Graphical Abstracts

Solution-Phase Synthesis of Novel Δ^2-Isoxazoline Libraries via 1,3-Dipolar Cycloaddition and Their Antifungal Properties

Bioorg. Med. Chem. 11 (2003) 4539

Basappa, M. P. Sadashiva, K. Mantelingu, S. Nanjunda Swamy and K. S. Rangappa*

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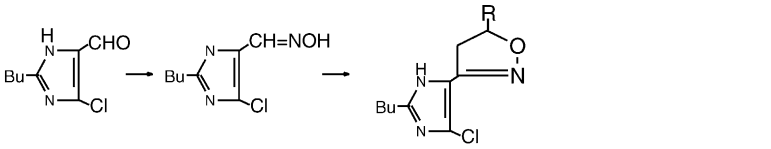
The synthesis and antifungal activities of 3-(-2-butyl-4-chloro-1*H*-imidazolyl)-substituted δ^2-isoxazolines was accomplished via 1,3-dipolar cycloaddition of *insitu* generated nitryl oxides from aldoximes with mono substituted alkenes to obtain the compound libraries contains an imidazole functionality in addition to the isoxazoline rings. The newly synthesized compounds when tested in vitro in solid agar culture exerted a potent antifungal activity against *Aspergillus flavus*, *Fusarium moniliforme* and *Botrydiplodia theobromae* also MIC values were determined. The title 5-substituted-3-imidazolyl-δ^2-isoxazoline compounds represent a novel class of potent antifungal agents.



Where:**R**=(I) -CN(II) $-C_6H_5$(III) $-COOC_6H_5$(IV) $-COOC_2H_5$(V) $-CH_2COOCH_3$(VI) $-CH_2OH$(VII) $-COOCH_3$

Anti-Tumor Activity of the Farnesyl-protein Transferase Inhibitors Arteminolides, Isolated from *Artemisa*

Bioorg. Med. Chem. 11 (2003) 4545

Seung Ho Lee,[a] Mi-Young Lee,[a] Hyun-Mi Kang,[a] Dong Cho Han,[a] Kwang-Hee Son,[a] Deok Cho Yang,[b] Nack-Do Sung,[c] Chang Woo Lee,[a] Hwan Mook Kim[a] and Byoung-Mog Kwon[a,*]

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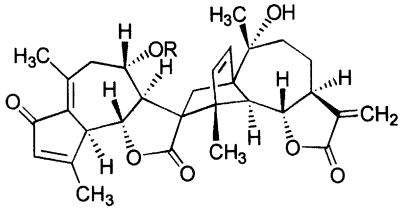
Arteminolides, isolated from aerial parts of *Artemisia*, strongly inhibited human tumor cells. Arteminolide C blocked in vivo growth of human colon SW620 and lung tumor NCI H-23 xenograft without the loss of body weight in nude mice.



One-Electron Reduction Characteristics of N(3)-Substituted 5-Fluorodeoxyuridines Synthesized as Radiation-Activated Prodrugs

Bioorg. Med. Chem. 11 (2003) 4551

Kazuhito Tanabe, Youhei Mimasu, Akira Eto, Yukihiro Tachi, Shingo Sakakibara, Mayuko Mori, Hiroshi Hatta and Sei-ichi Nishimoto*

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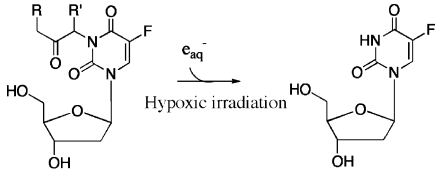
A series of 5-fluorodeoxyuridine derivatives possessing a 2-oxoalkyl group at the N(3)-position were synthesized as radiation-activated prodrugs of the antitumor agent 5-fluorodeoxyuridine.



8-Quinolinamines and Their Pro Prodrug Conjugates as Potent Blood-Schizontocidal Antimalarial Agents

Bioorg. Med. Chem. 11 (2003) 4557

Suryanarayana Vangapandu, Sandeep Sachdeva, Meenakshi Jain, Savita Singh, Prati Pal Singh, Chaman Lal Kaul and Rahul Jain*

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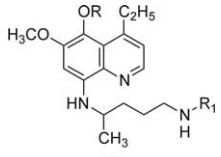
The synthesis and antimalarial activities of N^8-(4-amino-1-methylbutyl)-5-alkoxy-4-ethyl-6-methoxy-8-quinolinamines and their pro prodrug conjugates are described. Many of the compounds were found to possess potent in vivo activities against drug-sensitive and drug-resistant malaria strains.



