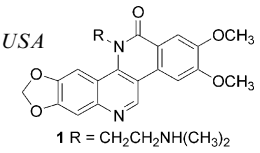
Bioorg. Med. Chem. Lett. 13 (2003) 3395

5*H*-8,9-Dimethoxy-5-(2-*N*,*N*-dimethylaminoethyl)dibenzo[*c*,*h*][1,6] naphthyridin-6-ones and Related Compounds as TOP1-Targeting Agents: Influence of Structure on the Ternary Cleavable Complex Formation

John E. Kerrigan,[a,b,*] Daniel S. Pilch,[a,b] Alexander L. Ruchelman,[c] Nai Zhou,[a] Angela Liu,[a] Leroy Liu[a,b] and Edmond J. LaVoie[b,c]

[a]*Department of Pharmacology, The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway, NJ 08854, USA*
[b]*The Cancer Institute of New Jersey, New Brunswick, NJ 08901, USA*
[c]*Department of Pharmaceutical Chemistry, School of Pharmacy, Rutgers University, Piscataway, NJ, 08854-8020, USA*

A model of the drug/DNA/topoisomerase I ternary cleavable complex for a novel series of TOP1 targeting agents is reported.



1 R = $CH_2CH_2NH(CH_3)_2$

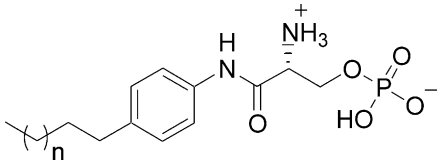
Bioorg. Med. Chem. Lett. 13 (2003) 3401

Synthesis of *Para*-Alkyl Aryl Amide Analogues of Sphingosine-1-phosphate: Discovery of Potent S1P Receptor Agonists

Jeremy J. Clemens,[a] Michael D. Davis,[b] Kevin R. Lynch[b,c] and Timothy L. Macdonald[a,*]

[a]*Department of Chemistry, University of Virginia, McCormick Road, PO Box 400319, Charlottesville, VA 22904, USA*
[b]*Department of Biochemistry and Molecular Biology, University of Virginia, McCormick Road, PO Box 400319, Charlottesville, VA 22904, USA*
[c]*Department of Pharmacology, University of Virginia, McCormick Road, PO Box 400319, Charlottesville VA 22904, USA*

We report the synthesis and potencies of several novel S1P receptor agonists.

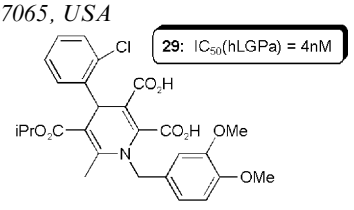


Bioorg. Med. Chem. Lett. 13 (2003) 3405

Glucose-Lowering in a *db*/*db* Mouse Model by Dihydropyridine Diacid Glycogen Phosphorylase Inhibitors

Anthony K. Ogawa,[a,*] Chris A. Willoughby,[a] Raynald Bergeron,[b] Kenneth P. Ellsworth,[b] Wayne M. Geissler,[b] Robert W. Myers,[b] Jun Yao,[b] Georgianna Harris[b] and Kevin T. Chapman[a]

[a]*Department of Basic Chemistry, Merck Research Laboratories, Rahway, NJ 07065, USA*
[b]*Department of Metabolic Disorders-Diabetes, Merck Research Laboratories, Rahway, NJ 07065, USA*

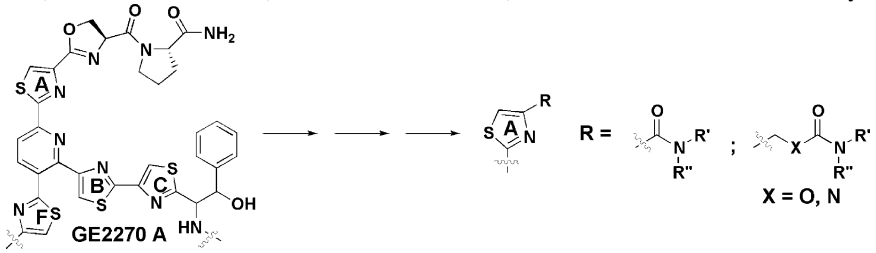


Bioorg. Med. Chem. Lett. 13 (2003) 3409

Combinatorial Modification of Natural Products: Synthesis and In Vitro Analysis of Derivatives of Thiazole Peptide Antibiotic GE2270 A: A-Ring Modifications

Jeffrey Clough,[a] Shaoqing Chen,[a] Eric M. Gordon,[a] Corinne Hackbarth,[a] Stuart Lam,[a] Joaquim Trias,[a] Richard J. White,[a] Gianpaolo Candiani,[b] Stefano Donadio,[b] Gabriella Romanò,[b] Romeo Ciabatti[b] and Jeffrey W. Jacobs[a,*]

[a]*Vicuron, Inc., 34790 Ardentech Court, Fremont, CA 94555, USA*
[b]*Vicuron, Inc., 21040 Gerenzano (VA), Italy*



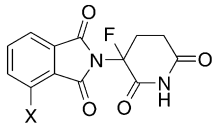
Bioorg. Med. Chem. Lett. 13 (2003) 3415

α-Fluoro-Substituted Thalidomide Analogues

Hon-Wah Man,* Laura G. Corral, David I. Stirling and George W. Muller*

Celgene Corporation, Warren, NJ 07059, USA

The synthesis and biological evaluation of α-fluoro-substituted thalidomide analogues are described.



X = H or NH_2

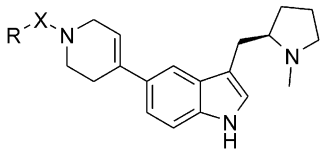
Bioorg. Med. Chem. Lett. 13 (2003) 3419

(*R*)-3-(*N*-Methylpyrrolidin-2-ylmethyl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indole Derivatives as High-Affinity h5-$HT_{1B/1D}$ Ligands

Ian Egle,* Neil MacLean, Lidia Demchyshyn, Louise Edwards, Abdelmalik Slassi and Ashok Tehim

NPS Pharmaceuticals Inc., 6850 Goreway Dr., Mississauga, Ontario, Canada L4V 1V7

A series of (*R*)-3-(*N*-methylpyrrolidin-2-ylmethyl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1*H*-indole derivatives (**2**) have been prepared using parallel synthesis, and their structure–activity relationship studied. High affinity human 5-$HT_{1B/1D}$ (h5-$HT_{1B/1D}$) ligands have been identified.



