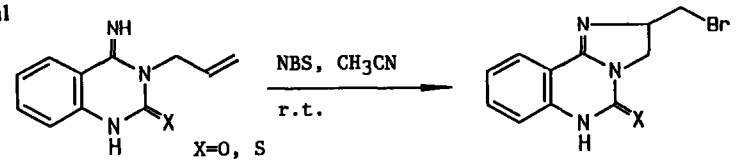
GRAPHICAL ABSTRACTS

BioMed. Chem. Lett. **1991**, *1*, 571

STUDIES ON QUINAZOLINONES. 3: [1] NOVEL AND EFFICIENT ROUTE TO THE SYNTHESIS OF CONFORMATIONALLY RESTRICTED ANALOGUES OF KETANSERIN AND SGB-1534 AS ANTIHYPERTENSIVE AGENTS

Ji-Wang Chern*, Chia-Yang Shiau and Guan-Yu Lu

Institute of Pharmacy and Medical Laboratories, National Defense Medical Center, P. O. Box 90048-512, Taipei, Taiwan, Republic of China (100)



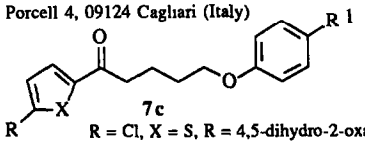
BioMed. Chem. Lett. **1991**, *1*, 575

SYNTHESIS OF NEW DISOXARIL ANALOGUES WITH POTENT AND SELECTIVE ANTI-HRV-14 ACTIVITY

Massa S.[a], Artico M.[a], Mai A.[a], Ragno R.[a], Corelli F.[b], Pani A.[c], Marongiu M.E.[c], Tramontano E.[c], La Colla P.[c]

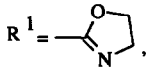
[a]Dipartimento di Studi Farmaceutici, Università "La Sapienza", P.le A. Moro 5, 00185 Roma (Italy)
[b]Dipartimento Farmaco-Chimico-Tecnologico, Università di Siena, Banchi di Sotto 55, 53100 Siena (Italy)
[c]Dipartimento di Biologia Sperimentale, Università di Cagliari, v. Porcell 4, 09124 Cagliari (Italy)

New analogues of disoxaril have been prepared and tested against DNA and RNA viruses. Derivative **7c** showed low cytotoxicity and significant selectivity index (ratio MTL/MIC) against HRV-14.



7c
R = Cl, X = S, R = 4,5-dihydro-2-oxazolyl

R = H, Cl, CH_3
X = S, NH, O



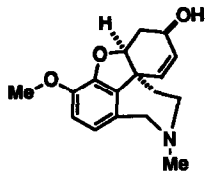
$CO_2C_2H_5$,
CO_2H

BioMed. Chem. Lett. **1991**, *1*, 579

SYNTHESIS AND BIOLOGICAL ACTIVITY OF GALANTHAMINE DERIVATIVES AS ACETYLCHOLINESTERASE (AChE) INHIBITORS

So-Yeop Han, Scott C. Mayer, Edwin J. Schweiger, Bonnie M. Davis, and Madeleine M. Joullié*
Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104-6323

The syntheses of several ester and carbamate derivatives of galanthamine are described. These compounds are potential therapeutic agents in the treatment of Alzheimer's disease (AD). The inhibition of cortical acetylcholinesterase (AChE) by these drug candidates with different side chains was investigated. Side chain length as well as branching affected the AChE inhibitory activity. Esters were generally less effective than carbamates.

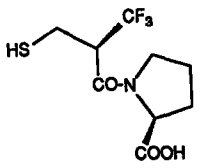


BioMed. Chem. Lett. **1991**, *1*, 581

A NEW POTENT INHIBITOR FOR ANGIOTENSIN CONVERTING ENZYME: *(R,S)*-CAPTOPRIL-F_3

Iwao Ojima* and Fabian A. Jameison
Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY 11794-3400

Synthesis and enzyme inhibitory activity of a new potent ACE inhibitor, (R,S)-captopril-f_3.



