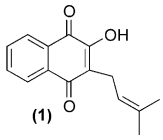
Inhibitory Effects of Lapachol Derivatives on Epstein–Barr Virus Activation

Bioorg. Med. Chem. 11 (2003) 483

Elisa Pérez Sacau,[a] Ana Estévez-Braun,[a,*] Ángel G. Ravelo,[a,*] Esteban A. Ferro,[b,*] Harunkuni Tokuda,[c] Teruo Mukainaka[c] and Hoyoku Nishino[c]

[a]*Instituto Universitario de Bio-Orgánica 'Antonio González', Universidad de La Laguna, Avda. Astrofísico Fco. Sánchez No. 2, La Laguna, E-38206, Tenerife, Spain*
[b]*Departamento de Fitoquímica, Univ. de Asunción, PO Box 1055 Asunción, Paraguay*
[c]*Department of Biochemistry, Kyoto Prefectural University of Medicine, Japan*



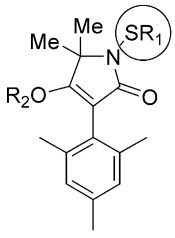
Sixteen derivatives (**2–17**) synthesized from the naphthoquinone lapachol (**1**), were tested for inhibitory activity against 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced Epstein–Barr virus early antigen (EBV-EA) activation in Raji cells. Some of them exhibited significant inhibitory activity.

Synthesis and Insecticidal Activity of Novel Dihydropyrrole Derivatives with *N*-Sulfanyl, Sulfinyl, and Sulfonyl Moieties

Bioorg. Med. Chem. 11 (2003) 489

Mitsuru Ito,[a,*] Hideshi Okui,[a] Harumi Nakagawa,[a] Shigeru Mio,[a] Ayako Kinoshita,[a] Takashi Obayashi,[a] Takako Miura,[a] Junko Nagai,[a] Shinji Yokoi,[a] Reiji Ichinose,[b] Keiji Tanaka,[a] Seiichiro Kodama,[c] Toshiaki Iwasaki,[d] Takaaki Miyake,[d] Miho Takashio[d] and Jun Iwabuchi[d]

[a]*Agroscience Research Laboratories, Sankyo Co., Ltd., 1041 Yasu, Yasu-cho, Yasu-gun, Shiga, 520-2342, Japan*
[b]*Crop Protection Department, Sankyo Co., Ltd., 7-12, Ginza 2-chome, Chuo-ku, Tokyo, 104-8113, Japan*
[c]*Marketing Department, Agrochemicals Division, Agro & Specialty Chemicals Group, Nippon Kayaku Co., Ltd., 11-2, Fujimi 1-chome, Chiyoda-ku, Tokyo, 102-8172, Japan*
[d]*Research & Development Laboratories, Agro & Specialty Chemicals Group, Nippon Kayaku Co., Ltd., 225-1, Koshikiya, Ageo-city, Saitama, 362-0064, Japan*



A series of novel dihydropyrrole derivatives with sulfur moieties was synthesized and evaluated for insecticidal activity against brown rice planthoppers and green rice leafhoppers.

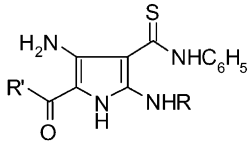
Synthesis and In Vitro Antitumoral Activity of New *N*-Phenyl-3-pyrrolecarbothioamides

Bioorg. Med. Chem. 11 (2003) 495

Maria T. Cocco,* Cenzo Congiu and Valentina Onnis

Dipartimento di Tossicologia, Università degli Studi di Cagliari, Via Ospedale 72, Cagliari, I-09124, Italy

N-Phenylpyrrolecarbothioamides demonstrated inhibitory effects on the growth of a wide range of cancer cell lines generally at 10^{-6} M level and in some cases at 10^{-8} M concentrations.

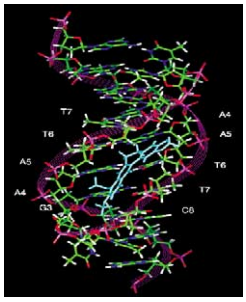


Mode of Binding of the Cytotoxic Alkaloid Berberine with the Double Helix Oligonucleotide D(AAGAATTCTT)$_2$

Bioorg. Med. Chem. 11 (2003) 505

Stefania Mazzini, Maria Cristina Bellucci and Rosanna Mondelli*

Dipartimento di Scienze Molecolari Agroalimentari, Sezione di Chimica, Università degli Studi di Milano, Via Celoria 2, Milan 20133, Italy



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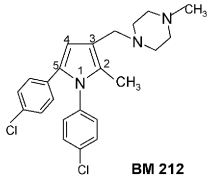
Importance of the Thiomorpholine Introduction in New Pyrrole Derivatives as Antimycobacterial Agents Analogues of BM 212

