## Graphical Abstracts

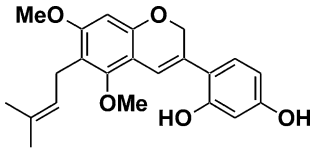
*Bioorg. Med. Chem. Lett. 13 (2003) 4267*

### Phenolics with PPAR-γ Ligand-Binding Activity Obtained from Licorice (*Glycyrrhiza uralensis* Roots) and Ameliorative Effects of Glycyrin on Genetically Diabetic KK-A$^y$ Mice

Minpei Kuroda,[a] Yoshihiro Mimaki,[a,*] Yutaka Sashida,[a] Tatsumasa Mae,[b] Hideyuki Kishida,[c] Tozo Nishiyama,[b] Misuzu Tsukagawa,[b] Eisaku Konishi,[b] Kazuma Takahashi,[d] Teruo Kawada,[e] Kaku Nakagawa[b] and Mikio Kitahara[b]

[a]*Laboratory of Medicinal Plant Science, School of Pharmacy, Tokyo University of Pharmacy and Life Science, Hachioji, Tokyo 192-0392, Japan*
[b]*Functional Foods Development Division, Kaneka Corporation, Takasago, Hyogo 676-8688, Japan*
[c]*Life Science Research Laboratories, Life Science RD Center, Kaneka Corporation, Takasago, Hyogo 676-8688, Japan*
[d]*Department of Internal Medicine, Division of Molecular Metabolism and Diabetes, Tohoku University School of Medicine, Sendai, Miyagi 980-8575, Japan*
[e]*Laboratory of Nutrition Chemistry, Division of Food Science and Biotechnology, Graduate School of Agriculture, Kyoto University, Kyoto, Kyoto 606-8502, Japan*

A new possible application of licorice and its ingredients to the amelioration of type-2 (insulin independent) diabetes has been discovered.



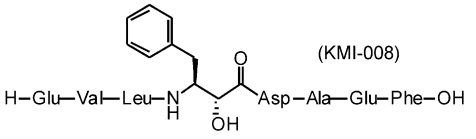

Dehydroglyasperin D (**1**)

*Bioorg. Med. Chem. Lett. 13 (2003) 4273*

### KMI-008, a Novel β-Secretase Inhibitor Containing a Hydroxymethylcarbonyl Isostere as a Transition-State Mimic: Design and Synthesis of Substrate-Based Octapeptides

Daisuke Shuto,[a] Soko Kasai,[a] Tooru Kimura,[a] Ping Liu,[a] Koushi Hidaka,[a] Takashi Hamada,[a] Saeko Shibakawa,[a] Yoshio Hayashi,[a] Chinatsu Hattori,[b] Beata Szabo,[b] Shoichi Ishiura[b] and Yoshiaki Kiso[a,*]

[a]*Department of Medicinal Chemistry, Center for Frontier Research in Medicinal Science, Kyoto Pharmaceutical University, Yamashina-ku, Kyoto 607-8412, Japan*
[b]*Department of Life Sciences, Graduate School of Arts and Sciences, University of Tokyo, Megro-ku, Tokyo 153-8902, Japan*

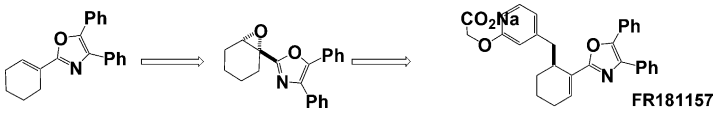



*Bioorg. Med. Chem. Lett. 13 (2003) 4277*

### A Simple Stereoselective Synthesis and Biological Evaluation of FR181157: Orally Active Prostacyclin Mimetic

Kouji Hattori,* Seiichiro Tabuchi, Osamu Okitsu and Kiyoshi Taniguchi

*Medicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co. Ltd, 1-6, Kashima 2-Chome, Yodogawa-Ku, Osaka, Japan*



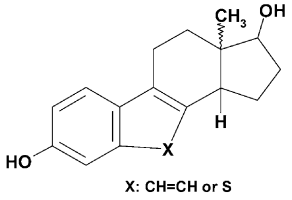

*Bioorg. Med. Chem. Lett. 13 (2003) 4281*

### B-Ring Unsaturated Estrogens: Biological Evaluation of 17α-Dihydroequilein and Novel B-Nor-6-thiaequilenins as Tissue Selective Estrogens

Charles W. Lugar, III, David Magee, Mary D. Adrian, Pamela Shetler, Henry U. Bryant and Jeffrey A. Dodge*

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

17α-Dihydroequilenin was found to prevent bone loss after 5 weeks of oral administration to ovariectomized rats. The stereochemical significance of the D-ring was investigated with a series of analogues based on a benzothiophene platform.



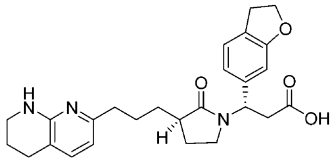
*Bioorg. Med. Chem. Lett. 13 (2003) 4285*

## Non-peptide $\alpha_v\beta_3$ Antagonists: Identification of Potent, Chain-Shortened RGD Mimetics that Incorporate a Central Pyrrolidinone Constraint

James J. Perkins,[a,*] Le T. Duong,[b] Carmen Fernandez-Metzler,[d] George D. Hartman,[a] Donald B. Kimmel,[b] Chih-Tai Leu,[b] Joseph J. Lynch,[d] Thomayant Prueksaritanont,[c] Gideon A. Rodan,[b] Sevgi B. Rodan,[b] Mark E. Duggan[a] and Robert S. Meissner[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, Merck Research Laboratories, West Point, PA 19486, USA*
[d]*Department of Pharmacology, Merck Research Laboratories, West Point, PA 19486, USA*

Antagonists of the integrin receptor $\alpha_v\beta_3$ are expected to have utility in the treatment of osteoporosis through inhibition of bone resorption. A series of potent, chain-shortened, pyrrolidinone-containing $\alpha_v\beta_3$ receptor antagonists is described. Two sets of diasteromeric pairs of high-affinity antagonists demonstrated marked differences in log P values, which translated into differing dog pharmacokinetic properties. One member of this set was demonstrated to be effective in reducing bone resorption in rats.



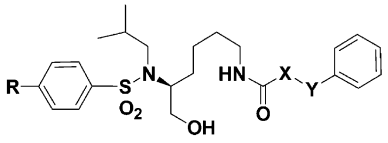
*Bioorg. Med. Chem. Lett. 13 (2003) 4289*

## Lysine Sulfonamides as Novel HIV-Protease Inhibitors: Optimization of the *N*ε-Acyl-Phenyl Spacer

Brent R. Stranix,* Gilles Sauvé, Abderrahim Bouzide, Alexandre Coté, Guy Sévigny and Jocelyn Yelle

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

A series of *N*α-isobutyl-*N*α-arylsulfonamido-(*N*ε acyl) lysine and lysinol derivatives were prepared and evaluated as inhibitors of HIV protease and wild type virus.

