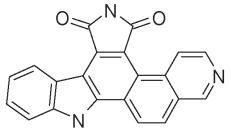
Bioorg. Med. Chem. Lett. 13 (2003) 1231

Synthesis of Quinolinyl/Isoquinolinyl[*a*]pyrrolo [3,4-*c*] Carbazoles as Cyclin D1/CDK4 Inhibitors

Guoxin Zhu,* Scott Conner, Xun Zhou, Chuan Shih, Harold B. Brooks, Eileen Considine, Jack A. Dempsey, Cathy Ogg, Bharvin Patel, Richard M. Schultz, Charles D. Spencer, Beverly Teicher and Scott A. Watkins

Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, USA

A novel series of pyrrolo[3,4-*c*] carbazoles fused with a quinolinyl/isoquinolinyl moiety was synthesized and their D1/CDK4 inhibitory and anti proliferative activity were evaluated.



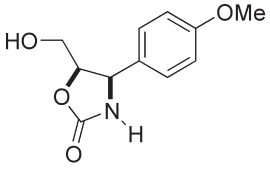
Bioorg. Med. Chem. Lett. 13 (2003) 1237

A New Synthesis of Cytoxazone and Its Diastereomers Provides Key Initial SAR Information

Percy H. Carter,* Jacob R. LaPorte, Peggy A. Scherle and Carl P. Decicco

Bristol-Myers Squibb Company, Pharmaceutical Research Institute, Princeton, NJ 08543-4000, USA

A short, enantioselective, and diastereoselective synthesis of cytoxazone, a Th2-selective immunomodulator from *Streptomyces*, is described. The route was readily adapted to the synthesis of the three other stereoisomers of natural cytoxazone. Evaluation of these compounds revealed that the stereochemical configuration of the oxazolidinone ring did not influence their biological activity.

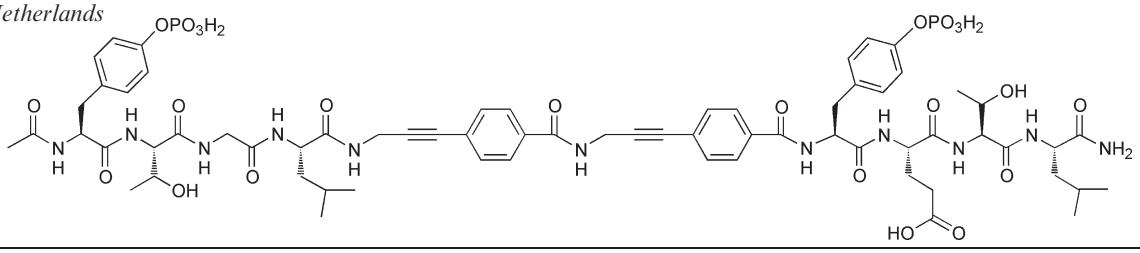


Bioorg. Med. Chem. Lett. 13 (2003) 1241

Amino Propynyl Benzoic Acid Building Block in Rigid Spacers of Divalent Ligands Binding to the Syk SH2 Domains with Equally High Affinity as the Natural Ligand

Frank J. Dekker, Nico J. de Mol, Marcel J. E. Fischer and Rob M. J. Liskamp*

Department of Medicinal Chemistry, Utrecht Institute of Pharmaceutical Sciences, Utrecht University, PO Box 80.082, 3508 TB Utrecht, The Netherlands



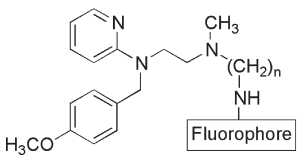
Bioorg. Med. Chem. Lett. 13 (2003) 1245

Synthesis and Pharmacological Activity of Fluorescent Histamine H_1 Receptor Antagonists Related to Mepyramine

Liantao Li,[a] Julia Kracht,[b] Shiqi Peng,[a] Günther Bernhardt[b] and Armin Buschauer[b,*]

[a]*College of Pharmaceutical Sciences, Peking University, 100083 Beijing, PR China*
[b]*Institute of Pharmacy, University of Regensburg, D-93040 Regensburg, Germany*

Fluorescently labeled H_1 antagonists were synthesized from N-demethylmepyramine by introduction of ω-aminoalkyl chains (n = 2-8) and derivatization with various fluorophores. The highest H_1 antagonistic activities were found in 5- and 6-carboxyfluorescein labeled compounds with hexa- and octamethylene spacers and in an analogous NBD-aminohexanoyl derivative (pA_2 or pK_B values (isolated guinea pig ileum and Ca^{2+} assay on U373MG cells) in the range 8.3–9.0, compared to 9.3–9.4 for mepyramine).



