Graphical Abstracts

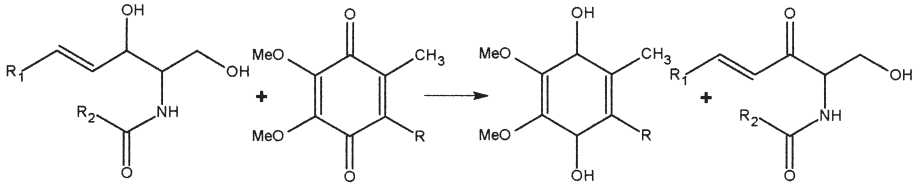
Bioorg. Med. Chem. 11 (2003) 2123

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.



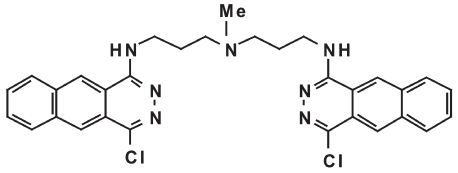
Bioorg. Med. Chem. 11 (2003) 2143

Synthesis and Cytotoxic Activity of *N*,*N*-bis-{3-[*N*-(4-Chlorobenzo[*g*]-phthalazin-1-yl)]aminopropyl}-*N*-methylamine: A New Potential DNA Bisintercalator

Marinela Rodríguez-Ciria,[a] Ana M. Sanz,[a] Maria J. R. Yunta,[a] Fernando Gomez-Contreras,[a,*] Pilar Navarro,[b] Isabel Fernandez,[c] Mercedes Pardo[a] and Carmen Cano[a]

[a]*Departamento de Quimica Organica I, Facultad de Quimica, Universidad Complutense, 28040 Madrid, Spain*
[b]*Instituto de Quimica Medica, C.S.I.C., Juan de la Cierva, 3, 28006 Madrid, Spain*
[c]*Laboratorios Knoll, Avda. de Burgos 91, 28050 Madrid, Spain*

The design, synthesis and cytotoxic activities of some benzo[*g*]phthalazine derivatives are described, and the DNA bisintercalating mode of the most active ligand is discussed with the help of molecular modeling techniques.



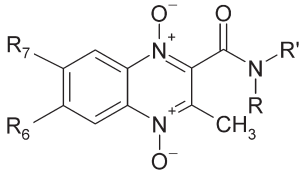
Bioorg. Med. Chem. 11 (2003) 2149

Synthesis and Antimycobacterial Activity of New Quinoxaline-2-carboxamide 1,4-di-*N*-Oxide Derivatives

Belén Zarranz, Andrés Jaso, Ignacio Aldana* and Antonio Monge

Unidad en Investigación y Desarrollo de Medicamentos, Centro de Investigación en Farmacobiología Aplicada (CIFA), Universidad de Navarra, Pamplona, Spain

As a continuation of our research and with the aim of obtaining new antituberculosis agents which can improve the current chemotherapeutic antituberculosis treatments, new series of quinoxaline-2-carboxamide 1,4-di-*N*-oxide derivatives were synthesized and evaluated for in vitro antituberculosis activity against *Mycobacterium tuberculosis* strain $H_{37}Rv$, using the radiometric BACTEC 460-TB methodology. Active compounds were also screened by serial dilution to assess toxicity to a VERO cell line. The results indicate that some compounds exhibited a good antituberculosis activity and the arylcarboxamide analogues **3**, **8** and **9** were the most active compounds (EC_{90}/MIC 1). Also, the cytotoxic effects indicate that these compounds have a good Selectivity Index (SI).

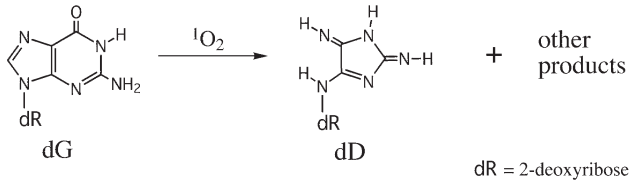


Bioorg. Med. Chem. 11 (2003) 2157

Formation of a Diimino-Imidazole Nucleoside from 2′-Deoxyguanosine by Singlet Oxygen Generated by Methylene Blue Photooxidation

Toshinori Suzuki, Marlin D. Friesen and Hiroshi Ohshima*

International Agency for Research on Cancer, 150 Cours Albert Thomas, F 69372 Lyon Cedex 08, France