2

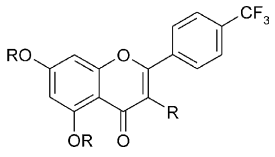
Bioorg. Med. Chem. Lett. 13 (2003) 3423

Synthesis and Anticancer Effect of B-Ring Trifluoromethylated Flavonoids

Xing Zheng,[a] Jian-Guo Cao,[b] Wei-Dong Meng[a] and Feng-Ling Qing[a,c,*]

[a]*College of Chemistry and Chemical Engineering, Donghua University, 1882 West Yanan Lu, Shanghai 200051, China*
[b]*Cancer Research Institute, Nanhua University, Hengyang, Hunan 421001, China*
[c]*Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*

A series of B-ring trifluoromethylated flavonoids were prepared and tested for their in vitro anticancer activities against SGC-7901 cell.



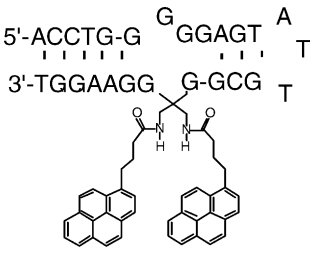
Bioorg. Med. Chem. Lett. 13 (2003) 3429

Bis-Pyrene Labeled DNA Aptamer as an Intelligent Fluorescent Biosensor

Kazushige Yamana,[a,c,*] Yusuke Ohtani,[a] Hidehiko Nakano[a] and Isao Saito[b,c]

[a]*Department of Applied Chemistry, Himeji Institute of Technology, 2167 Shosha, Himeji 671-2201, Japan*
[b]*Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan*
[c]*SORST of Japan Science Technology Corporation (JST), Japan*

The site-directed incorporation of bis-pyrenyl fluorophore into anti-ATP DNA aptamer results in a creation of an intelligent fluorescent sensor with high signal intensity and specificity for detecting the target ligand in a homogeneous system.



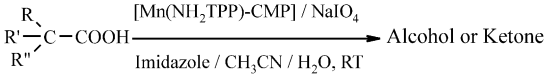
Bioorg. Med. Chem. Lett. 13 (2003) 3433

Efficient Oxidative Decarboxylation of Carboxylic Acids with Sodium Periodate Catalyzed by Supported Manganese(III) Porphyrin

Valiollah Mirkhani,[a,*] Shahram Tangestaninejad,[a] Majid Moghadam[b] and Zohreh Karimian[a]

[a]*Department of Chemistry, Isfahan University, Isfahan 81744, Iran*
[b]*Department of Chemistry, Yasouj University, Yasouj 75914-353, Iran*

Oxidative decarboxylation of carboxylic acids by 5,10,15,20-tetrakis(4-aminophenyl)porphyrinatomanganese (III) chloride supported on crosslinked chloromethylated polystyrene, [Mn(H_2NTPP)-CMP], to the corresponding carbonyl compounds with sodium periodate was investigated.



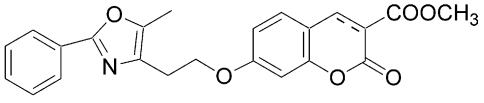
Bioorg. Med. Chem. Lett. 13 (2003) 3437

Synthesis and Insulin-Sensitizing Activity of a Novel Kind of Benzopyran Derivative

Lei Tang, Juanhong Yu, Ying Leng, Ying Feng, Yushe Yang* and Ruyun Ji

State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China

A series of benzopyran derivatives was synthesized and their insulin-sensitizing activities were evaluated in 3T3-L1 cells. Compounds **6** and **11** exhibited more potent insulin-sensitizing activity than rosiglitazone.



6 (double bond)
11 (single bond)

Bioorg. Med. Chem. Lett. 13 (2003) 3441

Novel Sulfated Gangliosides, High-Affinity Ligands for Neural Siglecs, Inhibit NADase Activity of Leukocyte Cell Surface Antigen CD38

Miki Hara-Yokoyama,[a,*] Hiromi Ito,[b] Kaori Ueno-Noto,[c] Keiko Takano,[c] Hideharu Ishida[b] and Makoto Kiso[b,*]

[a]*Biochemistry, Department of Hard Tissue Engineering, Division of Bio-Matrix, Graduate School, Tokyo Medical and Dental University, 1-5-45 Yusima, Bunkyo-ku, Tokyo 113-8549, Japan*
[b]*Department of Applied Bio-organic Chemistry, Gifu University, Gifu 501-1193, Japan*
[c]*Graduate School of Humanities and Sciences, Ochanomizu University, 2-1-1 Otsuka, Bunkyo-ku, Tokyo 112-8610, Japan*

Novel di-sulfated gangliosides were found to be potent inhibitors of NADase activity of leukocyte cell-surface antigen CD38.

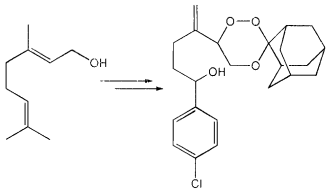
SO_3^-
6
NeuAcα2,3Galβ1,4(3)GalNAcβ1,4Galβ1,4Glc1→Cer
3
SO_3^-

Bioorg. Med. Chem. Lett. 13 (2003) 3447

Geraniol-Derived 1,2,4-Trioxanes with Potent In-Vivo Antimalarial Activity

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*

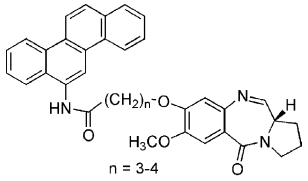


Bioorg. Med. Chem. Lett. 13 (2003) 3451

Design and Synthesis of Novel Chrysene-Linked Pyrrolo[2,1-*c*][1,4] Benzodiazepine Hybrids as Potential DNA-Binding Agents

Ahmed Kamal,* G. Ramesh, P. Ramulu, O. Srinivas, Tasneem Rehana and G. Sheelu

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500007, India

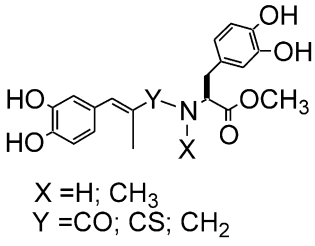


Bioorg. Med. Chem. Lett. 13 (2003) 3455

Design and Synthesis of Small Chemical Inhibitors Containing Different Scaffolds for *lck* SH2 Domain

