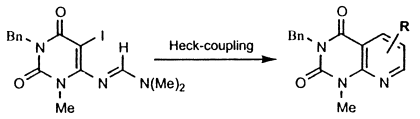
Syntheses and Evaluation of Pyrido[2,3-*d*]pyrimidine-2,4-diones as PDE 4 Inhibitors

Bioorg. Med. Chem. Lett. 11 (2001) 611

Ghilsoo Nam,[a] Cheol Min Yoon,[b] Euikyung Kim,[c] Chung K. Rhee,[c] Joong Hyup Kim,[a] Jung Hyu Shin[d] and Sung Hoon Kim[a,*]

[a]*Biochemicals Research Center, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul 130-650, South Korea*
[b]*Department of Chemistry, College of Science and Technology, Korea University, Jochiwon, Choong-nam, 339-700, South Korea*
[c]*Cheiljedang Corp., 522-1, Dokpyong-ri, Majang-myon, Ichon-si, Kyonggi-do, 467-810, South Korea*
[d]*School of Chemistry and Molecular Engineering, Seoul National University, Seoul 151-742, South Korea*

The synthesis and in vitro evaluation of a new series of pyrido[2,3-*d*]pyrimidine-2,4-diones bearing substituents at C-3 and/or C-4 positions on the pyridine ring is described. Some of these compounds, especially **5l** and **6f**, were found to be potent phosphodiesterase 4 (PDE 4) inhibitors exhibiting improved ratio of PDE 4 inhibitory activity:rolipram binding affinity (RBA).



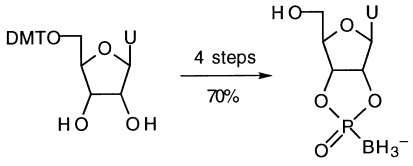
R = OBu, CN, CO_2Et, Ph, Ph(4-F), Ph(4-Cl), Ph(4-OEt), Ph(2-F), Ph(2-CF_3), Ph(3-CF_3), Ph(3-NO_2), CH_2Ph, CH_2OPr, CH_2OPh, CH_2OBn

Synthesis and Separation of Diastereomers of Uridine 2′,3′-Cyclic Boranophosphate

Bioorg. Med. Chem. Lett. 11 (2001) 615

Kaizhang He and Barbara Ramsay Shaw*

Department of Chemistry, Gross Chemical Laboratory, Duke University, Durham, NC 27708, USA



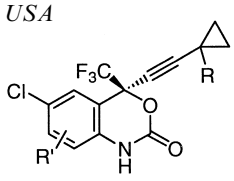
Synthesis and Biological Activities of Potential Metabolites of the Non-Nucleoside Reverse Transcriptase Inhibitor Efavirenz

Bioorg. Med. Chem. Lett. 11 (2001) 619

Jay A. Markwalder,* David D. Christ, Abdul Mutlib, Beverly C. Cordova, Ronald M. Klabe and Steven P. Seitz

DuPont Pharmaceuticals Company, Experimental Station, PO Box 80500, Wilmington, DE 19880-0500, USA

Efavirenz undergoes species-specific metabolism in vivo. Several primary and secondary metabolites were prepared by total synthesis, and their antiviral activities were determined.



Efavirenz metabolites

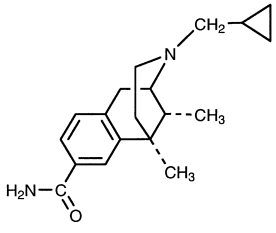
8-Carboxamidocyclazocine Analogues: Redefining the Structure–Activity Relationships of 2,6-Methano-3-benzazocines

Bioorg. Med. Chem. Lett. 11 (2001) 623

Mark P. Wentland,[a,*] Rongliang Lou,[a] Yingchun Ye,[a] Dana J. Cohen,[b] Gregory P. Richardson[b] and Jean M. Bidlack[b]

[a]*Department of Chemistry, Rensselaer Polytechnic Institute, Troy, NY 12180, USA*
[b]*Department of Pharmacology and Physiology, School of Medicine and Dentistry, University of Rochester, Rochester, NY 14642, USA*

Unexpectedly high affinity binding to μ and κ opioid receptors has been identified in a series of novel 2,6-methano-3-benzazocin-8-carboxamide derivatives.



