Bioorg. Med. Chem. 11 (2003) 1607

Solution-Phase Synthesis of Combinatorial Libraries Designed to Modulate Protein–Protein or Protein–DNA Interactions

Dale L. Boger*

Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA

A short personal perspective on the development of an approach to the solution-phase synthesis of combinatorial libraries for modulating cellular signaling by inhibiting, promoting, or mimicking protein–protein or protein–DNA interactions is provided.

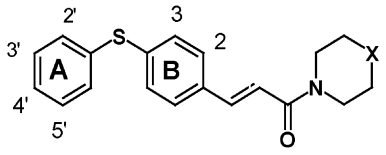
Bioorg. Med. Chem. 11 (2003) 1615

QSAR Study on Some *p*-Arylthio Cinnamides as Antagonists of Biochemical ICAM-1/LFA-1 Interaction and ICAM-1/JY-8 Cell Adhesion in Relation to Anti-inflammatory Activity

Bikash Debnath, Soma Samanta, Kunal Roy and Tarun Jha*

Division of Pharmaceutical and Medicinal Chemistry, Department of Pharmaceutical Technology, PO Box 17020, Jadavpur University, Kolkata 700 032, India

QSAR study was performed on some *p*-arylthio cinnamides using Hansch approach for their antagonistic activity against biochemical ICAM-1/LFA-1 interaction and ICAM-1/JY-8 cell adhesion.

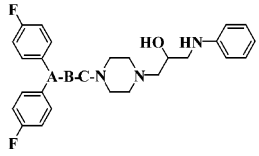


Bioorg. Med. Chem. 11 (2003) 1621

Syntheses of Novel Diphenyl Piperazine Derivatives and Their Activities as Inhibitors of Dopamine Uptake in the Central Nervous System

Makoto Kimura,[a,*] Tomoko Masuda,[a] Koji Yamada,[a] Masaki Mitani,[a] Nobuo Kubota,[a] Nobuyuki Kawakatsu,[a] Kenichi Kishii,[a] Masato Inazu,[b] Yuji Kiuchi,[c] Katsuji Oguchi[d] and Takayuki Namiki[a,*]

[a]*POLA Chemical Industries, Inc., Pharmaceutical R&D Laboratories, 560 Kashio-cho, Totsuka-ku, Yokohama, Kanagawa 244-0812, Japan*
[b]*Department of Pharmacology, and Intractable Disease Research Center, Tokyo Medical University, 6-1-1 Shinjuku, Shinjuku-ku, Tokyo 160-8402, Japan*
[c]*Department of Pathophysiology, School of Pharmaceutical Sciences, Showa University, 1-5-8Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan*
[d]*Department of Pharmacology, School of Medicine, Showa University, 1-5-8Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan*



A-B-C= CH-$(CH_2)_n$-, C=CH-$(CH_2)_2$-, CH-O-$(CH_2)_2$-, N-$(CH_2)_3$-, C(OH)-$(CH_2)_3$-

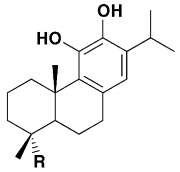
Bioorg. Med. Chem. 11 (2003) 1631

Catechols from Abietic Acid: Synthesis and Evaluation as Bioactive Compounds

B. Gigante,[a,*] C. Santos,[a] A. M. Silva,[a] M. J. M. Curto,[a] M. S. J. Nascimento,[b] E. Pinto,[b] M. Pedro,[b] F. Cerqueira,[b] M. M. Pinto,[b] M. P. Duarte,[c] A. Laires,[c] J. Rueff,[c] J. Gonçalves,[d] M. I. Pegado[d] and M. L. Valdeira[d]

[a]*INETI, Departamento de Tecnologia de Indústrias Químicas, Estrada do Paço do Lumiar, 22, 1649-038 Lisbon, Portugal*
[b]*Centro de Estudos de Química Orgânica, Fitoquímica e Farmacologia da Universidade do Porto, Faculdade de Farmácia, Rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*
[c]*Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Rua da Junqueira 96, 1349-008 Lisbon, Portugal*
[d]*Faculdade de Farmácia, Universidade de Lisboa, Av. Prof. Gama Pinto, 1649-003 Lisbon, Portugal*

Catechols from abietic acid were prepared by a short and good yielding chemical process and further evaluated for several biological activities namely, antifungal, antitumoral, antimutagenic, antiviral, antiproliferative and inhibitory activity of nitric oxide (NO) production. Their properties were compared with those of carnosic acid, a bioactive naturally occurring catechol possessing an abietane skeleton. In general, these catechols have shown better biological profile than carnosic acid.