See-Hyoung Park,[a] Sun-Hee Kang,[b] Sang-Hyeong Lim,[b] Hyun-Sik Oh[b] and Keun-Hyeung Lee[b,*]

[a]*Signal Transduction Laboratory, Mogam Biotechnology Research Institute, 341 Pojung-Ri, Koosung-Myun, Yongin-City, Kyunggi-Do 449-910, South Korea*
[b]*Department of Chemistry, Inha University, 253 Younghyong-Dong, Nam-Gu, Inchon-City 402-751, South Korea*



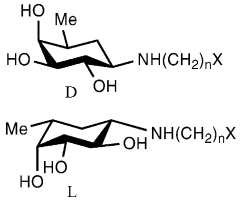
Bioorg. Med. Chem. Lett. 13 (2003) 3461

Synthesis and Glycosidase Inhibitory Activity of Some *N*-Substituted 6-Deoxy-5a-carba-β-DL- and L-galactopyranosylamines

Seiichiro Ogawa,* Shigeo Fujieda, Yuko Sakata, Masahiro Ishizaki, Seiichi Hisamatsu and Kensuke Okazaki

Department of Biosciences and Informatics, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan

N-Alkyl and phenylalkyl derivatives of 6-deoxy-5a-carba-β-DL-galactopyranosylamines have been demonstrated to be very strong inhibitors of β-galactosidase and β-glucosidase.



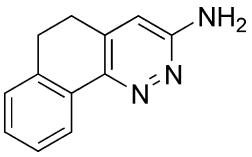
Bioorg. Med. Chem. Lett. 13 (2003) 3465

An Aminopyridazine-Based Inhibitor of a Pro-apoptotic Protein Kinase Attenuates Hypoxia-Ischemia Induced Acute Brain Injury

Anastasia V. Velentza,[a,b] Mark S. Wainwright,[d] Magdalena Zasadzki,[a,b] Salida Mirzoeva,[c] Andrew M. Schumacher,[a,b] Jacques Haiech,[e] Pamela J. Focia,[b] Martin Egli[f] and D. Martin Watterson[a,*]

[a]*Drug Discovery Program, Northwestern University, 303 E. Chicago Avenue, Ward 8-196, Chicago, IL 60611, USA*
[b]*Department of Molecular Pharmacology and Biological Chemistry, Northwestern University, Chicago, IL 60611, USA*
[c]*Department of Medicine, Northwestern University, Chicago, IL 60611, USA*
[d]*Department of Pediatrics, Northwestern University, Chicago, IL 60611, USA*
[e]*Institut G. Laustriat, Faculté de Pharmacie, Université Louis Pasteur, Illkirch, France*
[f]*Department of Biochemistry, Vanderbilt University, Nashville, TN, USA*

An aminopyridazine based inhibitor of death associated protein kinase (DAPK) diminishes brain damage in vivo when administered 6 h after hypoxia-ischemia induced injury. The high-resolution crystal structure of the kinase catalytic domain in complex with an aminopyridazine inhibitor fragment was determined in order to provide a precedent for the field and a foundation for future structure-assisted design of compounds with appropriate molecular properties.



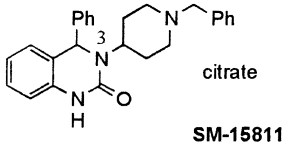
Bioorg. Med. Chem. Lett. 13 (2003) 3471

Discovery of a Novel Potent Na^+/Ca^{2+} Exchanger Inhibitor: Design, Synthesis and Structure–Activity Relationships of 3,4-Dihydro-2(1*H*)-quinazolinone Derivatives

Hirohiko Hasegawa,[a,*] Masami Muraoka,[a] Kazuki Matsui[a] and Atsuyuki Kojima[b]

[a]*Research Center, Sumitomo Pharmaceuticals Co., Ltd., 1-98, Kasugadenaka 3-Chome, Konohana-ku, Osaka 554-0022, Japan*
[b]*Takarazuka Organic Synthesis Department, Sumika Technoservice Co., Ltd., 2-1, Takatsukasa 4-Chome, Takarazuka City, Hyogo 665-0051, Japan*

Design, synthesis and structure–activity relationships for 3,4-dihydro-2(1*H*)-quinazolinone derivatives with the inhibitory activities of the Na^+/Ca^{2+} exchanger are discussed. These studies led to the discovery of a structurally novel and highly potent inhibitor against the Na^+/Ca^{2+} exchanger **SM-15811**, which directly inhibited the Na^+-dependent Ca^{2+} influx via the Na^+Ca^{2+} exchanger in cardiomyocytes with a high potency.



SM-15811

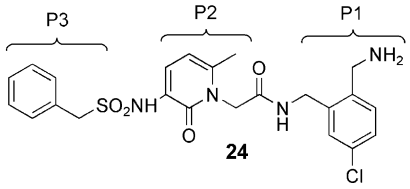
Bioorg. Med. Chem. Lett. 13 (2003) 3477

Unexpected Enhancement of Thrombin Inhibitor Potency with *o*-Aminoalkylbenzylamides in the P1 Position

Kenneth E. Rittle,[a,*] James C. Barrow,[a] Kellie J. Cutrona,[a] Kristen L. Glass,[a] Julie A. Krueger,[b] Lawrence C. Kuo,[c] S. Dale Lewis,[b] Bobby J. Lucas,[b] Daniel R. McMasters,[d] Matthew M. Morrissette,[a] Philippe G. Nantermet,[a] Christina L. Newton,[a] William M. Sanders,[a] Youwei Yan,[c] Joseph P. Vacca[a] and Harold G. Selnick[a]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA 19486, USA*
[b]*Department of Biological Chemistry, Merck Research Laboratories, West Point, PA 19486, USA*
[c]*Department of Structural Biology, Merck Research Laboratories, West Point, PA 19486, USA*
[d]*Department of Molecular Systems, Merck Research Laboratories, West Point, PA 19486, USA*

Thrombin inhibitors incorporating *o*-aminoalkylbenzylamides in the P1 position were designed, synthesized and found to enhance potency and selectivity in several different structural classes. X-ray crystallographic analysis of Compound **24** bound in the α-thrombin-hirugen complex provides an explanation for these surprising results.



