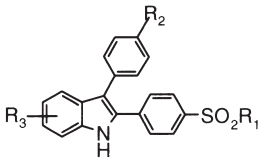
Bioorg. Med. Chem. 11 (2003) 1153

Synthesis and Biological Evaluation of Substituted 2-Sulfonyl-phenyl-3-phenyl-indoles: A New Series of Selective COX-2 Inhibitors

Wenhui Hu,[a] Zongru Guo,[a,*] Fengming Chu,[a] Aiping Bai,[a] Xiang Yi,[a] Guifang Cheng[b] and Jing Li[b]

[a]*Department of Synthetic Medicinal Chemistry, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China*
[b]*Department of Pharmacology, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China*



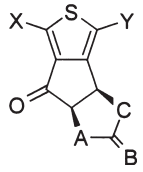
Bioorg. Med. Chem. 11 (2003) 1161

Synthesis and Biological Evaluation of Five-Membered Heterocycles Fused to Cyclopenta[*c*]thiophene as New Antitumor Agents

Patrick Dallemagne,* Lan Pham Khanh, Abdellah Alsaïdi, Isabelle Varlet, Valérie Collot, Magalie Paillet, Ronan Bureau and Sylvain Rault

Centre d'Etudes et de Recherche sur le Médicament de Normandie, U.F.R. des Sciences Pharmaceutiques, Université de Caen, 1, rue Vaubénard 14032 Caen cedex, France

A series of new compounds issued from the fusion of various heterocycles to cyclopenta[*c*]thiophene were synthesized and evaluated for antitumor interest. Some oxazolidinone derivatives displayed in vitro and in vivo antitumor activity.

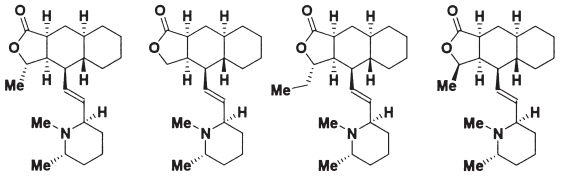


Bioorg. Med. Chem. 11 (2003) 1169

Synthetic Studies on Himbacine, a Potent Antagonist of the Muscarinic M_2 Subtype Receptor. Part 2: Synthesis and Muscarinic M_2 Subtype Antagonistic Activity of the Novel Himbacine Congeners Modified at the C-3 Position of Lactone Moiety

Masanori Takadoi,[a,*] Kentaro Yamaguchi[b] and Shiro Terashima[c]

[a]*Discovery Research Laboratories, Kyorin Pharmaceutical Co. Ltd., 2399-1 Nogi, Nogi-machi, Tochigi 329-0114, Japan*
[b]*Chemical Analysis Center, Chiba University, 1-33 Yayoicho, Inage-ku, Chiba 263-8522, Japan*
[c]*Sagami Chemical Research Center, 2743-1 Hayakawa, Ayase, Kanagawa 252-1193, Japan*



himbacine **1** 3-demethylhimbacine **2** (*ent*-**2**) 4-*epi*-3-demethylhimbacine 4-*epi*-**2** (*ent*-4-*epi*-**2**) 11-methylhimbacine **3** 3-*epi*-himbacine **4**

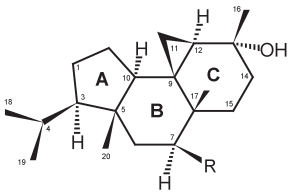
Bioorg. Med. Chem. 11 (2003) 1187

Pharmaco-toxicological Study of Diterpenoids

Carla Delporte,[a,*] Nadine Backhouse,[a] Pedro Salinas,[a] Aurelio San-Martín,[b] Jorge Bórquez[b] and Alberto Loyola[c]

[a]*Departamento de Química Farmacológica y Toxicológica, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile, Casilla 233, 1-Santiago, Chile*
[b]*Departamento de Química, Facultad de Ciencias, Universidad de Chile, Chile*
[c]*Departamento de Química, Facultad de Ciencias Básicas, Universidad de Antofagasta, Antofagasta, Chile*

Azorellanol, 13-hydroxy-7-oxoazorellane and 7-deacetylazorellanol, three diterpenoids previously isolated only from *Azorella compacta*, *Azorella yareta* and *Laretia acaulis*, Apiaceae, were subjected to in vivo farmaco-toxicological evaluation. 13-hydroxy-7-oxoazorellane (**3**) was the most potent analgesic but it was less effective than sodium naproxen, the reference drug. Azorellanol (**1**) exhibited the highest topical antiinflammatory potency on arachidonic acid and 12-deoxyphorbol 13-tetradecanoate induced oedema, and it effect was similar to the reference drugs (nimesulide and indomethacin respectively). Its mechanism of action could be explained through the inhibition to cyclo-oxygenase activity. Our results corroborate the antiinflammatory and analgesic effects of these species, and it justifies their use in folk medicine.



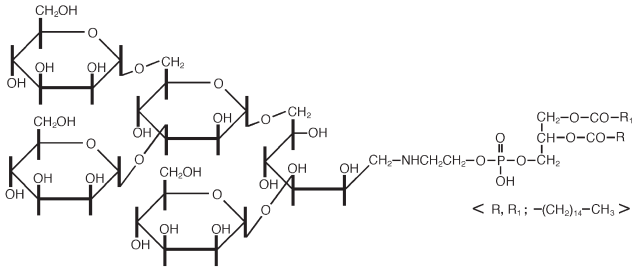
R	
1	OAc
2	OH
3	=O

Bioorg. Med. Chem. 11 (2003) 1191

Protection against *Leishmania major* Infection by Oligomannose-Coated Liposomes

Yoshitaka Shimizu,[a] Kazuo Yamakami,[b] Takao Gomi,[a] Munehiro Nakata,[a] Hideki Asanuma,[a] Takushi Tadakuma[c] and Naoya Kojima[a,*]

