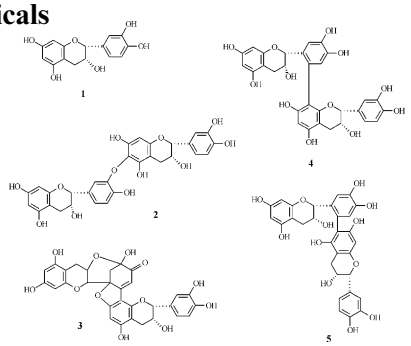
Bioorg. Med. Chem. 11 (2003) 3371

Chemical Studies of the Antioxidant Mechanism of Tea Catechins: Radical Reaction Products of Epicatechin with Peroxyl Radicals

Shengmin Sang,[a,*] Shiying Tian,[b] Hsin Wang,[b] Ruth E. Stark,[b] Robert T. Rosen,[a] Chung S. Yang[c] and Chi-Tang Ho[a]

[a]*Department of Food Science and Center for Advanced Food Technology, Rutgers University, 65 Dudley Road, New Brunswick, NJ 08901-8520, USA*
[b]*Department of Chemistry, CUNY Graduate Center and College of Staten Island, Staten Island, NY 10314-6600, USA*
[c]*Department of Chemical Biology, Ernest Mario School of Pharmacy, Rutgers University, 164 Frelinghuysen Road, Piscataway, NJ 08854-8020, USA*

Eight major reaction products (**2**–**9**) were isolated and identified from the oxidation reaction between Epicatechin (**1**) and peroxyl radicals generated by thermolysis of the azo initiator azo-bis-isobutyrylnitrile (AIBN). Their structures were determined on the basis of detailed high-field 1D and 2D NMR spectral analysis. The identification of these compounds confirmed that the B-ring is the initial site for formation of all these reaction products in the peroxyl radical oxidant system.

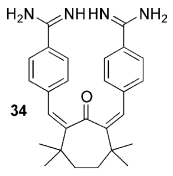


Bioorg. Med. Chem. 11 (2003) 3379

Design and Synthesis of Highly Constrained Factor Xa Inhibitors: Amidine-Substituted Bis(benzoyl)-[1,3]-diazepan-2-ones and Bis(benzylidene)-bis(*gem*-dimethyl)cycloketones

Jian Cui,[a,b] David Crich,[b] Donald Wink,[b] Matthew Lam,[c] Arnold L. Rheingold,[c] David A. Case,[d] WenTao Fu,[a] Yasheen Zhou,[a] Mohan Rao,[d] Arthur J. Olson[d] and Michael E. Johnson[a,*]

[a]*Center for Pharmaceutical Biotechnology, University of Illinois at Chicago, 900 S. Ashland Avenue, M/C 870, Chicago, IL 60607-7173, USA*
[b]*Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL 60607, USA*
[c]*Department of Chemistry, University of Delaware, Newark, DE 19716, USA*
[d]*Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA 92037, USA*



Compound **34** exhibited ~40 nN activity against Factor Xa, and good selectivity against thrombin, trypsin and plasmin.

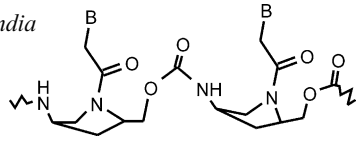
Bioorg. Med. Chem. 11 (2003) 3393

Pyrrolidine Carbamate Nucleic Acids: Synthesis and DNA Binding Studies

Meena and Vaijayanti A. Kumar*

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411008, India

Synthesis, characterization and DNA binding studies of chiral Carbamate-PNA analogue with conformation of constrained flexibility.

