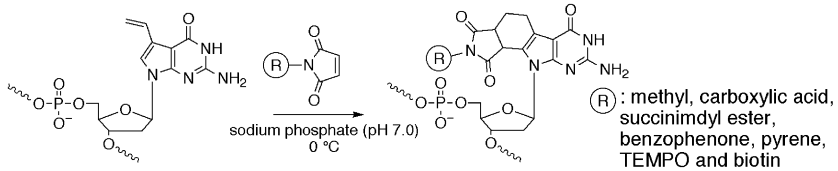
Bioorg. Med. Chem. Lett. 12 (2002) 1895

Oligonucleotides Containing 7-Vinyl-7-deazaguanine as a Facile Strategy for Expanding the Functional Diversity of DNA

Akimitsu Okamoto, Toshiji Taiji, Kazuki Tainaka and Isao Saito

Department of Synthetic Chemistry and Biological Chemistry, Faculty of Engineering, Kyoto University, SORST, Japan Science and Technology Corporation, Kyoto 606-8501, Japan



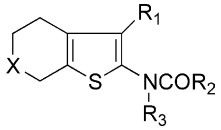
Bioorg. Med. Chem. Lett. 12 (2002) 1897

Synthesis and Bioactivities of Novel Bicyclic Thiophenes and 4,5,6,7-Tetrahydrothieno[2,3-*c*]pyridines as Inhibitors of Tumor Necrosis Factor-α (TNF-α) Production

Masakazu Fujita,* Taketsugu Seki and Naoko Ikeda

Pharmaceutical Research Laboratories, Nikken Chemicals Co., Ltd., 1-346, Kitabukuro-cho, Saitama-shi, Saitama 330-0835, Japan

Novel bicyclic thiophenes and 4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine derivatives were synthesized and evaluated for their ability to inhibit LPS-stimulated production of TNF-α. Several compounds revealed excellent in vivo activity. Furthermore, an effective compound was found in adjuvant-induced arthritic model (AIA) of rat.

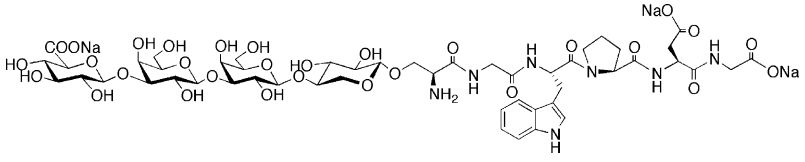


Bioorg. Med. Chem. Lett. 12 (2002) 1901

Synthesis of Betaglycan-type Tetraosyl Hexapeptide: A Possible Precursor Regulating Enzymatic Elongation Toward Heparin

Jun-ichi Tamura,[a,b,*] Akihiro Yamaguchi[a] and Junko Tanaka[a,b]

[a]*Department of Environmental Sciences, Faculty of Education & Regional Sciences, Tottori University, Tottori, 680-8551 Japan*
[b]*CREST, Japan Science and Technology Corporation (JST), Japan*



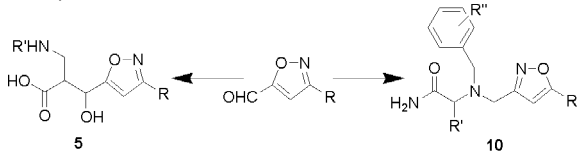
Bioorg. Med. Chem. Lett. 12 (2002) 1905

Combinatorial Synthesis and Biological Evaluation of Isoxazole-Based Libraries as Antithrombotic Agents

S. Batra,[a,*] T. Srinivasan,[a] S. K. Rastogi,[a] B. Kundu,[a] A. Patra,[a] A. P. Bhaduri[a] and M. Dixit[b]

[a]*Medicinal Chemistry Division, Central Drug Research Institute, Lucknow 226001, India*
[b]*Pharmacology Division, Central Drug Research Institute, Lucknow 226001, India*

The 3-substituted-phenyl-5-isoxazolecarboxaldehydes have been identified as activated aldehydes for the generation of isoxazole-based combinatorial libraries on solid phase through automation. Three highly functionalized isoxazole-based libraries comprising of 32, 96 and 45 compounds each have been synthesized in parallel format and evaluated for antithrombin activity.