5-7
$R=C_3H_7 - C_8H_{17}$
R_1=H, Pro prodrug linker

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Piericidins C_5 and C_6: New 4-Pyridinol Compounds Produced by *Streptomyces* sp. and *Nocardioides* sp.

Natsuki K. Kubota,[a] Emi Ohta,[a] Shinji Ohta,[a,*] Fumito Koizumi,[b] Makoto Suzuki,[b] Michio Ichimura[b] and Susumu Ikegami[a,c,*]

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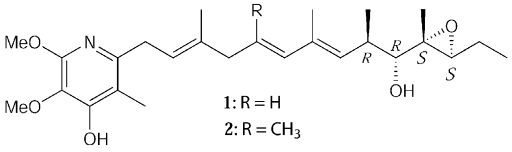
[b]*Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., 3-6-6 Asahi-machi, Machida, Tokyo 194-8533, Japan*
[c]*Laboratory of Environmental Biology, Nagahama Institute of Bio-science and Technology, 1266 Tamura-cho, Nagahama, Shiga 526-0829, Japan*

The structures of piericidins C_5 (**1**) and C_6 (**2**) were determined on the basis of their spectroscopic data. Both compounds inhibited cell division of fertilized starfish eggs at the minimum inhibitory concentration of 0.09 μg/mL.



Bioorg. Med. Chem. 11 (2003) 4577

Antifungal Diterpenoids of *Pseudolarix kaempferi*, and Their Structure–Activity Relationship Study

Sheng-Ping Yang, Lei Dong, Ying Wang, Yan Wu and Jian-Min Yue*

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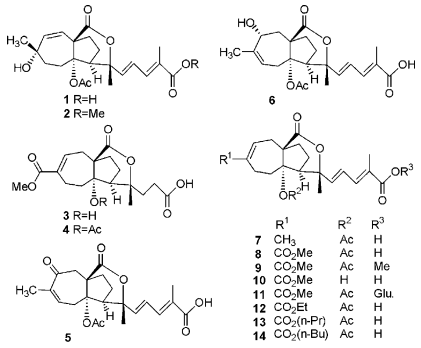
The in vitro antifungal activities of 19 structurally diversified analogues of pseudolaric acids tested against the major pathogenic fungus *Candida albicans* has led to establishment of a very clear structure–activity relationship of pseudolaric acids derivatives. Pseudolaric acid A was first found to be a potent antifungal component. Among the tested 19 diterpenoids, Compounds **1**–**4** are new isolates, and their structures were elucidated mainly by 2D-NMR techniques and chemical methods. Compounds **15**–**19** were first semi-synthesized by efficient routines from pseudolaric acid B.



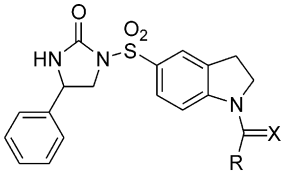
Bioorg. Med. Chem. 11 (2003) 4585

The 3D-QSAR Study of Antitumor Arylsulfonylimidazolidinone Derivatives by CoMFA and CoMSIA

Hea-Young Park Choo,[a,*] Suyoung Choi,[a] Sang-Hun Jung,[b] Hun Yeong Koh[c] and Ae Nim Pae[c,*]

[a]*School of Pharmacy, Ewha Womans University, Seoul 120-750, South Korea*
[b]*College of Pharmacy, Chung-Nam National University, Taejon 305-764, South Korea*
[c]*Biochemicals Research Center, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul 130-650, South Korea*

The 3-D-QSAR studies for a series of arylsulfonylimidazolidinone derivatives having antitumor activity were conducted using CoMFA and CoMSIA.



