Graphical Abstracts

Evaluation of the Cytotoxic Activity of Polyethers Isolated from *Laurencia*

Bioorg. Med. Chem. 6 (1998) 2237

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We report the conformational analysis of several polyether triterpenes with squalene carbon skeleton which exhibited a significant cytotoxic activity using a Monte Carlo conformational search and spectroscopical data.

Ligand Binding to I_2 Imidazoline Receptor: The Role of Lipophilicity in Quantitative Structure–Activity Relationship Models

Bioorg. Med. Chem. 6 (1998) 2245

M. Pigini,[a] P. Bousquet,[b] L. Brasili,[c] A. Carrieri,[d] R. Cavagna,[b] M. Dontenwill,[b] F. Gentili,[a] M. Giannella,[a] F. Leonetti,[d] A. Piergentili,[a] W. Quaglia[a] and A. Carotti[d]

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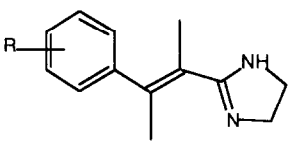
[d]*Dipartimento Farmaco-Chimico, Università degli Studi, via E. Orabona 4, 70125 Bari, Italy*

The important role of lipophilicity on the I_2 imidazoline receptor binding of a large series of tracizoline (**2**) congeners has been pointed out by means of 2-D and 3-D QSAR (CoMFA) studies. In addition, a comprehensive CoMFA model, based on about sixty I_2 ligands, has allowed the detection and location, at the 3-D level, of the key physicochemical interactions governing the receptor ligand binding.



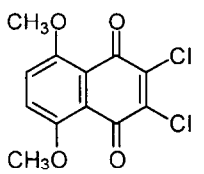
2

Synthesis and Antiplatelet, Antiinflammatory, and Antiallergic Activities of Substituted 3-Chloro-5,8-dimethoxy-1,4-naphthoquinone and Related Compounds

Bioorg. Med. Chem. 6 (1998) 2261

Li-Jiau Huang,[a] Fu-Chaio Chang,[a] Kuo-Hsiung Lee,[b] Jih-Pyang Wang,[c] Che-Ming Teng[d] and Sheng-Chu Kuo[a]

[a]*Graduate Institute of Pharmaceutical Chemistry, China Medical College, Taichung, Taiwan*
[b]*Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599, U.S.A.*
[c]*Department of Medical Research, Taichung Veterans General Hospital, Taichung, Taiwan*
[d]*Pharmacological Institute, College of Medicine, National Taiwan University, Taiwan*



4

Synthesis and antiplatelet, antiinflammatory, and antiallergic activities of derivatives of 2,3-dichloro-5,8-dimethoxy-1,4-naphthoquinone (**4**) are described.

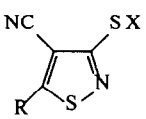
Synthesis and Antiviral Activity of a New Series of 4-Isothiazolecarbonitriles

Bioorg. Med. Chem. 6 (1998) 2271

Christian C. C. Cutrí,[a] Adriana Garozzo,[b] Maria A. Siracusa,[a] Maria C. Sarvá,[a] Gianna Tempera,[b] Ernesto Geremia,[c] Maria R. Pinizzotto[b] and Francesco Guerrera[a]

[a]*Dipartimento di Scienze Farmaceutiche, Universitá di Catania, Viale A. Doria 6, 95125 Catania, Italy*
[b]*Dipartimento di Scienze Microbiologiche e Ginecologiche, Universitá di Catania, Via Androne 81, 95124 Catania, Italy*
[c]*Istituto di Biologia Generale, Universitá di Catania, Via Androne 81, 95124 Catania, Italy*

New 4-isothiazolecarbonitrile derivatives were synthesized and tested as potential antiviral agents against both RNA and DNA viruses. Our compounds were effective as inhibitors of enteroviruses (polio 1 and ECHO 9).



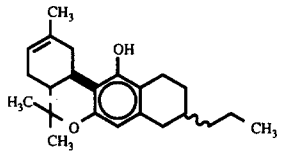
Bioorg. Med. Chem. 6 (1998) 2281

Synthesis of a Tetracyclic, Conformationally Constrained Analogue of Δ^8-THC

John W. Huffman and Shu Yu

H. L. Hunter Chemistry Laboratory, Clemson University, Clemson, SC 29634-1905, USA

A conformationally constrained analogue of Δ^8-THC, in which C2 and C2′ are connected has been synthesized. The compound shows weak affinity for the cannabinoid brain receptor ($K_i = 703 \pm 98$ nM).