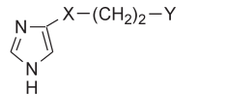
Bioorg. Med. Chem. 11 (2003) 2163

Imidazole Derivatives as a Novel Class of Hybrid Compounds with Inhibitory Histamine *N*-Methyltransferase Potencies and Histamine hH_3 Receptor Affinities

Sven Graßmann,[a] Joachim Apelt,[a] Wolfgang Sippl,[b] Xavier Ligneau,[c] Heinz H. Pertz,[a] Yuan Hui Zhao,[d] Jean-Michel Arrang,[e] C. Robin Ganellin,[d] Jean-Charles Schwartz,[e] Walter Schunack[a] and Holger Stark[f,*]

[a]*Institut für Pharmazie, Freie Universität Berlin, Königin-Luise-Strasse 2+4, 14195 Berlin, Germany*
[b]*Institut für Pharmazeutische Chemie, Heinrich-Heine-Universität Düsseldorf, Universitätsstrasse 1, 40225 Düsseldorf, Germany*
[c]*Laboratoire Bioprojet, 30 rue des Francs-Bourgeois, 75003 Paris, France*
[d]*Department of Chemistry, Christopher Ingold Laboratories, University College London, 20 Gordon Street, London WC1H 0AJ, UK*
[e]*Unité de Neurobiologie et Pharmacologie Moléculaire (U. 573), Centre Paul Broca de l'INSERM, 2ter rue d'Alésia, 75014 Paris, France*
[f]*Johann Wolfgang Goethe-Universität, Biozentrum, Institut für Pharmazeutische Chemie, Marie-Curie-Strasse 9, 60439 Frankfurt am Main, Germany*

Syntheses, inhibitory histamine *N*-methyltransferase activities, and histamine hH_3 receptor binding affinities of novel highly active imidazole derivatives are described.



X = -, $-CH_2-$, $-CH=CH-CH_2-$, $-(CH_2)_3-$
Y = -O-carbocycle, -O-heterocycle, -NH-heterocycle

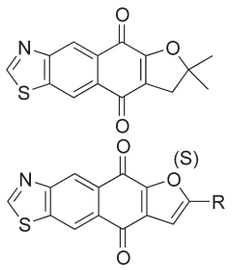
Bioorg. Med. Chem. 11 (2003) 2175

Synthesis and Antiprotozoal Activity of Naphthofuranquinones and Naphthothiophenequinones Containing a Fused Thiazole Ring

Ricardo A. Tapia,[a,*] Luz Alegria,[a] Carlos D. Pessoa,[a] Cristian Salas,[a] Manuel J. Cortés,[a] Jaime A. Valderrama,[a] Marie-Elisabeth Sarciron,[b] Félix Pautet,[c] Nadia Walchshofer[c] and Houda Fillion[c,*]

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

Tetracyclic quinones and their regiosomers were prepared and evaluated for their antiprotozoal properties.

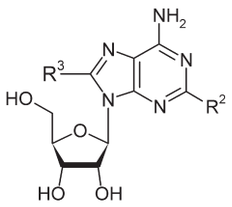


Bioorg. Med. Chem. 11 (2003) 2183

2,8-Disubstituted Adenosine Derivatives as Partial Agonists for the Adenosine A_{2A} Receptor

Erica W. van Tilburg,* Matty Gremmen, Jacobien von Frijtag Drabbe Künzel, Miriam de Groote and Ad P. IJzerman

Leiden/Amsterdam Center for Drug Research, Division of Medicinal Chemistry, PO Box 9502, 2300 RA Leiden, The Netherlands



Bioorg. Med. Chem. 11 (2003) 2193

Synthesis of β-(1→6)-Branched β-(1→3) Glucohexaose and Its Analogues Containing an α-(1→3) Linked Bond with Antitumor Activity

Jun Ning,[a,*] Wenhui Zhang,[a] Yuetao Yi,[a] Guangbin Yang,[a] Zhikui Wu,[b] Jie Yi[b] and Fanzuo Kong[a,*]

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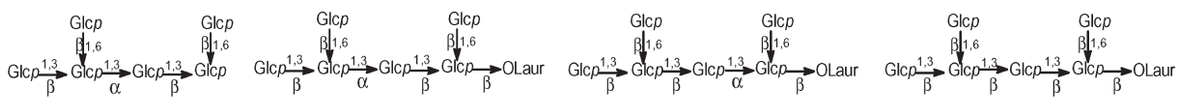
[b]*Guang Anmen Hospitol, Chinese Academy of Traditional Chinese Medicine, PR China*