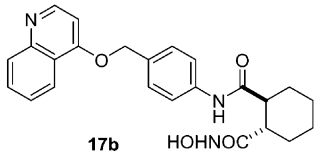


*Bioorg. Med. Chem. Lett. 13 (2003) 4293*

## Rational Design, Synthesis and Structure–Activity Relationships of a Cyclic Succinate Series of TNF-$\alpha$ Converting Enzyme Inhibitors. Part 1: Lead Identification

Chu-Biao Xue,* Xiaohua He, John Roderick, Ronald L. Corbett, James J.-W. Duan, Rui-Qin Liu, Maryanne B. Covington, Robert C. Newton, James M. Trzaskos, Ronald L. Magolda, Ruth R. Wexler and Carl P. Decicco

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

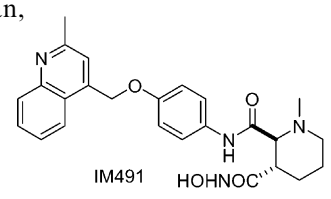



*Bioorg. Med. Chem. Lett. 13 (2003) 4299*

## Rational Design, Synthesis and Structure–Activity Relationships of a Cyclic Succinate Series of TNF-$\alpha$ Converting Enzyme Inhibitors. Part 2: Lead Optimization

Chu-Biao Xue,* Xiaohua He, John Roderick, Ronald L. Corbett, James J.-W. Duan, Rui-Qin Liu, Maryanne B. Covington, Mingxin Qian, Maria D. Ribadeneira, Krishna Vaddi, David D. Christ, Robert C. Newton, James M. Trzaskos, Ronald L. Magolda, Ruth R. Wexler and Carl P. Decicco

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

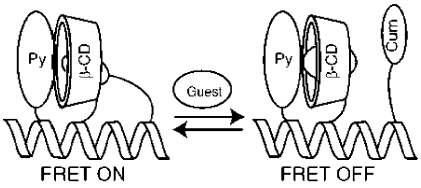


Bioorg. Med. Chem. Lett. 13 (2003) 4305

## Fluorescence Resonance Energy Transfer in a Novel Cyclodextrin–Peptide Conjugate for Detecting Steroid Molecules

Mohammed Akhter Hossain, Hisakazu Mihara* and Akihiko Ueno

*Department of Bioengineering, Tokyo Institute of Technology, 4259 Nagatsuta, Midori, Yokohama 226-8501, Japan*

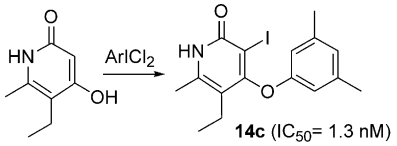



Bioorg. Med. Chem. Lett. 13 (2003) 4309

## 3-Iodo-4-phenoxypyridinones (IOPY's), a New Family of Highly Potent Non-nucleoside Inhibitors of HIV-1 Reverse Transcriptase

Abdellah Benjahad,[a,*] Jérôme Guillemont,[b] Koen Andries,[c] Chi Hung Nguyen[a,*] and David S. Grierson[a]

[a]*UMR 176 CNRS-Institut Curie, Laboratoire de Pharmacochimie, Section de Recherche, Batiment 110, Centre Universitaire, 91405 Orsay, France*
[b]*Johnson & Johnson Pharmaceutical Research and Development, Medicinal Chemistry Department, Campus de Maigremont BP315, Val de reuil, France*
[c]*Johnson & Johnson Pharmaceutical Research and Development, Virology Drug Discovery, Tumhoutseweg 30 B-2340 Beerse, Belgium*




**14c** ($IC_{50}$= 1.3 nM)

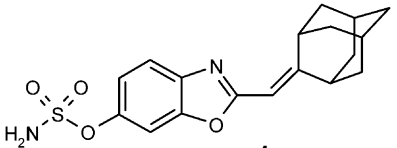
Bioorg. Med. Chem. Lett. 13 (2003) 4313

## 6-(2-Adamantan-2-ylidene-hydroxybenzoxazole)-*O*-sulfamate: A Potent Non-steroidal Irreversible Inhibitor of Human Steroid Sulfatase

Erwin P. Schreiner,* Barbara Wolff, Anthony P. Winiski and Andreas Billich

*Novartis Forschungsinstitut, Brunner Strasse 59, A-1235 Vienna, Austria*

We have identified the title compound **1** as the first potent non-estrogenic irreversible inhabitor of human steroid sulfatase featuring a 5,6-bicyclic ring system as a mimicry for the steroidal A- and B-ring.



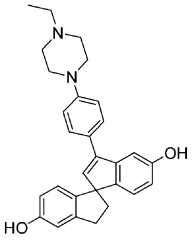

**1**

Bioorg. Med. Chem. Lett. 13 (2003) 4317

## 4-(4-Alkylpiperazin-1-yl)phenyl Group: A Novel Class of Basic Side Chains for Selective Estrogen Receptor Modulators

Nobuhide Watanabe,[a,*] Hiroshi Nakagawa,[a] Akihisa Ikeno,[b] Hisao Minato,[b] Chie Kohayakawa[b] and Jun-ichi Tsuji[b]

[a]*Chemistry Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Enoki-cho 33-94, Suita, Osaka 564-0053, Japan*
[b]*Pharmacology & Microbiology Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Enoki-cho 33-94, Suita, Osaka 564-0053, Japan*




**4m**

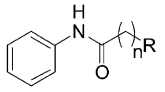
*Bioorg. Med. Chem. Lett. 13 (2003) 4321*

## Novel Histone Deacetylase Inhibitors: Design, Synthesis, Enzyme Inhibition, and Binding Mode Study of SAHA-Based Non-hydroxamates

Takayoshi Suzuki,[a] Yuki Nagano,[a] Azusa Matsuura,[a] Arihiro Kohara,[b] Shin-ichi Ninomiya,[b] Kohfuku Kohda[a] and Naoki Miyata[a,*]

[a]*Graduate School of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho-ku, Nagoya, Aichi 467-8603, Japan*
[b]*Daiichi Pure Chemicals Co., Ltd., 2117 Muramatsu, Tokai, Ibaraki 319-1182, Japan*

A series of SAHA-based non-hydroxamates was designed and synthesized, and semicarbazide **8b** and bromoacetamides **18b**,**c** were found to be potent HDAC inhibitors for non-hydroxamates. The binding mode analyses by computer calculation of **8b** and **18c** are also reported.



**8b**: n = 5, R = -NHCONHNH$_2$
**18b**: n = 6, R = -NHCOCH$_2$Br
**18c**: n = 5, R = -NHCOCH$_2$Br

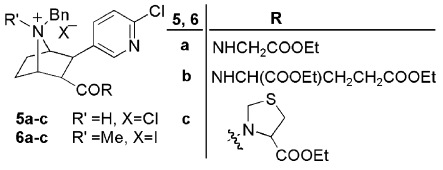
*Bioorg. Med. Chem. Lett. 13 (2003) 4327*

## Synthesis and Analgesic Activity of Hydrochlorides and Quaternary Ammoniums of Epibatidine Incorporated with Amino Acid Ester

Jing-Chao Dong, Xin Wang, Run-Tao Li,* Hong-Mei Zhang, Tie-Ming Cheng and Chang-Ling Li

*School of Pharmaceutical Sciences, Peking University, Beijing 100083, PR China*

Hydrochloride derivatives **5a**–**c** and quaternary ammonium derivatives **6a**–**c** of epibatidine incorporated with amino acid ester were synthesized and evaluated for their in vivo analgesic activity and toxicity.



| 5, 6 | R |
|---|---|
| a | NHCH$_2$COOEt |
| b | NHCH(COOEt)CH$_2$CH$_2$COOEt |
| c |  |

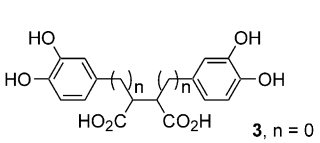
**5a-c** R' =H, X=Cl
**6a-c** R' =Me, X=I

*Bioorg. Med. Chem. Lett. 13 (2003) 4331*

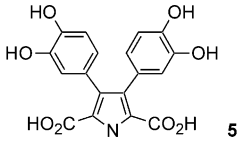
## Catechol-Substituted L-Chicoric Acid Analogues as HIV Integrase Inhibitors

Jae Yeol Lee, Kwon Joong Yoon and Yong Sup Lee*

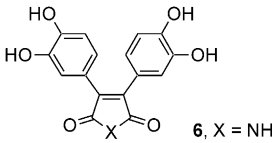
*Division of Life Sciences, Korea Institute of Science & Technology, PO Box 131, Cheongryang, Seoul 130-650, South Korea*



**3**, n = 0
**4**, n = 1



**5**



**6**, X = NH
**7**, X = O

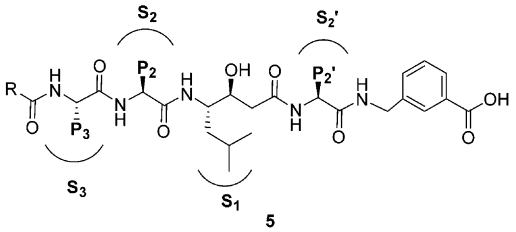
*Bioorg. Med. Chem. Lett. 13 (2003) 4335*

## Design and Synthesis of Statine-Containing BACE Inhibitors

Jingdan Hu,* Cynthia L. Cwi, David L. Smiley, David Timm, Jon A. Erickson, James E. McGee, Hsiu-Chiung Yang, David Mendel, Patrick C. May, Mike Shapiro and James R. McCarthy

*Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285, USA*

Structure-based design and synthesis of statine-containing tetrapeptide BACE inhibitors are reported. Computational analysis and the X-ray structure of BACE-inhibitor **38** are discussed.



