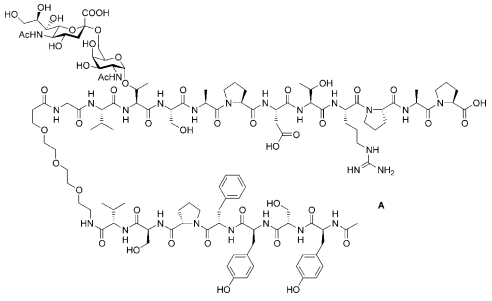
Bioorg. Med. Chem. 10 (2002) 3085

Synthesis of Tumor-Associated Glycopeptide Antigens

Constanze Brocke and Horst Kunz

Institut für Organische Chemie, Johannes Gutenberg-Universität Mainz, Duesbergweg 10-14, 55128 Mainz, Germany

Different strategies for the synthesis of tumor-associated glycopeptides such as **A** are discussed in this review.



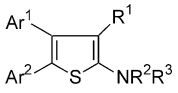
Bioorg. Med. Chem. 10 (2002) 3113

Design, Synthesis and Bioactivities of Novel Diarylthiophenes: Inhibitors of Tumor Necrosis Factor-α (TNF-α) Production

Masakazu Fujita, Tetsuya Hirayama and Naoko Ikeda

Pharmaceutical Research Laboratories, Nikken Chemicals Co., Ltd., 1-346, Kitabukuro-cho, Saitama-shi, Saitama 330-0835, Japan

The design, synthesis and SAR of novel diarylthiophene derivatives were performed. These compounds were designed by structural hybridization of TNF-α production inhibitors bearing 4-fluorophenyl and 4-pyridyl groups such as FR133605, FR167653 and SB210313, and 6-acetyl-3-ethoxycarbonyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine (**1**) found previously by us. As a result, several compounds were more potent in vitro than FR133605 against TNF-α production stimulated with lipopolysaccharide (LPS).



7-17

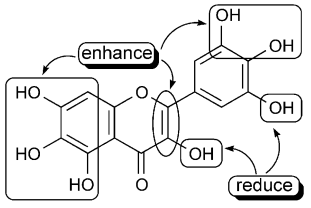
Bioorg. Med. Chem. 10 (2002) 3123

Structural Requirements of Flavonoids for Inhibition of Antigen-Induced Degranulation, TNF-α and IL-4 Production from RBL-2H3 Cells

Hisashi Mastuda, Toshio Morikawa, Kazuho Ueda, Hiromi Managi and Masayuki Yoshikawa

Kyoto Pharmaceutical University, Misasagi, Yamashina-ku, Kyoto 607-8412, Japan

To clarify the structure–activity relationships of flavonoids for antiallergic activity, the inhibitory effects of 52 flavonoids on the release of β-hexosaminidase, as a marker of degranulation of RBL-2H3 cells, were examined. Among them, luteolin ($IC_{50} = 3.0\,\mu M$), diosmetin (2.1 μM), and fisetin (3.0 μM) were found to show potent inhibitory activity, and the some additional and revised structural requirements for the activity were clarified. In addition, several flavonoids, that is, apigenin, luteolin, diosmetin, fisetin, and quercetin, inhibited the antigen-IgE-mediated TNF-α and IL-4 production from RBL-2H3 cells, both of which participate in the late phase of type I allergic reactions.



Bioorg. Med. Chem. 10 (2002) 3129

Biological Effects of G1 Phase Arrest Compound, Sesquicillin, in Human Breast Cancer Cell Lines

Ha-Won Jeong,[a] Ho-Jae Lee,[a] Yung-Hee Kho,[a] Kwang-Hee Son,[a] Mi Young Han,[a] Jong-Seok Lim,[a] Mi-Young Lee,[a] Dong Cho Han,[a] Ji-Hong Ha[b] and Byoung-Mog Kwon[a]

[a]*Korea Research Institute of Bioscience and Biotechnology, PO Box 115, Yoosung, Taejon 305-600, Republic of Korea*
[b]*Department of Genetic Engineering, Kyungpook National University, Taegu 702-701, Republic of Korea*