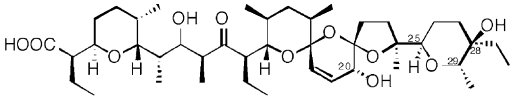


Bioorg. Med. Chem. 11 (2003) 3401

Cloning of Modular Type I Polyketide Synthase Genes from Salinomycin Producing Strain of *Streptomyces albus*

Miho Izumikawa,[a] Michio Murata,[b] Kazuo Tachibana,[a] Yutaka Ebizuka[c] and Isao Fujii[c,*]

[a]*Department of Chemistry, School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan*
[b]*Department of Chemistry, Graduate School of Science, Osaka University, 1-16 Machikaneyama, Toyonaka, Osaka 560-0043, Japan*
[c]*Graduate School of Pharmaceutical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan*

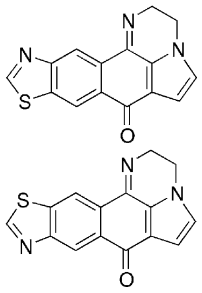


Bioorg. Med. Chem. 11 (2003) 3407

Synthesis and Antiprotozoal Evaluation of Benzothiazolopyrroloquinoxalinones, Analogues of Kuanoniamine A

Ricardo A. Tapia,[a,*] Yolanda Prieto,[a] Félix Pautet,[b] Nadia Walchshofer,[b] Houda Fillion,[b,*] Bernard Fenet[c] and Marie-Elizabeth Sarciron[d]

[a]*Facultad de Química, Pontificia Universidad Católica de Chile, Correo 22, Santiago, Chile*
[b]*Laboratoire de Chimie Organique, EA 635, Faculté de Pharmacie, Université Claude Bernard Lyon 1, 8 Avenue Rockefeller, F-69373 Lyon Cedex 08, France*
[c]*Centre de RMN, Université Claude Bernard Lyon 1, 69622 Villeurbanne Cedex, France*
[d]*Laboratoire de Parasitologie EA 1887, Faculté de Pharmacie, Université Claude Bernard Lyon 1, 8 Avenue Rockefeller, F-69373 Lyon Cedex 08, France*



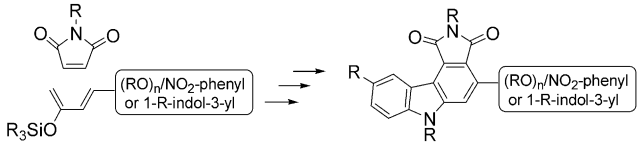
Quinoeimines analogues of Kuanoniamine A were prepared and evaluated for their antiprotozoal properties.

Bioorg. Med. Chem. 11 (2003) 3413

Synthesis and Cytotoxic Activity of Different Open Indolocarbazole Alkaloid Analogues

Esther Caballero,[a,*] Marta Adeva,[a] Suzanne Calderón,[a] Heidi Sahagún,[a] Fernando Tomé,[a] Manuel Medarde,[a] José Luis Fernández,[b] Miguel López-Lázaro[c] and Maria Jesús Ayuso[c]

[a]*Laboratorio de Química Orgánica y Farmacéutica, Facultad de Farmacia, 37007 Salamanca, Spain*
[b]*Instituto Biomar SA. 24231 Onzonilla, León, Spain*
[c]*Departamento de Farmacología, Facultad de Farmacia, Sevilla, Spain*

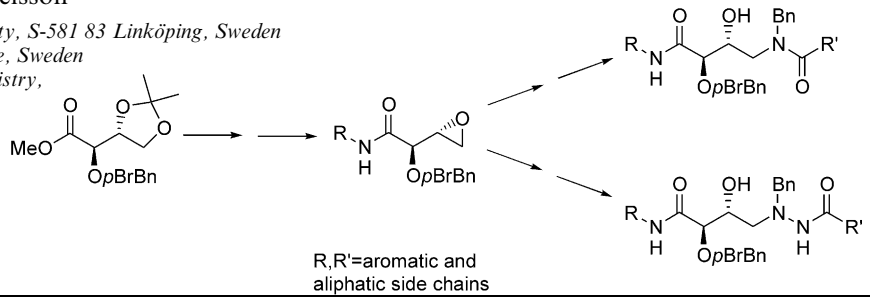


Bioorg. Med. Chem. 11 (2003) 3423

New Inhibitors of the Malaria Aspartyl Proteases Plasmepsin I and II

Anders Dahlgren,[a] Ingemar Kvarnström,[a] Lotta Vrang,[b] Elizabeth Hamelink,[b] Anders Hallberg,[c] Åsa Rosenquist[a,b,*] and Bertil Samuelsson[b,d,*]

