Bioorg. Med. Chem. 11 (2003) 4161

New Strategies for the Synthesis of A_3 Adenosine Receptor Antagonists

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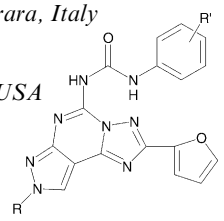
Novel synthetic strategies and biological evaluation of new A_3 adenosine receptor antagonists have been described.



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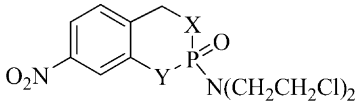
Nitrobenzocyclophosphamides as Potential Prodrugs for Bioreductive Activation: Synthesis, Stability, Enzymatic Reduction, and Antiproliferative Activity in Cell Culture

Zhuorong Li,[a] Jiye Han,[a] Yongying Jiang,[a] Patrick Browne,[b] Richard J. Knox[b] and Longqin Hu[a,*]

[a]*Department of Pharmaceutical Chemistry, Ernest Mario School of Pharmacy, Rutgers, the State University of New Jersey, 160 Frelinghuysen Road, Piscataway, NJ 08854, USA*
[b]*Enact Pharma PLC, Porton Down Science Park, Salisbury, Wiltshire, SP4 0JQ, UK*

A series of four nitrobenzocyclophosphamide analogues were synthesized and evaluated as substrates of *E. coli* nitroreductase and as potential prodrugs for bioreductive activation in gene-directed enzyme prodrug therapy.



X, Y = O or NH

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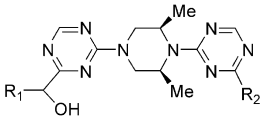
Design and Synthesis of a Novel Family of Triazine-Based Inhibitors of Sorbitol Dehydrogenase with Oral Activity: 1-{4-[3*R*,5*S*-Dimethyl-4-(4-methyl-[1,3,5] triazin-2-yl)-piperazin-1-yl]-[1,3,5]triazin-2-yl}-(*R*) Ethanol

Banavara L. Mylari,* Gregory J. Withbroe, David A. Beebe, Nathaniel S. Brackett, Edward L. Conn, James B. Coutcher, Peter J. Oates and William J. Zembrowski

Pfizer Global Research and Development, Groton Laboratories, Groton, CT 06340, USA

We report here the design and synthesis of novel sorbitol dehydrogenase inhibitors with strategically placed hydroxyalkyl groups onto triazine-piperazine-triazine back bones.



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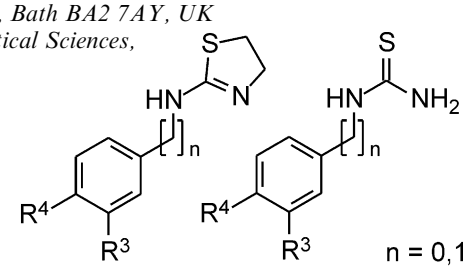
Synthesis of *N*-Benzyl- and *N*-Phenyl-2-amino-4,5-dihydrothiazoles and Thioureas and Evaluation as Modulators of the Isoforms of Nitric Oxide Synthase

Claire L. M. Goodyer,[a] Edwin C. Chinje,[b] Mohammed Jaffar,[b] Ian J. Stratford[b] and Michael D. Threadgill[a,*]

[a]*Department of Pharmacy & Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, UK*
[b]*MRC Experimental Oncology Laboratory, School of Pharmacy and Pharmaceutical Sciences, University of Manchester, Oxford Road, Manchester M13 9PL, UK*

Compounds inhibit or stimulate NOS activity, depending on R^3 and R^4.



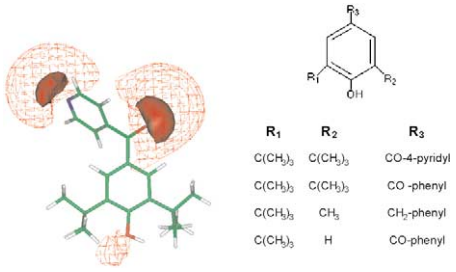
Bioorg. Med. Chem. 11 (2003) 4207

QSAR Study of Dual Cyclooxygenase and 5-Lipoxygenase Inhibitors 2,6-di-*tert*-Butylphenol Derivatives

Juan Ruiz,* Carmen Pérez and Ramon Pouplana

Departament de Fisicoquímica, Facultat de Farmàcia, Universitat de Barcelona, Avda Joan XXIII s/n, 08028 Barcelona, Spain

The QSAR study is analyzed quantifying the essential structural, electronic and physicochemical requirements for dual inhibition of both cyclooxygenase and 5-lipoxygenase enzymes by a set of 2,6-di-*tert*-butyl phenol derivatives.



