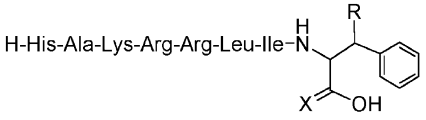
Peptide Inhibitors of CDK2-cyclin A that Target the Cyclin Recruitment-Site: Structural Variants of the C-Terminal Phe

Bioorg. Med. Chem. Lett. 12 (2002) 2501

Gail E. Atkinson,[a] Angela Cowan,[b] Campbell McInnes,[b] Daniella I. Zheleva,[b] Peter M. Fischer[b] and Weng C. Chan[a,*]

[a]*School of Pharmaceutical Sciences, University of Nottingham, University Park, Nottingham NG7 2RD, UK*
[b]*Cyclacel Ltd., James Lindsay Place, Dundee DD1 5JJ, UK*



Synthesis of Tag Introducible (3-Trifluoromethyl)phenyldiazirine Based Photoreactive Phenylalanine

Bioorg. Med. Chem. Lett. 12 (2002) 2507

Makoto Hashimoto,[a,*] Yasumaru Hatanaka,[b] Yutaka Sadakane[b] and Kensuke Nabeta[a]

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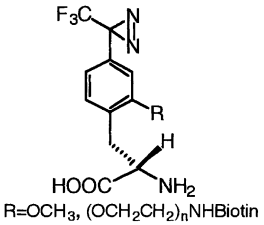
[b]*Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, 2360 Sugitani, Toyama, 930-0194 Japan*



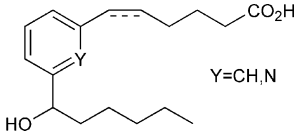
Synthesis and Antiaggregant Properties of Stabilized Analogues of Polyunsaturated Fatty Acid Metabolites

Bioorg. Med. Chem. Lett. 12 (2002) 2511

Ali Hachem,[a] Patrick Roussel,[a] Eric Ménager,[a] Danielle Grée,[a] Yves Le Floc'h,[a] René Grée,[a,*] Chiara Cerletti,[b] Yves Rolland,[c] Serge Simonet[d] and Tony Verbeuren[d]

[a]*ENSCR, Synthèses et Activations de Biomolécules, CNRS UMR 6052, Avenue du Gal Leclerc, 35700 Rennes, France*
[b]*Consorzio Mario Negri Sud, 66030 S. Maria Imbaro, Chieti, Italy*
[c]*Les Laboratoires Servier, 22 rue Garnier, 92200 Neuilly/Seine, France*
[d]*Institut de Recherches Servier, 11 rue des Moulineaux, 92150 Suresnes, France*

Synthesis of new structural analogues of 13-HODE and 12-HETE and study of their activity as inhibitors of platelet aggregation.



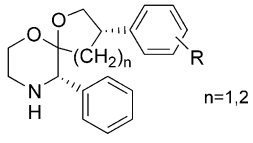
Spirocyclic NK_1 Antagonists I: [4.5] and [5.5]-Spiroketals

Bioorg. Med. Chem. Lett. 12 (2002) 2515

Eileen M. Seward,[a,*] Emma Carlson,[b] Timothy Harrison,[a] Karen E. Haworth,[a] Richard Herbert,[a] Fintan J. Kelleher,[a] Marc M. Kurtz,[c] Jonathan Moseley,[a] Simon N. Owen,[a] Andrew P. Owens,[a] Sharon J. Sadowski,[c] Christopher J. Swain[a] and Brian J. Williams[a]

[a]*Department of Medicinal Chemistry, Merck Sharp and Dohme Research Laboratories, The Neuroscience Research Centre, Terlings Park, Eastwick Road, Harlow, Essex, UK*
[b]*Department of Pharmacology, Merck Sharp and Dohme Research Laboratories, The Neuroscience Research Centre, Terlings Park, Eastwick Road, Harlow, Essex, UK*
[c]*Department of Biochemistry, Merck Research Laboratories, Rahway, NJ 07065, USA*

A series of novel spiroketal-based NK_1 antagonists is described. The effect of modifications to the spiroether ring and aromatic substituents are discussed, leading to the identification of compounds with high affinity and excellent CNS penetration.



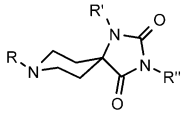
Bioorg. Med. Chem. Lett. 12 (2002) 2519

Parallel Solution- and Solid-Phase Synthesis of Spirohydantoin Derivatives as Neurokinin-1 Receptor Ligands

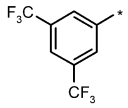
Konrad H. Bleicher,* Yves Wüthrich, Maxime De Boni, Sabine Kolczewski, Torsten Hoffmann and Andrew J. Sleight

F. Hoffmann-La Roche AG, Pharma Research, CH-4070 Basel, Switzerland

The generation of a compound library consisting of spirohydantoin as a privileged GPCR scaffold and the 3,5-bis(trifluoromethyl)phenyl motive as a neurokinin-1 specific needle is described. A series of nanomolar actives are disclosed.



