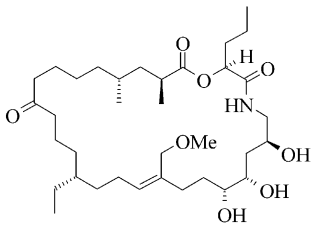
Myxovirescin Analogues Via Macrocyclic Ring-Closing Metathesis

Bioorg. Med. Chem. Lett. 13 (2003) 321

Stéphane Content, Christopher J. Dutton* and Lee Roberts

Pfizer Global Research and Development, Sandwich, Kent CT13 9NJ, UK

A short, efficient route has been developed to analogues of myxovirescin using ring-closing metathesis whereby the antibacterial activity has been retained.

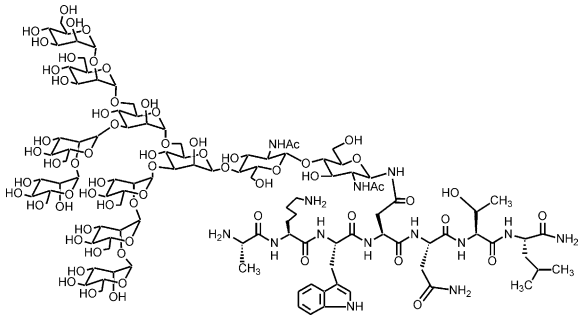


Chemoenzymatic Synthesis of High-Mannose Type HIV-1 Gp120 Glycopeptides

Bioorg. Med. Chem. Lett. 13 (2003) 327

Suddham Singh, Jiahong Ni and Lai-Xi Wang*

Institute of Human Virology, University of Maryland Biotechnology Institute, University of Maryland, 725 West Lombard Street, Baltimore, MD 21201, USA



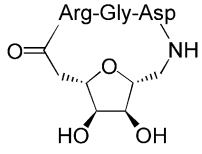
Solid-Phase Synthesis of Cyclic RGD-Furanoid Sugar Amino Acid Peptides as Integrin Inhibitors

Bioorg. Med. Chem. Lett. 13 (2003) 331

Renate M. van Well,[a] Herman S. Overkleeft,[a] Gijsbert A. van der Marel,[a] Dan Bruss,[b] Gaétan Thibault,[c] Phillip G. de Groot,[d] Jacques H. van Boom[a] and Mark Overhand[a,*]

[a]*Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University, PO Box 9502, 2300 RA Leiden, The Netherlands*
[b]*Department of Chemistry, Central College, 812 University, Pella, IA 50219, USA*
[c]*Laboratory of Cell Biology of Hypertension, Clinical Research Institute Montreal, 110 Pines Avenue West, Montreal, Quebec, Canada H2W 1R7*
[d]*Department of Haematology, University Medical Center, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands*

Novel cyclic RGD peptides containing one or two furanoid sugar amino acids were synthesized via a cyclization-cleavage approach using Kaiser's oxime resin. Evaluation of their ability to bind to the integrin receptors $\alpha_v\beta_3$ and $\alpha_{IIb}\beta_3$ revealed that compound **1** has the highest affinity for both receptors.



1

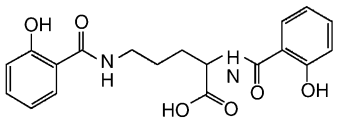
$IC_{50}\ \alpha_{IIb}\beta_3 = 0.384\ \mu M$
$IC_{50}\ \alpha_v\beta_3 = 1.49\ \mu M$

2,5-Bis-(2-hydroxybenzoylamino)pentanoic Acid, a Salicylic Acid-metabolite Isolated from Chicken: Characterization and Independent Synthesis

Bioorg. Med. Chem. Lett. 13 (2003) 335

Ulrik Hillaert,[a] Kris Baert,[b] Jef Rozenski,[c] Siska Croubels,[b] Denis De Keukeleire,[d] Patrick De Backer[b] and Serge Van Calenbergh[a,*]

[a]*Ghent University, Faculty of Pharmaceutical Sciences, Laboratory for Medicinal Chemistry, Harelbekestraat 72, B-9000 Ghent, Belgium*
[b]*Ghent University, Faculty of Veterinary Medicine, Department of Pharmacology, Pharmacy and Toxicology, Salisburylaan 133, B-9820 Merelbeke, Belgium*
[c]*Katholieke Universiteit Leuven, Rega Institute, Laboratory for Medicinal Chemistry, Minderbroedersstraat 10, B-3000 Leuven, Belgium*
[d]*Ghent University, Faculty of Pharmaceutical Sciences, Laboratory for Pharmacognosy and Phytochemistry, Harelbekestraat 72, B-9000 Ghent, Belgium*



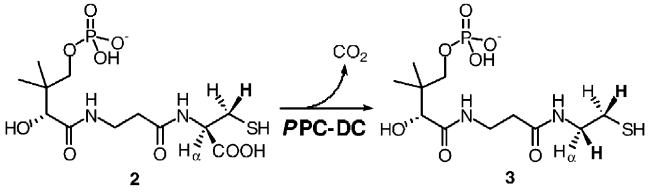
Bioorg. Med. Chem. Lett. 13 (2003) 339

Stereochemical Studies on Phosphopantothenoylcysteine Decarboxylase from *Escherichia coli*

Erick Strauss and Tadhg P. Begley*

Department of Chemistry and Chemical Biology, Cornell University, Baker Laboratory, Ithaca, NY 14853, USA

Stereochemical studies of the reaction catalyzed by *P*PC-DC indicate decarboxylation with retention at C_α and removal of the pro-*R* proton at C_β of the cysteine moiety of the substrate **2** during a reversible oxidation to a thioaldehyde intermediate.



2 **3**

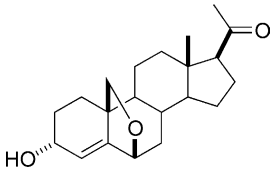
Bioorg. Med. Chem. Lett. 13 (2003) 343

Synthesis and $GABA_A$ Receptor Activity of a 6,19-Oxido Analogue of Pregnanolone

Adriana S. Veleiro,[a] Ruth E. Rosenstein,[b] Carolina O. Jaliffa,[b] María L. Grilli,[b] Florencia Speroni[a] and Gerardo Burton[a,*]

[a]*Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, C1428EHA Buenos Aires, Argentina*
[b]*Departamento de Bioquímica Humana, Facultad de Medicina, Universidad de Buenos Aires, Argentina*

The synthesis and biological activity in vitro and in vivo of the neurosteroid analogue **4** are reported.



4

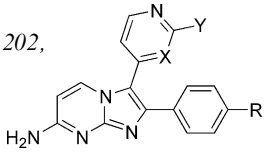
Bioorg. Med. Chem. Lett. 13 (2003) 347

Imidazopyrimidines, Potent Inhibitors of p38 MAP Kinase

Kenneth C. Rupert,* James R. Henry,* John H. Dodd, Scott A. Wadsworth, Druie E. Cavender, Gilbert C. Olini, Bohumila Fahmy and John J. Siekierka

Drug Discovery, Johnson & Johnson Pharmaceutical Research and Development, L.L.C., 1000 Route 202, Raritan, NJ 08869, USA

A novel series of imidazopyrimidines have been developed that potently inhibit p38α and suppress the production of TNF-α in vivo.