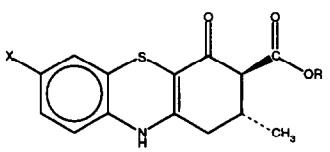


Bioorg. Med. Chem. 6 (1998) 2289

Synthesis, Characterization, and Anticonvulsant Activity of Enaminones. Part 5: Investigations on 3-Carboalkoxy-2-methyl-2,3-dihydro-1*H*-phenothiazin-4[10*H*]-one Derivatives

Mia L. Laws,[a] Ralph R. Roberts,[b] Jesse M. Nicholson,[c] Raymond Butcher,[c] James P. Stables,[d] Angela M. Goodwin,[e] Carlynn A. Smith[e] and K.R. Scott[e]

[a]*DuPont Merck Company, Chemical & Physical Sciences, R & D Experimental Station, E-500 - 4205B Route 141, Wilmington, DE 19880-0500, USA*
[b]*Science Research Laboratory, 3M Corporate Research, 3M Center, Building 201-2N-21, St. Paul, MN 55144-1000, USA*
[c]*Department of Chemistry, Graduate School of Arts and Sciences, Howard University, Washington, DC 20059, USA*
[d]*Epilepsy Branch, Division of Convulsive, Developmental and Neuromuscular Disorders, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892, USA*
[e]*Department of Pharmaceutical Sciences, College of Pharmacy, Nursing and Allied Health Sciences, Howard University, Washington, DC 20059, USA*



4a–k
R = CH_3, C_2H_5, $C(CH_3)_3$
X = H, Cl, Br, CH_3

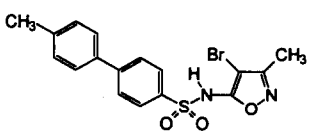
Bioorg. Med. Chem. 6 (1998) 2301

The Discovery and Structure–Activity Relationships of Non-peptide, Low Molecular Weight Antagonists Selective for the Endothelin ET_B Receptor

Ming Fai Chan, Adam Kois, Erik J. Verner, Bore G. Raju, Rosario S. Castillo, Chengde Wu, Ilya Okun, Fiona D. Stavros and V. N. Balaji

ImmunoPharmaceutics, Inc. (a subsidiary of Texas Biotechnology Corp.), 11011 Via Frontera, San Diego, CA 92127, USA

The SAR of several classes of ET_B selective antagonists were described. The best compound **4h** has IC_{50} of 17 nM and ET_B selectivity of 290.



4h

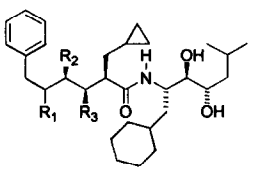
Bioorg. Med. Chem. 6 (1998) 2317

Novel Small Renin Inhibitors Containing 4,5- or 3,5-Dihydroxy-2-substituted-6-phenylhexanamide Replacements at the P_2–P_3 Sites

Grace L. Jung, Paul C. Anderson, Murray Bailey, Monique Baillet, Gary W. Bantle, Sylvie Berthiaume, Pierre Lavallée, Montse Llinas-Brunet, Bounkham Thavonekham, Diane Thibeault and Bruno Simoneau

Bio-Méga Research Division, Boehringer Ingelheim (Canada) Ltd, 2100 rue Cunard, Laval, Québec, Canada H7S 2G5

Most potent diastereomers **1a** and **2c** have a molecular weight of only 503 and IC_{50} values of 23 and 20 nM in a human plasma renin assay at pH 6.0.



