

Synthesis and Antiplatelet, Antiinflammatory, and Antiallergic Activities of 2-Substituted 3-Chloro-1,4-naphthoquinone Derivatives

Bioorg. Med. Chem. 1997, 5, 2111

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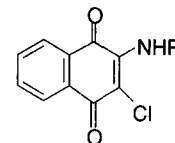
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Synthesis and antiplatelet, antiinflammatory, and antiallergic activities of 2-alkyl(aryl)-carboxamido- and 2-alkyl(aryl)amino-3-chloro-1,4-naphthoquinones are described.



Quantitative Structure–Activity Studies of Octopaminergic 2-(Arylimino)thiazolidines and Oxazolidines against the Nervous System of *Periplaneta americana* L.

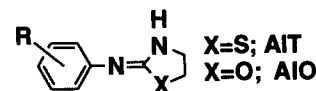
Bioorg. Med. Chem. 1997, 5, 2121

Akinori Hirashima,^{a,*} Jun Tomita,^a Canping Pan,^a Eiji Taniguchi^a and Morifusa Eto^b

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The quantitative structure–activity relationship (QSAR) of octopaminergic 2-(arylimino)thiazolidines (AITs) and 2-(arylimino)oxazolidines (AIOs) against the thoracic nerve cord of American cockroach, *Periplaneta americana* L., was analysed using reported physicochemical parameters and regression analysis.



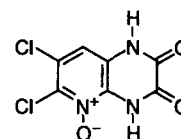
2,3-Dihydro-6,7-dichloro-pyrido[2,3-*b*]pyrazine-8-oxide as Selective Glycine Antagonist with In Vivo Activity

Bioorg. Med. Chem. 1997, 5, 2129

F. Micheli,^{a,*} A. Cugola,^a D. Donati,^a A. Missio,^a A. Percunioso,^{a,*} A. Reggiani^a and G. Tarzia^b

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Anti-AIDS Agents—XXVII. Synthesis and Anti-HIV Activity of Betulinic Acid and Dihydrobetulinic Acid Derivatives

Bioorg. Med. Chem. 1997, 5, 2133

F. Hashimoto,^{a,f} Y. Kashiwada,^{b,f} L. M. Cosentino,^c C.-H. Chen,^d P. E. Garrett^e and K.-H. Lee^{f,*}

^aKumamoto University, Kumamoto 862, Japan

^bNiigata College of Pharmacy, Niigata, 950-21, Japan

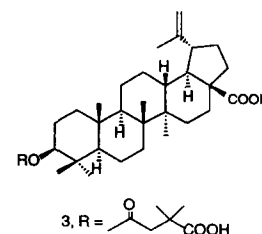
^cBiotech Research Laboratories, Rockville, MD 20850, U.S.A.

^dDuke University Medical Center, Durham, NC 27710, U.S.A.

^eBoston Biomedica, Inc., West Bridgewater, MA 02379, U.S.A.

^fSchool of Pharmacy, University of North Carolina, Chapel Hill, NC 27599-7360, U.S.A.

Derivatives of betulinic acid dihydrobetulinic acid were synthesized and evaluated for anti-HIV activity. 3-*O*-(3',3'-dimethylsuccinyl)-betulinic acid (**3**) had a remarkable EC₅₀ value of $<3.5 \times 10^{-4}$ μ M and a TI of 20,000.



Polyamine Derivatives as Inhibitors of Trypanothione Reductase and Assessment of their Trypanocidal Activities

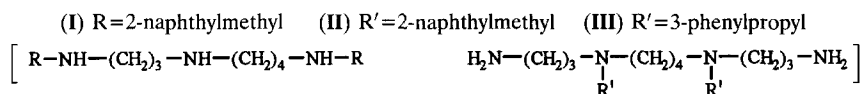
Bioorg. Med. Chem. 1997, 5, 2145

Mary C. O'Sullivan,^{a,*} Qibing Zhou,^a Zhili Li,^a Timothy B. Durham,^a Donna Rattendi,^b Schennella Lane^b and Cyrus J. Bacchi^b

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^bHaskins Laboratories and Department of Biology, Pace University, New York, NY 10038, U.S.A.

The inhibiting effects of several polyamine derivatives on *T. cruzi* TR were investigated. The most effective TR inhibitors studied **I**, **II**, and **III** were potent trypanocides in vitro (IC₅₀ 0.19–0.83 μM). (**I**) R = 2-naphthylmethyl, (**II**) R' = 2-naphthylmethyl and (**III**) R' = 3-phenylpropyl.



