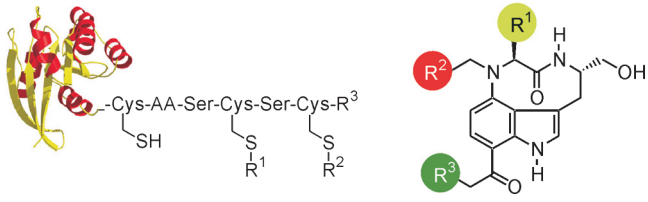
Bioorg. Med. Chem. 11 (2003) 3045

At the Crossroads of Chemistry and Biology

H. Waldmann[a,b,*]

[a]*Max-Planck-Institut für molekulare Physiologie, Abt. Chemische Biologie, Otto-Hahn-Str. 11, D-44227 Dortmund, Germany*
[b]*Fachbereich 3, Organische Chemie, Universität Dortmund, Germany*

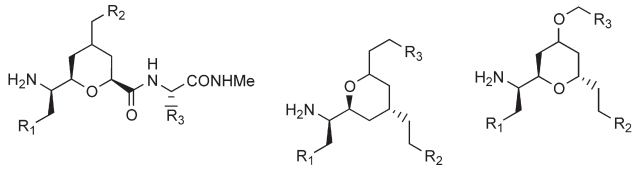


Bioorg. Med. Chem. 11 (2003) 3053

Novel Tetrahydropyran-Based Peptidomimetics from a Bioisosteric Transformation of a Tripeptide. Evidence of Their Activity at Melanocortin Receptors

Adam W. Mazur,* Anna Kulesza, Rajesh K. Mishra, Doreen Cross-Doersen, Anne F. Russell and Frank H. Ebetino

Procter & Gamble Pharmaceuticals, Health Care Research Center, Mason, OH 45040, USA



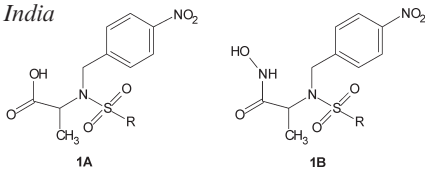
Bioorg. Med. Chem. 11 (2003) 3065

A Quantitative Structure–Activity Relationship Study on *Clostridium histolyticum* Collagenase Inhibitors: Roles of Electrotopological State Indices

S. P. Gupta[a,*] and S. Kumaran[b]

[a]*Department of Chemistry, Birla Institute of Technology and Science, Pilani-333031, India*
[b]*Department of Pharmacy, Birla Institute of Technology and Science, Pilani-333031, India*

A QSAR study has been made on different series of sulfonylated amino acids and their corresponding hydroxamtes, for example **1A** and **1B**, acting as *Clostridium histolyticum* collagenase inhibitors, to find that electrotopological state indices of their nitrogen and sulfur atoms can be good descriptors of their activity.



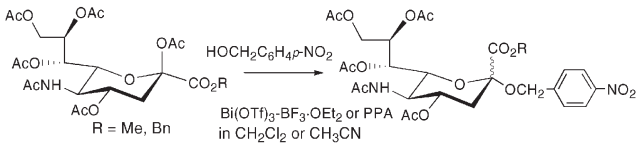
Bioorg. Med. Chem. 11 (2003) 3073

Glycosylation of Sialyl Acetates with a Novel Catalyst Combination: Bismuth Triflate and $BF_3{\cdot}OEt_2$ System

Kiyoshi Ikeda,[a,*] Yasuhiro Torisawa,[b] Takao Nishi,[b] Junichi Minamikawa,[b] Kiyoshi Tanaka[a] and Masayuki Sato[a,*]

[a]*School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Shizuoka 422-8526, Japan*
[b]*Process Research Laboratory, Second Tokushima Factory, Otsuka Pharmaceutical Co. Ltd., Kawauchi, Tokushima 771-0182, Japan*

A combined system of bismuth triflate [$Bi(OTf)_3$] and boron trifluoride etherate ($BF_3{\cdot}OEt_2$) in dichloromethane is an efficient promoter for the new glycosylation of *N*-acetylneuraminic acid derivatives.



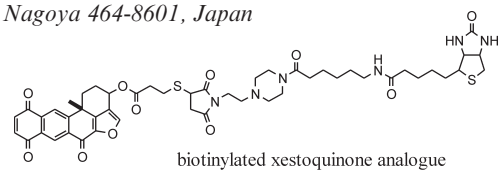
Bioorg. Med. Chem. 11 (2003) 3077

Synthesis of Biotinylated Xestoquinone That Retains Inhibitory Activity Against Ca^{2+} ATPase of Skeletal Muscle Myosin

Mitsuhiro Nakamura, Takahiko Kakuda, Yuichi Oba,* Makoto Ojika and Hideshi Nakamura

Graduate School of Bioagricultural Sciences, Nagoya University, Chikusa-ku, Nagoya 464-8601, Japan

Xestoquinone, a myosin Ca^{2+} ATPase inhibitor, was biotinylated on the basis of the study of the relationships between structure and activity. The biotinylated xestoquinone analogue retained the original Ca^{2+} ATPase inhibitory activity.