GPCR scaffold



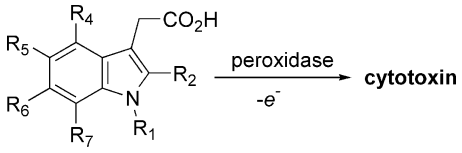
NK-1 needle

Bioorg. Med. Chem. Lett. 12 (2002) 2523

Halogenated Indole-3-acetic Acids as Oxidatively Activated Prodrugs with Potential for Targeted Cancer Therapy

Sharon Rossiter,* Lisa K. Folkes and Peter Wardman

Gray Cancer Institute, PO Box 100, Mount Vernon Hospital, Northwood, Middlesex HA6 2JR, UK



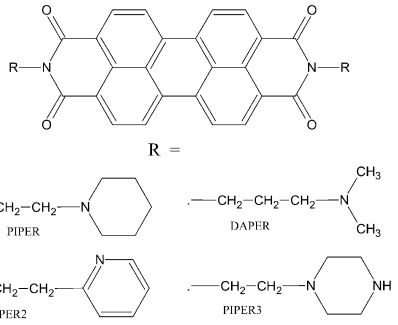
Bioorg. Med. Chem. Lett. 12 (2002) 2527

Perylene Diimides with Different Side Chains are Selective in Inducing Different G-Quadruplex DNA Structures and in Inhibiting Telomerase

Luigi Rossetti,[a] Marco Franceschin,[a,b] Armandodoriano Bianco,[b] Giancarlo Ortaggi[b] and Maria Savino[a,*]

[a]*Dipartimento di Genetica e Biologia Molecolare, Fondazione Istituto Pasteur-Fondazione Cenci Bolognetti, Università di Roma 'La Sapienza', Piazzale A. Moro 5, 00185 Rome, Italy*
[b]*Dipartimento di Chimica, Università di Roma 'La Sapienza', Piazzale A. Moro 5, 00185 Rome, Italy*

The electrostatic properties of the side chains of four *N,N′*-disubstituted perylene diimides influence the amount and the topology of the induced G-quadruplex structures, as well as the ability of inhibiting telomerase.



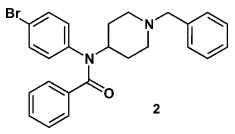
Bioorg. Med. Chem. Lett. 12 (2002) 2535

A New Series of M3 Muscarinic Antagonists Based on the 4-Amino-piperidine Scaffold

O. Diouf,[a] S. Gadeau,[a] F. Chellé,[a] M. Gelbcke,[a] P. Talaga,[b] B. Christophe,[b] M. Gillard,[b] R. Massingham[b] and M. Guyaux[b,*]

[a]*Laboratoire de Chimie Pharmaceutique Organique, Université Libre de Bruxelles, Institut de Pharmacie, Campus Plaine CP205/5, Boulevard du Triomphe, B-1050 Bruxelles, Belgium*
[b]*UCB S.A., Pharma Sector, Preclinical Research, Chemin du Foriest, B-1420 Braine-l'Alleud, Belgium*

A series of 4-amino-piperidine containing molecules have been synthesized and structure–affinity relationship toward the M3-muscarinic receptor has been investigated. Chemical modulations provided molecules with K_i for the human M3-R up to 1 nM with variable selectivity (3- to 40-fold) over the human M2-R. Compounds **2** ($pA_2 = 8.3, 8.6$) demonstrates in vitro on guinea pig bladder and ileal strips potent anticholinergic properties and tissue selectivity.



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Bioorg. Med. Chem. Lett. 12 (2002) 2541

New *N*-Alkyl-1,2-dihydro-2-thioxo-3-pyridinecarbothioamides as Antituberculous Agents with Improved Pharmacokinetics

Daniela Ubiali,[a] Giuseppe Pagani,[a] Massimo Pregnolato,[a] Claudio Piersimoni,[b] José L. Pedraz Muñoz,[c] Alicia Rodríguez Gascón[c] and Marco Terreni[a,*]

[a]*Dipartimento di Chimica Farmaceutica, Via Taramelli 12, Università degli Studi, I-27100 Pavia, Italy*
[b]*Dipartimento di Microbiologia Clinica, Policlinico 'Umberto I-Torrette', I-60020 Ancona, Italy*
[c]*Laboratory of Pharmacy and Pharmaceutical Technology, University of the Basque Country, Vitoria, Spain*

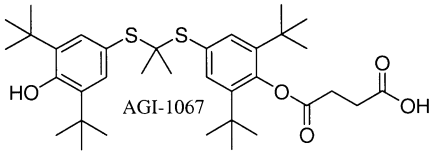
The in vitro antimycobacterial activity and pharmacokinetics of novel *N*-alkyl-1,2-dihydro-2-thioxo-3-pyridinecarbothioamides are reported.