Sesquicillin, isolated from fumgal fermentation broth, strongly induced G1 phase arrest in human breast cancer cells. During G1 phase arrest, the expression level of cyclin D1, cyclin A, and cyclin E was decreased, and the expression of CDK inhibitor protein p21, was increased in a time-dependent manner in a breast cancer cell MCF-7

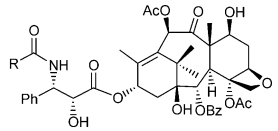
Bioorg. Med. Chem. 10 (2002) 3135

Synthesis, Biological Activity and Receptor-Based 3-D QSAR Study of 3′-*N*-Substituted-3′-*N*-debenzoylpaclitaxel Analogues

Eun Joo Roh,[a,b] Deukjoon Kim,[b] Jun Yong Choi,[c] Bon-Su Lee,[c] Chong Ock Lee[d] and Choong Eui Song[a]

[a]*Life Sciences Division, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul, 130-650, Republic of Korea*
[b]*College of Pharmacy, Seoul National University, Shinrim-Dong, Kwanak-ku, Seoul, 152-742, Republic of Korea*
[c]*Department of Chemistry, Inha University, Yonghyun-Dong 253, Nam-ku, Inchon, 402-751, Republic of Korea*
[d]*Screening Center, Korea Research Institute of Chemical Technology, PO Box 107, Yusong, Daejeon, 305-606, Republic of Korea*

A series of the 3′-*N*-substituted-3′-*N*-debenzoylpaclitaxel analogues were synthesized and investigated for their 3-D QSAR by using CoMFA (comparative molecular field analysis) study. The CoMFA model obtained from receptor(microtubule)-paclitaxel binding structure displays an excellent predictive power to forecast the biological activity of new 3′-*N*-substituted-3′-*N*-debenzoylpaclitaxel analogues as well as the ability to explain the activity of the known paclitaxel analogues.



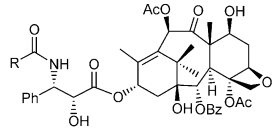
Bioorg. Med. Chem. 10 (2002) 3145

Structure–Activity Relationship Study at the 3′-*N*-Position of Paclitaxel: Synthesis and Biological Evaluation of 3′-*N*-Acyl-Paclitaxel Analogues

Eun Joo Roh,[a,b] Deukjoon Kim,[b] Chong Ock Lee,[c] Sang Un Choi[c] and Choong Eui Song[a]

[a]*Life Sciences Division, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul 130-650, Republic of Korea*
[b]*College of Pharmacy, Seoul National University, Shinrim-Dong, Kwanak-ku, Seoul 152-742, Republic of Korea*
[c]*Screening Center, Korea Research Institute of Chemical Technology, PO Box 107, Yusong, Daejeon 305-606, Republic of Korea*

A series of 3′-*N*-acyl-paclitaxel analogues were synthesized and their cytotoxicity in vitro against several human tumor cell lines was examined. It has been shown that distinct correlation between activity and *N*-acyl-substituent. It was found that appropriate size of *N*-acyl group was indispensable for cytotoxicity, and moreover, the presence of conjugated double and triple bond to *N*-carbonyl generally resulted in increase of activity.

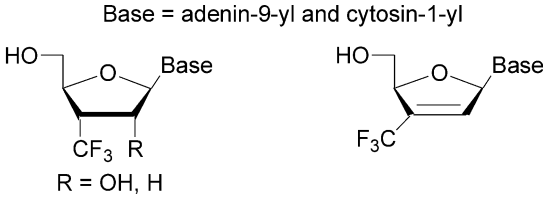


Bioorg. Med. Chem. 10 (2002) 3153

Synthesis and Studies of 3′-*C*-trifluoromethyl Nucleoside Analogues Bearing Adenine or Cytosine as the Base

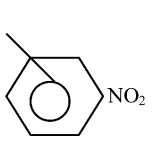
Frédéric Jeannot,[a] Gilles Gosselin,[a,b] David Standring,[c] Martin Bryant,[c] Jean-Pierre Sommadossi,[c] Anna Giulia Loi,[d] Paolo La Colla[d] and Christophe Mathé[a]