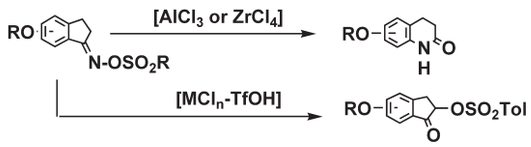


Bioorg. Med. Chem. 11 (2003) 2205

A Study on the Conversion of Indanones into Carbostyrils

Yasuhiro Torisawa,* Takao Nishi and Jun-ichi Minamikawa

Process Research Laboratory, Second Tokushima Factory, Otsuka Pharmaceutical Co., Ltd., Kawauchi, Tokushima, 771-0182, Japan



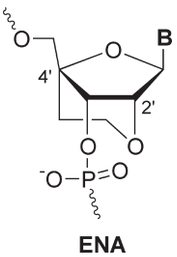
Bioorg. Med. Chem. 11 (2003) 2211

Synthesis and Properties of 2′-*O*,4′-*C*-Ethylene-Bridged Nucleic Acids (ENA) as Effective Antisense Oligonucleotides

Koji Morita,[a] Miho Takagi,[a] Chikako Hasegawa,[a] Masakatsu Kaneko,[a] Shinya Tsutsumi,[b] Junko Sone,[b] Tomio Ishikawa,[b] Takeshi Imanishi[c] and Makoto Koizumi[a,*]

[a]*Exploratory Chemistry Research Laboratories, Sankyo Co., Ltd., Tokyo 140-8710, Japan*
[b]*Biomedical Research Laboratories, Sankyo Co., Ltd., Tokyo 140-8710, Japan*
[c]*Graduate School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan*

Novel bicyclo nucleosides, 2′-*O*,4′-*C*-ethylene nucleosides and 2′-*O*,4′-*C*-propylene nucleosides, were synthesized as building blocks for antisense oligonucleotides.



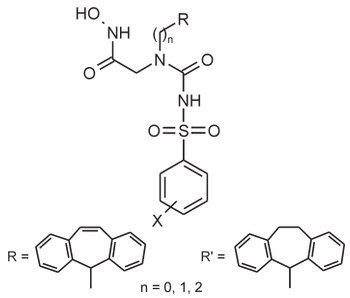
ENA

Bioorg. Med. Chem. 11 (2003) 2227

Protease Inhibitors: Synthesis of Bacterial Collagenase and Matrix Metalloproteinase Inhibitors Incorporating Arylsulfonylureido and 5-Dibenzo-suberenyl/suberyl Moieties

Monica Ilies,[a,b] Mircea D. Banciu,[c] Andrea Scozzafava,[a] Marc A. Ilies,[b] Miron T. Caproiu[d] and Claudiu T. Supuran[a,*]

[a]*Università degli Studi, Laboratorio di Chimica Inorganica e Bioinorganica, Via della Lastruccia 3, Rm 188, Polo Scientifico, 50019-Sesto Fiorentino, Firenze, Italy*
[b]*University of Agricultural Sciences and Veterinary Medicine, Faculty of Biotechnologies, Department of Chemistry, B-dul Marasti 59, 71331-Bucharest, Romania*
[c]*Polytechnic University, Department of Organic Chemistry, Splaiul Independentei 313, Bucharest, Romania*
[d]*'C.D. Nenitzescu' Institute of Organic Chemistry, Splaiul Independentei 202B, Bucharest, Romania*

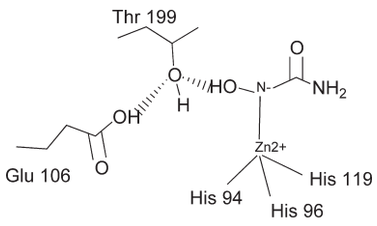


Bioorg. Med. Chem. 11 (2003) 2241

Hydroxyurea Is a Carbonic Anhydrase Inhibitor

Andrea Scozzafava and Claudiu T. Supuran*

Università degli Studi di Firenze, Dipartimento di Chimica, Laboratorio di Chimica Bioinorganica, Via della Lastruccia 3, Rm. 188, I-50019 Sesto Fiorentino, Firenze, Italy



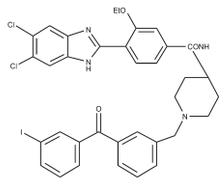
Bioorg. Med. Chem. 11 (2003) 2247

Synthesis of Photoactivable Inhibitors of Osteoclast Vacuolar ATPase

Barbara Biasotti,[a] Sabrina Dallavalle,[a] Lucio Merlini,[a,*] Carlo Farina,[b] Stefania Gagliardi,[b,*] Carlo Parini[b] and Pietro Belfiore[c]

[a]*Dipartimento di Scienze Molecolari Agroalimentari, Università di Milano, Via Celoria 2, 20133 Milan, Italy*
[b]*NiKem Research Srl, Via Zambeletti 25, 20021 Baranzate di Bollate (Mi), Italy*
[c]*GlaxoSmithKline, MuscoloSkeletal Disease, 709 Swedeland Road, King of Prussia, PA 19406, USA*

A series of inhibitors of vacuolar ATPase containing a photoactivable group were synthesized.