[a]*Department of Chemistry, Linköping University, S-581 83 Linköping, Sweden*
[b]*Medivir AB, Lunastigen 7, S-141 44 Huddinge, Sweden*
[c]*Department of Organic Pharmaceutical Chemistry, BMC, Uppsala University, Box 596, S-751 24 Uppsala, Sweden*
[d]*Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden*



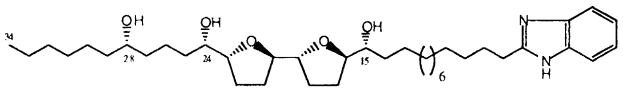
Bioorg. Med. Chem. 11 (2003) 3439

Semisynthesis of Heterocyclic Analogues of Squamocin, a Cytotoxic Annonaceous Acetogenin, by an Unusual Oxidative Decarboxylation Reaction

R. Duval, G. Lewin* and R. Hocquemiller

Laboratoire de Pharmacognosie (BioCis, UMR 8076 CNRS), Faculté de Pharmacie, rue J. B. Clément, 92296 Châtenay-Malabry Cedex, France

Two couples of heterocyclic analogues of squamocin have been semisynthetised from derived α-ketoesters and 1,2-diamines, trough classical condensation reactions or via an unusual condensation-oxydative decarboxylation process. In particular, benzimidazole analogue **I** exhibited potent though significantly reduced cytotoxicity relatively to squamocin.



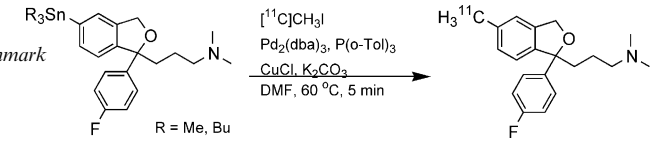
I

Bioorg. Med. Chem. 11 (2003) 3447

Synthesis and Biological Evaluation of Novel Carbon-11-Labelled Analogues of Citalopram as Potential Radioligands for the Serotonin Transporter

Jacob Madsen,[a,*] Pinelopi Merachtsaki,[b,c] Padideh Davoodpour,[d] Mats Bergström,[d] Bengt Långström,[d] Kim Andersen,[e] Christian Thomsen,[f] Lars Martiny[g] and Gitte M. Knudsen[h]

[a]*PET & Cyclotron Unit 3982, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark*
[b]*Department of Pharmaceutical Biosciences, Uppsala University, SE-751 24 Uppsala, Sweden*
[c]*Hospital Pharmacy, University Hospital, Uppsala University, SE-751 85 Uppsala, Sweden*
[d]*Uppsala Research Imaging Solutions AB, UAS, SE-751 85 Uppsala, Sweden*
[e]*Medicinal Chemistry Research, H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark*
[f]*Molecular Pharmacology, H. Lundbeck A/S, Ottiliavej 9, 2500 Valby, Denmark*
[g]*Isotope Chemistry, Novo Nordisk, 2760 Måløv, Denmark*
[h]*Neurobiology Research Unit 9201, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark*



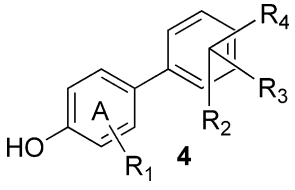
Bioorg. Med. Chem. 11 (2003) 3457

ER_β Ligands. Part 1: The Discovery of ER_β Selective Ligands which Embrace the 4-Hydroxy-biphenyl Template

Richard J. Edsall, Jr.,[a] Heather A. Harris,[b] Eric S. Manas[a] and Richard E. Mewshaw[a,*]

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

A systematic structure–activity relationship study within a series of 4-OH-biphenyls (**4**) revealed compounds with ERβ selectivity on the order of 20–70-fold.



