2=R_3=R_4=H

1b: R_2=Cl, R_1=R_3=R_4=H

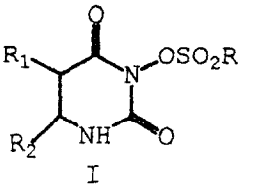
1c: R_3=Cl, R_1=R_2=R_4=H

1d: R_4=Cl, R_1=R_2=R_3=H

BioMed. Chem. Lett. **1992**, *2*, 1565

A GENERAL APPROACH TOWARD THE DESIGN OF INHIBITORS OF SERINE PROTEINASES:INHIBITION OF HUMAN LEUKOCYTE ELASTASE BY SUBSTITUTED DIHYDROURACILS.

William C. Groutas*, He Huang, Jeffrey B. Epp, Michael J. Brubaker, Charles E. Keller, Jerald J. McClenahan,
Department of Chemistry, Wichita State University, Wichita, KS 67208.



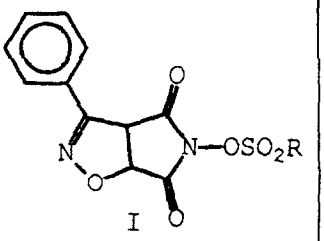
I

The rational design of potential inhibitors of serine proteinases is described and validated using substituted dihydrouracils **I**.

BioMed. Chem. Lett. **1992**, *2*, 1571

INHIBITION OF HUMAN LEUKOCYTE ELASTASE AND AND CATHEPSIN G BY ISOXAZOLINE DERIVATIVES.

William C. Groutas*, Lee S. Chong, Jeffrey B. Epp, Michael J. Brubaker, Michael A. Stanga, Eun-Hong Kim, Charles E. Keller,
Department of Chemistry, Wichita State University, Wichita, KS 67208.



I

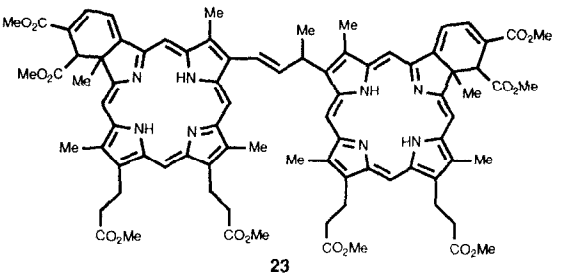
The interaction of a series of isoxazoline derivatives **I** with elastase and cathepsin G is described.

BioMed. Chem. Lett. **1992**, *2*, 1575

NEW SYNTHESES OF BENZOPORPHYRIN DERIVATIVES AND ANALOGUES FOR USE IN PHOTODYNAMIC THERAPY

Isabelle Meunier, Ravindra K Pandey,* Michelle M Walker, Mathias O Senge, Thomas J Dougherty, and Kevin M Smith*
Department of Chemistry, University of California, Davis, CA 95616, and Department of Radiation Medicine, Roswell Park Memorial Institute, 666 Elm St , Buffalo, NY 14263, USA

New syntheses of pure "benzoporphyrin derivative" ring isomers, as well as dimer analogues (e g **23**) are reported

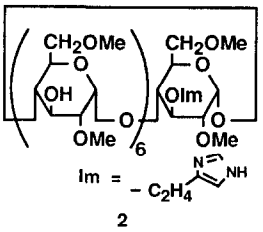


23

BioMed. Chem. Lett. **1992**, *2*, 1581

SUBSTRATE SELECTIVITY OF IMIDAZOLE-APPENDED DIMETHYL-β-CYCLODEXTRIN

Hiroshi Ikeda*, Tsukasa Ikeda, and Fujio Toda*
Department of Bioengineering, Tokyo Institute of Technology,
4259 Nagatsuta-cho, Midori-ku, Yokohama 227 Japan.



2

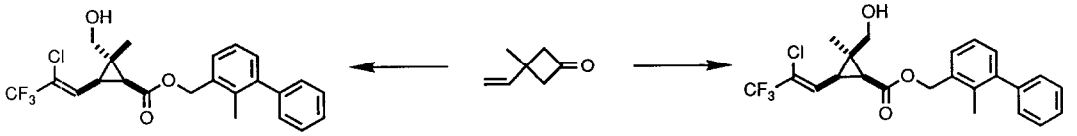
The substrate selectivity of imidazole-appended dimethyl-β-cyclodextrin (**2**) was studied using some kinds of *p*-nitrophenyl esters of amino acids. The tendency for the hydrolysis reaction of the amino acid ester by **2** reflected difference in K_m rather than in k_{cat}. **2** had the ability to undergo a stereo-selective hydrolysis reaction.

BioMed. Chem. Lett. **1992**, *2*, 1585

STEREOSELECTIVE SYNTHESIS OF HYDROXYLATED BIFENTHRIN ISOMERS

Scott McN. Sieburth*, Syed F. Ali, Charles M. Langevine and Robert H. Tullman
Agricultural Chemical Group, FMC Corporation
Princeton, New Jersey 08543

Two possible metabolites of bifenthrin, a potent insecticide/acaricide, were prepared from 4-methyl-4-vinylcyclobutanone with substantial control of stereochemistry.