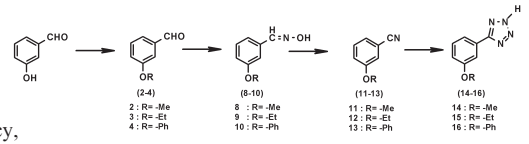
Bioorg. Med. Chem. Lett. 13 (2003) 1249

Synthesis of Low Molecular Weight Compounds with Complement Inhibition Activity

Hoshang E. Master,[a,*] Shabana I. Khan[b] and Krishna A. Poojari[a]

[a]*Department of Chemistry, St. Xavier's College, 5, Mahapalika Road, Mumbai 400 001, India*
[b]*National Centre for Natural Product Research, School of Pharmacy, University of Mississippi, MS 38677, USA*

An attempt was made to synthesise a series of non-cytotoxic low molecular weight meta-substituted aromatic ethers (**2**–**4**) and some of their bioisosteres (**14**–**16**) and to evaluate their activity on the activation of human complement (classical pathway) and their intrinsic hemolytic activity. The in vitro assay results of the inhibition of complement-mediated hemolysis by these analogues indicate that the aldehydic meta substituted aromatic ethers show inhibitory potency, while some of the bioisosteres exhibit both inhibitory as well as hemolytic property.



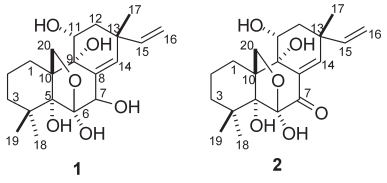
Bioorg. Med. Chem. Lett. 13 (2003) 1253

Antimycobacterial Pimarane Diterpenes from the Fungus *Diaporthe* Sp.

Suppamit Dettrakul,[a] Prasat Kittakoop,[b,*] Masahiko Isaka,[b] Sombat Nopichai,[b] Chotika Suyarnsestakorn,[b] Morakot Tanticharoen[b] and Yodhathai Thebtaranonth[a,b]

[a]*Department of Chemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*
[b]*National Center for Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency (NSTDA), Science Park, 113, Paholyothin Road, Klong 1, Klong Luang, Pathumthani 12120, Thailand*

Two new antimycobacterial primarane diterpenes were isolated from *Diaporthe* sp.

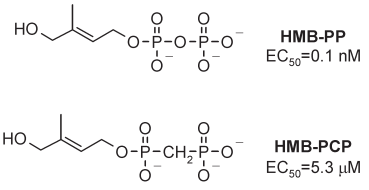


Bioorg. Med. Chem. Lett. 13 (2003) 1257

Replacing the Pyrophosphate Group of HMB-PP by a Diphosphonate Function Abrogates Its Potential to Activate Human γδ T Cells but does not lead to Competitive Antagonism

Armin Reichenberg,[a] Martin Hintz,[a] Yvonne Kletschek,[a] Tanja Kuhl,[a] Christian Haug,[a] Rosel Engel,[b] Jens Moll,[b] Dmitry N. Ostrovsky,[c] Hassan Jomaa[a,b] and Matthias Eberl[b,*]

[a]*Jomaa Pharmaka GmbH, Frankfurter Str. 50, D-35392 Giessen, Germany*
[b]*Biochemisches Institut, Justus-Liebig-Universität Giessen, Friedrichstr. 24, D-35392 Giessen, Germany*
[c]*Bakh Institute of Biochemistry, Leninsky prospect 33, 119071 Moscow, Russia*



Bioorg. Med. Chem. Lett. 13 (2003) 1261

The Inhibitory Effects of Squalene-Derived Triterpenes on Protein Phosphatase PP2A

María L. Souto,[a] Claudia P. Manríquez,[a] Manuel Norte,[a] Francisco Leira[b] and José J. Fernández[a,*]

[a]*Instituto Universitario de Bio-Orgánica, Universidad de La Laguna, Astrofísico Francisco Sánchez 2, 38206 La Laguna, Spain*
[b]*ANFACO, CECOPESCA, Campus Universitario, Lagoas (Marcosende), Vigo, Spain*

This paper reports the activity of 15 polyether triterpenes with a squalene carbon skeleton when tested for inhibitory effects on type 2A protein phosphatase. Two compounds, 16-hydroxydehydrothyrsiferol **10** and thyrsenol B **14**, exhibited significant inhibitory action at a concentration of 10 μM, and comparison with thyrsiferyl 23 acetate **1** showed a similar spatial disposition for the hydroxy group at C-15 or C-16 as a common structural moiety in these metabolites.

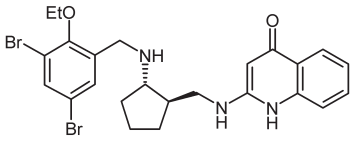
Bioorg. Med. Chem. Lett. 13 (2003) 1265

Conformational Restriction of Methionyl tRNA Synthetase Inhibitors Leading to Analogues with Potent Inhibition and Excellent Gram-Positive Antibacterial Activity

Richard L. Jarvest,[a,*] John M. Berge,[a] Pamela Brown,[a] Catherine S. V. Houge-Frydrych,[a] Peter J. O'Hanlon,[a] David J. McNair,[a] Andrew J. Pope[a] and Stephen Rittenhouse[b]

[a]*GlaxoSmithKline, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK*
[b]*GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19426, USA*

Conformationally restricted analogues of the central linker unit of bacterial methionyl tRNA synthetase inhibitors have been prepared. The (1*S*,2*R*)-cyclopentylmethyl moiety is the preferred cyclic linker, with significant diastereo- and enantioselectivity activity. Combination with an optimal right-hand side results in exceptionally good antibacterial activity against staphylococci and enterococci, including antibiotic resistant strains.