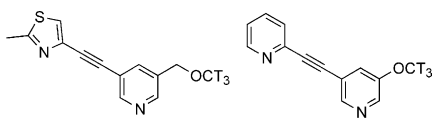


Bioorg. Med. Chem. Lett. 13 (2003) 351

[^{3}H]-Methoxymethyl-MTEP and [^{3}H]-Methoxy-PEPy: Potent and Selective Radioligands for the Metabotropic Glutamate Subtype 5 (mGlu5) Receptor

Nicholas D. P. Cosford,[a,*] Jeffrey Roppe,[a] Lida Tehrani,[a] Edwin J. Schweiger,[a] T. Jon Seiders,[a] Ashok Chaudary,[c] Sara Rao[b] and Mark A. Varney[b]

[a]*Department of Chemistry, Merck Research Laboratories, MRLSDB2, 3535, General Atomics Court, San Diego, CA 92121, USA*
[b]*Department of Neuropharmacology, Merck Research Laboratories, MRLSDB1, 3535, General Atomics Court, San Diego, CA 92121, USA*
[c]*Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ 07065, USA*



[^{3}H]-Methoxymethyl-MTEP [^{3}H]-Methoxy-PEPy

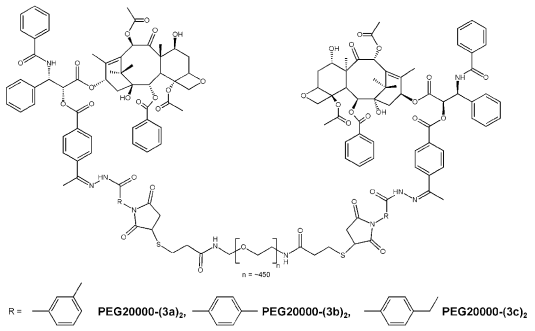
Bioorg. Med. Chem. Lett. 13 (2003) 355

Synthesis and In Vitro Efficacy of Acid-Sensitive Poly(ethylene glycol) Paclitaxel Conjugates

Paula C. A. Rodrigues,[a,c] Karin Scheuermann,[a] Cornelia Stockmar,[a] Gerhard Maier,[b] Heinz H. Fiebig,[b] Clemens Unger,[a] Rolf Mülhaupt[c] and Felix Kratz[a,*]

[a]*Tumor Biology Center, Department of Medical Oncology, Clinical Research, Breisacher Straße 117, 79106 Freiburg, FRG*
[b]*Oncotest GmbH, Am Flugplatz 12-14, 79108 Freiburg, FRG*
[c]*Institute of Macromolecular Chemistry, University of Freiburg, 79104 Freiburg, FRG*

Three maleimide derivatives of the anticancer drug paclitaxel that incorporate an acid-sensitive carboxylic hydrazone linker were prepared and coupled to bifunctional PEGs (MW 20,000 g/mol). The conjugates showed in vitro activity in three human cancer lines in the low micromolar range.



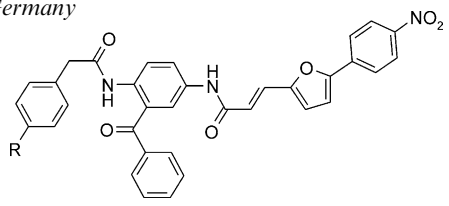
Bioorg. Med. Chem. Lett. 13 (2003) 361

Structure–Activity Relationships of Novel Anti-Malarial Agents: Part 5. *N*-(4-acylamino-3-benzoylphenyl)-[5-(4-nitrophenyl)-2-furyl]acrylic Acid Amides

Jochen Wiesner,[b,c] Katja Kettler,[a] Jacek Sakowski,[a] Regina Ortmann,[a] Hassan Jomaa[c] and Martin Schlitzer[a,*]

[a]*Department für Pharmazie, Zentrum für Pharmaforschung, Ludwig-Maximilians-Universität München, Butenandtstraße 5-13, D-81377 München, Germany*
[b]*Biochemisches Institut der Universitätsklinik Gießen, Friedrichstraße 24, Gießen, Germany*
[c]*Jomaa Pharmaka GmbH, Frankfurter Straße 50, D-35249 Gießen, Germany*

We have developed a [5-(4-nitrophenyl)-2-furyl]acrylic acid substituted benzophenone as a novel lead for anti-malarial agents. Here, we demonstrated that the acyl residue at the 2-amino group of the benzophenone core structure has to be a phenylacetic acid substructure substituted in its *para*-position with methyl or other substituents of similar size like chlorine, bromine or trifluoromethyl.



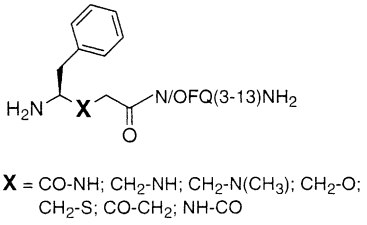
Bioorg. Med. Chem. Lett. 13 (2003) 365

Nociceptin/Orphanin FQ(1–13)NH_2 Analogues Modified in the Phe[1]-Gly[2] Peptide Bond

Remo Guerrini,[a,*] Daniela Rizzi,[b] Marina Zucchini,[a] Roberto Tomatis,[a] Domenico Regoli,[b] Girolamo Calo'[b] and Severo Salvadori[a]

[a]*Department of Pharmaceutical Sciences and Biotechnology Center, University of Ferrara, via Fossato di Mortara, 17/19, 44100 Ferrara, Italy*
[b]*Department of Experimental and Clinical Medicine, Section of Pharmacology, University of Ferrara, via Fossato di Mortara, 17/19, 44100 Ferrara, Italy*

The synthesis and the mouse vas deferens activity of a series of Nociceptin/orpanin FQ(1–13)NH_2 analogues are reported.



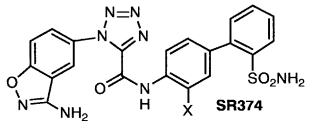
Bioorg. Med. Chem. Lett. 13 (2003) 369

Nonbenzamidine Tetrazole Derivatives as Factor Xa Inhibitors

Mimi L. Quan,* Christopher D. Ellis, Ming Y. He, Ann Y. Liauw, Francis J. Woerner, Richard S. Alexander, Robert M. Knabb, Patrick Y. S. Lam, Joseph M. Luettgen, Pancras C. Wong, Matthew R. Wright and and Ruth R. Wexler

Bristol-Myers Squibb Co., PO Box 80500 Wilmington, DE 19880-0500, USA

A series of tetrazole fXa inhibitors containing benzamidine mimic as the P_1 substrate is described. The aminobenzisoxaole moiety was found to be the most potent benzamidine mimic. SR374 inhibits fXa with a K_i value of 0.35 nM and is very selective for fXa over thrombin and trypsin.



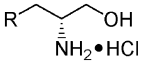
Bioorg. Med. Chem. Lett. 13 (2003) 375

Synthesis and In Vivo Anti-inflammatory Activity of Long-Chain 2-Amino-alcohols

Victoria Magrioti,[a] Dimitra Hadjipavlou-Litina[b] and Violetta Constantinou-Kokotou[a,*]

[a]*Chemical Laboratories, Agricultural University of Athens, Iera Odos 75, 118 55 Athens, Greece*
[b]*Department of Pharmaceutical Chemistry, University of Thessaloniki, 540 06 Thessaloniki, Greece*

The synthesis, anti-inflammatory and analgesic activity of long-chain 2-amino-alcohols is reported.



