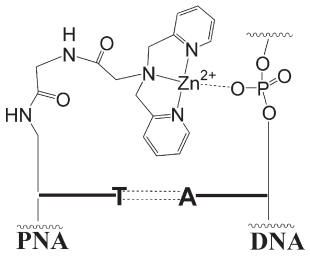
Bioorg. Med. Chem. Lett. 13 (2003) 1399

Peptide Nucleic Acid–Metal Complex Conjugates: Facile Modulation of PNA–DNA Duplex Stability

Andriy Mokhir, Roman Stiebing and Roland Kraemer*

Anorganisch-Chemisches Institut, Universität Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany

Stability of duplexes of bis-picolylamine–PNA conjugates and DNA was found to be modulated by equimolar concentrations of bioavailable metal ions: Ni^{2+}, $Zn^{2+} > Cu^{2+}$.



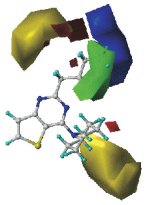
Bioorg. Med. Chem. Lett. 13 (2003) 1403

3D-QSAR Studies on Thieno[3,2-*d*]pyrimidines as Phosphodiesterase IV Inhibitors

Asit K. Chakraborti,* B. Gopalakrishnan, M. Elizabeth Sobhia and Alpeshkumar Malde

Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Sector-67, S.A.S. Nagar-160 062, Punjab, India

The CoMFA and CoMSIA studies of thieno[3,2-*d*]pyrimidines is reported.



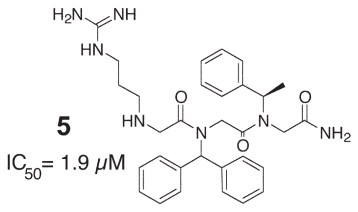
Bioorg. Med. Chem. Lett. 13 (2003) 1409

Peptoid Mimics of Agouti Related Protein

Darren A. Thompson,[a,*] Biao-Xin Chai,[b] Hilary L. E. Rood,[a] Michael A. Siani,[c] Nicholai R. Douglas,[a] Ira Gantz[b] and Glenn L. Millhauser[a]

[a]*Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA*
[b]*Department of Surgery, University of Michigan Medical Center, 6504 MSRB I 1150 W. Medical Center Drive, Ann Arbor, MI 48109-0682, USA*
[c]*Department of Bioinformatics Affymetrix - Berkeley, 6550 Vallejo Street, Emeryville, CA 94608, USA*

A peptoid antagonist of the human Melanocortin 4 Receptor **5** ($IC_{50} = 1.9$ μM) is reported.

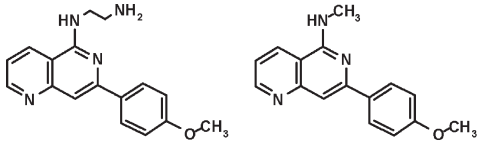


Bioorg. Med. Chem. Lett. 13 (2003) 1415

Discovery and SAR of Novel [1,6]Naphthyridines as Potent Inhibitors of Spleen Tyrosine Kinase (SYK)

Charles L. Cywin,[a,*] Bao-Ping Zhao,[b] Daniel W. McNeil,[a] Matt Hrapchak,[a] Anthony S. Prokopowicz, III,[a] Daniel R. Goldberg,[a] Tina M. Morwick,[a] Amy Gao,[a] Scott Jakes,[a] Mohammed Kashem,[a] Ronald L. Magolda,[a] Richard M. Soll,[b] Mark R. Player,[b] Mark A. Bobko,[b] James Rinker,[b] Renee L. DesJarlais[b] and Michael P. Winters[b]

[a]*Boehringer Ingelheim Pharmaceuticals, Inc., 900 Ridgebury Road, Ridgefield, CT 06801-0368, USA*
[b]*3-Dimensional Pharmaeuticals, Inc., 665 Stockton Drive, Suite 104, Exton, PA 19341, USA*



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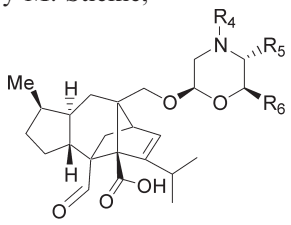
Bioorg. Med. Chem. Lett. 13 (2003) 1419

Identification of a Broad-Spectrum Azasordarin with Improved Pharmacokinetic Properties

Michael H. Serrano-Wu,[a,*] Denis R. St. Laurent,[a] Tina M. Carroll,[a] Marco Dodier,[b] Qi Gao,[a] Patrice Gill,[b] Claude Quesnelle,[b] Anne Marinier,[b] Charles E. Mazzucco,[a] Alicia Regueiro-Ren,[a] Terry M. Stickle,[a] Dedong Wu,[a] Hyekyung Yang,[a] Zheng Yang,[a] Ming Zheng,[a] Mary E. Zoeckler,[a] Dolatrai M. Vyas[a] and Balu N. Balasubramanian[a]

[a]*Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*
[b]*Bristol-Myers Squibb Pharmaceutical Research Institute, 100, boul. de l'Industrie, Candiac, Québec, Canada J5R 1J1*

The synthesis and antifungal activity of novel azasordarin derivatives are described.