[a]*The Institute of Glycotechnology and the Department of Applied Biochemistry, Tokai University, Hiratsuka, Kanagawa 259-1292, Japan*
[b]*Department of Public Health, National Defense Medical College, Tokorozawa, Saitama 359-5813, Japan*
[c]*Department of Parasitology and Immunology, National Defense Medical College, Tokorozawa, Saitama 359-5813, Japan*



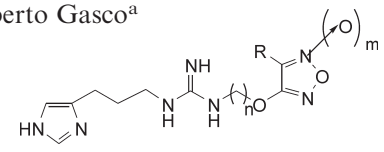
Man5-DPPE

Bioorg. Med. Chem. 11 (2003) 1197

[3-(1*H*-Imidazol-4-yl)propyl]guanidines Containing Furoxan Moieties: A New Class of H_3-Antagonists Endowed with NO-Donor Properties

Massimo Bertinaria,[a] Antonella Di Stilo,[a] Paolo Tosco,[a] Giovanni Sorba,[b] Enzo Poli,[c] Cristina Pozzoli,[c] Gabriella Coruzzi,[c] Roberta Fruttero[a,*] and Alberto Gasco[a]

[a]*Dipartimento di Scienza e Tecnologia del Farmaco, Università degli Studi di Torino, Via Pietro Giuria 9, I-10125 Turin, Italy*
[b]*Dipartimento di Scienze Chimiche, Alimentari, Farmaceutiche e Farmacologiche, Università degli Studi del Piemonte Orientale, Viale Ferrucci 33, I-28100 Novara, Italy*
[c]*University of Parma, School of Medicine, Dipartimento di Anatomia Umana, Farmacologia e Scienze Medico-Forensi, via Volturno 39, I-43100 Parma, Italy*



n = 2, 3
m = 0, 1
R = Ph, SO_2Ph

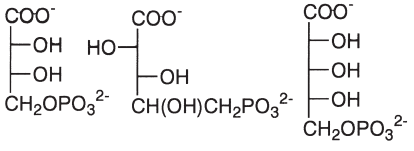
Bioorg. Med. Chem. 11 (2003) 1207

Sugar Derivatives as New 6-Phosphogluconate Dehydrogenase Inhibitors Selective for the Parasite *Trypanosoma brucei*

Claudia Pasti,[a] Eliana Rinaldi,[a] Carlo Cervellati,[a] Franco Dallocchio,[a] Renaud Hardré,[b] Laurent Salmon[b] and Stefania Hanau[a,*]

[a]*Dipartimento di Biochimica e Biologia Molecolare, Università di Ferrara, Via L. Borsari 46, 44100, Ferrara, Italy*
[b]*Laboratoire de Chimie Bioorganique et Bioinorganique, CNRS-FRE 2127, ICMMO, Bât. 420, Université Paris-XI, 91405 Orsay, France*

A number of 4-carbon and 5-carbon aldonates, acyl derivatives, and phosphonate analogues are strong inhibitors of the *Trypanosoma brucei* 6PGDH with a good selectivity for the parasite enzyme over the sheep liver counterpart.



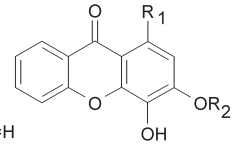
Bioorg. Med. Chem. 11 (2003) 1215

Inhibition of Protein Kinase C by Synthetic Xanthone Derivatives

Lucília Saraiva,[a,b] Paula Fresco,[a] Eugénia Pinto,[b] Emília Sousa,[c] Madalena Pinto[c] and Jorge Gonçalves[a,*]

[a]*Serviço de Farmacologia, CEQOFFUP, Faculdade de Farmácia, Universidade do Porto, rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*
[b]*Serviço de Microbiologia, CEQOFFUP, Faculdade de Farmácia, Universidade do Porto, rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*
[c]*Serviço de Química Orgânica, CEQOFFUP, Faculdade de Farmácia, Universidade do Porto, rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*

The modulatory activity of two xanthones (**1** and **2**) on isoforms α, βI, δ, η and ζ of protein kinase C (PKC) was evaluated using an in vivo yeast phenotypic assay. Both xanthones caused an eect compatible with PKC inhibition, similar to that elicited by known PKC inhibitors. PKC inhibition caused by these xanthones was confirmed using an in vitro kinase assay. The present results suggest that xanthone derivatives can be explored to develop new PKC isoform-selective inhibitors.



1 R1=R2=H
2 R1=CHO R2=Me

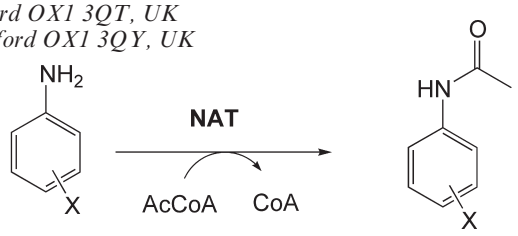
Bioorg. Med. Chem. 11 (2003) 1227

An Approach to Identifying Novel Substrates of Bacterial Arylamine *N*-Acetyltransferases

Edward W. Brooke,[a] Stephen G. Davies,[b,*] Andrew W. Mulvaney,[b] Frédérique Pompeo,[a] Edith Sim[a] and Richard J. Vickers[b]

[a]*Department of Pharmacology, University of Oxford, Mansfield Road, Oxford OX1 3QT, UK*
[b]*The Dyson Perrins Laboratory, University of Oxford, South Parks Rd, Oxford OX1 3QY, UK*

A novel assay to determine the activity of arylamine *N*-acetyltransferases (NATs) has been used to determine the substrate specificity of two recombinant prokaryotic NATs. A link between the lipophilicity of the substrate and the acetylation activity has been observed. This SAR has been related to in silico docking studies and key lipophilic substrate binding residues have been identified.

