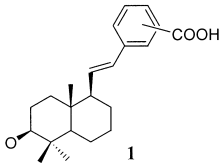
Bioorg. Med. Chem. Lett. 11 (2001) 1619

Enantioselective Synthesis and Complement Inhibitory Assay of A/B-Ring Partial Analogues of Oleanolic Acid

Haregewein Assefa,[a] Alison Nimrod,[b] Larry Walker[b,c] and Robert Sindelar[a,b,*]

[a]*Department of Medicinal Chemistry, School of Pharmacy, University of Mississippi, University, MS 38677, USA*
[b]*National Center for Natural Product Research, School of Pharmacy, University of Mississippi, University, MS 38677, USA*
[c]*Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677, USA*



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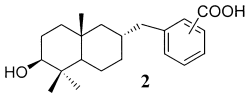


2

A series of oleanlic acid A/B-ring parital analogues (**1** and **2**) was synthesized and tested for their complement inhibitory activity as well as cytotoxic properties.

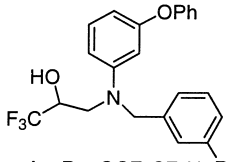
Bioorg. Med. Chem. Lett. 11 (2001) 1625

Novel Heteroaryl Replacements of Aromatic 3-Tetrafluoroethoxy Substituents in Trifluoro-3-(tertiaryamino)-2-propanols as Potent Inhibitors of Cholesteryl Ester Transfer Protein

Mark A. Massa,* Dale P. Spangler, Richard C. Durley, Brian S. Hickory, Daniel T. Connolly, Bryan J. Witherbee, Mark E. Smith and James A. Sikorski

Pharmacia Discovery Research, 700 Chesterfield Parkway North, St. Louis, MO 63198, USA

A series of novel *N*,*N*-disubstituted trifluoro-3-amino-2-propanols has been prepared as potent inhibitors of cholesteryl ester transfer protein (CETP). Modifying the aromatic 3-tetrafluoroethoxy group in the lead molecule **1a** with various heteroaryl moieties produced new 2-furyl analogues **2a**,**b** with submicromolar potency in vitro.



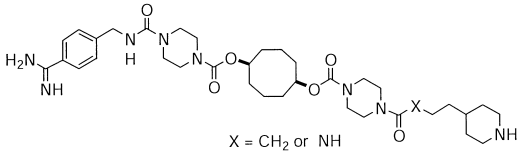
1a: R = OCF_2CF_2H R
2a: R = 2-furyl

Bioorg. Med. Chem. Lett. 11 (2001) 1629

Dibasic Inhibitors of Human Mast Cell Tryptase. Part 3: Identification of a Series of Potent and Selective Inhibitors Containing the Benzamidine Functionality

Jeffrey M. Dener,* Kenneth D. Rice, William S. Newcomb, Vivian R. Wang, Wendy B. Young, Anthony R. Gangloff, Elaine Y.-L. Kuo, Lynne Cregar, Daun Putnam and Martin Wong

Departments of Medicinal Chemistry, Biochemistry, and Enzymology, Axys Pharmaceuticals, Inc., 180 Kimball Way, South San Francisco, CA 94080, USA



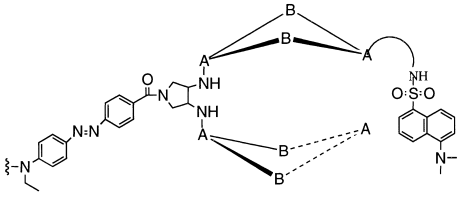
Bioorg. Med. Chem. Lett. 11 (2001) 1635

Sequence-Selective Peptide Detection by Small Synthetic Chemosensors Selected from an Encoded Combinatorial Chemosensor Library

Edward James Iorio,* Yuefei Shao, Chao-Tsen Chen, Holger Wagner and W. Clark Still

Department of Chemistry, Columbia University, New York, NY 10027, USA

Synthetic chemosensors hold great potential in many diagnostic applications. In this study, we describe the design and preparation of the first encoded combinatorial library of chemosensors for tripeptides. Subsequent screening of the library resulted in the discovery of novel chemosensors able to distinguish between random tripeptides.



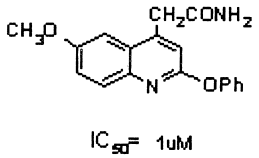
Bioorg. Med. Chem. Lett. 11 (2001) 1639

Quinoline-4-acetamides as $sPLA_2$ Inhibitors

Ying Liu, Yabing Feng, Renxiao Wang, Ying Gao and Luhua Lai*

Institute of Physical Chemistry & College of Chemistry and Molecular Engineering, Peking University, State Key Laboratory for Structural Chemistry of Unstable and Stable Species, Beijing 100871, PR China

Design and synthesis of novel quinoline-4-acetamides tested as $sPLA_2$ inhibitors.