1a: R_1 = (*S*)-OH, R_2 = OH, R_3 = H
2c: R_1 = (*R*)-OH, R_2 = H, R_3 = OH

Bioorg. Med. Chem. 6 (1998) 2337

Structural Basis for Selective Inhibition of COX-2 by Nimesulide

Gabriel F. Fabiola,[a] Vasantha Pattabhi[a] and Kuppuswamy Nagarajan[b]

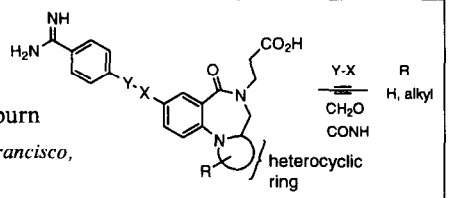
[a]*Department of Crystallography & Biophysics, University of Madras, Madras 600 025, India*
[b]*Recon Limited, Bangalore 560 076, India*

Bioorg. Med. Chem. 6 (1998) 2345

Preparation and Biological Activity of Novel Tricyclic GPIIb/IIIa Antagonists

Kirk D. Robarge, Michael S. Dina, Todd C. Somers, Arthur Lee, Thomas E. Rawson, Alan G. Olivero, Maureen H. Tischler, Robert R. Webb, II, Kenneth J. Weese, Ignacio Aliagas, Brent K. Blackburn

Department of Bioorganic Chemistry, Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080, USA



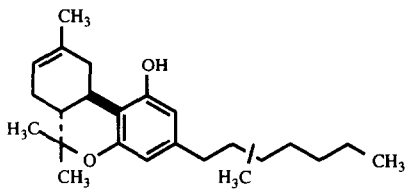
Novel tricyclic nonpeptidal GPIIb/IIIa antagonists have been prepared and evaluated in vitro as antagonists of fibrinogen binding to the purified GPIIb/IIIa receptor and as inhibitors of platelet aggregation. The work presented demonstrates the robustness of the benzodiazepinedione (BZDD) scaffold, which can be functionalized at the N^1–C^2 amide as well as at C^7, to provide structural diversity and allow optimization of the physiochemical and pharmacological properties ot the BZDD based GPIIb/IIIa antagonists.

Bioorg. Med. Chem. 6 (1998) 2383

Synthesis and Pharmacology of the Isomeric Methylheptyl-Δ^8-tetrahydrocannabinols

John W. Huffman,[a] John Liddle,[a] Sammy G. Duncan, Jr.,[a] Shu Yu,[a] Billy R. Martin[b] and Jenny L. Wiley[b]

[a]*Howard L. Hunter Laboratory, Clemson University, Clemson, SC 29634-1905, USA*
[b]*Department of Pharmacology and Toxicology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298-0613, USA*



The synthesis of eleven isomeric monomethylheptyl-Δ^8-tetrahydrocannabinols has been carried out. Both epimers of the 1′-, 2′- and 3′-methylheptyl analogues were considerably more potent than Δ^8-THC, both in vitro and in vivo.

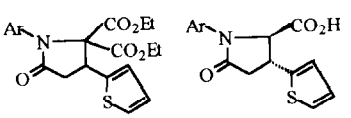
Bioorg. Med. Chem. 6 (1998) 2397

Synthesis of Some Thieno Gamma Lactam Monocarboxylic Acids with High Antibacterial Activity: A New Look at an Old Molecular System

Gandhi K. Kar,[a] Bidhan C. Roy,[a] Sujit Das Adhikari,[a] Jayanta K. Ray[a] and Nitosh K. Brahma[b]

[a]*Department of Chemistry, Indian Institute of Technology, Kharagpur 721 302, West Bengal, India*
[b]*Department of Chemical Engineering, Indian Institute of Technology, Kharagpur 721 302, West Bengal, India*

Synthesis and antibacterial activity of some novel monocyclic gamma lactams are reported.

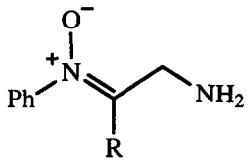


Bioorg. Med. Chem. 6 (1998) 2405

Syntheses of Amino Nitrones. Potential Intramolecular Traps for Radical Intermediates in Monoamine Oxidase-catalyzed Reactions

Boyu Zhong, Xingliang Lu and Richard B. Silverman

Department of Chemistry and Department of Biochemistry, Molecular Biology, and Cell Biology, Northwestern University, Evanston, IL 60208-3113, USA



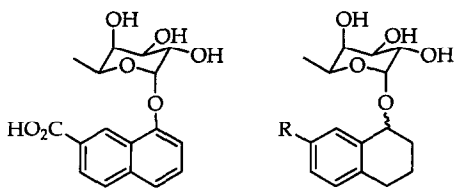
Syntheses of seven different amino nitrones, three acyclic, and four cyclic analogues were attempted. The acyclic analogues were unstable. One of the cyclic analogues was very stable, one stable only in organic solvents, and one stable below pH 6.5. None was found useful to detect radical intermediates in monoamine oxidase, but the approach should be viable for use with other enzymes.