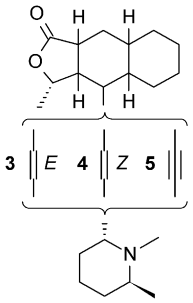


Bioorg. Med. Chem. Lett. 12 (2002) 1909

Synthesis and Affinity Studies of Himbacine Derived Muscarinic Receptor Antagonists

Ling-Jie Gao,[a] Magali Waelbroeck,[b] Sven Hofman,[a] Dirk Van Haver,[a] Marco Milanesio,[c] Davide Viterbo[c] and Pierre J. De Clercq[a,*]

[a]*Department of Organic Chemistry, Ghent University, Krijgslaan 281, B-9000 Gent, Belgium*
[b]*Laboratoire de Chimie Biologique et de la Nutrition, Université Libre de Bruxelles, Route de Lennik 808, B-1070 Brussels, Belgium*
[c]*Dipartimento di Scienze e Tecnologie Avanzate, Università del Piemonte Orientale 'A. Avogadro', Corso T. Borsalino 54, I-15100 Alessandria, Italy*



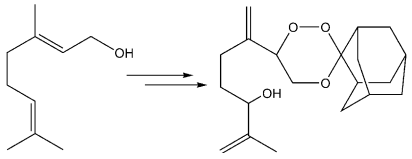
A series of nine himbacine-like derivatives, **3a**–**c**, **4a**–**c** and **5a**–**c**, in which **a**, **b** and **c** (natural) correspond to different configurations of the B-ring, has been synthesised. Binding affinity studies for the M_1, M_2, M_3 and M_4 muscarinic receptor subtypes showed that **3a** and **5c** display a 10-fold selectivity for the M_2 receptor as compared to the M_4 receptor.

Bioorg. Med. Chem. Lett. 12 (2002) 1913

Photo-Oxygenation of Geraniol: Synthesis of a Novel Series of Hydroxy-Functionalized Anti-Malarial 1,2,4-Trioxanes

Chandan Singh,[a,*] Nitin Gupta[a] and Sunil K. Puri[b]

[a]*Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow-226001, India*
[b]*Division of Parasitology, Central Drug Research Institute, Lucknow-226001, India*

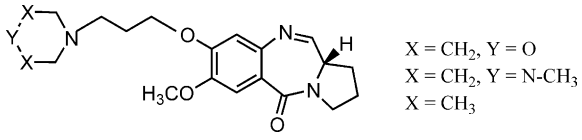


Bioorg. Med. Chem. Lett. 12 (2002) 1917

Synthesis of C-8 Alkylamino Substituted Pyrrolo[2,1-*c*][1,4]-benzodiazepines as Potential Anti-Cancer Agents

Ahmed Kamal,* N. Laxman, G. Ramesh, O. Srinivas and P. Ramulu

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India

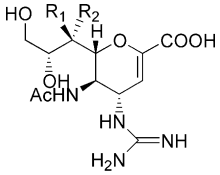


Bioorg. Med. Chem. Lett. 12 (2002) 1921

Synthesis and Anti-Influenza Virus Activity of 4-Guanidino-7-substituted Neu5Ac2en Derivatives

Takeshi Honda,[a,*] Takeshi Masuda,[a] Shuku Yoshida,[b] Masami Arai,[a] Yoshiyuki Kobayashi[a] and Makoto Yamashita[b]

[a]*Medicinal Chemistry Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan*
[b]*Biological Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan*



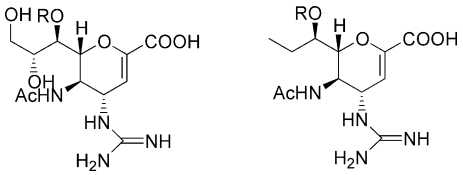
R_1 = F, OMe, OEt, N_3
R_2 = H

Bioorg. Med. Chem. Lett. 12 (2002) 1925

Synthesis and Anti-Influenza Virus Activity of 7-*O*-Alkylated Derivatives Related to Zanamivir

Takeshi Honda,[a,*] Takeshi Masuda,[a] Shuku Yoshida,[b] Masami Arai,[a] Satoru Kaneko[a] and Makoto Yamashita[b]

[a]*Medicinal Chemistry Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan*
[b]*Biological Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan*

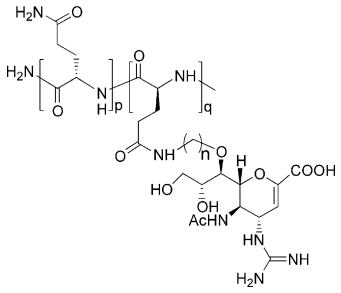


Bioorg. Med. Chem. Lett. 12 (2002) 1929

Synthesis and Anti-Influenza Evaluation of Polyvalent Sialidase Inhibitors Bearing 4-Guanidino-Neu5Ac2en Derivatives