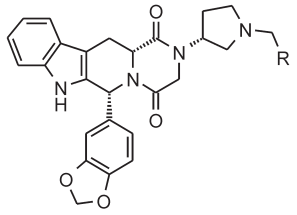


Bioorg. Med. Chem. Lett. 13 (2003) 1425

Design, Synthesis and Biological Activity of β-Carboline-Based Type-5 Phosphodiesterase Inhibitors

Graham N. Maw,* Charlotte M. N. Allerton, Eugene Gbekor and William A. Million

Department of Discovery Chemistry, Pfizer Global Research and Development, Sandwich Laboratories (IPC351), Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK

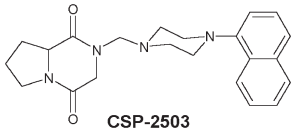


Bioorg. Med. Chem. Lett. 13 (2003) 1429

Design and Synthesis of *S*-(−)-2-[4-(napht-1-yl)piperazin-1-yl]methyl]-1,4-dioxoperhydropyrrolo[1,2-*a*]pyrazine (CSP-2503) Using Computational Simulation. A 5-HT_{1A} Receptor Agonist

María L. López-Rodríguez,[a,*] Mª José Morcillo,[b] Esther Fernández,[a] Bellinda Benhamú,[a] Ignacio Tejada,[a] David Ayala,[a] Alma Viso,[a] Mireia Olivella,[c] Leonardo Pardo,[c] Mercedes Delgado,[d] Jorge Manzanares[d] and José A. Fuentes[d]

[a]*Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense, E-28040 Madrid, Spain*
[b]*Sección de Química, Facultad de Ciencias, Universidad Nacional de Educación a Distancia, E-28040 Madrid, Spain*
[c]*Unitat Bioestadística, Institut de Neurociències, Universitat Autònoma, E-08913 Cerdanyola del Vallès, Barcelona, Spain*
[d]*Unidad de Cartografía Cerebral, Instituto Pluridisciplinar, Universidad Complutense, E-28040 Madrid, Spain*



Bioorg. Med. Chem. Lett. 13 (2003) 1433

Leporin B: A Novel Hexokinase II Gene Inducing Agent from an Unidentified Fungus

Chaowei Zhang, Liang Jin, Belinda Mondie, Scott S. Mitchell,* Arlindo L. Castelhano, Weizhong Cai and Nils Bergenhem

OSI Pharmaceuticals Inc., 1 Bioscience Park Drive, Farmingdale, NY 11735, USA

The isolation, structural characterization, and biological activity of leporin B, a novel hexokinase II gene inducing agent, is described.

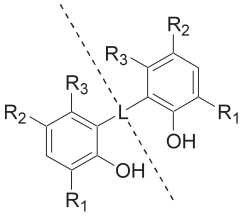
Bioorg. Med. Chem. Lett. 13 (2003) 1437

Novel Openers of Ca^{2+}-Dependent Large-Conductance Potassium Channels: Symmetrical Pharmacophore and Electrophysiological Evaluation of Bisphenols

Yi Li,[a,*] Graham Johnson,[b] Jeffrey L. Romine,[b] Nicholas A. Meanwell,[b] Scott W. Martin,[b] Steven I. Dworetzky,[c] Christopher G. Boissard,[c] Valentin K. Gribkoff[c] and John E. Starrett, Jr.[b]

[a]*Computer-Assisted Drug Design, The Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*
[b]*Department of Discovery Chemistry, The Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*
[c]*Department of Neuroscience Drug Discovery, The Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*

Electrophysiological evaluation of bisphenols (**2**) as maxi-K channel openers is reported.