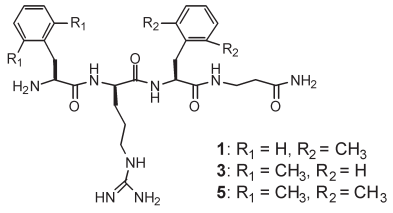


Bioorg. Med. Chem. Lett. 13 (2003) 1269

Dermorphin Tetrapeptide Analogues with 2′,6′-dimethylphenylalanine (Dmp) Substituted for Aromatic Amino Acids have High μ Opioid Receptor Binding and Biological Activities

Akihiro Ambo, Hideko Niizuma, Ai Sasaki, Hirokazu Kohara and Yusuke Sasaki*

Tohoku Pharmaceutical University, 4-1 Komatsushima 4-chome, Aoba-ku, Sendai 981-8558, Japan



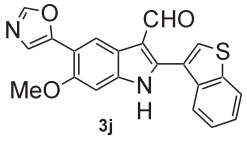
Bioorg. Med. Chem. Lett. 13 (2003) 1273

Novel Indole-Based Inhibitors of IMPDH: Introduction of Hydrogen Bond Acceptors at Indole C-3

Scott H. Watterson,* T. G. Murali Dhar, Shelley K. Ballentine, Zhongqi Shen, Joel C. Barrish, Daniel Cheney, Catherine A. Fleener, Katherine A. Rouleau, Robert Townsend, Diane L. Hollenbaugh and Edwin J. Iwanowicz

Bristol-Myers Squibb PRI, PO Box 4000, Princeton, NJ 08543-4000, USA

The development of a series of novel indole-based inhibitors of 5′-inosine monophosphate dehydrogenase (IMPDH) is described. Various hydrogen bond acceptors at C-3 of the indole were explored. The synthesis and the structure–activity relationships (SARs) derived from in vitro studies are outlined.



3j

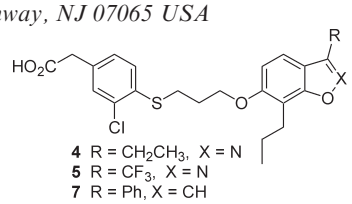
Bioorg. Med. Chem. Lett. 13 (2003) 1277

Phenylacetic Acid Derivatives as hPPAR Agonists

Conrad Santini,[a,*] Gregory D. Berger,[a] Wei Han,[a] Ralph Mosley,[a] Karen MacNaul,[b] Joel Berger,[b] Thomas Doebber,[b] Margaret Wu,[b] David E. Moller,[b] Richard L. Tolman[a] and Soumya P. Sahoo[a,*]

[a]*Department of Basic Chemistry, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065 USA*
[b]*Department of Molecular Endocrinology, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065 USA*

A new series of hPPAR agonists was developed. Significant in vivo glucose and triglyceride lowering activity was displayed by compounds **4**, **5** and **7**. **7** was of comparable potency in insulin resistant rodents to BRL 49653.



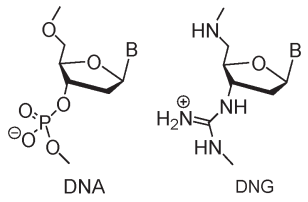
Bioorg. Med. Chem. Lett. 13 (2003) 1281

Solid-Phase Synthesis of Positively Charged Deoxynucleic Guanidine (DNG) Oligonucleotide Mixed Sequences

Putta Mallikarjuna Reddy and Thomas C. Bruice*

Department of Chemistry and Biochemistry, University of California at Santa Barbara, CA 93106, USA

Positively charged DNG oligonucleotide mixed sequences containing A/T bases were synthesized by solid-phase synthesis. Synthesis proceeds in 3′→5′ direction and involves coupling of 3′-Fmoc protected thiourea in the presence of $HgCl_2$/TEA with the corresponding 5′-amine of the growing oligo chain. DNG binding characteristics with complimentary DNA and with itself have been evaluated.