**5**

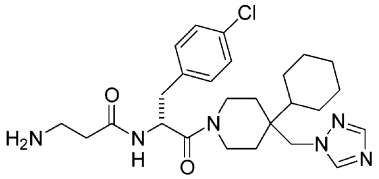
Bioorg. Med. Chem. Lett. 13 (2003) 4341

## β-Alanine Dipeptides as MC4R Agonists

Réjean Ruel,[a,*] Timothy F. Herpin,[c] Lawrence Iben,[b] Guanglin Luo,[b] Alain Martel,[a] Helen Mason,[c] Gail Mattson,[b] Brigitte Poirier,[a] Edward H. Ruediger,[a] Dan Shi,[c] Carl Thibault,[a] Guixue Yu,[c] Ildiko Antal Zimanyi,[c] Graham S. Poindexter[b] and John E. Macor[b]

[a]*Bristol-Myers Squibb Pharmaceutical Research Institute, 100 boul. de l'Industrie, Candiac, Quebec, Canada J5R 1J1*
[b]*Department of Neuroscience, 5 Research Parkway, Wallingford, CT 06492, USA*
[c]*Department of Metabolic Research, POB 5400 Princeton, NJ 08543-5400, USA*

β-Alanine derivative **2** ($IC_{50}$ = 16 nM) and related compounds were found to be potent MC4R agonists.



**2** MC4R $IC_{50}$ = 16 nM

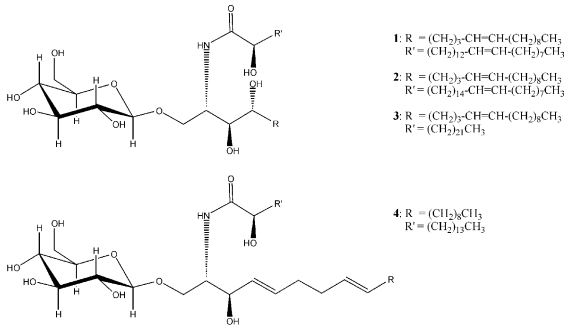
Bioorg. Med. Chem. Lett. 13 (2003) 4345

## New Cerebrosides from *Euphorbia peplis* L.: Antimicrobial Activity Evaluation

Francesca Cateni,[a,*] Jelena Zilic,[a] Gioacchino Falsone,[a] Giuditta Scialino[b] and Elena Banfi[b]

[a]*Department of Pharmaceutical Sciences, University of Trieste, P.zle Europa 1, 34127 Trieste, Italy*
[b]*Department of Biomedical Sciences, Microbiology sect., University of Trieste, Via A. Fleming 22, 34127 Trieste, Italy*

The isolation and structure elucidation of four cerebrosides with antifungal and antitubercular activity from *Euphorbia peplis* L. is reported.



**1**: R = $(CH_2)_5$-CH=CH-$(CH_2)_8CH_3$, R' = $(CH_2)_{12}$-CH=CH-$(CH_2)_7CH_3$
**2**: R = $(CH_2)_5$-CH=CH-$(CH_2)_8CH_3$, R' = $(CH_2)_{14}$-CH=CH-$(CH_2)_7CH_3$
**3**: R = $(CH_2)_5$-CH=CH-$(CH_2)_8CH_3$, R' = $(CH_2)_{21}CH_3$
**4**: R = $(CH_2)_8CH_3$, R' = $(CH_2)_{13}CH_3$

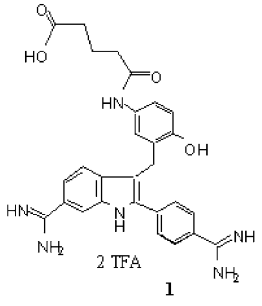
Bioorg. Med. Chem. Lett. 13 (2003) 4351

## DAPI Derivative: A Fluorescent DNA Dye that Can Be Covalently Attached to Biomolecules

Min Li,* Robert S. Wu and Jane S. C. Tsai

*Roche Diagnostics Corporation, 9115Hague Road, Indianapolis, IN 46250, USA*

The preparation of a DAPI (4′,6-diamidino-2-phenylindole) derivative (**1**) is described. The resulting derivative retains the fluorogenic property upon binding to double-stranded DNA. Its ability for bioconjugation through amide linkage is demonstrated.



2 TFA

**1**

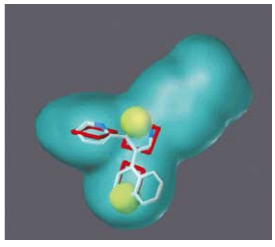
Bioorg. Med. Chem. Lett. 13 (2003) 4355

## Successful Shape-Based Virtual Screening: the Discovery of a Potent Inhibitor of the Type I TGFβ Receptor Kinase (TβRI)

Juswinder Singh,* Claudio E. Chuaqui, P. Ann Boriack-Sjodin, Wen-Cherng Lee, Timothy Pontz, Michael J. Corbley, H.-Kam Cheung, Robert M. Arduini, Jonathan N. Mead, Miki N. Newman, James L. Papadatos, Scott Bowes, Serene Josiah and Leona E. Ling

*Biogen Inc., 12 Cambridge Center, Cambridge, MA 02142, USA*

We describe the discovery, using shape-based virtual screening, of a potent, ATP site-directed inhibitor of the TβRI kinase, an important and novel drug target for fibrosis and cancer.



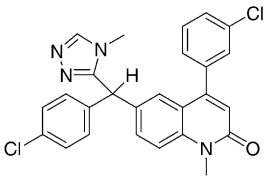
Bioorg. Med. Chem. Lett. 13 (2003) 4361

## 4-Methyl-1,2,4-triazol-3-yl Heterocycle as an Alternative to the 1-Methylimidazol-5-yl Moiety in the Farnesyltransferase Inhibitor ZARNESTRA™

Patrick Angibaud,[a,*] Ashis K. Saha,[b] Xavier Bourdrez,[a] David W. End,[b] Eddy Freyne,[c] Patricia Lezouret,[a] Geert Mannens,[d] Laurence Mevellec,[a] Christophe Meyer,[a] Isabelle Pilatte,[a] Virginie Poncelet,[a] Bruno Roux,[a] Gerda Smets,[c] Jacky Van Dun,[c] Marc Venet[a] and Walter Wouters[e]

[a]*Medicinal Chemistry Department Johnson & Johnson Pharmaceutical Research & Development (J&JPRD), Campus de Maigremont BP615, 27106 Val de Reuil, France*
[b]*Oncology Drug Discovery, J&JPRD L.L.C. Welsh and McKean Roads, Spring-House, PA 19477-0776, USA*
[c]*Oncology Drug Discovery, J&JPRD, Turnhoutseweg 30, B-2340, Belgium*
[d]*Preclinical Pharmacokinetics, J&JPRD, Turnhoutseweg 30, B-2340, Belgium*
[e]*Drug Evaluation, J&JPRD, Turnhoutseweg 30, B-2340, Belgium*

The synthesis and inhibiting potency of 4-methyl-1,2,4-triazol-3-yl analogues of R115777 are reported.