2, Symmetrical bisphenols

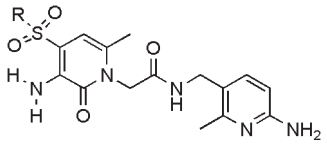
Bioorg. Med. Chem. Lett. 13 (2003) 1441

3-Amino-4-sulfonylpyridinone Acetamide and Related Pyridothiadiazine Thrombin Inhibitors

Philip E. J. Sanderson,[a,*] Kellie J. Cutrona,[a] Kelly L. Savage,[a] Adel M. Naylor-Olsen,[b] Denise J. Bickel,[c] Dennis L. Bohn,[c] Franklin C. Clayton,[c] Julie A. Krueger,[d] S. Dale Lewis,[d] Bobby J. Lucas,[d] Elizabeth A. Lyle,[c] Audrey A. Wallace,[c] Denice C. Welsh[c] and Youwei Yan[e]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA 19486, USA*
[b]*Department of Molecular Design and Diversity, Merck Research Laboratories, West Point, PA 19486, USA*
[c]*Department of Pharmacology, Merck Research Laboratories, West Point, PA 19486, USA*
[d]*Department of Biological Chemistry, Merck Research Laboratories, West Point, PA 19486, USA*
[e]*Department of Structural Biology, Merck Research Laboratories, West Point, PA 19486, USA*

We describe the design, synthesis, biological activity and a co-crystal structure of 4-sulfonylpyridinone and pyridothiadiazine thrombin inhibitors.



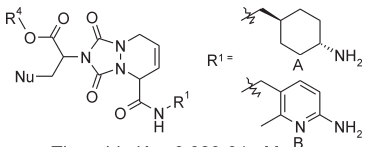
Bioorg. Med. Chem. Lett. 13 (2003) 1445

High-Throughput Synthesis and Optimization of Thrombin Inhibitors Via Urazole α-Addition and Michael Addition

P. Douglas Boatman,[a,*] Jan Urban,[a] Minh Nguyen,[a] Maher Qabar[a] and Michael Kahn[b]

[a]*Molecumetics, 2023 120th Ave NE, Bellevue, WA 98005, USA*
[b]*Pacific Northwest Research Institute, 720 Broadway, Seattle, WA 98122, USA*

A novel α-addition of propiolates to urazoles followed by Michael addition of a variety of nucleophiles for rapid thrombin lead identification and optimization is reported.



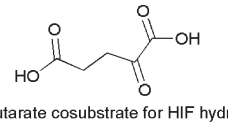
Thrombin K_i = 0.023-91 nM

Bioorg. Med. Chem. Lett. 13 (2003) 1451

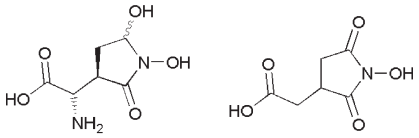
Analogues of Dealanylalahopcin Are Inhibitors of Human HIF Prolyl Hydroxylases

Imre Schlemminger,[a] David R. Mole,[b] Luke A. McNeill,[a] Anupma Dhanda,[a] Kirsty S. Hewitson,[a] Ya-Min Tian,[b] Peter J. Ratcliffe,[b] Christopher W. Pugh[b] and Christopher J. Schofield[a,*]

[a]*Oxford Centre for Molecular Sciences, Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, UK*
[b]*Wellcome Trust Centre for Human Genetics, Roosevelt Drive, Oxford OX3 7BN, UK*



2-oxoglutarate cosubstrate for HIF hydroxylases



Dealanylalahopcin

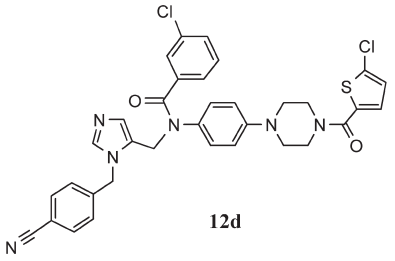
Bioorg. Med. Chem. Lett. 13 (2003) 1455

Synthesis and Evaluation of a Novel Series of Farnesyl Protein Transferase Inhibitors as Non-Peptidic CAAX Tetrapeptide Analogues

Michel Perez,[a,*] Catherine Maraval,[a] Stephan Dumond,[a] Marie Lamothe,[a] Philippe Schambel,[b] Chantal Etiévant[c] and Bridget Hill[c]

[a]*Department of Medicinal Chemistry 4, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France*
[b]*Department of Molecular Modeling, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France*
[c]*Department of Cancerology, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France*

Optimization of a novel series of 4-amino-phenyl piperazine derivatives has led to potent inhibitors of FPTase both on isolated enzyme and on cell culture (i.e. compound **12d**).