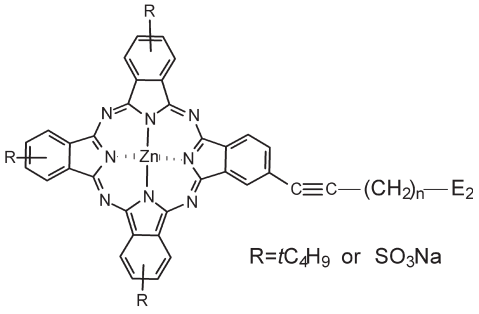
Bioorg. Med. Chem. Lett. 13 (2003) 1287

Synthesis and Biological Activities of Phthalocyanine–Estradiol Conjugates

Ehtsham H. Khan,[a] Hasrat Ali,[b] Hongjian Tian,[b] Jacques Rousseau,[b] Guillame Tessier,[b] Shafiullah[a] and Johan E. van Lier[b,*]

[a]*Department of Chemistry, A.M.U. Aligarh (U.P.) India*
[b]*Department of Nuclear Medicine and Radiobiology, Faculty of Medicine, Université de Sherbrooke, Sherbrooke (QC), Canada J1H 5N4*

Phthalocyanine-based photosensitizers, coupled via a 17α-ethynyl group to estradiol using Pd(II) as a catalyst, were synthesized and evaluated for their estrogen receptor binding affinity and in vitro photocytotoxicity.



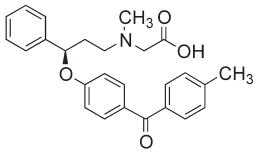
Bioorg. Med. Chem. Lett. 13 (2003) 1291

[^{3}H]-(*R*)-NPTS, a Radioligand for the Type 1 Glycine Transporter

John A. Lowe, III,* Susan E. Drozda, Katherine Fisher, Christine Strick, Lorraine Lebel, Christopher Schmidt, Donna Hiller and Kathleen S. Zandi

Central Research Division, Pfizer Inc., Eastern Point Road, Groton, CT 06340, USA

The synthesis of NPTS, **6**, a potent inhibitor of the type 1 glycine transporter (GlyT1) is described, as well as preparation of **6** in optically active and tritiated form for use as a radioligand for affinity displacement assay of GlyT1.



6, **(R)-NPTS**

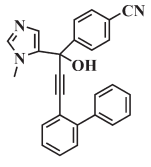
Bioorg. Med. Chem. Lett. 13 (2003) 1293

Synthesis and Biological Evaluation of 4-[3-biphenyl-2-yl-1-hydroxy-1-(3-methyl-3*H*-Imidazol-4-yl)-prop-2-ynyl]-1-yl-benzonitrile as Novel Farnesyltransferase Inhibitor

Nan-Horng Lin,* Le Wang, Jerry Cohen, Wen-Zhen Gu, David Frost, Haiying Zhang, Saul Rosenberg and Hing Sham

Cancer Research, D-47B, Global Pharmaceutical Products Division, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-3500, USA

Analogues of compound **1** were synthesized and tested in vitro for farnesyltransferase inhibition activity.



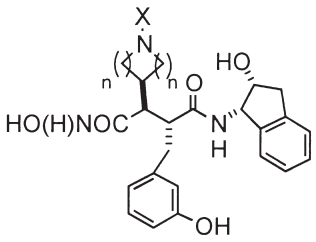
1

Bioorg. Med. Chem. Lett. 13 (2003) 1297

Potent and Selective Aggrecanase Inhibitors Containing Cyclic P1 Substituents

Robert J. Cherney,* Ruowei Mo, Dayton T. Meyer, Li Wang, Wenqing Yao, Zelda R. Wasserman, Rui-Qin Liu, Maryanne B. Covington, Micky D. Tortorella, Elizabeth C. Arner, Mingxin Qian, David D. Christ, James M. Trzaskos, Robert C. Newton, Ron L. Magolda and Carl P. Decicco

Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08543-4000, USA



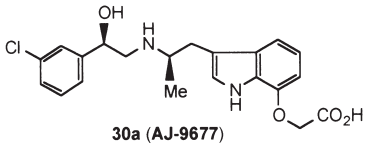
Bioorg. Med. Chem. Lett. 13 (2003) 1301

Novel and Potent Human and Rat β_3-Adrenergic Receptor Agonists Containing Substituted 3-Indolylalkylamines

Hiroshi Harada,[a,*] Yoshimi Hirokawa,[a] Kenji Suzuki,[a] Yoichi Hiyama,[a] Mayumi Oue,[b] Hitoshi Kawashima,[b] Naoyuki Yoshida,[b] Yasuji Furutani[b] and Shiro Kato[a]

[a]*Chemistry Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Enoki 33-94, Suita 564-0053, Japan*
[b]*Pharmacology & Microbiology Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Enoki 33-94, Suita 564-0053, Japan*

The synthesis and biological evaluation of indole β_3-AR agonists, including **30a** are described.