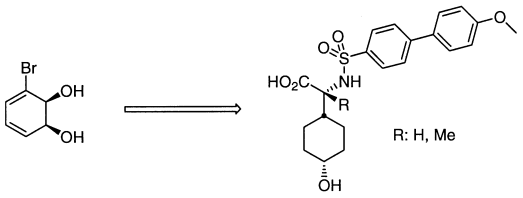
(±)-**15**: K_i = 0.41 nM (μ) and 0.53 nM (κ)

Bioorg. Med. Chem. Lett. 11 (2001) 627

Chemoenzymatic Synthesis of Functionalized Cyclohexylglycines and α-Methylcyclohexylglycines via Kazmaier–Claisen Rearrangement

Tomas Hudlicky,[a] Kofi Oppong,[a] Caiming Duan,[a] Charles Stanton,[a] Matthew J. Laufersweiler[b] and Michael G. Natchus[b,*]

[a]*Department of Chemistry, University of Florida, Gainesville, FL 32611-7200, USA*
[b]*Procter and Gamble Pharmaceuticals, Health Care Research Center, 8700 Mason-Montgomery Road, Mason, OH 45040, USA*



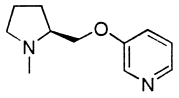
Bioorg. Med. Chem. Lett. 11 (2001) 631

Synthesis and Structure–Activity Relationships of 5-Substituted Pyridine Analogues of 3-[2-((*S*)-Pyrrolidinyl)methoxy]pyridine, A-84543: A Potent Nicotinic Receptor Ligand

Nan-Horng Lin,* Yihong Li, Yun He, Mark W. Holladay, Theresa Kuntzweiler, David J. Anderson, Jeffrey E. Campbell and Stephen P. Arneric

Neurological and Urological Diseases Research, D-47W, Pharmaceutical Products Division, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-3500, USA

Compound **1** substituted with bulky groups at the 5-position was synthesized and tested in vitro for nicotinic receptor binding affinity.



1 (A-84543)

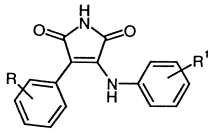
Bioorg. Med. Chem. Lett. 11 (2001) 635

3-Anilino-4-arylmaleimides: Potent and Selective Inhibitors of Glycogen Synthase Kinase-3 (GSK-3)

David G. Smith,* Marianne Buffet, Ashley E. Fenwick, David Haigh, Robert J. Ife, Martin Saunders, Brian P. Slingsby, Rachel Stacey and Robert W. Ward

SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK

Potent 3-anilino-4-arylmaleimide glycogen synthase kinase-3 (GSK-3) inhibitors have been prepared using automated array methodology. A number of these are highly selective, having little inhibitory potency against more than 20 other protein kinases.



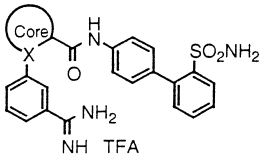
Bioorg. Med. Chem. Lett. 11 (2001) 641

Synthesis and SAR of Benzamidine Factor Xa Inhibitors Containing a Vicinally-Substituted Heterocyclic Core

John M. Fevig,* Donald J. Pinto,* Qi Han, Mimi L. Quan, James R. Pruitt, Irina C. Jacobson, Robert A. Galemmo, Jr., Shuaige Wang, Michael J. Orwat, Lori L. Bostrom, Robert M. Knabb, Pancras C. Wong, Patrick Y. S. Lam and Ruth R. Wexler

DuPont Pharmaceuticals Company, PO Box 80500, Wilmington, DE 19880-0500, USA

The selective inhibition of coagulation factor Xa has emerged as an attractive strategy for the discovery of novel antithrombotic agents. Here we describe highly potent benzamidine factor Xa inhibitors based on a vicinally-substituted heterocyclic core.