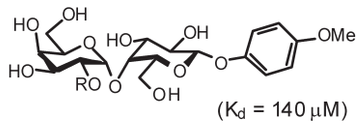
Bioorg. Med. Chem. 11 (2003) 2255

Quantitative Studies of the Binding of the Class II PapG Adhesin from Uropathogenic *Escherichia coli* to Oligosaccharides

Andreas Larsson,[a] Jörgen Ohlsson,[b] Karen W. Dodson,[c] Scott J. Hultgren,[c] Ulf Nilsson[b] and Jan Kihlberg[a,*]

[a]*Organic Chemistry, Department of Chemistry, Umeå University, SE-901 87 Umeå, Sweden*
[b]*Bioorganic Chemistry, Lund University, PO Box 124, SE-221 00 Lund, Sweden*
[c]*Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO 63110, USA*

Surface plasmon resonance was used to determine dissociation constants for binding of the class II PapG adhesin to globoseries di-pentasaccharides, and to modified galabiose derivatives.



GalNAcα3GalNAcβ3Galα4Galβ4GlcβOTMSEt
(K_d = 91 μM)

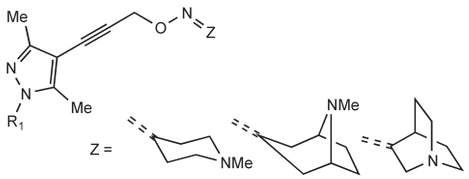
Bioorg. Med. Chem. 11 (2003) 2263

Synthesis and Muscarinic Activities of *O*-[(Benzyl- or Benzoyl-pyrazolyl)propynyl]-oximes of *N*-Methylpiperidinone, 3-Tropinone, and 3-Quinuclidinone

María Isabel Rodríguez-Franco,[a,*] Isabel Dorronsoro,[a] Ana Castro,[a] Ana Martínez,[a] Albert Badía[b] and Josep E. Baños[b]

[a]*Instituto de Química Médica (C.S.I.C.), Juan de la Cierva 3, 28006 Madrid, Spain*
[b]*Departamento de Farmacología, Terapéutica, y Toxicología, Facultad de Medicina, Universidad Autónoma de Barcelona, 08913 Bellaterra, Spain*

The synthesis of *O*-propynyloximes of *N*-methylpiperidinone, 3-tropinone, and 3-quinuclidinone, containing several pyrazole frameworks, is described, together with their muscarinic receptor affinities.



R_1 = H, $CH_2C_6H_5$, $CH_2C_6H_4$(4-OMe), COC_6H_2(2,4,6-Me)

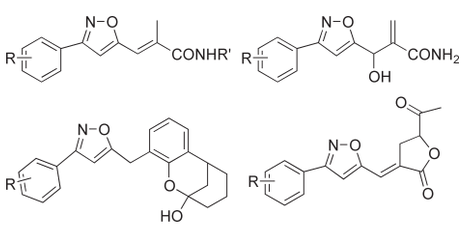
Bioorg. Med. Chem. 11 (2003) 2269

Isoxazole-Based Derivatives from Baylis–Hillman Chemistry: Assessment of Preliminary Hypolipidemic Activity

A. Patra,[a] S. Batra,[a,*] A. P. Bhaduri,[a] A. Khanna,[b] R. Chander[b] and M. Dikshit[c]

[a]*Medicinal Chemistry Division, Central Drug Research Institute, PO Box, 173, Lucknow 226001, India*
[b]*Biochemistry Division, Central Drug Research Institute, PO Box, 173, Lucknow 226001, India*
[c]*Pharmacology Division, Central Drug Research Institute, PO Box, 173, Lucknow 226001, India*

The synthesis of isoxazole-based derivatives utilizing Baylis–Hillman chemistry and results of their preliminary bioevaluation as hypolipidemic agents are described.