Bioorg. Med. Chem. Lett. 12 (2002) 2545

Novel Phenolic Antioxidants as Multifunctional Inhibitors of Inducible VCAM-1 Expression for Use in Atherosclerosis

Charles Q. Meng,* Patricia K. Somers, Carolyn L. Rachita, Lisa A. Holt, Lee K. Hoong, X. Sharon Zheng, Jacob E. Simpson, Russell R. Hill, Lynda K. Olliff, Charles Kunsch, Cynthia L. Sundell, Sampath Parthasarathy, Uday Saxena, James A. Sikorski and Martin A. Wasserman

AtheroGenics, Inc., 8995 Westside Parkway, Alpharetta, GA 30004, USA



AGI-1067

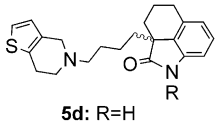
Bioorg. Med. Chem. Lett. 12 (2002) 2549

Tetrahydrothienopyridylbutyl-tetrahydrobenzindoles: New Selective Ligands of the 5-HT_7 Receptor

Chika Kikuchi,* Toyokazu Hiranuma and Masao Koyama

Pharmaceutical Research Center, Meiji Seika Kaisha, Ltd., 760 Morooka-cho, Kohoku-ku, Yokohama 222-8567, Japan

Tetrahydrothienopyridylbutyl-tetrahydrobenzindoles **5d** and **5h** were potent ligands for the 5-HT_7 receptor, with high selectivity over the 5-HT_2 receptor and other receptors.



5d: R=H
5h: R=CH_3

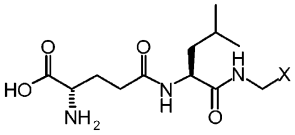
Bioorg. Med. Chem. Lett. 12 (2002) 2553

Glutathione-like Tripeptides as Inhibitors of Glutathionylspermidine Synthetase. Part 1: Substitution of the Glycine Carboxylic Acid Group

Katie Amssoms,[a] Sandra L. Oza,[b] Esteban Ravaschino,[c] Abdellah Yamani,[a] Anne-Marie Lambeir,[d] Padinchare Rajan,[a] Gunther Bal,[a] Juan Bautista Rodriguez,[c] Alan H. Fairlamb,[b] Koen Augustyns[a] and Achiel Haemers[a,*]

[a]*Department of Medicinal Chemistry, University of Antwerp (UIA), Belgium*
[b]*Department of Biochemistry, University of Dundee, Scotland, UK*
[c]*Departamanto de Quimica Organica, FCEyN, Universidad de Buenos Aires, Argentina*
[d]*Department of Medical Biochemistry, University of Antwerp (UIA), Belgium*

The structure–activity of a series of glutathione analogues as inhibitors of glutathionylspermidine synthetase is reported.



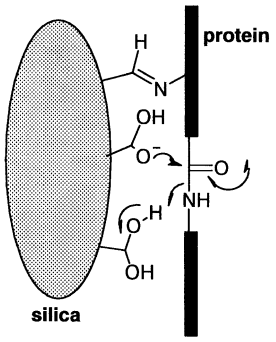
Bioorg. Med. Chem. Lett. 12 (2002) 2557

Silica-Based Artificial Protease Exploiting Aldehyde Groups as Catalytic Elements

Hyunsook Kim, Hyesun Paik, Myoung-soon Kim, Yeon-Sook Chung and Junghun Suh*

School of Chemistry and Center for Molecular Catalysis, Seoul National University, Seoul 151-747, Republic of Korea

An artificial protease synthesized by covering the surface of silica gel with aldehyde and indole groups effectively hydrolyzed albumin and γ-globulin.