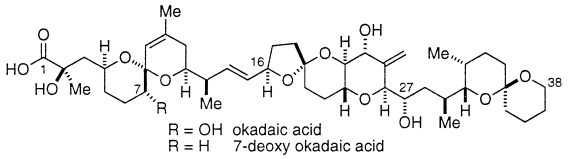
Bioorg. Med. Chem. Lett. 11 (2001) 647

Importance of the C28–C38 Hydrophobic Domain of Okadaic Acid for Potent Inhibition of Protein Serine-Threonine Phosphatases 1 and 2A

Valerie A. Frydrychowski, Rebecca A. Urbanek, Amy B. Dounay and Craig J. Forsyth*

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455, USA

Okadaic acid is a potent inhibitor of select serine/threonine protein phosphatases. The importance of the C28–C38 hydrophobic domain of okadaic acid for inhibition of PP1 and PP2A was investigated. The hydrophobic domain is required but not sufficient for potent inhibition, and it also contributes to differential inhibition between PP1 and PP2A.



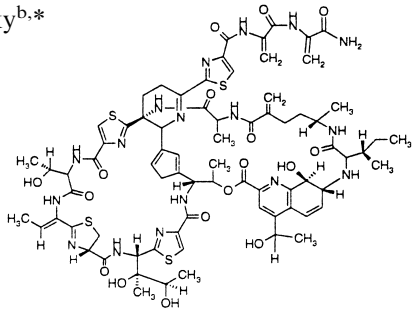
Bioorg. Med. Chem. Lett. 11 (2001) 651

Anion Recognition by Thiostrepton

Carolina Godoy-Alcántar,[a] Ismael León Rivera[a] and Anatoly K. Yatsimirsky[b,*]

[a]*Centro de Investigaciones Químicas, Universidad Autónoma del Estado de Morelos, 62210 Cuernavaca, Morelos, Mexico*
[b]*Facultad de Química, Universidad Nacional Autónoma de México, 04510 Mexico D.F., Mexico*

A bicyclic polypeptide antibiotic thiostrepton forms both 1:1 and 1:2 complexes with anions (as tetrabutylammonium salts) in organic solvents with $K_2 > K_1$ for F^- and $K_2 \ll K_1$ for all other anions studied. Relative stabilities of 1:1 complexes in DMSO are $AcO^- \sim F^- \gg Cl^-$, Br^-, HSO_4^-, $H_2PO_4^-$, but in $CHCl_3$ they follow a different order: $Cl^- \sim HSO_4^- > F^- \sim AcO^- > Br^- > H_2PO_4^-$.

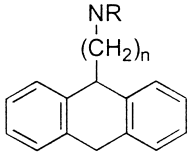


Bioorg. Med. Chem. Lett. 11 (2001) 655

Influence of Chain Length and *N*-Alkylation on the Selective Serotonin Receptor Ligand 9-(Aminomethyl)-9,10-dihydroanthracene

Scott P. Runyon,[a] Jason E. Savage,[b,c] Mohamed Taroua,[a] Bryan L. Roth,[b,c] Richard A. Glennon[a] and Richard B. Westkaemper[a,*]

[a]*Department of Medicinal Chemistry, School of Pharmacy, Virginia Commonwealth University, R.B. Smith Building, 410 North 12th Street, PO Box 980540, Richmond 23298-0540, VA 23298, USA*
[b]*Departments of Biochemistry and Psychiatry, Case Western Reserve University School of Medicine, Cleveland, OH 44106, USA*
[c]*The NIMH Psychoactive Drug Screening Program, USA*



The 5-HT_{2A} receptor affinities of a parallel series of 9-(aminomethyl)-9,10-dihydroanthracene and imipramine analogues suggests that the two classes of compounds bind to the receptor in different fashions. Unlike imipramine, AMDA has low affinity for D_2 receptors, SERT, and NET.