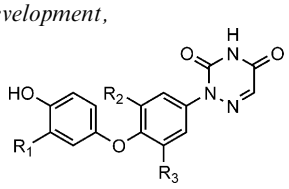
R=$(CH_2)_{12}CH_3$
$(CH_2)_5CH{=}CH(CH_2)_7CH_3$
$O(CH_2)_{11}CH_3$

Bioorg. Med. Chem. Lett. 13 (2003) 379

Discovery of a Novel Series of 6-Azauracil-Based Thyroid Hormone Receptor Ligands: Potent, TRβ Subtype-Selective Thyromimetics

Robert L. Dow,[a,*] Steven R. Schneider,[a] Ernest S. Paight,[a] Richard F. Hank,[a] Phoebe Chiang,[a] Peter Cornelius,[a] Eunsun Lee,[a] William P. Newsome,[a] Andrew G. Swick,[a] Josephine Spitzer,[a] Diane M. Hargrove,[a] Terrell A. Patterson,[a] Jayvardhan Pandit,[b] Boris A. Chrunyk,[b] Peter K. LeMotte,[b] Dennis E. Danley,[b] Michele H. Rosner,[b] Mark J. Ammirati,[b] Samuel P. Simons,[b] Gayle K. Schulte,[b] Bonnie F. Tate[b] and Paul DaSilva-Jardine[a]

[a]*Cardiovascular and Metabolic Diseases, Pfizer Global Research and Development, Groton, CT 06340, USA*
[b]*Exploratory Medicinal Sciences, Pfizer Global Research and Development, Groton, CT 06340, USA*



R_1 = $SO_2NR'R''$, C(O)NR'R''
R_2, R_3 = Cl, Me

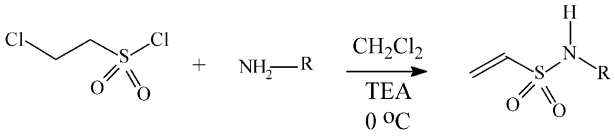
Bioorg. Med. Chem. Lett. 13 (2003) 383

Evaluation of Vinylsulfamides as Sulfhydryl Selective Alkylation Reagents in Protein Modification

Min Li,* Robert S. Wu, Jane S. C. Tsai and Salvatore J. Salamone

Roche Diagnostics Corporation, 9115Hague Road, Indianapolis, IN 46250, USA

Several model vinylsulfamides were prepared. Their excellent selective reactivity towards sulfhydryl group with regards to amino group has been demonstrated through kinetics study.



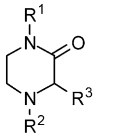
Bioorg. Med. Chem. Lett. 13 (2003) 387

Synthesis and Evaluation of δ-Lactams (Piperazones) as Elastase Inhibitors

Jürgen Seibel,[a] David Brown,[c] Augustin Amour,[c] Simon J. Macdonald,[b] Neil J. Oldham[a] and Christopher J. Schofield[a,*]

[a]*The Oxford Centre for Molecular Sciences and The Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, UK*
[b]*Medicinal Chemistry 1, GlaxoSmithKline Medicines Research Centre, Gunnels Wood Road, Stevenage SG1 2NY, UK*
[c]*Systems Research, GlaxoSmithKline Medicines Research Centre, Gunnels Wood Road, Stevenage SG1 2NY, UK*

A series of monocyclic δ-lactams (piperazones) was prepared and analysed as inhibitors of porcine pancreatic and human neutrophil elastase.



R^1 = Bn, R^2 = Ts, R^3 =

K_i = *ca.* 154 μM (PPE)

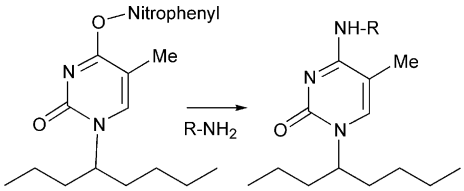
Bioorg. Med. Chem. Lett. 13 (2003) 391

Synthesis of Labelled PNA Oligomers by a Post-synthetic Modification Approach

Beatriz G. de la Torre and Ramon Eritja*

Institut de Biologia Molecular de Barcelona, C.S.I.C., Jordi Girona 18–26, E-08034 Barcelona, Spain

Fluorescently-labelled PNA oligomers are prepared using a reactive PNA monomer.



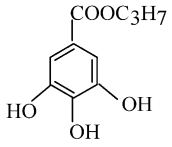
Bioorg. Med. Chem. Lett. 13 (2003) 395

Synthesis of Antioxidant Propyl Gallate Using Tannase from *Aspergillus Niger* Van Teighem in Nonaqueous Media

Shweta Sharma and Munishwar N. Gupta*

Chemistry Department, Indian Institute of Technology, Delhi, Hauz Khas, New Delhi 110016, India

The enzyme based synthesis of antioxidant food additive propyl gallate, is reported.



Propyl gallate

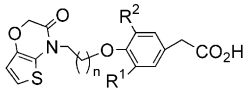
Bioorg. Med. Chem. Lett. 13 (2003) 399

Novel Thieno Oxazine Analogues as Antihyperglycemic and Lipid Modulating Agents

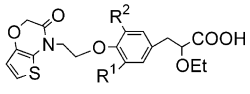
Saibal Kumar Das,[a,*] K. Anantha Reddy,[a] Chandrasekhar Abbineni,[a] Javed Iqbal,[a] J. Suresh,[b] M. Premkumar[b] and Ranjan Chakrabarti[b]

[a]*Discovery Chemistry, Dr. Reddy's Research Foundation, Bollaram Road, Miyapur, Hyderabad 500 050, India*
[b]*Discovery Biology, Dr. Reddy's Research Foundation, Bollaram Road, Miyapur, Hyderabad 500 050, India*

Synthesis and biological evaluation of **1** and **2** have been described.



1



2

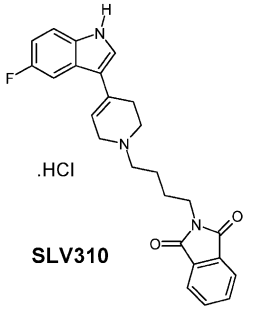
Bioorg. Med. Chem. Lett. 13 (2003) 405

SLV310, a Novel, Potential Antipsychotic, Combining Potent Dopamine D_2 Receptor Antagonism with Serotonin Reuptake Inhibition

Rolf van Hes, Pieter Smid,* Cees N. J. Stroomer, Koos Tipker, Martin Th. M. Tulp, Jan A. M. van der Heyden, Andrew C. McCreary, Mayke B. Hesselink and Chris G. Kruse

Solvay Pharmaceuticals Research Laboratories, PO Box 900, 1380 BA, Weesp, The Netherlands

SLV310 is presented as a novel antipsychotic, displaying the interesting combination of potent D_2 receptor antagonism and serotonin reuptake inhibition in one molecule. This paper describes the structure–activity relationship in a series of compounds leading to SLV310 together with pharmacological data showing the unique profile of this compound.



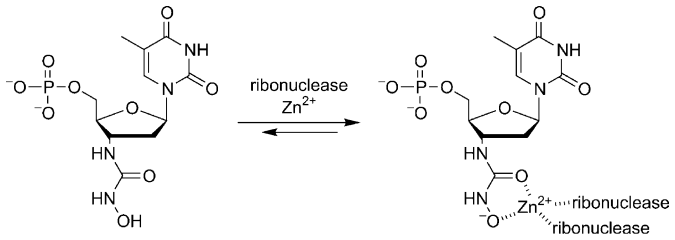
SLV310

Bioorg. Med. Chem. Lett. 13 (2003) 409

Zinc(II)-Mediated Inhibition of a Ribonuclease by an *N*-Hydroxyurea Nucleotide

Joshua J. Higgin,[a] Gennady I. Yakovlev,[b] Vladimir A. Mitkevich,[b] Alexander A. Makarov[b,*] and Ronald T. Raines[a,c,*]

[a]*Department of Chemistry, University of Wisconsin-Madison, Madison, WI 53706, USA*
[b]*Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Vavilov Street 32, 119991 Moscow, Russia*
[c]*Department of Biochemistry, University of Wisconsin-Madison, Madison, WI 53706, USA*



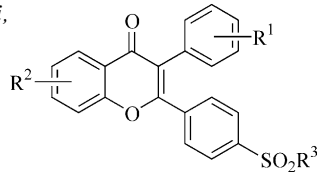
Bioorg. Med. Chem. Lett. 13 (2003) 413

2,3-Diarylbenzopyran Derivatives as a Novel Class of Selective Cyclooxygenase-2 Inhibitors

Yung Hyup Joo,* Jin Kwan Kim, Seon-Hwa Kang, Min-Soo Noh, Jun-Yong Ha, Jin Kyu Choi, Kyung Min Lim, Chang Hoon Lee and Shin Chung

Drug Discovery, AmorePacific Corporation R&D Center, 314-1 Bora-ri, Kiheung-eup, Yongin-si, Kyounggi-do 449-729, South Korea

A new series of benzopyrans has been synthesized and tested for cyclooxygenase inhibitory activity. Rational structural modifications were applied to potent COX-2 inhibitors to obtain the desired pharmacokinetic profiles for improved oral anti-inflammatory activity.