[a]*Laboratoire de Chimie Organique Biomoléculaire de Synthèse, UMR 5625 CNRS-UM II, Université Montpellier II, case courrier 008, Place Eugène Bataillon, 34095 Montpellier, cedex 5, France*
[b]*Laboratoire Coopératif Novirio-CNRS-Université Montpellier II, Université Montpellier II, case courrier 008, Place Eugène Bataillon, 34095 Montpellier, cedex 5, France*
[c]*Novirio-Pharmaceuticals, Inc., 125 Cambridge Park Drive, Cambridge, MA 02140, USA*
[d]*Dipartimento di Biologia Sperimentale, Università degli Studi di Cagliari, 09042 Cagliari, Italy*



Bioorg. Med. Chem. 10 (2002) 3163

Use of the PI Index in Predicting Toxicity of Nitrobenzene Derivatives



Padmakar V. Khadikar,[a] Sneha Karmarkar,[a] Shalini Singh[b] and Anjali Shrivastava[c]

[a]*Research Division, Laxmi Fumigation and Pest Control Pvt Ltd., 3, Khatipura, Indore 452 007, India*
[b]*Department of Chemistry, A.P.S. University, Rewa 480003, India*
[c]*Department of Chemistry, Govt. Holkar Model and Autonomous College, Indore 452 001, India*

We have used the PI Index for predicting toxicity of nitrobenzene derivatives in that we have observed that combination of the PI Index with other distance based topological indices gave excellent results. The predictive potential of the proposed models is discussed on the basis of cross-validation and other related parameters.

Bioorg. Med. Chem. 10 (2002) 3171

Enantioselective Formation of (*R*)-9-HPODE and (*R*)-9-HPOTrE in Marine Green Alga *Ulva Conglobata*

Yoshihiko Akakabe, Kenji Matsui and Tadahiko Kajiwara

Department of Biological Chemistry, Faculty of Agriculture, Yamaguchi University, 1677-1 Yoshida, Yamaguchi 753-8515, Japan

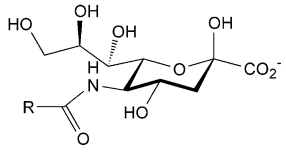
When linoleic and linolenic acid were incubated with a crude enzyme of marine green alga *Ulva conglobata*, the corresponding (*R*)-9-hydroperoxy-(10*E*, 12*Z*)-10, 12-octadecadienoic acid [(*R*)-9-HPODE] and (*R*)-9-hydroperoxy-(10*E*, 12*Z*, 15*Z*)-10, 12, 15-octadecatrienoic acid [(*R*)-9-HPOTrE] were formed with a high enantiomeric excess (>99%), respectively.

Bioorg. Med. Chem. 10 (2002) 3175

Biological Properties of *N*-Acyl and *N*-Haloacetyl Neuraminic Acids: Processing by Enzymes of Sialic Acid Metabolism, and Interaction with Influenza Virus

Andrew J. Humphrey,[a] Claire Fremann,[a] Peter Critchley,[b] Yanina Malykh,[c] Roland Schauer[c] and Timothy D. H. Bugg[b]

[a]*Department of Chemistry, University of Southampton, Highfield, Southampton SO17 1BJ, UK*
[b]*Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK*
[c]*Biochemical Institute, Christian-Albrechts University, Kiel, Germany*



N-acyl-D-neuraminic acid

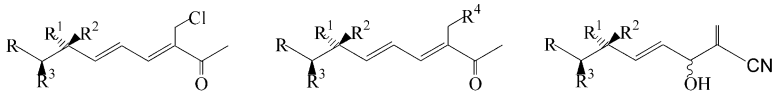
R = -CH_3,-CH_2CH_3, -$(CH_2)_5CH_3$, -Ph, -CH_2Cl, -CHF_2, -CF_3

Bioorg. Med. Chem. 10 (2002) 3187

Baylis–Hillman Reaction: Convenient Ascending Syntheses and Biological Evaluation of Acyclic Deoxy Monosaccharides as Potential Antimycobacterial Agents