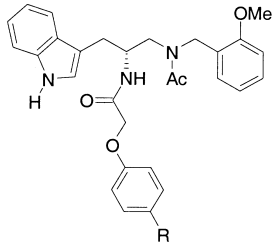
Bioorg. Med. Chem. Lett. 11 (2001) 1643

Expedited Discovery of Second Generation NK-1 Antagonists: Identification of a Nonbasic Aryloxy Substituent

James E. Fritz,* Philip A. Hipskind, Karen L. Lobb, James A. Nixon, Penny G. Threlkeld, Bruce D. Gitter, Carl L. McMillian and Stephen W. Kaldor

Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285, USA

Solution-phase, parallel-synthesis techniques were used to optimize a series of nonbasic side-chain replacements, resulting in the identification of a series of substituted aryloxy containing NK-1 antagonists with improved orally bioavailable subnanomolar potency.



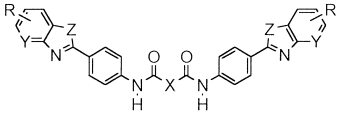
Bioorg. Med. Chem. Lett. 11 (2001) 1647

Biological Evaluation of Hepatitis C Virus Helicase Inhibitors

Chee Wee Phoon,[a] Poh Yong Ng,[b] Anthony E. Ting,[b] Su Ling Yeo[b] and Mui Mui Sim[a,*]

[a]*Medicinal and Combinatorial Chemistry Laboratory, Institute of Molecular and Cell Biology, 30 Medical Drive, Singapore 117609*
[b]*Collaborative Antiviral Research Laboratory, Institute of Molecular and Cell Biology, 30 Medical Drive, Singapore 117609*

The SAR study of HCV helicase inhibitors was reported.



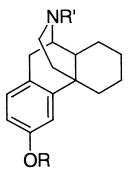
Bioorg. Med. Chem. Lett. 11 (2001) 1651

Anticonvulsant Effects of New Morphinan Derivatives

Hyoung-Chun Kim,[a,*] Toshitaka Nabeshima,[b] Wang-Kee Jhoo,[a] Kwang Ho Ko,[c] Won-Ki Kim,[d] Eun-Joo Shin,[a] Minkyoung Cho[e] and Phil Ho Lee[e]

[a]*Neurotoxicology Program, Department of Pharmacy, College of Pharmacy, Korea Institute of Drug Abuse, Kangwon National University, Chunchon 200-701, South Korea*
[b]*Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Showa-Ku, Nagoya 466-8560, Japan*
[c]*Department of Pharmacy, College of Pharmacy, Seoul National University, Seoul 151-742, South Korea*
[d]*Department of Pharmacology, College of Medicine, Ewha Medical Research Center, Ewha Women's University, Seoul 158-056, South Korea*
[e]*Department of Chemistry, Kangwon National University, Chunchon 200-701, South Korea*

We synthesized a series of compounds that are modified in positions 3 and 17 of the morphinan ring system, with the intention of developing ideal anticonvulsant agents. We examined the effects of these compounds on kainic acid (KA)-induced seizures, and on locomotor patterns in rats. We found that compounds **5** (R = allyl, R′ = methyl), **6** (R = cyclopropylmethyl, R′ = methyl) and **8** (R = allyl, R′ = H) exhibit novel anticonvulsant effects, with negligible psychotropic effects.



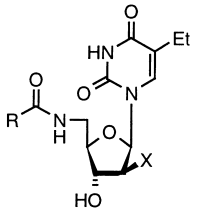
Bioorg. Med. Chem. Lett. 11 (2001) 1655

Nucleoside Analogues as Highly Potent and Selective Inhibitors of Herpes Simplex Virus Thymidine Kinase

Joseph A. Martin,[a,*] Robert W. Lambert,[a] John H. Merrett,[a] Kevin E. B. Parkes,[a] Gareth J. Thomas,[a] Stewart J. Baker,[a] David J. Bushnell,[a] Julie E. Cansfield,[a] Stephen J. Dunsdon,[a] Andrew C. Freeman,[a] Richard A. Hopkins,[a] Ian R. Johns,[a] Elizabeth Keech,[a] Heather Simmonite,[a] Andrea Walmsley,[a] Philippe Wong Kai-In[b] and Mark Holland[b]

[a]*Department of Medicinal Chemistry, Roche Discovery Welwyn, Broadwater Road, Welwyn Garden City, Herts AL7 3AY, UK*
[b]*Department of Antiviral Biology, Roche Discovery Welwyn, Broadwater Road, Welwyn Garden City, Herts AL7 3AY, UK*

A new series of highly potent and selective inhibitors of herpes simplex virus thymidine kinase is described.

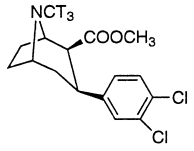


Bioorg. Med. Chem. Lett. 11 (2001) 1659

[^{3}H]MFZ 2-12: A Novel Radioligand for the Dopamine Transporter

Amy Hauck Newman,[a,*] Mu-Fa Zou,[a] Jasmine V. Ferrer[b] and Jonathan A. Javitch[b]

[a]*Medicinal Chemistry Section, National Institute on Drug Abuse—Intramural Research Program, 5500 Nathan Shock Drive, Baltimore, MD 21224, USA*
[b]*Center for Molecular Recognition and Departments of Pharmacology and Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY, 10032, USA*



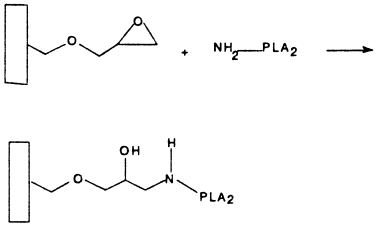
Bioorg. Med. Chem. Lett. 11 (2001) 1663

A Simple Method to Obtain a Covalent Immobilized Phospholipase A_2

R. R. Madoery[a,*] and G. D. Fidelio[b]

[a]*Facultad de Ciencias Agropecuarias, Universidad Nacional de Córdoba, 5000 Córdoba, Argentina*
[b]*Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, 5000 Córdoba, Argentina*

The obtention of a covalent immobilized phospholipase A_2 from cobra venom is reported.