Bioorg. Med. Chem. Lett. 13 (2003) 419

QSAR Study on Solubility of Alkanes in Water and Their Partition Coefficients in Different Solvent Systems Using PI Index

Padmakar V. Khadikar,[a,*] Dheeraj Mandloi,[b] Amrit V. Bajaj[c] and Sheela Joshi[c]

[a]*Research Division, Laxmi Fumigation and Pest Control, 3, Khatipura, Indore 452007, India*
[b]*Institute of Engineering and Technology, D.A. University, Indore 452017, India*
[c]*School of Chemical Sciences, D.A. University, Indore 452017, India*

The aqueous solubility as well as partition coefficients in different solvent systems have been modeled using the newly introduced PI index. Results show that the PI index gives better results than the Wiener index (W).

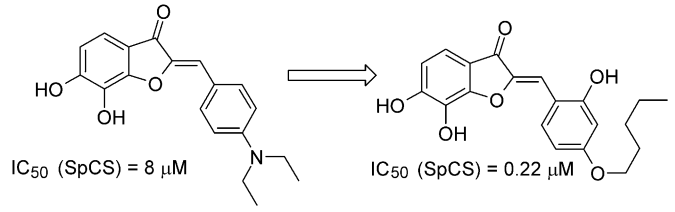
Bioorg. Med. Chem. Lett. 13 (2003) 423

A Series of 2(*Z*)-2-Benzylidene-6,7-dihydroxybenzofuran-3[2H]-ones as Inhibitors of Chorismate Synthase

Michael G. Thomas,* Chris Lawson, Nigel M. Allanson, Bruce W. Leslie, Joanna R. Bottomley, Andrew McBride and Oyinkan A. Olusanya

PanTherix Ltd., Todd Campus, West of Scotland Science Park, Glasgow G20 0XA, Scotland, UK

We have synthesized a series of 2(*Z*)-2-benzylidene-6,7-dihydroxybenzofuran-3[2H]-ones. Inhibitory activity of *Streptococcus pneumoniae* chorismate synthase is reported.

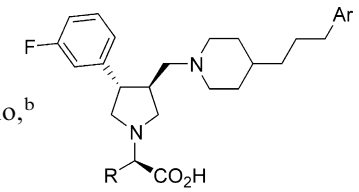


Bioorg. Med. Chem. Lett. 13 (2003) 427

1,3,4 Trisubstituted Pyrrolidine CCR5 Receptor Antagonists Bearing 4-Aminoheterocycle Substituted Piperidine Side Chains

Christopher A. Willoughby,[a,*] Keith G. Rosauer,[a] Jeffery J. Hale,[a] Richard J. Budhu,[a] Sander G. Mills,[a] Kevin T. Chapman,[a] Malcolm MacCoss,[a] Lorraine Malkowitz,[b] Martin S. Springer,[b] Sandra L. Gould,[b] Julie A. DeMartino,[b] Salvatore J. Siciliano,[b] Margaret A. Cascieri,[b] Anthony Carella,[c] Gwen Carver,[c] Karen Holmes,[c] William A. Schleif,[c] Renee Danzeisen,[c] Daria Hazuda,[c] Joseph Kessler,[c] Janet Lineberger,[c] Michael Miller[c] and Emilio A. Emini[c]

Optimization of 4(3-arylpropyl)piperidine derived 1,3,4-trisubstituted pyrrolidine CCR5 antagonists is reported.



9a; Ar = -2,4-$C_6H_3F_2$, R = -CH_2cBu
CCR5 IC_{50} = 0.1 nM
PBMC IC_{95} = 38 nM

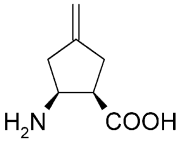
Bioorg. Med. Chem. Lett. 13 (2003) 433

Novel Antifungal β-Amino Acids: Synthesis and Activity Against *Candida albicans*

Joachim Mittendorf,[a,*] Franz Kunisch,[b] Michael Matzke,[a] Hans-Christian Militzer,[b] Axel Schmidt[c] and Wolfgang Schönfeld[c]

[a]*Medicinal Chemistry, Business Group Pharma, Bayer AG, D-42096 Wuppertal, Germany*
[b]*Central Research, Bayer AG, D-51368 Leverkusen, Germany*
[c]*Antiinfective Research, Business Group Pharma, Bayer AG, D-42096 Wuppertal, Germany*

A series of novel β-amino acids has been synthesized and tested for their in vitro antifungal activity against *Candida albicans*. A steep SAR was observed. β-Amino acid **21** (BAY 10-8888/PLD-118) revealed the most favourable activity-tolerability profile and was selected for clinical studies as a novel antifungal for the oral treatment of yeast infections.



BAY 10-8888 / PLD-118 **21**

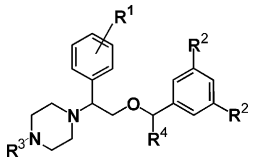
Bioorg. Med. Chem. Lett. 13 (2003) 437

Discovery of Orally Bioavailable NK_1 Receptor Antagonists

C. Genicot,[a,*] B. Christophe,[b] P. Collart,[d] M. Gillard,[b] L. Goossens,[e] J.-P. Hénichart,[e] M.-A. Lassoie,[a] F. Moureau,[a] M. Neuwels,[a] J.-M. Nicolas,[d] P. Pasau,[a] L. Quéré,[a] T. Ryckmans,[a] F. Stiernet,[c] T. Taverne[e] and B. J. Van Keulen[a]

[a]*Chemistry Department, UCB Pharma, Chemin du Foriest, B-1420, Braine-l'Alleud, Belgium*
[b]*In vitro Pharmacology, UCB Pharma, Chemin du Foriest, B-1420, Braine-l'Alleud, Belgium*
[c]*A/R Pharmacology, UCB Pharma, Chemin du Foriest, B-1420, Braine-l'Alleud, Belgium*
[d]*In vitro DMPK, R&D, UCB Pharma, Chemin du Foriest, B-1420, Braine-l'Alleud, Belgium*
[e]*Institut de Chimie Pharmaceutique A. Lespagnol, Université de Lille II, 3 rue du Professeur Laguesse, F-59006, Lille, France*

Benzyloxyphenethylpiperazines are a new class of high affinity NK_1 receptor antagonists. Oral bioavailability and selectivity can be fine tuned by the nature of the substituents on the basic nitrogen atom.