12d

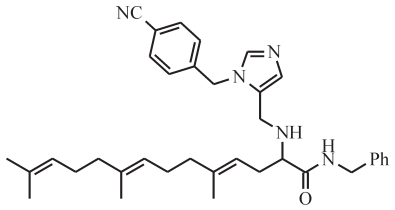
Bioorg. Med. Chem. Lett. 13 (2003) 1459

From Pure FPP to Mixed FPP and CAAX Competitive Inhibitors of Farnesyl Protein Transferase

Marc Lannuzel,[a] Marie Lamothe,[a,*] Philippe Schambel,[b] Chantal Etiévant,[c] Bridget Hill[c] and Michel Perez[a]

[a]*Department of Medicinal Chemistry 4, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France*
[b]*Department of Molecular Modeling, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France*
[c]*Department of Cancerology, Centre de Recherche Pierre Fabre, 17, Avenue Jean Moulin, 81106 Castres Cedex, France*

Compound **3c** was prepared and identified as a powerful inhibitor of FPTase, partially competitive versus FPP and fully competitive versus dansyl-GCVLS.



3c

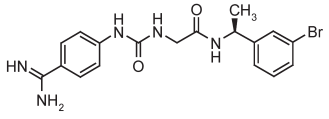
Bioorg. Med. Chem. Lett. 13 (2003) 1463

Design, Synthesis, and Structure–Activity Relationship of a New Class of Amidinophenylurea-Based Factor VIIa Inhibitors

Otmar Klingler,[a,*] Hans Matter,[a] Manfred Schudok,[a] S. Paul Bajaj,[b] Joerg Czech,[a] Martin Lorenz,[a] Hans Peter Nestler,[a] Herman Schreuder[a] and Peter Wildgoose[a]

[a]*Aventis Pharma Deutschland GmbH, Building G878, D-65926 Frankfurt, Germany*
[b]*Department of Pharmacological & Physiological Sciences and Internal Medicine, Saint Louis University Health Sciences Center, St. Louis, MI 63110, USA*

The most potent compounds display K_i values between 23 nM and 35 nM for factor VIIa.



Bioorg. Med. Chem. Lett. 13 (2003) 1469

Structure-Based Design of Inhibitors of Human L-Xylulose Reductase Modelled Into the Active Site of the Enzyme

Vincenzo Carbone,[a] Connie Darmanin,[a] Shuhei Ishikura,[b] Akira Hara[b] and Ossama El-Kabbani[a,*]

[a]*Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, 381 Royal Parade, Parkville, Victoria 3052, Australia*
[b]*Laboratory of Biochemistry, Gifu Pharmaceutical University, Mitahora-higashi, Gifu 502-8585, Japan*

Inhibitors of human L-xylulose reductase were designed based on a model of the enzyme/*n*-butyric acid complex.

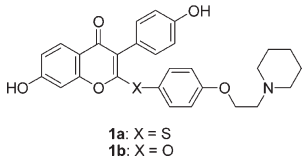
Bioorg. Med. Chem. Lett. 13 (2003) 1475

Synthesis and Estrogen Receptor Binding Affinities of 7-Hydroxy-3-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-ones Containing a Basic Side Chain

Young-Woo Kim,[a] James A. Mobley[b] and Robert W. Brueggemeier[a,*]

[a]*Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, 500 West 12th Avenue, Columbus, OH 43210, USA*
[b]*Division of Urology, Department of Surgery, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655, USA*

The synthesis of isoflavones **1** and their binding affinities for the estrogen receptors are reported.



1a: X = S
1b: X = O

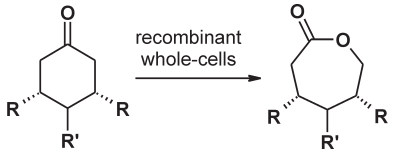
Bioorg. Med. Chem. Lett. 13 (2003) 1479

First Enantiodivergent Baeyer–Villiger Oxidation by Recombinant Whole-Cells Expressing Two Monooxygenases from *Brevibacterium*

Marko D. Mihovilovic,* Florian Rudroff, Bernhard Müller and Peter Stanetty

Vienna University of Technology, Institute of Applied Synthetic Chemistry, Getreidemarkt 9/163, A-1060 Vienna, Austria

Enantiodivergent Baeyer–Villiger oxidations of prochiral ketones with recombinant *Escherichia coli* cells expressing two monooxygenases from *Brevibacterium* are reported.