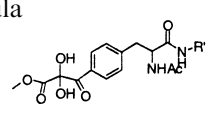
Bioorg. Med. Chem. Lett. 11 (2001) 1665

Selective Inhibition of Src SH2 by a Novel Thiol-Targeting Tricarbonyl-Modified Inhibitor and Mechanistic Analysis by ^{1}H/^{13}C NMR Spectroscopy

Raji Sundaramoorthi,* Chris Siedem, Chi B. Vu, David C. Dalgarno, Ellen C. Laird, Martyn C. Botfield, Amanda B. Combs, Susan E. Adams, Ruth W. Yuan, Manfred Weigele and Surinder S. Narula

ARIAD Pharmaceuticals, Inc., 26 Landsdowne Street, Cambridge, MA 02139, USA

Synthesis and detailed analysis of Src SH2 binding by peptidyl and non-peptidyl compounds incorporating tricarbonyl-modified pTyr are described. A mechanistic analysis of ^{13}C-labeled tricarbonyl derivatives **6a–c** by ^{1}H and ^{13}C NMR is also presented.



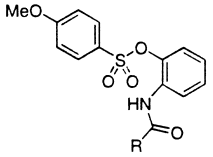
Bioorg. Med. Chem. Lett. 11 (2001) 1671

Novel Sulfonate Derivatives: Potent Antimitotic Agents

Stephen L. Gwaltney, II,* Hovis M. Imade, Qun Li, Laura Gehrke, R. Bruce Credo, Robert B. Warner, Jang Yun Lee, Peter Kovar, David Frost, Shi-Chung Ng and Hing L. Sham

Cancer Research, D47B, Building AP-10, Abbott Laboratories, Abbott Park, IL 60064-6101, USA

The synthesis and biological evaluation of novel sulfonate analogues of **E-7010** are reported. Several of the compounds are potent inhibitors of cell proliferation and tubulin polymerization. Importantly, these compounds are also active against P-glycoprotein positive (+) cancer cells, which are resistant to many other antitumor agents.



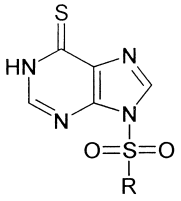
Bioorg. Med. Chem. Lett. 11 (2001) 1675

Antimycobacterial Activity of 9-Sulfonylated/Sulfenylated-6-mercaptopurine Derivatives

Andrea Scozzafava,[a] Antonio Mastrolorenzo[b] and Claudiu T. Supuran[a,*]

[a]*Laboratorio di Chimica Inorganica e Bioinorganica, Università degli Studi, Via Gino Capponi 7, I-50121, Florence, Italy*
[b]*Dipartimento di Scienze Dermatologiche, Università degli Studi, Centro MTS, Via degli Alfani 37, I-50121, Florence, Italy*

A series of 9-sulfonylated/sulfenylated-6-mercaptopurines has been prepared by reaction of 6-mercaptopurine with sulfonyl/sulfenyl halides. These compounds constitute a new class of potent antimycobacterial agents, possessing MIC values against *Mycobacterium tuberculosis* H37Rv in the range of 0.39–3.39 μg/mL, as well as appreciable activity against *Mycobacterium avium*. Furthermore, a compound of this small series exhibited good activity (MIC under 1 μg/mL) against several drug resistant strains of *M. tuberculosis*.



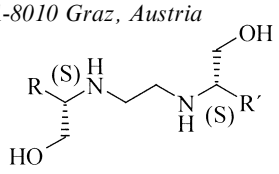
Bioorg. Med. Chem. Lett. 11 (2001) 1679

Ethambutol Analogues as Potential Antimycobacterial Agents

Herwig Häusler,[a] R. Pamela Kawakami,[b] Eva Mlaker,[a] Wayne B. Severn[b] and Arnold E. Stütz[a,*]

[a]*Glycogroup, Institut für Organische Chemie der Technischen Universität Graz, Stremayrgasse 16, A-8010 Graz, Austria*
[b]*AgResearch, Wallaceville Animal Research Centre, PO Box 40063, Upper Hutt, New Zealand*

A range of symmetrical as well as unsymmetrical ethambutol derivatives was prepared and inhibitory properties were screened against *Mycobacterium smegmatis*.



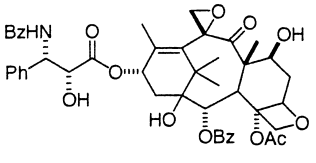
Bioorg. Med. Chem. Lett. 11 (2001) 1683

Synthesis of a Novel C-10 Spiro-Epoxide of Paclitaxel

Michael A. Walker,* Timothy D. Johnson, Stella Huang, Dolatorai M. Vyas and John F. Kadow

Bristol-Myers Squibb, Pharmaceutical Research Institute, Richard L. Gelb Center for Pharmaceutical Research and Development, 5 Research Parkway, Wallingford, CT 06492, USA

New analogues of paclitaxel were synthesized containing an epoxide at the C-10 position.