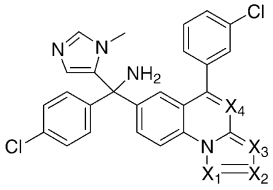
Bioorg. Med. Chem. Lett. 13 (2003) 4365

## Substituted Azoloquinolines and -quinazolines as New Potent Farnesyl Protein Transferase Inhibitors

Patrick Angibaud,[a,*] Xavier Bourdrez,[a] David W. End,[b] Eddy Freyne,[c] Michel Janicot,[b] Patricia Lezouret,[a] Yannick Ligny,[a] Geert Mannens,[d] Siegrid Damsch,[e] Laurence Mevellec,[a] Christophe Meyer,[a] Philippe Muller,[a] Isabelle Pilatte,[a] Virginie Poncelet,[a] Bruno Roux,[a] Gerda Smets,[b] Jacky Van Dun,[c] Pieter Van Remoortere,[e] Marc Venet[a] and Walter Wouters[e]

[a]*Medicinal Chemistry Dept. Johnson&Johnson Pharmaceutical Research & Development (J&JPRD), Campus de Maigremont BP615, 27106 Val de Reuil, France*
[b]*Oncology Drug Discovery, J&JPRD L.L.C. Welsh and McKean Roads, Spring-House, PA 19477-0776, USA*
[c]*Oncology Drug Discovery, J&JPRD, Turnhoutseweg 30, B-2340, Belgium*
[d]*Preclinical Pharmacokinetics, J&JPRD, Turnhoutseweg 30, B-2340, Belgium*
[e]*Drug Evaluation, J&JPRD, Turnhoutseweg 30, B-2340, Belgium*

The synthesis and inhibiting potency of farnesyltransferase inhibitors derived from R115777 is reported.



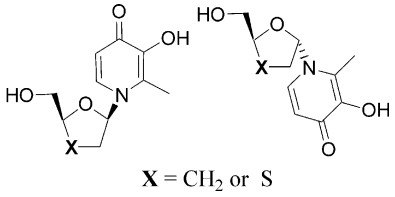
Bioorg. Med. Chem. Lett. 13 (2003) 4371

## Synthesis and Antiviral Evaluation of 3-Hydroxy-2-methylpyridin-4-one Dideoxynucleoside Derivatives

Karine Barral,[a] Robert C. Hider,[b] Jan Balzarini,[c] Johan Neyts,[c] Erik De Clercq[c] and Michel Camplo[a,*]

[a]*Laboratoire des Matériaux Moléculaires et des Biomatériaux (UMR-CNRS 6114), Faculté des Sciences de Luminy, case 901, 13288 Marseille cedex 09, France*
[b]*King's College London, Department of Pharmacy, Franklin-Wilkins Building, 150 Stamford Street, London SE1 9NN, UK*
[c]*Rega Institute for Medical Research, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium*

Novel α and β dideoxynucleoside derivatives in which the base has been replaced by a 3-hydroxy-2-methylpyridin-4-one showed moderate activity on herpes simplex virus (HSV) type 1 and type 2.



**X** = $CH_2$ or S

Bioorg. Med. Chem. Lett. 13 (2003) 4375

## 3D-QSAR Studies on Natural Acetylcholinesterase Inhibitors of *Sarcococca saligna* by Comparative Molecular Field Analysis (CoMFA)

Zaheer-ul-Haq,[a,*] Bernd Wellenzohn,[a] Somsak Tonmunphean,[b] Asaad Khalid,[c] M. Iqbal Choudhary[c] and Bernd M. Rode[a]

[a]*Department of Theoretical Chemistry, Institute of General, Inorganic and Theoretical Chemistry, University of Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria*
[b]*Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand*
[c]*HEJ Research Institute of Chemistry, University of Karachi, Karachi-75270, Pakistan*

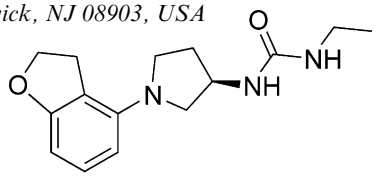
Bioorg. Med. Chem. Lett. 13 (2003) 4381

## Heterocyclic Aminopyrrolidine Derivatives as Melatoninergic Agents

Li-Qiang Sun,[a,*] Jie Chen,[a] Ronald J. Mattson,[a] James R. Epperson,[a] Jeffrey A. Deskus,[a] Wen-Sen Li,[b] Katherine Takaki,[a] Donald B. Hodges,[a] Lawrence Iben,[a] Cathy D. Mahle,[a] Astrid Ortiz,[a] David Molstad,[a] Elaine Ryan,[a] Krishnaswamy Yeleswaram,[a] Cen Xu[a] and Guanglin Luo[a,*]

[a]*Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT 06492, USA*
[b]*Bristol-Myers Squibb Pharmaceutical Research Institute, One Squibb Drive, New Brunswick, NJ 08903, USA*

A series of chiral heterocyclic aminopyrrolidine derivatives was synthesized as novel melatoninergic ligands. Binding affinity assays were performed on cloned human $MT_1$ and $MT_2$ receptors, stably expressed in NIH3T3 cells. Compound **16** was identified as an orally bioavailable agonist at $MT_1$ and $MT_2$ melatonin receptors with low vasoconstrictive activity.



**16**

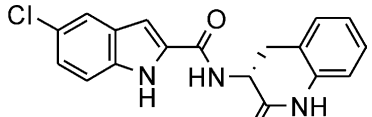
Bioorg. Med. Chem. Lett. 13 (2003) 4385

## Novel 3,4-Dihydroquinolin-2(1*H*)-one Inhibitors of Human Glycogen Phosphorylase *a*

Keith G. Rosauer,[a,*] Anthony K. Ogawa,[a] Chris A. Willoughby,[a] Kenneth P. Ellsworth,[b] Wayne M. Geissler,[b] Robert W. Myers,[b] Qiaolin Deng,[c] Kevin T. Chapman,[a] Georgianna Harris[b] and David E. Moller[b]

[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*
[c]*Department of Molecular Systems, Merck Research Laboratories, Rahway, NJ 07065, USA*

The preparation and SAR of 3,4-dihydroquinolin-2(1*H*)-one human glycogen phosphorylase inhibitors is discussed.



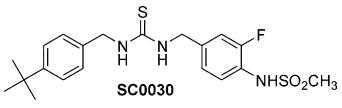
**7:** $IC_{50}$(hLGPa) =25nM

Bioorg. Med. Chem. Lett. 13 (2003) 4389

## Novel Non-vanilloid VR1 Antagonist of High Analgesic Effects and Its Structural Requirement for VR1 Antagonistic Effects

Young-Ger Suh,[a,*] Yong-Sil Lee,[a] Kyung-Hoon Min,[a] Ok-Hui Park,[a] Ho-Sun Seung,[a] Hee-Doo Kim,[c] Hyoung-Geun Park,[a] Ji-Yeon Choi,[a] Jeewoo Lee,[a] Sang-Wook Kang,[a] Uh-taek Oh,[b] Jae-yeon Koo,[b] Yung-Hyup Joo,[d] Sun-Young Kim,[d] Jin Kwan Kim[d] and Young-Ho Park[d]

[a]*College of Pharmacy, Seoul National University, San 56-1, Shinlim-Dong, Kwanak-Gu, Seoul 151-742, South Korea*
[b]*Sensory Research Center, CRI, Seoul National University, San 56-1, Shinlim-Dong, Kwanak-Gu, Seoul 151-742, South Korea*
[c]*College of Pharmacy, Sookmyung Women's University, 53-12, Chungpa-Dong, Yongsan-Gu, Seoul 140-742, South Korea*
[d]*R&D Center of AmorePacific Corp., 314-1, Bora-Ri, Giheung-Eup, Yongin-Si, Gyounggi-Do 449-900, South Korea*



**SC0030**

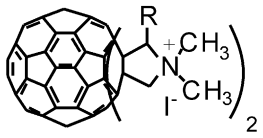
Bioorg. Med. Chem. Lett. 13 (2003) 4395

## Antibacterial and Antiproliferative Activity of Cationic Fullerene Derivatives

Tadahiko Mashino,[a,*] Dai Nishikawa,[a] Kyoko Takahashi,[a] Noriko Usui,[a] Takao Yamori,[b] Masako Seki,[a] Toyoshige Endo[a] and Masataka Mochizuki[a]

[a]*Kyoritsu College of Pharmacy, Shibakoen 1-5-30, Minato-ku, Tokyo 105-8512, Japan*
[b]*Japanese Foundation for Cancer Research, Kami-ikebukuro 1-37-1, Toshima-ku, Tokyo 170-8455, Japan*

We examined the antibacterial and antiproliferative activities of alkylated $C_{60}$-bis(*N,N*-dimethylpyrrolidinium iodide) derivatives. The fullerene derivatives inhibited bacteria and cancer cell growth effectively. However, the fullerene derivatives with a long alkyl chain did not show antibacterial activity.