R = CO_2CH_3, CH_2OH, CO_2H, CH_3

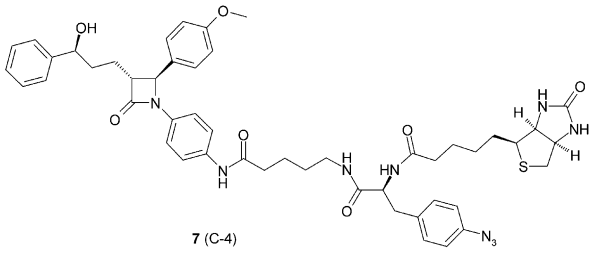
Bioorg. Med. Chem. 11 (2003) 1639

Synthesis of a Biotin-Tagged Photoaffinity Probe of 2-Azetidinone Cholesterol Absorption Inhibitors

Wendelin Frick, Andrea Bauer-Schäfer, Jochen Bauer, Frank Girbig, Daniel Corsiero, Hubert Heuer and Werner Kramer*

Aventis Pharma Deutschland GmbH, Disease Group Metabolic Diseases Industriepark Höchst, Building G 879 D-65926, Frankfurt am Main, Germany

The design and synthesis of a biotin-tagged photoreactive analogue C-4 of the cholesterol absorption inhibitor Ezetimibe is described to purify the target protein(s) for cholesterol absorption inhibitors from enterocyte brush border membranes.



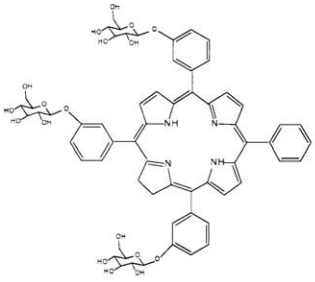
7 (C-4)

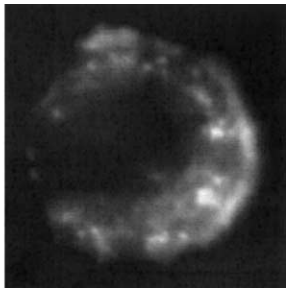
Bioorg. Med. Chem. 11 (2003) 1643

Synthesis, Cellular Internalization and Photodynamic Activity of Glucoconjugated Derivatives of Tri and Tetra(*meta*-hydroxyphenyl)chlorins

I. Laville,[a] T. Figueiredo,[b] B. Loock,[b] S. Pigaglio,[a] Ph. Maillard,[b] D. S. Grierson,[b] D. Carrez,[c] A. Croisy[c] and J. Blais[a,*]

[a]*LPBC, UMR CNRS 7033 and Université Pierre et Marie Curie, 4 Place Jussieu, case 138, 75252 Paris Cedex 05, France*
[b]*UMR 176 CNRS-Institut Curie, Section de Recherche, Bat 110 Centre Universitaire, 91405 Orsay, France*
[c]*INSERM U-350, Institut Curie, Section de Recherche, Bat 112 Centre Universitaire, 91405 Orsay, France*





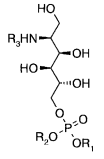
Bioorg. Med. Chem. 11 (2003) 1653

Hydrophobic Derivatives of 2-Amino-2-deoxy-D-glucitol-6-phosphate: A New Type of D-Glucosamine-6-phosphate Synthase Inhibitors with Antifungal Action

Agnieszka M. Janiak,[a] Maria Hoffmann,[b] Maria J. Milewska[b] and Sławomir Milewski[a,*]

[a]*Department of Pharmaceutical Technology and Biochemistry, Technical University of Gdañsk, 11/12 Narutowicza St., 80-952 Gdañsk, Poland*
[b]*Department of Organic Chemistry, Technical University of Gdañsk, 80-952 Gdañsk, Poland*

N-acyl and ester derivatives of 2-amino-2-deoxy-D-glucitol-6-phosphate (ADGP) were found to be poorer inhibitors of the enzyme, D-glucosamine-6-phosphate synthase, than the parent compound but a few of them exhibited much better antifungal activity. Some of the examined derivatives behaved as 'pro-drugs' and after internalization were in the cell-free extract converted into ADGP.



R_1, R_2=H; CH_3; C_2H_5
R_3=H; C(O)CH_3; C(O)C_4H_9; C(O)C_8H_{13}; C(O)CH_2Cl; C(O)CH_2I

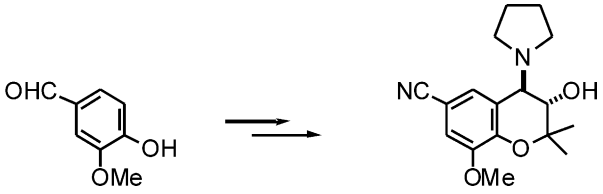
Bioorg. Med. Chem. 11 (2003) 1663

Potassium Channel Activators Based on the Benzopyran Substructure: Synthesis and Activity of the C-8 Substituent

Rona Thompson,[a] Sheila Doggrell[b,*] and John O. Hoberg[a,*]

[a]*School of Chemical and Physical Sciences, Victoria University of Wellington, Box 600, Wellington, New Zealand*
[b]*Department of Physiology and Pharmacology, School of Biomedical Sciences, The University of Queensland, Brisbane, Queensland 4072, Australia*

Potassium channel activators bearing both electron withdrawing and electron donating moieties were synthesized from vanillin. Evaluation of their biological properties indicate that substitution at the methoxy bearing carbon represents a key site of activity.