Bioorg. Med. Chem. 11 (2003) 4591

Synthesis and Cytotoxic Activity of Some New Azapyranoxanthenone Aminoderivatives

George Kolokythas,[a] Ioannis K. Kostakis,[a] Nicole Pouli,[a] Panagiotis Marakos,[a,*] Dimitris Kletsas[b] and Harris Pratsinis[b]

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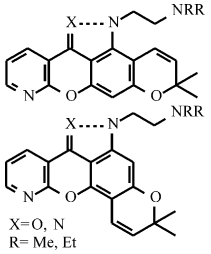
[b]*Laboratory of Cell Proliferation & Ageing, Institute of Biology, NCSR 'Demokritos', 15310 Athens, Greece*



Bioorg. Med. Chem. 11 (2003) 4599

A System of Protein Target Sequences for Anti-RNA-viral Chemotherapy by a Vitamin B_6-Derived Zinc-Chelating Trioxa-adamantane-triol

Andreas J. Kesel*

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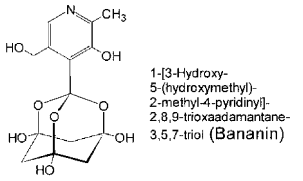
The synthesis and theoretically deduced anti-RNA-viral activity of the structurally unusual heterotricyclic compound 1-[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]-2,8,9-trioxaadamantane-3,5,7-triol are critically evaluated.



Bioorg. Med. Chem. 11 (2003) 4615

Synthesis and Antiparasitic Activity of Albendazole and Mebendazole Analogues

Gabriel Navarrete-Vázquez,[a,*] Lilián Yépez,[b] Alicia Hernández-Campos,[a] Amparo Tapia,[b] Francisco Hernández-Luis,[a] Roberto Cedillo,[c] José González,[a] Antonio Martínez-Fernández,[d] Mercedes Martínez-Grueiro[d] and Rafael Castillo[a,*]

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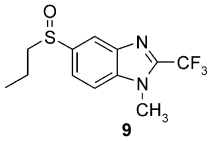
[b]*Unidad de Investigación Médica en Enfermedades Infecciosas y Parasitarias, IMSS, DF 06720, Mexico*
[c]*Unidad Interinstitucional de Investigación Médica, IMSS-UADY, Mérida, Yucatán, Mexico*
[d]*Departamento de Parasitología, Facultad de Farmacia, Universidad Complutense de Madrid, Madrid 28040, Spain*

Albendazole (Abz) and Mebendazole (Mbz) analogues have been synthesized and in vitro tested against 2 protozoa and 2 helminths. Results indicate that two Abz analogues and two Mbz analogues were as active as Metronidazole against *G. lamblia*. Compound **9** was 58 times more active than Abz against *T. vaginalis*. The anthelminthic activity presented by these compounds was poor.



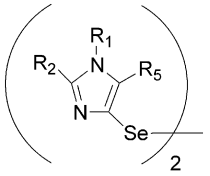
Bioorg. Med. Chem. 11 (2003) 4623

Design, Synthesis and Glutathione Peroxidase-Like Properties of Ovothiol-Derived Diselenides

Fabrice Bailly,[a,*] Nathalie Azaroual[b] and Jean-Luc Bernier[a]

[a]*Laboratoire de Chimie Organique Macromoléculaire, CNRS UMR 8009, USTL, Bâtiment C3, UST Lille I, 59655 Villeneuve d'Ascq, France*
[b]*Laboratoire de RMN, Faculté de Pharmacie, CNRS UMR 8009, BP83, 59006 Lille Cedex, France*

A series of imidazole diselenides derived from the naturally occurring antioxidant ovothiols were synthesized and investigated for their glutathione peroxidase-like properties and their capacity to be reduced by glutathione. The most active molecules of the series were 4 times more potent in the GSH Px-like test than the widely known reference compound, ebselen. This catalytic activity was mediated by the formation of the antioxidant selenol form upon partial but significant exchange reaction with glutathione.



Bioorg. Med. Chem. 11 (2003) 4631

Inhibition of Bovine Plasma Amine Oxidase by 1,4-Diamino-2-butenes and -2-butynes

Heung-Bae Jeon, Younghee Lee, Chunhua Qiao, He Huang and Lawrence M. Sayre*

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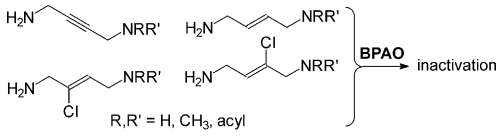
1,4-Diamino-2-butyne is a known inactivator of diamine oxidases. Whereas propargylamine and 2- and 3-chloroallylamines are known inactivators of bovine plasma amine oxidase (BPAO), diamine versions of these monoamines are here shown to be potent inactivators also of BPAO. Simple allylamine-based diamines are weaker inhibitors. Alkylation or acylation of one end of the bis-primary amine inhibitors greatly reduces their potency.