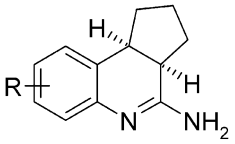
Bioorg. Med. Chem. Lett. 12 (2002) 2561

Dihydroquinolines as Novel n-NOS Inhibitors

Stefan Jaroch,[a,*] Peter Hölscher,[a] Hartmut Rehwinkel,[a] Detlev Sülzle,[b] Gerardine Burton,[c] Margrit Hillmann[c] and Fiona M. McDonald[c]

[a]*Department of Medicinal Chemistry, Corporate Research, Schering AG, D-13342-Berlin, Germany*
[b]*Department of Computational Chemistry, Corporate Research, Schering AG, D-13342-Berlin, Germany*
[c]*CNS-Research, Corporate Research, Schering AG, D-13342-Berlin, Germany*

Dihydroquinolines have been synthesized and have been shown to be potent n-NOS inhibitors. Selectivity versus e-NOS was increased to approximately 100-fold through appropriate substitution at the benzene ring.



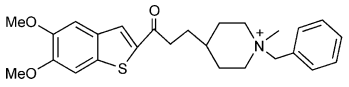
Bioorg. Med. Chem. Lett. 12 (2002) 2565

Quaternary Salts of E2020 Analogues as Acetylcholinesterase Inhibitors for the Reversal of Neuromuscular Block

John K. Clark,[a,*] Phill Cowley,[a] Alan W. Muir,[b] Ronald Palin,[a] Eleanor Pow,[b] Alan B. Prosser,[a] Robert Taylor[a] and Ming-Qiang Zhang[a]

[a]*Department of Medicinal Chemistry, Organon Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, UK*
[b]*Department of Pharmacology, Organon Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, UK*

A series benzylpiperidinium and benzylpyridinium quaternary salts have been synthesised and tested for inhibition of acetylcholinesterase and reversal of neuromuscular block induced by vecuronium.



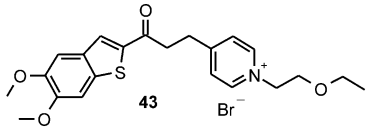
Bioorg. Med. Chem. Lett. 12 (2002) 2569

Novel Piperidinium and Pyridinium Agents as Water-Soluble Acetylcholinesterase Inhibitors for the Reversal of Neuromuscular Blockade

Ronald Palin,[a,*] John K. Clark,[a] Phill Cowley,[a] Alan Muir,[b] Eleanor Pow,[b] Alan B. Prosser,[a] Robert Taylor[a] and Ming-Qiang Zhang[a]

[a]*Department of Medicinal Chemistry, Organon Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, UK*
[b]*Department of Pharmacology, Organon Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, UK*

The synthesis of novel pyridinium salts as powerful acetylcholinesterase inhibitors with improved water solubility is reported, for example **43** (IC_{50} = 0.007 μM, 50 mg/mL).



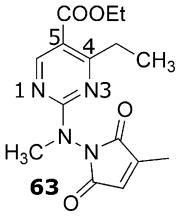
Bioorg. Med. Chem. Lett. 12 (2002) 2573

Structure–Activity Relationship Studies of Ethyl 2-[(3-Methyl-2,5-dioxo(3-pyrrolinyl))amino]-4-(trifluoromethyl)pyrimidine-5-carboxylate: An Inhibitor of AP-1 and NF-κB Mediated Gene Expression

Moorthy S. S. Palanki,* Leah M. Gayo-Fung, Graziella I. Shevlin, Paul Erdman, Mark Sato, Mark Goldman, Lynn J. Ransone and Cheryl Spooner

Celgene Signal Research Division, 5555 Oberlin Drive, San Diego, CA 92121, USA

Several analogues of ethyl 2-(3-methyl-2, 5-dioxo(3-pyrrolinyl))amino]-4- (trifluoromethyl)pyrimidine-5-carboxylate (**1**) were synthesized and tested as inhibitors of AP-1 and NF-kB mediated transcriptional activation in Jurkat T cells. From our SAR work, ethyl 2-(3-methyl-2,5-dioxo(3-pyrrolinyl))-*N*-methylamino]-4-(trifluoro-methyl)-pyrimidine-5-carboxylate (**63**) was identified as a novel and potent inhibitor.



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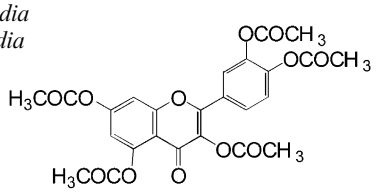
Bioorg. Med. Chem. Lett. 12 (2002) 2579

Comparison of the Prevention of Aflatoxin B_1-Induced Genotoxicity by Quercetin and Quercetin Pentaacetate

Ekta Kohli,[a] Hanumantharao G. Raj,[a] Ranju Kumari,[a] Vishwajit Rohil,[a] Narendra K. Kaushik,[b] Ashok K. Prasad[b] and Virinder S. Parmar[b,*]

[a]*Department of Biochemistry, V. P. Chest Institute, University of Delhi, Delhi-110 007, India*
[b]*Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007, India*

Quercetin penta acetate (QPA) unlike quercetin demonstrated time-dependent inhibition of liver microsome-catalyzed AFB_1 epoxidation as measured by AFB_1 binding to DNA. In the present work, we have demonstrated the transacetylase-mediated action of QPA in the prevention of genotoxicity due to AFB_1.