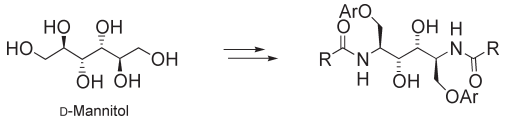


Bioorg. Med. Chem. 11 (2003) 1235

New Potent C_2-Symmetric Malaria Plasmepsin I and II Inhibitors

Karin Oscarsson,[a] Stefan Oscarson,[a] Lotta Vrang,[b] Elizabeth Hamelink,[b] Anders Hallberg[c] and Bertil Samuelsson[a,b,*]

[a]*Department of Organic Chemistry, Arrhenius Laboratory, Floor 6, Stockholm University, S-106 91 Stockholm, Sweden*
[b]*Medivir AB, Lunastigen 7, S-141 44 Huddinge, Sweden*
[c]*Department of Organic Pharmacutical Chemistry, BMC, Uppsala University, Box 574, S-751 23 Uppsala, Sweden*

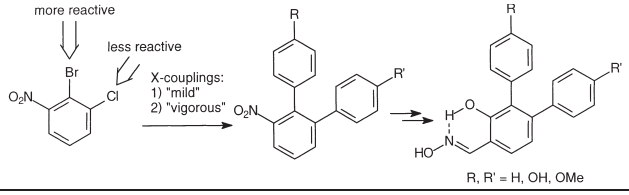


Bioorg. Med. Chem. 11 (2003) 1247

Synthesis, Binding Affinity, and Transcriptional Activity of Hydroxy- and Methoxy-Substituted 3,4-Diarylsalicylaldoximes on Estrogen Receptors α and β

Filippo Minutolo,[a] Michela Antonello,[a] Simone Bertini,[a] Simona Rapposelli,[a] Armando Rossello,[a] Shubin Sheng,[b] Kathryn E. Carlson,[c] John A. Katzenellenbogen[c] and Marco Macchia[a,*]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Pisa, Via Bonanno 6, 56126 Pisa, Italy*
[b]*Department of Molecular and Integrative Physiology University of Illinois, 407 S. Goodwin Avenue, Urbana, IL 61801, USA*
[c]*Department of Chemistry, University of Illinois, 600 S. Mathews Avenue, Urbana, IL 61801, USA*



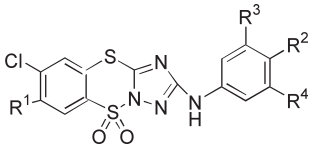
Bioorg. Med. Chem. 11 (2003) 1259

Synthesis and Anticancer Activity of 2-Amino-8-chloro-5,5-dioxo[1,2,4]triazolo[2,3-*b*][1,4,2]benzodithiazine Derivatives

Elżbieta Pomarnacka[a,*] and Maria Gdaniec[b]

[a]*Department of Chemical Technology of Drugs, Medical University of Gdańsk, 107 Gen.J.Hallera Str., 80-416 Gdańsk, Poland*
[b]*Faculty of Chemistry, A. Mickiewicz University, 60-780 Poznań, Poland*

The title compounds **17**–**29** were synthesized and evaluated for inhibitory activity against 59 human cancer cells.The compound **17** (R^1 = CN, R^2 = R^3 = R^4 = H) showed significant activity against the leukemia SR cell line (log GI_{50} = −7.67).

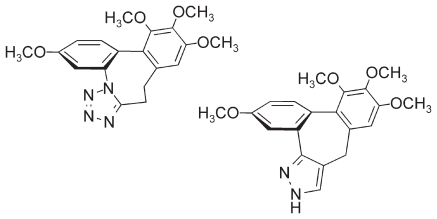


Bioorg. Med. Chem. 11 (2003) 1269

Novel B-Ring Modified Allocolchicinoids of the NCME Series: Design, Synthesis, Antimicrotubule Activity and Cytotoxicity

Silke Bergemann,[c] René Brecht,[a] Frank Büttner,[a] Daniel Guénard,[b] Ronald Gust,[c] Gunther Seitz,[a,*] Milton T. Stubbs[a] and Sylviane Thoret[b]

[a]*Pharmazeutisch-Chemisches Institut der Philipps-Universität, Marbacher Weg 6, D-35032 Marburg, Germany*
[b]*Institut de Chimie des Substances Naturelles, Centre National de la Recherche Scientifique, Avenue de la Terrasse, 91198 Gif-Sur-Yvette Cedex, France*
[c]*Institut für Pharmazie I der Freien Universität Berlin, Königin-Luise-Str. 2 u. 4, D-14195 Berlin, Germany*



Two series of NCME-type allocolchicinoids were synthesized and evaluated for their antimicrotubule and antiproliferative activity.

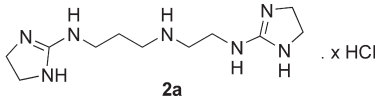
Bioorg. Med. Chem. 11 (2003) 1283

Synthesis and Analgesic Activity of a Series of New Azaalkane Bis-guanidinium and Bis(2-aminoimidazolinium) Compounds

Christophe Dardonville,[a,*] Isabel Rozas,[b] Pilar Goya,[a] Rocío Girón,[c] Carlos Goicoechea[c] and M[a] Isabel Martín[c]

[a]*Instituto de Química Médica (CSIC), Juan de la Cierva 3, 28006-Madrid, Spain*
[b]*Department of Chemistry, Trinity College Dublin, Dublin 2, Ireland*
[c]*Unidad de Farmacología, Facultad de Ciencias de la Salud, Universidad Rey Juan Carlos, 28922-Alcorcón, Madrid, Spain*

The synthesis and antinociceptive activity of a series of new azaalkane bis(2-aminoimidazolinium) compounds from which, *N*,*N*′-di(4,5-dihydro-1*H*-imidazol-2-yl)-3-aza-1,6-hexanediamine **2a** has shown the best analgesic properties in vivo in two different assays (i.e., acetic acid-induced writhing test and hot-plate test in mice), as well as oral bioavailability is reported.