Bioorg. Med. Chem. 11 (2003) 4643

Design of EGFR Kinase Inhibitors: A Ligand-Based Approach and Its Confirmation with Structure-Based Studies

Aparna Vema,[a] Sunil K. Panigrahi,[a] G. Rambabu,[c] B. Gopalakrishnan,[b,*] J. A. R. P. Sarma[c,*] and Gautam R. Desiraju[a,*]

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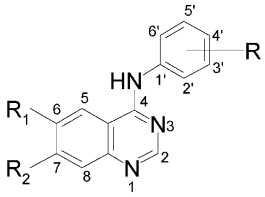
[c]*gvk bioSciences Pvt. Ltd., #210 'My Home Tycoon', 6-3-1192 Begumpet, Hyderabad 500 016, India*

Robust and predictive 3D-QSAR models were developed for anilinoquinazolines inhibiting EGFR kinase. The results were compared with docking to confirm the distinct nature of the 6- and 7-positions in the quinazoline nucleus.

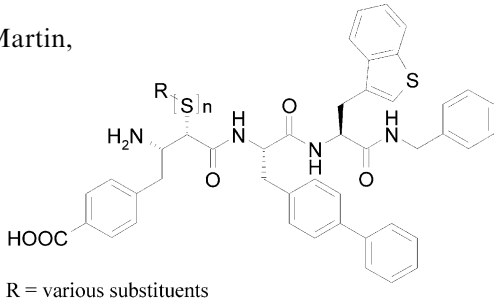


Bioorg. Med. Chem. 11 (2003) 4655

Thio-Derived Disulfides as Potent Inhibitors of Botulinum Neurotoxin Type B: Implications for Zinc Interaction

Christine Anne, Armand Blommaert, Serge Turcaud, Anne-Sophie Martin, Hervé Meudal and Bernard P. Roques*

Département de Pharmacochimie Moléculaire et Structurale, INSERM U266, UFR des Sciences Pharmaceutiques et Biologiques, 4 avenue de l'Observatoire, 75270 Paris cedex 06, France



R = various substituents
n = 0, 1 or 2

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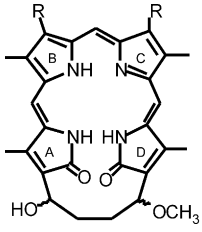
On How the Conformation of Biliverdins Influences Their Reduction to Bilirubins: A Biological and Molecular Modeling Study

María E. Mora,[a] Sara E. Bari,[b] Josefina Awruch[a] and José M. Delfino[b,*]

[a]*Departamento de Química Orgánica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, 1113 Buenos Aires, Argentina*
[b]*Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, 1113 Buenos Aires, Argentina*

Bridged biliverdin **2** is excreted in bile without reduction to a bilirubin. Monte Carlo and molecular dynamics simulations support the view that **2**, although very similar in overall shape to biliverdin IX α, adopts a 'locked lock washer' conformation unable to undergo fluctuations necessary to fit into the active site of biliverdin reductase.



2

R=$CH_2CH_2CO_2H$

Bioorg. Med. Chem. 11 (2003) 4673

Antisense Phosphorothioate Oligodeoxyribonucleotide Targeted against ICAM-1: Synthetic and Biological Characterization of a Process-Related Impurity Formed During Oligonucleotide Synthesis

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Isis Pharmaceuticals, Inc., 2292 Faraday Avenue, Carlsbad, CA 92008, USA

A phosphorothioate-linked oligonucleotide bearing a 3′-terminal phosphorothioate monoester has been synthesized and characterized. This oligonucleotide has been identified as a process-related impurity formed during synthesis of ISIS 2302. Biological properties of the compound have been determined. Based on these data, it can be concluded that this species (3′-TPT) has biological properties similar to parent drug.