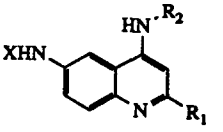


BioMed. Chem. Lett. **1992**, *2*, 1589

THE SYNTHESIS AND IDENTIFICATION OF 4,6-DIAMINOQUINOLINE DERIVATIVES AS POTENT IMMUNOSTIMULANTS

Mikel P. Moyer*, Frederick H. Weber†, Jonathan L. Gross, Joseph W. Isaac, and Ralph Saint Fort, Central Research Division, Pfizer Inc, Groton, CT 06340 and †Terre Haute, IN 47808

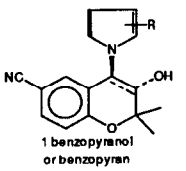
The synthesis of a number of 4,6-diaminoquinoline derivatives is described as well as their evaluation in a mouse protection model designed to identify immunostimulant activity. These compounds represent a novel series of potent immunostimulants.



BioMed. Chem. Lett. **1992**, *2*, 1595

PYRROLE ANALOGUES OF THE PYRROLIDINONE MOIETY OF THE POTASSIUM CHANNEL ACTIVATOR CROMAKALIM AS RELAXANTS OF GUINEA PIG TRACHEALIS.

D.G. Smith*, D.R. Buckle, A. Faller, and I.L. Pinto.
SmithKline Beecham Pharmaceuticals, Great Burgh, Yew Tree Bottom Rd, Epsom, Surrey, KT18 5XQ, UK.



1 benzopyranol
or benzopyran

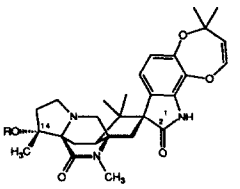
A series of pyrrole derivatives of general structure 1 is described. Compounds where R is an electron withdrawing group are potent relaxants of guinea pig tracheal spirals, appearing to act via potassium channel opening.

BioMed. Chem. Lett. **1992**, *2*, 1599

THE PREPARATION AND UTILIZATION OF PARAHERQUAMIDE-2-O-METHYL IMIDATE IN THE SYNTHESIS OF 14-O-SUBSTITUTED PARAHERQUAMDE DERIVATIVES

Peter J. Sinclair*, James M. Schaeffer, W. L. Shoop and Helmut Mrozik, Merck Research Laboratories, P.O. Box 2000, Rahway, N.J. 07065.

The 2-O-methylmidate of the antiparasitic oxindole alkaloid paraherquamide **1**, was prepared and subsequently utilized in the synthesis of 14-O-alkyl paraherquamide analogs.

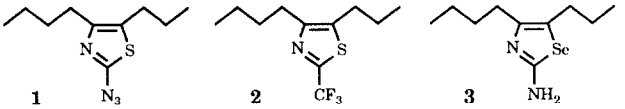


1 R = H Paraherquamide

BioMed. Chem. Lett. **1992**, *2*, 1603

SYNTHESIS OF THIAZOLE AND SELENAZOLE DERIVATIVES WITH AFFINITY FOR THE ODORANT-BINDING PROTEIN.

Elio Napolitano[a], Paolo Pelosi*[b]
[a] *Dipartimento di Chimica Bioorganica*
[b] *Istituto di Industrie Agrarie*
University of Pisa
Via S. Michele, 4 - 56124 Pisa, Italy



1 **2** **3**

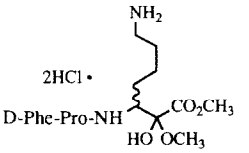
Abstract. Compounds **1-3**, designed as probes to investigate the binding site of OBP by photoaffinity labelling, NMR, and X-ray, respectively, bind the bovine OBP with dissociation constants in the micromolar range.

BioMed. Chem. Lett. **1992**, *2*, 1607

α-HYDROXY- AND α-KETOESTER FUNCTIONALIZED THROMBIN INHIBITORS

Edwin J. Iwanowicz,* James Lin, Daniel G.M. Roberts, Inge M. Michel and Steven M. Seiler
Bristol-Myers Squibb Pharmaceutical Research Institute
Princeton, NJ 08543-4000

Abstract: α-Hydroxy- and α-ketoester functionalized D-Phe-Pro-Lys tripeptides were found to be potent thrombin active site inhibitors. The ketoester derivatives were characterized by slow binding kinetics. The most potent of the series was **11** (**BMS 181,412-01**) with an overall inhibition constant K_I^* of 0.0017 μM.

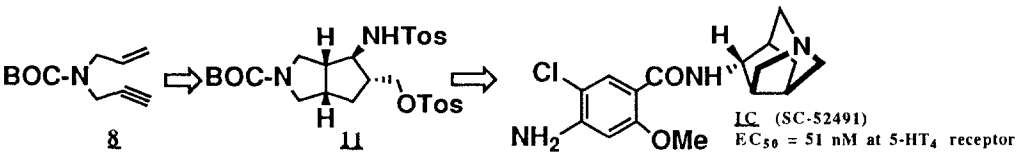


11

BMS 181,412-01

BioMed. Chem. Lett. **1992**, *2*, 1613

NEW AZA(NOR)ADAMANTANES ARE AGONISTS AT THE NEWLY IDENTIFIED SEROTONIN 5-HT4 RECEPTOR AND ANTAGONISTS AT THE 5-HT3 RECEPTOR Daniel L. Flynn*[a], Daniel P. Becker [a], Dale P. Spangler [a], Roger Nosal [a], Gary W. Gullikson [b], Chafiq Moummi [b], and Dai-Chang Yang [b], Depts of Chemistry[a] and Neurological Diseases Research[b] *Searle Research and Development, Skokie, Illinois 60077*



8 **11**

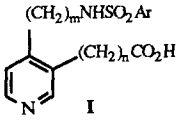
IC (SC-52491)
EC_{50} = 51 nM at 5-HT_4 receptor

BioMed. Chem. Lett. **1992**, *2*, 1619

Thromboxane Receptor Antagonism Combined with Thromboxane Synthase Inhibition. 6. 4-Substituted 3-Pyridinylalkanoic Acids.

