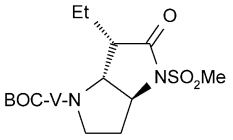
Bioorg. Med. Chem. Lett. 12 (2002) 3359

Design and Synthesis of Ethyl Pyrrolidine-5,5-*trans*-lactams as Inhibitors of Hepatitis C Virus NS3/4A Protease

Martin J. Slater,* David M. Andrews, Graham Baker, Susanne S. Bethell, Seb Carey, Helene Chaignot, Berwyn Clarke, Barry Coomber, Malcolm Ellis, Andrew Good, Norman Gray, George Hardy, Paul Jones, Gail Mills and Ed Robinson

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

Using a pyrrolidine-5,5-*trans*-lactam template, we have designed small, neutral, mechanism-based inhibitors of hepatitis C NS3/4A protease. Compound **11a**, with an alpha-ethyl P1 substituent and a Boc-valine substituent at the pyrrolidine nitrogen, has an $IC_{50} = 30\ \mu M$.



11a

Bioorg. Med. Chem. Lett. 12 (2002) 3363

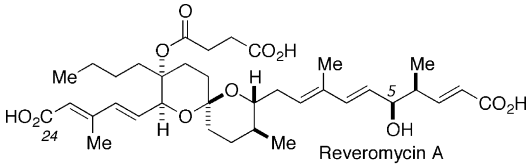
Chemical Modification of Reveromycin A and Its Biological Activities

Takeshi Shimizu,[a,*] Takeo Usui,[b] Kiyotaka Machida,[b] Kouichi Furuya,[a] Hiroyuki Osada[b] and Tadashi Nakata[a]

[a]*Synthetic Organic Chemistry Laboratory, RIKEN (The Institute of Physical and Chemical Research), Wako, Saitama 351-0198, Japan*

[b]*Antibiotic Laboratory, RIKEN (The Institute of Physical and Chemical Research), Wako, Saitama 351-0198, Japan*

Various derivatives of reveromycin A, a novel inhibitor of eukaryotic cell growth, were prepared and their inhibitory effects on both isoleucyl-tRNA synthetase activity and in vitro protein synthesis, and activities on the morphological reversion of *src*^{ts}-NRK cells were assayed. The C5 hydroxyl group and C24 carboxyl group are particularly important for these activities.



Reveromycin A

Bioorg. Med. Chem. Lett. 12 (2002) 3367

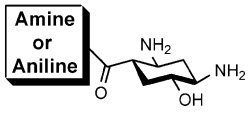
Novel 2,5-Dideoxystreptamine Derivatives Targeting the Ribosomal Decoding Site RNA

Dionisios Vourloumis,[a,*] Masayuki Takahashi,[a] Geoffrey C. Winters,[a] Klaus B. Simonsen,[a] Benjamin K. Ayida,[a] Sofia Barluenga,[a] Seema Qamar,[b] Sarah Shandrick,[b] Qiang Zhao[b] and Thomas Hermann[b,*]

[a]*Department of Medicinal Chemistry, Anadys Pharmaceuticals, Inc., 9050 Camino Santa Fe, San Diego, CA 92121, USA*

[b]*Departments of RNA Biochemistry and Computational Chemistry and Structure, Anadys Pharmaceuticals, Inc., 9050 Camino Santa Fe, San Diego, CA 92121, USA*

We have synthesized and tested RNA-targeted 2,5-dideoxystreptamine-4-amides in which a sugar moiety in natural aminoglycosides is replaced by heterocycles.

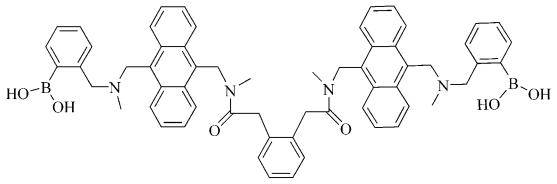


Bioorg. Med. Chem. Lett. 12 (2002) 3373

A Glucose-Selective Fluorescence Sensor Based on Boronic Acid-Diol Recognition

Vishnu Vardhan Reddy Karnati, Xingming Gao, Shouhai Gao, Wenqian Yang, Weijuan Ni, Sabapathy Sankar and Binghe Wang*

Department of Chemistry, North Carolina State University, Raleigh, NC 27695-8204, USA