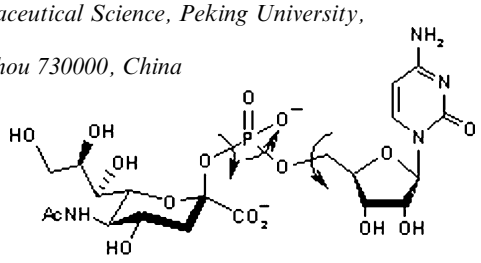
Bioorg. Med. Chem. 11 (2003) 4217

3D-QSAR Analysis of Sialyltransferase Inhibitors

Xiaofang Wang,[a] Youhong Niu,[a,b] Xiaoping Cao,[b] Liangren Zhang,[a] Li-He Zhang[a] and Xin-Shan Ye[a,*]

[a]*The State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Science, Peking University, Xue Yuan Road #38, Beijing 100083, China*
[b]*National Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China*

A 3D-QSAR model of sialyltransferase inhibitors using the CoMFA (comparative molecular field analysis) method was established.



1 (CMP–Neu5Ac)

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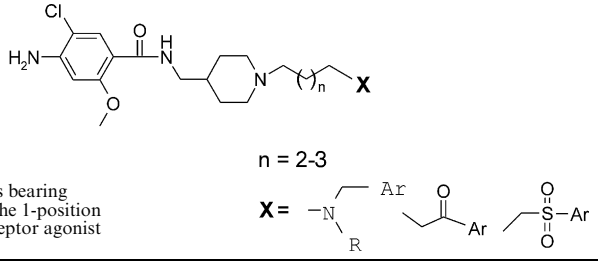
Design and Synthesis of Orally Active Benzamide Derivatives as Potent Serotonin 4 Receptor Agonist

Shuji Sonda,[a,*] Toshio Kawahara,[a] Takahiro Murozono,[b] Noriko Sato,[d] Kiyoshi Asano[c] and Keiichiro Haga[e]

[a]*Pharmaceutical Development Laboratories, Technology & Production Division, Mitsubishi Pharma Corporation, 955, Koiwai, Yoshitomi-cho, Chikujo-gun Fukuoka 871-8550, Japan*
[b]*Pharmacokinetics Laboratory, Research & Development Division, Mitsubishi Pharma Corporation, 1-1-1, Kazusa-kamatari, Kisarazu, Chiba 292-0818, Japan*
[c]*Research Laboratory I, Research & Development Division, Mitsubishi Pharma Corporation, 1000, Kamoshida-cho, Aoba-ku, Yokahama 227-0033, Japan*
[d]*Research Laboratory III, Research & Development Division, Mitsubishi Pharma Corporation, 1000, Kamoshida-cho, Aoba-ku, Yokahama 227-0033, Japan*
[e]*Protein Research Laboratory, Research & Development Division, Mitsubishi Pharma Corporation, 2-25-1, Shodai-ohtani, Hirakata Osaka 573-1153, Japan*

A series of 4-amino-5-chloro-2-methoxy-*N*-(piperidin-4-ylmethyl)benzamide derivatives bearing an aralkylamino, alkylamino, benzoyl or phenylsulfonyl group at its side chain part at the 1-position on the piperidine ring was synthesized. They were evaluated for serotonin 4 (5-HT_4) receptor agonist activity by testing their ability to contract the isolated guinea-pig ascending colon.



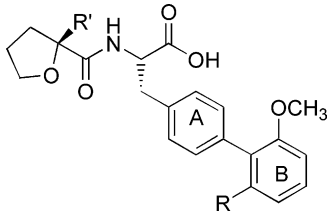
Bioorg. Med. Chem. 11 (2003) 4235

3-D-QSAR CoMFA and CoMSIA Studies on Tetrahydrofuroyl-L-phenylalanine Derivatives as VLA-4 Antagonists

Akash Khandelwal,[a] Ramamurthi Narayanan[b] and Bulusu Gopalakrishnan[a,*]

[a]*Department of Molecular Modeling and Drug Design, Dr. Reddy's Laboratories Ltd, Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India*
[b]*Discovery Chemistry, Dr. Reddy's Laboratories Ltd, Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India*

Robust 3-D-QSAR CoMFA and CoMSIA models were generated using a training set of 25 title compounds as VLA-4 antagonists and validated using a test set of 11 compounds.