Redesigning the Active-site of an Acyl-CoA Dehydrogenase: New Evidence Supporting a One-base Mechanism

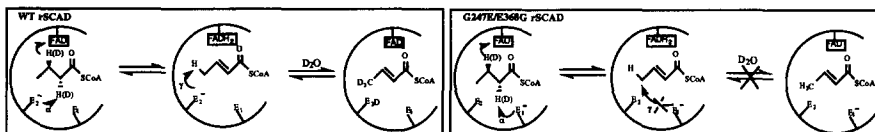
Bioorg. Med. Chem. 1997, 5, 2157

Srikanth Dakoiji,^a Injae Shin,^a Kevin P. Battaile,^b Jerry Vockley^c and Hung-wen Liu^{a,*}

^aDepartment of Chemistry, University of Minnesota, Minneapolis, MN 55455, U.S.A.

^bDepartment of Biochemistry and Molecular Biology ^cDepartment of Medical Genetics at Mayo Clinic and Mayo Foundation, Rochester, MN 55905, U.S.A.

Both the wild-type and mutant enzymes (rat short-chain acyl-CoA dehydrogenases (rSCAD)) display identical stereochemical preference for catalysis; however, mutant enzyme whose catalytic base has been moved from E₁ to the E₂ site is unable to carry out γ-proton abstraction.



O-Methylasparvenone, a Nitrogen-free Serotonin Antagonist

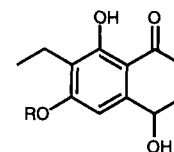
Bioorg. Med. Chem. 1997, 5, 2165

Michael Bös,^{a,*} Rolf Canesso,^a Noriko Inoue-Ohga,^b Atsuko Nakona,^b Yuki Takehana^b and Andrew J. Sleight^a

^aPharma Division, Preclinical CNS Research, F. Hoffmann–La Roche Ltd, CH-4070 Basel, Switzerland

^bNippon Roche Research Center, Department of Screening, 200 Kajiwara, Kamakura 247, Japan

O-Methylasparvenone (**1**) and asparvenone (**2**) represent the first nitrogen-free serotonin antagonists (pK_i 5-HT_{2c} = 6.7 and 6.4, respectively).



1 R = CH₃
2 R = H

Enantiomers of Cis- and Trans-3-(4-propyl-cyclopent-2-enyl) Propyl Acetate. A Study on the Bioactive

Bioorg. Med. Chem. 1997, 5, 2173

Conformation and Chiral Recognition of a Moth Sex Pheromone Component

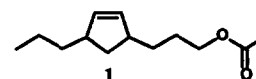
Anna-Lena Gustavsson,^a Mattias C. Larsson,^b Bill S. Hansson^b and Tommy Liljefors^{c,*}

^aOrganic Chemistry 1, Center for Chemistry and Chemical Engineering, Lund University, P.O. Box 124, S-221 00 Lund, Sweden

^bDepartment of Ecology, Lund University, S-223 62 Lund, Sweden

^cDepartment of Medicinal Chemistry, The Royal Danish School of Pharmacy, DK-2100 Copenhagen, Denmark

The enantiomers of cis- and trans-**1**, analogues of a sex pheromone component of *Agrotis segetum*, have been prepared and tested by single-cell electrophysiology.



Anti-Plasmodial and Anti-Trypanosomal Activity of Synthetic Naphtho[2,3-*b*]thiophen-4,9-quinones

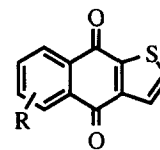
Carlos L. Zani,^{a,*} Egler Chiari,^b Antoniana U. Krettli,^a Silvane M. F. Murta,^a Mark L. Cunningham,^c Alan. H. Fairlamb^c and Alvaro J. Romanha^a

^aCentro de Pesquisas René Rachou—Fundação Oswaldo Cruz (FIOCRUZ), Av. Augusto de Lima, 1715 CEP 30190-002, Belo Horizonte, MG, Brazil

^bDepartamento de Parasitologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil

^cDepartment of Medical Parasitology, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, U.K.

Naphthothiophenquinones (NTQs) were prepared using Friedel–Crafts or tandem *ortho*-lithiation methodologies. These quinones were tested against *Plasmodium falciparum* and *Trypanosoma cruzi*. Some of them showed potent in vitro activity against these parasites. The in vitro trypanocidal effect does not correlate with the inhibition of the enzyme trypanothione reductase. Furthermore, despite reaching blood concentrations of 40 μ M in mice after a single 500 mg/kg oral dose, the parent compound (R = H) was not active against *P. berghei* in infected mice.