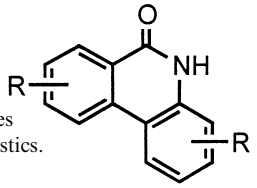


Bioorg. Med. Chem. Lett. 11 (2001) 1687

Synthesis of Substituted 5[*H*]Phenanthridin-6-ones as Potent Poly(ADP-ribose)polymerase-1 (PARP1) Inhibitors

Jia-He Li,* Larisa Serdyuk, Dana V. Ferraris, Ge Xiao, Kevin L. Tays, Paul W. Kletzly, Weixing Li, Susan Lautar, Jie Zhang and Vincent J. Kalish

Guilford Pharmaceuticals Inc., 6611 Tributary Street, Baltimore, MD 21224, USA



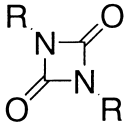
1-, 2-, 3-, 4-, 8-, or 10-Substituted 5(*H*)phenanthridin-6-ones were synthesized in three different pathways and found to be potent PARP1 inhibitors. Among the 28 compounds prepared, some showed not only low IC_{50} values (compound **1b**, 10 nM) against recombinant human PARP1 in vitro but also desirable water solubility characteristics.

Bioorg. Med. Chem. Lett. 11 (2001) 1691

Inhibition of Serine Proteases: Activity of 1,3-Diazetidine-2,4-diones

Yasunori Aoyama,[a,*] Masaaki Uenaka,[a] Toshiro Konoike,[b,*] Yoko Hayasaki-Kajiwara,[c] Noriyuki Naya[c] and Masatoshi Nakajima[c]

[a]*Shionogi Research Laboratories, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553-0002, Japan*
[b]*Shionogi Research Laboratories, Shionogi & Co., Ltd., Amagasaki, Hyogo 660-0813, Japan*
[c]*Shionogi Research Laboratories, Shionogi & Co., Ltd., Futaba-cho, Toyonaka, Osaka 561-0825, Japan*



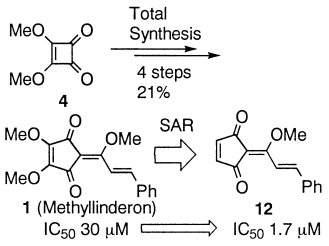
We discovered a new class of serine protease inhibitors, 1,3-diazetidine-2,4-dione derivatives. The present work demonstrates that the 1,3-diazetidine-2,4-dione nucleus is effective as a scaffold of serine protease inhibitors.

Bioorg. Med. Chem. Lett. 11 (2001) 1695

Total Synthesis of Human Chymase Inhibitor Methyllinderone and Structure–Activity Relationships of Its Derivatives

Yasunori Aoyama,[a,*] Toshiro Konoike,[b,*] Akiko Kanda,[a] Noriyuki Naya[c] and Masatoshi Nakajima[c]

[a]*Shionogi Research Laboratories, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553-0002, Japan*
[b]*Shionogi Research Laboratories, Shionogi & Co., Ltd., Amagasaki, Hyogo 660-0813, Japan*
[c]*Shionogi Research Laboratories, Shionogi & Co., Ltd., Futaba-cho, Toyonaka, Osaka 561-0825, Japan*



Bioorg. Med. Chem. Lett. 11 (2001) 1699

Antioxidant Activity of Water-Soluble Chitosan Derivatives

Wenming Xie, Peixin Xu* and Qing Liu

Department of Chemistry, Yuquan Campus, Zhejiang University, Hangzhou 310027, China

Water-soluble chitosan derivatives were prepared by graft copolymerization of maleic acid sodium onto hydroxypropyl chitosan and carboxymethyl chitosan sodium. Their scavenging activities against hydroxyl radical ·OH were investigated by chemiluminescence technique. They exhibit IC_{50} values ranging from 246 to 498 μg/mL, which should be attributed to their different content of hydroxyl and amino groups and different substituting groups.

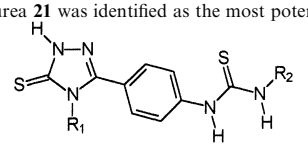
Bioorg. Med. Chem. Lett. 11 (2001) 1703

Some 3-Thioxo/Alkylthio-1,2,4-triazoles with a Substituted Thiourea Moiety as Possible Antimycobacterials

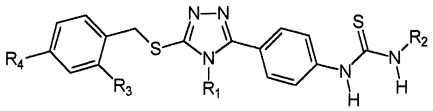
Ilkay Küçükgüzel,[a,*] S. Güniz Küçükgüzel,[a] Sevim Rollas[a] and Muammer Kiraz[b]

[a]*Department of Pharmaceutical Chemistry, Marmara University, Faculty of Pharmacy, Haydarpasa 81010 Istanbul, Turkey*
[b]*Center for Research and Application of Culture Collections of Microorganisms, University of Istanbul, Faculty of Medicine, Çapa, Istanbul, Turkey*

A series of novel *N*-alkyl/aryl-*N*′-[4-(4-alkyl/aryl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione-5-yl)phenyl]thioureas **1**–**19** and their 3-alkylthio derivatives **20**–**22** were synthesized and tested for antimycobacterial activity against *Mycobacterium tuberculosis H37Rv* as well as *M. fortuitum ATCC 6841*. *N*-Allyl-*N*′-{4-[3-[(2,4-dichlorobenzyl)thio]-4-methyl-4*H*-1,2,4-triazole-5-yl]phenyl}thiourea **21** was identified as the most potent derivative of the **1**–**22** series by an MIC value of 6.25 μg/mL and selectivity index of 1.6.