Bioorg. Med. Chem. 6 (1998) 2421

The Design, Synthesis, and Evaluation of Novel Conformationally Rigid Analogues of Sialyl Lewis[x]

Paul V. Murphy,[a] Rod E. Hubbard,[a] David T. Manallack,[b] Ruth E. Wills,[b] John G. Montana[b] and Richard J. K. Taylor[a]

[a]*Department of Chemistry, University of York, Heslington, York YO1 5DD, U.K.*
[b]*Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE, U.K.*



R = $CONHCH_2CO_2H$
R = $CONHCH(Me)CO_2H$ (*R*)
R = $CONHCH(Me)CO_2H$ (*S*)
R = $CH_2CH_2CH_2CO_2H$
R = $CH_2CH_2C(Me)_2CO_2H$
R = $C{\equiv}CC(Me)_2CO_2H$
R = CO_2H
R = H

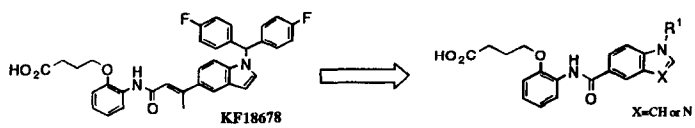
Bioorg. Med. Chem. 6 (1998) 2441

Indole and Benzimidazole Derivatives as Steroid 5α-Reductase Inhibitors in the Rat Prostate

Hitoshi Takami, Nobuyuki Kishibayashi, Akio Ishii and Toshiaki Kumazawa

Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd, Nagaizumi, Shizuoka 411-8731, Japan

Indole and benzimidazole derivatives, deleting the link unit between the benzene ring and indole skeleton of parent compound KF18678, were synthesized and evaluated for inhibitory activity on rat prostatic 5α-reductase. Several potent compounds showed IC_{50} values of 10^{-8}–10^{-9} M order.



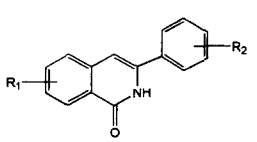
Bioorg. Med. Chem. 6 (1998) 2449

Synthesis and Comparative Molecular Field Analysis (CoMFA) of Antitumor 3-Arylisoquinoline Derivatives

Won-Jea Cho,[a] Eui-Ki Kim,[a] Myun-Ji Park,[a] Sang-Un Choi,[b] Chong-Ock Lee,[b] Seung Hoon Cheon,[a] Bo-Gil Choi[a] and Byung-Ho Chung[a]

[a]*College of Pharmacy, Chonnam National University, Yongbong-dong, Buk-gu, Kwangju 500-757, Korea*
[b]*Korea Research Institute Chemical Technology, DaeJeon, Korea*

A series of 3-arylisoquinoline derivatives was synthesized and cytotoxicity against human tumor cell evaluated, and the comparative molecular field analysis (CoMFA) was investigated.



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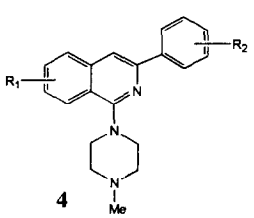


4

Hybrid Peptides Constructed from RES-701-1, an Endothelin B Receptor Antagonist, and Endothelin; Binding Selectivity for Endothelin Receptors and their Pharmacological Activity

Bioorg. Med. Chem. 6 (1998) 2459

Kenji Shibata,[a] Toshiyuki Suzawa,[a] Tetsuji Ohno,[b] Koji Yamada,[b] Takeo Tanaka,[a] Eiji Tsukuda,[a] Yuzuru Matsuda[a] and Motoo Yamasaki[a]

[a]*Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, 3-6-6, Asahi-machi, Machida-shi, Tokyo 194-8533, Japan*
[b]*Drug Discovery Research Laboratories, Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd, 1188, Shimotogari, Nagaizumi-cho, Sunto-gun, Shizuoka 411-8731, Japan*

We have found four types of ET receptor-binding peptides; (1) ET_B-selective agonist with weak ET_A antagonism (KT7421); (2) ET_B-selective antagonist with weak ET_A antagonism (KT7539); (3) ET_B agonist with potent ET_A antagonism (KT7538); and (4) non-selective ET_A/ET_B antagonist (KT7540).