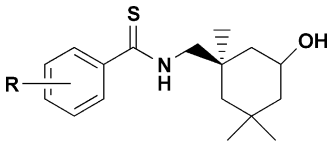
Bioorg. Med. Chem. Lett. 12 (2002) 3379

Structure–Activity Relationships for a Series of Thiobenzamide Influenza Fusion Inhibitors Derived from 1,3,3-Trimethyl-5-hydroxy-cyclohexylmethylamine

Kuo-Long Yu,[a,*] Albert F. Torri,[b] Guangxiang Luo,[b] Christopher Cianci,[b] Katharine Grant-Young,[a] Stephanie Danetz,[b] Lawrence Tiley,[b] Mark Krystal[b] and Nicholas A. Meanwell[a,*]

[a]*Departments of Chemistry, The Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*
[b]*Department of Virology, The Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*

The synthesis and SAR of a series of thiobenzamide influenza fusion inhibitors derived from 1,3,3-trimethyl-5-hydroxy-cyclohexylmethylamine are discussed. Axial disposition of the thioamide moiety is essential for influenza inhibitory activity and potency exhibits dependence on the substitution pattern of the aryl ring.



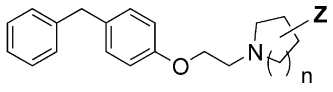
Bioorg. Med. Chem. Lett. 12 (2002) 3383

Pyrrolidine and Piperidine Analogues of SC-57461A as Potent, Orally Active Inhibitors of Leukotriene A_4 Hydrolase

Thomas D. Penning,[a,*] Nizal S. Chandrakumar,[a] Bipin N. Desai,[a] Stevan W. Djuric,[a] Alan F. Gasiecki,[a] Chi-Dean Liang,[a] Julie M. Miyashiro,[a] Mark A. Russell,[a] Leslie J. Askonas,[b] James K. Gierse,[b] Elizabeth I. Harding,[b] Maureen K. Highkin,[b] James F. Kachur,[b] Suzanne H. Kim,[b] Doreen Villani-Price,[b] E. Yvonne Pyla,[b] Nayereh S. Ghoreishi-Haack[b] and Walter G. Smith[b]

[a]*Department of Medicinal Chemistry, Pharmacia Corporation, 4901 Searle Parkway, Skokie, IL 60077, USA*
[b]*Departments of Inflammatory Diseases Research and Molecular Pharmacology, Pharmacia Corporation, 4901 Searle Parkway, Skokie, IL 60077, USA*

The synthesis and biological evaluation of a series of functionalized pyrrolidine- and piperidine-containing analogues of our lead LTA_4 hydrolase inhibitor, SC-57461A, is described.



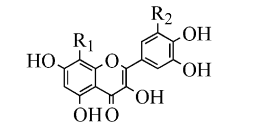
Bioorg. Med. Chem. Lett. 12 (2002) 3387

Natural PTP1B Inhibitors from *Broussonetia papyrifera*

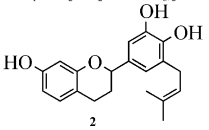
Rong Min Chen, Li Hong Hu,* Tian Ying An, Jia Li and Qiang Shen

Chinese National Center for Drug Screening, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological sciences, Chinese Academy of Sciences, Shanghai 200031, China

Two new compounds, 8-(1,1-dimethylallyl)-5′-(3-methylbut-2-enyl)-3′,4′,5,7-tetrahydroxyflanvonol (**1**),3′-(3-methylbut-2-enyl)-3′,4′,7-trihydroxyflavane (**2**) and three known compounds 3,3′,4′,5,7-pentahydroxyflavone (**3**), uralenol (**4**), broussochalcone A (**5**) were isolated from the roots of *Broussonetia papyrifera,* and their structures determined by spectroscopic methods. Compounds **1**, **3**, **4** and **5** significantly show the inhibitory activities against the PTP1B enzyme.