30a (**AJ-9677**)

Bioorg. Med. Chem. Lett. 13 (2003) 1307

Structure–Activity Relationship of Cyclic Peptide Penta-c[Asp-His^6-DPhe^7-Arg^8-Trp^9-Lys]-NH_2 at the Human Melanocortin-1 and -4 Receptors: His^6 Substitution

Adrian Wai-Hing Cheung,* Waleed Danho, Joseph Swistok, Lida Qi, Grazyna Kurylko, Karen Rowan, Mitch Yeon, Lucia Franco, Xin-Jie Chu, Li Chen and Keith Yagaloff

Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ 07110, USA

A series of MT-II related cyclic peptides, based on potent but non-selective hMC4R agonist (Penta-c[Asp-His^6-DPhe^7-Arg^8-Trp^9-Lys]-NH_2) was prepared in which His^6 residue was systematically substituted. Two of the most interesting peptides identified in this study are Penta-c[Asp-**5-ClAtc**-DPhe-Arg-Trp-Lys]-NH_2 and Penta-c[Asp-**5-ClAtc**-DPhe-**Cit**-Trp-Lys]-NH_2 which are potent hMC4R agonists and are either inactive or weak partial agonists in hMC1R, hMC3R and hMC5R agonist assays.

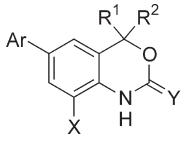
Bioorg. Med. Chem. Lett. 13 (2003) 1313

Novel 6-Aryl-1,4-dihydrobenzo[*d*][1,3]oxazine-2-thiones as Potent, Selective, and Orally Active Nonsteroidal Progesterone Receptor Agonists

Puwen Zhang,[a,*] Eugene A. Terefenko,[a] Andrew Fensome,[a] Jay Wrobel,[a] Richard Winneker[b] and Zhiming Zhang[b]

[a]*Chemical Sciences, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*
[b]*Women's Health Research Institute, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*

In contrast to the progesterone receptor (PR) antagonists **1**, novel 6-aryl benzoxazine-2-thiones (**2-47**) were generally potent PR agonists.



1, Y = O
2-47, Y = S

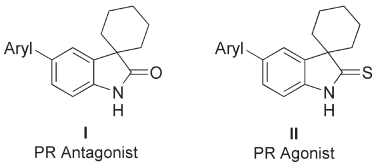
Bioorg. Med. Chem. Lett. 13 (2003) 1317

Novel 5-Aryl-1,3-dihydro-indole-2-thiones: Potent, Orally Active Progesterone Receptor Agonists

Andrew Fensome,[a,*] Marci Koko,[a] Jay Wrobel, Puwen Zhang,[a] Zhiming Zhang,[b] Jeffrey Cohen,[b] Scott Lundeen,[b] Kelly Rudnick,[b] Yuan Zhu[b] and Richard Winneker[b]

[a]*Chemical Sciences, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*
[b]*Women's Health Research Institute, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*

During the course of our work on oxindole derived progesterone receptor antagonists **I**, we noted that when we converted the oxindole **I** into a thio-oxidole **II**, the compounds became potent progesterone receptor agonists. The synthesis and biological characterization of this series is discussed.



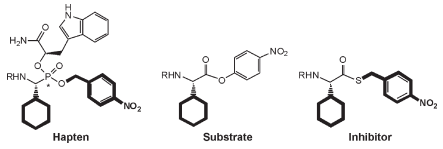
I PR Antagonist II PR Agonist

Bioorg. Med. Chem. Lett. 13 (2003) 1321

Investigation of an Antibody-Ligase. Evidence for Strain-Induced Catalysis

Sergey N. Savinov,[a] Ralph Hirschmann,[a,*] Stephen J. Benkovic[b,*] and Amos B. Smith, III[a,*]

[a]*Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104, USA*
[b]*Department of Chemistry, Pennsylvania State University, University Park, PA 16802, USA*



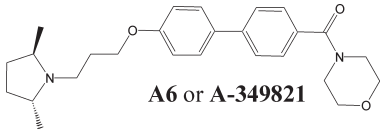
Bioorg. Med. Chem. Lett. 13 (2003) 1325

Synthesis and SAR of Aminoalkoxy-biaryl-4-carboxamides: Novel and Selective Histamine H_3 Receptor Antagonists

Ramin Faghih,* Wesley Dwight, Jia Bao Pan, Gerard B. Fox, Kathy M. Krueger, Timothy A. Esbenshade, Jill M. McVey, Kennan Marsh, Youssef L. Bennani and Arthur A. Hancock

Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL 60064-6123, USA

Solution-phase parallel synthesis and a matrix approach were employed to prepare selective, orally bioavailable histamine H_3 receptor antagonists (e.g., **A6** or **A-349821**).



A6 or **A-349821**

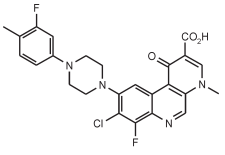
Bioorg. Med. Chem. Lett. 13 (2003) 1329

Benzo[*f*]naphtyridones: A New Family of Topical Antibacterial Agents Active on Multi-Resistant Gram-Positive Pathogens

Michel Tabart,* Guy Picaut, Marc Lavergne, Sylvie Wentzler, Jean-Luc Malleron, Sylvie Dutka-Malen and Nadine Berthaud

Aventis Pharma, Centre de Recherche de Vitry Alfortville, 13 Quai Jules Guesde, 94403 Vitry sur Seine, France

The synthesis and biological activity of a series of benzo[*f*] [1,7]naphtyridone, new topical antibacterial agents, are reported.