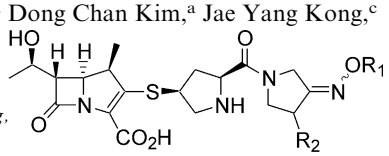
Bioorg. Med. Chem. Lett. 13 (2003) 4399

## Synthesis and Biological Activity of Novel 1β-Methylcarbapenems with Oxyiminopyrrolidinylamide Moiety

Ji Hoon Lee,[a,b] Kyung Seok Lee,[a] Yong Koo Kang,[a] Kyung Ho Yoo,[a] Kye Jung Shin,[a] Dong Chan Kim,[a] Jae Yang Kong,[c] Yeonhee Lee,[d] Sook Ja Lee[b,*] and Dong Jin Kim[a,*]

[a]*Medicinal Chemistry Research Center, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul 130-650, South Korea,* [b]*Department of Chemistry, Hankuk University of Foreign Studies, Seoul 130-791, South Korea,* [c]*Medicinal Science Division, Korea Research Institute of Chemical Technology, PO Box 107, Yusung, Daejeon 305-606, South Korea,* [d]*Department of Biology, Seoul Women's University, Seoul 139-774, South Korea*

The synthesis and antibacterial activity of novel 1β-methylcarbapenems **1a**–**f** bearing oxyimino-pyrrolidinylamide moiety at C-5 position of pyrrolidine are described. Most compounds exhibited comparable antibacterial activity to meropenem against a wide range of Gram-positive and Gram-negative organisms including *Pseudomonas aeruginosa* isolates. Of these carbapenems, **1a** showed potent and broad spectrum of antibacterial activity and similar stability to DHP-I to meropenem. Against clinical isolates of 40 Gram-negative bacterial species including MDR and ESBL-producing strains, the selected carbapenem **1a** possessed excellent in vitro activity except for MDR *P. aeruginosa*, and was comparable in potency to meropenem.



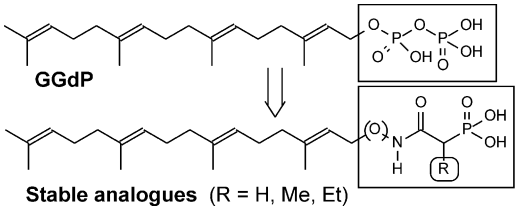
**1a:** $R_1$=$R_2$=H
**1b:** $R_1$=Me, $R_2$=H
**1c:** $R_1$=H, $R_2$=$CH_2NH_2$
**1d:** $R_1$=Me, $R_2$=$CH_2NH_2$
**1e:** $R_1$=H, $R_2$=$CO_2H$
**1f:** $R_1$=H, $R_2$=$CO_2Et$

Bioorg. Med. Chem. Lett. 13 (2003) 4405

## Stable Analogues of Geranylgeranyl Diphosphate Possessing Improved Geranylgeranyl Versus Farnesyl Protein Transferase Inhibitory Selectivity

Filippo Minutolo,[a] Simone Bertini,[a] Laura Betti,[b] Romano Danesi,[c] Gianbattista Gervasi,[d] Gino Giannaccini,[b] Chiara Papi,[a] Giorgio Placanica,[a] Silvia Barontini,[a] Simona Rapposelli[a] and Marco Macchia[a,*]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Pisa, Via Bonanno 6, 56126 Pisa, Italy*
[b]*Dipartimento di Psichiatria, Neurobiologia, Farmacologia e Biotecnologie, Università di Pisa, via Bonanno 6, 56126 Pisa, Italy*
[c]*Dipartimento di Oncologia, dei Trapianti e delle Nuove Tecnologie in Medicina, Divisione di Farmacologia e Chemioterapia, Università di Pisa, Via Roma 55, 56126 Pisa, Italy*
[d]*Laboratori Baldacci SpA, Via S. Michele degli Scalzi 73, 56124 Pisa, Italy*



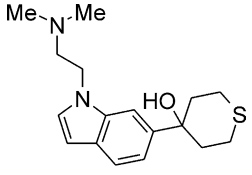

Bioorg. Med. Chem. Lett. 13 (2003) 4409

## Design, Synthesis and Biological Activity of Novel Dimethyl-{2-[6-substituted-indol-1-yl]-ethyl}-amine as Potent, Selective, and Orally-bioavailable 5-$HT_{1D}$ Agonists

Methvin Isaac,[a,*] Malik Slassi,[a] Tao Xin,[a] Jalaj Arora,[a] Anne O'Brien,[a] Louise Edwards,[a] Neil MacLean,[a] Julie Wilson,[a] Lidia Demschyshyn,[a] Phillipe Labrie,[a] Angela Naismith,[a] Shawn Maddaford,[a] Damon Papac,[b] Shuree Harrison,[b] Hua Wang,[b] Stan Draper[b] and Ashok Tehim[a]

[a]*NPS Pharmaceuticals Inc., 6850 Goreway Drive, Mississauga, ON, Canada L4V 1V7*
[b]*NPS Pharmaceuticals Inc., 420 Chipeta Way, Salt Lake City, UT 84108, USA*

A novel series of dimethyl-{2-[6-substituted-indol-1-yl]-ethyl}-amine derivatives was synthesized and found to be potent and selective 5-$HT_{1D}$ receptor agonist.



**11b (ALX-2732)**
$K_i$ (5$HT_{1D}$)=2.4 nM

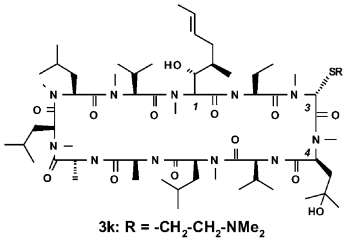
Bioorg. Med. Chem. Lett. 13 (2003) 4415

## Synthesis of Non-immunosuppressive Cyclophilin-Binding Cyclosporin A Derivatives as Potential Anti-HIV-1 Drugs

Michel Evers, Jean-Claude Barrière, Georges Bashiardes, Anne Bousseau, Jean-Christophe Carry, Norbert Dereu, Bruno Filoche, Yvette Henin, Serge Sablé, Marc Vuilhorgne and Serge Mignani*

*Aventis Pharma S.A., Centre de Recherche de Paris, 13 quai Jules Guesde, BP 14, 94403, Vitry-sur-Seine Cedex, France*

Original [2-(dimethyl or diethylamino)ethylthio-Sar]$^3$[(4′-OH)MeLeu]$^4$-CsA derivatives—**3k** and **3l**, respectively—display potent in vitro anti-HIV-1 ($IC_{50}$∼46 nM) and low immunosuppressive activities ($IC_{50}$≥1500 nM).