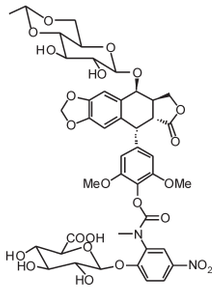
Bioorg. Med. Chem. 11 (2003) 2277

Prodrug Mono Therapy: Synthesis and Biological Evaluation of an Etoposide Glucuronide-Prodrug

Frédéric Schmidt* and Claude Monneret

UMR 176 CNRS/Institut Curie, Section Recherche, 26, rue d'Ulm, 75248 Paris Cedex 05, France

The synthesis and biological evaluation of a glucuronide-based prodrug are reported. This compound fulfils all the requirements for a Prodrug Mono Therapy strategy in cancer chemotherapy.



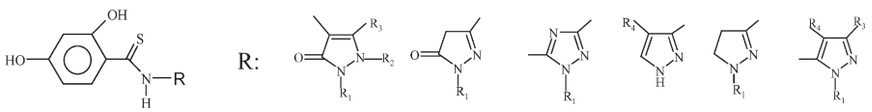
Bioorg. Med. Chem. 11 (2003) 2285

Synthesis and Antimycotic Activity of *N*-azolyl-2,4-dihydroxythiobenzamides

Joanna Matysiak and Andrzej Niewiadomy*

Department of Chemistry, University of Agriculture, Akademicka 15, 20-950 Lublin, Poland

A series of *N*-azolyl-2,4-dihydroxythiobenzamides have been synthesised and their fungistatic properties were described.

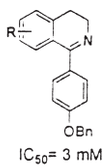


Bioorg. Med. Chem. 11 (2003) 2293

Structure-Based Approach to Falcipain-2 Inhibitors: Synthesis and Biological Evaluation of 1,6,7-Trisubstituted Dihydroisoquinolines and Isoquinolines

Sanjay Batra,[a,*] Yogesh A. Sabnis,[b] Philip J. Rosenthal[c] and Mitchell A. Avery[b,d,*]

[a]*Medicinal Chemistry Division, Central Drug Research Institute, Lucknow 226001, India*
[b]*Department of Medicinal Chemistry, National Center for Natural Products Research, School of Pharmacy, University of Mississippi, University, MI 38677-1848, USA*
[c]*Department of Medicine, University of California at San Francisco, San Francisco, CA, USA*
[d]*Department of Chemistry, PO Box 1848, University of Mississippi, University, MI 38677-1848, USA*



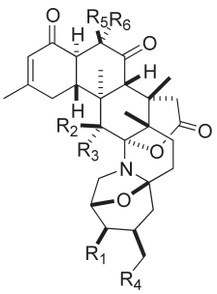
Bioorg. Med. Chem. 11 (2003) 2301

Evaluation of the Effects of Several Zoanthamine-type Alkaloids on the Aggregation of Human Platelets

Rosa M. Villar,[b] José Gil-Longo,[b] Antonio H. Daranas,[c] María L. Souto,[c] José J. Fernández,[c] Solange Peixinho,[d] Miguel A. Barral,[a] Gilmar Santafé,[a] Jaime Rodríguez[a] and Carlos Jiménez[a,*]

[a]*Departamento de Química Fundamental, Facultade de Ciencias, Universidade de A Coruña, 15071 A Coruña, Spain*
[b]*Departamento de Farmacoloxía, Facultade de Farmacia, Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain*
[c]*Instituto Universitario de Bio-Orgánica 'Antonio González', Universidad de La Laguna, 38206 La Laguna, Spain*
[d]*Departamento de Zoologia, Instituto de Biologia, Universidade Federal de Bahía, 4071-290 Salvador da Bahía, Brazil*

Ten zoanthamine-type alkaloids from two marine zoanthids belonging to the *Zoanthus* genus (*Z. nymphaeus* and *Zoanthus* sp.) along with one semisynthetic derivative were evaluated for their antiplatelet activities on human platelet aggregation induced by several stimulating agents.



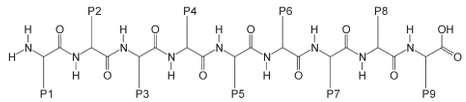
Bioorg. Med. Chem. 11 (2003) 2307

A Comparative Molecular Similarity Indices (CoMSIA) Study of Peptide Binding to the HLA-A3 Superfamily

Pingping Guan, Irini A. Doytchinova and Darren R. Flower*

Edward Jenner Institute for Vaccine Research, Compton, Berkshire RG20 7NN, UK

The motif of the peptides binding to the HLA-A3 superfamily was produced.