24

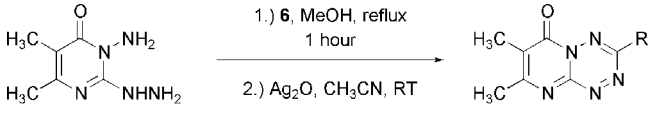
Bioorg. Med. Chem. Lett. 13 (2003) 3483

Pyrimido[1,2-*b*]-1,2,4,5-tetrazin-6-ones as HCMV Protease Inhibitors: A New Class of Heterocycles with Flavin-Like Redox Properties

Martin J. Di Grandi,[a,*] Kevin J. Curran,[a] Ellen Z. Baum,[a] Geraldine Bebernitz,[a] George A. Ellestad,[a] Wei-Dong Ding,[a] Stanley A. Lang,[a] Miriam Rossi[b] and Jonathan D. Bloom[a]

[a]*Wyeth Research, 401 N. Middletown Rd., Pearl River, NY 10965, USA*
[b]*Department of Chemistry, Vassar College, Poughkeepsie, NY 12601, USA*

Tetrazines **2** were found to be inhibitors of HMCV protease via redox chemistry.



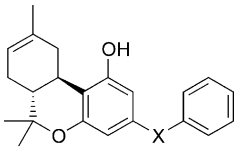
3 **2**

Bioorg. Med. Chem. Lett. 13 (2003) 3487

Synthesis and Testing of Novel Phenyl Substituted Side-Chain Analogues of Classical Cannabinoids

Mathangi Krishnamurthy,[a] Antonio M. Ferreira[b] and Bob M. Moore, II[c,*]

[a]*Department of Pharmaceutical Sciences, College of Pharmacy, University of Tennessee-Memphis, Memphis, TN 38163, USA*
[b]*Computational Research on Materials Institute, Department of Chemistry, University of Memphis, Memphis, TN 38152, USA*
[c]*University of Tennessee, College of Pharmacy, Department of Pharmaceutical Sciences, 847 Monroe Ave., Room 327D, Memphis, TN 38163, USA*



X = $C(CH_3)_2$
$C(\text{-S-}CH_2\text{-})_2$
CH_2
CO

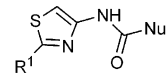
Bioorg. Med. Chem. Lett. 13 (2003) 3491

A Catch-and-Release Strategy for the Combinatorial Synthesis of 4-Acylamino-1,3-thiazoles as Potential CDK5 Inhibitors

Scott D. Larsen,[a,*] Carl F. Stachew,[a] Paula M. Clare,[b] Jerry W. Cubbage[c] and Karen L. Leach[b]

[a]*Medicinal Chemistry Research, Pharmacia Corporation, 333 Portage St., Kalamazoo, MI 49007, USA*
[b]*Cellular & Molecular Biochemistry, Pharmacia Corporation, 333 Portage St., Kalamazoo, MI 49007, USA*
[c]*Structural & Computational Chemistry, Pharmacia Corporation, 333 Portage St., Kalamazoo, MI 49007, USA*

Two-dimensional libraries of 4-acylamino-1,3-thiazoles were prepared via Curtius rearrangement of 1,3-thiazole-4-carbonyl azides, trapping of the intermediate isocyanates with oxime resin, and thermal regeneration of the isocyanates from the washed resin in the presence of nucleophiles, NuH.



Nu = $R^2R^3NNR^4$ or RONH

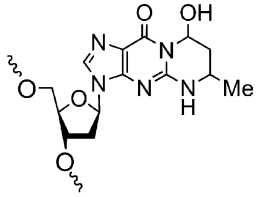
Bioorg. Med. Chem. Lett. 13 (2003) 3497

Histones Accelerate the Cyclic 1,N^2-Propanoguanine Adduct-Formation of DNA by the Primary Metabolite of Alcohol and Carcinogenic Crotonaldehyde

Magoichi Sako,* Shinsuke Inagaki, Yukihiro Esaka and Yoshihiro Deyashiki

Gifu Pharmaceutical University, Mitahora-higashi, Gifu 502-8585, Japan

The impressive role of histones for the formation of cyclic *1,N2*-propanoguanine adducts in the reactions of DNA with acetaldehyde and crotonaldehyde is reported.



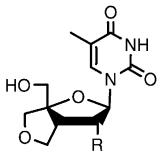
Bioorg. Med. Chem. Lett. 13 (2003) 3499

Synthesis and Biological Evaluation of Thymine Nucleosides Fused with 3′,4′-Tetrahydrofuran Ring

Myong Jung Kim,[a] Hea Ok Kim,[b] Hee-Doo Kim,[c] Joong Hyup Kim,[d] Lak Shin Jeong[e] and Moon Woo Chun[a,*]

[a]*College of Pharmacy, Seoul National University, Seoul 151-742, South Korea*
[b]*Division of Chemistry and Molecular Engineering, Seoul National University, Seoul 151-742, South Korea*
[c]*College of Pharmacy, Sookmyung Women's University, Seoul 140-742, South Korea*
[d]*Korea Institute of Science and Technology, Seoul 136-791, South Korea*
[e]*College of Pharmacy, Ewha Womans University, Seoul 120-750, South Korea*

Conformationally restricted nucleosides were synthesized and tested for antiviral activity.



5 (R=OH)
6 (R=H)

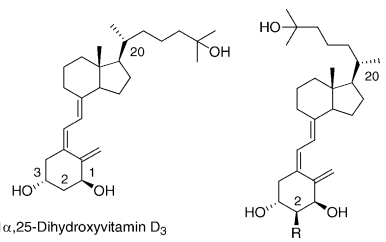
Bioorg. Med. Chem. Lett. 13 (2003) 3503

Concise Synthesis and Biological Activities of 2α-Alkyl- and 2α-(ω-Hydroxyalkyl)-20-*epi*-1α,25-dihydroxyvitamin D_3

Shinobu Honzawa,[a] Yoshitomo Suhara,[a] Ken-ichi Nihei,[a] Nozomi Saito,[a] Seishi Kishimoto,[b] Toshie Fujishima,[a] Masaaki Kurihara,[c] Takayuki Sugiura,[b] Keizo Waku,[b] Hiroaki Takayama[a] and Atsushi Kittaka[a,*]

[a]*Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-0195, Japan*
[b]*Department of Hygienic Chemistry and Nutrition, Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-0195, Japan*
[c]*National Institute of Health Sciences, Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan*

The novel three analogues of 2α-alkyl- and four analogues of 2α-(ω-hydroxyalkyl)-20-*epi*-1α,25-dihydroxyvitamin D_3 showed higher binding affinity for vitamin D receptor (VDR) and more potent activity in induction of HL-60 cell differentiation than those of the natural hormone.