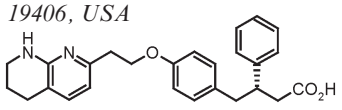
Bioorg. Med. Chem. Lett. 13 (2003) 1483

Phenylbutyrates as Potent, Orally Bioavailable Vitronectin Receptor (Integrin $\alpha v\beta 3$) Antagonists

William H. Miller,[a,*] Peter J. Manley,[a] Russell D. Cousins,[a] Karl F. Erhard,[b] Dirk A. Heerding,[a] Chet Kwon,[a] Stephen T. Ross,[b] James M. Samanen,[a] Dennis T. Takata,[a] Irene N. Uzinskas,[a] Catherine C. K. Yuan,[a] R. Curtis Haltiwanger,[b] Catherine J. Gress,[b] Michael W. Lark,[b] Shing-Mei Hwang,[b] Ian E. James,[b] David J. Rieman,[b] Robert N. Willette,[b] Tian-Li Yue,[b] Leonard M. Azzarano,[b] Kevin L. Salyers,[b] Brian R. Smith,[b] Keith W. Ward,[b] Kyung O. Johanson[b] and William F. Huffman[a]

[a]*GlaxoSmithKline Pharmaceuticals, 1250 S. Collegeville Rd., PO Box 5089, Collegeville, PA 19426, USA*
[b]*GlaxoSmithKline Pharmaceuticals, 709 Swedeland Road, PO Box 1539, King of Prussia, PA 19406, USA*

A new series of potent, phenylbutyrate-based vitronectin receptor antagonists with excellent oral bioavailability (approximately 100% in rats) is described.



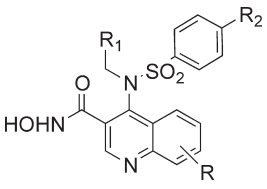
Bioorg. Med. Chem. Lett. 13 (2003) 1487

Synthesis and SAR of Bicyclic Heteroaryl Hydroxamic Acid MMP and TACE Inhibitors

A. Zask,[a,*] Y. Gu,[a] J. D. Albright,[a] X. Du,[a] M. Hogan,[a] J. I. Levin,[a] J. M. Chen,[a] L. M. Killar,[b] A. Sung,[b] J. F. DiJoseph,[b] M. A. Sharr,[b] C. E. Roth,[b] S. Skala,[b] G. Jin,[a] R. Cowling,[a] K. M. Mohler,[c] D. Barone,[c] R. Black,[c] C. March[c] and J. S. Skotnicki[a]

[a]*Wyeth-Ayerst Research, 401 N. Middletown Road, Pearl River, NY 10965, USA*
[b]*Wyeth Research, PO Box CN800, Princeton, NJ 08543, USA*
[c]*Immunex Corporation, Seattle, WA 98101, USA*

Potent and selective bicyclic heteroaryl hydroxamic acid MMP and TACE inhibitors were synthesized by a novel convergent route. Selectivity and efficacy versus MMPs and TACE could be controlled by appropriate substitution on the scaffolds and by variation of the P1′ group. Select compounds were found to be effective in in vivo models of arthritis.

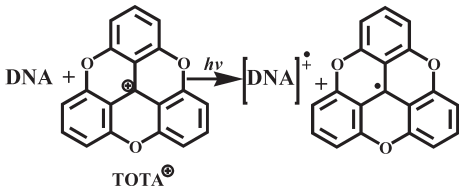


Bioorg. Med. Chem. Lett. 13 (2003) 1491

Photo-Oxidation of Duplex DNA with the Stable Trioxatriangulenium Ion

Arti Pothukuchy,[a] Sampathkumar Ellapan,[a] Karickal R. Gopidas[b,*] and Miguel Salazar[a,*]

[a]*Division of Medicinal Chemistry, College of Pharmacy, and Institute for Cellular and Molecular Biology, The University of Texas at Austin, Austin, TX 78712, USA*
[b]*Photochemistry Research Unit, Regional Research Laboratory (CSIR), Trivandrum 695 019, India*



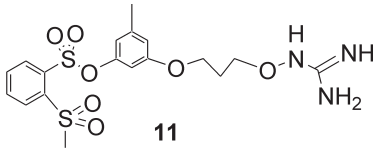
Bioorg. Med. Chem. Lett. 13 (2003) 1495

Oxyguanidines: Application to Non-peptidic Phenyl-Based Thrombin Inhibitors

Bruce Tomczuk,* Tianbao Lu, Richard M. Soll, Cynthia Fedde, Aihua Wang, Larry Murphy, Carl Crysler, Malini Dasgupta, Stephen Eisennagel, John Spurlino and Roger Bone

3-Dimensional Pharmaceuticals, Inc., 665 Stockton Drive, Exton, PA 19341 USA

We report here novel non-peptidic phenyl-based, highly potent, highly selective and orally bioavailable thrombin inhibitors exemplified by **11** using oxyguanidines as guanidine-mimetics.



11