**3k:** R = -$CH_2$-$CH_2$-$NMe_2$
**3l:** R = -$CH_2$-$CH_2$-$NEt_2$

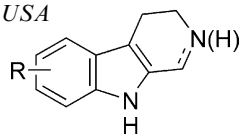
Bioorg. Med. Chem. Lett. 13 (2003) 4421

## Binding of β-Carbolines at 5-$HT_2$ Serotonin Receptors

Brian Grella,[a] Milt Teitler,[b] Carol Smith,[b] Katharine Herrick-Davis[b] and R. A. Glennon[a,*]

[a]*Department of Medicinal Chemistry, School of Pharmacy, Virginia Commonwealth University, Richmond, VA 23298-0540, USA*
[b]*Center for Neuropharmacology and Neuroscience, Albany Medical College, Albany, New York 12208, USA*

Certain bromo-substituted derivatives of 3,4-dihydro- and 1,2,3,4-tetrahydro-β-carboline bind with 20- to >150-fold enhanced affinity at 5-$HT_{2A}$ serotonin receptors relative to their parent unsubstituted counterparts.



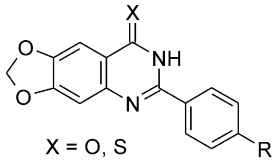

Bioorg. Med. Chem. Lett. 13 (2003) 4427

## 1-Aryl-6,7-methylenedioxy-3*H*-quinazolin-4-ones as Anticonvulsant Agents

Maria Zappalà,[a] Silvana Grasso,[a,*] Nicola Micale,[a] Giuseppe Zuccalà,[a] Frank S. Menniti,[b] Guido Ferreri,[c] Giovambattista De Sarro[c] and Carlo De Micheli[d]

[a]*Dipartimento Farmaco-Chimico, Università di Messina, viale Annunziata, 98168 Messina, Italy*
[b]*Pfizer Global Research and Development, Eastern Point Road, Groton, CT 06340, USA*
[c]*Dipartimento di Medicina Sperimentale e Clinica, Università di Catanzaro, Via T. Campanella, 88100 Catanzaro, Italy*
[d]*Istituto di Chimica Farmaceutica, Università di Milano, viale Abruzzi, 42, 20131 Milan, Italy*

A set of 1-aryl-6,7-methylenedioxy-3*H*-quinazolin-4-(thi)ones (**3a**–**f**) were synthesized and evaluated for either their anticonvulsant properties and their ability to bind the noncompetitive site of AMPA receptors.




**3a-3f**

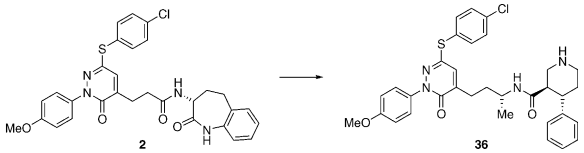
Bioorg. Med. Chem. Lett. 13 (2003) 4431

## Design and Syntheses of Melanocortin Subtype-4 Receptor Agonists: Evolution of the Pyridazinone Archetype

Feroze Ujjainwalla,[a,*] Daniel Warner,[a] Thomas F. Walsh,[a] Matthew J. Wyvratt,[a] Changyou Zhou,[a] Lihu Yang,[a] Rubana N. Kalyani,[b] Tanya MacNeil,[b] Lex H.T. Van der Ploeg,[b] Charles I. Rosenblum,[b] Rui Tang,[b] Aurawan Vongs,[b] David H. Weinberg[b] and Mark T. Goulet[a]

[a]*Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ 07065-0900, USA*
[b]*Department of Obesity and Metabolic Research, Merck Research Laboratories, Rahway, NJ 07065-0900, USA*

The discovery and optimization of a new class of non-peptidyl, pyridazinone derived melanocortin subtype-4 receptor agonists is disclosed. This work culminated in the identification of **36** which is a potent and selective agonist of the human MC4R.

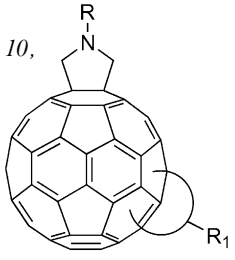



Bioorg. Med. Chem. Lett. 13 (2003) 4437

## Synthesis and Anti-HIV Properties of New Water-Soluble Bis-functionalized[60]fullerene Derivatives

Susanna Bosi,[a] Tatiana Da Ros,[a] Giampiero Spalluto,[a] Jan Balzarini[b,*] and Maurizio Prato[a,*]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Trieste, Piazzale Europa 1, I-34127 Trieste, Italy*
[b]*Rega Institute for Medical Research, Laboratory of Virology and Chemotherapy, Minderbroedersstraat 10, B-3000 Leuven, Belgium*



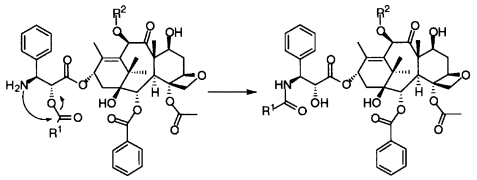
Bioorg. Med. Chem. Lett. 13 (2003) 4441

## O–N Intramolecular Acyl Migration Strategy in Water-Soluble Prodrugs of Taxoids

Mariusz Skwarczynski, Youhei Sohma, Maiko Kimura, Yoshio Hayashi,* Tooru Kimura and Yoshiaki Kiso*

*Department of Medicinal Chemistry, Center for Frontier Research in Medicinal Science, Kyoto Pharmaceutical University, Yamashina-Ku, Kyoto 607-8412, Japan*

The first water-soluble prodrug of canadensol based on O–N intramolecular acyl migration strategy is reported. A similar design of docetaxel prodrug is also considered.



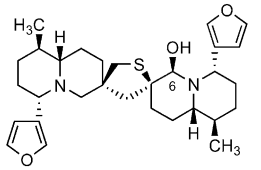
Bioorg. Med. Chem. Lett. 13 (2003) 4445

## Potent Anti-metastatic Activity of Dimeric Sesquiterpene Thioalkaloids from the Rhizome of *Nuphar pumilum*

Hisashi Matsuda, Toshio Morikawa, Mamiko Oda, Yasunobu Asao and Masayuki Yoshikawa*

*Kyoto Pharmaceutical University, Misasagi, Yamashina-ku, Kyoto 607-8412, Japan*

The methanolic extract and its alkaloid fraction from the rhizomes of *Nuphar pumilum* inhibited invasion of B16 melanoma cells across collagen-coated filters in vitro. Dimeric sesquiterpene thioalkaloids with the 6-hydroxyl group, (6-hydroxythiobinupharidine, 6,6′-dihydroxythiobinupharidine, and 6-hydroxythionuphlutine B), showed potent activity with $IC_{50}$ values of 0.029, 0.087, and 0.36 μM, respectively, but dimeric sesquiterpene thioalkaloids lacking the 6-hydroxyl group (thiobinupharidine, neothiobinupharidine, *syn*-thiobinupharidine sulfoxide, thionuphultine B β-sulfoxide, and neothiobinupharidine β-sulfoxide) and monomeric sesquiterpene alkaloids (nupharidine, deoxynupharidine, 7-epideoxynupharidine, and nupharolutine) showed weak activity. The alkaloid fraction (20 mg/kg/d, po) and the principal dimeric sesquiterpene thioalkaloid 6-hydroxythiobinupharidine (5 mg/kg/d, po) significantly inhibited lung tumor formation by more than 90% 10 days after injection of B16 melanoma cells in mice.



6-hydroxythiobinupharidine

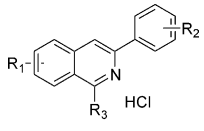
Bioorg. Med. Chem. Lett. 13 (2003) 4451

## Synthesis of New 3-Arylisoquinolinamines: Effect on Topoisomerase I Inhibition and Cytotoxicity

Won-Jea Cho,* Sun Young Min, Thanh Nguyen Le and Tae Sung Kim

*College of Pharmacy, Chonnam National University, Yong-Bong dong, Buk-gu, Kwangju 500-757, South Korea*

3-Arylisoquinolinamines were synthesized and tested in vitro antitumor and topoisomerase I inhibitory activities.