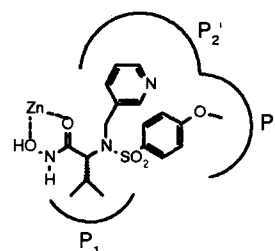
Bioorg. Med. Chem. 1997, 5, 2185

Bioactive Conformation of a Potent Stromelysin Inhibitor Determined by X-nucleus Filtered and Multidimensional NMR Spectroscopy

Nina C. Gonnella,^{*} Yu-Chin Li, Xiaolu Zhang and C. Gregory Paris

Novartis Pharmaceuticals Corp., 556 Morris Ave., Summit, NJ 07901, U.S.A.

The bioactive conformation of a potent, nonpeptidic stromelysin inhibitor was determined using NMR methods. This study established the enzyme–inhibitor binding mode and provided a structural template for the design of more potent stromelysin inhibitors.



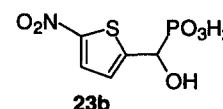
Bioorg. Med. Chem. 1997, 5, 2193

Nitroarylhydroxymethylphosphonic Acids as Inhibitors of CD45

Scott A. Beers,^{*} Elizabeth A. Malloy, Wei Wu, Michael P. Wachter, Uma Gunnia, Druie Cavender, Crafford Harris, Janet Davis, Ruth Brosius, J. Lee Pellegrino-Gensey and John Siekierka.

The R.W. Johnson Pharmaceutical Research Institute, 1000 Route 202, Raritan NJ 08869, U.S.A.

Compound **23b** is a member of a new class of phosphonic acids that inhibit CD45 with IC₅₀ values from 2–20 μ M. Both nitro and hydroxy groups are essential for potency. Lineweaver–Burk kinetics have shown these to be competitive inhibitors of CD45.



Bioorg. Med. Chem. 1997, 5, 2203

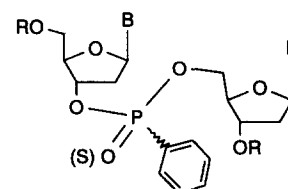
Synthesis and Binding Properties of Oligodeoxynucleotides Containing Phenylphosphon(othio)ate Linkages

Matthias Mag,^a Jochen Muth,^b Kerstin Jahn,^a Anusch Peyman,^a Gerhard Kretzschmar,^a Joachim W. Engels^{b,*} and Eugen Uhlmann^a

^aHoechst Aktiengesellschaft, G 838, D-65926 Frankfurt am Main, Germany

^bInstitut für Organische Chemie, Johann Wolfgang Goethe-Universität, D-60439 Frankfurt am Main, Germany

Novel oligodeoxynucleotides containing phenylphosphonate and phenylphosphonothioate linkages, and their synthesis and binding properties to complementary nucleic acids are described.



Bioorg. Med. Chem. 1997, 5, 2213

Binding to δ and μ Opioid Receptors by Deltorphin I/II Analogues Modified at the Phe³ and Asp⁴/Glu⁴ Side Chains: a Report of 32 New Analogues and a QSAR Study

Bioorg. Med. Chem. 1997, 5, 2221

Stephen E. Schullery,^a Tasneem Mohammedshah,^a Hafida Makhoul,^a Eleanor L. Marks,^a Benjamin S. Wilenkin,^a Sharleen Escobar,^a Carol Mousigian^b and Deborah L. Heyl^{a*}

^aDepartment of Chemistry, Eastern Michigan University, Ypsilanti, MI 48197 U.S.A.
^bCollege of Pharmacy, The University of Michigan, Ann Arbor, MI 48109 U.S.A.

Thirty-two new X³Gly⁴ analogues of deltorphin I/II opioid peptides are described. A QSAR study of the X³Gly⁴, X³Asp⁴, and Phe³X⁴ analogue series using a potential well model reveals the roles of hydrophobic, van der Waals, electrostatic, hydrogen bonding and steric interactions in δ and μ receptor binding of X³ and X⁴ side chains.

Biologically Active Oligodeoxyribonucleotides—IX. Synthesis and Anti-HIV-1 Activity of Hexadeoxyribonucleotides, TGGGAG, Bearing 3'- and 5'-End-modification

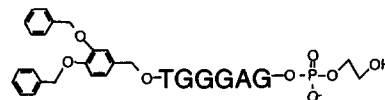
Bioorg. Med. Chem. 1997, 5, 2235

Makoto Koizumi,^{a,*} Rika Koga,^a Hitoshi Hotoda,^a Kenji Momota,^b Toshinori Ohmine,^b Hidehiko Furukawa,^b Toshinori Agatsuma,^b Takashi Nishigaki,^b Koji Abe,^c Toshiyuki Kosaka,^c Shinya Tsutsumi,^c Junko Sone,^c Masakatsu Kaneko,^a Satoshi Kimura^d and Kaoru Shimada^d

^aExploratory Chemistry Research Laboratory, ^bBiological Research Laboratory, ^cAnalytical and Metabolic Research Laboratory, Sankyo Co., Ltd, Tokyo 140, Japan

^dDepartment of Infectious Diseases, Institute of Medical Science, University of Tokyo, Tokyo 108, Japan

A 6-mer (R-95288) bearing a 3,4-dibenzyloxybenzyl group at the 5'-end and a 2-hydroxyethylphosphate group at the 3'-end with anti-HIV-1 activity is described.