1 R_1=C(CH$_3$)-CH=CH$_2$, R_2=CH$_2$-CH=C(CH$_3$)$_2$
3 R_1=R_2=H
4 R_1=H, R_2=CH$_2$-CH=C(CH$_3$)$_2$



2

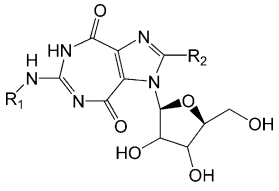
Bioorg. Med. Chem. Lett. 12 (2002) 3391

In Vitro Inhibition of the Measles Virus by Novel Ring-Expanded ('Fat') Nucleoside Analogues Containing the Imidazo[4,5-*e*][1,3]diazepine Ring System

Ning Zhang,[a] Huan-Ming Chen,[a] Ramesh Sood,[b] Kishna Kalicharran,[b] Ali I. Fattom,[b] Robert B. Naso,[b] Dale L. Barnard,[c] Robert W. Sidwell[c] and Ramachandra S. Hosmane[a,*]

[a]*Laboratory for Drug Design and Synthesis, Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, 1000 Hilltop Circle Baltimore, MD 21250, USA*
[b]*W. W. Karakawa Microbial Pathogenesis Laboratory, Nabi, 12280 Wilkins Avenue, Rockville, MD 20852, USA*
[c]*Institute for Antiviral Research, Utah State University, Logan, UT 84322, USA*

The synthesis and in vitro anti-measles virus activity of ring-expanded nucleosides **1**–**4** are reported.



1: R_1=R_2=H
2: R_1=H; R_2=Ph
3: R_1=CH_3; R_2=H
4: R_1=C_2H_5; R_2=H

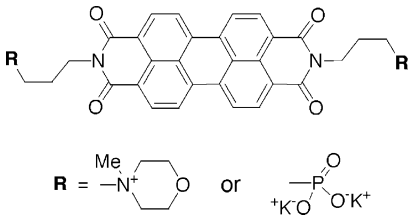
Bioorg. Med. Chem. Lett. 12 (2002) 3395

The Aggregation and G-Quadruplex DNA Selectivity of Charged 3,4,9,10-perylenetetracarboxylic Acid Diimides

Jonathan T. Kern and Sean M. Kerwin*

Division of Medicinal Chemistry, College of Pharmacy, University of Texas at Austin, Austin, TX 78712, USA

Charged G-quadruplex DNA binding perylene diimides were prepared. A bis(cationic) ligand binds in a cooperative fashion to G-quadruplex and duplex DNA, but a bis(phosphonate) analogue binds selectively to G-quadruplex DNA.

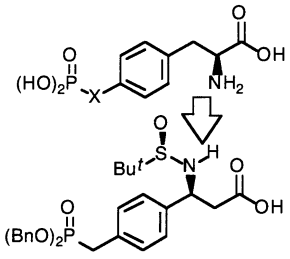


Bioorg. Med. Chem. Lett. 12 (2002) 3399

Design and Synthesis of a β-Amino Phosphotyrosyl Mimetic Suitably Protected for Peptide Synthesis

Kyeong Lee,[a] Manchao Zhang,[b] Dajun Yang[b] and Terrence R. Burke, Jr.[a,*]

[a]*Laboratory of Medicinal Chemistry, Center for Cancer Research, NCI-Frederick, National Institutes of Health, Frederick, MD 21702, USA*
[b]*Department of Hematology/Oncology, University of Michigan, Ann Arbor, MI 48109, USA*



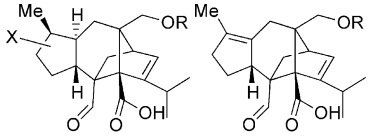
Bioorg. Med. Chem. Lett. 12 (2002) 3403

Core-Modified Sordaricin Derivatives: Synthesis and Antifungal Activity

Alicia Regueiro-Ren,* Tina M. Carroll, Yijun Chen, James A. Matson, Stella Huang, Charles E. Mazzucco, Terry M. Stickle, Dolatrai M. Vyas and Balu N. Balasubramanian

Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA

The synthesis and biological activity of core-modified sordaricin analogues are reported.