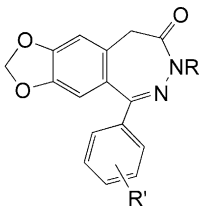
Bioorg. Med. Chem. Lett. 13 (2003) 443

Characterization of the Mechanism of Anticonvulsant Activity for a Selected Set of Putative AMPA Receptor Antagonists

Silvana Grasso,[a] Nicola Micale,[a] Maria Zappalà,[a] Alessandro Galli,[b] Chiara Costagli,[b] Frank S. Menniti[c] and Carlo De Micheli[d,*]

[a]*Dipartimento Farmaco-Chimico, Università di Messina, viale Annunziata, 98168 Messina, Italy*
[b]*Dipartimento di Farmacologia Preclinica e Clinica, Università di Firenze, viale G. Pieraccini, 6, 50134 Firenze, Italy*
[c]*Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340, USA*
[d]*Istituto di Chimica Farmaceutica, Università di Milano, viale Abruzzi, 42, 20131 Milano, Italy*

A selected set of 1-aryl-7,8-methylenedioxy-2,3-benzodiazepin-4-ones and their analogues were evaluated for their ability to bind the competitive and noncompetitive sites of AMPA receptors as well as glycine/NMDA receptor site.



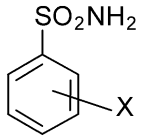
Bioorg. Med. Chem. Lett. 13 (2003) 447

Modelling of Carbonic Anhydrase Inhibitory Activity of Sulfonamides Using Molecular Negentropy

Vijay K. Agrawal[a] and Padmakar V. Khadikar[b,*]

[a]*QSAR and Computer Chemical Laboratories, A.P.S. University, Rewa, 486 003, India*
[b]*Research Division, Laxmi Fumigation and Pest Control Pvt. Ltd, 3, Khatipura, Indore 452 007, India*

The present paper deals with the modelling of carbonic anhydrase inhibitory activity of sulfonamides using molecular negentropy (*N*). Excellent results are obtained in multiple regression analysis upon introduction of indicator parameters. The results are critically discussed on the basis of statistical data obtained from regression analysis.



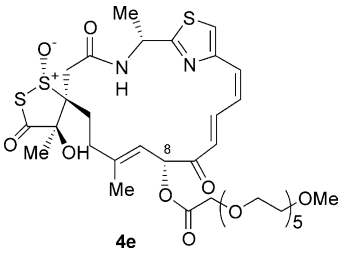
Bioorg. Med. Chem. Lett. 13 (2003) 455

Synthesis and Antitumor Activity of Novel C-8 Ester Derivatives of Leinamycin

Yutaka Kanda,* Tadashi Ashizawa, Kenji Kawashima, Shun-ichi Ikeda and Tatsuya Tamaoki

Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., 1188 Shimotogari, Nagaizumi-cho, Sunto-gun, Shizuoka 411-8731, Japan

Synthesis and antitumor activity of novel C-8 ester derivatives of leinamycin are reported. Introduction of acyl groups containing polyether moiety resulted in the derivatives, such as **4e**, with potent antitumor activity.



4e

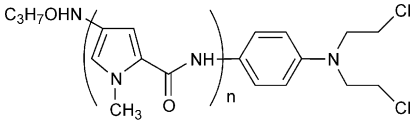
Bioorg. Med. Chem. Lett. 13 (2003) 459

Synthesis and Preliminary Cytotoxicity of Nitrogen Mustard Derivatives of Distamycin A

Yuqiang Wang,* Susan C. Wright and James W. Larrick

Panorama Research, Inc., 2462 Wyandotte Street, Mountain View, CA 94043, USA

Synthesis of new nitrogen mustard and distamycin A derivatives is reported.



1, n = 1
2, n = 2
3, n = 3

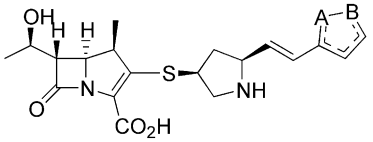
Bioorg. Med. Chem. Lett. 13 (2003) 463

Synthesis and Biological Evaluation of Novel 1β-Methylcarbapenems with Isothiazoloethenyl Side Chains

Yong Koo Kang,[a] Kyung Seok Lee,[a] Kyung Ho Yoo,[a] Kye Jung Shin,[a] Dong Chan Kim,[a] Chang-Seok Lee,[b] Jae Yang Kong[c] and Dong Jin Kim[a,*]

[a]*Medicinal Chemistry Research Center, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul 130-650, South Korea*
[b]*LG Life Sciences Ltd., R&D Park, PO Box 61, Yusung, Daejeon 305-380, South Korea*
[c]*Medicinal Science Division, Korea Research Institute of Chemical Technology, PO Box 107, Yusung, Daejeon 305-606, South Korea*

The synthesis of novel 1β-methylcarbapenems **1a**,**b** bearing isothiazoloethenyl moieties at C-5 position of pyrrolidine ring and their biological evaluation are described. Both compounds showed potent and well-balanced antibacterial activity as well as high stability to DHP-I. Especially, 5-isothiazole derivative **1a** exhibited excellent DHP-I stability and advanced pharmacokinetics profiles, compared to 5-isoxazole derivative **2**, imipenem, and meropenem.



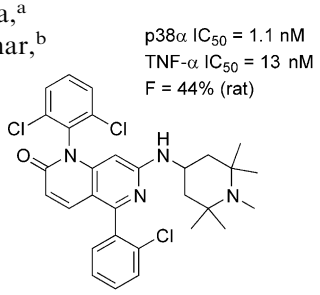
1a: A=S, B=N
1b: A=N, B=S

Bioorg. Med. Chem. Lett. 13 (2003) 467

p38 Inhibitors: Piperidine- and 4-Aminopiperidine-Substituted Naphthyridinones, Quinolinones, and Dihydroquinazolinones

Julianne A. Hunt,[a,*] Florida Kallashi,[a] Rowena D. Ruzek,[a] Peter J. Sinclair,[a] Ida Ita,[a] Sherrie X. McCormick,[a] James V. Pivnichny,[a] Cornelis E. C. A. Hop,[b] Sanjeev Kumar,[b] Zhen Wang,[b] Stephen J. O'Keefe,[c] Edward A. O'Neill,[c] Gene Porter,[c] James E. Thompson,[c] Andrea Woods,[c] Dennis M. Zaller[c] and James B. Doherty[a]

[a]*Department of Medicinal Chemistry, Merck & Co., Inc., PO Box 2000, Rahway, NJ 07065, USA*
[b]*Department of Drug Metabolism, Merck & Co., Inc., PO Box 2000, Rahway, NJ 07065, USA*
[c]*Department of Inflammation and Rheumatology, Merck & Co., Inc., PO Box 2000, Rahway, NJ 07065, USA*



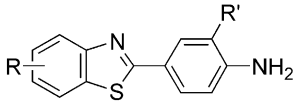
Bioorg. Med. Chem. Lett. 13 (2003) 471

Antitumour Benzothiazoles. Part 20:† 3′-Cyano and 3′-Alkynyl-Substituted 2-(4′-Aminophenyl)benzothiazoles as New Potent and Selective Analogues

Ian Hutchinson, Tracey D. Bradshaw, Charles S. Matthews, Malcolm F. G. Stevens and Andrew D. Westwell*

Cancer Research Laboratories, School of Pharmaceutical Sciences, University of Nottingham, Nottingham NG7 2RD, UK

The synthesis and in vitro antitumour evaluation of a series of new 3′-cyano and 3′-alkynyl-substituted 2-(4′-aminophenyl)benzothiazoles is reported.