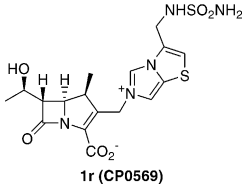
Bioorg. Med. Chem. 11 (2003) 3475

CP0569, A New Broad-Spectrum Injectable Carbapenem. Part 1: Synthesis and Structure–Activity Relationships

Kazuhiro Aihara,* Yuko Kano, Sohjiro Shiokawa, Toshiro Sasaki, Fumihito Setsu, Yumiko Sambongi, Miyuki Ishii, Kazuyo Tohyama, Takashi Ida, Atsushi Tamura, Kunio Atsumi and Katsuyoshi Iwamatsu

Pharmaceutical Research Center, Meiji Seika Kaisha, Ltd., 760 Morooka-cho, Kohoku-ku, Yokohama 222-8567, Japan

Compared with currently available β-lactams, CP0569 (**1r**) has stronger anti-MRSA and similar activity against Gram-negative bacteria, including *Pseudomonas aeruginosa*. Furthermore, CP0569 (**1r**) is less susceptible to porcine or mouse renal DHP-1 than clinically used injectable carbapenems, that is IPM, PAPM, and MEPM.



1r (CP0569)

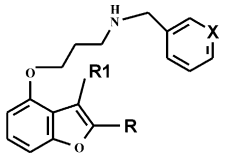
Bioorg. Med. Chem. 11 (2003) 3487

3D-QSAR of *N*-Myristoyltransferase Inhibiting Antifungal Agents by CoMFA and CoMSIA Methods

P. Purushottamachar and Vithal M. Kulkarni*

Pharmaceutical Division, Institute of Chemical Technology, University of Mumbai, Matunga, Mumbai 400019, India

A 3D-QSAR study using CoMFA and CoMSIA was performed on a series of benzofuran antifungals. The results indicated the importance of steric, electrostatic, hydrogen bond donor and acceptor fields for antifungal activity.



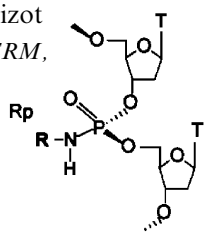
Bioorg. Med. Chem. 11 (2003) 3499

Synthesis and Properties of Oligo-2′-deoxyribonucleotides Containing Internucleotidic Phosphoramidate Linkages Modified with Pendant Groups Ending with either Two Amino Or Two Hydroxyl Functions

Ulysse Asseline,* Marcel Chassignol, Jolanta Draus, Maurice Durand and Jean-Claude Maurizot

Centre de Biophysique Moléculaire, CNRS UPR 4301, affiliated with the University of Orléans and with INSERM, Rue Charles Sadron, 45071 Orléans Cedex 02, France

We report single and multiple incorporations of phosphoramidate linkages, modified with pendant groups (R) ending with either two amino or two hydroxyl functions, into triple helix forming oligonucleotides. Only the modified phosphate groups with the R_P configuration are stabilizing the triplexes. The strongest stabilization is obtained with the aminated compounds.