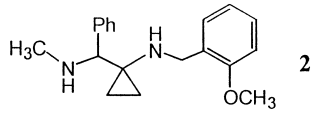
Bioorg. Med. Chem. Lett. 11 (2001) 659

Synthesis, Modelling and NK_1 Antagonist Evaluation of a Non-Rigid Cyclopropane-Containing Analogue of CP-99,994

David J. Aitken,[a,b,*] Sandrine Ongeri,[a] Danielle Vallée-Goyet,[b] Jean-Claude Gramain[b] and Henri-Philippe Husson[a]

[a]*Laboratoire de Chimie Thérapeutique associé au CNRS et à l'Université René Descartes (UMR 8638), Faculté des Sciences Pharmaceutiques et Biologiques, 4 avenue de l'Observatoire, 75270 Paris cedex 06, France*
[b]*Laboratoire SEESIB-CNRS (UMR 6504), Département de Chimie, Université Blaise Pascal - Clermont-Ferrand II, 24 avenue des Landais, 63177 Aubière cedex, France*

Compound **2** (synthesised racemic) has moderate NK_1 receptor binding affinity. Molecular dynamics calculations indicate conformational freedom and validate a pharmacophore model.



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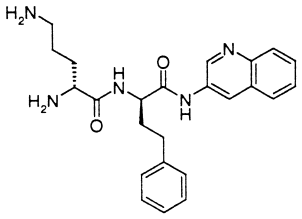
Bioorg. Med. Chem. Lett. 11 (2001) 663

Addressing the Stability of *C*-Capped Dipeptide Efflux Pump Inhibitors that Potentiate the Activity of Levofloxacin in *Pseudomonas aeruginosa*

Thomas E. Renau,[a,*] Roger Léger,[a] Eric M. Flamme,[a] Miles W. She,[a] Carla L. Gannon,[a] Kristina M. Mathias,[a] Olga Lomovskaya,[a] Suzanne Chamberland,[a] Ving J. Lee,[a] Toshiharu Ohta,[b] Kiyoshi Nakayama[b] and Yohei Ishida[b]

[a]*Microcide Pharmaceuticals, Inc., 850 Maude Ave., Mountain View, CA 94043, USA*
[b]*New Product Research Laboratories I, Daiichi Pharmaceutical Co. Ltd., 1-16-13, Kita-Kasai, Edogawa, Tokyo 134-8630, Japan*

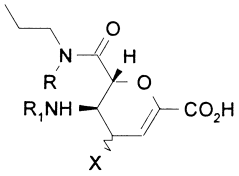


Bioorg. Med. Chem. Lett. 11 (2001) 669

Sialidase Inhibitors Related to Zanamivir. Further SAR Studies of 4-Amino-4*H*-pyran-2-carboxylic Acid-6-propylamides

Paul G. Wyatt,[a,*] Barry A. Coomber,[a] Derek N. Evans,[a] Torquil I. Jack,[a] Heather E. Fulton,[a] Alan J. Wonacott,[b] Peter Colman[c] and Jose Varghese[c]

[a]*Department of Medicinal Chemistry, GlaxoWellcome Medicines Research Centre, Gunnels Wood Road, Stevenage, Herts SG1 2NY, UK*
[b]*Department of Molecular Recognition, GlaxoWellcome Medicines Research Centre, Gunnels Wood Road, Stevenage, Herts SG1 2NY, UK*
[c]*Biomolecular Research Institute, Parkville, Victoria, Australia*



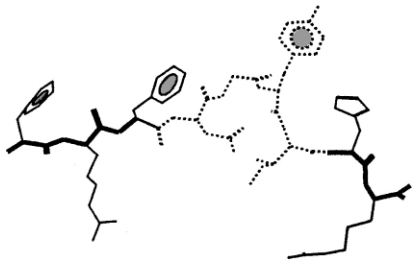
SAR investigations of the 4- and 5-positions of a series 4-amino-4*H*-pyran-2-carboxylic acid 6-carboxamides are reported. Potent inhibitors of influenza A sialidase with marked selectivity over the influenza B enzyme were obtained.