Takeshi Honda,[a,*] Shuku Yoshida,[b] Masami Arai,[a] Takeshi Masuda[a] and Makoto Yamashita[b]

[a]*Medicinal Chemistry Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan*
[b]*Biological Research Laboratories, Sankyo Co., Ltd., 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140-8710, Japan*

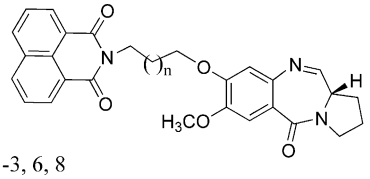


Bioorg. Med. Chem. Lett. 12 (2002) 1933

Design and Synthesis of C-8 Linked Pyrrolobenzodiazepine–Naphthalimide Hybrids as Anti-Tumour Agents

Ahmed Kamal,* B. S. Narayan Reddy, G. Suresh Kumar Reddy and G. Ramesh

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India



n = 1-3, 6, 8

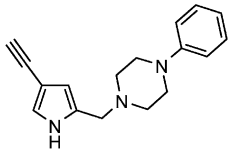
Bioorg. Med. Chem. Lett. 12 (2002) 1937

2,4-Disubstituted Pyrroles: Synthesis, Traceless Linking and Pharmacological Investigations Leading to the Dopamine D4 Receptor Partial Agonist FAUC 356

Markus Bergauer, Harald Hübner and Peter Gmeiner*

Department of Medicinal Chemistry, Emil Fischer Center, Friedrich-Alexander University, Schuhstraße 19, D-91052 Erlangen, Germany

The ethynylpyrrole **1d** (FAUC 356) proved to have selective D4 binding and substantial ligand efficacy (66%, $EC_{50} = 1.9$ nM).



1d

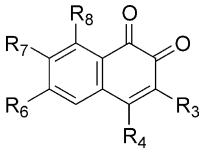
Bioorg. Med. Chem. Lett. 12 (2002) 1941

Synthesis and PTP1B Inhibition of 1,2-Naphthoquinone Derivatives as Potent Anti-Diabetic Agents

Jin Hee Ahn, Sung Yun Cho, Jae Du Ha, So Young Chu, Sun Ho Jung, Yoon Sung Jung, Ji Yoen Baek, In Kyung Choi, Eun Young Shin, Seung Kyu Kang, Sung Soo Kim, Hyae Gyeong Cheon, Sung-Don Yang and Joong-Kwon Choi*

Medicinal Science Division, Korea Research Institute of Chemical Technology, Taejon, 305-600, Republic of Korea

A new series of 1,2-naphthoquinone derivatives was synthesized by various synthetic methods and evaluated for their ability to inhibit protein tyrosine phosphatase 1B (PTP1B).



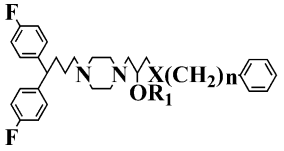
Bioorg. Med. Chem. Lett. 12 (2002) 1947

Novel Diphenylalkyl Piperazine Derivatives with Dual Calcium Antagonistic and Antioxidative Activities

Makoto Kimura,* Tomoko Masuda, Koji Yamada, Nobuo Kubota, Nobuyuki Kawakatsu, Masaki Mitani, Kenichi Kishii, Masato Inazu and Takayuki Namiki*

Pharmaceutical R & D Laboratories, POLA Chemical Industries Inc., 560, Kashio-cho, Totsuka-ku, Yokohama, Kanagawa, 244-0812, Japan

Two types of novel diphenylalkyl piperazine derivatives containing the thio or aminopropanol moiety substituted by phenyl or benzyl group were synthesized and evaluated for calcium antagonistic and antioxidative activities.



X=S or NR_2
n=0 or 1

Bioorg. Med. Chem. Lett. 12 (2002) 1951

The Synthesis and Effect of Fluorinated Chalcone Derivatives on Nitric Oxide Production

Javier Rojas,[a] Miguel Payá,[a] José N. Dominguez[b] and M. Luisa Ferrándiz[a,*]

[a]*Departamento de Farmacología, Universidad de Valencia, 46100 Burjasot, Valencia, Spain*
[b]*Laboratorio de Síntesis Orgánica, Facultad de Farmacia, Universidad Central de Venezuela, Caracas 1051, Venezuela*

Dimethoxy- and trimethoxychalcone derivatives, with various patterns of fluorination, were synthesized and evaluated for their influence on nitric oxide production. Some of them, chalcones **1**, **5**, **7**, **10**, **11** and **17**, inhibited NO production with IC_{50} in the *submicromolar* range; **17** is especially noteworthy because of its potency (IC_{50} 30 nM). These effects were not the consequence of a direct inhibitory action on enzyme activity but the inhibition of enzyme expression.