2a

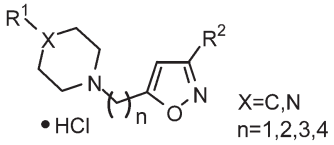
Bioorg. Med. Chem. 11 (2003) 1293

QSAR Studies on Piperazinylalkylisoxazole Analogues Selectively Acting on Dopamine D_3 Receptor by HQSAR and CoMFA

Mi Young Cha, In Young Lee, Joo Hwan Cha, Kyung Il Choi, Yong Seo Cho, Hun Yeong Koh and Ae Nim Pae*

Biochemicals Research Center, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul, 130-650, South Korea

QSAR studies for piperazinylalkylisoxazole analogues were conducted by hologram QSAR (HQSAR) and comparative molecular field analysis (CoMFA) to explain the binding affinities of 264 ligands acting on dopamine D_3 receptor.

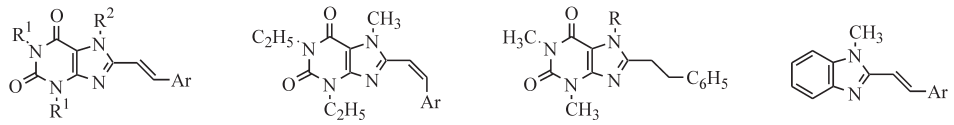


Bioorg. Med. Chem. 11 (2003) 1299

Inhibition of Monoamine Oxidase B by Selective Adenosine A_{2A} Receptor Antagonists

Jacobus P. Petzer,[a] Salome Steyn,[a] Kay P. Castagnoli,[a] Jiang-Fan Chen,[b] Michael A. Schwarzschild,[b] Cornelis J. Van der Schyf[a] and Neal Castagnoli[a,*]

[a]*Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, USA*
[b]*Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02129, USA*

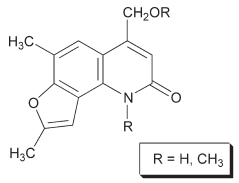


Bioorg. Med. Chem. 11 (2003) 1311

4-Hydroxymethyl- and 4-Methoxymethylfuro[2,3-*h*]quinolin-2(1*H*)-ones: Synthesis and Biological Properties

Adriana Chilin,* Cristina Marzano, Francarosa Baccichetti, Morena Simonato and Adriano Guiotto

Department of Pharmaceutical Sciences, University of Padova, Via Francesco Marzolo 5, I-35131 Padova, Italy

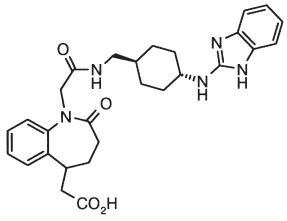


Bioorg. Med. Chem. 11 (2003) 1319

Design and Synthesis of 1,5- and 2,5-Substituted Tetrahydrobenzazepinones as Novel Potent and Selective Integrin $\alpha_V\beta_3$ Antagonists

Andreas Kling,[a,*] Gisela Backfisch,[b] Jürgen Delzer,[b] Hervé Geneste,[a] Claudia Graef,[c] Wilfried Hornberger,[a] Udo E. W. Lange,[c] Arnulf Lauterbach,[c] Werner Seitz[c] and Thomas Subkowski[c]

[a]*Neuroscience, Medicinal Chemistry, Abbott GmbH and Co KG, Discovery Research, D-67008 Ludwigshafen, PO Box 210805, Germany*
[b]*Abbott GmbH and Co KG, Pharmaceutical Development, D-67008 Ludwigshafen, Germany*
[c]*BASF AG, Main Research Laboratory, D-67056 Ludwigshafen, Germany*

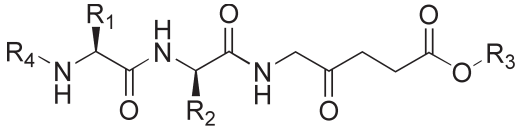


Bioorg. Med. Chem. 11 (2003) 1343

Evaluation of Dipeptide-Derivatives of 5-Aminolevulinic Acid as Precursors for Photosensitizers in Photodynamic Therapy

Yann Berger,[a] Laurent Ingrassia,[a] Reinhard Neier[a] and Lucienne Juillerat-Jeanneret[b,*]

[a]*Institute of Chemistry, Neuchâtel University, avenue de Bellevaux, PO Box 2, CH-2007 Neuchâtel, Switzerland*
[b]*University Institute of Pathology, CHUV, Bugnon 25, CH-1011 Lausanne, Switzerland*



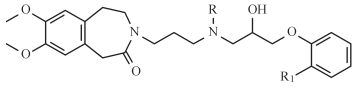
Bioorg. Med. Chem. 11 (2003) 1353

Cardiovascular Hybrid Drugs: New Benzazepinone Derivatives as Bradycardic Agents Endowed with Selective β_1-non-competitive Antagonism

Alessandra Bisi,[a,*] Angela Rampa,[a] Roberta Budriesi,[a] Silvia Gobbi,[a] Federica Belluti,[a] Pierfranco Ioan,[a] Ermanno Valoti,[b] Alberto Chiarini[a] and Piero Valenti[a]

[a]*Department of Pharmaceutical Sciences, University of Bologna, via Belmeloro 6, 40126 Bologna, Italy*
[b]*Institute of Medicinal Chemistry, University of Milano, viale Abruzzi 42, 20131 Milano, Italy*

The synthesis and pharmacological profile of some hybrid compounds bearing both a benzazepinone moiety and typical β-blocker aryloxypropanolamine groups are described.