Bioorg. Med. Chem. Lett. 11 (2001) 675

Customized Versus Universal Scoring Functions: Application to Class I MHC–Peptide Binding Free Energy Predictions

Antoine Logean,[a] Alessandro Sette[b] and Didier Rognan[a,*]

[a]*Laboratoire de Pharmacochimie de la Communication Cellulaire, UMR 7081, F-67401 Illkirch, France*
[b]*Epimmune Inc., San Diego, CA 92121, USA*



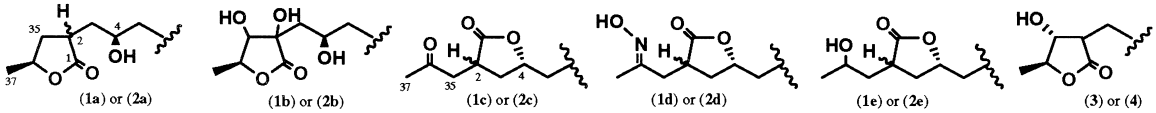
A customized scoring function (Fresno) is shown to outperform universal scoring functions for predicting binding free energies of peptide ligands to a class I MHC protein.

Bioorg. Med. Chem. Lett. 11 (2001) 681

γ-Lactone-Functionalized Antitumoral Acetogenins are the Most Potent Inhibitors of Mitochondrial Complex I

José R. Tormo,[a] Ernesto Estornell,[b] Teresa Gallardo,[a] M. Carmen González,[a] Adrien Cavé,[c] Susana Granell,[a] Diego Cortes[a,*] and M. Carmen Zafra-Polo[a]

[a]*Departamento de Farmacología, Farmacognosia y Farmacodinamia, Universidad de Valencia, 46100 Burjassot, Valencia, Spain*
[b]*Departamento de Bioquímica y Biologia Molecular, Facultad de Farmacia, Universidad de Valencia, 46100 Burjassot, Valencia, Spain*
[c]*Centre de Biochimie Structurale, Faculté de Pharmacie, 34060 Montpellier Cédex 1, France*

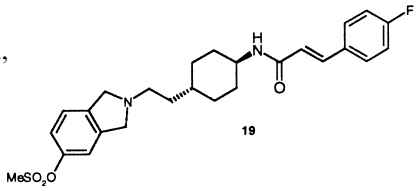


Bioorg. Med. Chem. Lett. 11 (2001) 685

Design and Synthesis of Novel 2,3-Dihydro-1*H*-isoindoles with High Affinity and Selectivity for the Dopamine D_3 Receptor

Nigel E. Austin, Kim Y. Avenell, Izzy Boyfield, Clive L. Branch,* Michael S. Hadley, Phillip Jeffrey, Christopher N. Johnson, Gregor J. Macdonald, David J. Nash, Graham J. Riley, Alexander B. Smith, Geoffrey Stemp, Kevin M. Thewlis, Antonio K. K. Vong and Martyn D. Wood

SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK



19

A novel series of 2,3-dihydro-1*H*-isoindoles (e.g., **19**) is described.

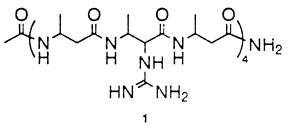
Bioorg. Med. Chem. Lett. 11 (2001) 689

The Synthesis of β-Peptides Containing Guanidino Groups

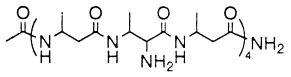
Ke Wen,[a] Hyunsoo Han,[b,*] Timothy Z. Hoffman,[b] Kim D. Janda[b,*] and Leslie E. Orgel[a,*]

[a]*The Salk Institute for Biological Studies, PO Box 85800, San Diego, CA, 92186, USA*
[b]*Department of Chemistry, The Scripps Research Institute and The Skaggs Institute for Chemical Biology, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*

The synthesis of the β-peptide **1** by the postsynthetic modification of the corresponding amino-containing peptide **3** is described. The potential of **1** to act as a template for the ligation of complementary negatively-charged peptides is discussed.