Rashmi Pathak,[a] Chandra Shekhar Pant,[a] Arun K. Shaw,[a] Amiya P. Bhaduri,[a] Anil N. Gaikwad,[b] Sudhir Sinha,[b] Anil Srivastava,[c] Kishore K. Srivastava,[c] Vinita Chaturvedi,[c] Ranjana Srivastava[c] and Brahm S. Srivastava[c]

[a]*Medicinal Chemistry Division, Central Drug Research Institute, Lucknow-226001, India*
[b]*Biochemistry Division, Central Drug Research Institute, Lucknow-226001, India*
[c]*Microbiology Division Central Drug Research Institute, Lucknow-226001, India*

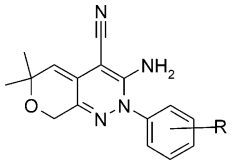


Bioorg. Med. Chem. 10 (2002) 3197

Synthesis and Biological Activity of a Novel Class of Pyridazine Analogues as Non-competitive Reversible Inhibitors of Protein Tyrosine Phosphatase 1B (PTP1B)

Charlotta Liljebris,[a] Jessica Martinsson,[a] Lars Tedenborg,[a] Meredith Williams,[a] Emma Barker,[b] James E. S. Duffy,[b] Alf Nygren[a] and Stephen James[a]

[a]*Biovitrum AB, Department of Medicinal Chemistry and Biology, SE-75137 Uppsala, Sweden*
[b]*BioFocus, Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AZ, UK*

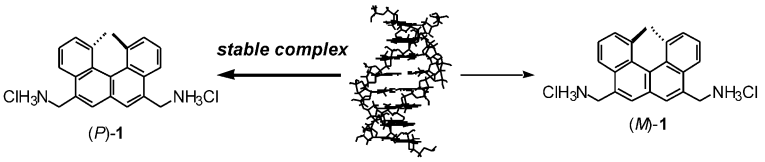


Bioorg. Med. Chem. 10 (2002) 3213

Chiral Recognition in the Binding of Helicenediamine to Double Strand DNA: Interactions between Low Molecular Weight Helical Compounds and a Helical Polymer

Shinobu Honzawa,[a] Hitoshi Okubo[a], Shuzo Anzai[a], Masahiko Yamaguchi[a], Kohei Tsumoto[b] and Izumi Kumagai[b]

[a]*Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba, Sendai 980-8578, Japan*
[b]*Department of Biomolecular Engineering, Graduate School of Engineering, Tohoku University, Aoba, Sendai 980-8579, Japan*



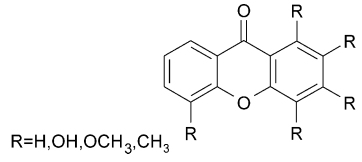
Bioorg. Med. Chem. 10 (2002) 3219

Synthesis and In Vivo Modulatory Activity of Protein Kinase C of 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, Faculdade de Farmácia, Universidade do Porto, rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*
[b]*Serviço de Microbiologia, Faculdade de Farmácia, Universidade do Porto, rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*
[c]*Serviço de Química Orgânica, Faculdade de Farmácia, Universidade do Porto, rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*

The modulatory activity of 20 simple xanthones on isoforms α, βI, δ, η and ζ of protein kinase C (PKC) was evaluated using an in vivo yeast phenotypic assay. The majority of these compounds caused an effect compatible with PKC activation. Some xanthone derivatives showed high potency and selectivity towards individual PKC isoforms.



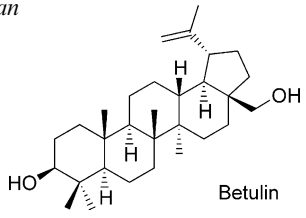
Bioorg. Med. Chem. 10 (2002) 3229

Synthesis of Betulin Derivatives and Their Protective Effects against the Cytotoxicity of Cadmium

Kou Hiroya, Taisuke Takahashi, Nobuhiko Miura, Akira Naganuma and Takao Sakamoto

Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba-ku, Sendai 980-8578, Japan

The protecting effect of betulin against cadmium toxicity was investigated using 11 kinds of analogues.