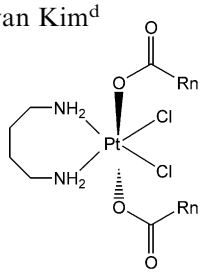
Bioorg. Med. Chem. 11 (2003) 1669

Synthesis, Characterization and Antitumor Activity of Novel Octahedral Pt(IV) Complexes

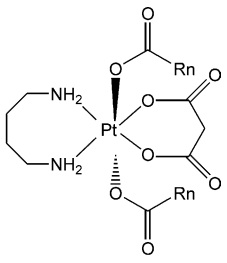
Young-Ee Kwon,[a,*] Kyu-Ja Whang,[b] Young-Ja Park[c] and Kuk Hwan Kim[d]

[a]*Drug Discovery Institute of STC Life Science Center, 6-13, Nonhyun-Dong, Kangnam-Gu, Seoul, 135-010, South Korea*
[b]*College of Pharmacy, Sookmyung Women's University, Chungpa-dong, Yongsan-ku, Seoul, 140-742, South Korea*
[c]*Department of Chemistry, Sookmyung Women's University, Chungpa-dong, Yongsan-ku, Seoul, 140-742, South Korea*
[d]*College of Pharmacy, Dongduk Women's University, Worlkok-dong, Sungbuk-Gu, Seoul, 136-714, South Korea*

Synthesis and antitumor acivity of (1,4-butanediamine)Pt(IV) complexes having axial ligands, **12**, **13**, **17**, **18** was reported.



12: $R_1 = CH_3$; **13**: $R_2 = CF_3$



17: $R_1 = CH_3$; **18**: $R_2 = CF_3$

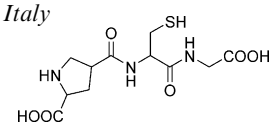
Bioorg. Med. Chem. 11 (2003) 1677

Proline–Glutamate Chimeras in Isopeptides. Synthesis and Biological Evaluation of Conformationally Restricted Glutathione Analogues

Mario Paglialunga Paradisi,[a] Adriano Mollica,[a] Ivana Cacciatore,[b] Antonio Di Stefano,[b] Francesco Pinnen,[b] Anna Maria Caccuri,[c] Giorgio Ricci,[c] Silvestro Duprè,[d] Alessandra Spirito[d] and Gino Lucente[a,*]

[a]*Istituto di Chimica Biomolecolare, CNR Sezione di Roma, c/o Dipartimento di Studi Farmaceutici, Università di Roma 'La Sapienza', P.le A. Moro, 00185 Rome, Italy*
[b]*Dipartimento di Scienze del Farmaco, Università 'G. D'Annunzio', Via dei Vestini 31, 66100 Chieti, Italy*
[c]*Dipartimento di Biologia, Università 'Tor Vergata', Via della Ricerca Scientifica, 00133 Rome, Italy*
[d]*Dipartimento di Scienze Biologiche, Università di Roma 'La Sapienza', P.le A. Moro, 00185 Rome, Italy*

The synthesis and biological activity on γ-GT and hGST P1-1 of two novel conformationally restricted glutathione analogues, containing the residue of *cis*- and *trans*-4-carboxy-L-proline replacing the γ-glutamylic moiety, are reported.



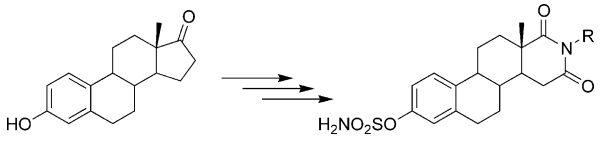
Bioorg. Med. Chem. 11 (2003) 1685

D-Ring Modified Estrone Derivatives as Novel Potent Inhibitors of Steroid Sulfatase

Delphine S. Fischer,[a] L.W. Lawrence Woo,[a] Mary F. Mahon,[b] Atul Purohit,[c] Michael J. Reed[c] and Barry V. L. Potter[a,*]

[a]*Medicinal Chemistry, Department of Pharmacy and Pharmacology and Sterix Ltd., University of Bath, Claverton Down, Bath BA2 7AY, UK*
[b]*Department of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY, UK*
[c]*Endocrinology and Metabolic Medicine and Sterix Ltd., Imperial College, Faculty of Medicine, St. Mary's Hospital, London W2 1NY, UK*

Some new D-ring derivatives of estrone were synthesized and found to be powerful steroid sulfatase inhibitors as their sulfamates. The most active compounds were up to 18-fold more potent than EMATE, the benchmark steroidal inhibitor.