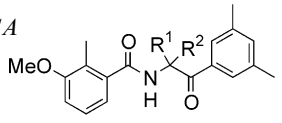
R = H, F; R' = CN, C≡CH

Bioorg. Med. Chem. Lett. 13 (2003) 475

Synthesis and SAR of α-Acylaminoketone Ligands for Control of Gene Expression

Colin M. Tice,[a,*] Robert E. Hormann,[a] Christine S. Thompson,[a] Jennifer L. Friz,[a] Caitlin K. Cavanaugh,[a] Enrique L. Michelotti,[b] Javier Garcia,[b,c] Ernesto Nicolas[c] and Fernando Albericio[c]

[a]*RHeoGene, PO Box 949, 727 Norristown Road, Spring House, PA 19477-0949, USA*
[b]*Rohm and Haas Company, PO Box 904, 727 Norristown Road, Spring House, PA 19477-0904, USA*
[c]*Department of Organic Chemistry, University of Barcelona, 08028-Barcelona, Spain*



R^1, R^2 = -$(CH_2)_4$-, Me, *i*-Pr

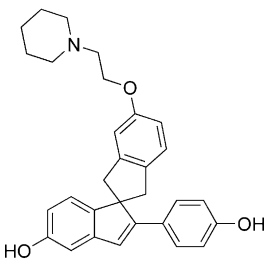
Bioorg. Med. Chem. Lett. 13 (2003) 479

2-Phenylspiroindenes: A Novel Class of Selective Estrogen Receptor Modulators (SERMs)

Timothy A. Blizzard,* Jerry D. Morgan, II, Ralph T. Mosley, Elizabeth T. Birzin, Katalin Frisch, Susan P. Rohrer and Milton L. Hammond

Merck Research Laboratories, RY800-B116, PO Box 2000, Rahway, NJ 07065, USA

A series of 2-phenylspiroindenes was prepared. The most active analogue (**2**) was found to be comparable in potency to raloxifene as an estrogen receptor ligand.



2

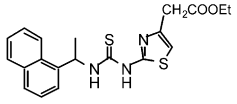
Bioorg. Med. Chem. Lett. 13 (2003) 485

Inhibition of Mast Cell Leukotriene Release by Thiourea Derivatives

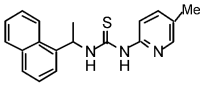
Taracad K. Venkatachalam,[a] Sanjive Qazi,[b] Peter Samuel[c] and Fatih M. Uckun[d,*]

[a]*Department of Chemistry, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[b]*Department of Immunology, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[c]*Department of Virology, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[d]*Drug Discovery Program, Parker Hughes Cancer Center, 2848 Patton Road, Roseville, MN 55113, USA*

Substituted halopyridyl, indolyl and naphthylthiourea compounds were synthesized and examined for their in vitro effects on IgE/FcεRI receptor mediated mast cell leukotriene release. Compounds 3004R and 3002R were identified as lead compounds with a IC_{50} of 2–5 nM.



(3004)



(3002)

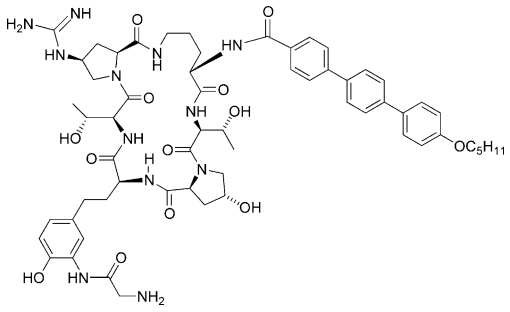
Bioorg. Med. Chem. Lett. 13 (2003) 489

Discovery, SAR, Synthesis, Pharmacokinetic and Biochemical Characterization of A-192411: A Novel Fungicidal Lipopeptide-(I)

Weibo Wang,* Qun Li, Lisa Hasvold, Beth Steiner, Daniel A. Dickman, Hong Ding, Akyio Clairborne, Hui-Ju Chen, David Frost, Robert C. Goldman, Kennan Marsh, Yu-Hua Hui, Brian Cox, Angela Nilius, Darlene Balli, Paul Lartey, Jacob J. Plattner and Youssef L. Bennani*

Infectious Diseases Research, Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL 60064, USA

The discovery, SAR, synthesis, PK and biochemical characterization of the cyclic lipopepetide A192411 is described.



Bioorg. Med. Chem. Lett. 13 (2003) 495

In Vivo Characterization of A-192411: A Novel Fungicidal Lipopeptide (II)

Jonathan A. Meulbroek,* Angela M. Nilius, Qun Li, Weibo Wang, Lisa Hasvold, Beth Steiner, Daniel A. Dickman, Hong Ding, David Frost, Robert C. Goldman, Paul Lartey, Jacob J. Plattner and Youssef L. Bennani*

Infectious Diseases Research, Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL 60064, USA

The in vivo characterization of the cyclic lipopepetide A192411 in both acute and chronic *candidiasis* settings are described.

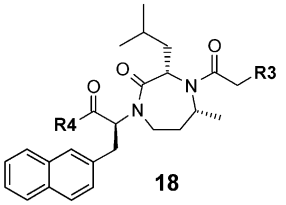
Bioorg. Med. Chem. Lett. 13 (2003) 499

1,4-Diazepane-2-ones as Novel Inhibitors of LFA-1

Sompong Wattanasin,[a,*] Rainer Albert,[b] Claus Ehrhardt,[b] Didier Roche,[a] Michael Sabio,[a] Ulrich Hommel,[b] Karl Welzenbach[b] and Gabriele Weitz-Schmidt[b]

[a]*Novartis Institute for Biomedical Research, Novartis Pharmaceuticals Corporation, 556 Morris Avenue, Summit, NJ 07901, USA*
[b]*Novartis Pharma A.G., Preclinical Research, Basel, Switzerland*

The design, synthesis, and biological evaluation of 1,4-diazepane-2-ones as novel LFA-1 antagonists from a scaffold-based combinatorial library are described. Initial optimization of the library lead has resulted in high-affinity antagonists of the LFA-1/ICAM-1 interaction, such as compounds **18d** and **18e** with IC_{50} values of 110 and 70 nM, respectively.



18

18d: R_3=6-quinolyl; R_4=NH_2
18e: R_3=3-quinolyl; R_4=NH_2

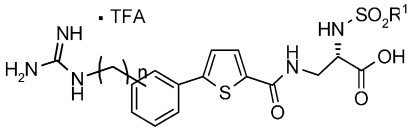
Bioorg. Med. Chem. Lett. 13 (2003) 503

Thiophene-Based Vitronectin Receptor Antagonists

Monica Bubenik,* Karen Meerovitch, Frédéric Bergeron, Giorgio Attardo and Laval Chan

Shire BioChem Inc., 275 Armand-Frappier Blvd., Laval, Québec, Canada H7V 4A7

A series of $\alpha_v\beta_3$ antagonists based on a thiophene scaffold were synthesized via two routes and evaluated for in vitro biological activity. We have identified several structurally similar antagonists with different selectivities towards $\alpha_{IIb}\beta_3$, $\alpha_v\beta_5$ and $\alpha_5\beta_1$ at the cellular level. In addition, these antagonists exerted an antiangiogenic effect in the chick chorioallantoic membrane (CAM) assay.



o, *m*, *p*; n= 0, 1; R_1=Ph, Mes

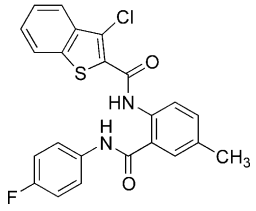
Bioorg. Med. Chem. Lett. 13 (2003) 507

Structure–Activity Relationships of Substituted Benzothiophene-anthranilamide Factor Xa Inhibitors

Yuo-Ling Chou,* David D. Davey, Keith A. Eagen, Brian D. Griedel, Rushad Karanjawala, Gary B. Phillips, Karna L. Sacchi, Kenneth J. Shaw, Shung C. Wu, Dao Lentz, Amy M. Liang, Lan Trinh, Michael M. Morrissey and Monica J. Kochanny*

Departments of Medicinal Chemistry and Molecular Pharmacology, Berlex Biosciences, PO Box 4099, Richmond, CA 94804-0099, USA

A novel benzothiophene-anthranilamide compound was identified by high throughput screening as a potent, non-amidine factor Xa inhibitor. A series of modifications of the three aromatic groups was investigated, leading to the discovery of subnanomolar inhibitors.