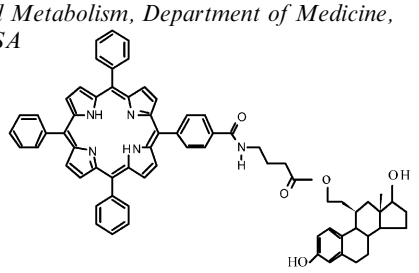
Bioorg. Med. Chem. 10 (2002) 3237

An Estradiol-Porphyrin Conjugate Selectively Localizes Into Estrogen Receptor-Positive Breast Cancer Cells

Narasimha Swamy,[a] David A. James,[a] Scott C. Mohr,[b] Robert N. Hanson[c] and Rahul Ray[a]

[a]*Bioorganic Chemistry and Structural Biology, Section in Endocrinology, Diabetes and Metabolism, Department of Medicine, Boston University School of Medicine, 80 East Concord Street Boston, MA 02118, USA*
[b]*Department of Chemistry, Boston University, Boston, MA, USA*
[c]*Department of Chemistry, Northeastern University, Boston, MA, USA*

A conjugate of a C_{11}-β-derivative of estradiol and an asymmetric tetraphenylporphyrin was synthesized to study its potential selective uptake by breast cancer over-expressing the nuclear estrogen receptor, ER.



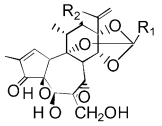
Bioorg. Med. Chem. 10 (2002) 3245

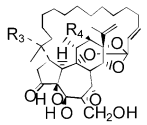
Neurotrophic and Antileukemic Daphnane Diterpenoids from *Synaptolepis kirkii*

Weidong He,[a] Miroslav Cik,[b] Luc Van Puyvelde,[a] Jacky Van Dun,[c] Giovanni Appendino,[d] Anne Lesage,[b] Ilse Van der Lindin,[b] Josée E. Leysen,[b] Walter Wouters,[c] Simon G. Mathenge,[e] Francis P. Mudida[f] and Norbert De Kimpe[a]

[a]*Department of Organic Chemistry, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium*
[b]*Department of Receptor Pharmacology, Janssen Research Foundation, Turnhoutseweg 30, B-2340 Beerse, Belgium*
[c]*Department of Oncology, Janssen Research Foundation, Turnhoutseweg 30, B-2340 Beerse, Belgium*
[d]*DISCAFF, Università del Piemonte Orientale, Viale Ferrucci 33, 28100 Novara, Italy*
[e]*Botany Department, University of Nairobi, Kenya*
[f]*TRAMEDA, PO Box 66514, Nairobi, Kenya*

A bioassay-guided fractionation led to the isolation of kirkinine (**6**), kirkinine B (**7**), C (**8**), D (**3**), E (**9**), synaptolepis factor K_7 (**1**), excoecariatoxin (**2**), yuanhuadine (**4**) and 12β-acetoxyhuratoxin (**5**) from the root of *Synaptolepis kirkii*, which possess potential neurotrophic and antileukaemia activities.


(**1**) - (**6**)

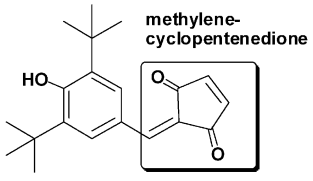

(**7**) - (**9**)

Bioorg. Med. Chem. 10 (2002) 3257

TX-1123: An Antitumor 2-Hydroxyarylidene-4-cyclopentene-1, 3-Dione as a Protein Tyrosine Kinase Inhibitor Having Low Mitochondrial Toxicity

Hitoshi Hori,[a] Hideko Nagasawa,[a] Masaki Ishibashi,[a] Yoshihiro Uto,[a] Akihiko Hirata,[a] Kouichi Saijo,[a] Kazuto Ohkura,[a] Kenneth L. Kirk[b] and Yoshimasa Uehara[c]