QPA

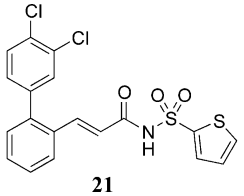
Bioorg. Med. Chem. Lett. 12 (2002) 2583

Structure–Activity Relationship of Biaryl Acylsulfonamide Analogues on the Human EP_3 Prostanoid Receptor

M. Gallant,* M. C. Carrière, A. Chateauneuf, D. Denis, Y. Gareau, C. Godbout, G. Greig, H. Juteau, N. Lachance, P. Lacombe, S. Lamontagne, K. M. Metters, C. Rochette, R. Ruel, D. Slipetz, N. Sawyer, N. Tremblay and M. Labelle

Merck Frosst Centre for Therapeutic Research, PO Box 1005, Pointe Claire-Dorval, Québec, Canada H9R 4P8

Potent and selective ligands for the human EP_3 prostanoid receptor are described. Biaryl compounds bearing a tethered *ortho* substituted acidic moiety were identified as potent EP_3 antagonists based on the SAR described herein. The binding affinity of key compounds on all eight human prostanoid receptors is reported.



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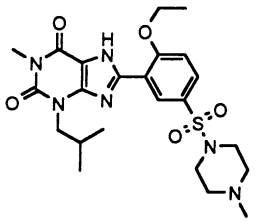
Bioorg. Med. Chem. Lett. 12 (2002) 2587

8-Aryl Xanthines Potent Inhibitors of Phosphodiesterase 5

Ruth Arnold,[a] David Beer,[a] Gurdip Bhalay,[a] Urs Baettig,[a] Stephen P. Collingwood,[a,*] Sarah Craig,[a] Nicholas Devereux,[a] Andrew Dunstan,[a] Angela Glen,[a] Sylvie Gomez,[a] Sandra Haberthuer,[a] Trevor Howe,[a] Stephen Jelfs,[a] Heinz Moser,[a] Reto Naef,[b] Paul Nicklin,[a] David Sandham,[a] Rowan Stringer,[a] Katharine Turner,[a] Simon Watson[a] and Mauro Zurini[b]

[a]*Novartis Horsham Research Centre, Wimblehurst Road, Horsham, West Sussex RH12 5AB, UK*
[b]*Novartis Pharma AG, Lichtstrasse 35, CH-4056 Basel, Switzerland*

A series of 8-aryl xanthine derivatives which function as potent PDE5 inhibitors with, in many cases, high levels of selectivity versus other PDE isoforms is described.



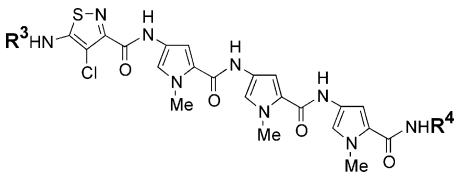
Bioorg. Med. Chem. Lett. 12 (2002) 2591

DNA Binding Ligands with Excellent Antibiotic Potency Against Drug-Resistant Gram-Positive Bacteria

Roland W. Bürli,* Yigong Ge, Sarah White, Eldon E. Baird, Sofia M. Touami, Matthew Taylor, Jacob A. Kaizerman and Heinz E. Moser

Genesoft Inc, 7300 Shoreline Court, South San Francisco, CA 94080, USA

An efficient synthesis of DNA binding molecules consisting of four heterocyclic carboxamide units and various substituents at both termini is described. The minor-groove binding ligands showed excellent activity against a broad range of Gram-positive bacteria; no cross-resistance to known antibacterial drugs was observed.



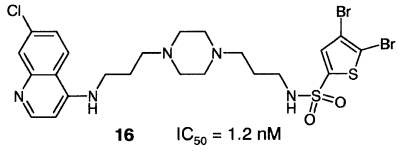
Bioorg. Med. Chem. Lett. 12 (2002) 2595

Parallel Synthesis and Anti-Malarial Activity of a Sulfonamide Library

A. Ryckebusch,[a] R. Déprez-Poulain,[a] M.-A. Debreu-Fontaine,[a] R. Vandaele,[a] E. Mouray,[b] P. Grellier[b] and C. Sergheraert[a,*]

[a]*Institut de Biologie et Institut Pasteur de Lille, UMR CNRS 8525, Université de Lille II, 1 rue du Professeur Calmette, B.P. 447, 59021 Lille, France*
[b]*Laboratoire de Biologie Parasitaire, FR CNRS 63, Muséum National d'Histoire Naturelle, 61 rue Buffon, 75005 Paris, France*

The synthesis and antimalarial evaluation of a library of 31 sulfonamides are described. Compound **16** displayed an activity 100-fold better than chloroquine. Fluorescence experiments suggest an intraparasitical localisation different from that of chloroquine.