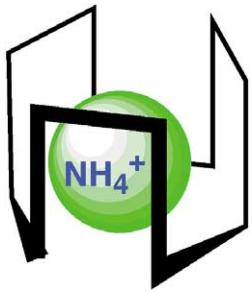
1α,25-Dihydroxyvitamin D_3

Bioorg. Med. Chem. Lett. 13 (2003) 3507

Complexation of Cyclic Dodecadepsipeptide, Cereulide with Ammonium Salts

Suthasinee Pitchayawasin,[a] Masaki Kuse,[a] Kazushi Koga,[a] Minoru Isobe,[a,*] Norio Agata[b] and Michio Ohta[c]

[a]*Laboratory of Organic Chemistry, School of Bioagricultural Sciences, Nagoya University, Chikusa, Nagoya 464-8601, Japan*
[b]*Nagoya City Public Health Research Institute, 1-11 Hagiyamacho, Mizuho, Nagoya 467-0011, Japan*
[c]*Department of Bacteriology, School of Medicine, Nagoya University, 65 Tsurumaicho, Showa, Nagoya 466-8550, Japan*



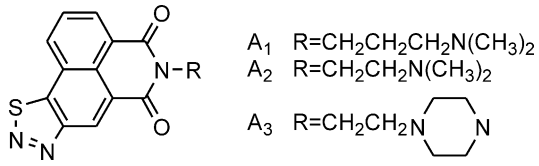
Bioorg. Med. Chem. Lett. 13 (2003) 3513

Thiadiazole: A New Family of Intercalative Photonuclease with Electron Transfer and Radical Mechanisms

Yonggang Li,[a,c] Yufang Xu,[a,c] Xuhong Qian[b,*] and Baoyuan Qu[a,c]

[a]*East China University of Science and Technology, Shanghai 200237, China*
[b]*State Key Lab. Fine Chemicals, Dalian University of Technology, Dalian 116012, China*
[c]*Shanghai Key Lab. Chem. Biology, Shanghai 200237, China*

A new family of intercalative photonuclease, thiadiazole-naphthalimide were synthesized and evaluated.

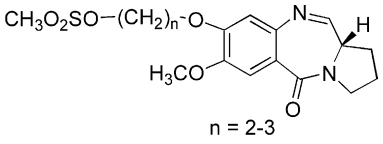


Bioorg. Med. Chem. Lett. 13 (2003) 3517

Synthesis of C-8 Methanesulphonate Substituted Pyrrolobenzodiazepines as Potential Antitumour Agents

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

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500007, India



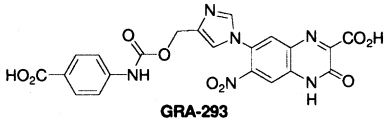
Bioorg. Med. Chem. Lett. 13 (2003) 3521

Synthesis and AMPA Receptor Antagonistic Activity of a Novel Class of Quinoxalinecarboxylic Acid with a Substituted Phenyl Group at the C-7 Position

Yasuo Takano,* Futoshi Shiga, Jun Asano, Naoki Ando, Hideharu Uchiki and Tsuyosi Anraku

Discovery Research Laboratories, Kyorin Pharmaceutical Co., Ltd., 2399-1, Nogi, Nogi-machi, Simotsuga-gun, Tochigi 329-0114, Japan

The synthesis and biological properties of a novel class of 7-heterocycle-substituted quinoxalinecarboxylic acid, which bears a substituted phenyl group through a urethane linkage at the C-7 position, are described. One of the synthesized compounds, GRA-293, which is water-soluble, was found to possess high potency in vitro and showed excellent neuroprotective efficacy in vivo.



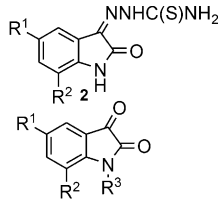
Bioorg. Med. Chem. Lett. 13 (2003) 3527

Synthesis and Evaluation of Isatins and Thiosemicarbazone Derivatives against Cruzain, Falcipain-2 and Rhodesain

Idan Chiyanzu,[a] Elizabeth Hansell,[b] Jiri Gut,[c] Philip J. Rosenthal,[c] James H. McKerrow[b] and Kelly Chibale[a,*]

[a]*Department of Chemistry, University of Cape Town, Rondebosch 7701, South Africa*
[b]*Department of Pathology, Tropical Diseases Research Unit, University of California San Francisco, 513 Parnassus Avenue, Box 0511, HSW 511, San Francisco, CA 94143, USA*
[c]*Department of Medicine, San Francisco General Hospital, University of California San Francisco, 1001 Potrero Avenue, Box 0811, San Francisco, CA 94110, USA*

A series of thiosemicarbazones (**2**) and *N*-substituted isatins (**3**) were synthesised and tested against the parasitic cysteine proteases cruzain, falcipain-2 and rhodesain.



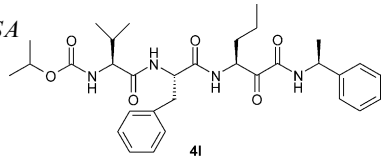
Bioorg. Med. Chem. Lett. 13 (2003) 3531

Synthesis and Evaluation of Tripeptidyl α-Ketoamides as Human Rhinovirus 3C Protease Inhibitors

Shu-Hui Chen,[a,*] Jason Lamar,[a] Frantz Victor,[a] Nancy Snyder,[a] Robert Johnson,[b] Beverly A. Heinz,[b] Mark Wakulchik[b] and Q. May Wang[b,*]

[a]*Discovery Chemistry Research and Technology, Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, USA*
[b]*Department of Infectious Diseases, Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, USA*

A number of tripeptidyl α-ketoamides described herein displayed impressive inhibitory activity against HRV 3C protease with IC_{50} values <0.5 μM.