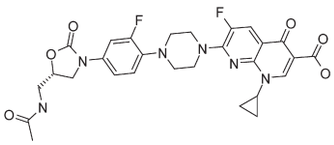


Bioorg. Med. Chem. 11 (2003) 2313

Design, Synthesis and Biological Evaluation of Oxazolidinone–Quinolone Hybrids

Christian Hubschwerlen,* Jean-Luc Specklin, Christine Sigwalt, Susanne Schroeder and Hans H. Locher

Morphochem AG, Schwarzwaldallee 215, CH-4058 Basel, Switzerland

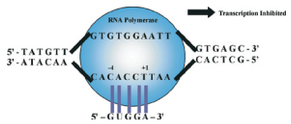


Bioorg. Med. Chem. 11 (2003) 2321

Transcription Inhibition Using Modified Pentanucleotides

Jae-Taeg Hwang,[a] Francis E. Baltasar,[b] Daniel L. Cole,[b] David S. Sigman[a,b] Chi-hong B. Chen[b,*] and Marc M. Greenberg[c,*]

[a]*Department of Chemistry, Colorado State University, Fort Collins, CO 80523, USA*
[b]*Department of Biological Chemistry, School of Medicine, Department of Chemistry and Biochemistry, Molecular Biology Institute, University of California, Los Angeles, Los Angeles, CA 90095-1570, USA*
[c]*Department of Chemistry, Johns Hopkins University, 3400 N. Charles St., Baltimore, MD 21218, USA*



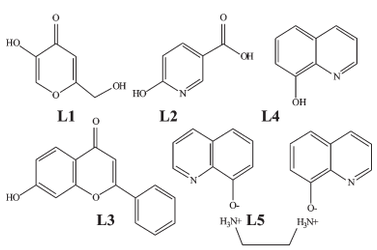
Bioorg. Med. Chem. 11 (2003) 2329

Manganese-Based Complexes of Radical Scavengers as Neuroprotective Agents

Opa Vajragupta,[a,*] Preecha Boonchoong,[a] Yaowared Sumanont,[a] Hiroshi Watanabe,[b] Yuvadee Wongkrajang[a] and Naparat Kammasud[a]

[a]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Mahidol University, 447 Sri-Ayudhya Road, Bangkok 10400, Thailand*
[b]*Department of Pharmacology, Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan*

Manganese complexes from ligands **1**–**5** showed potent SOD and action against lipid peroxidation in vitro. In vivo, Mn complexes of **L1** and **L3** significantly suppressed MAP-induced hypermotility but did not significantly decrease the locomotor activity in normal condition. Manganese complex **3** (12.5 mg/kg) protected the learning and memory impairment in transient cerebral ischemic mice.



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Structure–Activity Studies of Glucose Transfer: Determination of the Spontaneous Rates of Hydrolysis of Uridine 5′-Diphospho-α-D-glucose (UDPG) and Uridine 5′-Diphospho-α-D-glucuronic Acid (UDPGA)

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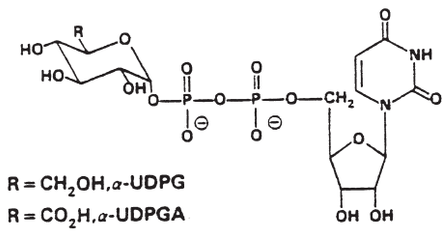
From the measured pH-rate profiles for the hydrolysis of UDPG and UDPGA, the catalytic power (k_{cat}/k_{uncat}) of the glycosltransferases has been estimated for the first time to be in the order of 10^{11-13}.



Bioorg. Med. Chem. 11 (2003) 2347

Assessment of the Sequence Dependency for the Binding of 2-Aminonaphthyridine to the Guanine Bulge

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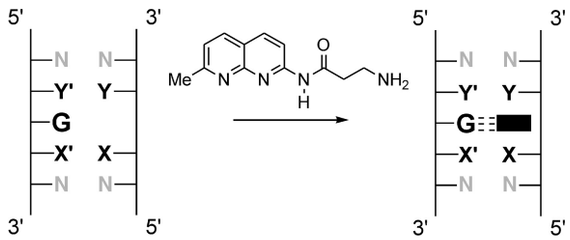
The sequence dependency for the binding of naphthyridine derivative was investigated.



Bioorg. Med. Chem. 11 (2003) 2355

Synthesis and Evaluation of Peptidomimetics That Bind DNA

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