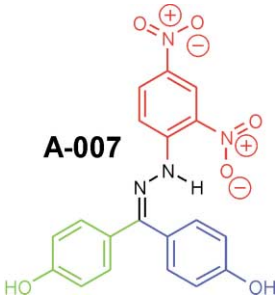
Bioorg. Med. Chem. Lett. 12 (2002) 3407

Anticancer Activity for 4,4′-Dihydroxybenzophenone-2,4-dinitrophenylhydrazone (A-007) Analogues and Their Abilities to Interact with Lymphoendothelial Cell Surface Markers

Lee Roy Morgan,[a] Branko S. Jursic,[b,*] Catherine L. Hooper,[a] Donna M. Neumann,[b] Kanappan Thangaraj[a] and Blaise LeBlanc[a]

[a]*DEKK-TEC, Inc, New Orleans, LA 70119, USA*
[b]*Department of Chemistry, University of New Orleans, New Orleans, LA 70122, USA*

A-007 has been modified through SAR and the analogue anticancer activity and modulation of HH T-cell leukemia cell surface markers were evaluated and discussed.



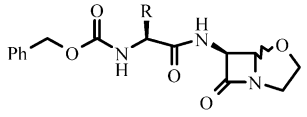
Bioorg. Med. Chem. Lett. 12 (2002) 3413

Design and Synthesis of 6-Substituted Amino-4-oxa-1-azabicyclo[3,2,0]heptan-7-one Derivatives as Cysteine Proteases Inhibitors

Nian E. Zhou,[a] Deqi Guo,[a] Jadwiga Kaleta,[a] Enrico Purisima,[b] Robert Menard,[b] Ronald G. Micetich[a] and Rajeshwar Singh[a,*]

[a]*SynPhar Laboratories, currently NAEJA Pharmaceutical Inc.,4290-91A Street, Edmonton, Alberta, Canada T6E 5V2*
[b]*National Research Council Canada, BRI, 6100 Royalmount Ave, Montreal, Quebec, Canada, H4P-2R2*

A series of 6-substituted amino-4-oxa-1-azabicyclo[3,2,0]heptan-7-one compounds was synthesized with excellent cysteine protease inhibitory activity is reported.



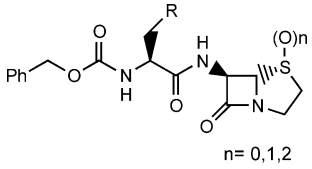
Bioorg. Med. Chem. Lett. 12 (2002) 3417

6-Acylamino-penam Derivatives: Synthesis and Inhibition of Cathepsins B, L, K, and S

Nian E. Zhou,[a] Jadwiga Kaleta,[a] Enrico Purisima,[b] Robert Menard,[b] Ronald G. Micetich[a] and Rajeshwar Singh[a,*]

[a]*SynPhar Laboratories, currently NAEJA Pharmaceutical Inc., 4290-91A Street, Edmonton, Alberta, Canada T6E 5V2*
[b]*National Research Council Canada, BRI, 6100 Royalmount Ave, Montreal, Quebec, Canada H4P 2R2*

The synthesis of 6-acylamino penam derivatives with excellent cysteine proteases inhibitory activity is reported.



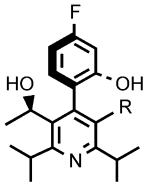
Bioorg. Med. Chem. Lett. 12 (2002) 3421

Integration of Optimized Substituent Patterns to Produce Highly Potent 4-Aryl-pyridine Glucagon Receptor Antagonists

Gaetan H. Ladouceur,[a,*] James H. Cook,[a] Donald L. Hertzog,[a] J. Howard Jones,[a] Thomas Hundertmark,[a] Mary Korpusik,[a] Timothy G. Lease,[a] James N. Livingston,[b] Margit L. MacDougall,[b] Martin H. Osterhout,[a] Kathleen Phelan,[a] Romulo H. Romero,[a] William R. Schoen,[a] Chunning Shao[a] and Roger A. Smith[a]

[a]*Department of Chemistry Research, Bayer Research Center, 400 Morgan Lane, West Haven, CT 06516, USA*
[b]*Department of Metabolic Disorders Research, Bayer Research Center, 400 Morgan Lane, West Haven, CT 06516, USA*

Optimized substituent patterns in 4-aryl-pyridine glucagon receptor antagonists were merged to produce highly potent derivatives containing both a 3-[(1*R*)-hydroxyethyl] and a 2′-hydroxy group. Due to restricted rotation of the phenyl–pyridine bond, these analogues exist as four isomers. A diastereoselective methylcopper reaction was developed to facilitate the synthesis, and single isomers were isolated with activities in the range $IC_{50} = 10–25$ nM.