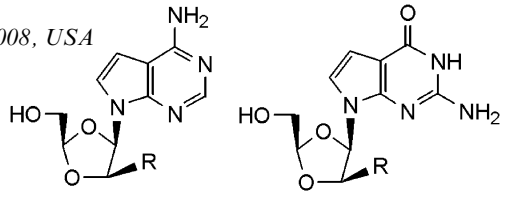


Bioorg. Med. Chem. Lett. 13 (2003) 4455

## Synthesis and Evaluation of Optically Pure Dioxolanes as Inhibitors of Hepatitis C Virus RNA Replication

Sanjib Bera,[a] Leila Malik,[a] Balkrishen Bhat,[a] Steven S. Carroll,[b] Malcolm MacCoss,[c] David B. Olsen,[b] Joanne E. Tomassini[b] and Anne B. Eldrup[a,*]

[a]*Department of Medicinal Chemistry, Isis Pharmaceuticals, Carlsbad, CA 92008, USA*
[b]*Department of Biological Chemistry, Merck Research Laboratories, West Point, PA 19486, USA*
[c]*Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ 07065, USA*



R can be H or Me

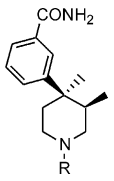
Bioorg. Med. Chem. Lett. 13 (2003) 4459

## *trans*-3,4-Dimethyl-4-(3-carboxamidophenyl)piperidines: A Novel Class of μ-Selective Opioid Antagonists

Bertrand Le Bourdonnec,[a,*] Serge Belanger,[b] Joel A. Cassel,[b] Gabriel J. Stabley,[b] Robert N. DeHaven[b] and Roland E. Dolle[a]

[a]*Department of Chemistry, Adolor Corporation, 700 Pennsylvania Drive, Exton, PA 19341, USA*
[b]*Department of Pharmacology, Adolor Corporation, 700 Pennsylvania Drive, Exton, PA 19341, USA*

The discovery and SAR studies of a series of *trans*-3,4-dimethyl-4-(3-carboxamidophenyl)piperidines as novel μ opioid receptor antagonists is reported.



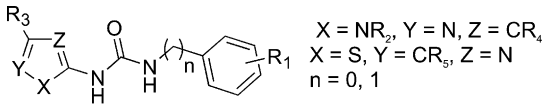

Bioorg. Med. Chem. Lett. 13 (2003) 4463

## Ureas of 5-Aminopyrazole and 2-Aminothiazole Inhibit Growth of Gram-Positive Bacteria

John L. Kane, Jr.,* Bradford H. Hirth, Beirong Liang, Brian B. Gourlie, Sharon Nahill and Gary Barsomian

*Genzyme Drug Discovery and Development, Genzyme Corp., Cambridge MA 02139, USA*

The discovery of antibacterial activity in ureas of 5-aminopyrazole and 2-aminothiazole inhibitors is described. Structure–activity relationships and in vivo behavior of these compounds is discussed. Data on drug resistant organisms is presented.

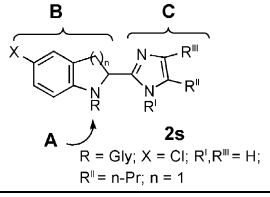



Bioorg. Med. Chem. Lett. 13 (2003) 4467

## Tripeptidyl-peptidase II (TPP II) Inhibitory Activity of (*S*)-2,3-Dihydro-2-(1*H*-imidazol-2-yl)-1*H*-indoles, a Systematic SAR Evaluation. Part 2

Henry J. Breslin,[a,*] Tamara A. Miskowski,[a] Michael J. Kukla,[a] Hans L. De Winter,[b] Maria V. F. Somers,[b] Peter W. M. Roevens[b] and Robert W. Kavash[a]

[a]*Johnson & Johnson Pharmaceutical Research & Development, L.L.C., Welsh and McKean Roads, PO Box 776, Spring House, PA 19477-0776, USA*
[b]*Johnson & Johnson Pharmaceutical Research & Development, L.L.C., Turnhoutseweg 30, B-2340 Beerse, Belgium*



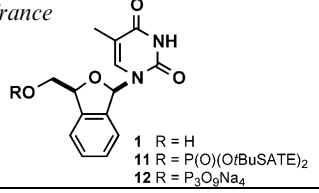

Bioorg. Med. Chem. Lett. 13 (2003) 4473

## 1,3-Dihydrobenzo[*c*]furan Nucleoside Analogues: Additional Studies of the Thymine Derivative

David Egron,[a] Christian Périgaud,[a] Gilles Gosselin,[a,c] Anne-Marie Aubertin,[b] Abdesslem Faraj,[c] Majid Sélouane,[d] Denis Postel[d] and Christophe Len[d,*]

[a]*UMR 5625 CNRS-UM II, Université Montpellier II, cc 008, place E. Bataillon, 34095 Montpellier Cedex 5, France*
[b]*Institut de Virologie de la Faculté de Médecine de Strasbourg, U. INSERM 74, 3 rue Koeberlé, 67000 Strasbourg, France*
[c]*Laboratoire Coopératif Idenix CNRS-UM II, place E. Bataillon, 34095 Montpellier Cedex 5, France*
[d]*Laboratoire des Glucides, Université de Picardie Jules Verne, 80039 Amiens, France*

Synthesis and biological tests for 1,3-dihydrobenzo[*c*]furan derivative of thymine **1**, its bis(*t*BuSATE) phosphotriester **11** and triphosphate **12** are reported.



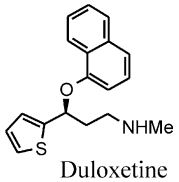
Bioorg. Med. Chem. Lett. 13 (2003) 4477

## Duloxetine (Cymbalta™), a Dual Inhibitor of Serotonin and Norepinephrine Reuptake

F. P. Bymaster,[a] E. E. Beedle,[a] J. Findlay,[b] P. T. Gallagher,[b,*] J. H. Krushinski,[a] S. Mitchell,[b] D. W. Robertson,[a] D. C. Thompson,[a] L. Wallace[b] and D. T. Wong[a]

[a]*Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, USA*
[b]*Eli Lilly and Company, Ltd, Lilly Research Centre, Windlesham, Surrey GU20 6PH, UK*

A series of naphthalenyloxy-arylpropylamines have been prepared and are demonstrated to be inhibitors of both serotonin and norepinephrine reuptake. One member of this series, duloxetine (Cymbalta™) has proven to be effective in clinical trials for the treatment of depression.



Duloxetine

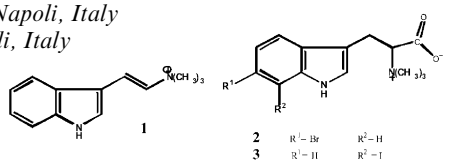
Bioorg. Med. Chem. Lett. 13 (2003) 4481

## Conicamin, a Novel Histamine Antagonist from the Mediterranean Tunicate *Aplidium conicum*

Anna Aiello,[a] Francesca Borrelli,[b] Raffaele Capasso,[b] Ernesto Fattorusso,[a,*] Paolo Luciano[a] and Marialuisa Menna[a]

[a]*Dipartimento di Chimica delle Sostanze Naturali, via D. Montesano, 49, I-80131 Napoli, Italy*
[b]*Dipartimento di Farmacologia Sperimentale, via D. Montesano, 49, I-80131 Napoli, Italy*

The methanol extract of Mediterranean tunicate *Aplidium conicum* was shown to contain, in addition to the known 6-bromo-hypaphorine (**2**) and plakohypaphorine-A (**3**), conicamin (**1**), a novel alkaloid having histamine-antagonistic activity, which structure was determined on the basis of the spectral data.