[a]*Department of Biological Science & Technology, Faculty of Engineering, The University of Tokushima, Tokushima 770-8506, Japan*
[b]*Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Health, Bethesda, MD 20892, USA*
[c]*Department of Bioactive Molecules, National Institute of Infectious Diseases, 1-23-1 Shinjuku-ku, Tokyo 162-8640, Japan*



TX-1123

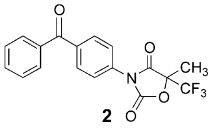
Bioorg. Med. Chem. 10 (2002) 3267

N-Arylated Pyrrolidin-2-ones and Morpholin-3-ones as Potassium Channel Openers

Pi-Hui Liang, Ling-Wei Hsin and Chen-Yu Cheng

Institute of Pharmaceutical Sciences, College of Medicine, National Taiwan University, Taipei 10018, Taiwan

Among a series of rigid analogues of ZD6169 (**2**–**13**), compounds **6** and **9** (X = Y = CH_3) were found to be potent and selective KCO's at the bladder.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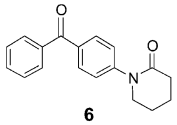
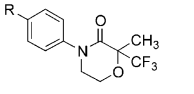

6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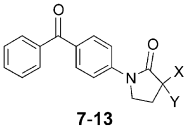
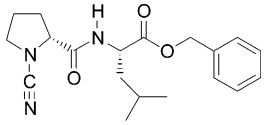

7-13

Bioorg. Med. Chem. 10 (2002) 3277

Peptidic 1-Cyanopyrrolidines: Synthesis and SAR of a Series of Potent, Selective Cathepsin Inhibitors

Robert M. Rydzewski,[a] Clifford Bryant,[a] Renata Oballa,[b] Gregg Wesolowski,[c] Sevgi B. Rodan,[c] Kathryn E. Bass[d] and Darren H. Wong[d]

[a]*Department of Medicinal Chemistry, Celera, 180 Kimball Way, South San Francisco, CA 94080, USA*
[b]*Department of Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, Quebec, Canada H9H 3L1*
[c]*Department of Bone Biology and Osteoporosis, Merck Research Laboratories, West Point, PA 19486, USA*
[d]*Department of Molecular and Cellular Pharmacology, Celera, 180 Kimball Way, South San Francisco, CA 94080, USA*


12 Cathepsin L K_i = 94 pM

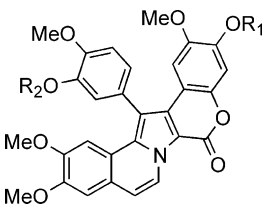
Total Synthesis and Evaluation of Lamellarin α 20-Sulfate Analogues

Bioorg. Med. Chem. 10 (2002) 3285

Christian P. Ridley,[a] M. Venkata Rami Reddy,[a] Genalyn Rocha,[b] Frederic D. Bushman[b] and D. John Faulkner[a]

[a]*Scripps Institution of Oceanography, University of California at San Diego, La Jolla, CA 92093-0212, USA*
[b]*Infectious Disease Laboratory, The Salk Institute, 10010 North Torrey Pines Rd., La Jolla, CA, 92037, USA*

Lamellarin α ($R_1 = R_2 = H$), lamellarin α 13,20-disulfate ($R_1 = R_2 = SO_3Na$) and lamellarin H were synthesized and their activity against HIV-1 integrase and cytotoxicity were compared with those of lamellarin α 20-sulfate ($R_1 = SO_3Na$, $R_2 = H$).



Cocaine Detoxification by Combinatorially Substituted β-Cyclodextrin Libraries

Bioorg. Med. Chem. 10 (2002) 3291

Jiaxin Yu,[a] Yongzhong Zhao,[a] Mark Holterman[b] and Duane L. Venton[a]

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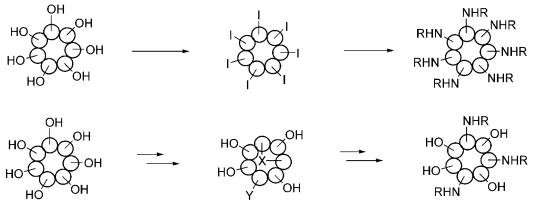
[b]*Department of Surgery, College of Medicine, The University of Illinois at Chicago, 833 S. Wood Street, Chicago, IL 60612, USA*