S S. Bhagwat*, C Boswell, C. Gude, N. Contardo, D. S. Cohen, J. Mathis, R. Dotson, W. Lee, and S. Shetty
Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, 556 Morris Avenue, Summit, New Jersey 07901.

Pyridinylalkanoic acids (I) with an arylsulfonylaminoalkyl substituent at the 4-position were synthesized and found to be antagonists of the platelet receptor for thromboxane A_2 and inhibit thromboxane synthase.



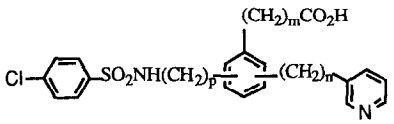
I

BioMed. Chem. Lett. **1992**, *2*, 1623

Thromboxane Receptor Antagonism Combined with Thromboxane Synthase Inhibition. 7. Pyridinylalkyl-Substituted Arylsulfonylamino Arylalkanoic Acids.

S S. Bhagwat*, D. M. Roland, A. J. Main, C Gude, K. Grim, R. Goldstein, D. S. Cohen, R Dotson, J. Mathis, and W. Lee
Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, 556 Morris Avenue, Summit, New Jersey 07901.

Arylsulfonylamino arylalkanoic acids (I) substituted with a pyridinylalkyl group were synthesized and found to have the dual activity of antagonizing the receptor for thromboxane A_2 and inhibiting thromboxane synthase.

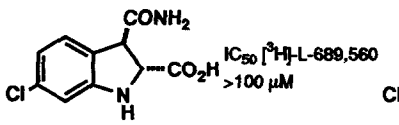


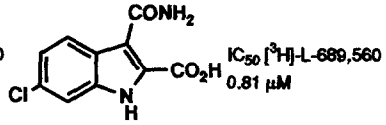
I

BioMed. Chem. Lett. **1992**, *2*, 1627

2-CARBOXY INDOLINES AND INDOLES AS POTENTIAL GLYCINE/NMDA ANTAGONISTS: EFFECT OF FIVE-MEMBERED RING CONFORMATION ON AFFINITY.

Michael Rowley,* Paul D. Leeson, Sarah Grimwood, Alan Foster, and Kay Saywell.
Merck Sharp and Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Eastwick Road, Harlow, Essex CM20 2QR, UK.





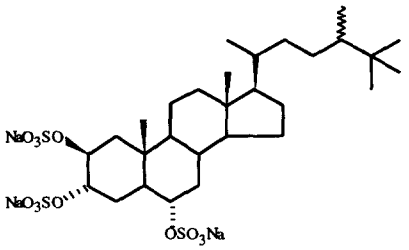
Molecular modelling suggests that 2-carboxyindolines may not bind to the Glycine/NMDA receptor due to the lack of coplanarity between the aromatic ring and the carboxylate.

BioMed. Chem. Lett. **1992**, *2*, 1631

A NOTE OF CAUTION IN THE USE OF RECEPTOR BINDING ASSAYS TO SCREEN MARINE ORGANISMS: THE ACTION OF HALISTANOL TRISULPHATE ON ADENOSINE RECEPTORS.

Roger W. Moni, Roger J. Willis and Ronald J. Quinn*
School of Science, Griffith University, Brisbane, 4111, Australia

The adenosine A_1 receptor binding assay was used to screen marine extracts. Following the isolation of halistanol trisulphate, non-specific interference causing reduction in affinity and the number of binding sites of the radioligand was identified to be associated with this detergent. Methods for detection of non-specific receptor interactions and optimization of the assays for natural product screening are discussed.

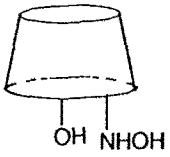


BioMed. Chem. Lett. **1992**, *2*, 1635

HYDROGEN BONDING EFFECTS ON THE REACTIVITY OF A PREASSOCIATING α-NUCLEOPHILE. THE SECONDARY-SIDE βCD HYDROXYLAMINE

Mark A. Mortellaro and Anthony W. Czarnik*
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

The secondary-side hydroxylamine derivative of β-cyclodextrin demonstrates base-catalyzed transesterification from pH 6.5-9.5, while the primary-side derivative does not.

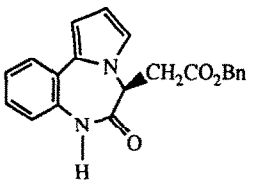


BioMed. Chem. Lett. **1992**, *2*, 1639

SYNTHESIS AND ANTI-HIV ACTIVITY OF PYRROLO-[1,2-d]-(1,4)-BENZODIAZEPIN-6-ONES

George V. De Lucca* and Michael J. Otto
Du Pont Merck Pharmaceutical Company
Experimental Station P.O. Box 80353
Wilmington, DE 19880-0353

The synthesis of novel pyrrolo annulated 1,4-benzodiazepines is described. These pyrrolo[1,2-d]-(1,4)-benzodiazepines (e.g. **4**) have been found to have antiviral activity against HIV-1. Like other non nucleoside HIV-1 RT inhibitors, these compounds appear to be specific for HIV-1.