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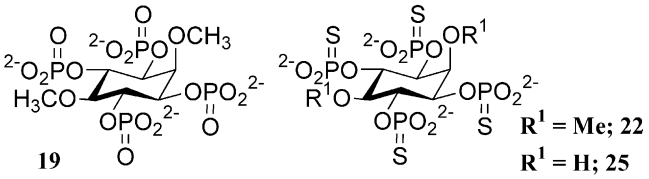
Synthesis of Potent Ins(1,4,5)P_3 5-Phosphatase Inhibitors by Modification of *myo*-Inositol 1,3,4,6-Tetrakisphosphate

Stephen J. Mills and Barry V. L. Potter*

Wolfson Laboratory of Medicinal Chemistry, Department of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath BA2 7AY, UK



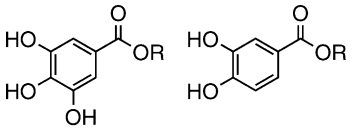
Bioorg. Med. Chem. 11 (2003) 4255

Molecular Design of Multifunctional Antibacterial Agents Against Methicillin Resistant *Staphylococcus aureus* (MRSA)

Isao Kubo,* Ken-ichi Fujita and Ken-ichi Nihei

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

Antibacterial activity of a series of alkyl gallates and protocatechuates against Gram-positive bacteria, especially methicillin resistant *Staphylococcus aureus* (MRSA) strains was evaluated. Dodecyl gallate was the most effective against MRSA ATCC 33591 strain with the minimum bactericidal concentration of 25 μg/mL (74 μM). The time-kill curve study showed that dodecyl gallate was bactericidal against this MRSA strain at any growth stage. The bactericidal activity of medium-chain alkyl gallates was noted in combination with their ability to disrupt the native membrane-associated function nonspecifically as surfactants and to inhibit the respiratory electron transport.

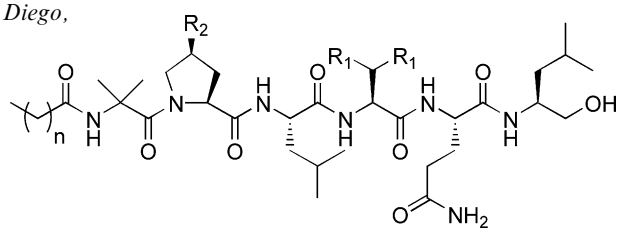


Bioorg. Med. Chem. 11 (2003) 4263

Halovirs A–E, New Antiviral Agents from a Marine-Derived Fungus of the Genus *Scytalidium*

David C. Rowley,* Sara Kelly, Christopher A. Kauffman, Paul R. Jensen and William Fenical

Center for Marine Biotechnology and Biomedicine, Scripps Institution of Oceanography, University of California-San Diego, La Jolla, CA 92093-0204, USA



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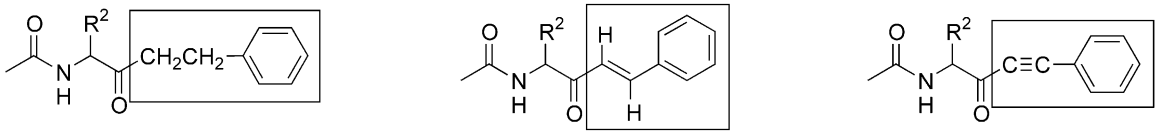
Functionalized Amido Ketones: New Anticonvulsant Agents

Cécile Béguin,[a] Shridhar V. Andurkar,[a,b] Albert Y. Jin,[c] James P. Stables,[d] Donald F. Weaver[e] and Harold Kohn[f,*]

[a]*Department of Chemistry, University of Houston, Houston, TX 77204-5641, USA*
[b]*School of Pharmacy, Midwestern University, 555 31st Street, Downers Grove, IL 60515, USA*
[c]*Department of Chemistry, Queen's University, Kingston, Ontario, Canada K7L 3N6*
[d]*Epilepsy Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, 6001 Executive Boulevard, Suite 2106, Rockville, MD 20852, USA*
[e]*Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4J3*
[f]*Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599-7360, USA*



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Evaluation of Copper Chelation Agents as Anti-Angiogenic Therapy

Kevin Camphausen, Mary Sproull, Steve Tantama, Sandeep Sankineni, Tamalee Scott, Cynthia Ménard, C. Norman Coleman and Martin W. Brechbiel*

Radiation Oncology Branch, National Cancer Institute, National Institutes of Health, 10 Center Drive, Building 10, Room B3B69, Bethesda, MD 20892-1002, USA

The design, synthesis and evaluation of *N*,*N*′,*N*′-tris(2-pyridylmethyl)-*cis*,*cis*-1,3,5,-triaminocyclohexane (tachpyr) derivatives as copper chelators for novel anti-angiogenic therapy performed in an in vitro endothelial cell proliferation assay to assess their cytotoxicity and selectivity is reported.