1-19



20-22

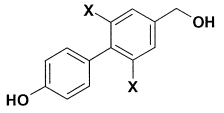
Bioorg. Med. Chem. Lett. 11 (2001) 1709

Biphenyls as Surrogates of the Steroidal Backbone. Part 1: Synthesis and Estrogen Receptor Affinity of an Original Series of Polysubstituted Biphenyls

Dominique Lesuisse,[a,*] Eva Albert,[a] Françoise Bouchoux,[b] E. Cérède,[a] Jean-Michel Lefrançois,[a] Marc-Olivier Levif,[a] Sophie Tessier,[a] Bernadette Tric[a] and Georges Teutsch[a]

[a]*Medicinal Chemistry, Aventis, 102 route de Noisy, 93235 Romainville Cedex, France*
[b]*Bone Diseases Group, Aventis, 102 route de Noisy, 93235 Romainville Cedex, France*

A series of original biphenyls was synthesized and evaluated for their binding affinity for the estrogen receptor. Some of them demonstrated better or equivalent binding as estradiol.



X = Br (RBA = 425 % of estradiol)
X = Cl (RBA = 106 % of estradiol)

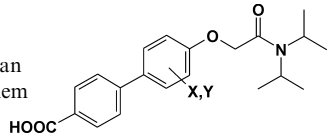
Bioorg. Med. Chem. Lett. 11 (2001) 1713

Biphenyls as Surrogates of the Steroidal Backbone. Part 2: Discovery of a Novel Family of Non-steroidal 5-α-Reductase Inhibitors

Dominique Lesuisse,[a,*] Jean-François Gourvest,[b] Eva Albert,[a] Bernard Doucet,[b] Catherine Hartmann,[b] Jean-Michel Lefrançois,[a] Sophie Tessier,[a] Bernadette Tric[a] and Georges Teutsch[a]

[a]*Medicinal Chemistry, Aventis, 102 route de Noisy, 93235 Romainville Cedex, France*
[b]*Bone Diseases Group, Aventis, 102 route de Noisy, 93235 Romainville Cedex, France*

A new family of non-steroidal 5-α-reductase inhibitors was designed by replacing the steroid skeleton of an inhibitor related to estrone by a biphenyl moiety. This gave rise to a new family of inhibitors, some of them in the nanomolar range, placing them amongst the best non-steroidal inhibitors of this enzyme.



Bioorg. Med. Chem. Lett. 11 (2001) 1717

3-Carboxamido Analogues of Morphine and Naltrexone: Synthesis and Opioid Receptor Binding Properties

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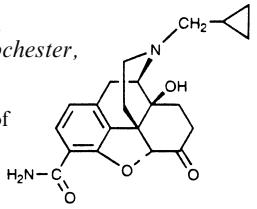
[b]*Department of Pharmacology and Physiology, School of Medicine and Dentistry, University of Rochester, Rochester, NY 14642, USA*

High-affinity binding to μ opioid receptors has been identified in a series of novel 3-carboxamido analogues of morphine and naltrexone.



Naltrexone analogue **9**: K_i = 1.9 nM (μ)

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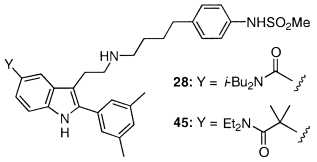
Substituted Indole-5-carboxamides and -acetamides as Potent Nonpeptide GnRH Receptor Antagonists

Wallace T. Ashton,[a,*] Rosemary M. Sisco, Yi Tien Yang,[b] Jane-Ling Lo,[b] Joel B. Yudkovitz,[b] Kang Cheng[b] and Mark T. Goulet[a]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065-0900, USA*
[b]*Department of Biochemistry and Physiology, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065-0900, USA*

The 2-aryltryptamine class of GnRH receptor antagonists has been modified to incorporate carboxamide and acetamide substituents at the indole 5-position. With either a phenol or methanesulfonamide terminus on the *N*-aralkyl side chain, potent binding affinity to the GnRH receptor was achieved. A functional assay for GnRH antagonism was even more sensitive to structural modification and revealed a strong preference fro branched chain amides such as **28** and **45.**



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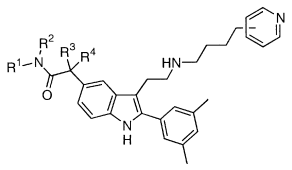
Potent Nonpeptide GnRH Receptor Antagonists Derived from Substituted Indole-5-carboxamides and -acetamides Bearing a Pyridine Side-Chain Terminus

Wallace T. Ashton,[a,*] Rosemary M. Sisco,[a] Yi Tien Yang,[b] Jane-Ling Lo,[b] Joel B. Yudkovitz,[b] Patrice H. Gibbons,[b] George R. Mount,[b] Rena Ning Ren,[b] Bridget S. Butler,[b] Kang Cheng[b] and Mark T. Goulet[a]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065-0900, USA*
[b]*Department of Biochemistry and Physiology, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065-0900, USA*

Indole-5-carboxamides and -acetamides containing a pyridine terminus were found to be potent functional GnRH antagonists.