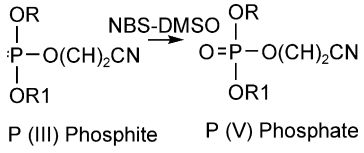
Bioorg. Med. Chem. Lett. 13 (2003) 3537

NBS–DMSO as a Nonaqueous Nonbasic Oxidation Reagent for the Synthesis of Oligonucleotides

Matthew C. Uzagare,[a] Kamlesh J. Padiya,[a] Manikrao M. Salunkhe[a] and Yogesh S. Sanghvi[b,*]

[a]*The Institute of Science, 15 Madam Cama Road, Mumbai 400 032, India*
[b]*Isis Pharmaceuticals, 2292 Faraday Avenue, Carlsbad, CA 92008, USA*

A new method for the oxidation of nucleoside phosphite triester into phosphate triester under nonbasic and nonaqueous conditions using NBS–DMSO in CH_3CN has been developed. The utility of this method for solution- and solid-phase synthesis of oligonucleotide is demonstrated.



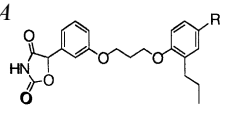
Bioorg. Med. Chem. Lett. 13 (2003) 3541

Aryloxazolidinediones: Identification of Potent Orally Active PPAR Dual α/γ Agonists

Ranjit C. Desai,[a,*] Dominick F. Gratale,[a] Wei Han,[a] Hiroo Koyama,[a] Edward Metzger,[a] Victoria K. Lombardo,[a] Karen L. MacNaul,[b] Thomas W. Doebber,[b] Joel P. Berger,[b] Kwan Leung,[c] Ronald Franklin,[c] David E. Moller,[b] James V. Heck[a] and Soumya P. Sahoo[a,*]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065, USA*
[b]*Department of Metabolic Disorders, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065, USA*
[c]*Department of Drug Metabolism, Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065, USA*

A novel series of potent, orally efficacious dual PPAR α/γ agonists was identified.



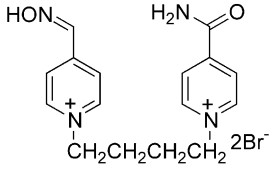
Bioorg. Med. Chem. Lett. 13 (2003) 3545

Synthesis of a New Reactivator of Tabun-Inhibited Acetylcholinesterase

Kamil Kuča,* Jiří Bielavský, Jiří Cabal and Jiří Kassa

Department of Toxicology, Purkyně Military Medical Academy, 500 01 Hradec Králové, Czech Republic

Synthesis of a new asymmetric bisquaternary reactivator of tabun-inhibited acetylcholinesterase and comparison of its reactivation potency with currently used reactivators.



Bioorg. Med. Chem. Lett. 13 (2003) 3549

Lupane Triterpenes and Derivatives with Antiviral Activity

L. A. Baltina,[a,*] O. B. Flekhter,[a] L. R. Nigmatullina,[a] E. I. Boreko,[b] N. I. Pavlova,[b] S. N. Nikolaeva,[b] O. V. Savinova[b] and G. A. Tolstikov[a]

[a]*Institute of Organic Chemistry, Ufa Research Center of RAS, 71, prospect Oktyabrya, 450054 Ufa, Russia*
[b]*Belarussian Research Institute for Epidemiology and Microbiology, 4, K. Zetkin str., 220050 Minsk, Belarus*

Betulin and betulinic acid have been modified at the C-3 and C-28 positions and the antiviral activity of derivatives has been evaluated in vitro. It was found that simple modifications of the parent structure of lupane triterpenes produced highly effective agents against influenza A and herpes simplex type 1 viruses.

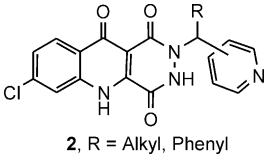
Bioorg. Med. Chem. Lett. 13 (2003) 3553

Synthesis of 7-Chloro-2,3-dihydro-2-[1-(pyridinyl)alkyl]-pyridazino[4,5-*b*]quinoline-1,4,10(5*H*)-triones as NMDA Glycine-Site Antagonists

Dean G. Brown,* Rebecca A. Urbanek, Thomas M. Bare, Frances M. McLaren, Carey L. Horchler, Megan Murphy, Gary B. Steelman, James R. Empfield, Janet M. Forst, Keith J. Herzog, Wenhua Xiao, Martin C. Dyroff, Chi-Ming C. Lee, Shephali Trivedi, Kathy L. Neilson and Richard A. Keith

AstraZeneca Pharmaceuticals, 1800 Concord Pike, Wilmington, DE 19850, USA

Potent NMDA-glycine site antagonists (**2**) have been identified with improved physical properties (e.g., solubility and oral absorption) over the initial lead structure.



2, R = Alkyl, Phenyl

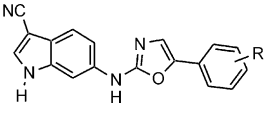
Bioorg. Med. Chem. Lett. 13 (2003) 3557

3-Cyanoindole-Based Inhibitors of Inosine Monophosphate Dehydrogenase: Synthesis and Initial Structure–Activity Relationships

T. G. Murali Dhar,* Zhongqi Shen, Henry H. Gu, Ping Chen, Derek Norris, Scott H. Watterson, Shelley K. Ballentine, Catherine A. Fleener, Katherine A. Rouleau, Joel C. Barrish, Robert Townsend, Diane L. Hollenbaugh and Edwin J. Iwanowicz*

Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08543-4000, USA

The synthesis and SAR of a series of novel small molecule inhibitors of inosine monophosphate dehydrogenase based upon a 3-cyanoindole core are described.



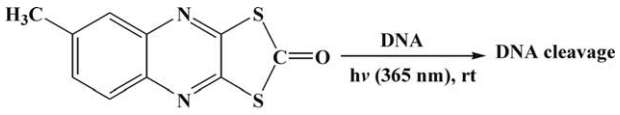
Bioorg. Med. Chem. Lett. 13 (2003) 3561

Fungicide Chinomethionate as a New Family of Photoinducible DNA-Cleaving Agents

Jianying Qi, Tianhu Li* and Albert S. C. Chan*

Open Laboratory of Chirotechnology of the Institute of Molecular Technology for Drug Discovery and Synthesis and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong

It is demonstrated for the first time in this report that chinomethionate is capable of causing efficient DNA cleavage under mild irradiation conditions, a fungicide molecule that processes the simple group of 1,3-dithio-2-one as its reactive functionality.