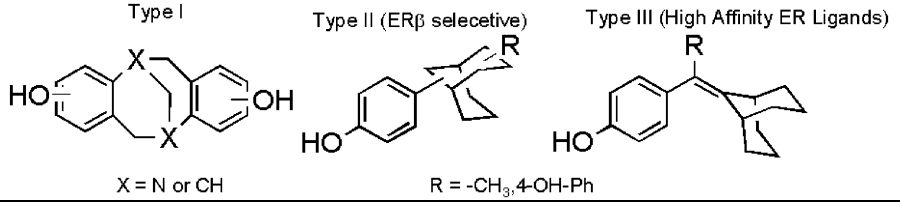



Bioorg. Med. Chem. Lett. 13 (2003) 4485

## Exploration of the Bicyclo[3.3.1]nonane System as a Template for the Development of New Ligands for the Estrogen Receptor

Rajeev S. Muthyala, Kathryn E. Carlson and John A. Katzenellenbogen*

*Department of Chemistry, University of Illinois, 600 S Mathews Avenue, Urbana, IL 61801, USA*



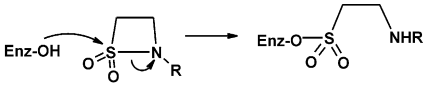

Bioorg. Med. Chem. Lett. 13 (2003) 4489

## Novel Mechanism of Inhibiting β-Lactamases by Sulfonylation Using β-Sultams

Michael I. Page,* Paul S. Hinchliffe, J. Matthew Wood, Lindsay P. Harding and Andrew P. Laws

*Department of Chemical and Biological Sciences, The University of Huddersfield, Queensgate, Huddersfield HD1 3DH, UK*

β-Sultams inactivate a class C β-lactamase by sulfonylation of the active site serine.



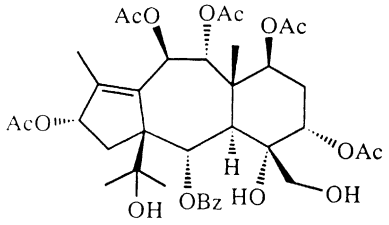
*Bioorg. Med. Chem. Lett. 13 (2003) 4493*

## Microbial Transformation of Baccatin VI and 1β-Hydroxy Baccatin I by *Aspergillus niger*

Ya-Ching Shen,* Kuang-Liang Lo, Chun-Ling Lin and Rupak Chakraborty

*Institute of Marine Resources, National Sun Yat-sen University, 70 Lien Hai Road, Kaohsiung 80424, Taiwan, ROC*

The biotransformation of baccatin VI and 1β-hydroxybaccatin I with *Aspergillus niger* produced four new taxane diterpenoids.



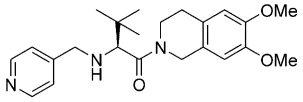

*Bioorg. Med. Chem. Lett. 13 (2003) 4497*

## *N*-Acyl 6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline: The First Orexin-2 Receptor Selective Non-peptidic Antagonist

Masaaki Hirose, Shin-ichiro Egashira, Yasuhiro Goto, Takashi Hashihayata, Norikazu Ohtake, Hisashi Iwaasa, Mikiko Hata, Takehiro Fukami, Akio Kanatani and Koji Yamada

*Banyu Tsukuba Research Institute, Banyu Pharmaceutical Co., Ltd, Okubo 3, Tsukuba, 300-2611 Ibaraki, Japan*

The discovery of a novel orexin-2 receptor selective antagonist **29** ($IC_{50}$: 40 nM, $OX_1R/OX_2R = >250$-fold) is described.




**29**

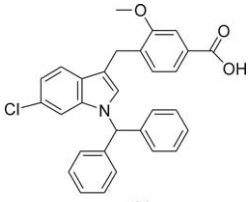
*Bioorg. Med. Chem. Lett. 13 (2003) 4501*

## Structure–Activity Relationships of Indole Cytosolic Phospholipase $A_2\alpha$ Inhibitors: Substrate Mimetics

John C. McKew,[a,*] Frank Lovering,[a] James D. Clark,[b] Jean Bemis,[a] YiBin Xiang,[a] Marina Shen,[b] Wen Zhang,[b] Juan C. Alvarez[a] and Diane Joseph-McCarthy[a]

[a]*Departments of Chemical and Screening Sciences, Wyeth Research, 200 Cambridge Park Drive, Cambridge, MA 02140, USA*
[b]*Inflammation Research, Wyeth Research, 200 Cambridge Park Drive, Cambridge, MA 02140, USA*

The synthesis of a $cPLA_2$ α inhibitor with potent activity in both an isolated enzyme assay and cell-based assays with good pharmacokinetic properties is reported.




**21**

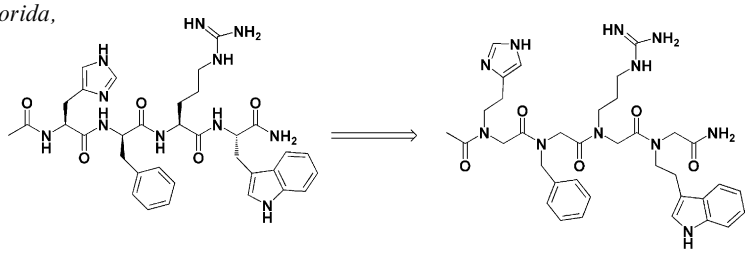
$IC_{50}$ = 0.8 uM
MC-9 $LTB_4$ $IC_{50}$ = 0.8 uM
% F (rat) = 63%

*Bioorg. Med. Chem. Lett. 13 (2003) 4505*

## Design and Pharmacology of Peptoids and Peptide–Peptoid Hybrids Based on the Melanocortin Agonists Core Tetrapeptide Sequence

Jerry Ryan Holder, Rayna M. Bauzo, Zhimin Xiang, Joseph Scott and Carrie Haskell-Luevano*

*Department of Medicinal Chemistry, University of Florida, PO Box 100485, Gainesville, FL 32610, USA*

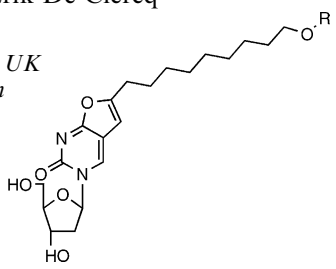


*Bioorg. Med. Chem. Lett. 13 (2003) 4511*

## Novel Bicyclic Furanopyrimidines with Dual Anti-VZV and -HCMV Activity

Christopher McGuigan,[a,*] Andrea Brancale,[a] Graciela Andrei,[b] Robert Snoeck,[b] Erik De Clercq[b] and Jan Balzarini[b]

[a]*Welsh School of Pharmacy, Cardiff University, King Edward VII Avenue, Cardiff CF10 3XF, UK*
[b]*Rega Institute for Medical Research, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium*



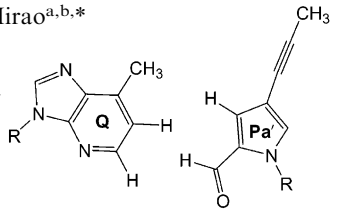

Novel bicyclic nucleoside analogues bearing long alkyl side-chains were prepared and tested as inhibitors of VZV. In particular, analogues with long alkyoxy side chains are noted to be the first ever examples of this class on these bicyclic nucleoside analogues (BCNAs) to display dual anti-VZV and -HCMV action.

*Bioorg. Med. Chem. Lett. 13 (2003) 4515*

## An Unnatural Hydrophobic Base, 4-Propynylpyrrole-2-carbaldehyde, as an Efficient Pairing Partner of 9-Methylimidazo[(4,5)-*b*]pyridine

Tsuneo Mitsui,[a] Michiko Kimoto,[b] Akira Sato,[b] Shigeyuki Yokoyama[b,c,d] and Ichiro Hirao[a,b,*]

[a]*Research Center for Advanced Science and Technology, The University of Tokyo, 4-6-1 Komaba, Meguro-ku, Tokyo 153-8904, Japan*
[b]*Protein Synthesis Technology Team, Protein Research Group, RIKEN Genomic Sciences Center (GSC), 1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan*
[c]*Department of Biophysics and Biochemistry, Graduate School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan*
[d]*RIKEN Harima Institute at Spring-8, 1-1-1 Kouto, Mikazuki-cho, Sayo, Hyogo 679-5148, Japan*

The unnatural Q-Pa′ 

pair

An unnatural hydrophobic base, 4-propynylpyrrole-2-carbaldehyde, as an efficient pairing partner of 9-methylimidazo[(4,5)-*b*]pyridine.