16 IC_{50} = 1.2 nM

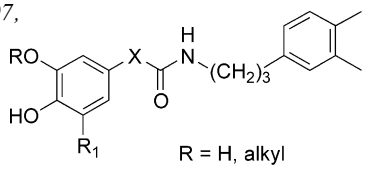
Bioorg. Med. Chem. Lett. 12 (2002) 2599

Synthesis and Evaluation of 4-Hydroxyphenylacetic Acid Amides and 4-Hydroxycinnamamides as Antioxidants

Young-Sik Jung,[a] Tae-Souk Kang,[a] Joong-Ho Yoon,[a] Bo-Young Joe,[a] Hee-Jong Lim,[a] Churl-Min Seong,[a] Woo-Kyu Park,[a] Jae-Yang Kong,[a] Jungsook Cho[b] and No-Sang Park[a,*]

[a]*Medicinal Science Division, Korea Research Institute of Chemical Technology, PO Box 107, Yusong, Taejon 305-606, Republic of Korea*
[b]*Department of Pharmacology, College of Medicine, Dongguk University, Kyongju, Kyongbuk 780-714, Republic of Korea*

4-Hydroxyphenylacetic acid amides and 4-hydroxycinnamamides were synthesized and their antioxidant and neuroprotective activities were evaluated.



R = H, alkyl
R_1 = H, OH, OCH_3
X = CH_2, CH=CH

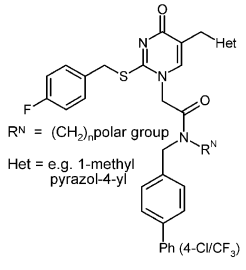
Bioorg. Med. Chem. Lett. 12 (2002) 2603

The Discovery of SB-435495: A Potent, Orally Active Inhibitor of Lipoprotein-Associated Phospholipase A_2 for Evaluation in Man

Josie A. Blackie, Jackie C. Bloomer, Murray J. B. Brown, Hung-Yuan Cheng, Richard L. Elliott, Beverley Hammond, Deirdre M. B. Hickey, Robert J. Ife, Colin A. Leach, V. Ann Lewis, Colin H. Macphee, Kevin J. Milliner, Kitty E. Moores, Ivan L. Pinto, Stephen A. Smith,* Ian G. Stansfield, Steven J. Stanway, Maxine A. Taylor, Colin J. Theobald and Caroline M. Whittaker

GlaxoSmithKline, Medicines Research Centre, Gunnels Wood Road, Stevenage SG1 2NY, UK

Sub-nanomolar inhibitors of recombinant lipoprotein-associated phospholipase A_2 with very encouraging developability properties have been developed from a series of 1-(biphenylmethylamidoalkyl)pyrimidones. Diethylaminoethyl derivative **32**, SB-435495 was selected for progression to man.

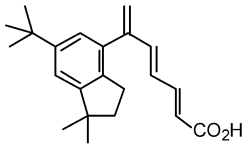


Bioorg. Med. Chem. Lett. 12 (2002) 2607

Synthesis and Characterization of a New RXR Agonist Based on the 6-*tert*-Butyl-1,1-dimethylindanyl Structure

Beatriz Domínguez,[a] M. Jesús Vega,[a] Fredy Sussman[b] and Angel R. de Lera[a,*]

[a]*Departamento de Química Orgánica, Facultad de Ciencias, Universidade de Vigo, 36200 Vigo, Spain*
[b]*Departamento de Química Orgánica, Facultad de Química, Universidade de Santiago de Compostela, 15706 Santiago de Compostela, Spain*



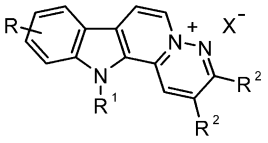
Bioorg. Med. Chem. Lett. 12 (2002) 2611

Synthesis and Cytotoxic Activity of Pyridazino[1′,6′:1,2]pyrido [3,4-*b*]indol-5-inium Derivatives as Anti-Cancer Agents

Alberto Fontana,[a] Enrique J. Benito,[a] M. Justina Martín,[a] Nuria Sánchez,[a] Ramón Alajarín,[a] J. José Vaquero,[a] Julio Alvarez-Builla,[a,*] Stéphanie Lambel-Giraudet,[b] Stéphane Leonce,[b] Alain Pierré[b] and Daniel Caignard[b]

[a]*Departamento de Química Orgánica, Universidad de Alcalá, 28871-Alcalá de Henares, Madrid, Spain*
[b]*Institut de Recherche Servier, 11 rue des Molineaux, 92450 Suresnes, France*

New pyridazino[1′,6′:1,2]pyrido[3,4-*b*]indol-5-inium derivatives were synthesised and their anti-cancer activity was evaluated against L1210 cancer cells.