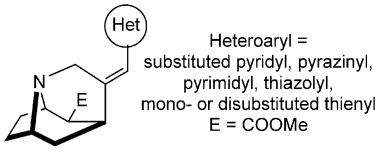
Chinomethionate

Bioorg. Med. Chem. Lett. 13 (2003) 3565

Synthesis and Pharmacological Evaluation of (*Z*)-9-(Heteroarylmethylene)-7-azatricyclo[4.3.1.0^{3,7}]decanes: Thiophene Analogues as Potent Norepinephrine Transporter Inhibitors

Jia Zhou,[a] Thomas Kläß,[a] Ao Zhang,[a] Kenneth M. Johnson,[b] Cheng Z. Wang,[b] Yanping Ye[b] and Alan P. Kozikowski[a,*]

[a]*Drug Discovery Program, Department of Neurology, Georgetown University Medical Center, 3970 Reservoir Road, NW, Washington, DC 20057-2197, USA*
[b]*Department of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77555-1031, USA*



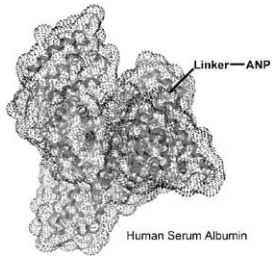
Bioorg. Med. Chem. Lett. 13 (2003) 3571

Synthesis and In Vitro Analysis of Atrial Natriuretic Peptide-Albumin Conjugates

Roger Léger,* Martin Robitaille, Omar Quraishi, Elizabeth Denholm, Corinne Benquet, Julie Carette, Pieter van Wyk, Isabelle Pellerin, Nathalie Bousquet-Gagnon, Jean-Paul Castaigne and Dominique Bridon

Research Department, ConjuChem Inc., 225 President-Kennedy Ave., Suite 3950, Montréal, QC, Canada H2X 3Y8

Atrial natriuretic peptide (ANP) is a clinically useful anti-hypertensive hormone. Maleimide derivatives of ANP have been prepared and conjugated to cysteine 34 of human serum albumin. The conjugates were analyzed to assess their stability, receptor binding affinity and ability to stimulate guanylyl-cyclase activity in rat lung fibroblasts.

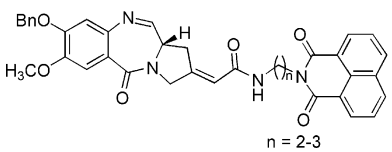


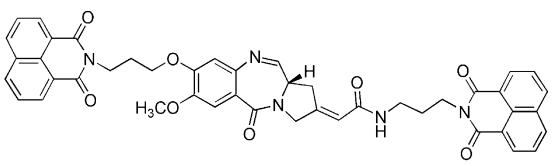
Bioorg. Med. Chem. Lett. 13 (2003) 3577

Synthesis of Novel C2 and C2–C8 Linked Pyrrolo[2,1-*c*][1,4]benzodiazepine-naphthalimide Hybrids as DNA-Binding Agents

Ahmed Kamal,* O. Srinivas, P. Ramulu, G. Ramesh and P. Praveen Kumar

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500007, India





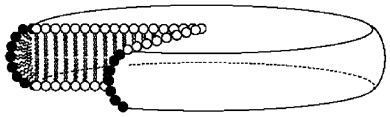
Bioorg. Med. Chem. Lett. 13 (2003) 3583

The Packing of Lipid Chains Changes the Character of Bacteriorhodopsin Reconstituted in a Model Membrane

Hirotaka Sasaki, Mayumi Araki, Seketsu Fukuzawa* and Kazuo Tachibana*

Department of Chemistry, Graduate School of Science, The University of Tokyo and CREST, Japan Science and Technology Corporation (JST), Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Comparison of the packing of lipid chains in bicelles with that in mixed micelles at the temperature between 298 and 318 K is reported. The influence of the packing on the character of reconstituted bacteriorhodopsin is also provided.



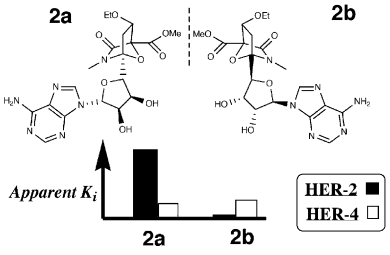
Bioorg. Med. Chem. Lett. 13 (2003) 3587

Adenosine-Anchored Triphosphate Subsite Probing: Distinguishing between HER-2 and HER-4 Tyrosine Protein Kinases

Fei Liu,[a] Eric F. Johnson,[b] David J. Austin[a,*] and Karen S. Anderson[b,*]

[a]*Department of Chemistry, 225 Prospect Street, Yale University, New Haven, CT 06520, USA*
[b]*Department of Pharmacology, 333 Cedar Street, Yale University School of Medicine, New Haven, CT 06520, USA*

A strategy of full-site occupancy and stereospecific recognition in the triphosphate subsite was used to study the specific inhibition of two protein kinases HER-2 and HER-4 from the EGFR family. The SAR profiles of a panel of adenosine-anchored bicyclic heterocycles against HER-2 and HER-4 indicated that specificity can be derived for highly homologous protein kinases from stereospecific recognition in the triphosphate-subsite.