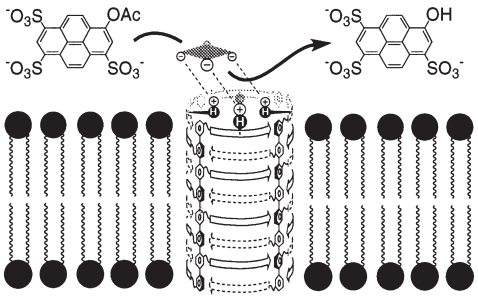


Bioorg. Med. Chem. 11 (2003) 1363

Complementary Characteristics of Homologous *p*-Octiphenyl β-Barrels with Ion Channel and Esterase Activity

Abhigyan Som, Naomi Sakai and Stefan Matile*

Department of Organic Chemistry, University of Geneva, CH-1211 Geneva 4, Switzerland



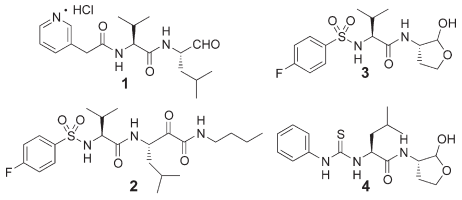
Bioorg. Med. Chem. 11 (2003) 1371

Exploration of Cornea Permeable Calpain Inhibitors as Anticataract Agents

Masayuki Nakamura,* Masazumi Yamaguchi, Osamu Sakai and Jun Inoue

Research Laboratory, Senju Pharmaceutical Co., Ltd., 1-5-4 Murotani Nishiku Kobe 651-2241, Japan

To explore cornea permeable calpain inhibitors, four compounds displaying different characteristics were designed and synthesized.



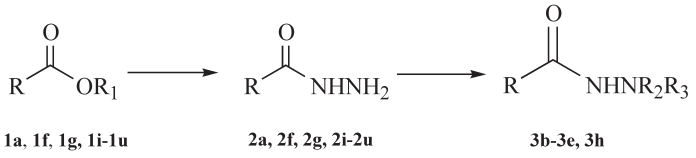
Bioorg. Med. Chem. 11 (2003) 1381

Synthesis and In Vitro Leishmanicidal Activity of Some Hydrazides and Their Analogues

Khalid Mohammad Khan,* Maimona Rasheed, Zia-Ullah, Safdar Hayat, Farhana Kaukab, M. Iqbal Choudhary, Atta-ur-Rahman and Shahnaz Perveen

International Center for Chemical Sciences, HEJ Research Institute of Chemistry, University of Karachi, Karachi-75270, Pakistan

Twenty-one hydrazides were synthesized by treating different esters with hydrazine hydrate. Some of these compounds exhibit potential in vitro leishmanicidal activity.

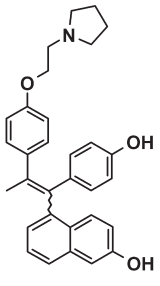


Bioorg. Med. Chem. 11 (2003) 1389

De Novo Design, Synthesis and Evaluation of a Non-Steroidal Diphenylnaphthyl Propylene Ligand for the Estrogen Receptor

Jonathan M. Schmidt,[a] Julie Mercure,[a] Gilles B. Tremblay,[b] Martine Pagé,[b] Miklos Feher,[a] Robert Dunn-Dufault,[a] Markus G. Peter[a] and Peter R. Redden[a,*]

[a]*SignalGene Inc., 335 Laird Road, Unit 2, Guelph, Ontario, Canada N1G 4P7,*
[b]*SignalGene Inc., 8475 Avenue Christophe-Colomb, bureau 1000, Montreal, Quebec, Canada H2M 2N9*

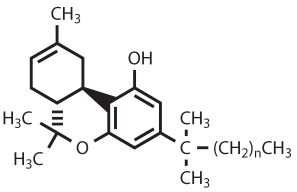


Bioorg. Med. Chem. 11 (2003) 1397

Structure–Activity Relationships for 1′,1′-dimethylalkyl-Δ^8-tetrahydrocannabinols

John W. Huffman,[a,*] John R. A. Miller,[a] John Liddle,[a] Shu Yu,[a] Brian F. Thomas,[b] Jenny L. Wiley[c] and Billy R. Martin[c]

[a]*Howard L. Hunter Laboratory, Clemson University, Clemson, SC 29634-0973, USA*
[b]*Department of Chemistry and Life Sciences, Research Triangle Institute, PO Box 12194, Research Triangle Park, NC 27709-2194, USA*
[c]*Department of Pharmacology and Toxicology, Medical College of Virginia Campus of Virginia Commonwealth University, Richmond, VA 23298-0613, USA*



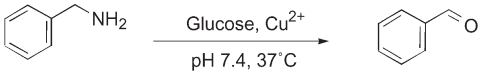
The structure–activity relationships for a series of 1′, 1′-dimethylalkyl-Δ^8-THCs ($n = 0$–10) are discussed in terms of the conformation of the side chain.