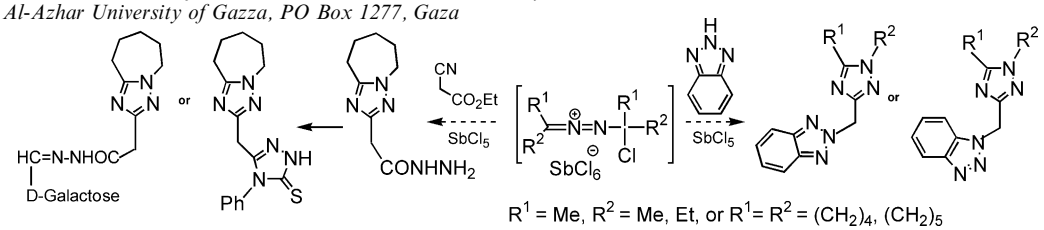
Bioorg. Med. Chem. 11 (2003) 1701

Synthesis and Properties of New Substituted 1,2,4-Triazoles: Potential Antitumor Agents

Yaseen A. Al-Soud,[a] Najim A. Al-Masoudi[b,*] and Abd El-Rahman S. Ferwanah[c]

[a]*Department of Chemistry, College of Science, University of Al al-Bayt, Al-Mafraq, Jordan*
[b]*Fakultät für Chemie, Universität Konstanz, Potfach 5560, D-78457 Konstanz, Germany*
[c]*Department of Chemistry, Al-Azhar University of Gazza, PO Box 1277, Gaza*

The title compounds were prepared by cycloaddition reactions. Six of the new compounds were screened against a variety of tumor cell lines.



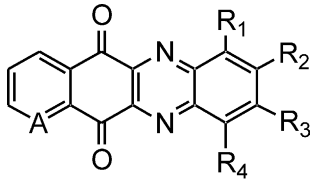
R^1 = Me, R^2 = Me, Et, or $R^1 = R^2 = (CH_2)_4$, $(CH_2)_5$

Bioorg. Med. Chem. 11 (2003) 1709

Synthesis and Cytotoxicity of 6,11-Dihydro-pyrido- and 6,11-Dihydro-benzo[2,3-b]phenazine-6,11-dione Derivatives

Young-Shin Kim,[a] Se-Young Park,[a] Hyun-Jung Lee,[a] Myung-Eun Suh,[a,*] Dieter Schollmeyer[b] and Chong-Ock Lee[c]

[a]*Division of Medicinal Chemistry, College of Pharmacy, Ewha Woman's University, Seoul 120-750, South Korea*
[b]*Department of Chemistry and Pharmacy, Institute of Organic Chemistry, University of Mainz, Duesbergweg 10-14, 55099 Mainz, Germany*
[c]*Pharmaceutical Screening Division, Korea Research Institute of Chemical Technology, TaeJon 305-606, South Korea*



A = C or N

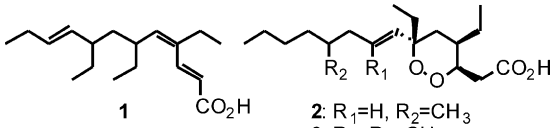
Bioorg. Med. Chem. 11 (2003) 1715

A New α,β,γ,δ-Unsaturated Carboxylic Acid and Three New Cyclic Peroxides From the Marine Sponge, *Monotria japonica*, Which Selectively Lyse Starfish Oocytes Without Affecting Nuclear Morphology

Mihoko Yanai,[a] Shinji Ohta,[a] Emi Ohta,[a] Toshifumi Hirata[b] and Susumu Ikegami[a,*]

[a]*Instrument Center for Chemical Analysis, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan*
[b]*Department of Mathematical and Life Sciences, Graduate School of Science, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan*

The structures of monotriajaponides A–D (**1**–**4**) were determined on the basis of their spectroscopic data. These compounds lysed immature starfish (*Asterina pectinifera*) oocytes without affecting nuclear morphology.



1

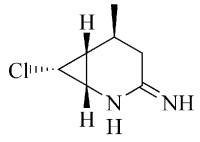
2: R_1=H, R_2=CH_3
3: R_1=R_2=CH_3
4: R_1=CH_3, R_2=C_2H_5

Bioorg. Med. Chem. 11 (2003) 1723

Design and Synthesis of Orally Bioavailable Inhibitors of Inducible Nitric Oxide Synthase. Identification of 2-Azabicyclo[4.1.0]heptan-3-imines

Yasufumi Kawanaka,[a,*] Kaoru Kobayashi,[b] Shinya Kusuda,[b] Tadashi Tatsumi,[b] Masayuki Murota,[b] Toshihiko Nishiyama,[b] Katsuya Hisaichi,[b] Atsuko Fujii,[b] Keisuke Hirai,[b] Masao Naka,[b] Masaharu Komeno,[a] Yshihiko Odagaki,[b] Hisao Nakai[b] and Masaaki Toda[b]

[a]*Fukui Research Institute, Ono Pharmaceutical Co., Ltd., Technoport, Yamagishi, Mikuni, Sakai, Fukui 913-8538, Japan*
[b]*Minase Research Institute, Ono Pharmaceutical Co., Ltd., Shimamoto, Mishima, Osaka 618-8585, Japan*