1



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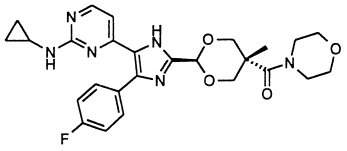
Bioorg. Med. Chem. Lett. 11 (2001) 693

RPR203494 a Pyrimidine Analogue of the p38 Inhibitor RPR200765A with an Improved In Vitro Potency

Alan J. Collis, Martyn L. Foster, Frank Halley,* Christopher Maslen, Iain M. McLay, Kenneth M. Page, E. Jane Redford, John E. Souness and Nicola E. Wilsher

Aventis Pharma, Dagenham Research Centre, Rainham Road South, Dagenham, Essex, RM10 7XS UK

Following the discovery of RPR200765, a series of pyrimidine analogues have been prepared as backups. Amongst them, RPR203494 was identified with a better in vitro profile than RPR200765A.



RPR203494. IC50 = 9 nM, EC50 = 60 nM.

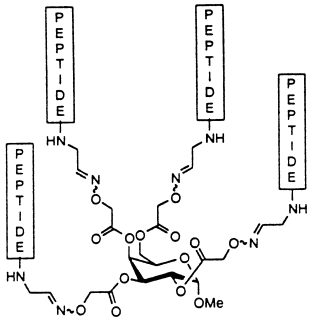
Bioorg. Med. Chem. Lett. 11 (2001) 697

Carboproteins: A 4-α-Helix Bundle Protein Model Assembled on a D-Galactopyranoside Template

Jesper Brask and Knud J. Jensen*

Department of Organic Chemistry, Technical University of Denmark, Building 201, Kemitorvet, DK-2800 Kgs. Lyngby, Denmark

A 64 amino acid protein model was synthesized by chemoselective oxime ligation of C-terminal peptide aldehydes to a tetra-aminooxy functionalized D-galactopyranoside template. The 'carboprotein' showed characteristics of a 4-α-helix bundle, according to CD spectroscopy and H–D exchange experiments.



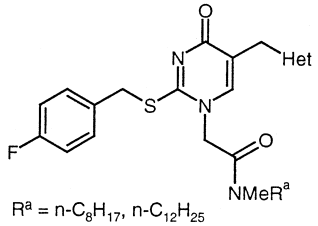
Bioorg. Med. Chem. Lett. 11 (2001) 701

The Identification of a Potent, Water Soluble Inhibitor of Lipoprotein-Associated Phospholipase A_2

Helen F. Boyd, Beverley Hammond, Deirdre M. B. Hickey, Robert J. Ife, Colin A. Leach, V. Ann Lewis, Colin H. Macphee, Kevin J. Milliner, Ivan L. Pinto, Stephen A. Smith,* Ian G. Stansfield, Colin J. Theobald and Caroline M. Whittaker

GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK

Modification of the 5-substituent in a series of 1-((amidolinked)-alkyl)-pyrimidones, has given a potent, highly water soluble, CNS penetrant inhibitor of human lipoprotein-associated phospholipase A_2 that is suitable for intravenous administration.



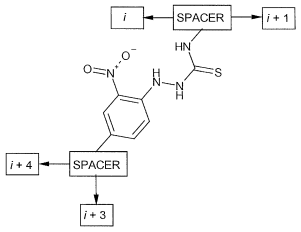
R^a = n-C_8H_{17}, n-$C_{12}H_{25}$
Het = substituted (pyrimidin-5-yl)

Bioorg. Med. Chem. Lett. 11 (2001) 705

Design of Non-Peptide CCK_2 and NK_1 Peptidomimetics Using 1-(2-Nitrophenyl)thiosemicarbazide as a Novel Common Scaffold

Edward K. Dziadulewicz,* Christopher S. Walpole, Christopher R. Snell, Roger Wrigglesworth, Glyn A. Hughes, David Beattie, John N. Wood, Margaret M. Beech and Paul R. Coote

Novartis Institute for Medical Sciences, 5 Gower Place, London WC1E 6BN, UK



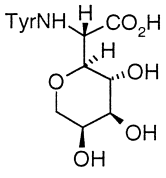
Bioorg. Med. Chem. Lett. 11 (2001) 711

Synthetic Analogues of SB-219383. Novel *C*-Glycosyl Peptides as Inhibitors of Tyrosyl tRNA Synthetase