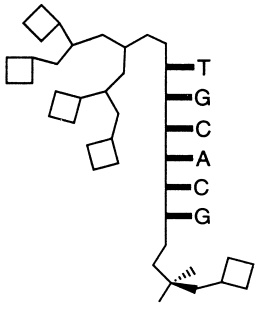
Bioorg. Med. Chem. Lett. 11 (2001) 1733

Synthesis and Nuclease Stability of Trilysyl Dendrimer–Oligodeoxyribonucleotide Hybrids

David A. Sarracino and Clemens Richert*

Department of Chemistry, Tufts University, Medford, MA 02155, USA

A dendrimer–oligonucleotide hybrid with terminal nalidixic acid residues shows increased resistance to endo- and exonucleases, particularly at low pH, as well as enhanced affinity for a target strand.



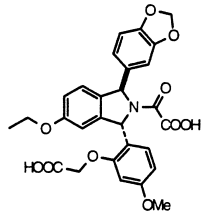
Bioorg. Med. Chem. Lett. 11 (2001) 1737

Isoindolines: A New Series of Potent and Selective Endothelin-A Receptor Antagonists

Paivi J. Kukkola,* Natalie A. Bilci, Theodore Ikler, Paula Savage, Suraj S. Shetty, Dominick DelGrande and Arco Y. Jeng

Metabolic and Cardiovascular Diseases, Novartis Institute for Biomedical Research, Summit NJ 07901, USA

1,3-Disubstituted isoindolines have been discovered as a new class of potent functional ET_A selective receptor antagonists through pharmacophore analysis of existing nonpeptide endothelin antagonists. The structure–activity relationships for both the *trans* and the *cis* series of isoindolines are discussed.



ET_A-IC_{50} = 4.1 nM; pK_B = 7.7

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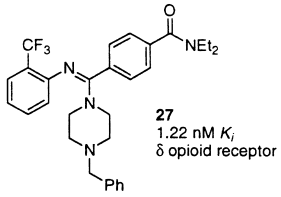
Piperazinyl Benzamidines: Synthesis and Affinity for the Delta Opioid Receptor

Samuel O. Nortey,* Ellen W. Baxter, Ellen E. Codd, Sui-Po Zhang and Allen B. Reitz

Drug Discovery Division, R. W. Johnson Pharmaceutical Research Institute, Welsh and McKean Roads, Spring House, PA 19477, USA

Piperazinyl benzamides such as **27** are potent and selective δ opioid receptor ligands.



27
1.22 nM K_i
δ opioid receptor

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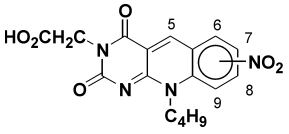
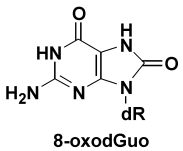
Promotion of Radiation-Induced Formation of 8-Oxo-7,8-dihydro-2′-deoxyguanosine by Nitro 5-Deazaflavin Derivatives

Tetsuji Kawamoto,[a,*] Yoshihiro Ikeuchi,[a] Yuji Mikata,[b,*] Maki Kishigami,[b] Shigenobu Yano,[b] Chieko Murayama,[c,*] Tomoyuki Mori[c] and Fumio Yoneda[a,*]

[a]*Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan*
[b]*Department of Chemistry, Faculty of Science, Nara Women's University, Nara 630-8506, Japan*
[c]*Department of Radiation Oncology, School of Medicine, Tokai University, Bohseidai Isehara 259-1193, Japan*





8-oxodGuo

Prominent promotion of radiation-induced formation of 8-oxodGuo by nitro 5-deazaflavin derivatives has been found both in deaerated and N_2O saturated aqueous dGuo solutions.

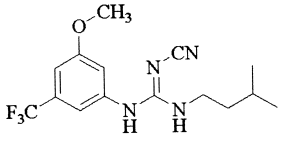
Bioorg. Med. Chem. Lett. 11 (2001) 1749

Phenylcyanoguanidines as Inhibitors of Glucose-Induced Insulin Secretion from Beta Cells

Tina M. Tagmose,[a] John P. Mogensen,[a] Pia C. Agerholm,[a] Per O. G. Arkhammar,[a,b] Philip Wahl,[a] Anne Worsaae[a] and J. Bondo Hansen[a,*]

[a]*Discovery and Development, Novo Nordisk A/S, Novo Nordisk Park, DK-2760, Måløv, Denmark*
[b]*BioImage A/S, Mørkhøj Bygade 28, DK-2860, Søborg, Denmark*

Phenylcyanoguanidines, for example **6**, have been identified as vasodilators and as potent inhibitors of insulin release from beta cells in vitro. Compound **6** activates human SUR1/Kir6.2 K_{ATP} channels expressed in HEK293 cells.