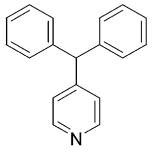
Bioorg. Med. Chem. Lett. 13 (2003) 513

Pharmacophore-Based Discovery of Substituted Pyridines as Novel Dopamine Transporter Inhibitors

Istvan J. Enyedy,[a] Sukumar Sakamuri,[a] Wahiduz A. Zaman,[b] Kenneth M. Johnson[b] and Shaomeng Wang[a,*]

[a]*Departments of Internal Medicine and Medicinal Chemistry, University of Michigan, Ann Arbor, MI 48109-0934, USA*
[b]*Department of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77555-1031, USA*

The discovery of novel dopamine transporter inhibitors using a new pharmacophore model through 3D-database pharmacophore searching is described. A simple substituted pyridine has a K_i value of 79 nM in inhibition of dopamine reuptake.



K_i = 79 nM

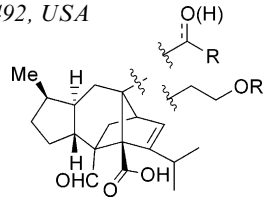
Bioorg. Med. Chem. Lett. 13 (2003) 519

Sordaricin Antifungal Agents

Claude A. Quesnelle,[a,*] Patrice Gill,[a] Marco Dodier,[a] Denis St. Laurent,[b] Michael Serrano-Wu,[b] Anne Marinier,[a] Alain Martel,[a] Charles E. Mazzucco,[b] Terry M. Stickle,[b] John F. Barrett,[b] Dolatrai M. Vyas[b] and Balu N. Balasubramanian[b]

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

The synthesis of antifungal agents derived from sordarin is reported.



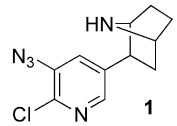
Bioorg. Med. Chem. Lett. 13 (2003) 525

5-Azidoepibatidine: An Exceptionally Potent Photoaffinity Ligand for Neuronal α4β2 and α7 Nicotinic Acetylcholine Receptors

Nanjing Zhang, Motohiro Tomizawa and John E. Casida*

Environmental Chemistry and Toxicology Laboratory, Department of Environmental Science, Policy and Management, University of California, Berkeley, CA 94720-3112, USA

Racemic 5-azidoepibatidine [(±)-**1**] was synthesized via 5-aminoepibatidine as a candidate photoaffinity ligand with exceptionally high affinity at the mammalian neuronal nicotinic receptors (K_i values of 0.027 nM for α4β2 and 9.7 nM for α7) and excellent photoreactivity.



K_i = 0.027 nM for α4β2
9.7 nM for α7

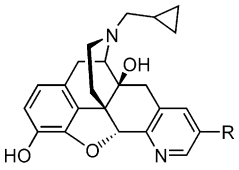
Bioorg. Med. Chem. Lett. 13 (2003) 529

Synthesis, Opioid Receptor Binding, and Functional Activity of 5′-Substituted 17-Cyclopropylmethylpyrido[2′,3′:6,7]morphinans

Subramaniam Ananthan,[a,*] Hollis S. Kezar, III,[a] Surendra K. Saini,[a] Naveen K. Khare,[a] Peg Davis,[b] Christina M. Dersch,[c] Frank Porreca[b] and Richard B. Rothman[c]

[a]*Organic Chemistry Department, Southern Research Institute, Birmingham, AL 35255, USA*
[b]*Department of Pharmacology, The University of Arizona Health Sciences Center, Tucson, AZ 85724, USA*
[c]*Clinical Psychopharmacology Section, IRP, National Institute on Drug Abuse, Baltimore, MD 21224, USA*

A series of 5′-substituted analogues of **3** were synthesized and evaluated. While a pyrrole substituent (**6h**) improved the δ selectivity and antagonist potency of **3**, a guanidine group (**6i**) transformed it to a κ selective antagonist.



3, R = H
6h, R = 1-pyrrolyl
6i, R = NH-C(=NH)-NH2

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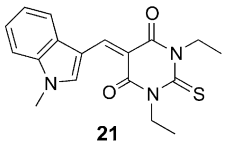
Both 5-Arylidene-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-diones and 3-Thioxo-2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-1-ones are Light-Dependent Tumor Necrosis Factor-α Antagonists

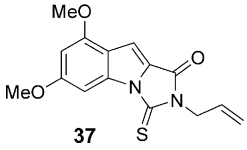
Matthew E. Voss, Percy H. Carter,* Andrew J. Tebben, Peggy A. Scherle, Gregory D. Brown, Lorin A. Thompson, Meizhong Xu, Yvonne C. Lo, Gengjie Yang, Rui-Qin Liu, Paul Strzemienski, J. Gerry Everlof, James M. Trzaskos and Carl P. Decicco

Bristol-Myers Squibb Pharmaceuticals, Experimental Station, Rt. 141 & Henry Clay Road, Wilmington, DE 19880-0500, USA

Compounds such as **21** (IC_{50} = 0.13 μM) and **37** (IC_{50} = 0.28 μM) are selective, but light-dependent, inhibitors of TNFRc1.



21



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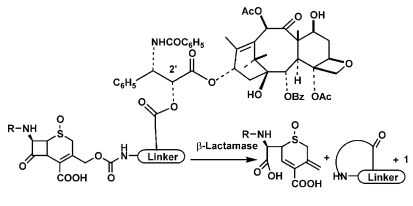
Cephalosporin Prodrugs of Paclitaxel for Immunologically Specific Activation by L-49-sFv-β-Lactamase Fusion Protein

Vivekananda M. Vrudhula,* David E. Kerr, Nathan O. Siemers, Gene M. Dubowchik and Peter D. Senter

Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA

Paclitaxel conjugates of 7-phenylacetamidocephalosporanic acid were prepared as prodrugs for site specific activation by targeted β-lactamase. Immunologically specific activation of the prodrug **5** containing 3,3-dimethyl-4-amino-butyric acid as linker in combination with the fusion protein L-49-sFv-β-lactamase was demonstrated in vitro on 3677 melanoma cells.



Compd	R	Linker
3	$PhCH_2CO$	$-(CH_2)_3-$
5	$PhCH_2CO$	$-CH_2-C(Me)_2-CH_2-$
6	$PhCH_2CO$	

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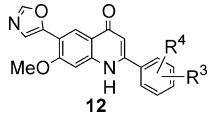
Novel Inhibitors of IMPDH: A Highly Potent and Selective Quinolone-Based Series

Scott H. Watterson,* Marianne Carlsen, T. G. Murali Dhar, Zhongqi Shen, William J. Pitts, Junqing Guo, Henry H. Gu, Derek Norris, John Chorba, Ping Chen, Daniel Cheney, Mark Witmer, Catherine A. Fleener, Katherine Rouleau, Robert Townsend, Diane L. Hollenbaugh and Edwin J. Iwanowicz

Bristol-Myers Squibb PRI, PO Box 400, Princeton, NJ 08543-4000, USA

The preparation and in vitro biological evaluation of a novel series of potent, selective quinolone-based small molecule inhibitors of IMPDH are described.