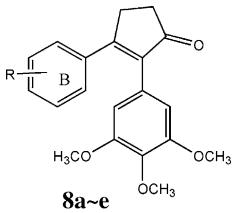
Bioorg. Med. Chem. Lett. 12 (2002) 1955

Synthesis and Anti-Tumor Activity of Novel Combretastatins: Combretocyclopentenones and Related Analogues

Nguyen-Hai Nam,[a] Yong Kim,[a] Young-Jae You,[a] Dong-Ho Hong,[a] Hwan-Mook Kim[b] and Byung-Zun Ahn[a,*]

[a]*College of Pharmacy, Chungnam National University, Taejon 305-764, Republic of Korea*
[b]*Korea Research Institute of Bioscience and Biotechnology, Taejon 305-600, Republic of Korea*

Five compounds **8a**–**8e** and their related analogues were synthesized and evaluated for cytotoxicity and anti-tumor activity. These compounds showed strong cytotoxicity with IC_{50} values in the range of 8–34 ng/mL. Compound **8e** exhibited significant anti-tumor activity in BDF1 mice bearing Lewis lung carcinoma cells with an inhibition ratio of 59%.



8a~e

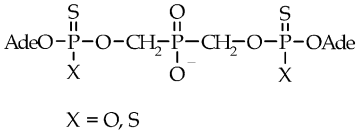
Bioorg. Med. Chem. Lett. 12 (2002) 1959

Inhibition of ADP-Triggered Blood Platelet Aggregation by Diadenosine Polyphosphate Analogues

Bogdan Walkowiak,[a,b,*] Janina Baraniak,[c] Czeslaw S. Cierniewski[a] and Wojciech Stec[c]

[a]*Department of Molecular and Medical Biophysics, Institute of Physiology and Biochemistry, Medical University of Lodz, Lodz, Poland*
[b]*Department of Biophysics, Institute of Material Engineering, Technical University of Lodz, Lodz, Poland*
[c]*Department of Bioorganic Chemistry, Center for Molecular and Macromolecular Research, Polish Academy of Science, Lodz, Poland*

The synthesis and biological evaluation of new diadenosine polyphosphate analogues on blood platelet aggregation are reported. The most active are compounds with a sulfur atom replacing one or both non-bridging oxygens at phosphorus bound to adenosyl residues and hydroxymethyl groups of bis(hydroxymethyl)phosphinic acid.



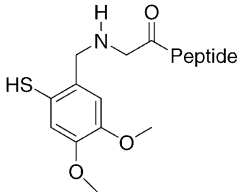
Bioorg. Med. Chem. Lett. 12 (2002) 1963

Synthesis and Application of an Auxiliary Group for Chemical Ligation at the X-Gly Site

Jean Vizzavona, Fritz Dick and Thomas Vorherr*

BACHEM AG, Hauptstrasse 144, CH-4416 Bubendorf, Switzerland

Synthesis and application of the 2-mercapto-4,5-dimethoxybenzyl (Dmmb) moiety for chemical ligation are reported.



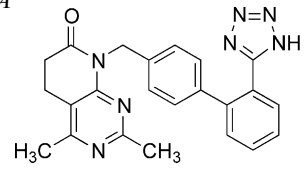
Bioorg. Med. Chem. Lett. 12 (2002) 1967

Novel Human Metabolites of the Angiotensin-II Antagonist Tasosartan and Their Pharmacological Effects

Hassan M. Elokdah,[a,*] Gregory S. Friedrichs,[b] Sie-Yearl Chai,[a] Boyd L. Harrison,[a] John Primeau,[a] Michael Chlenov[a] and David L. Crandall[b]

[a]*Medicinal Chemistry, Chemical Sciences, Wyeth Research, CN 8000, Princeton, NJ 08543, USA*
[b]*Cardiovascular/Women's Health, Wyeth Research, PO Box 42528, Philadelphia, PA 19101, USA*

Three novel metabolites of the angiotensin-II (A-II) receptor antagonist tasosartan (**1**) have been recently identified in plasma from the individuals treated with the compound. The syntheses of these metabolites, their in vitro inhibition of A-II receptor binding in human cell cultures, and their in vivo effects in attenuating the pressor response to angiotensin-II challlenge in anesthetized rats are reported.