Pamela Brown,[a,*] Drake S. Eggleston,[a] R. Curtis Haltiwanger,[b] Richard L. Jarvest,[a] Lucy Mensah,[a] Peter J. O'Hanlon[a] and Andrew J. Pope[a]

[a]*GlaxoSmithKline, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK*
[b]*GlaxoSmithKline, 709 Swedeland Road, King of Prussia, PA 19406, USA*

Novel inhibitors of bacterial tyrosyl tRNA synthetase have been synthesised in which the cyclic hydroxylamine moiety of SB-219383 is replaced by *C*-pyranosyl derivatives. The L-arabinose derivative is a potent and selective inhibitor.



IC_{50} 100 nM

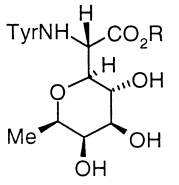
Bioorg. Med. Chem. Lett. 11 (2001) 715

Potent Synthetic Inhibitors of Tyrosyl tRNA Synthetase Derived from *C*-Pyranosyl Analogues of SB-219383

Richard L. Jarvest, John M. Berge, Pamela Brown,* Dieter W. Hamprecht, David J. McNair, Lucy Mensah, Peter J. O'Hanlon and Andrew J. Pope

GlaxoSmithKline, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK

Novel pyranosyl analogues of SB-219383 have been synthesised to elucidate the SARs around the pyran ring. Analogues with highly potent stereoselective and bacterioselective inhibition of bacterial tyrosyl tRNA synthetase have been identified.



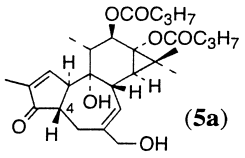
R = H IC_{50} 4.0 nM
R= Bu IC_{50} 0.8 nM

Bioorg. Med. Chem. Lett. 11 (2001) 719

The C4 Hydroxyl Group of Phorbol Esters is Not Necessary for Protein Kinase C Binding

Minoru Tanaka,[a] Kazuhiro Irie,[a,*] Yu Nakagawa,[a] Yoshimasa Nakamura,[b] Hajime Ohigashi[a] and Paul A. Wender[c]

[a]*Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Sakyo-ku, Kyoto 606-8502, Japan*
[b]*Laboratory of Food and Biodynamics, Graduate School of Bioagricultural Sciences, Nagoya University, Nagoya 464-8601, Japan*
[c]*Department of Chemistry, Stanford University, Stanford, CA 94305-5080, USA*



(**5a**)

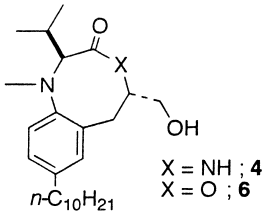
Synthesis of 4β-deoxy-phorbol-12,13-dibutyrate (**5a**) and its biological activities related to tumor promotion are reported.

Bioorg. Med. Chem. Lett. 11 (2001) 723

The Amide Hydrogen of (−)-Indolactam-V and Benzolactam-V8's Plays a Critical Role in Protein Kinase C Binding and Tumor-Promoting Activities

Yu Nakagawa,[a] Kazuhiro Irie,[a,*] Yoshimasa Nakamura[b] and Hajime Ohigashi[a]

[a]*Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Sakyo-ku, Kyoto 606-8502, Japan*
[b]*Laboratory of Food and Biodynamics, Graduate School of Bioagricultural Sciences, Nagoya University, Nagoya 464-8601, Japan*



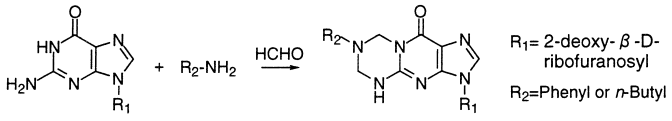
Synthesis, PKC surrogate binding, and tumor-promoting activities in vitro of the new lactone analogue (**6**) of 8-decylbenzolactam-V8 (**4**) are described.