BioMed. Chem. Lett. **1991**, *1*, 585

NOVEL *IN VITRO* AND *IN VIVO* INHIBITORS OF PROLYL ENDOPEPTIDASE

Alice V Bakker, June Daffeh, Stanley Jung, Lawrence A Vincent, Arthur A Nagel, Robin W Spencer, Fredric J Vinick, and W. Stephen Faraci*

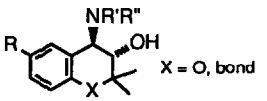
Central Research Division, Pfizer Inc , Groton, CT 06340

Abstract. Inhibition of prolyl endopeptidase by Z-cyclohexyl prolinal and Z-indolinyl prolinal occurs with slow, tight binding inhibition and K_i values of 2 - 3 nM *In vivo* enzyme inhibition is also observed with a half time for recovery of enzyme activity of 3 - 4 h

BioMed. Chem. Lett. **1991**, *1*, 591

ANTIHYPERTENSIVE BENZOPYRAN-RELATED POTASSIUM CHANNEL ACTIVATORS: A ROLE FOR LIPOPHILICITY

Richard M Soll,* ~ Dominick A Quagliato,~ David D Deininger,~ Paul J Dollings,~ Betsy L Joslyn,~ Terrence M Dolak,~ Sung J Lee,~ Chris Bohan,~ Alexandra Wojdan," Mary Ellen Monn," and George Oshiro"
~Department of Medicinal Chemistry and "Department of Experimental Therapeutics, Wyeth-Ayerst Research, CN 8000, Princeton, NJ 08543



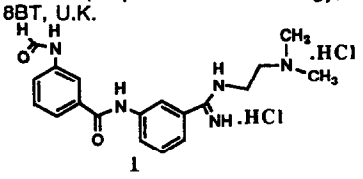
A series of benzopyran-related potassium channel activators were prepared and evaluated in the spontaneously hypertensive rat. The duration of the blood pressure lowering effect at the calculated ED_{30} dose was found to be related to the lipophilicity of the agent and was independent of the potency

BioMed. Chem. Lett. **1991**, *1*, 595

SYNTHESIS AND DNA BINDING PROPERTIES OF AN AMIDINE-LINKED AND PHENYL-CONTAINING ANALOGUE OF DISTAMYCIN A

Moses Lee,* Lori A. White, Jennifer A. Nobles, Stephen M. Forrow† and John A. Hartley†
Department of Chemistry, Furman University, Greenville, SC 29613, and †Department of Oncology, University College and Middlesex School of Medicine, London, W1P 8BT, U.K.

A phenyl-containing and amidine-linked analogue 1 of distamycin A has improved water solubility while retaining the minor groove and AT sequence binding selectivity to DNA.



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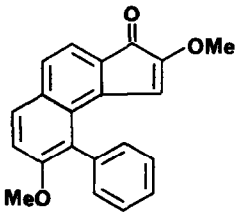
BioMed. Chem. Lett. **1991**, *1*, 599

A BIOACTIVE BENZOINDENONE FROM *EICHHORNIA CRASSIPES* SOLM

Marina Della Greca, Rosa Lanzetta, Lorenzo Mangoni, Pietro Monaco, Lucio Previtera*
Dipartimento di Chimica Organica e Biologica, Università Federico II, Via Mezzocannone 16, I-80134 Napoli, Italy



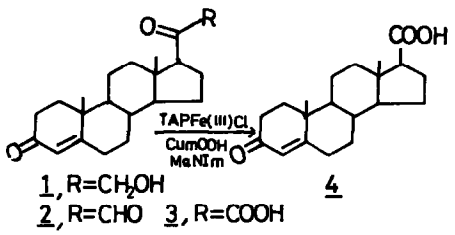
The structure of the benzoindenone **1**, isolated from *E. crassipes*, was determined mainly by spectroscopic methods. The compound was found active against the fungus *Candida albicans*.