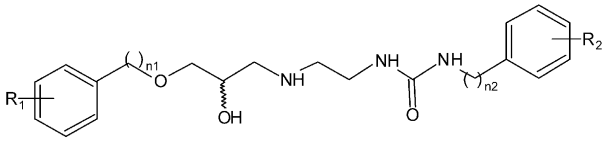
Bioorg. Med. Chem. 11 (2003) 3513

Design of New β_1-Selective Adrenoceptor Ligands as Potential Radioligands for In Vivo Imaging

Klaus Kopka,[a,*] Stefan Wagner,[a] Burkhard Riemann,[a,b] Marilyn P. Law,[a] Carsten Puke,[a] Sajinder K. Luthra,[c] Victor W. Pike,[d] Thomas Wichter,[e] Wilhelm Schmitz,[b] Otmar Schober[a] and Michael Schäfers[a]

[a]*Department of Nuclear Medicine, Albert-Schweitzer-Str. 33, University Hospital Münster, 48149 Münster, Germany;* [b]*Institute of Pharmacology and Toxicology, Domagkstr. 12, University Hospital Münster, 48149 Münster, Germany;* [c]*Imaging Research Solutions Limited, Cyclotron Building, Hammersmith Hospital, Du Cane Road, London W12 ONN, UK;* [d]*Molecular Imaging Branch, National Institute of Mental Health, National Institutes of Health, 10 Center Drive, Rm B3C346A, MSC 1003, Bethesda, MD 20892-1003, USA;* [e]*Department of Cardiology and Angiology, Albert-Schweitzer Str. 33, University Hospital Münster, 48149 Münster, Germany*

A series of new 3-aryloxy-2-propanolamines and chain-elongated derivatives were synthesized and tested as potential β_1-selective adrenoceptor ligands. Nine of these compounds showed an improved β_1-selectivity and affinity compared to the known β_1-selective adrenoceptor antagonist, ICI 89,406 **8i** (R_1 = 2-CN, n1 = n2 = 0, R_2 = H). Most of these ligands can serve as precursors or reference counterparts of potential radioligands for the non-invasive in vivo imaging of β_1-adrenoceptor density in the human heart using SPECT or PET relevant for patients suffering from cardiac diseases like heart failure and ventricular arrhythmias.

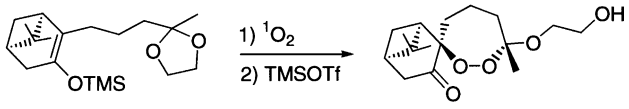


Bioorg. Med. Chem. 11 (2003) 3529

Synthesis and Antioxidant Activity Evaluation of Novel Antiparkinsonian Agents, Aminoadamantane Derivatives of Nitroxyl Free Radical

Janusz Skolimowski,[a] Agata Kochman,[b] Lidia Gębicka[c] and Diana Metodiewa[c,*]

[a]*Department of Organic Chemistry, University of Łódź, Narutowicza 68, 90-136 Łódź, Poland*
[b]*Department of Pathological Anatomy, Medical University of Wrocław, Marcinkowskiego 1, 50-368 Wrocław, Poland*
[c]*Institute of Applied Radiation Chemistry, Technical University of Łódź, Wróblewskiego 15, 93-590 Łódź, Poland*



Bioorg. Med. Chem. 11 (2003) 3541

Synthesis and Structure–Activity Relationships of a New Set of 1,2,4-Triazolo[4,3-*a*]quinoxalin-1-one Derivatives as Adenosine Receptor Antagonists

Vittoria Colotta,[a,*] Daniela Catarzi,[a] Flavia Varano,[a] Guido Filacchioni,[a] Claudia Martini,[b] Letizia Trincavelli[b] and Antonio Lucacchini[b]

[a]*Dipartimento di Scienze Farmaceutiche, Universita' di Firenze, Via G. Capponi, 9, 50121 Florence, Italy*
[b]*Dipartimento di Psichiatria, Neurobiologia, Farmacologia e Biotecnologie, Via Bonanno, 6, 50126 Pisa, Italy*

The synthesis and A_1, A_{2A} and A_3 adenosine receptor binding activity of some 2-phenyl-1,2,4-triazolo[4,3-*a*]quinoxalin-1,4-diones (series **A**) and 4-amino-1-ones (series **B**), bearing simple substituents at different positions of the benzofused moiety, are reported.