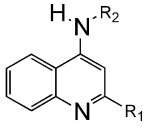
Bioorg. Med. Chem. Lett. 12 (2002) 2615

4-Aminoquinolines as a Novel Class of NR1/2B Subtype Selective NMDA Receptor Antagonists

Emmanuel Pinard,[a,*] Alexander Alanine,[a] Anne Bourson,[b] Bernd Büttelmann,[a] Marie-Paule Heitz,[a] Vincent Mutel,[b] Ramanjit Gill,[b] Gerhard Trube[b] and René Wyler[a]

[a]*Pharma Division, Discovery Chemistry, F. Hoffmann-La Roche Ltd., CH-4070 Basel, Switzerland*
[b]*Pharma Division, Preclinical CNS Research, F. Hoffmann-La Roche Ltd., CH-4070 Basel, Switzerland*

Screening of the Roche compound library led to the identification of 4-aminoquinolines as structurally novel NR1/2B subtype selective NMDA receptor antagonists. The SAR which was developed in this series resulted in the discovery of highly potent and in vivo active blockers.



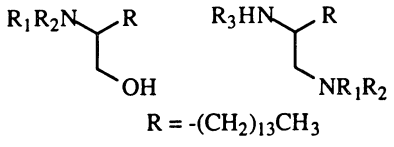
Bioorg. Med. Chem. Lett. 12 (2002) 2621

Long-Chain Aminoalcohol and Diamine Derivatives Induce Apoptosis through a Caspase-3 Dependent Pathway

Esther del Olmo,[a,*] Antonio Macho,[b] Mario Alves,[a] José L. López,[a] Fadwa el Banoua,[b] Eduardo Muñoz[b] and Arturo San Feliciano[a]

[a]*Departamento Química Farmacéutica, Facultad de Farmacia, Univ. de Salamanca, 37007-Salamanca, Spain*
[b]*Departamento Biología Celular, Fisiología e Inmunol, Fac. Medicina, Avda. Menendez Pidal s/n, 14004 Córdoba, Spain*

Some aliphatic diamine and aminoalcohols and their alkyl, acyl and carbamoyl derivatives, have been synthesized and their apoptotic activities evaluated. They induce mitochondrial transmembrane potential disruption and caspase-3 activation, which provokes DNA fragmentation at the G_1/S phase of the cell cycle.

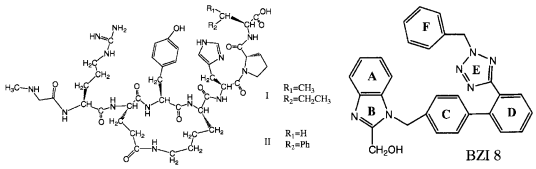


Bioorg. Med. Chem. Lett. 12 (2002) 2627

Design, Synthesis and Biological Evaluation of Cyclic Angiotensin II Analogues with 3,5 Side-Chain Bridges: Role of C-Terminal Aromatic Residue and Ring Cluster for Activity and Implications in the Drug Design of AT1 Non-peptide Antagonists

Panagiota Roumelioti,[a] Ludmila Polevaya,[b] Panagiotis Zoumpoulakis,[c] Nektarios Giatas,[a] Ilze Mutule,[b] Tatjana Keivish,[b] Anastasia Zoga,[c] Demetrios Vlahakos,[d] E. Iliodromitis,[d] Demetrios Kremastinos,[d] Simona Golic Grdadolnik,[e] Thomas Mavromoustakos,[b,*] and John Matsoukas[a]

[a]*Department of Chemistry, University of Patras, 26500 Patras, Greece*
[b]*Laboratory of Peptide Chemistry, Latvian Institute of Organic Synthesis, Riga, LV-1006, Latvia*
[c]*Institute of Organic and Pharmaceutical Chemistry, National Hellenic Research Foundation, Athens, 11635, Greece*
[d]*Onassis Cardiac Surgery Center, 17674, Athens, Greece*
[e]*National Institute of Chemistry, Hajdrihova 19, POB 30 SI-1115 Ljubljana, Slovenia*