RPR203246

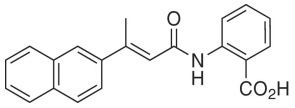
Bioorg. Med. Chem. Lett. 13 (2003) 1333

Inhibition of Telomerase by BIBR 1532 and Related Analogues

D. K. Barma, Anissa Elayadi, J. R. Falck and David R. Corey*

Departments of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX 75390-9041, USA

BIBR 1532 has been reported to be a potent, small molecule inhibitor of human telomerase, suggesting it as a lead for the development of anti-telomerase therapy. We confirm the ability of BIBR 1532 to inhibit telomerase and report the discovery of an equally potent analogue. IC_{50} values in cell extract are considerably higher than those previously reported using assays for purified enzyme.

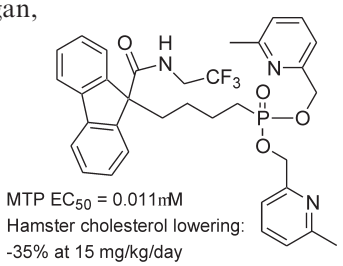


Bioorg. Med. Chem. Lett. 13 (2003) 1337

Microsomal Triglyceride Transfer Protein Inhibitors: Discovery and Synthesis of Alkyl Phosphonates as Potent MTP Inhibitors and Cholesterol Lowering Agents

David R. Magnin,* Scott A. Biller, John Wetterau, Jeffrey A. Robl, John K. Dickson, Jr., Prakash Taunk, Thomas W. Harrity, R. Michael Lawrence, C.-Q. Sun, Tammy Wang, Janette Logan, Olga Fryszman, Fergal Connolly, Kern Jolibois and Lori Kunselman

Department of Discovery Chemistry and Department of Metabolic Disease, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08543-4000, USA



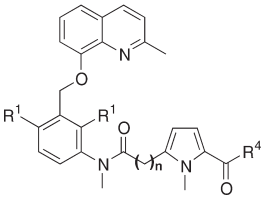
Bioorg. Med. Chem. Lett. 13 (2003) 1341

Synthesis and Structure–Activity Relationships of Aroylpyrrole Alkylamide Bradykinin (B_2) Antagonists

Mark A. Youngman, John R. Carson, Jung S. Lee, Scott L. Dax, Sui-Po Zhang, Ray W. Colburn, Dennis J. Stone, Ellen E. Codd and Michele C. Jetter*

Johnson & Johnson Pharmaceutical Research and Development, Welsh & McKean Roads, PO Box 776, Spring House, PA 19477-0776, USA

The synthesis and structure–activity relationships of a novel series of aroylpyrrole alkylamides as potent selective bradykinin B_2 receptor antagonists are described.



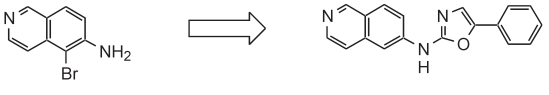
Bioorg. Med. Chem. Lett. 13 (2003) 1345

Identification of Novel and Potent Isoquinoline Aminooxazole-Based IMPDH Inhibitors

Ping Chen,[a,*] Derek Norris,[a] Kristin D. Haslow,[a] T. G. Murali Dhar,[a] William J. Pitts,[a] Scott H. Watterson,[a] Daniel L. Cheney,[b] Donna A. Bassolino,[b] Catherine A. Fleener,[c] Katherine A. Rouleau,[c] Diane L. Hollenbaugh,[c] Robert M. Townsend,[c] Joel C. Barrish[a] and Edwin J. Iwanowicz[a]

[a]*Discovery Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute PO Box 4000 Princeton, NJ 08543, USA*
[b]*Computer Aided Drug Design, Bristol-Myers Squibb Pharmaceutical Research Institute PO Box 4000 Princeton, NJ 08543, USA*
[c]*Immunology, Inflammation and Pulmonary Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute PO Box 4000 Princeton, NJ 08543, USA*

Screening of our in-house compound collection followed by subsequent structural optimization afforded a series of novel 2-isoquinolinoamino-oxazole based human IMPDH-II inhibitors. As a representative of this class, compound **17** displayed single-digit nanomolar potency against the enzyme.



1 IMPDH-II IC_{50}= 0.55 μM

17 IMPDH-II IC_{50} = 5 nM

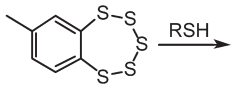
Bioorg. Med. Chem. Lett. 13 (2003) 1349

Reaction of Thiols with 7-Methylbenzopentathiepin

Tonika Chatterji and Kent S. Gates*

Departments of Chemistry and Biochemistry, University of Missouri-Columbia, Columbia, MO 65211, USA

Thiols react readily with the pentathiepin heterocycle to generate a complex mixture of polysulfides. The reactions studied here may shed light on the cytotoxic activity of naturally-occurring pentathiepin-containing antibiotics such as varacin and lissoclinotoxin A.