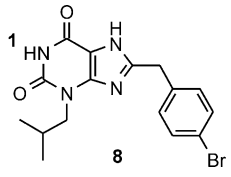
Bioorg. Med. Chem. Lett. 12 (2002) 1973

A Solid-Phase Approach Towards the Synthesis of PDE5 Inhibitors

David Beer, Gurdip Bhalay,* Andrew Dunstan, Angela Glen, Sandra Haberthuer and Heinz Moser

Novartis Horsham Research Centre, Wimblehurst Road, Horsham, West Sussex RH12 5AB, UK

Synthesis of analogues of xanthine **8** modified at *N*-1 is described using a practical solid-phase protocol.



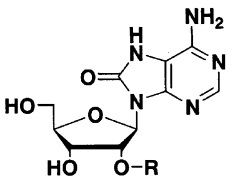
Bioorg. Med. Chem. Lett. 12 (2002) 1977

Base Pairing Properties of 8-Oxo-7,8-dihydroadenosine in cDNA Synthesis by Reverse Transcriptases

Sang Kook Kim, Ji Young Kim, Ae Kyeong Baek and Byung Jo Moon*

Department of Biochemistry, College of Natural Sciences, Kyungpook National University, Taegu 702–701, Republic of Korea

Incorporation of nucleotides opposite 8-oxo-7,8-dihydroadenosine (8-oxoA) in oligonucleotides with dNTPs by three reverse transcriptases (AMV-, MMRV-, RAV2-RT) in cDNA synthesis was studied. Guanine as well as thymine was incorporated preferentially by all reverse transcriptases. In the melting temperature experiment, 8-oxoA and 8-oxoA-Me formed base pairs with thymine and guanine with similar stabilities.



R=H: 8-oxoA
R=CH_3:8-oxoA-Me

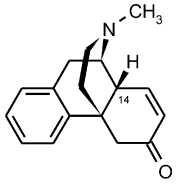
Bioorg. Med. Chem. Lett. 12 (2002) 1981

A Convenient Synthesis of $\Delta^{7,8}$-Morphinan-6-one and Its Direct Oxidation to 14-Hydroxy-$\Delta^{7,8}$-Morphinan-6-one

Daniele Passarella,* Alessandra Consonni, Alessandra Giardini, Giordano Lesma and Alessandra Silvani

Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano, Via Venezian 21, 20133 Milan, Italy

Synthesis of $\Delta^{7,8}$-morphinan-6-one and direct oxidation by MnO_2 to 14-hydroxy derivative is described.



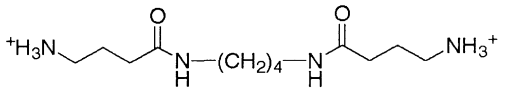
Bioorg. Med. Chem. Lett. 12 (2002) 1985

Discovery of Non-Zwitterionic $GABA_A$ Receptor Full Agonists and a Superagonist

Paul R. Carlier,[a,*] Ella S.-H. Chow,[a] Rebecca L. Barlow[b] and Jeffrey R. Bloomquist[b]

[a]*Department of Chemistry, Virginia Tech, Blacksburg, VA 24061, USA*
[b]*Department of Entomology, Virginia Tech, Blacksburg, VA 24061, USA*

Functional assays (chloride flux) demonstrate that appropriately functionalized GABA amides are partial, full, or superagonists of the $GABA_A$ receptor.



superagonist
maximal ion flux ~50% greater than that of GABA

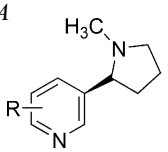
Bioorg. Med. Chem. Lett. 12 (2002) 1989

A Comparison of the Binding of Three Series of Nicotinic Ligands

Mase Lee,[a] Malgorzata Dukat,[a] Liang Liao,[a] Dwight Flammia,[a] M. Imad Damaj,[b] Billy Martin[b] and Richard A. Glennon[a,b]

[a]*Department of Medicinal Chemistry, School of Pharmacy, Box 980540, Virginia Commonwealth University, Richmond, VA 23298, USA*
[b]*Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298, USA*

Comparison of K_i values for 24 examples of aryl-substituted derivatives of nicotine and their corresponding ring-opened and ether analogues suggests that it is unlikely they bind at nicotinic acetylcholine receptors with precisely superimposed pyridine rings.