BioMed. Chem. Lett. **1991**, *1*, 601

BIOMIMETIC OXIDATION OF 21-HYDROXY, 21-FORMYL AND 21-CARBOXYLIC PREGN-4-EN-3, 20-DIONE WITH CHEMICAL CYTOCHROME P450 MODEL SYSTEMS

S.M.S. Chauhan* and P.C. Ray
Department of Chemistry, University of Delhi, Delhi - 110 007, INDIA

The oxidation of 1, 2 and 3 with the electron withdrawing 5,10,15,20-tetraarylporphyrinate/N-Methylimidazole/CumOOH system gives 4 in 60-84% yields.

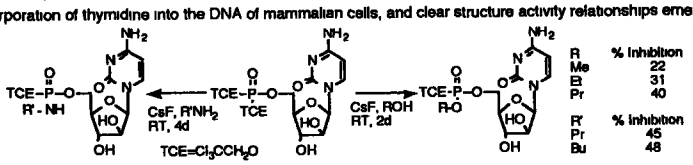


BioMed. Chem. Lett. **1991**, *1*, 607

TRANS-ESTERIFICATION REACTIONS YIELD NOVEL MASKED PHOSPHATE DERIVATIVES OF THE ANTI-CANCER AGENT araC

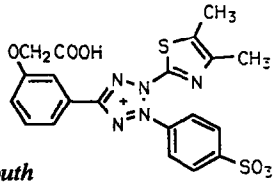
Christopher McGuigan*, B Colin N.M. Jones, and Patrick A Riley†
Department of Chemistry, University of Southampton, Southampton, SO9 5NH, UK † Department of Chemical Pathology, University College and Middlesex School of Medicine, Windeyer Building, Cleveland Street, London, W1P 6DB, UK

Phosphate and phosphoramidate derivatives of the anti-leukemic agent araC have been prepared and tested for their ability to inhibit the incorporation of thymidine into the DNA of mammalian cells, and clear structure activity relationships emerged



BioMed. Chem. Lett. **1991**, *1*, 611

5-(3-CARBOXYMETHOXYPHENYL)-2-(4,5-DIMETHYLTHIAZOLYL) -3-(4-SULFOPHENYL)TETRAZOLIUM, INNER SALT (MTS) AND RELATED ANALOGS OF 3-(4,5-DIMETHYLTHIAZOLYL)-2,5-DIPHENYLTETRAZOLIUM BROMIDE (MTT) REDUCING TO PURPLE WATER-SOLUBLE FORMAZANS AS CELL-VIABILITY INDICATORS



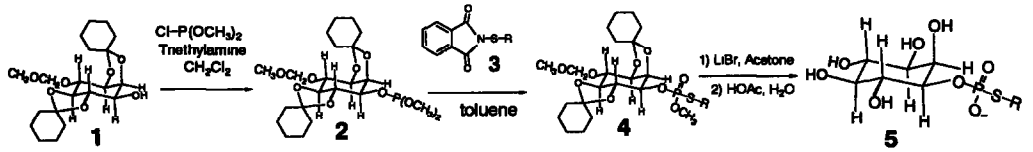
John A. Barltrop, Terence C. Owen*, *Department of Chemistry, University of South Florida, Tampa, Florida 33620;* Ann H. Cory, Joseph G. Cory, *Department of Biochemistry, East Carolina University School of Medicine, Greenville, North Carolina 27858*

Abstract. Analogs of MTT have been synthesized and evaluated as cell-viability indicators.

BioMed. Chem. Lett. **1991**, *1*, 615

A THIOPHOSPHATE SUBSTRATE FOR A CONTINUOUS SPECTROPHOTOMETRIC ASSAY OF PHOSPHATIDYL-INOSITOL-SPECIFIC PHOSPHOLIPASE C: HEXADECYLTHIOPHOSPHORYL-1-*myo*-INOSITOL

Elizabeth K. Hendrickson, Jeannette L. Johnson, and H. Stewart Hendrickson*
Department of Chemistry, St. Olaf College, Northfield, MN 55057-1098