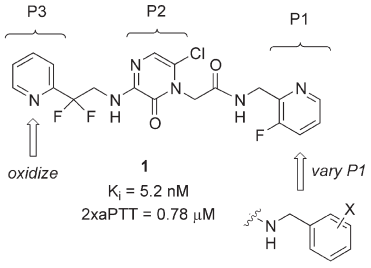
Bioorg. Med. Chem. Lett. 13 (2003) 1353

Pharmacokinetic Optimization of 3-Amino-6-chloropyrazinone Acetamide Thrombin Inhibitors. Implementation of P3 Pyridine N-Oxides to Deliver an Orally Bioavailable Series Containing P1 *N*-Benzylamides

Christopher S. Burgey,[a,*] Kyle A. Robinson,[a] Terry A. Lyle,[a] Philippe G. Nantermet,[a] Harold G. Selnick,[a] Richard C. A. Isaacs,[a] S. Dale Lewis,[b] Bobby J. Lucas,[b] Julie A. Krueger,[b] Rominder Singh,[c] Cynthia Miller-Stein,[c] Rebecca B. White,[c] Bradley Wong,[c] Elizabeth A. Lyle,[d] Maria T. Stranieri,[d] Jacquelynn J. Cook,[d] Daniel R. McMasters,[e] Janetta M. Pellicore,[a] Swati Pal,[a] Audrey A. Wallace,[d] Franklin C. Clayton,[d] Dennis Bohn,[d] Denise C. Welsh,[d] Joseph J. Lynch, Jr.,[d] Youwei Yan,[f] Zhongguo Chen,[f] Lawrence Kuo,[f] Stephen J. Gardell,[b] Jules A. Shafer[b] and Joseph P. Vacca[a]

[a]*Department of Medicinal Chemistry,* [b]*Department of Biological Chemistry,* [c]*Department of Drug Metabolism,* [d]*Department of Pharmacology,* [e]*Department of Molecular Systems,* [f]*Department of Structural Biology, Merck Research Laboratories, West Point, PA 19486, USA*

A modification principally directed toward the improvement of the aqueous solubility (i.e., introduction of a P3 pyridine N-oxide) of the previous lead compound **1** afforded a new series of potent orally bioavailable P1 *N*-benzylamide thrombin inhibitors.



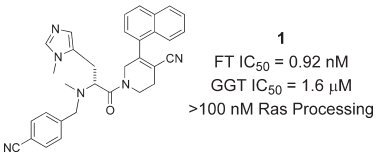
Bioorg. Med. Chem. Lett. 13 (2003) 1359

Aryl Tetrahydropyridine Inhibitors of Farnesyltransferase: Glycine, Phenylalanine and Histidine Derivatives

Stephen L. Gwaltney, II,* Stephen J. O'Connor, Lissa T. J. Nelson, Gerard M. Sullivan, Hovis Imade, Weibo Wang, Lisa Hasvold, Qun Li, Jerome Cohen, Wen-Zhen Gu, Stephen K. Tahir, Joy Bauch, Kennan Marsh, Shi-Chung Ng, David J. Frost, Haiying Zhang, Steve Muchmore, Clarissa G. Jakob, Vincent Stoll, Charles Hutchins, Saul H. Rosenberg and Hing L. Sham

Pharmaceutical Discovery, R47B, Building AP-10, Abbott Laboratories, Abbott Park, IL 60064-6101, USA

In our effort to develop new farnesyltransferase inhibitors, we have discovered a series of aryl tetrahydropyridines that incorporate substituted glycine, phenylalanine and histidine residues. The design, synthesis, SAR and biological properties of these compounds will be discussed.



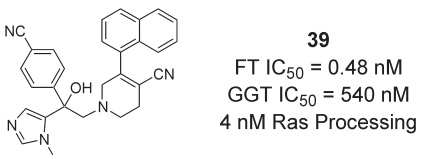
Bioorg. Med. Chem. Lett. 13 (2003) 1363

Aryl Tetrahydropyridine Inhibitors of Farnesyltransferase: Bioavailable Analogues with Improved Cellular Potency

Stephen L. Gwaltney, II,* Stephen J. O'Connor, Lissa T. J. Nelson, Gerard M. Sullivan, Hovis Imade, Weibo Wang, Lisa Hasvold, Qun Li, Jerome Cohen, Wen-Zhen Gu, Stephen K. Tahir, Joy Bauch, Kennan Marsh, Shi-Chung Ng, David J. Frost, Haiying Zhang, Steve Muchmore, Clarissa G. Jakob, Vincent Stoll, Charles Hutchins, Saul H. Rosenberg and Hing L. Sham

Pharmaceutical Discovery, R47B, Building AP-10, Abbott Laboratories, Abbott Park, IL 60064-6101, USA

In our effort to develop new farnesyltransferase inhibitors, we have discovered bioavailable aryl tetrahydropyridines that are potent in cell culture. The design, synthesis, SAR and biological properties of these compounds will be discussed.