Bioorg. Med. Chem. 11 (2003) 1411

Oxidative Deamination of Benzylamine by Glycoxidation

Mitsugu Akagawa, Takeshi Sasaki and Kyozo Suyama*

Department of Applied Bioorganic Chemistry, Division of Life Science, Graduate School of Agricultural Science, Tohoku University, Sendai, 981-8555, Japan

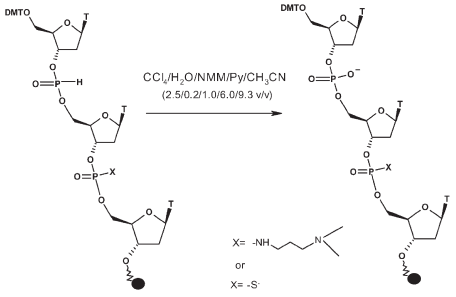


Bioorg. Med. Chem. 11 (2003) 1419

An Efficient Oxidizing Reagent for the Synthesis of Mixed Backbone Oligonucleotides via the H-Phosphonate Approach

Nikhil U. Mohe, Kamlesh J. Padiya and Manikrao M. Salunkhe*

Department of Chemistry, The Institute of Science, 15-Madam Cama Road, Mumbai-400 032, India



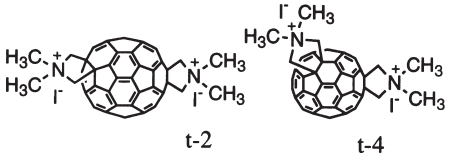
Bioorg. Med. Chem. 11 (2003) 1433

Respiratory Chain Inhibition by Fullerene Derivatives: Hydrogen Peroxide Production Caused by Fullerene Derivatives and a Respiratory Chain System

Tadahiko Mashino,[a,*] Noriko Usui,[a] Kensuke Okuda,[b] Takashi Hirota[b] and Masataka Mochizuki[a]

[a]*Kyoritsu College of Pharmacy, Shibakoen 1-5-30, Minato-ku, Tokyo 105-8512, Japan*
[b]*Faculty of Pharmaceutical Sciences, Okayama University, Tsushimanaka 1-1-1, Okayama 700-8530, Japan*

We studied the effects of fullerene derivatives, t-2 and t-4, on *Escherichia coli* growth and respiratory chain activity and found H_2O_2 production activity. We also found that a reduced form of the fullerene derivatives reacted with dioxygen.



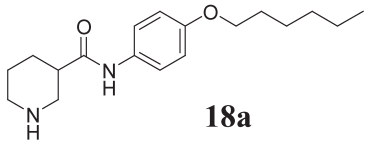
Bioorg. Med. Chem. 11 (2003) 1439

Investigation of Platelet Aggregation Inhibitory Activity by Phenyl Amides and Esters of Piperidinecarboxylic Acids

Modesto de Candia,[a] Luciana Summo,[a] Antonio Carrieri,[a] Cosimo Altomare,[a,*] Adele Nardecchia,[b] Saverio Cellamare[c] and Angelo Carotti[a]

[a]*Dipartimento Farmaco-chimico, Università degli Studi, Via Orabona 4, 70125, Bari, Italy*
[b]*Dipartimento di Medicina e Oncologia, Ospedale Policlinico, P.zza G. Cesare 1, 70125, Bari, Italy*
[c]*Dipartimento di Scienze del Farmaco, Università 'G. D'Annunzio', Via dei Vestini, 66100, Chieti, Italy*

A series of phenyl amides and esters of piperidinecarboxylic acids were synthesized. Among them, 4-hexyloxyanilide of nipecotic acid (**18a**) showed the highest inhibitory activity of the platelet aggregation in vitro, and a Hansch-type QSAR study highlighted lipophilicity and electron density of the phenyl ring as the properties which mainly increase the antiplatelet activity ($r^2 = 0.74$, $q^2 = 0.64$).



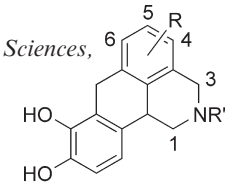
18a

Bioorg. Med. Chem. 11 (2003) 1451

Synthesis and Pharmacological Evaluation of Substituted Naphth[1,2,3-*de*]isoquinolines (Dinapsoline Analogues) as D_1 and D_2 Dopamine Receptor Ligands

Amjad M. Qandil,[a] Mechelle M. Lewis,[b] Amy Jassen,[b] Sarah K. Leonard,[b] Richard B. Mailman[b] and David E. Nichols[a,*]

[a]*Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907, USA*
[b]*Neuroscience Center, Departments of Psychiatry, Pharmacology, and Medicinal Chemistry, University of North Carolina School of Medicine, Chapel Hill, NC 27599-7160, USA*



R = 4-CH_3
R = 6-CH_3

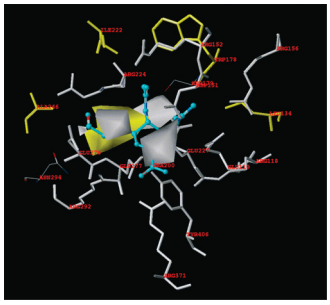
Bioorg. Med. Chem. 11 (2003) 1465

Study on Molecular Mechanism and 3D-QSAR of Influenza Neuraminidase Inhibitors

Xiang Yi, Zongru Guo* and Feng Ming Chu

Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China

The binding mode of a series of neuraminidase (NA) inhibitors with various scaffold structures were investigated by application of molecular simulation methods. A robust QSAR model was obtained using CoMSIA method. The resulting information provided a significant guide to further modification of NA inhibitors.



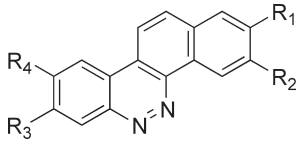
Bioorg. Med. Chem. 11 (2003) 1475

Substituted Dibenzo[*c*,*h*]cinnolines: Topoisomerase I-Targeting Anticancer Agents

Younong Yu,[a] Sudhir K. Singh,[a] Angela Liu, Tsai-Kun Li,[b] Leroy F. Liu[b,c] and Edmond J. LaVoie[a,c,*]

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

Where R_1,R_2 = OCH_3, OCH_3; and R_3, R_4 = H, H; OCH_3, OCH_3; H, OCH_3; OCH_3, H; OCH_3,Bn; OCH_3, OH. Where R_3R_4–OCH_2O–; and R_1, R_2 = OCH_3, OCH_3; OCH_3, H; H, OCH_3, H, Bn; H, OH; OCH_3, CH_2OH.