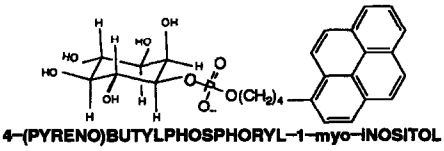


BioMed. Chem. Lett. **1991**, *1*, 619

A FLUORESCENT SUBSTRATE FOR THE ASSAY OF PHOSPHATIDYLINOSITOL-SPECIFIC PHOSPHOLIPASE C: 4-(1-PYRENO)BUTYLPHOSPHORYL-1-*myo*-INOSITOL

Elizabeth K. Hendrickson, Jeannette L. Johnson, and H. Stewart Hendrickson*
Department of Chemistry, St. Olaf College, Northfield, MN 55057-1098

A pyrene-labeled analog of phosphatidylinositol was synthesized as a substrate for a sensitive assay of phosphatidylinositol-specific phospholipase C from *Bacillus cereus*. The substrate and product (pyrenebutanol) were separated by HPLC and quantified by fluorescence detection.



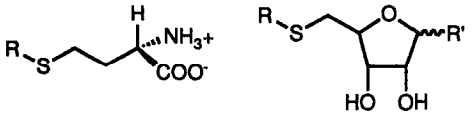
4-(PYRENO)BUTYLPHOSPHORYL-1-myo-INOSITOL

BioMed. Chem. Lett. **1991**, *1*, 623

Synthesis and Biological Activity of Fluorinated Intermediates of the Methionine Salvage Pathway

Michael E. Houston Jr ,[a] David L. Vander Jagt,[b] and John F Honek[a*]
[a]Department of Chemistry, (GWC)[2],University of Waterloo, Waterloo, Ontario, Canada, N2L 3G1
[b]Department of Biochemistry, University of New Mexico, School of Medicine, Albuquerque, New Mexico, USA 87131

The synthesis and antimalarial, anticancer and anti-HIV-1 activities of fluorinated analogs of the methionine salvage pathway are reported



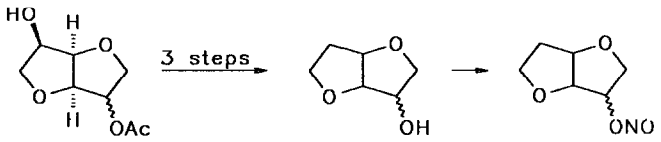
R = fluoroalkyl, R' = adenine, OH

BioMed. Chem. Lett. **1991**, *1*, 629

MONODEOXY-1,4:3,6-DIANHYDROHEXITOL NITRATES

Peter Stoss* and Siegfried Erhardt

Chemical R & D, Heinrich Mack Nachf.,
Chem. - Pharm. Fabrik,
D-7918 Illertissen, Germany

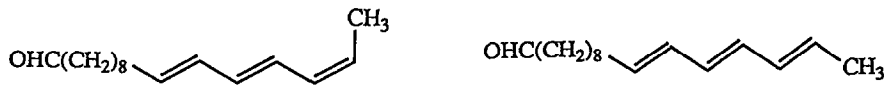


Both the endo- and exo-configurated monodeoxy-1,4:3,6-dianhydrohexitol nitrates have been prepared. Attempts to generate an unsaturated nitrate ester resulted in a DBN alkylation produkt.

BioMed. Chem. Lett. **1991**, *1*, 635

NEW STEREOSPECIFIC SYNTHESES OF (E,E,Z)- AND (E,E,E)-10,12,14-HEXADECATRIENAL SEX PHEROMONAL COMPONENTS OF MANDUCTA SEXTA

Frédérique Tellier: INRA, Laboratoire des Médiateurs Chimiques, Domaine de Brouessy, 78114, Magny-les-Hameaux. (France)



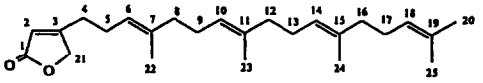
Trienic compounds are obtained by two sequential palladium-catalyzed cross-coupling reactions between adequate organometallic reagents and (E)-1,2-dibromoethylene.