Mariangela Biava,[a,*] Giulio Cesare Porretta,[a] Delia Deidda,[b] Raffaello Pompei,[b] Andrea Tafi[c] and Fabrizio Manetti[c]

[a]*Dipartimento di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive, Università 'La Sapienza', P. le A Moro 5, 00185 Rome, Italy*
[b]*Cattedra di Microbiologia Applicata, Facoltà di Scienze Matematiche Fisiche Naturali, Università degli Studi di Cagliari, Via Porcell 4, 09124 Cagliari, Italy*
[c]*Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, Via Aldo Moro snc, 53100 Siena, Italy*

Previously we have identified **BM 212**, a pyrrole derivative with good in vitro activity against *mycobacteria* and *candidae*. These findings prompted us to prepare new pyrrole derivatives in the hope of increasing the activity. The microbiological data showed interesting in vitro activity against *Mycobacterium tuberculosis* and atypical mycobacteria.



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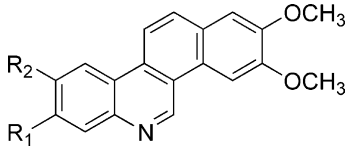
2,3-Dimethoxybenzo[*i*]phenanthridines: Topoisomerase I-Targeting Anticancer Agents

Dajie Li,[a] Baoping Zhao,[a] Sai-Peng Sim,[b] Tsai-Kun Li,[b] Angela Liu,[b] Leroy F. Liu[b,c] and Edmond J. LaVoie[a,c,*]

[a]*Department of Pharmaceutical Chemistry, Rutgers, The State University of New Jersey, 160 Frelinghuysen Road, 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_2 = H, and R_1 = NH_2, CN, CH_2OH, OBn, OCH_3, OH, or $NHCOCH_3$ and where R_1,R_2 = $–OCH_2O–$.



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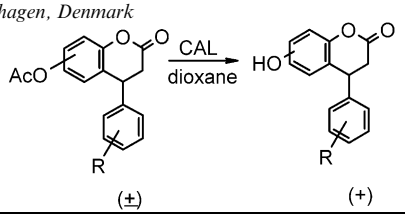
Synthetic and Novel Biocatalytic Resolution Studies on (±)-5/6/7-Acetoxy-4-aryl-3,4-dihydrocoumarins

Ishwar Singh,[a] Ashok K. Prasad,[a] Ajendra K. Sharma,[a,d] Rajendra K. Saxena,[b] Carl E. Olsen,[c] Ashok L. Cholli,[d] Lynne A. Samuelson,[d] Jayant Kumar,[d] Arthur C. Watterson[d] and Virinder S. Parmar[a,d,*]

[a]*Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007, India*
[b]*Department of Microbiology, University of Delhi South Campus, New Delhi-110 021, India*
[c]*Chemistry Department, Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Copenhagen, Denmark*
[d]*INSET, Department of Chemistry, University of Massachusetts, One University Avenue, Lowell, MA 01854, USA*

Eleven (±)-5/6/7-acetoxy-4-aryl-3,4-dihydrocoumarins have been synthesised by the coupling of appropriate analogues of cinnamic acid and phenol, followed by the acetylation of the resulting hydroxycoumarin. As a rare example of phenolic acetoxy group serving as a remote handle for chiral recognition, *Candida antarctica* lipase (CAL)-catalysed deacetylation of these acetoxycoumarins in dioxane occurred with moderate enantioselectivity.



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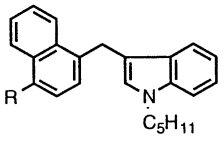
3-Indolyl-1-naphthylmethanes: New Cannabimimetic Indoles Provide Evidence for Aromatic Stacking Interactions with the CB_1 Cannabinoid Receptor

John W. Huffman,[a,*] Ross Mabon,[a] Ming-Jung Wu,[a] Jianzhong Lu,[a] Richard Hart,[b] Dow P. Hurst,[b] Patricia H. Reggio,[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 Biochemistry, Kennesaw State University, 1000 Chastain Road, Kennesaw, GA 30144, USA*
[c]*Department of Pharmacology and Toxicology, Medical College of Virginia Campus of Virginia Commonwealth University, Richmond, VA 23298-0613, USA*

The synthesis and pharmacology of 3-indolyl-1-naphthylmethanes (R = H, CH_3, OCH_3) and related compounds are described. These compounds have CB_1 receptor affinities similar to those of 3-(1-naphthoyl)indoles.