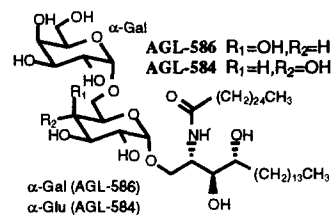
Immunostimulatory Activities of Monoglycosylated α -D-Pyranosylceramides

Bioorg. Med. Chem. 1997, 5, 2245

Akira Uchimura, Toshiyuki Shimizu, Masahiro Morita, Hitomi Ueno, Kazuhiro Motoki, Hideaki Fukushima, Takenori Natori and Yasuhiko Koezuka*

Pharmaceutical Research Laboratory, Kirin Brewery Co., Ltd, 3 Miyahara-cho, Takasaki-shi, Gunma 370-12, Japan

We compared the immunostimulatory effects of α -galactosylceramides (α -GalCers), α -glucosylceramides (α -GluCers), 6-monoglycosylated α -GalCer and 6- or 4-monoglycosylated α -GluCer which were chemically synthesized, and found; 1) the lengths of the fatty acid side chain in the ceramide portion greatly affect the immunostimulatory effects of α -GalCers and α -GluCers; 2) the configuration of 4-hydroxyl group of the inner pyranose moiety plays an important role in the immunostimulatory effects of monoglycosylated α -D-pyranosylceramides.



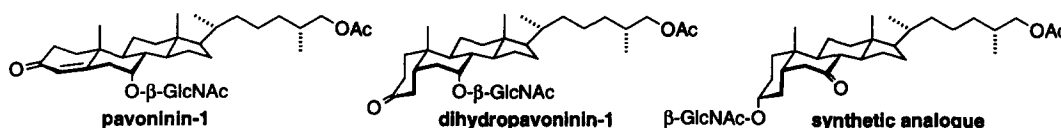
Synthesis of Pavoninin-1, a Shark Repellent Substance, and its Structural Analogues toward Mechanistic Studies on their Membrane Perturbation

Bioorg. Med. Chem. 1997, 5, 2251

Yuki Ohnishi and Kazuo Tachibana*

Department of Chemistry, School of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan

Pavoninin-1 and its structural analogues were synthesized using anomeric sulfoxide glycosidation as a key step, and the mode of action for their perturbation on liposomal membrane was evaluated by the fluorescence dye leakage.

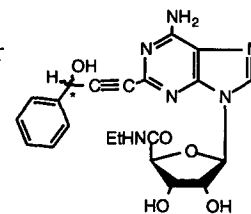


Adenosine Receptor Agonists: Synthesis and Biological Evaluation of the Diastereoisomers of 2-(3-Hydroxy-3-phenyl-1-propyn-1-yl)NECA

Bioorg. Med. Chem. 1997, 5, 2267

Emidio Camaioni, Emanuela Di Francesco, Sauro Vittori, Rosaria Volpini and Gloria Cristalli*
Dipartimento di Scienze Chimiche, Università di Camerino, 62032 Camerino, Italy.

A very potent inhibitor of rabbit platelet aggregation was obtained by diastereoisomer separation of a 2-alkynyl derivative of NECA.



Antitumor Agents—CLXXV. Anti-tubulin Action of (+)-Thiocolchicine Prepared by Partial Synthesis

Bioorg. Med. Chem. 1997, 5, 2277

Qian Shi,^a Pascal Verdier-Pinard,^b Arnold Brossi,^{a,*} Ernest Hamel^b and Kuo-Hsiung Lee^{a,*}

^aNatural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill, North Carolina 27599

^bLaboratory of Drug Discovery Research and Development, Developmental Therapeutics Program, Division of treatment, Diagnosis and Centers, National Cancer Institute, Frederick Cancer Research and Development Center, Frederick, MD 21702, U.S.A.

(+)-Thiocolchicine (**2b**) is 15-fold and 29-fold less potent for tubulin polymerization and inhibiting growth of lymphoma cells than (–)-thiocolchicine, suggesting that the proper configuration of colchicine-related compounds is important for their anti-tubulin action.