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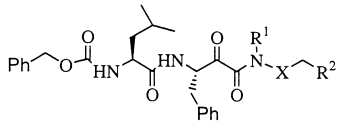
Bioorg. Med. Chem. Lett. 11 (2001) 1753

Significance of Hydrogen Bonding at the S_1' Subsite of Calpain I

Isaac O. Donkor,* Xiaozhang Zheng, Jie Han, Calvin Lacy and Duane D. Miller

Department of Pharmaceutical Sciences, The University of Tennessee, Johnson Bldg. Room 327E, 847 Monroe Avenue, Memphis, TN 38163, USA



R^1 = H Me, or Et R^2 = Me or Ph X = O or CH_2

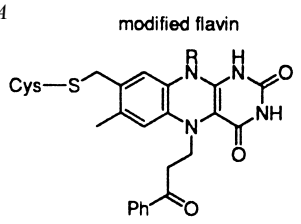
Bioorg. Med. Chem. Lett. 11 (2001) 1757

Inactivation of Monoamine Oxidase B by 1-Phenylcyclopropylamine: Mass Spectral Evidence for the Flavin Adduct

Deanna J. Mitchell,[a] Dejan Nikolic,[b] Richard B. van Breemen[b] and Richard B. Silverman[a,*]

[a]*Department of Chemistry and Department of Biochemistry, Molecular Biology, and Cell Biology, Northwestern University, Evanston, IL 60208-3113, USA*
[b]*Department of Medicinal Chemistry and Pharmacognosy, University of Illinois, Chicago, IL 60612-7231, USA*

Incubation of 1-phenylcyclopropylamine with bovine liver MAO (MAO B), followed by complete enzymatic digestion to single amino acid residues and subsequent analysis by on-line liquid chromatography–electrospray ionization mass spectrometry, was used to investigate the structure of the resulting flavin adduct.



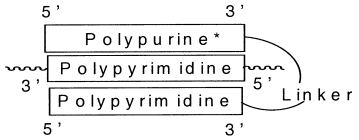
Bioorg. Med. Chem. Lett. 11 (2001) 1761

Parallel-Stranded Hairpins Containing 8-Aminopurines. Novel Efficient Probes for Triple-Helix Formation

Anna Aviñó,[a] Juan Carlos Morales,[b] Miriam Frieden,[a] Beatriz G. de la Torre,[b] Ramon Güimil García,[b] Elena Cubero,[c] F. Javier Luque,[c] Modesto Orozco,[c] Ferran Azorín[a] and Ramon Eritja[a,*]

[a]*Cygene Spain S.L., Parc Científic de Barcelona, Baldiri i Reixac, 10-12, E-08028 Barcelona, Spain*
[b]*Institut de Biología Molecular de Barcelona, C.S.I.C., Jordi Girona 18-26, E-08034 Barcelona, Spain*
[c]*Universitat de Barcelona, Martí i Franquès 1-11, E-08028 Barcelona, Spain*

Parallel-stranded oligonucleotides with 8-aminopurines form a stable triplex.

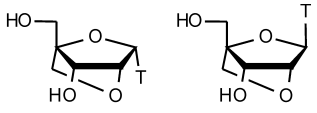


Bioorg. Med. Chem. Lett. 11 (2001) 1765

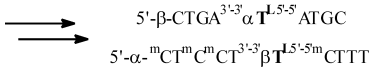
Incorporation of α- and β-LNA (Locked Nucleic Acid) Monomers in Oligodeoxynucleotides with Polarity Reversals

Nanna K. Christensen,[a] Britta M. Dahl[b] and Poul Nielsen[a,*]

[a]*Department of Chemistry, University of Southern Denmark, Odense University, DK-5230 Odense M, Denmark*
[b]*Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark*



The thymidine monomers of LNA with both α- and β-configuration are incorporated with polarity reversals in oligodeoxynucleotides with β- and α-configuration. Thermal stabilities of duplexes with complementary DNA and RNA are evaluated.

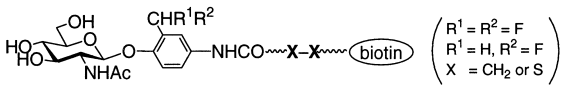


Bioorg. Med. Chem. Lett. 11 (2001) 1769

A Mechanism-Based Affinity-Labeling Agent for Possible Use in Isolating *N*-Acetylglucosaminidase

Mie Ichikawa and Yoshitaka Ichikawa*

Department of Pharmacology and Molecular Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA



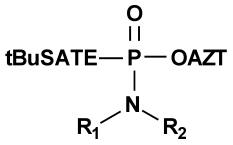
Bioorg. Med. Chem. Lett. 11 (2001) 1775

Rational Design of a New Series of Pronucleotide

Thierry Beltran,[a] David Egron,[a] Alain Pompon,[a] Isabelle Lefebvre,[a] Christian Périgaud,[a] Gilles Gosselin,[a] Anne-Marie Aubertin[b] and Jean-Louis Imbach[a,*]

[a]*UMR 5625 CNRS-UM II, Université Montpellier II, cc 008, place E. Bataillon, 34095 Montpellier Cedex 05, France*
[b]*Laboratoire de virologie de la Faculté de Médecine, Unité 74 I.N.S.E.R.M., Université L. Pasteur, 3, rue Koeberlé, 67000 Strasbourg, France*

A new pronucleotide series is described involving a two-step degradation process mediated by, respectively, carboxylesterase and phosphoramidase. Taking AZT as the nucleosidyl moiety, it is shown that most of the compounds inhibit HIV replication in the TK^- cell line, which proves 5′-AZTMP delivery.