4

BioMed. Chem. Lett **1992**, *2*, 1645

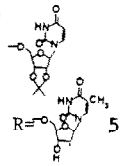
SYNTHESIS AND TUMORICIDAL ACTIVITY OF WATER SOLUBLE PORPHYRINYL-THYMIDINES AND RELATED PORPHYRINS

Leszek Czuchajowski*, Halina Niedbala, Department of Chemistry, University of Idaho, Moscow, ID 83843, Terry Shultz* and Wanda Seaman, Department of Food Science and Human Nutrition, Washington State University, Pullman, WA 99164.

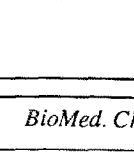
The cobalt(II)porphyrinyl-thymidine **5**, the most efficient among the porphyrins **1-5**, suppressed the growth of human malignant melanoma cells by 95% as a 2.5×10^{-5} M solution in tris buffer.

1 R=OCH_3 **2** R=OH

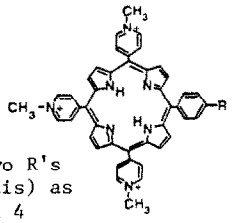
3 R=



4 R=



5 two R's (cis) as in **4**



BioMed. Chem. Lett. **1992**, *2*, 1649

P-3A and (-)-Desacetamido P-3A: Demonstration and Study of Their Effective Functional Cleavage of Duplex DNA, Dale L. Boger* and Wenjin Yang, *Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, California 92037 USA*

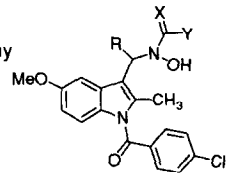
Abstract. A study of the Fe(II) complexes of P-3A (**1**) and (-)-desacetamido P-3A (**2**) abilities to cleave duplex DNA was conducted through examination of single-strand and double-strand cleavage of supercoiled ϕX174 RFI DNA (Form I) in the presence of O_2 to produce relaxed (Form II) and linear (Form III) DNA, respectively. Like Fe(II)-bleomycin A_2 and deglycobleomycin A_2, Fe(II)-**1** and **2** effectively produced both single- and double-strand cleavage of supercoiled ϕX174 DNA. Unlike Fe(II)-bleomycin A_2 or deglycobleomycin A_2, Fe(II)-**1** and **2** were found to cleave duplex w794 DNA with no discernible sequence selectively suggesting that the polynucleotide recognition of the C-terminus tetrapeptide S subunit of the bleomycins including the bithiazole may dominate the bleomycin A_2 DNA cleavage selectivity.

BioMed. Chem. Lett. **1992**, *2*, 1655

SYNTHESIS OF REVERSED HYDROXAMIC ACIDS OF INDOMETHACIN: DUAL INHIBITORS OF CYCLOOXYGENASE AND 5-LIPOXYGENASE

J.B.Kramer, D.H.Boschelli, D.T.Connor, C.R.Kostlan, D.L.Flynn, R.D.Dyer, D.A.Bornemeier, J.A.Kennedy, C.D.Wright, P.J.Kuipers
Departments of Medicinal Chemistry, Biochemistry and Immunopathology
Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company
2800 Plymouth Road, Ann Arbor, Michigan 48105

Replacement of the carboxylic acid function of indomethacin with reversed hydroxamic acids converted a selective cyclooxygenase (CO) inhibitor into dual inhibitors of CO and 5-lipoxygenase (5-LO).



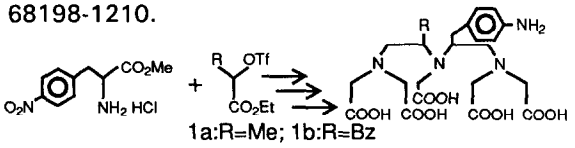
R = H, CH_3
X = O, S
Y = CH_3, NH_2, $NHCH_3$

BioMed. Chem. Lett. **1992**, *2*, 1661

SYNTHESIS OF 2-P-AMINOBENZYL-3-METHYL- AND 2-P-AMINOBENZYL-3-BENZYL DERIVATIVES OF DIETHYLENETRIAMINEPENTAACETIC ACIDS: CARBON BACKBONE MODIFIED BIFUNCTIONAL CHELATING AGENTS.

Syed M Quadri* and Hamid Mohammadpour, Univ. of Nebraska Med. Center, Dept. of Int. Med., 600 S. 42nd St., Omaha, NE 68198-1210.

The new chelating agents (**1a** and **1b**) are synthesized starting from optically active p-nitro-L-phenylalanine and triflates of ethyl esters of L-lactic and L-phenyl lactic acids.



1a:R=Me; 1b:R=Bz

BioMed. Chem. Lett. **1992**, *2*, 1665

AUTOMATED SYNTHESIS OF FLUOROGENIC PROTEASE SUBSTRATES: DESIGN OF PROBES FOR ALZHEIMER'S DISEASE-ASSOCIATED PROTEASES

Gary T. Wang and Grant A. Krafft*
Structural Biology, Pharmaceutical Discovery, Abbott Laboratories, Abbott Park, Illinois, 60064-3500.

A facile automated solid phase method for the synthesis of internally quenched, fluorogenic protease substrates is described. Two coumpounds, **3** and **4**, were synthesized for studies of proteases related to Alzheimer's Disease using this method.