BioMed. Chem. Lett. **1991**, *1*, 639

LINEAR SESTERTERPENES FROM THE CARIBBEAN SPONGE *THORECTA HORRIDUS* WITH INFLAMMATORY ACTIVITY

Ernesto Fattorusso*, Virginia Lanzotti[1], Silvana Magno, Luciano Mayol, *Dipartimento di Chimica delle Sostanze Naturali, Via D. Montesano, 49, I-80131, Napoli (Italy)*

Massimo Di Rosa and Armando Ialenti, *Dip.to di Farmacologia Sperimentale, Via D. Montesano 49, I-80131 Napoli (Italy)*



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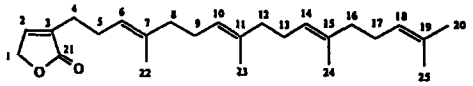


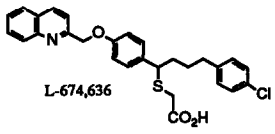
2

Structures of two new linear sesterterpenes 1 and 2 from the sponge *Thorecta horridus*, determined through HREIMS, 1D and 2D NMR experiments, are reported. Compound 1 exhibits inflammatory activity.

BioMed. Chem. Lett. **1991**, *1*, 645

A New Class of Leukotriene Biosynthesis Inhibitors: The Development of ((4- (4 - Chlorophenyl)-1- (4- (2-quinolinylmethoxy)phenyl) butyl)thio)acetic acid, L-674,636,

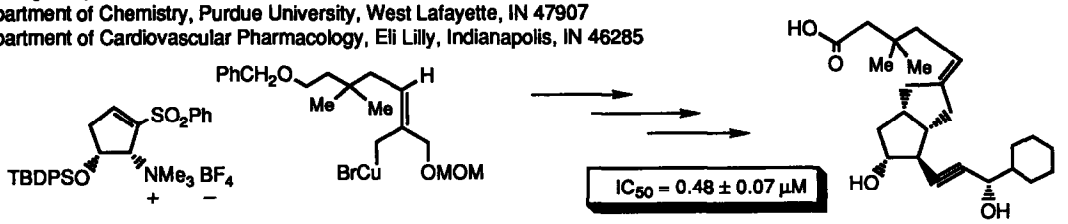
P. Prasit *, M. Belley, J. F. Evans, J.Y. Gauthier, C. Léveillé, C. S. McFarlane, E. MacIntyre °°, L. Peterson °°, H. Piechuta, M. Thérien, R. N. Young and R. Zamboni. *Merck Frosst Centre for Therapeutic Research, P.O. Box 1005, Pointe Claire-Dorval, Québec H9R 4P8, CANADA.* °°*Merck and Co. Inc., P.O. Box 2000, Rahway, NJ 07065, USA.*



BioMed. Chem. Lett. **1991**, *1*, 649

TRIPLY-CONVERGENT SYNTHESIS OF A HOMOCHIRAL 3,3-DIMETHYL,15-CYCLOHEXYL PROSTACYCLIN ANALOG

R.A. Berglund†, T.F. Braish†, J. A. Jakubowski§, P.L. Fuchs*,†
†Department of Chemistry, Purdue University, West Lafayette, IN 47907
§Department of Cardiovascular Pharmacology, Eli Lilly, Indianapolis, IN 46285

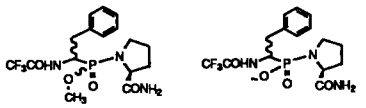


BioMed. Chem. Lett. **1991**, *1*, 653

PHOSPHONAMIDATES AND PHOSPHONAMIDATE ESTERS AS HIV-1 PROTEASE INHIBITORS:

Donald A. McLeod†, Ross I Brinkworth‡, Jon A Ashley†, Kim D. Janda†‡, and Peter Wirsching†, (†The Scripps Research Institute, Department of Molecular Biology & Chemistry, 10666 North Torrey Pines Road, La Jolla, California 92033 & ‡The Centre for Drug Design & Development, The University of Queensland, Qld 4072, Australia)

Abstract - Simple dipeptides incorporating phosphonamidate and phosphonamidate ester isosteres for the scissile peptide bond are modest inhibitors of the HIV-1 protease. Their synthesis and inhibition studies are described.



6 IC_{50} = 102 uM 4 IC_{50} = 121 uM