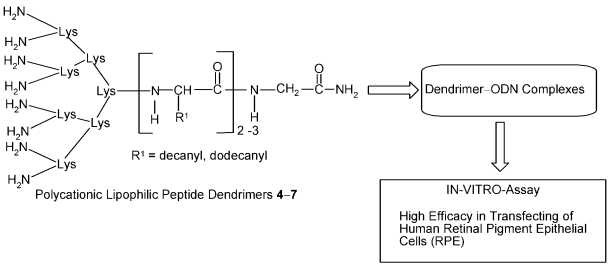


Bioorg. Med. Chem. Lett. 12 (2002) 2635

Syntheses of Polycationic Dendrimers on Lipophilic Peptide Core for Complexation and Transport of Oligonucleotides

Norbert Wimmer,[a] Robert J. Marano,[b] Philip S. Kearns,[a] Elizabeth P. Rakoczy[b] and Istvan Toth[a,*]

[a]*School of Pharmacy, The University of Queensland, Steele Building, St. Lucia, Qld 4072, Australia*
[b]*Centre for Ophthalmology and Visual Science and Lions Eye Institute, University of Western Australia, 2 Verdun Street, Nedlands, WA 6009, Australia*



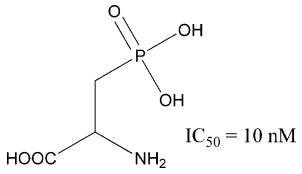
Bioorg. Med. Chem. Lett. 12 (2002) 2639

Multisubstrate Analogue Inhibitors of Glucosamine-6-phosphate Synthase from *Candida albicans*

Sridar V. Chittur* and Robert K. Griffith

Department of Basic Pharmaceutical Sciences, School of Pharmacy, West Virginia University, Morgantown, WV 26505, USA

2-Amino-3-phosphono propionic acid (AP3) is a potent multisubstrate inhibitor of GFAT.



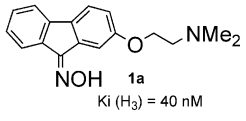
Bioorg. Med. Chem. Lett. 12 (2002) 2643

The Synthesis of Substituted Fluorenes as Novel Non-Imidazole Histamine H_3 Inhibitors

Pauline C. Ting,* Joe F. Lee, Margaret M. Albanese, Wing C. Tom, Daniel M. Solomon, Robert Aslanian, Neng-Yang Shih and Robert West

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

A novel non-imidazole fluorene oxine **1a** has been identified as a histamine H_3 inhibitor, and its structure–activity relationship has been evaluated.



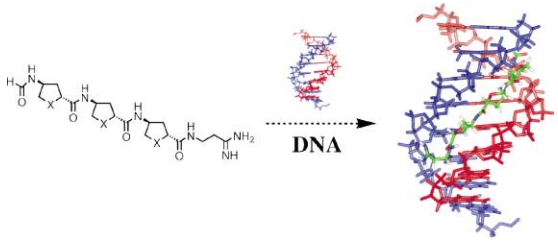
Bioorg. Med. Chem. Lett. 12 (2002) 2647

Synthesis and DNA Binding Properties of Saturated Distamycin Analogues

Craig R. Woods,[a] Nicolas Faucher,[a] Bernd Eschgfaller,[b] Kenneth W. Bair[b,*] and Dale L. Boger[a,*]

[a]*Department of Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*
[b]*Novartis Institute for Biomedical Research, Novartis Pharmaceuticals Corporation—Oncology, 556 Morris Avenue, Summit, NJ 07901-1398, USA*

A series of saturated heterocyclic analogues of distamycin was prepared and DNA binding affinity evaluated with a fluorescent intercalator displacement (FID) assay.



Bioorg. Med. Chem. Lett. 12 (2002) 2651

Oligonucleotides Comprised of Alternating 2′-Deoxy-2′-fluoro-β-D-arabinonucleosides and D-2′-deoxyribonucleosides (2′F-ANA/DNA 'Altimers') Induce Efficient RNA Cleavage Mediated by RNase H

Kyung-Lyum Min, Ekaterina Viazovkina, Annie Galarneau, Michael A. Parniak* and Masad J. Damha*

Department of Chemistry, McGill University, 801 Sherbrooke Street West, Montreal, QC, Canada H3A 2K6

Oligomers comprising alternating three-nucleotide segments of 2′F-ANA and three-nucleotide segments of DNA ('altimers') are very efficient at eliciting RNase H degradation of target RNA, and were significantly better than oligomers entirely comprised of DNA, or oligomers comprised of 2′-*O*-methyl RNA wings and a DNA gap ('gapmers'). This suggests that 2′F-ANA/DNA 'altimers' may be potent antisense agents.