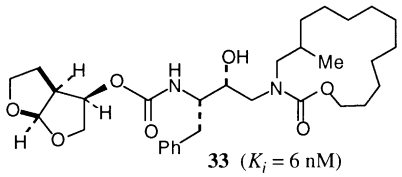
Bioorg. Med. Chem. Lett. 12 (2002) 1993

Novel Cyclourethane-Derived HIV Protease Inhibitors: A Ring-Closing Olefin Metathesis Based Strategy

Arun K. Ghosh,[a,*] Lisa M. Swanson,[a] Chunfeng Liu,[a] Khaja Azhar Hussain,[a] Hanna Cho,[a] D. Eric Walters,[b] Louis Holland[c] and Jim Buthod[c]

[a]*Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL 60607, USA*
[b]*Department of Biological Chemistry, Finch University of Health Sciences/ The Chicago Medical School, North Chicago, IL 60064, USA*
[c]*IIT Research Institute, Life Science Department, Chicago, IL 60616, USA*

A series of novel cyclourethanes containing a (*R*)-hydroxyethylamine isostere was designed and synthesized. Inhibitors with 14- to 16-membered rings exhibited low nanomolar inhibitory potencies.



33 (K_i = 6 nM)

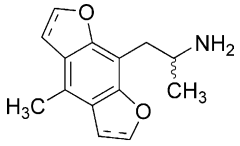
Bioorg. Med. Chem. Lett. 12 (2002) 1997

Translocation of the 5-Alkoxy Substituent of 2,5-Dialkoxyarylalkylamines to the 6-Position: Effects on 5-$HT_{2A/2C}$ Receptor Affinity

James J. Chambers, Deborah M. Kurrasch-Orbaugh and David E. Nichols*

Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907-1333, USA

Positional modification of 2,5-dimethoxyamphetamine analogues has been studied. The rigid compounds possessed increased affinity for the 5-HT_{2A} receptor when compared to 2,5- or 2,6-dimethoxy-4-methyl-amphetamine.



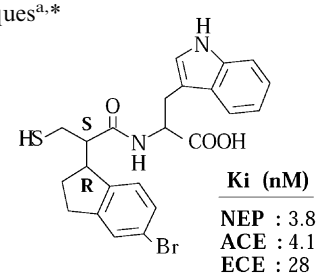
Bioorg. Med. Chem. Lett. 12 (2002) 2001

N-[2-(Indan-1-yl)-3-mercapto-propionyl] Amino Acids as Highly Potent Inhibitors of the Three Vasopeptidases (NEP, ACE, ECE): In Vitro and In Vivo Activities

Nicolas Inguimbert,[a] Hervé Poras,[a] Franck Teffo,[a] Françoise Beslot,[a] Mohamed Selkti,[b] Alain Tomas,[b] Elizabeth Scalbert,[c] Caroline Bennejean,[c] Pierre Renard,[c] Marie-Claude Fournié-Zaluski[a] and Bernard-Pierre Roques[a,*]

[a]*Département de Pharmacochimie Moléculaire et Structurale, U266 INSERM, UMR 8600 CNRS, UFR des Sciences Pharmaceutiques et Biologiques, 4, avenue de l'observatoire, 75270 Paris Cedex 06, France*
[b]*Laboratoire de Cristallographie et RMN Biologiques, CNRS UMR 8015, 4, avenue de l'Observatoire, 75270 Paris Cedex 06, France*
[c]*Institut de Recherches Internationales Servier, 6, place des Pleiades, 92415 Courbevoie Cedex, France*

This paper reports the synthesis and pharmacology of the first triple NEP, ACE, ECE inhibitor.



Ki (nM)
NEP : 3.8
ACE : 4.1
ECE : 28

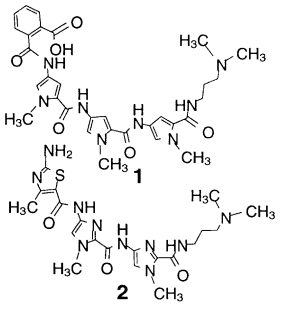
Bioorg. Med. Chem. Lett. 12 (2002) 2007

Inhibition of Feline Immunodeficiency Virus (FIV) Replication by DNA Binding Polyamides

Sanjay K. Sharma,[a] Jean-Noel Billaud,[b] Manju Tandon,[a] Olivier Billet,[b] Sam Choi,[b] Mary L. Kopka,[c] Tom R. Phillips[b] and J. William Lown[a,*]

[a]*Department of Chemistry, University of Alberta, Edmonton, AB, Canada T6G 2G2*
[b]*Vaccine Research Institute of San Diego, San Diego, CA 92121, USA*
[c]*Molecular Biology Institute, University of California, Los Angeles, CA 90095, USA*

Two DNA minor-groove binding polyamides **1** and **2** were designed and synthesized and evaluated for inhibition of FIV-34TF10 replication. Both **1** and **2** decreased the replicationof FIV-34TF10 by 75% at 0.1 nM concentration by acting at the level of the virus but outside of the LTR or env region.