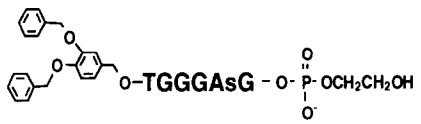
H-GNWHGTAPDWVYFAHLX$_1$X$_2$IW-OH
X$_1$; Asp, X$_2$; Ile: KT7421
X$_1$; Thr, X$_2$; 2-thienyl-Ala: KT7539
X$_1$; Thr, X$_2$; 2-cyclohexyl-Ala: KT7538
X$_1$; Ser, X$_2$; Met: KT7540

Biologically Active Oligodeoxyribonucleotides. Part 11: The Least Phosphate-modification of Quadruplex-forming Hexadeoxyribonucleotide TGGGAG, Bearing 3′- and 5′-End-modification, with Anti-HIV-1 Activity

Bioorg. Med. Chem. 6 (1998) 2469

Makoto Koizumi,[a] Rika Koga,[a] Hitoshi Hotoda,[a] 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,e] and Kaoru Shimada[d,f]

[a]*Exploratory Chemistry Research Lab., Sankyo Co., Ltd, Tokyo 140, Japan*
[b]*Biological Research Lab., Sankyo Co., Ltd, Tokyo 140, Japan*
[c]*Analytical and Metabolic Research Lab., Sankyo Co., Ltd, Tokyo 140, Japan*
[d]*Department of Infectious Diseases, Institute of Medical Science, University of Tokyo, Tokyo 108, Japan*
[e]*Department of Infection Control and Prevention, The University of Tokyo Hospital, Tokyo 113, Japan*
[f]*Tokyo Senbai Hospital, Tokyo 108, Japan*

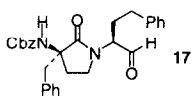


Structure-Based Design, Synthesis and Evaluation of Conformationally Constrained Cysteine Protease Inhibitors

Bioorg. Med. Chem. 6 (1998) 2477

Karl A. Scheidt,[a,b] William R. Roush,[a,b] James H. McKerrow,[c] Paul M. Selzer,[c] Elizabeth Hansell,[c] Philip J. Rosenthal[d]

[a]*Department of Chemistry, Indiana University, Bloomington, IN 47405, USA*
[b]*Department of Chemistry, University of Michigan, Ann Arbor, MI 48109, USA*
[c]*Department of Pathology, University of California, San Francisco, CA 94121, USA*
[d]*Department of Medicine, University of California, San Francisco, CA 94143, USA*



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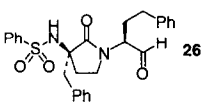
	IC$_{50}$ (μM)
cruzain	0.6
cathepsin B	1
leishmania cpB	0.03



26

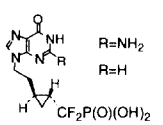
	IC$_{50}$ (μM)
cruzain	2
cathepsin B	1
leishmania cpB	0.02
falcipain	0.05

Synthesis of 1,1-Difluoro-5-(1*H*-9-purinyl)-2-pentenylphosphonic Acids and the Related Methano Analogues. Remarkable Effect of the Nucleobases and the Cyclopropane Rings on Inhibitory Activity Toward Purine Nucleoside Phosphorylase

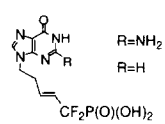
Bioorg. Med. Chem. 6 (1998) 2495

Tsutomu Yokomatsu,[a] Hiroshi Abe,[a] Mutsumi Sato,[a] Kenji Suemune,[a] Taro Kihara,[b] Shinji Soeda,[b] Hiroshi Shimeno[b] and Shiroshi Shibuya[a]

[a]*School of Pharmacy, Tokyo University of Pharmacy & Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan*
[b]*Faculty of Pharmaceutical Science, Fukuoka University, 8-19-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan*



R=NH$_2$ Ki = 28.2 nM; IC$_{50}$ =390 nM
R=H Ki = 8.8 nM; IC$_{50}$ = 70 nM



R=NH$_2$ Ki = 20.4 nM; IC$_{50}$ = 170 nM
R=H Ki = 11.4 nM; IC$_{50}$ = 280 nM