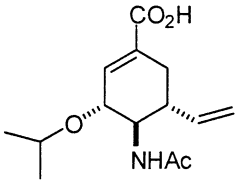


Bioorg. Med. Chem. Lett. 12 (2002) 3425

Design, Synthesis, and Neuraminidase Inhibitory Activity of GS-4071 Analogues that Utilize a Novel Hydrophobic Paradigm

Stephen Hanessian,[a,*] Jianchio Wang,[a] Debra Montgomery,[b] Vincent Stoll,[b] Kent D. Stewart,[b] Warren Kati,[b] Clarence Maring,[b] Dale Kempf,[b] Charles Hutchins[b] and W. Graeme Laver[c]

[a]*Department of Chemistry, Université de Montréal, PO Box 6128, Station Centre-ville, Montréal, QC, Canada H3C 3J7*
[b]*Abbott Laboratories, Abbott Park, IL 60064, USA*
[c]*The Australian National University, Canberra 260, Australia*



K_i = 45 nM

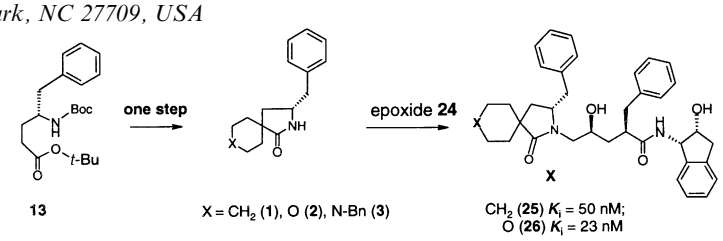
Bioorg. Med. Chem. Lett. 12 (2002) 3431

Novel Spirocyclic Pyrrolidones as P2/P1 Mimetics in Potent Inhibitors of HIV-1 Protease

Wieslaw M. Kazmierski,* Eric Furfine, Andrew Spaltenstein and Lois L. Wright

GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, NC 27709, USA

We have developed concise and efficient syntheses of novel spirocyclic pyrrolidones **1**–**3**, which involve the alkylation of pyrrolidone precursor **13** with 1,5-dibromopentane, **16** and **15**, followed by an in situ lactamization. Conjugates of **1** and **2** with P1′/P2′ hydroxy-indanolamine moiety resulted in novel and potent inhibitors of HIV-1 protease **25** and **26**, suggesting that **1** and **2** are novel P2/P1 HIV-PI mimetics.



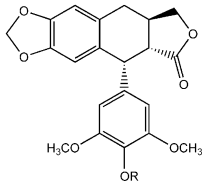
Bioorg. Med. Chem. Lett. 12 (2002) 3435

Prodrugs of 4′-Demethyl-4-deoxypodophyllotoxin: Synthesis and Evaluation of the Antitumor Activity

Yong Kim, Young-Jae You, Nguyen-Hai Nam and Byung-Zun Ahn*

College of Pharmacy, Chungnam National University, Taejon 305-764, South Korea

A series of prodrugs of 4′-demethyl-4-deoxypodophyllotoxin (DDPT) including carbamates (**3**–**8**), a carbonate (**9**) and water-soluble amino acid derivatives (**10**–**17**) were prepared and tested for their antitumor activity. The carbamate **6** (2-hydroxyethylcarbamoyl-DDPT), carbonate **9** (2-chloroethyl-oxycarbonyl-DDPT), and most of amino acid prodrugs (**12**–**17**) showed enhanced antitumor activity.



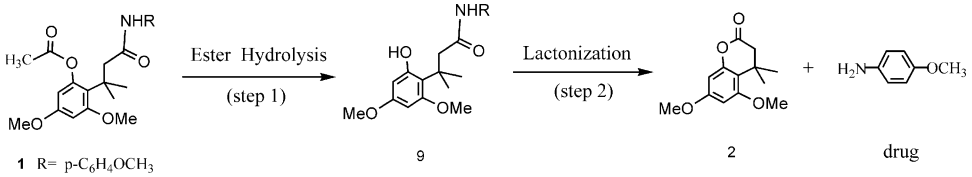
Bioorg. Med. Chem. Lett. 12 (2002) 3439

Synthesis and Stability Study of a Modified Phenylpropionic Acid Linker-Based Esterase-Sensitive Prodrug

Xiaoping Song and Teruna J. Siahaan*

Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS 66047, USA

An esterase-sensitive amide prodrug **1** with a modified phenylpropionic acid linker was synthesized. The prodrug can be converted to the drug using isolated porcine esterase and human plasma. Paraoxon, an esterase inhibitor, can inhibit the prodrug to drug conversion. The conversion of prodrug **1** was via phenol intermediate **9** followed by a lactonization reaction to give lactone **2** and the drug.