4

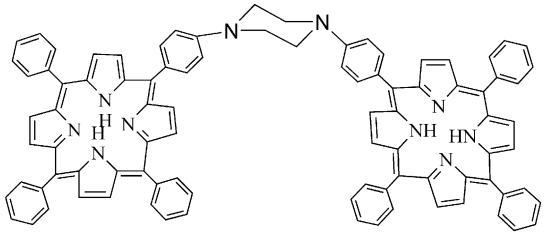
(1*S*,5*S*,6*R*,7*R*)-7-Chloro-5-methyl-2-azabicyclo[4.1.0]heptan-3-imine **4** was identified as a potent inhibitor of inducible nitric oxide synthase.

Bioorg. Med. Chem. 11 (2003) 1745

Study on Synthesis, Characterization and Biological Activity of Some New Nitrogen Heterocycle Porphyrins

Can-Cheng Guo,* He-Ping Li and Xiao-Bing Zhang

College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410082 China



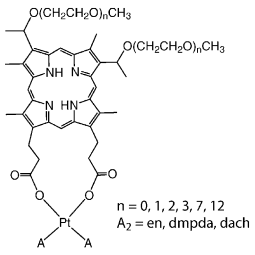
Bioorg. Med. Chem. 11 (2003) 1753

Synthesis, Biodistribution and Antitumor Activity of Hematoporphyrin–Platinum(II) Conjugates

Yeong-Sang Kim,[a,c] Rita Song,[b] Dong Hyun Kim[b], Moo Jin Jun[c,*] and Youn Soo Sohn[a]

[a]*Department of Chemistry, Ewha Womans University, Seoul 120-750, South Korea*
[b]*Division of Life Sciences, Korea Institute of Science and Technology, Seoul 136-791, South Korea*
[c]*Department of Chemistry, Yonsei University, Seoul 120-749, South Korea*

A new series of antitumor platinum(II) complexes of pegylated hematoporphyrin derivatives with controlled hydrophobic/hydrophilic balance were synthesized by introducting different kinds of poly(ethylene glycol) and amine ligands to the porphyrin ring.



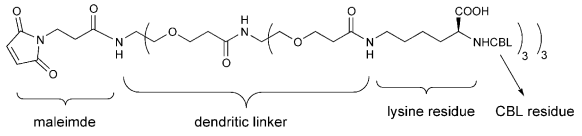
Bioorg. Med. Chem. 11 (2003) 1761

Enabling ScFvs as Multi-Drug Carriers: A Dendritic Approach

Chengzao Sun, Peter Wirsching* and Kim D. Janda*

Department of Chemistry, The Scripps Research Institute and the Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA

Soluble dendritic molecules that enable scFvs as multi-drug carriers were synthesized.

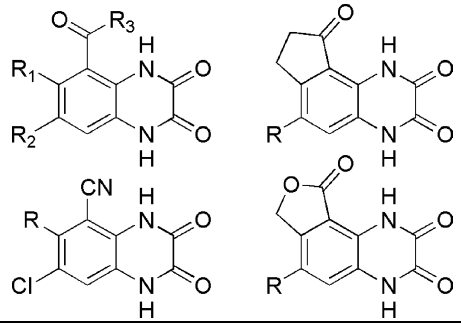


Bioorg. Med. Chem. 11 (2003) 1769

Synthesis and SAR of Novel Di- and Trisubstituted 1,4-dihydroquinoxaline-2,3-diones Related to Licostinel (Acea 1021) as NMDA/Glycine Site Antagonists

Zhang-Lin Zhou,[a] Sunil M. Kher,[a] Sui Xiong Cai,[b] Edward R. Whittemore,[b] Stephen A. Espitia,[b] Jon E. Hawkinson,[b] Minhtam Tran,[b] Richard M. Woodward,[b] Eckard Weber[b] and John F. W. Keana[a,*]

[a]*Department of Chemistry, University of Oregon, Eugene, OR 97403, USA*
[b]*CoCensys, Inc., 201 Technology Drive, Irvine, CA 92618, USA*



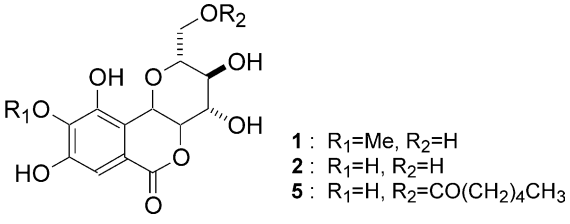
Bioorg. Med. Chem. 11 (2003) 1781

Synthesis and Neuroprotective Activity of Bergenin Derivatives with Antioxidant Activity

Hironobu Takahashi, Masamiti Kosaka, Yasutoshi Watanabe, Kousuke Nakade and Yoshiyasu Fukuyama*

Institute of Pharmacognosy, Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770-8514, Japan

A series of bergenin derivatives were synthesized and their anti-oxidative activities were evaluated. Among these compounds, **5** showed the highest antioxidant activity as well as neuroprotective activity on the primary culture of rat cortical neurons.