Ac-Glu-Glu-Glu-Val-Lys-Met-Asp-Ala-Glu-Phe-Lys-Glu-NH_2 (Edans, Dabcyl) **3**

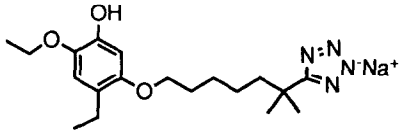
Ac-Glu-Glu-Val-His-His-Gln-Lys-Leu-Val-Phe-Lys-Glu-NH_2 (Edans, Dabcyl) **4**

BioMed. Chem. Lett. **1992**, *2*, 1669

Ortho-Alkoxyphenol Leukotriene B_4 Receptor Antagonists

Michael J. Sofia *, William T. Jackson, David L. Saussy, Jr., Steven A. Silbaugh, Larry L. Froelich, Sandra L. Cockerham and Peter W. Stengel
Lilly Research Labs, Eli Lilly & Co., Indianapolis, IN. 46285

	Receptor Binding Against [^{3}H]LTB_4
Human Neutrophils	4.8 nM (IC_{50})
Guinea Pig Lung Membranes	14.2±2.9 nM (Ki)

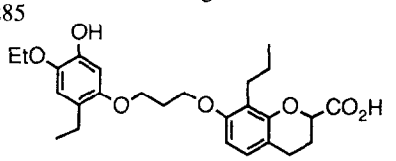


BioMed. Chem. Lett. **1992**, *2*, 1675

Ortho-Alkoxyphenol Leukotriene B_4 Receptor Antagonists: Effect of a Chroman Carboxylic Acid.

Michael J. Sofia *, David L. Saussy, Jr., William T. Jackson, Philip Marder, Steven A. Silbaugh, Larry L. Froelich, Sandra L. Cockerham and Peter W. Stengel
Lilly Research Labs, Eli Lilly & Co., Indianapolis, IN. 46285

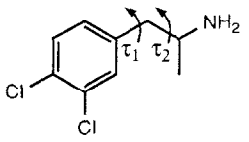
	Receptor Binding Against [^{3}H]LTB$_4$
Human Neutrophils	4.2 nM (IC_{50})
Guinea Pig Lung Membranes	3.51±2.42 nM (Ki)



BioMed. Chem. Lett. **1992**, *2*, 1681

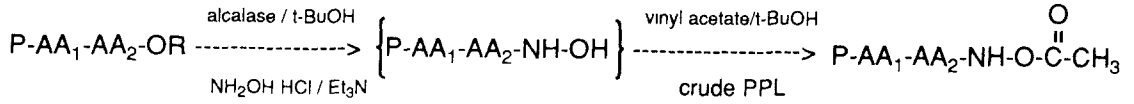
USE OF TRANSFERRED NUCLEAR OVERHAUSER EFFECTS TO DETERMINE THE CONFORMATION OF 1-(3,4-DICHLOROPHENYL)-2-AMINOPROPANE WHEN BOUND TO THE ACTIVE SITE OF PHENYLETHANOLAMINE *N*-METHYLTRANSFERASE (PNMT). *Gary L. Grunewald,* Moorthy S. S. Palanki, and David Vander Velde, Department of Medicinal Chemistry, The University of Kansas, Lawrence, KS 66045, USA*

Transferred two dimensional nuclear Overhauser effect spectroscopy (transferred NOESY) was used to show that the side chain of 1-(3,4-dichlorophenyl)-2-aminopropane (**1**) exists when bound at the active site of PNMT in an extended conformation (τ_2 = 167 - 180°) with the aromatic ring rotated out of the plane of the ethylamine side chain (τ_1 = 29 - 45°)



BioMed. Chem. Lett. **1992**, *2*, 1685

One-pot synthesis of Cathepsin inhibitors: N$^{\alpha}$-protected N-peptidyl-O-acetyl hydroxylamines catalyzed by alcalase followed by lipase in anhydrous t-butanol. S. T. Chen,[1*] S. L. Lin, S. C. Hsiao, and K. T. Wang.[1,2*]
1. Laboratory of Biocatalyst, Institute of Biological Chemistry, Academia Sinica,
2. Department of Chemistry, National Taiwan University.

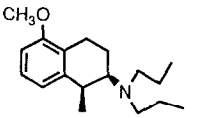


BioMed. Chem. Lett. **1992**, *2*, 1691

AN IMPROVED SYNTHESIS OF THE DOPAMINE AUTORECEPTOR ANTAGONIST (+)-*CIS*-8-METHOXY-1-METHYL-2-(DIPROPYLAMINO)TETRALIN (AJ-76).

Arthur G. Romero* and Jeffrey A. Leiby
Medicinal Chemistry Research
The Upjohn Company
Kalamazoo, MI 49001, USA

(+)-AJ-76



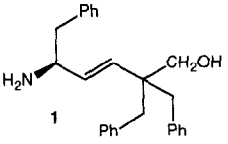
The efficient stereocontrolled synthesis of (+)-AJ-76 in 8 % yield is described.

Novel Peptidomimetics: Inhibitors of Substance P Endopeptidase

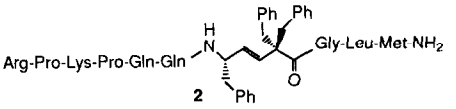
BioMed. Chem. Lett. **1992**, *2*, 1693

Annika Jenmalm,[a] Kristina Luthman,[a,*] Gunnar Lindeberg,[b] Fred Nyberg,[c] Lars Terenius,[d] and Uli Hacksell[a]
[a]Dept.of Organic Pharmaceutical Chemistry, Box 574, [b] Dept. of Immunology, Box 582, [c]Dept. of Pharmacology, Box 591, Uppsala Biomedical Center, Uppsala University, S-751 23 Uppsala, Sweden, [d]Dept. of Drug Dependence Research, Karolinska Institute, Box 60500, S-104 01 Stockholm, Sweden.