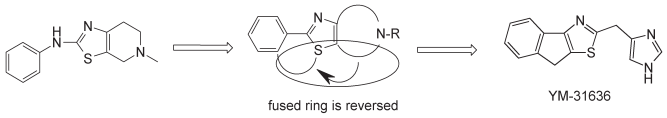
Bioorg. Med. Chem. 11 (2003) 1493

New Thiazole Derivatives as Potent and Selective 5-Hydroxytriptamine 3 (5-HT_3) Receptor Agonists for the Treatment of Constipation

Naoki Imanishi,* Kiyoshi Iwaoka, Hiroyuki Koshio, Shin-ya Nagashima, Ken-ichi Kazuta, Mitsuaki Ohta, Shuichi Sakamoto, Hiroyuki Ito, Shinobu Akuzawa, Tetsuo Kiso, Shin-ichi Tsukamoto and Toshiyasu Mase

Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., 21 Miyukigaoka, Tsukuba, Ibaraki 305-8585, Japan

YM-31636 showed high affinity and selectivity for the cloned human 5-HT_3 receptor; furthermore, it showed potent and selective 5-HT_3 receptor agonistic activity. YM-31636 was examined for its effects on defecation in animals, thus evaluating the compound as an agent against constipation.

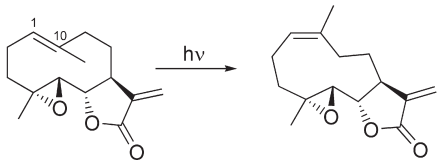


Bioorg. Med. Chem. 11 (2003) 1503

Parthenolide and Its Photochemically Synthesized 1(10)*Z* Isomer: Chemical Reactivity and Structure–Activity Relationship Studies in Human Leucocyte Chemotaxis

Hannes Neukirch,[a] Nicole C. Kaneider,[b] Christian J. Wiedermann,[b] Antonio Guerriero[a] and Michele D'Ambrosio[a,*]

[a]*Laboratorio di Chimica Bioorganica, Università degli Studi di Trento, Via Sommarive 14, 38050 Povo (Trento), Italy*
[b]*Division of General Internal Medicine, Department of Internal Medicine, University of Innsbruck, Anichstrasse 35, 6020 Innsbruck, Austria*



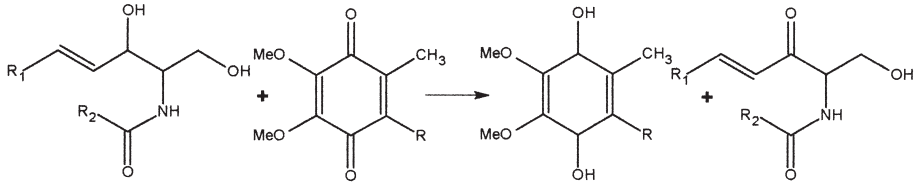
Bioorg. Med. Chem. 11 (2003) 1511

Designing Anticancer Drugs Via the Achilles Heel: Ceramide, Allylic Ketones, and Mitochondria

Norman S. Radin

Mental Health Research Institute, University of Michigan, Ann Arbor, MI, USA

This review hypothesizes that ceramide, the apoptosis-inducing sphingolipid, acts by undergoing oxidation to an allylic ketone in tumor mitochondria. The graphic suggests that the reaction occurs in complex III, with ubiquinone as the oxidant. The presence of an allylic alcohol or allylic ketone group in a drug seems to make it a good antineoplastic agent.



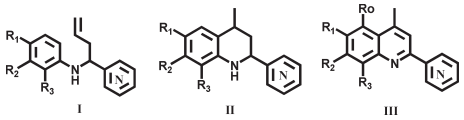
Bioorg. Med. Chem. 11 (2003) 1531

In Vitro Antifungal Activity of New Series of Homoallylamines and Related Compounds with Inhibitory Properties of the Synthesis of Fungal Cell Wall Polymers

Leonor Y. Vargas M.,[a] María V. Castelli,[b] Vladimir V. Kouznetsov,[a,*] Juan M. Urbina G.,[a] Silvia N. López,[b] Maximiliano Sortino,[b] Ricardo D. Enriz,[c] Juan C. Ribas[d] and Susana Zacchino[b,*]

[a]*Laboratory of Fine Organic Chemistry, School of Chemistry, Industrial University of Santander, A.A. 678, Bucaramanga, Colombia*
[b]*Farmacognosia, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario, Suipacha 531, (2000)-Rosario, Argentina*
[c]*Química Medicinal, Facultad de Química, Bioquímica y Farmacia, Chacabuco y Pedernera, (5700)-San Luis, Argentina*
[d]*Instituto de Microbiología Bioquímica, Campus 'Miguel de Unamuno', Edificio Departamental (37007)- Salamanca, Spain*

A new series of synthetic compounds type I–III has shown antifungal properties in cellular assays. *p*-Halogen-phenyl derivatives of structure I displayed potent activities against dermatophytes. A structure–activity relationship (SAR) supported by computational studies, aided to identify the electronic characteristics of active compounds. Regarding the mode of action, active structures inhibited (1,3)-β-glucan and mainly chitin synthases, enzymes that catalyze the synthesis of the two majors polymers of the fungal cell wall.