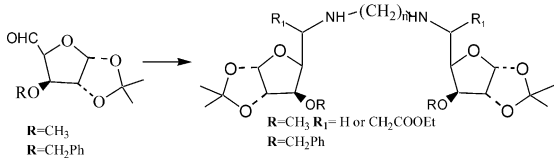


Bioorg. Med. Chem. 11 (2003) 1789

Synthesis and Antifilarial Evaluation of N^1,N^n- Xylofuranosylated Diaminoalkanes

V. K. Tiwari,[a] N. Tewari,[a] D. Katiyar,[a] R. P. Tripathi,[a,*] K. Arora,[b] S. Gupta,[b] R. Ahmad,[b] A. K. Srivastava,[b] M. A. Khan,[c] P. K. Murthy[c] and R. D. Walter[d]

[a]*Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow-226001, India*
[b]*Division of Biochemistry, Central Drug Research Institute, Lucknow-226001, India*
[c]*Division of Parasitology, Central Drug Research Institute, Lucknow-226001, India*
[d]*Abteilung fur Biochemie, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany*



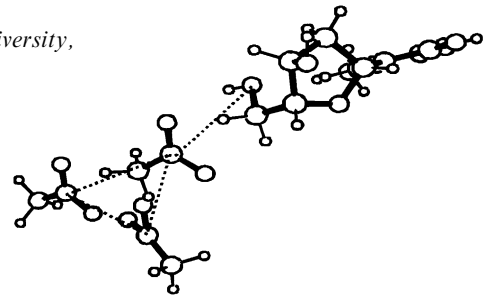
Bioorg. Med. Chem. 11 (2003) 1801

Pharmacophoric Features of Nucleosidic HIV-1RT Inhibitors

Arpita Yadav* and Sanjeev Kumar Singh

Department of Chemistry, Institute of Engineering and Technology, CSJM University, Kanpur-208024, India

A study on pharmacophoric features (conformational and electrostatic) of nucleoside inhibitor of HIV-1RT. Importance of interaction between phosphate and the catalytic triad in binding and controlling the potency is emphasized. All inhibitors show similar ribose ring puckering. MESP maps show charge complementarity between the drug and the receptor.



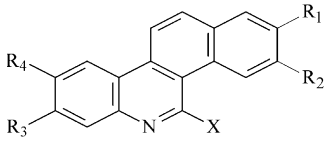
Bioorg. Med. Chem. 11 (2003) 1809

Substituted Benzo[*i*]phenanthridines as Mammalian Topoisomerase-Targeting Agents

Darshan Makhey,[a] 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, 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_1,R_2 = –OCH_2O-; R_3 = R_4 = OCH_3; X = H or CH_3 R_1 = R_2 = R_3 = R_4 = OCH_3; X = H or CH_3 R_1 = R_2 = R_3 = OCH_3; R_4 = X = H R_1 = R_2 = R_4 = OCH_3; R_3 = X = H R_1,R_2 = R_3,R_4 = -OCH_2O-; X = H.



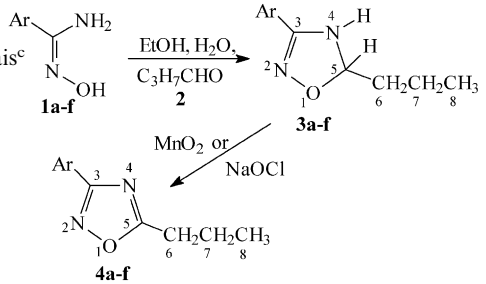
Bioorg. Med. Chem. 11 (2003) 1821

Antiinflammatory Property of 3-Aryl-5-(*n*-propyl)-1,2,4-oxadiazoles and Antimicrobial Property of 3-Aryl-5-(*n*-propyl)-4,5-dihydro-1,2,4-oxadiazoles: Their Syntheses and Spectroscopic Studies

Rajendra M. Srivastava,[a,*] Analice de Almeida Lima,[a] Osnir S. Viana,[a] Marcelo J. da Costa Silva,[a] Maria T. J. A. Catanho[b] and José Otamar F. de Morais[c]

[a]*Departamento de Química Fundamental, Universidade Federal de Pernambuco, Cidade Universitária, 50.740-540 Recife, PE, Brazil*
[b]*Departamento de Biofísica, Universidade Federal de Pernambuco, Cidade Universitária, 50.670-420 Recife, PE, Brazil*
[c]*Departamento de Antibióticos, Universidade Federal de Pernambuco, Cidade Universitária, 50.690-901 Recife, PE, Brazil*

Syntheses of 3-aryl-5-(*n*-propyl)-4,5-dihydro-1,2,4-oxadiazoles **3a**–**f** and 3-aryl-5-(*n*-propyl)-1,2,4-oxadiazoles **4a**–**f** and their biological activity tests are described.