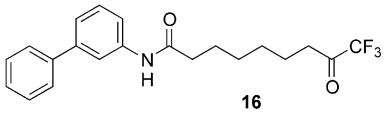
Bioorg. Med. Chem. Lett. 12 (2002) 3443

Trifluoromethyl Ketones as Inhibitors of Histone Deacetylase

Robin R. Frey,* Carol K. Wada, Robert B. Garland, Michael L. Curtin, Michael R. Michaelides, Junling Li, Lori J. Pease, Keith B. Glaser, Patrick A. Marcotte, Jennifer J. Bouska, Shannon S. Murphy and Steven K. Davidsen

Cancer Research, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064, USA

The synthesis and evaluation of a series of non-hydroxamate histone deacetylase (HDAC) inhibitors such as **16** (HDAC IC_{50} 380 nM) is described.



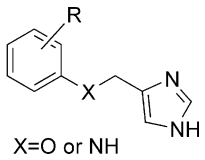
Bioorg. Med. Chem. Lett. 12 (2002) 3449

α_1-Adrenoceptor Activation: A Comparison of 4-(Anilinomethyl)imidazoles and 4-(Phenoxymethyl)imidazoles to Related 2-Imidazolines

Stephen J. Hodson, Eric C. Bigham, Deanna T. Garrison, Michael J. Gobel, Paul E. Irving, James A. Liacos, Frank Navas, III, David L. Saussy, Jr., Bryan W. Sherman, Jason D. Speake and Michael J. Bishop*

GlaxoSmithKline Research and Development, 5 Moore Drive, Research Triangle Park, NC 27709, USA

Novel 4-(anilinomethyl)imidazoles and 4-(phenoxymethyl)imidazoles are agonists of the cloned human α_1-adrenoceptors in vitro, and these imidazoles demonstrate similar potencies and α_1-subtype selectivities as the corresponding 2-substituted imidazolines.



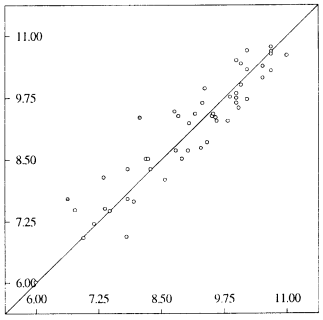
Bioorg. Med. Chem. Lett. 12 (2002) 3453

Six-Membered Cyclic Ureas as HIV-1 Protease Inhibitors: A QSAR Study Based on CODESSA PRO Approach

Alan R. Katritzky,[a,*] Alexander Oliferenko,[a] Andre Lomaka[b] and Mati Karelson[b]

[a]*Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, PO Box 11720, Gainesville, FL 32611-7200, USA*
[b]*Department of Chemistry, University of Tartu, 2 Jakobi Str., Tartu, Estonia*

A four-parameter QSAR model with $R^2 = 0.873$ for 51 aspartyl protease inhibitors has been obtained using CODESSA PRO descriptors and software.



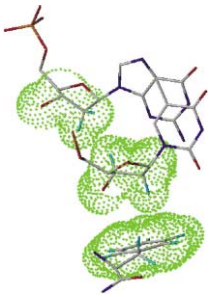
Bioorg. Med. Chem. Lett. 12 (2002) 3459

Understanding the Unique Mechanism of L-FMAU (Clevudine) against Hepatitis B Virus: Molecular Dynamics Studies

Youhoon Chong and Chung K. Chu*

Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA 30602, USA

The molecular dynamics simulation of HBV-polymerase·DNA·L-FMAU-TP complex is presented.