The synthesis of the novel *bis*-phenylalanine mimetic **1** and its incorporation into substance P giving **2** are described. Compounds **1** and **2** were able to inhibit a human substance P endopeptidase but lacked appreciable affinity for the rat NK_1-receptor.



1



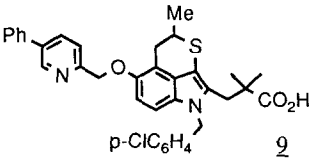
2

Development of L-689,065 - The Prototype of a New Class of Potent 5-Lipoxygenase Inhibitors.

BioMed. Chem. Lett. **1992**, *2*, 1699

J.H.Hutchinson, P.Prasit, L.Y.Choo, D.Riendeau, S.Charleson, J.F.Evans, H.Piechuta and R.G.Ball.
Merck Frosst Centre for Therapeutic Research, P.O. Box 1005, Pointe Claire-Dorval, Quebec, CANADA H9R 4P8

The development of a new class of direct 5-LO inhibitors is described. The prototype of this class is L-689,065 (9) and it contains the novel thiopyranoindole ring system in conjunction with a phenylpyridine substituent. The enzyme 5-LO is able to discriminate between the individual enantiomers, preferentially binding the (-) enantiomer.



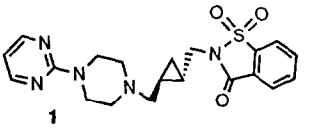
9

SYNTHESIS OF METABOLICALLY STABLE ARYLPIPERAZINE 5-HT_{1A} RECEPTOR AGONISTS

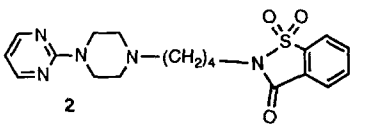
BioMed. Chem. Lett. **1992**, *2*, 1703

Arthur G. Romero*[1], William H. Darlington[1], Montford F. Piercey[2], Robert A. Lahti[2]
[1]Medicinal Chemistry Research, [2]CNS Disease Research
The Upjohn Company
Kalamazoo, MI 49001, USA

A cyclopropanated analog (**1**) of the 5-HT1A partial agonist ipsapirone (**2**) was synthesized and found to possess a longer duration of action in the *in vivo* hypothermia model, by both s.c. and oral dosing.



1

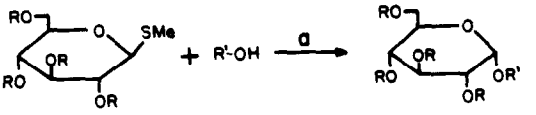


2

METHYL 2,3,4,6-TETRA-O-(4-METHOXYBENZYL)-1-THIO-β-D-GLUCOPYRANOSIDE - A NOVEL REAGENT FOR α-GLYCOSYLATION TOWARDS NITROPHENYL OR BENZYL GLYCOSIDES

BioMed. Chem. Lett. **1992**, *2*, 1707

R. K. Jain and K. L. Matta, Department of Gynecologic Oncology, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, NY 14263



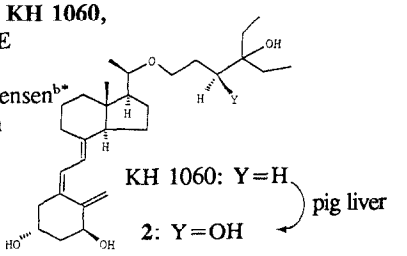
R = 4-MeOBn ; R' = Acceptor; a = $CuBr_2$-Bu_4NBr

BioMed. Chem. Lett. **1992**, *2*, 1713

IDENTIFICATION AND SYNTHESIS OF A METABOLITE OF KH 1060, A NEW POTENT 1α,25-DIHYDROXYVITAMIN D, ANALOGUE

Niels Rastrup Andersen[a], Frants A. Buchwald[b] and Gunnar Grue-Sørensen[b]*
[a] Department of Spectroscopy [b] Department of Chemical Research
Leo Pharmaceutical Products, DK-2750 Ballerup, Denmark

Compound **2** is identified by spectroscopy and chemical synthesis starting from *(S)*-malic acid.

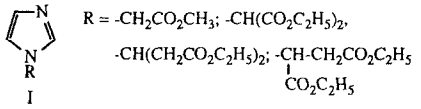


BioMed. Chem. Lett. **1992**, *2*, 1717

IMIDAZOL-1-YLALKANOATE ESTERS AND THEIR CORRESPONDING ACIDS. A NOVEL SERIES OF EXTRINSIC ^{1}H NMR PROBES FOR INTRACELLULAR pH

M. S. Gil, F. Cruz,# S. Cerdán# and P. Ballesteros*
Departamento de Química Orgánica y Biología, Facultad de Ciencias, UNED, 28040-Madrid, Spain and #Instituto de Investigaciones Biomédicas, CSIC, Arturo Duperier 4, 28029-Madrid, Spain

Imidazol-1-ylacetate, malonate, 3-glutarate and 2-succinate esters I, and the corresponding acids are described as a novel series of extrinsic probes for intracellular pH (pH_i) determination by ^{1}H NMR

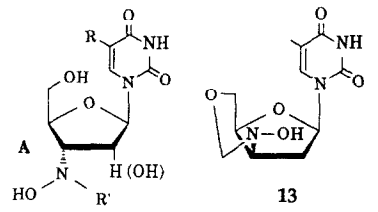


BioMed. Chem. Lett. **1992**, *2*, 1723

SYNTHESIS AND ANTI-HIV ACTIVITY OF 3'-DEOXY-3'-(*N*-HYDROXYAMINO) ANALOGUES OF NUCLEOSIDES

Jean M. J. Tronchet,* Martina Zsély, Karel Capek,+ and Fabienne de Villedon de Naide
Institute of Pharmaceutical Chemistry, University of Geneva, Sciences II, CH-1211 Geneva 4 (Switzerland)

A series of title compounds of the general structure **A** (R = H, Me, Br or I, R' = H, Me, $ArCH_2$, $C_{17}H_{33}CO$) have been prepared either by modification of a preexisting nucleoside or by nucleosidation of a modified ribose derivative. One of them (**13**) is active against HIV virus.