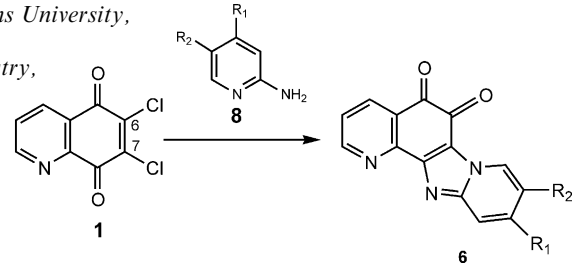


Bioorg. Med. Chem. 11 (2003) 1829

Regioselective Substitution of 6,7-dichloroquinoline-5,8-dione: Synthesis and X-ray Crystal Structure of 4a,10,11-triazabenzo[3,2-*a*]fluorene-5,6-diones

Young-Shin Kim,[a] So-Young Park,[a] Myung-Eun Suh,[a,*] Hyun-Jung Lee[a] and Dieter Schollmeyer[b]

[a]*Division of Medicinal Chemistry, College of Pharmacy, Ewha Womans University, 11-1 Daehyun-dong, Seodaemun-ku, Seoul 120-750, South Korea*
[b]*Department of Chemistry and Pharmacy, Institute of Organic Chemistry, University of Mainz, Duesbergweg 10-14, 55099 Mainz, Germany*



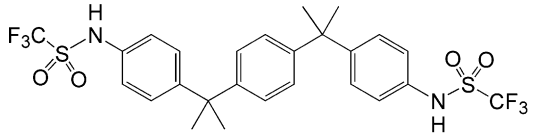
Bioorg. Med. Chem. 11 (2003) 1835

Structure-Based Design and Discovery of Novel Inhibitors of Protein Tyrosine Phosphatases

Ping Huang,* John Ramphal, James Wei, Congxin Liang, Bahija Jallal, Gerald McMahon and Cho Tang

SUGEN, Inc., 230 East Grand Ave., South San Francisco, CA 94080, USA

Structure-based design and synthesis have successfully led to the discovery of a novel series of trifluoromethyl sulfonyl and trifluoromethyl sulfonamido compounds as catalytic-site directed, reversible inhibitors of protein tyrosine phosphatases.



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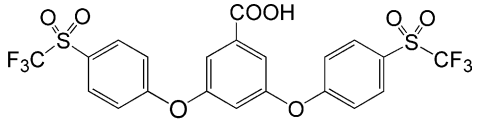

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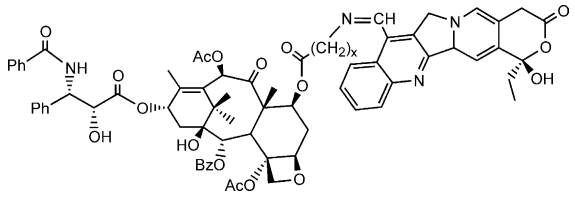
Bioorg. Med. Chem. 11 (2003) 1851

Antitumor Agents 216. Synthesis and Evaluation of Paclitaxel–Camptothecin Conjugates as Novel Cytotoxic Agents

Hironori Ohtsu,[a] Yuka Nakanishi,[a] Kenneth F. Bastow,[a] Fang-Yu Lee[b] and Kuo-Hsiung Lee[a,*]

[a]*Natural Products Laboratory, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA*
[b]*Yung-Shin Pharmaceutical Industrial Company, 1191, Section 1, Chung-Shan Road, Taichia, Taichung, Taiwan*

Five conjugates (**16**–**20**) composed of a paclitaxel and a camptothecin derivative joined by an imine linkage were synthesized and evaluated as cytotoxic agents and as inhibitors of DNA topoisomerase I. All of the conjugates were potent inhibitors of tumor cell replication with improved activity relative to camptothecin.



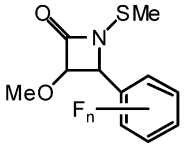
Bioorg. Med. Chem. 11 (2003) 1859

Effect of Aryl Ring Fluorination on the Antibacterial Properties of C_4 Aryl-Substituted *N*-Methylthio β-Lactams

Timothy E. Long,[a] Edward Turos,[a,*] Monika I. Konaklieva,[b] Allison L. Blum,[b] Amal Amry,[b] Ejae A. Baker,[b] Lita S. Suwandi,[b] Melodie D. McCain,[b] Miti F. Rahman,[b] Sonja Dickey[c] and Daniel V. Lim[c]

[a]*Department of Chemistry, 4202 E. Fowler Avenue-SCA400, University of South Florida, Tampa, FL 33620, USA*
[b]*Department of Chemistry, American University, Washington, DC 20016, USA*
[c]*Department of Biology, University of South Florida, Tampa, FL 33620, USA*

N-Methylthio β-lactams are members of a new family of antibacterial agents for *MRSA*. This paper describes the effect that fluorine substitution in the C_4 aryl ring has on the antimicrobial properties of these agents.