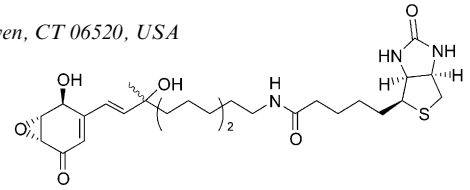
Bioorg. Med. Chem. Lett. 12 (2002) 3463

Inhibitors of NF-κB Signaling: Design and Synthesis of a Biotinylated Isopanepoxydone Affinity Reagent

J. Brad Shotwell,[a,b] Brian Koh,[b] Hui Won Choi,[a] John L. Wood[a] and Craig M. Crews[a,b,c,*]

[a]*Sterling Chemistry Laboratory, Yale University, New Haven, CT 06520, USA*
[b]*Department of Molecular, Cellular, and Developmental Biology, Yale University, New Haven, CT 06520, USA*
[c]*Department of Pharmacology, Yale University, New Haven, CT 06520, USA*

A number of inhibitors of NF-κB signaling arising from our recent syntheses of isopanepoxydone and panepoxydone have been identified. Structure–activity data have been correlated to allow the design and synthesis of an affinity reagent for the isolation and identification of relevant cellular target(s).



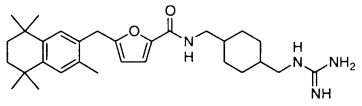
Bioorg. Med. Chem. Lett. 12 (2002) 3467

The Discovery of Novel Small Molecule Non-peptide Gonadotropin Releasing Hormone (GnRH) Receptor Antagonists

David R. Luthin,* Yufeng Hong, Ved P. Pathak, Genevieve Paderes, Karen D. Nared-Hood, Mary A. Castro, Haresh Vazir, Haitao Li, Eileen Tompkins, Lance Christie, John M. May and Mark B. Anderson

Pfizer Global Research and Development-La Jolla/Agouron Pharmaceuticals, Inc., 10724 Science Center Drive, San Diego, CA 92121, USA

The discovery of novel guanidine-derived GnRH receptor antagonists **1** (Human GnRH-R $K_i = 40$ nM) is reported.



1

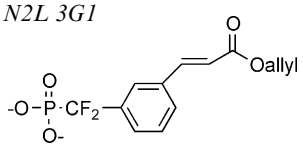
Bioorg. Med. Chem. Lett. 12 (2002) 3471

Synthesis of [Difluoro-(3-alkenylphenyl)-methyl]-phosphonic Acids on Non-crosslinked Polystyrene and Their Evaluation as Inhibitors of PTP1B

Gabriel Hum, Jason Lee and Scott D. Taylor*

Department of Chemistry, University of Waterloo, 200 University Avenue West, Ontario, Canada N2L 3G1

A series of phosphonic acids were prepared using soluble polymer-supported methodologies and examined for inhibition with protein tyrosine phosphatase 1B. Compound **20** was the most potent of this series of compounds, being a reversible, competitive inhibitor with a K_i of 8.0 ± 1.4 μM.



20

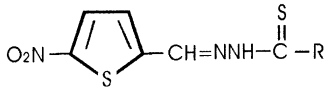
Bioorg. Med. Chem. Lett. 12 (2002) 3475

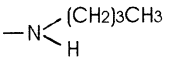
Synthesis and In Vitro Antiprotozoal Activity of 5-Nitrothiophene-2-carboxaldehyde Thiosemicarbazone Derivatives

Neelam Bharti,[a] Kakul Husain,[a] M.T. Gonzalez Garza,[b] Delia E. Cruz-Vega,[b] J. Castro-Garza,[b] Benito D. Mata-Cardenas,[b] Fehmida Naqvi[a] and Amir Azam[a,*]

[a]*Department of Chemistry, Jamia Millia Islamia, Jamia Nagar, New Delhi 110025, India*
[b]*Division de Biologia Celular of Molecular, Centro de Investigacion, Biomedica sdel Noreste, IMSS, Monetary, NL, Mexico*

Thiosemicarbazone derivatives were prepared from 5-nitrothiophene-2-carboxaldehyde and tested in vitro against *Entamoeba histolytica* (strain HK-9), *Giardia lamblia* (strain IMSS-0989) and *Trichomonas vaginalis* (strain tv-43). Compound **3** and **11** exhibited better antitrichomonial and antiamoebic activity respectively comparable to that of metronidazole.