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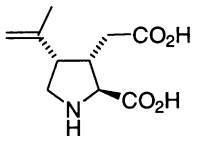
The Structural Basis for Kainoid Selectivity at AMPA Receptors Revealed by Low-Mode Docking Calculations

Luis M. Carcache, Jonierr Rodriguez and Kathleen S. Rein*

Department of Chemistry, Florida International University, 11200 SW 8th St., Miami, FL 33199, USA

Low-mode docking calculations for kainoids within the S1S2 binding site of iGluR2 are reported.



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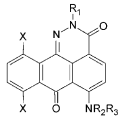
Synthesis and Biological Evaluation of 2,7-Dihydro-3*H*-dibenzo[*de*,*h*]cinnoline-3,7-dione Derivatives, a Novel Group of Anticancer Agents Active on a Multidrug Resistant Cell Line

Barbara Stefańska,[a] Małgorzata Arciemiuk,[a] Maria M. Bontemps-Gracz,[a] Maria Dzieduszycka,[a] Agnieszka Kupiec,[a] Sante Martelli[b] and Edward Borowski[a,*]

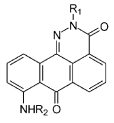
[a]*Department of Pharmaceutical Technology and Biochemistry, Gdańsk University of Technology, 80-952 Gdańsk, Poland*
[b]*Department of Chemistry, University of Camerino, 62033 Camerino, Italy*

Derivatives of 2,7-dihydro-3*H*-dibenzo[*de*,*h*]cinnoline-3,7-diones (structures **A** and **B**) have been synthesized and evaluated for their cytotoxicity against murine leukemia and human leukemia sensitive and MDR cell lines.



A

where: R_1 = H, alkylaminoalkyl
R_2 = H, CH_3
R_3 =H, alkylaminoalkyl
X = H, OH



B

where: R_1 = H, alkylaminoalkyl
R_2 = H, alkylaminoalkyl

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Non-antibiotic Antibacterial Activity of Dodecyl Gallate

Isao Kubo,* Ken-ichi Fujita, Ken-ichi Nihei and Noriyoshi Masuoka

Department of Environmental Science, Policy and Management, University of California, Berkeley, CA 94720-3112, USA

Dodecyl gallate was found to possess antibacterial activity specifically against Gram-positive bacteria, in addition to its potent antioxidant activity. The time–kill curve study indicates that this gallate exhibits bactericidal activity against methicillin resistant *Staphylococcus aureus* (MRSA) strains. Dodecyl gallate inhibited oxygen consumption in whole cells and oxidation of NADH in membrane preparation. The antibacterial activity of this gallate comes in part from its ability to inhibit the membrane respiratory chain. As far as alkyl gallates are concerned, their antimicrobial spectra and potency depend in part on the hydrophobic portion of the molecule.

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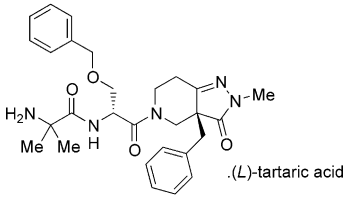
Pyrazolinone-piperidine Dipeptide Growth Hormone Secretagogues (GHSs): Discovery of Capromorelin

Philip A. Carpino*, Bruce A. Lefker, Steven M. Toler, Lydia C. Pan, John R. Hadcock, Ewell R. Cook, Joseph N. DiBrino, Anthony M. Campeta, Shari L. DeNinno, Kristin L. Chidsey-Frink, William A. Hada, John Inthavongsay, F. Michael Mangano, Michelle A. Mullins, David F. Nickerson, Oicheng Ng, Christine M. Pirie, John A. Ragan, Colin R. Rose, David A. Tess, Ann S. Wright, Li Yu, Michael P. Zawistoski, Paul A. DaSilva-Jardine, Theresa C. Wilson and David D. Thompson

Pfizer Global Research and Development, Groton Labs, MS8220-3004, Eastern Point Rd, Groton, CT 06340, USA

The discovery, synthesis and PK characterization of capromorelin (**5**, CP-424391-18), a novel dipeptide GHS, are described.



5 (CP-424391-18)

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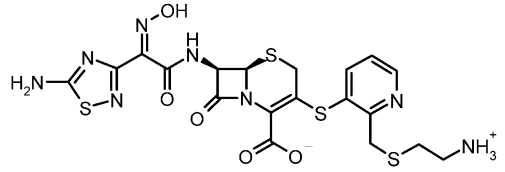
Relationships Between Structure, Antibacterial Activity, Serum Stability, Pharmacokinetics and Efficacy in 3-(Heteroarylthio)cephems. Discovery of RWJ-333441 (MC-04,546)

Tomasz Glinka,* Keith Huie, Aesop Cho, Maria Ludwikow, Johanne Blais, David Griffith, Scott Hecker and Michael Dudley

Essential Therapeutics, Inc., 850 Maude Ave., Mountain View, CA 94043, USA

In a series of 3-heteroarylthio cephalosporins, stability toward enzymatic decomposition in serum was very sensitive to structural modifications. The 3-pyridylthio analogue RWJ-333441 displays high serum stability, excellent activity against gram-positive bacteria (including MRSA), and good pharmacokinetic properties.