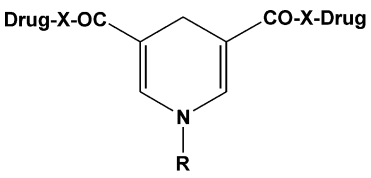
Bioorg. Med. Chem. 11 (2003) 1865

New Carrier for Specific Delivery of Drugs to the Brain

Mahmoud Sheha,[a,*] Ali Al-Tayeb,[b] Hosny El-Sherief[b] and Hassan Farag[a]

[a]*Medicinal Chemistry Department, Faculty of Pharmacy, Assiut University, Assuit 71526, Egypt*
[b]*Medicinal Chemistry Department, Faculty of Pharmacy, Al-Azhar University, Assiut 71526, Egypt*

N-Alkoxycarbonylmethyl derivatives of 1,4-dihydropyridine-3,5-dicarboxylate (**1** and **2**) were synthesized and investigated as a new carrier system for drug brain delivery.



1 and **2**

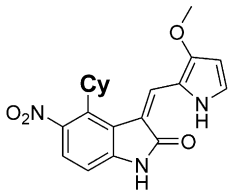
Bioorg. Med. Chem. 11 (2003) 1873

Synthesis of Potent Oxindole CDK2 Inhibitors

Apos Dermatakis,* Kin-Chun Luk and Wanda DePinto

Hoffmann-La Roche Inc., 340 Kingsland str., Nutley, NJ 07110-1199, USA

The synthesis of 5-nitro oxindoles that are substituted at C-4 with saturated cyclic moieties which serve as surrogates for the ribofuranoside of ATP is reported. The evaluation of these agents as CDK2 inhibitors and as inhibitors of the proliferation of RKO and MDA MB435 cancer cells is reported as well.



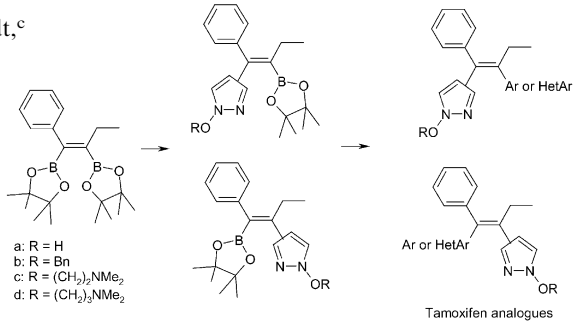
Cy= cyclic monosubstituted amine moiety

Bioorg. Med. Chem. 11 (2003) 1883

N-Alkoxypyrazoles as Biomimetics for the Alkoxyphenyl Group in Tamoxifen

Martin Wenckens,[a,b] Palle Jakobsen,[b] Per Vedsø,[a] Per Olaf Huusfeldt,[c] Birgitte Gissel,[b] Marianne Barfoed,[b] Bettina Lundin Brockdorff,[d] Anne E. Lykkesfeldt[d] and Mikael Begtrup[a,*]

[a]*Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen, Denmark*
[b]*Novo Nordisk A/S, Novo Nordisk Park, DK-2760 Måløv, Denmark*
[c]*Pantheco A/S Fruebjergvej 3, DK-2100 Copenhagen, Denmark*
[d]*Department of Tumour Endocrinology, Institute of Cancer Biology, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen, Denmark*



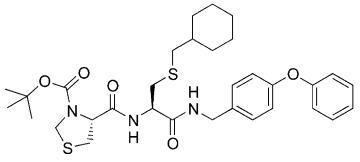
Bioorg. Med. Chem. 11 (2003) 1901

Structure–Activity Study of L-Amino Acid-Based N-Type Calcium Channel Blockers

Takuya Seko,* Masashi Kato, Hiroshi Kohno, Shizuka Ono, Kazuya Hashimura, Hideyuki Takimizu, Katsuhiko Nakai, Hitoshi Maegawa, Nobuo Katsube and Masaaki Toda

Minase Research Institute, Ono Pharmaceutical Co., Ltd., 3-1-1 Sakurai, Shimamoto, Mishima, Osaka 618-8585, Japan

The synthesis and SAR studies of L-cysteine-based N-type calcium channel blockers are described. L-Cysteine derivative **21f** was found to be a potent and selective N-type calcium channel blocker with an IC_{50} value of 0.14 μM.



21f IC_{50} = 0.14 μM

Bioorg. Med. Chem. 11 (2003) 1915

Topological Modelling of Analgesia

K. C. Mathur,[a] Sunita Gupta[a] and P. V. Khadikar[b,*]

[a]*Department of Chemistry, A.P.S. University, Rewa, 486003, India*
[b]*Research Division, Laxmi Fumigation and Pest Control, Pvt. Ltd., 3, Khatipura, Indore 452007, India*

Analgesic activity (log IC) for a large set of 97 analgesics were modelled topologically using distance-based topological indices. Due to familial behaviour, excellent results were obtained under splitted conditions.