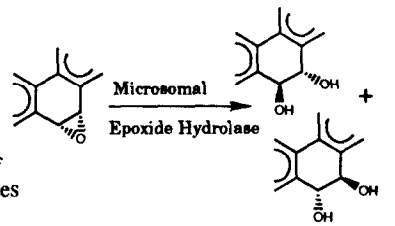


BioMed. Chem. Lett. **1992**, *2*, 1729

Enantiomeric Composition of Trans-Dihydrodiols Formed from Meso-K-Region Arene Oxides by Microsomal Epoxide Hydrolase

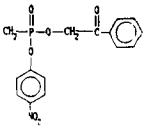
Martin T. Haber, Nashed T. Nashed, and Donald M. Jerina
Laboratory of Bioorganic Chemistry, NIDDK,
National Institutes of Health, Bethesda, MD 20892.

Absolute configurations for the enantiomers of trans-4,5-dihydroxy-4,5-dihydrobenzo[e]pyrene were assigned. Enantiomeric compositions of the products of enzyme-catalyzed hydrolysis of meso-K-region arene oxides of benzo[e]pyrene, pyrene, and phenanthrene were determined.



BioMed. Chem. Lett. **1992**, *2*, 1735

REVERSIBLE MODULATION OF SERINE PROTEASE ACTIVITY BY PHOSPHONATE ESTERS



Ildiko M. Kovach[a]* and Linda McKay[b]

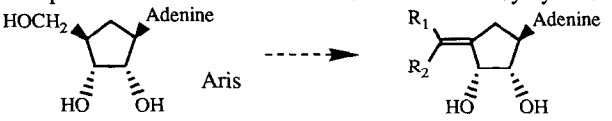
[a]The Catholic University of America, Department of Chemistry, Washington D.C. 20064
[b]The University of Kansas, Center for Biomedical Research, 2099 Constant Avenue Lawrence Kansas 66046

Abstract: Temporary modification of serine hydrolase activity with 4-nitrophenyl (4-H and 4-NO_2) phenacyl methyl-phosphonates occurs with self-catalyzed intramolecular reactivation of chymotrypsin, trypsin, thrombin and plasmin.

BioMed. Chem. Lett. **1992**, *2*, 1741

Synthesis and Evaluation of 4',5'-Dehydro-5'-Fluoroaristeromycins as S-Adenosyl-L-Homocysteine(AdoHcy) Hydrolase Inhibitors

Siming Liu, Michael S. Wolfe, Chongsheng Yuan, Syed Mashhood Ali and Ronald T. Borchardt*, Departments of Medicinal Chemistry and Biochemistry, The University of Kansas, Lawrence, Kansas 66045. 4',5'-Dehydro-5'-fluoro analogs of carbocyclic nucleoside aristeromycin were synthesized and shown to be potent inhibitors of recombinant rat liver AdoHcy hydrolase.



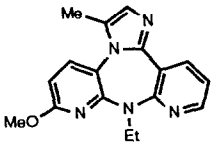
3 R_1 = H, R_2 = F (E)
4 R_1 = F, R_2 = H (Z)

BioMed. Chem. Lett. **1992**, *2*, 1745

IMIDAZO[2',3':6,5]DIPYRIDO[3,2-b:2',3'-e]-1,4-DIAZEPINES: NON-NUCLEOSIDE HIV-1 REVERSE TRANSCRIPTASE INHIBITORS WITH GREATER ENZYME AFFINITY THAN NEVIRAPINE

Nicholas K. Terrett,* Dejan Bojanic, James R. Merson, and Peter T. Stephenson
Pfizer Central Research, Sandwich, Kent, CT13 9NJ

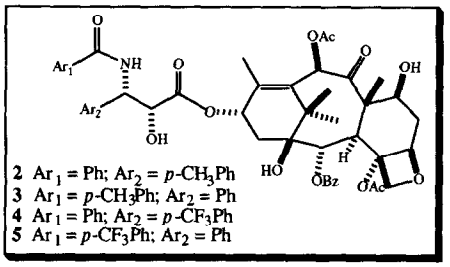
Abstract: The chemistry and SAR of a new series of imidazo[2',3':6,5]dipyrido-[3,2-b:2',3'-e]-1,4-diazepine HIV-1 RTase inhibitors is described.