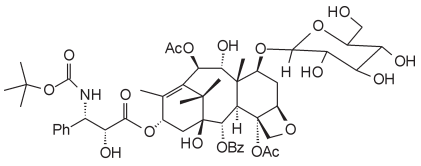
Bioorg. Med. Chem. 11 (2003) 1551

Semi-Synthesis of an *O*-Glycosylated Docetaxel Analogue

Anastasia Nikolakakis,[a] Khadidja Haidara,[a] Françoise Sauriol,[b] Orval Mamer[c] and Lolita O. Zamir[a,*]

[a]*Human Health Research Center, INRS-Institut Armand-Frappier, Université du Québec, 531 Boulevard des Prairies, Laval, Québec, Canada H7V 1B7*
[b]*Department of Chemistry, Queen's University, Kingston, Ontario, Canada K7L 3N6*
[c]*Biomedical Mass Spectrometry Unit, McGill University, 1130 Pine Avenue west, Montreal, Québec, Canada H3A 1A3*

A 7β-*O*-glycosylated taxane, 7-(β-D-glucopyranosyloxy)-9-dihydro-10-acetyldocetaxel **15** was semi-synthesized from 9-dihydro-13-acetylbaccatin III. The bioactivities towards both the tubulin and cytotoxicity assays against breast cancer cell lines MCF7 and MCF7-ADR (adriamycin resistant) will be discussed.



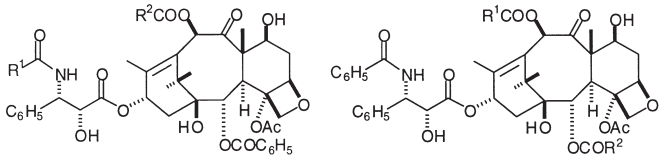
15

Bioorg. Med. Chem. 11 (2003) 1557

Synthesis and Biological Evaluation of C-3′NH/C-10 and C-2/C-10 Modified Paclitaxel Analogues

Erkan Baloglu,[a] Jeannine M. Hoch,[a] Sabarni K. Chatterjee,[b] Rudravajhala Ravindra,[b] Susan Bane[b] and David G. I. Kingston[a,*]

[a]*Department of Chemistry, M/C 0212, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA*
[b]*Department of Chemistry, State University of New York, Binghamton, NY 13902, USA*

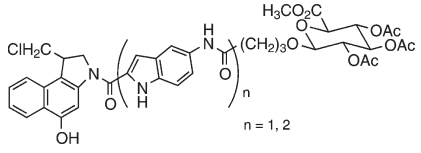


Bioorg. Med. Chem. 11 (2003) 1569

Synthesis and Preliminary Cytotoxicity Study of Glucuronide Derivatives of CC-1065 Analogues

Yuqiang Wang,* Huiling Yuan, Susan C. Wright, Hong Wang and James W. Larrick

Panorama Research, Inc., 2462 Wyandotte Street, Mountain View, CA 94043, USA



n = 1, 2

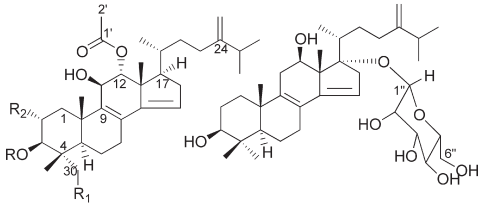
Bioorg. Med. Chem. 11 (2003) 1577

Integracides: Tetracyclic Triterpenoid Inhibitors of HIV-1 Integrase Produced by *Fusarium* Sp.

Sheo B. Singh,[a,*] Deborah L. Zink,[a] Anne W. Dombrowski,[a] Jon D. Polishook,[a] John G. Ondeyka,[a] Jorden Hirshfield,[a] Peter Felock[b] and Daria J. Hazuda[b]

[a]*Merck Research Laboratories, PO Box 2000, Rahway, NJ 07065, USA*
[b]*Merck Research Laboratories, West Point, PA 19486, USA*

Integracides are members of the tetracyclic triterpenoids family that were isolated from the fermentation broth of a *Fusarium* sp. Integracide A, a sulfated ester, exhibited significant inhibitory activity against strand transfer reaction of HIV-1 integrase.



R = SO_3H, R_1 = H, R_2 = OH (Integracide A)

Integracide D

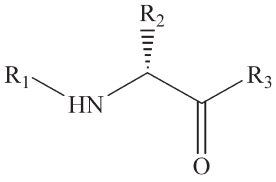
Bioorg. Med. Chem. 11 (2003) 1583

Combinatorial Enzymatic Assay for the Screening of a New Class of Bacterial Cell Wall Inhibitors

Ahmed El Zoeiby,[a] Mélanie Beaumont,[b] Eric Dubuc,[b] François Sanschagrin,[a] Normand Voyer[b] and Roger C. Levesque[a,*]

[a]*Centre de recherche sur la fonction, structure et ingénierie des protéines, Faculté de médecine, pavillon Charles-Eugène-Marchand, Université Laval, Sainte-Foy, Québec, Canada G1K 7P4*
[b]*Centre de recherche sur la fonction, structure et ingénierie des protéines, Département de chimie, Faculté des sciences et génie, Université Laval, Sainte-Foy, Québec, Canada G1K 7P4*

We report the combinatorial chemistry synthesis of more than 430 molecules with a D-amino acid central nucleus. These compounds were tested as bacterial cell wall inhibitors with our newly developed ATP-based assay.

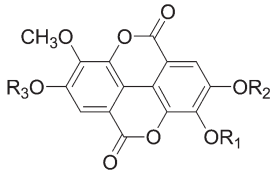


Bioorg. Med. Chem. 11 (2003) 1593

DNA Damaging Activity of Ellagic Acid Derivatives

Ya-ming Xu,[a] Jing-Zhen Deng,[a] Ji Ma,[a] Shao-Nong Chen,[a] Rebekah Marshall,[a] Shannon H. Jones,[a] Randall K. Johnson[b] and Sidney M. Hecht[a,*]

[a]*Departments of Chemistry and Biology, University of Virginia, Charlottesville, VA 22901, USA*
[b]*Department of Biomolecular Discovery, Glaxo SmithKline, King of Prussia, PA 19406, USA*



R_1	R_2	R_3
CH_3	H	β-D-Glc
CH_3	CH_3	β-D-Glc
-CH_2-		H
-CH_2-		β-D-Glc