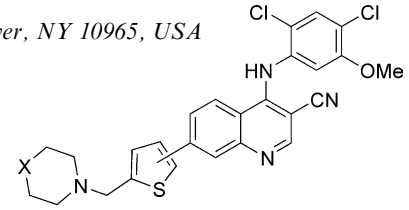
Bioorg. Med. Chem. Lett. 12 (2002) 2011

Inhibition of Src Kinase Activity by 4-Anilino-7-thienyl-3-quinolinecarbonitriles

Diane H. Boschelli,* Daniel Y. Wang, Fei Ye, Ayako Yamashita, Nan Zhang, Dennis Powell, Jennifer Weber and Frank Boschelli

Wyeth Research, Chemical Sciences and Oncology, 401 N. Middletown Road, Pearl River, NY 10965, USA

The preparation and Src kinase inhibitory activity of a series of 4-anilino-7-thienyl-3-quinolinecarbonitriles is reported.

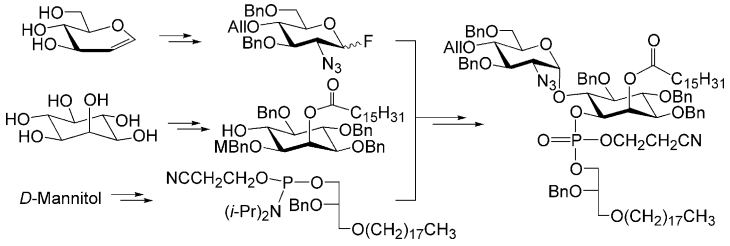


Bioorg. Med. Chem. Lett. 12 (2002) 2015

Convergent Synthesis of an Inner Core GPI of Sperm CD52

Jie Xue and Zhongwu Guo*

Department of Chemistry, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106, USA



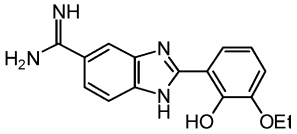
Bioorg. Med. Chem. Lett. 12 (2002) 2019

2-(2-Hydroxy-3-alkoxyphenyl)-1*H*-benzimidazole-5-carboxamidine Derivatives as Potent and Selective Urokinase-type Plasminogen Activator Inhibitors

Richard L. Mackman,* Hon C. Hui, J. Guy Breitenbucher, Bradley A. Katz, Christine Luong, Arnold Martelli, Danny McGee, Kesavan Radika, Martin Sendzik,* Jeffrey R. Spencer, Paul A. Sprengeler, James Tario, Erik Verner and Jing Wang

Celera, 180 Kimball Way, South San Francisco, CA 94080, USA

The development of potent and selective inhibitors of uPA based on the lead molecule **3a** is described.



3a

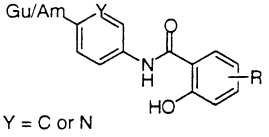
Bioorg. Med. Chem. Lett. 12 (2002) 2023

4-Aminoarylguanidine and 4-Aminobenzamidine Derivatives as Potent and Selective Urokinase-type Plasminogen Activator Inhibitors

Jeffrey R. Spencer, Danny McGee, Darin Allen, Bradley A. Katz, Christine Luong, Martin Sendzik,* Neil Squires and Richard L. Mackman*

Celera, 180 Kimball Way, South San Francisco, CA *94080, USA*

The structure-based design of potent and selective inhibitors of uPA with 4-aminoarylamidine or 4-aminoarylguanidine S1 binding groups, is described.



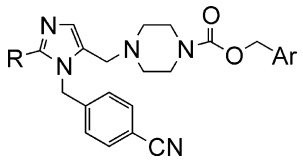
Bioorg. Med. Chem. Lett. 12 (2002) 2027

The Synthesis and Biological Evaluation of a Series of Potent Dual Inhibitors of Farnesyl and Geranyl-Geranyl Protein Transferases

Thomas J. Tucker,[a,*] Marc T. Abrams,[b] Carolyn A. Buser,[b] Joseph P. Davide,[b] Michelle Ellis-Hutchings,[b] Christine Fernandes,[b] Jackson B. Gibbs,[b] Samuel L. Graham,[a] George D. Hartman,[a] Hans E. Huber,[b] Dongming Liu,[b] Robert B. Lobell,[b] William C. Lumma,[a] Ronald G. Robinson,[b] John T. Sisko[a] and Anthony M. Smith[a]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, PO Box 4, Sumneytown Pike, West Point, PA 19486, USA*
[b]*Department of Cancer Biology, Merck Research Laboratories, PO Box 4, Sumneytown Pike, West Point, PA 19486, USA*

We have prepared a series of potent, dual inhibitors of the prenyl transferases FPTase (Farnesyl Protein Transferase) and GGPTase (Geranyl-Geranyl Protein Transferase I).