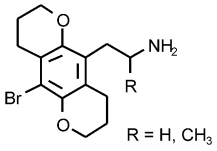
Substituted Hexahydrobenzodipyrans as 5-$HT_{2A/2C}$ Receptor Probes

Bioorg. Med. Chem. 10 (2002) 3301

Michael S. Whiteside,[a] Deborah Kurrasch-Orbaugh,[b] Danuta Marona-Lewicka,[b] David E. Nichols[b] and Aaron Monte[a]

[a]*Department of Chemistry, University of Wisconsin-La Crosse, La Crosse, WI 54601, USA*
[b]*Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907-1333, USA*

A pair of substituted hexahydrobenzodipyrans was designed as molecular probes for determining the steric restrictions of the agonist binding site of serotonin 5-HT_{2A} and 5-HT_{2C} receptors. The rationale for the design of these receptor ligands, their chemical synthesis, rat behavioral pharmacology in the two-lever drug discrimination assay using LSD-trained rats, affinity for cloned rat 5-HT_{2A} and 5-HT_{2C} receptors, and agonist functional activities are reported.



Probing the Phytopathogenic Stem Rot Fungus with Phytoalexins and Analogues: Unprecedented Glucosylation of Camalexin and 6-Methoxycamalexin

Bioorg. Med. Chem. 10 (2002) 3307

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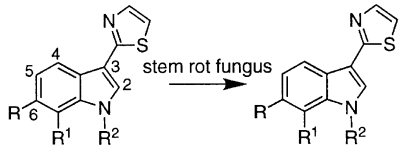


1 R = R^1 = R^2 = H
1a R = OMe; R^1 = R^2 = H
1b R = F; R^1 = R^2 = H
1c R = F; R^1 = H; R^2 = Me

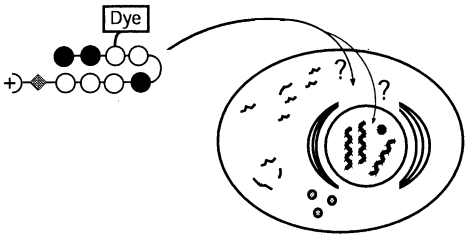
5 R = OH; R^1 = R^2 = H
5a R = O-β-D-gluc; R^1 = R^2 = H
5b R = OMe; R^1 = H; R^2 = β-D-gluc
5c R = F; R^1 = H; R^2 = β-D-gluc
5d R = F; R^1 = O-β-D-gluc; R^2 = Me

Bioorg. Med. Chem. 10 (2002) 3313

Cellular Uptake of *N*-Methylpyrrole/*N*-methylimidazole Polyamide-Dye Conjugates

Jason M. Belitsky,[a] Stephanie J. Leslie,[b] Paramjit S. Arora,[a] Terry A. Beerman[b] and Peter B. Dervan[a]

[a]*Division of Chemistry and Chemical Engineering and Beckman Institute, California Institute of Technology, Pasadena, CA 91125, USA*
[b]*Department of Pharmacology and Therapeutics, Roswell Park Cancer Institute, Buffalo, NY 14263, USA*



Bioorg. Med. Chem. 10 (2002) 3319

Probes for Narcotic Receptor Mediated Phenomena. Part 28: New Opioid Antagonists from Enantiomeric Analogues of 5-(3-Hydroxyphenyl)-*N*-phenylethylmorphan

Akihiro Hashimoto,[a] Arthur E. Jacobson,[a] Richard B. Rothman,[b] Christina M. Dersch,[b] Clifford George,[c] Judith L. Flippen-Anderson[c] and Kenner C. Rice[a]

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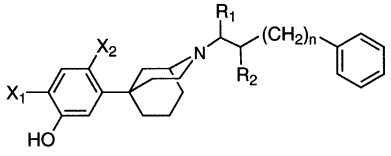
[b]*Clinical Psychopharmacology Section, National Institute on Drug Abuse, Addiction Research Center, Baltimore, MD 21224, USA*
[c]*Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, DC 20375, USA*