RWJ-333441 (MC-04,546)

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Inhibition and Kinetics of *Mycobacterium Tuberculosis* and *Mycobacterium Smegmatis* Mycothiol-*S*-conjugate Amidase by Natural Product Inhibitors

Gillian M. Nicholas,[a] Lisa L. Eckman,[a] Gerald L. Newton,[b] Robert C. Fahey,[b] Satyajit Ray[a] and Carole A. Bewley[a,*]

[a]*Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892-0820, USA*
[b]*Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA 92093, USA*

Identification of 13 natural products that inhibit the *Mycobacterium tuberculosis* and *Mycobacterium smegmatis* detoxification enzyme mycothiol-*S*-conjugate amidase (MCA) is reported. Kinetics experiments conducted with four compounds representing four different structural classes of inhibitors demonstrate that bromotyrosine-derived alkaloids containing a centrally located amide group compete directly with the substrate mycothiol bimane (MSmB) for MCA activity, while natural products that are likely to chelate metals are non-competitive inhibitors. Our results suggest that MCA is a metalloenzyme.

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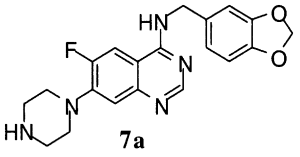
Structure–Activity Relationships of 6-Fluoroquinazolines: Dual-Acting Compounds with Inhibitory Activities Toward Both TNF-α Production and T Cell Proliferation

Masanori Tobe, Yoshiaki Isobe, Hideyuki Tomizawa, Takahiro Nagasaki, Fumihiro Obara and Hideya Hayashi*

Pharmaceuticals and Biotechnology Laboratory, Japan Energy Corporation, Toda-shi, Saitama 335-8502, Japan

Compound **7a** exhibited an anti-inflammatory effect as well as suppressing effects toward both TNF-α production and T cell proliferation.



7a

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Quantitative Structure–Activity Relationships of Phenolic Compounds Causing Apoptosis

Corwin Hansch,[a,*] Benjamin Bonavida,[b] Ali R. Jazirehi,[b] J. John Cohen,[c] Cheri Milliron[c] and Alka Kurup[a]

[a]*Department of Chemistry, Pomona College, 645 N. College Ave., Claremont, CA 91711, USA*
[b]*UCLA School of Medicine, Department of Microbiology, Immunology and Molecular Genetics, University of California at Los Angeles, 10833 LeConte Ave., Los Angeles, CA 90095, USA*
[c]*Department of Immunology, University of Colorado Medical School, Mail Stop B-184, 4200 E. 9th Ave., Denver, CO 80262, USA*

A QSAR study of a variety of phenolic compounds with apoptotic activity imply the significance of characterization in the development of new agents for cancer therapy.

Bioorg. Med. Chem. 11 (2003) 621

Searching for Allosteric Effects Via QSAR. Part II

Rajni Garg, Alka Kurup, Suresh B. Mekapati and Corwin Hansch*
Department of Chemistry, Pomona College, Claremont, CA 91711, USA

$-CMR + CMR^2 \Rightarrow$ Allosteric Interaction
(CMR is calculated molar refractivity)

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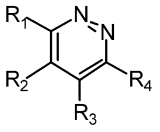
Estrogenic Diazenes: Heterocyclic Non-steroidal Estrogens of Unusual Structure with Selectivity for Estrogen Receptor Subtypes

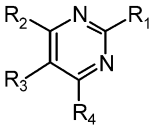
Usha Ghosh,[a] Deshanie Ganessunker,[b] Viswajanani J. Sattigeri,[a] Kathryn E. Carlson,[a] Deborah J. Mortensen,[a] Benita S. Katzenellenbogen[b] and John A. Katzenellenbogen[a,*]

[a]*Department of Chemistry, University of Illinois, Urbana, IL 61801, USA*
[b]*Department of Molecular and Integrative Physiology, University of Illinois, Urbana, IL 61801, USA*

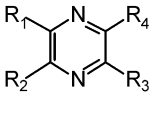
Various di- and triarylsubstituted diazenes were prepared and evaluated for their binding affinity and transcriptional activity for estrogen receptor subtypes alpha and beta. Certain analogues show significant selectivity in terms of affinity, potency and efficacy.



Pyridazine



Pyrimidine



Pyrazine