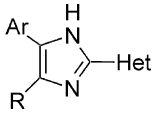


Bioorg. Med. Chem. Lett. 13 (2003) 3593

Structure–Activity Relationship Studies on 2-Heteroaryl-4-arylimidazoles NPY5 Receptor Antagonists

Richard L. Elliott,[a,*] Robert M. Oliver,[a] Janet A. LaFlamme,[a] Melissa L. Gillaspy,[a] Marlys Hammond,[a] Richard F. Hank,[a] Tristan S. Maurer,[a] Demetria L. Baker,[a] Paul A. DaSilva-Jardine,[a] Ralph W. Stevenson,[a] Christine M. Mack[b] and James V. Cassella[b]

[a]*Department of Cardiovascular and Metabolic Diseases, Pfizer Global Research and Development, Groton, CT 06340, USA*
[b]*Neurogen Corporation, Branford, CT 06405, USA*



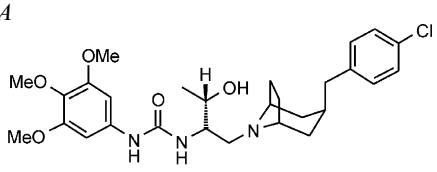
Bioorg. Med. Chem. Lett. 13 (2003) 3597

Design and Synthesis of Novel CCR3 Antagonists

Leyi Gong,[a,*] J. Heather Hogg,[a] James Collier,[a] Robert S. Wilhelm[b] and Carol Soderberg[b]

[a]*Department of Medicinal Chemistry, Roche Palo Alto, Palo Alto, CA 94304, USA*
[b]*Respiratory Disease Therapeutic Area, Roche Palo Alto, Palo Alto, CA 94304, USA*

A novel series of piperidine analogues was designed and prepared. Their inhibitory ability to CCR3 was evaluated. One of the most potent compounds in the series was **24c** with an IC_{50} of 0.0082 μM in the binding assay and 0.0024 μM in the chemotaxis assay.



24c

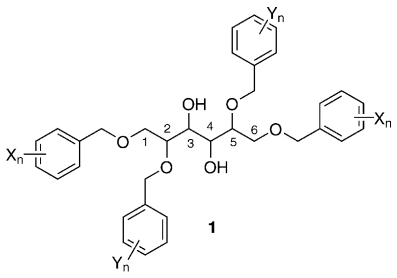
Bioorg. Med. Chem. Lett. 13 (2003) 3601

1,2,5,6-Tetra-*O*-benzyl-D-mannitol Derivatives as Novel HIV Protease Inhibitors

Abderrahim Bouzide, Gilles Sauvé,* Guy Sévigny and Jocelyn Yelle*

Pharmacor Inc., 535 West, Cartier blvd., Laval, Quebec, Canada H7V 3S8

The synthesis and structure–activity relationships of HIV protease inhibitors derived from carbohydrate alditols are reported.



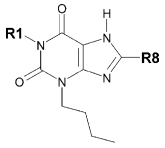
Bioorg. Med. Chem. Lett. 13 (2003) 3607

Modified 3-Alkyl-1,8-dibenzylxanthines as GTP-competitive Inhibitors of Phosphoenolpyruvate Carboxykinase

Louise H. Foley,[a,*] Ping Wang,[a] Pete Dunten,[a] Gwendolyn Ramsey,[b] Mary-Lou Gubler[b] and Stanley J. Wertheimer[b]

[a]*Department of Discovery Chemistry, Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ 07110, USA*
[b]*Department of Metabolic Diseases, Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ 07110, USA*

A HTS hit, 1-allyl-3-butyl-8-methylxanthine (**5**), was found to be a reversible inhibitor of human cytosolic PEPCK. Modifications of **5** at *N*-1 and *C*-8 that improved the in vitro activity of the HTS hit by 100-fold are presented.



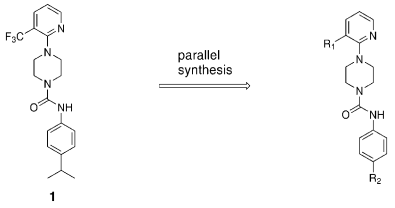
Bioorg. Med. Chem. Lett. 13 (2003) 3611

4-(2-Pyridyl)piperazine-1-carboxamides: Potent Vanilloid Receptor 1 Antagonists

Qun Sun,* Laykea Tafesse, Khondaker Islam, Xiaoming Zhou, Sam F. Victory, Chongwu Zhang, Mohamed Hachicha, Lori A. Schmid, Aniket Patel, Yakov Rotshteyn, Kenneth J. Valenzano and Donald J. Kyle

Purdue Pharma L.P., 6 Cedar Brook Drive, Cranbury, NJ 08512,USA

Synthesis and SAR studies of a series of 4-(2-pyridyl)piperazine-1-carboxamides as vanilloid receptor **1** antagonists is reported.



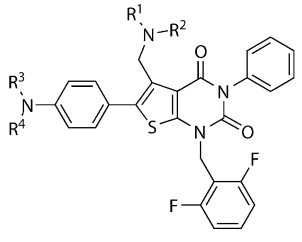
Bioorg. Med. Chem. Lett. 13 (2003) 3617

Synthesis and Structure–Activity Relationships of Thieno[2,3-*d*]-pyrimidine-2,4-dione Derivatives as Potent GnRH Receptor Antagonists

Zhiqiang Guo,[a,*] Yongsheng Chen,[a] Dongpei Wu,[a] Yun-Fei Zhu,[a] R. Scott Struthers,[b] John Saunders,[a] Qiu Xie[b] and Chen Chen[a,*]

[a]*Department of Medicinal Chemistry, Neurocrine Biosciences, Inc., 10555 Science Center Drive, San Diego, CA 92121, USA*
[b]*Department of Exploratory Discovery, 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 0.4 nM (K_i) binding affinity.



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Structure–Activity Relationships within a Series of Caspase Inhibitors: Effect of Leaving Group Modifications

Brett R. Ullman,[a,*] Teresa Aja,[a] Thomas L. Deckwerth,[a] Jose-Luis Diaz,[a] Julia Herrmann,[a] Vincent J. Kalish,[a] Donald S. Karanewsky,[a] Steven P. Meduna,[a] Kip Nalley,[a] Edward D. Robinson,[a] Silvio P. Roggo,[b] Robert O. Sayers,[a] Albert Schmitz,[b] Robert J. Ternansky,[a] Kevin J. Tomaselli[a] and Joe C. Wu[a]

[a]*Idun Pharmaceuticals, Inc., 9380 Judicial Drive, San Diego, CA 92121, USA*
[b]*Novartis Pharma Ltd., Pharma Research, CH-4002 Basel, Switzerland*

Various aryloxy methyl ketones of the 1-naphthyloxyacetyl-Val-Asp backbone have been prepared. A systematic study of their structure–activity relationship (SAR) related to caspases 1, 3, 6, and 8 is reported. Highly potent irreversible broad-spectrum caspase inhibitors have been identified. Their efficacy in cellular models of cell death and inflammation are also discussed.