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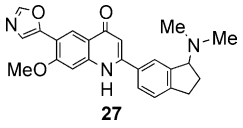
Quinolone-Based IMPDH Inhibitors: Introduction of Basic Residues on Ring D and SAR of the Corresponding Mono, Di and Benzofused Analogues

T. G. Murali Dhar,* Scott H. Watterson, Ping Chen, Zhongqi Shen, Henry H. Gu, Derek Norris, Marianne Carlsen, Kristin D. Haslow, William J. Pitts, Junqing Guo, John Chorba, Catherine A. Fleener, Katherine A. Rouleau, Robert Townsend, Diane Hollenbaugh and Edwin J. Iwanowicz*

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

The synthesis and SAR of quinolone-based IMPDH inhibitors derived from the introduction of basic residues are described. Improvement in aqueous solubility was observed.



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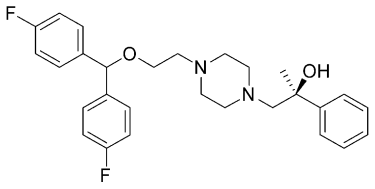
Synthesis and Dopamine Transporter Affinity of Chiral 1-[2-[Bis(4-fluorophenyl)methoxy]ethyl]-4-(2-hydroxypropyl)piperazines as Potential Cocaine Abuse Therapeutic Agents

Ling-Wei Hsin,[a] Thomas Prisinzano,[a] Chavon R. Wilkerson,[a] Christina M. Dersch,[b] Robert Horel,[b] Arthur E. Jacobson,[a] Richard B. Rothman[b] and Kenner C. Rice[a,*]

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



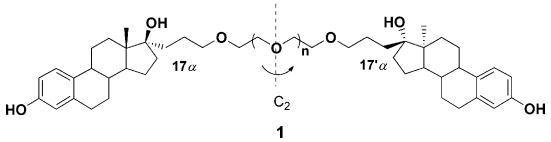
Bioorg. Med. Chem. Lett. 13 (2003) 557

A Facile Synthesis of C_2-Symmetric 17β-Estradiol Dimers

Daniel Rabouin,[a] Valérie Perron,[a] Blaise N'Zemba[a], René C.-Gaudreault[b] and Gervais Bérubé[a,*]

[a]*Département de Chimie-Biologie, Université du Québec à Trois-Rivières, C.P. 500, Trois-Rivières, Québec, Canada G9A 5H7*
[b]*Unité de Biotechnologie, Institut des Biomatériaux de Québec, C.H.U.Q., Hôpital Saint-François d'Assise, 10 Rue de l'Espinay, Québec, Canada G1L 3L5*

A rapid and efficient synthesis of a series of C_2-symmetric 17β-estradiol dimers is reported. Some of the dimers show selective cytotoxic activity against the MCF-7 (ER^+) human breast cancer cell line.



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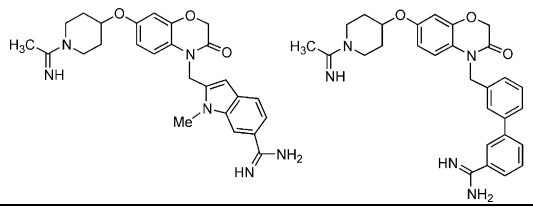
Design, Synthesis and Structure–Activity Relationships of Benzoxazinone-Based Factor Xa Inhibitors

Wenrong Huang, Penglie Zhang,* Jingmei F. Zuckett, Lingyan Wang, John Woolfrey, Yonghong Song, Zhaozhong J. Jia, Lane A. Clizbe, Ting Su, Katherine Tran, Brian Huang, Paul Wong, Uma Sinha, Gary Park, Andrea Reed, John Malinowski, Stanley J. Hollenbach, Robert M. Scarborough and Bing-Yan Zhu*

Millennium Pharmaceuticals, Inc., 256 E. Grand Avenue, South San Francisco, CA 94080, USA

Factor Xa inhibitors with a benzoxazinone template were designed and synthesized.



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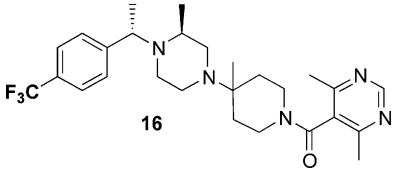
Piperazine-Based CCR5 Antagonists as HIV-1 Inhibitors. III: Synthesis, Antiviral and Pharmacokinetic Profiles of Symmetrical Heteroaryl Carboxamides

Stuart W. McCombie, Jayaram R. Tagat,* Susan F. Vice, Sue-Ing Lin, Ruo Steensma, Anandan Palani, Bernard R. Neustadt, Bahige M. Baroudy, Julie M. Strizki, Michael Endres, Kathleen Cox, Niya Dan and Chuan-Chu Chou

Schering-Plough Research Institute, 2015 Galloping Hill Road, K-15-2B-2800, Kenilworth, NJ 07033, USA

Compound **16** exemplifies a new class of CCR5 antagonists with improved overall profile over previous compounds.



16

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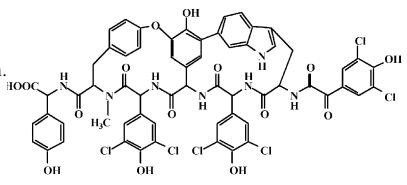
Condensed Aromatic Peptide Family of Microbial Metabolites, Inhibitors of CD28–CD80 Interactions

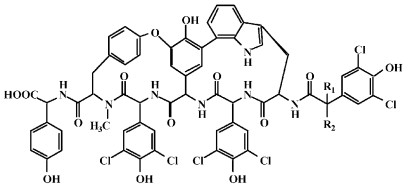
Vinod R. Hegde,* Mohindar S. Puar, Ping Dai, Mahesh Patel, Vincent P. Gullo, Tze-Ming Chan, Jack Silver, Birendra N. Pramanik and Chung-Her Jenh

Schering Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033, USA

Three condensed aromatic peptides SCH79235 (**1**), SCH79236 (**2**), and SCH204698 (**3**) were isolated from the fermentation broth of a *Streptomycete* microorganism. The structure of SCH204698 (**3**) was established by extensive NMR spectral data. All these compounds exhibited good activity against CD28–CD80 binding with an IC_{50} of 0.42, 0.38 and 0.22 μM, respectively.



1. Complestatin (Chloropeptin II)



2. R_1 & R_2 = O (Chloropeptin I)
3. R_1 = -OH, R_2 = CH_2COCH_3

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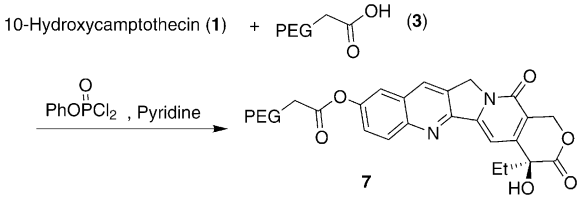
Selective Phenolic Acylation of 10-Hydroxycamptothecin Using Poly (Ethylene Glycol) Carboxylic Acid

Richard B. Greenwald,* Yun H. Choe and Dechun Wu

Enzon, Inc., 20 Kingsbridge Road, Piscataway, NJ 08854, USA



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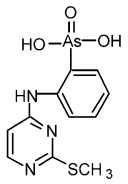
Organic Phenyl Arsonic Acid Compounds with Potent Antileukemic Activity

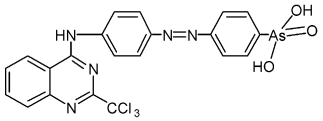
Xing-Ping Liu, Rama Krishna Narla and Fatih M. Uckun*

Parker Hughes Cancer Center, Parker Hughes Institute, 2699 Patton Road, St. Paul, MN 55113, USA

The organic arsonic acid compounds 2-trichloromethyl-4-[4′-(4″-phenylazo)phenylarsonic acid]aminoquinazoline (**PHI-P518**) and 2-methylthio-4-(2′-phenylarsonic acid)aminopyrimidine (**PHI-P381**) exhibit potent antileukemic activity at low micromolar concentrations.



PHI-P381



PHI-P518