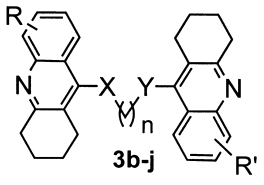


Bioorg. Med. Chem. Lett. 11 (2001) 1779

Novel and Potent Tacrine-Related Hetero- and Homobivalent Ligands for Acetylcholinesterase and Butyrylcholinesterase

Luisa Savini,[a,*] Giuseppe Campiani,[b] Alessandra Gaeta,[a] Cesare Pellerano,[a] Caterina Fattorusso,[c] Luisa Chiasserini,[a] James M. Fedorko[d] and Ashima Saxena[d]

[a]*Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, via Aldo Moro, 53100 Siena, Italy*
[b]*Dipartimento di Scienze Farmaceutiche, Università degli Studi di Salerno, via Ponte Don Melillo 11C, 84084 Fisciano, Italy*
[c]*Dipartimento di Chimica delle Sostanze Naturali, Università di Napoli Federico II, via D. Montesano 49, 80131 Napoli, Italy*
[d]*Division of Biochemistry, Walter Reed Forest Glen Annex, Forney Drive, Silver Spring, MD 20910, USA*

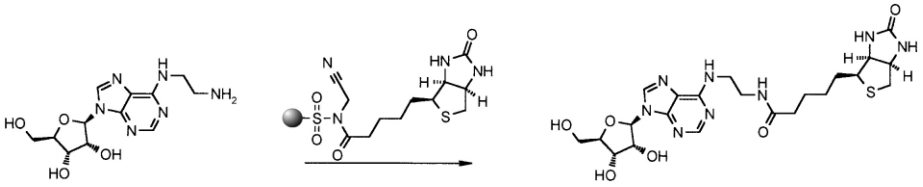


Bioorg. Med. Chem. Lett. 11 (2001) 1783

Biotin Labelling of Amines by Polymer-Assisted Solution-Phase Synthesis

Abolfasl Golisade, Claudia Herforth, Karen Wieking, Conrad Kunick and Andreas Link*

Universität Hamburg, Institut für Pharmazie, Bundesstraße 45, D-20146 Hamburg, Germany

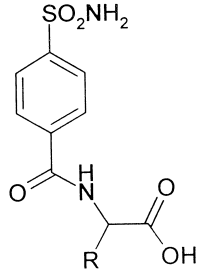


Bioorg. Med. Chem. Lett. 11 (2001) 1787

Carbonic Anhydrase Inhibitors: 4-Sulfamoyl-benzenecarboxamides and 4-Chloro-3-sulfamoyl-benzenecarboxamides with Strong Topical Antiglaucoma Properties

Francesco Mincione,[a,b] Michele Starnotti,[a,b] Luca Menabuoni,[c] Andrea Scozzafava,[d] Angela Casini[d] and Claudiu T. Supuran[d,e,*]

[a]*Università degli Studi, Istituto Oculistico, Viale Morgagni 85, I-50134 Firenze, Italy*
[b]*U.O. Oculistica Az. USL 3, Val di Nievole, Ospedale di Pescia, Pescia, Italy*
[c]*Ospedale San Giovanni di Dio, U.O. Oculistica, Via Torregalli 3, I-50123, Firenze, Italy*
[d]*Università degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Via Gino Capponi 7, I-50121, Firenze, Italy*
[e]*CSGI, c/o Università degli Studi di Firenze, Via Gino Capponi 7, I-50121, Firenze, Italy*

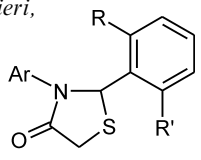


Bioorg. Med. Chem. Lett. 11 (2001) 1793

Discovery of 2,3-Diaryl-1,3-thiazolidin-4-ones as Potent Anti-HIV-1 Agents

Maria Letizia Barreca,[a] Alba Chimirri,[a] Laura De Luca,[a] Anna-Maria Monforte,[b] Pietro Monforte,[a,*] Angela Rao,[a] Maria Zappalà,[a] Jan Balzarini,[c] Erik De Clercq,[c] Christophe Pannecouque[c] and Myriam Witvrouw[c]

[a]*Dipartimento Farmaco-Chimico, Università di Messina, Viale Annunziata, 98168 Messina, Italy*
[b]*Dipartimento di Scienze Farmacobiologiche, Università Magna Græcia di Catanzaro, Complesso Ninì Barbieri, 88021 Roccelletta di Borgia (CZ), Italy*
[c]*Rega Institute for Medical Research, Katholieke Universiteit Leuven, 10 Minderbroedersstraat, B-3000, Leuven, Belgium*



Design, synthesis and anti-HIV activity of a series of 2,3-diaryl-1,3-thiazolidin-4-ones are reported.