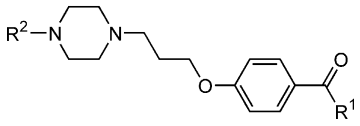
Bioorg. Med. Chem. Lett. 12 (2002) 2031

Structure–Activity Relationships of Non-imidazole H_3 Receptor Ligands. Part 1

Ramin Faghih,* Wesley Dwight, Robert Gentles, Kathleen Phelan, Timothy A. Esbenshade, Lynne Ireland, Thomas R. Miller, Chae-Hee Kang, Gerard B. Fox, Sujatha M. Gopalakrishnan, Arthur A. Hancock and Youssef L. Bennani

Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL 60064-6123, USA

SAR studies of novel non-imidazole containing H_3 receptor ligands are described.



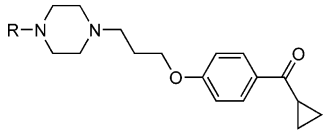
Bioorg. Med. Chem. Lett. 12 (2002) 2035

Structure–Activity Relationships of Non-imidazole H_3 Receptor Ligands. Part 2: Binding Preference for D-Amino Acids Motifs

Ramin Faghih,* Wesley Dwight, Larry Black, Huaqing Liu, Robert Gentles, Kathleen Phelan, Timothy A. Esbenshade, Lynne Ireland, Thomas R. Miller, Chae-Hee Kang, Kathy M. Krueger, Gerard B. Fox, Arthur A. Hancock and Youssef L. Bennani

Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL 60064-6123, USA

A series of D-amino acid containing ligands of histamine H_3 is described.



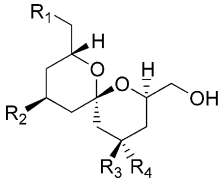
Bioorg. Med. Chem. Lett. 12 (2002) 2039

Synthesis and Biological Evaluation of a Spongistatin AB-Spiroketal Analogue

Amos B. Smith, III,[a,*] R. Michael Corbett,[a] George R. Pettit,[b] Jean-Charles Chapuis,[b] Jean M. Schmidt,[b] Ernest Hamel[c] and M. Katherine Jung[d]

[a]*Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104, USA*
[b]*Cancer Research Institute, Arizona State University, Tempe, AZ 85287, USA*
[c]*Screening Technologies Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute at Frederick, National Institutes of Health, Frederick, MD 21702, USA*
[d]*Science Applications International Corporation-Frederick, National Cancer Institute at Frederick, National Institutes of Health, Frederick, MD 21702, USA*

A short synthesis of a highly functionalized spongistatin AB-spiroketal mimic (−)-**4** is disclosed. Neither (−)-**4** nor the parent compound (−)-**3**, previously reported to possess growth inhibitory effects, was observed to have significant cytotoxic or antitubulin activity.



(−)-**3** R_1=OH, R_2=R_3=R_4=H
(−)-**4** R_1=CH_2OH, R_2=OAc, R_3=Me, R_4=OH

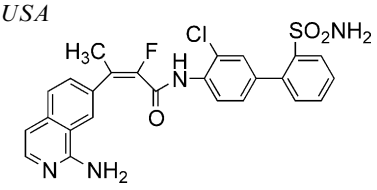
Bioorg. Med. Chem. Lett. 12 (2002) 2043

Substituted Acrylamides as Factor Xa Inhibitors: Improving Bioavailability by P1 Modification

Yonghong Song,* Lane Clizbe, Chhaya Bhakta, Willy Teng, Wenhao Li, Paul Wong, Brian Huang, Uma Sinha, Gary Park, Andrea Reed, Robert M. Scarborough and Bing-Yan Zhu

Millennium Pharmaceuticals, Inc., 256 East Grand Ave., South San Francisco, CA 94080, USA

To overcome the low bioavailability of our substituted acrylamide P1 benzamidine factor Xa inhibitors reported previously, neutral and less basic groups were used to replace the benzamidine. As a result, a series of P1 aminoisoquinoline substituted acrylamide Xa inhibitors was identified to be potent, selective, and orally bioavailable. Modification of P4 moiety of these compounds further improved their pharmacokinetic properties.



Bioorg. Med. Chem. Lett. 12 (2002) 2047

Preparation of Soluble and Insoluble Polymer Supported IBX Reagents

Neal N. Reed, Mercedes Delgado, Kristina Hereford, Bruce Clapham and Kim D. Janda*

Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA