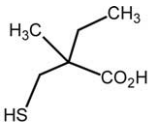
Bioorg. Med. Chem. 11 (2003) 4685

Synthesis and Evaluation of α,α-Disubstituted-3-mercaptopropanoic Acids as Inhibitors for Carboxypeptidase A and Implications with Respect to Enzyme Inhibitor Design

Hyun Soo Lee and Dong H. Kim

Center for Integrated Molecular Systems, and Division of Molecular and Life Sciences, Pohang University of Science and Technology, San 31 Hyojadong, Pohang 790-784, South Korea



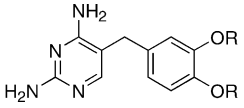
K_i = 0.11±0.012 μM

Bioorg. Med. Chem. 11 (2003) 4693

2,4-Diaminopyrimidines as Inhibitors of Leishmanial and Trypanosomal Dihydrofolate Reductase

Didier Pez,[a] Isabel Leal,[b] Fabio Zuccotto,[a] Cyrille Boussard,[a] Reto Brun,[c] Simon L. Croft,[d] Vanessa Yardley,[d] Luis M. Ruiz Perez,[b] Dolores Gonzalez Pacanowska[b] and Ian H. Gilbert[a,*]

[a]*Welsh School of Pharmacy, Cardiff University, Redwood Building, King Edward VII Avenue, Cardiff CF10 3XF, UK*
[b]*Instituto de Parasitologia y Biomedicina, Consejo Superior de Investigaciones Cientificas, C/ Ventanilla 11, 18001-Granada, Spain*
[c]*Swiss Tropical Institute, Socinstrasse 57, CH-4002 Basel, Switzerland*
[d]*London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK*



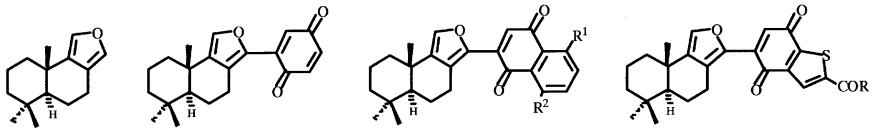
Bioorg. Med. Chem. 11 (2003) 4713

Studies on Quinones. Part 38: Synthesis and Leishmanicidal Activity of Sesquiterpene 1,4-Quinones

Jaime A. Valderrama,[a,*] Julio Benites,[a] Manuel Cortés,[a,*] Hernán Pessoa-Mahana,[b] Eric Prina[c] and Alain Fournet[d]

[a]*Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 306, Santiago-22, Chile*
[b]*Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile, Casilla 233, Santiago-1, Chile*
[c]*Groupe de Recherche sur les interactions macrophage-Leishmania, Unité d'Immunophysiologie et Parasitisme Intracellulaire, Institut Pasteur, rue du Dr. Roux 75724, Paris Cedex, France*
[d]*Institut de Recherche pour le Développment (IRD), 213 rue La Fayette 75480, Paris Cedex, France*

(+)-Euryfuran **1** reacts with benzo, naphtho, and benzo[*b*]thiophene-1,4-quinones in acetic acid to give the sesquiterpene 1,4-quinones **3**, **5**, **7**, **8**, **10**, **12**, and **14**. The reported quinones possess in vitro activity against *Leismania amazonensis*.

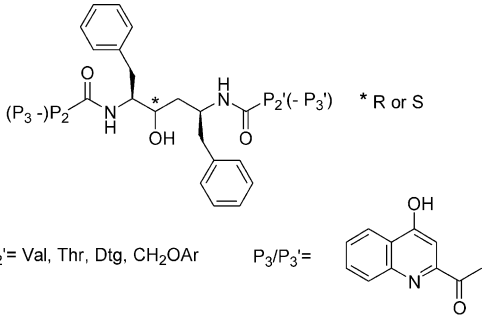


Bioorg. Med. Chem. 11 (2003) 4719

Small Hydroxyethylene-Based Peptidomimetics Inhibiting Both HIV-1 and *C. albicans* Aspartic Proteases

Alessandro Tossi,[a,b,*] Fabio Benedetti,[b,c] Stefano Norbedo,[b,c] Damiano Skrbec,[a] Federico Berti[b,c] and Domenico Romeo[a,b]

[a]*Department of Biochemistry, Biophysics and Macromolecular Chemistry, University of Trieste, Via Giorgieri 1, I-34127 Trieste, Italy*
[b]*Centre of Excellence on Biocrystallography, University of Trieste, Via Giorgieri 1, I-34127 Trieste, Italy*
[c]*Department of Chemical Sciences, University of Trieste, Via Giorgieri 1, I-34127 Trieste, Italy*



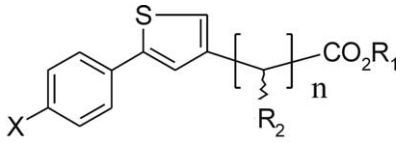
Bioorg. Med. Chem. 11 (2003) 4729

Synthesis and Structure–Activity Relationships of 5-Phenylthiophenecarboxylic Acid Derivatives as Antirheumatic Agents

Toshiya Noguchi,* Masahiro Hasegawa, Kazuyuki Tomisawa and Morihiro Mitsukuchi

Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., 403, Yoshino-cho, 1-chome, Kita-ku, Saitama-city, Saitama 330-8530, Japan

5-Phenylthiophenecarboxylic acid deriveatives were prepared.



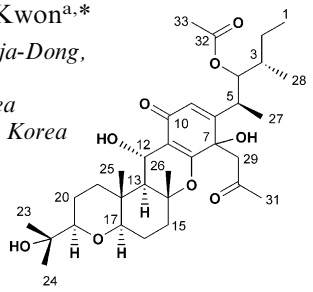
Bioorg. Med. Chem. 11 (2003) 4743

Cochlioquinone A1, a New Anti-Angiogenic Agent from *Bipolaris zeicola*

Hye Jin Jung,[a] Hyang Burm Lee,[b] Chi-Hwan Lim,[c] Chang-Jin Kim[b] and Ho Jeong Kwon[a,*]

[a]*Department of Bioscience and Biotechnology, Institute of Bioscience, Sejong University, 98 Kunja-Dong, Kwangjin-Gu, Seoul 143-747, South Korea*
[b]*Korea Research Institute of Bioscience and Biotechnology, Yusong, Taejon 305-600, South Korea*
[c]*College of Agriculture and Life Science, Chungnam National University, Taejon 305-760, South Korea*

Cochlioquinone A1 (CoA1) is a new anti-angiogenic agent isolated from a fungal strain, *Bipolaris zeicola*.



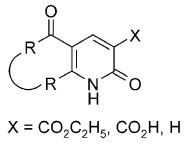
Bioorg. Med. Chem. 11 (2003) 4749

Synthesis and Pharmacological Characterization of Functionalized 2-Pyridones Structurally Related to the Cardiotonic Agent Milrinone

Paola Fossa,[a] Giulia Menozzi,[a] Paola Dorigo,[b] Maura Floreani[b] and Luisa Mosti[a,*]

[a]*Department of Pharmaceutical Sciences, University of Genova, Viale Benedetto XV 3, 16132 Genova, Italy*
[b]*Department of Pharmacology and Anaesthesiology, Pharmacology Section, University of Padova, Largo Meneghetti 2, 25131 Padova, Italy*

A new positive inotropic agent, milrinone analogue, with a specific mechanism of action via PDE3 inhibition is presented.

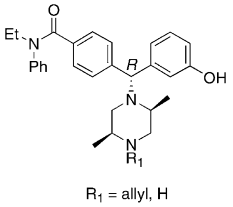


Bioorg. Med. Chem. 11 (2003) 4761

Diaryldimethylpiperazine Ligands with μ- and δ-Opioid Receptor Affinity: Synthesis of (+)-4-[(αR)-α-(4-allyl-(2S,5S)-dimethylpiperazin-1-yl)-(3-hydroxyphenyl)methyl]-*N*-ethyl-*N*-phenylbenzamide and (−)-4-[(αR)-α-(2S,5S)-dimethylpiperazin-1-yl)-(3-hydroxyphenyl)methyl]-*N*-ethyl-*N*-phenylbenzamide

In Jong Kim,[a] Thomas Ullrich,[a] James W. Janetka,[a] M. Scott Furness,[a] Arthur E. Jacobson,[a,*] Richard B. Rothman,[b] Christina M. Dersch,[b] Judith L. Flippen-Anderson,[c] Clifford George[c] and Kenner C. Rice[a,*]

[a]*Laboratory of Medicinal Chemistry, Building 8, Room B1-23, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Department of Health and Human Services, Bethesda, MD 20892, USA*
[b]*Clinical Psychopharmacology Section, National Institute on Drug Abuse, Addiction Research Center, Department of Health and Human Services, Baltimore, MD 21224, USA*
[c]*Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, DC 20375, USA*



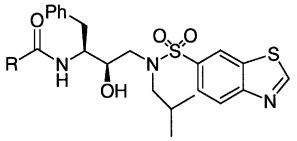
Bioorg. Med. Chem. 11 (2003) 4769

Discovery of Novel Benzothiazolesulfonamides as Potent Inhibitors of HIV-1 Protease

Srinivasan R. Nagarajan,[a,*] Gary A. De Crescenzo,[a] Daniel P. Getman,[a] Hwang-Fun Lu,[a] James A. Sikorski,[a] Jeffrey L. Walker,[a] Joseph J. McDonald,[a] Kathryn A. Houseman,[b] Geralyn P. Kocan,[b] Nandini Kishore,[a] Pramod P. Mehta,[a] Christie L. Funkes-Shippy[a] and Lisa Blystone[a]

[a]*Pfizer Global Research and Development, Pfizer Inc., 700 Chesterfield Parkway West, Chesterfield, MO 63017, USA*
[b]*Pfizer Global Research and Development, Pfizer Inc., 4901 Searle Parkway, Skokie, IL 60077, USA*

The human immunodeficiency virus (HIV) has been shown to be the causative agent for AIDS. Protease inhibitors have been useful in combating the disease. The inhibitors incorporate a variety of isosteres including the hydroxyethylurea at the protease cleavage site. We have shown that the replacement of t-butylurea moiety by benzothiazolesulfonamide provided inhibitors with improved potency, antiviral activity and good oral bioavailability.

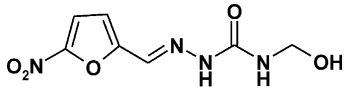


Bioorg. Med. Chem. 11 (2003) 4779

Synthesis and In Vitro Evaluation of Potential Antichagasic Hydroxymethylnitrofurazone (NFOH-121): A New Nitrofurazone Prodrug

Man-Chin Chung,[a] Rafael Victório Carvalho Güido,[a] Tatiane Favarato Martinelli,[b] Marinei Ferreira Gonçalves,[c] Michelle Carneiro Polli,[b] Katia Cirlene Alves Botelho,[b] Eliana Aparecida Varanda,[d] Walter Colli,[c] M. Terêsa M. Miranda[c] and Elizabeth Igne Ferreira[b,*]

[a]*Lapdesf- Laboratório de Pesquisa e Desenvolvimento de Fármacos, Departamento de Fármacos e Medicamentos, Faculdade de Ciências Farmacêuticas, UNESP, Araraquara, Caixa Postal 502, CEP 14.801-902, SP, Brazil*
[b]*Departamento de Farmácia, Faculdade de Ciências Farmacêuticas, USP, Caixa Postal 66083, CEP 05389-970, SP, Brazil*
[c]*Departamento de Bioquímica, Instituto de Química, USP, Caixa Postal 26077, CEP 05513-970, SP, Brazil*
[d]*Departamento de Ciências Biológicas, Faculdade de Ciências Farmacêuticas, UNESP, Araraquara, Caixa Postal 502, CEP 14.801-902, SP, Brazil*



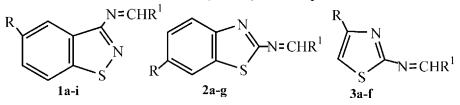
Bioorg. Med. Chem. 11 (2003) 4785

Synthesis and Biological Evaluation of Benzo[*d*]isothiazole, Benzothiazole and Thiazole Schiff Bases

Paola Vicini,[a,*] Athina Geronikaki,[b] Matteo Incerti,[a] Bernadetta Busonera,[c] Graziella Poni,[c] Carla Alba Cabras[c] and Paolo La Colla[c]

[a]*Dipartimento Farmaceutico Università degli Studi Parma, Parco Area delle Scienze 27/A, 43100 Parma, Italy*
[b]*Department of Pharmaceutical Chemistry, School of Pharmacy, Aristotelian University of Thessaloniki, Thessaloniki 54006, Greece*
[c]*Dipartimento di Scienze e Tecnologie Biomediche, Sez. Microbiologia e Virologia Generale e Biotecnologie Microbiche, Università di Cagliari, Cittadella Universitaria di Monserrato, S.S. 554, Km 4.500, 09042 Monserrato (CA), Italy*

Three new series of benzo[*d*]isothiazole, benzothiazole and thiazole Shiff bases were synthesized and tested in vitro for their antiviral, antimicrobial, antimycobacterial and antiproliferative activity.

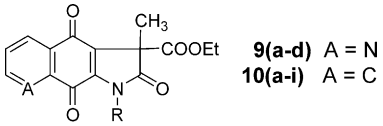


Bioorg. Med. Chem. 11 (2003) 4791

Synthesis and Cytotoxicity Evaluation of Pyridin[2,3-*f*]indole-2,4,9-trione and Benz[*f*]indole-2,4,9-trione Derivatives

Hyun-Jung Lee,[a] So-Young Park,[a] Jin Sung Kim,[a] Hyun Min Song,[a] Myung-Eun Suh[a,*] and Chong-Ock Lee[b]

[a]*Department of Medicinal Chemistry, College of Pharmacy, Ewha Woman's University, Seoul 120-750, South Korea*
[b]*Pharmaceutical Screening Division, Korea Research Institute of Chemical Technology, TaeJon 305-606, South Korea*

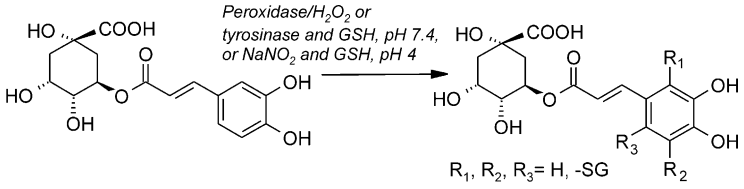


Bioorg. Med. Chem. 11 (2003) 4797

Oxidative Conjugation of Chlorogenic Acid with Glutathione: Structural Characterization of Addition Products and a New Nitrite-Promoted Pathway

Lucia Panzella, Alessandra Napolitano and Marco d'Ischia*

Department of Organic Chemistry and Biochemistry, University of Naples 'Federico II', Via Cinthia 4, I-80126 Naples, Italy



Bioorg. Med. Chem. 11 (2003) 4807

Design, Synthesis and Pharmacological Profile of Novel Dopamine D2 Receptor Ligands

Ricardo Menegatti,[a,b] Anna C. Cunha,[c] Vítor F. Ferreira,[c] Edna F. R. Perreira,[d] Ahmed El-Nabawi,[d] Amira T. Eldefrawi,[d] Edson X. Albuquerque,[d,e] Gilda Neves,[f] Stela M. K. Rates,[f] Carlos A. M. Fraga[a,b] and Eliezer J. Barreiro[a,b,*]

[a]*Laboratório de Avaliação e Síntese de Substâncias Bioativas (LASSBio), Faculdade de Farmácia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, PO Box 68006, RJ 21944-970, Brazil*
[b]*Instituto de Química, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil*
[c]*Departamento de Química Orgânica, Universidade Federal Fluminense, Rio de Janeiro, RJ, Brazil*
[d]*Department of Pharmacology and Experimental Therapeutic, University of Maryland, School of Medicine, Baltimore, MD 21201, USA*
[e]*Departamento de Farmacologia Básica e Clínica, Instituto de Ciências Biomédicas, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil*
[f]*Faculdade de Farmácia, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil*

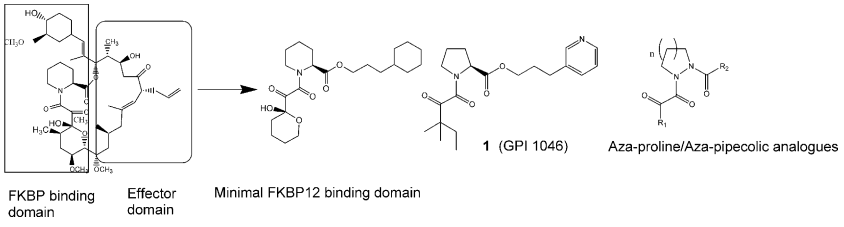
The synthesis and in vitro dopamine receptor ligand profile of new pyrazole and 1,2,3-triazole *N*-phenylpiperazines **3**–**5** is reported.

Bioorg. Med. Chem. 11 (2003) 4815

Synthesis, Molecular Modeling and Biological Evaluation of Aza-Proline and Aza-Pipecolic Derivatives as FKBP12 Ligands and Their In Vivo Neuroprotective Effects

Douglas E. Wilkinson, Bert E. Thomas, IV, David C. Limburg, Agnes Holmes, Hansjorg Sauer, Douglas T. Ross, Raj Soni, Yi Chen, Hong Guo, Pamela Howorth, Heather Valentine, Dawn Spicer, Mike Fuller, Joseph P. Steiner, Gregory S. Hamilton and Yong-Qian Wu*

Department of Research, Guilford Pharmaceuticals, Inc., Baltimore, MD 21224, USA

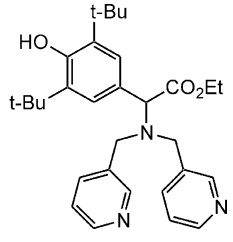


Bioorg. Med. Chem. 11 (2003) 4827

Inhibitors of Lipoprotein(a) Assembly

Karen E. Sexton,[a] Helen T. Lee,[a,*] Mark Massa,[c] Janak Padia,[d] William C. Patt,[a] Peggy Liao,[e] Jason K. Pontrello,[f] Bruce D. Roth,[a] Mark A. Spahr[b] and Randy Ramharack[b]

[a]*Department of Medicinal Chemistry, Pfizer Global Research and Development, 2800 Plymouth Road, Ann Arbor, MI, 48105, USA*
[b]*Department of Molecular Biology, Pfizer Global Research and Development, 2800 Plymouth Road, Ann Arbor, MI, 48105, USA*
[c]*Monsanto, St. Louis, MO, USA*
[d]*ChemRX Advanced Technologies, Phoenix, AZ, USA*
[e]*Duke University, Raleigh, NC, USA*
[f]*University of Wisconsin-Madison, Madison, WI, USA*



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