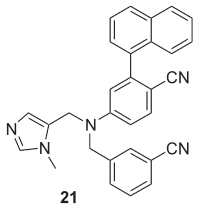
Bioorg. Med. Chem. Lett. 13 (2003) 1367

Novel and Selective Imidazole-Containing Biphenyl Inhibitors of Protein Farnesyltransferase

Michael L. Curtin,* Alan S. Florjancic, Jerome Cohen, Wen-Zhen Gu, David J. Frost, Steven W. Muchmore and Hing L. Sham

Departments of Cancer Research and Advanced Technology, Global Pharmaceutical Research and Development, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064, USA

The evaluation of farnesyltransferase inhibitor **21** (IC_{50} 0.39 nM) and related analogues is reported including an inhibitor/enzyme X-ray crystal structure.



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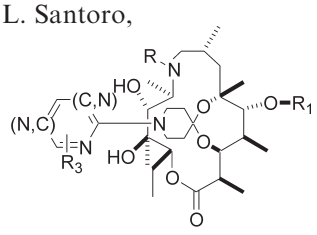
Bioorg. Med. Chem. Lett. 13 (2003) 1373

Azalide 3,6-Ketals: Antibacterial Activity and Structure–Activity Relationships of Aryl and Hetero Aryl Substituted Analogues

Subas M. Sakya,* Peter Bertinato, Bryan Pratt, Melani Suarez-Contreras, Kristin M. Lundy, Martha L. Minich, Hengmiao Cheng, Carl B. Ziegler, Barbara J. Kamicker, Shigeru F. Hayashi, Sheryl L. Santoro, David M. George and Camilla D. Bertsche

Veterinary Medicine Research and Development, Pfizer Inc, Eastern Point Road, PO Box 4063, Groton, CT 06340, USA

Aryl and hetero aryl substituted 3,6-ketals of 15-membered azalide analogues were synthesized and were found to have potent in vitro antibacterial activity against veterinary pathogens, including *Staphylococcus aureus* and *Pasteurella multocida*.



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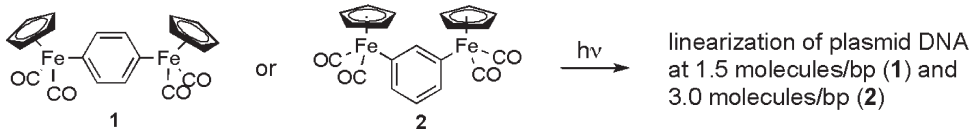
Bioorg. Med. Chem. Lett. 13 (2003) 1377

Photoinduced DNA Cleavage by Benzenediradical Equivalents: 1,3- and 1,4-Bis(dicarbonylcyclopentadienyliron)benzene

Debra L. Mohler,* Janet Gray Coonce and Daniel Predecki

Department of Chemistry, Emory University, 1515 Pierce Dr., Atlanta, GA 30322, USA



1 **2**

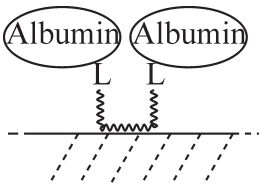
Bioorg. Med. Chem. Lett. 13 (2003) 1381

Adsorbed Surfactants for Affinity Chromatography: End-Group Modification of Ethylene Glycol Polymers

Cemile Yaniç,[a] Martin W. Bredenkamp,[b,*] Edmund P. Jacobs[a] and Pieter Swart[c]

[a]*Institute of Polymer Science, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa*
[b]*Department of Chemistry, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa*
[c]*Department of Biochemistry, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa*

Ligands were attached to Pluronic®F108 and the adduct adsorbed onto a membrane surface, providing a system that was used to extract albumin from sheep serum.



Bioorg. Med. Chem. Lett. 13 (2003) 1385

Further Exploration of 1-{2-[Bis-(4-fluorophenyl)methoxy]ethyl}piperazine (GBR 12909): Role of *N*-Aromatic, *N*-Heteroaromatic, and 3-Oxygenated *N*-Phenylpropyl Substituents on Affinity for the Dopamine and Serotonin Transporter

David Lewis,[a] Ying Zhang,[a] Thomas Prisinzano,[a] Christina M. Dersch,[b] Richard B. Rothman,[b] Arthur E. Jacobson[a] and Kenner C. Rice[a,*]

[a]*Laboratory of Medicinal Chemistry, NIDDK, NIH, Bethesda, MD, 20892, USA*
[b]*Psychopharmacology Section, NIDA, Addiction Research Center, Baltimore, MD 21224, USA*