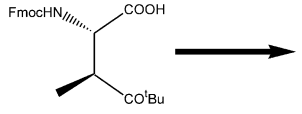
1*R*,5*S* and 1*S*,5*R* series

Bioorg. Med. Chem. 10 (2002) 3331

Incorporation of (2*S*,3*S*) and (2*S*,3*R*) β-Methyl Aspartic Acid into RGD-Containing Peptides

Silke Schabbert,[a] Michael D. Pierschbacher,[b] Ralph-Heiko Mattern[b] and Murray Goodman[a]

[a]*Department of Chemistry and Biochemistry, University of California at San Diego, La Jolla, CA 92093-0343, USA*
[b]*Integra LifeSciences Corporation, Corporate Research Center, San Diego, CA 92121, USA*



(2*S*,3*S*)

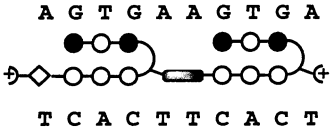
→ c[Arg-Gly-(S)β-Me-Asp-(S)β-Me-Asp-(tBuG)-(Mamb)]

Bioorg. Med. Chem. 10 (2002) 3339

Search for the Optimal Linker in Tandem Hairpin Polyamides

Inger Kers and Peter B. Dervan

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA



10-bp Binding Site:

$K_a = 5.4 \times 10^{10}\ M^{-1}$

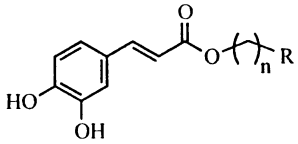
Bioorg. Med. Chem. 10 (2002) 3351

Selective Antiproliferative Activity of Caffeic Acid Phenethyl Ester Analogues on Highly Liver-Metastatic Murine Colon 26-L5 Carcinoma Cell Line

Takema Nagaoka, Arjun H. Banskota, Yasuhiro Tezuka, Ikuo Saiki and Shigetoshi Kadota

Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, 2630-Sugitani, Toyama 930-0194, Japan

Caffeic acid phenethyl ester (CAPE, **2**) and its 20 analogues (**1**, **3**–**21**) were prepared. These esters were tested by MTT assay on growth of murine colon 26-L5 carcinoma, murine B16-BL6 malonoma, murine Lewis lung carcinoma, human HT-1080 fibrosarcoma, human lung A549 adenocarcinoma, and human cervix HeLa adenocarcinoma cell lines. It was found that CAPE analogues possessed selective anti-proliferative activity toward highly liver-metastatic murine colon 26-L5 carcinoma cell line. Among them, 4-phenylbutyl caffeate (**4**), (*Z*)-8-phenyl-7-octenyl (**10a**) and (*E*)-8-phenyl-7-octenyl (**10b**) caffeate showed the most potent antiproliferative activity (EC_{50} value, 0.02 μM). In addition, CAPE (**2**) induced DNA fragmentation at concentrations of 1 to 10 μg/mL towards murine colon 26-L5 carcinoma cells.



R = methyl, phenyl, *cyclo*-hexyl, -CH=CHPh

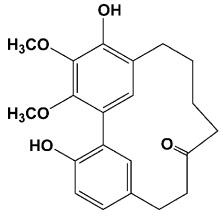
Bioorg. Med. Chem. 10 (2002) 3361

Chemopreventive Potential of Cyclic Diarylheptanoids

Junko Ishida,[a] Mutsuo Kozuka,[b] Harukuni Tokuda,[c] Hoyoku Nishino,[c] Seiji Nagumo,[a] Kuo-Hsiung Lee[b] and Masahiro Nagai[a]

[a]*Hoshi University, 2-4-41, Ebara, Shinagawa-ku, Tokyo 142-8501, Japan*
[b]*Natural Products Laboratory, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599-7360, USA*
[c]*Department of Biochemistry, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto 602-0841, Japan*

The cyclic diarylheptanoid myricanone (**2**) exhibited significant antitumor initiating activity in a two-stage carcinogenesis assay of mouse skin tumors induced by peroxynitrite as an initiator and TPA as a promoter.



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