BioMed. Chem. Lett. **1992**, *2*, 1751

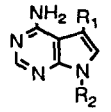
SEMISYNTHESIS AND BIOLOGICAL ACTIVITY OF TAXOL ANALOGUES: BACCATIN III 13-(*N*-BENZOYL-(2'*R*,3'*S*)-3'-(*p*-TOLYL)ISOSERINATE), BACCATIN III 13-(*N*-(*p*-TOLUOYL)-(2'*R*,3'*S*)-3'-PHENYLISOSERINATE), BACCATIN III 13-(*N*-BENZOYL-(2'*R*,3'*S*)-3'-(*p*-TRIFLUOROMETHYLPHENYL)-ISOSERINATE), AND BACCATIN III 13-(*N*-(*p*-TRIFLUORO-METHYLBENZOYL)-(2'*R*,3'*S*)-3'-PHENYLISOSERINATE)

Gunda I. Georg* and Zacharia S. Cheruvallath*
Richard H. Himes≠ and Magdalena R. Mejillano≠
Department of Medicinal Chemistry* and Department of Biochemistry≠
University of Kansas, Lawrence, KS 66045



2 Ar_1 = Ph; Ar_2 = *p*-CH_3Ph
3 Ar_1 = *p*-CH_3Ph; Ar_2 = Ph
4 Ar_1 = Ph; Ar_2 = *p*-CF_3Ph
5 Ar_1 = *p*-CF_3Ph; Ar_2 = Ph

BioMed. Chem. Lett. **1992**, *2*, 1755



R_1= CN, $CONH_2$, $CSNH_2$
R_2= Allyl, Propyl, Methyl

Design, Synthesis and Activity Against Human Cytomegalovirus of Non-Phosphorylatable Analogs of Toyocamycin, Sangivamycin and Thiosangivamycin

Thomas E. Renau[1], Mary S. Ludwig[2], John C. Drach[1,2] and Leroy B. Townsend*[1,3]. [1]Interdepartmental Program in Medicinal Chemistry, College of Pharmacy; [2]Department of Biologic and Material Sciences, School of Dentistry; [3]Department of Chemistry, College of Literature, Arts and Sciences, University of Michigan, Ann Arbor, Michigan 48109-1065.

Abstract: A number of 7-alkyl 4-aminopyrrolo[2,3-d]pyrimidine derivatives related to toyocamycin, sangivamycin and thiosangivamycin have been prepared and tested for their activity against human cytomegalovirus (HCMV).

BioMed. Chem. Lett. **1992**, *2*, 1761

STABILIZATION OF A PROSTAGLANDIN TERTIARY ALLYLIC ALCOHOL SYSTEM BY FLUORINE: SYNTHESIS, ACID STABILITY STUDIES AND PHARMACOLOGY OF A 16-FLUOROMETHYL ANALOG OF SC-46275, P.W. Collins*, R.L. Shone, A.F. Gasiecki, S.W. Kramer, W.E. Perkins and R.G. Bianchi. *Departments of Chemistry and Immunoinflammatory Diseases Research, G.D. Searle & Co., Skokie, Illinois 60067, USA.*

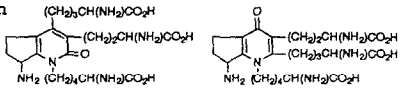
Abstract: The synthesis of a 16-fluoromethyl analog of SC-46275, a potent, long-acting and selective analog of enisoprost, is described. Introduction of a fluorine atom to the C-16 methyl group of SC-46275 conveys a remarkable increase in stability toward acid induced epimerization, dehydration and allylic rearrangement while having minimal influence on the pharmacological profile.

BioMed. Chem. Lett **1992**, *2*, 1767

TWO FLUORESCENT CROSSLINKING AMINO ACIDS HAVING N-SUBSTITUTED DIHYDROOXOPYRIDINE SKELETON ISOLATED FROM BOVINE ELASTIN

Kyozo Suyama* and Fumihiko Nakamura
Laboratory of Molecular Technology of Animal Products,
Faculty of Agriculture, Tohoku University, Sendai 981, Japan

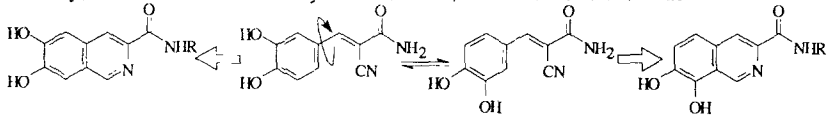
Two new fluorescent crosslinking amino acids named oxodesmosine and isooxodesmosine were isolated from bovine aorta elastin. These amino acids have unique structure, both N-substituted dihydrooxopyridine skeletons.



BioMed. Chem. Lett. **1992**, *2*, 1771

ARYLAMIDES OF HYDROXYLATED ISOQUINOLINES AS PROTEIN-TYROSINE KINASE INHIBITORS

Terrence R. Burke, Jr.,*,† Harry Ford,† Nir Osherov,‡ Alexander Levitzki,‡ Irena Stefanova,¶ Ivan D. Horak¶ and Victor E. Marquez,† †Laboratory of Medicinal Chemistry, Developmental Therapeutics Program, Division of Cancer Treatment, Bldg. 37, Rm 5C06, and ¶Metabolism Branch, Division of Cancer Biology, Diagnosis and Centers, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, ‡Department of Biological Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel



SUBSTITUTED PIPERIDINE-2-ONE BIPHENYLTETRAZOLES AS ANGIOTENSIN II ANTAGONISTS

W. V. Murray*, P. Lalan, A. Gill, M. Addo, J. Lewis, D. Lee, R. Rampulla, J. Hsi, M. P. Wachter, D. Underwood
The R. W. Johnson Pharmaceutical Research Institute,
P. O. Box 300, Route 202, Raritan, New Jersey 08869

A novel series of piperidine-2-ones have been identified as antagonists of angiotensin II. These compounds are potent in bovie adrenal cortex binding assays with IC_{50}'s as low as 20nM. They also show pA_2's of up to 9 in rabbit aortic ring assays. A number of these compounds are also orally active as antihypertensives in spontaneously hypertensive rat preparations.

BioMed. Chem. Lett. **1992**, 2, 1775