3 R = 

11 R = 

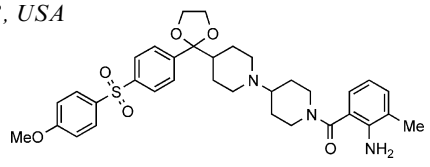
Bioorg. Med. Chem. Lett. 12 (2002) 3479

Enhancement of Pharmacokinetic Properties and In Vivo Efficacy of Benzylidene Ketal M_2 Muscarinic Receptor Antagonists Via Benzamide Modification

Craig D. Boyle,* Susan F. Vice, Jennifer Campion, Samuel Chackalamannil, Claire M. Lankin, Stuart W. McCombie, William Billard, Herbert Binch, III, Gordon Crosby, Mary-Cohen Williams, Vicki L. Coffin, Kathleen A. Cox, Diane E. Grotz, Ruth A. Duffy, Vilma Ruperto and Jean E. Lachowicz

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

We previously reported the initial discovery of a novel class of stabilized benzylidene ketal M_2 receptor antagonists. This paper discusses new analogues consisting of benzamide modifications which not only improved M_2 receptor affinity and selectivity, but also enhanced the pharmacokinetic properties of the series. These changes led to the discovery of a highly potent and selective M_2 antagonist, which demonstrated in vivo efficacy and had good bioavailability in multiple species.

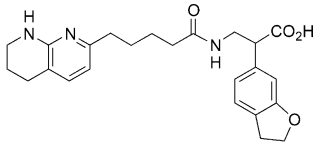


Bioorg. Med. Chem. Lett. 12 (2002) 3483

Non-Peptide $\alpha_v\beta_3$ Antagonists. Part 5: Identification of Potent RGD Mimetics Incorporating 2-Aryl β-Amino Acids as Aspartic Acid Replacements

Karen M. Brashear,[a,*] Cecilia A. Hunt,[a] Brian T. Kucer,[a] Mark E. Duggan,[a] George D. Hartman,[a] Gideon Rodan,[b] Sevgi Rodan,[b] Chi-Tai Leu,[b] Thomayant Prueksaritanont,[c] Carmen Fernandez-Metzler,[c] Andrea Barrish,[c] Carl F. Homnick,[a] John H. Hutchinson[a] and Paul J. Coleman[a]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA 19486, USA*
[b]*Department of Bone Biology and Osteoporosis Research, Merck Research Laboratories, West Point, PA 19486, USA*
[c]*Department of Drug Metabolism and Pharmacology, Merck Research Laboratories, West Point, PA 19486, USA*



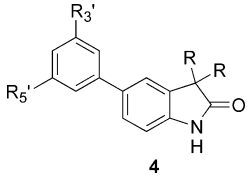
Bioorg. Med. Chem. Lett. 12 (2002) 3487

New Progesterone Receptor Antagonists: 3,3-Disubstituted-5-aryloxindoles

Andrew Fensome,[a,*] Reinhold Bender,[a] Jeffrey Cohen,[b] Mark A. Collins,[a] Valerie A. Mackner,[a] Lori L. Miller,[a] John W. Ullrich,[a] Richard Winneker,[b] Jay Wrobel,[a] Puwen Zhang,[a] Zhiming Zhang[b] and Yuan Zhu[b]

[a]*Chemical Sciences, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*
[b]*Women's Health Research Institute, Wyeth Research, 500 Arcola Road, Collegeville, PA 19426, USA*

The synthesis and SARs of a novel series of progesterone receptor antagonists **4** based upon a 5-aryl oxindole platform are discussed.



4

Bioorg. Med. Chem. Lett. 12 (2002) 3491

A Novel Synthesis of 7-Aryl-8-fluoro-pyrrolo[1,2-*a*]pyrimid-4-ones as Potent, Stable GnRH Receptor Antagonists

Fabio C. Tucci,* Yun-Fei Zhu, Zhiqiang Guo, Timothy D. Gross, Patrick J. Connors, Jr., R. Scott Struthers, Greg J. Reinhart, Xiaochuan Wang, John Saunders and Chen Chen*

Neurocrine Biosciences, Inc., 10555 Science Center Drive, San Diego, CA-92121, USA

The design and synthesis of this novel class of GnRH receptor antagonists is described. The best compound of this series showed 9 nM (K_i) binding affinity and improved stability towards acidic conditions.