Bioorg. Med. Chem. Lett. 11 (2001) 729

Formaldehyde-Mediated Modification of Natural Deoxyguanosine with Amines: One-Pot Cyclization as a Molecular Model for Genotoxicity

Hiroyasu Takahashi and Yuichi Hashimoto*

Institute of Molecular and Cellular Biosciences, University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113-0032, Japan

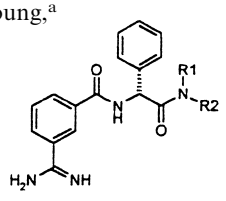


Bioorg. Med. Chem. Lett. 11 (2001) 733

The Design of Phenylglycine Containing Benzamidine Carboxamides as Potent and Selective Inhibitors of Factor Xa

Stuart D. Jones,[a,*] John W. Liebeschuetz,[a] Phillip J. Morgan,[a] Christopher W. Murray,[a] Andrew D. Rimmer,[a] Jonathan M. E. Roscoe,[a] Bohdan Waszkowycz,[a] Pauline M. Welsh,[a] William A. Wylie,[a] Stephen C. Young,[a] Harry Martin,[a] Jacqui Mahler,[a] Leo Brady[b] and Kay Wilkinson[b]

[a]*Protherics Molecular Design, Beechfield House, Lyme Green Business Park, Macclesfield, SK11 0JL, UK*
[b]*Department of Biochemistry, University of Bristol, Bristol BS8 1TD, UK*



Using PRO_SELECT, a number of highly focused libraries of compounds have been designed and synthesised giving rapid access to a series of potent and selective inhibitors of factor Xa. Key to the potency of these compounds is the lipophilic interaction between phenylglycine residue and the 'disulphide' pocket comprising Gln192, Cys191, Cys220 and Gly218.

Bioorg. Med. Chem. Lett. 11 (2001) 737

Structure–Activity Analysis of Truncated Orexin-A Analogues at the Orexin-1 Receptor

John G. Darker,[a,*] Roderick A. Porter,[a] Drake S. Eggleston,[a] Darren Smart,[b] Stephen J. Brough,[b] Cibele Sabido-David[a] and Jeffrey C. Jerman[b]

[a]*Discovery Chemistry, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK*
[b]*Neuroscience Research, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK*

Truncated peptide analogues of orexin-A were prepared and their biological activity assessed at the orexin-1 receptor.

Orexin-A

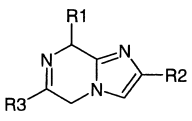
Bioorg. Med. Chem. Lett. 11 (2001) 741

Synthesis of Substituted Imidazopyrazines as Ligands for the Human Somatostatin Receptor Subtype 5

Marie-Odile Contour-Galcéra,[a,*] Lydie Poitout,[a] Christophe Moinet,[a] Barry Morgan,[b] Tom Gordon,[b] Pierre Roubert[a] and Christophe Thurieau[a,*]

[a]*Institut Henri Beaufour, 5, Avenue du Canada, F-91966 Les Ulis Cédex, France*
[b]*Biomeasure Inc., 27 Maple Street, Milford, MA 01757, USA*

A new preparation of trisubstituted imidazopyrazines and dihydro imidazopyrazines via parallel synthesis using aminoacids and bromoketones resulted in the discovery of non-peptidic sst_5 selective agonists.



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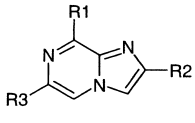

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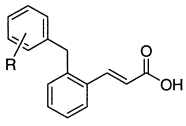
Bioorg. Med. Chem. Lett. 11 (2001) 747

Structure–Activity Relationship on the Human EP_3 Prostanoid Receptor by Use of Solid-Support Chemistry

Hélène Juteau,* Yves Gareau, Marc Labelle, Sonia Lamontagne, Nathalie Tremblay, Marie-Claude Carrière, Nicole Sawyer, Danielle Denis and Kathleen M. Metters

Merck Frosst & Co. PO Box 1005, Pointe-Claire, Dorval, Québec, Canada, H9R 4P8

Potent and selective EP_3 receptor ligands were found by making a library using solid-support chemistry. These compounds (**1**) can be obtained by a Suzuki coupling reaction of solid-supported benzyl bromide using various boronic acids.



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