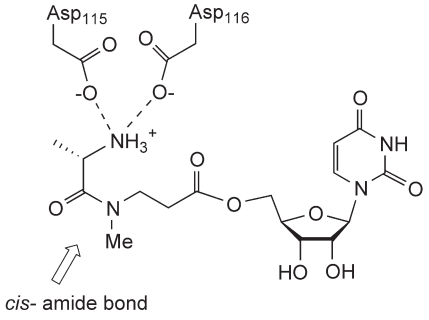
biotinylated xestoquinone analogue

Bioorg. Med. Chem. 11 (2003) 3083

Synthesis and Activity of 5′-Uridinyl Dipeptide Analogues Mimicking the Amino Terminal Peptide Chain of Nucleoside Antibiotic Mureidomycin A

Nigel I. Howard and Timothy D. H. Bugg*

Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK

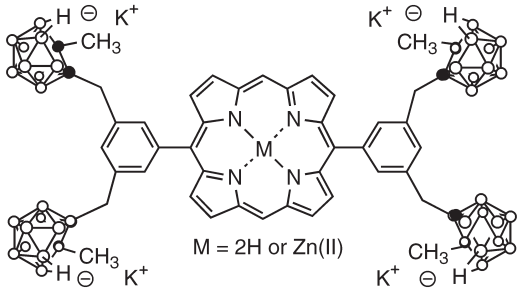


Bioorg. Med. Chem. 11 (2003) 3101

Synthesis, Toxicity and Biodistribution of Two 5,15-Di[3,5-(*nido*-carboranylmethyl)phenyl]porphyrins in EMT-6 Tumor Bearing Mice

M. Graça H. Vicente,[a,*] Anura Wickramasinghe,[b] Daniele J. Nurco,[b] Hong J. H. Wang,[b] Marta M. Nawrocky,[c] Michael S. Makar[c] and Michiko Miura[c]

[a]*Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA*
[b]*Department of Chemistry, University of California, Davis, CA 95616, USA*
[c]*Medical Department, Brookhaven National Laboratory, Upton NY 11973, USA*



Bioorg. Med. Chem. 11 (2003) 3109

An Engineered Chorismate Mutase with Allosteric Regulation

Sheng Zhang,[a] David B. Wilson[a] and Bruce Ganem[b,*]

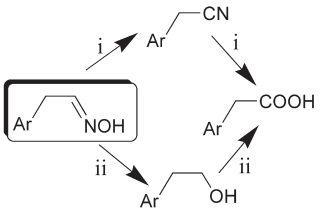
[a]*Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY 14853, USA*
[b]*Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14853, USA*

Bioorg. Med. Chem. 11 (2003) 3115

Probing Crucial Metabolic Pathways in Fungal Pathogens of Crucifers: Biotransformation of Indole-3-Acetaldoxime, 4-Hydroxyphenylacetaldoxime, and Their Metabolites

M. Soledade C. Pedras* and Sabine Montaut

Department of Chemistry, University of Saskatchewan, 110 Science Place, Saskatoon SK, Canada S7N 5C9



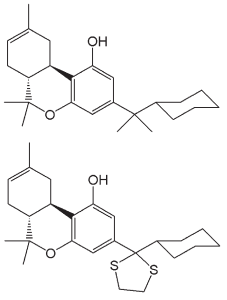
i) plant pathogen; ii) insect pathogen.

Bioorg. Med. Chem. 11 (2003) 3121

Synthesis and Testing of Novel Classical Cannabinoids: Exploring the Side Chain Ligand Binding Pocket of the CB1 and CB2 Receptors

Asha K. Nadipuram,[a] Mathangi Krishnamurthy,[a] Antonio M. Ferreira,[b] Wei Li[a] and Bob M. Moore, II[a,*]

[a]*Department of Pharmaceutical Sciences, College of Pharmacy, University of Tennessee-Memphis, Memphis, TN 38103, USA*
[b]*Computational Research on Materials Institute, Department of Chemistry, University of Memphis, Memphis, TN 38152, USA*

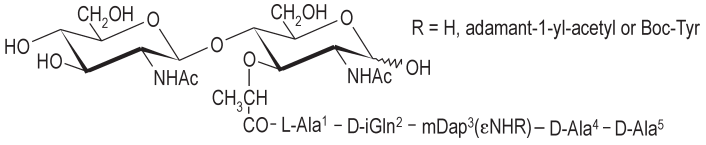


Bioorg. Med. Chem. 11 (2003) 3133

Modified Glycopeptides Related to Cell Wall Peptidoglycan: Conformational Studies by NMR and Molecular Modelling

Krisztina Fehér,[a] Primož Pristovšek,[b] László Szilágyi,[a,*] Đurdica Ljevaković[c] and Jelka Tomašić[c]

[a]*Department of Organic Chemistry, University of Debrecen, H-4010 Debrecen, Pf. 20., Hungary*
[b]*National Institute of Chemistry, Hajdrihova 19, SI-1001 Ljubljana, POB 660, Slovenia*
[c]*Institute of Immunology, Rockefellerova 2, HR-10 000 Zagreb, POB 266, Croatia*

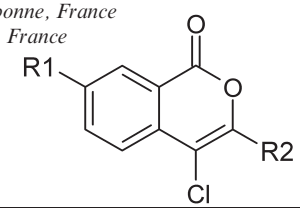


Bioorg. Med. Chem. 11 (2003) 3141

Synthesis of New 3-Alkoxy-7-amino-4-chloro-isocoumarin Derivatives as New β-Amyloid Peptide Production Inhibitors and Their Activities on Various Classes of Protease

Frédéric Bihel,[a] Gilles Quéléver,[a] Hugues Lelouard,[e] Agnès Petit,[b] Cristine Alvès da Costa,[b] Olivier Pourquié,[c] Frédéric Checler,[b] Annie Thellend,[d] Philippe Pierre[e] and Jean-Louis Kraus[a,*]

[a]*INSERM U-382, Developmental Biology Institute of Marseille (CNRS-INSERM-Univ. Méditerranée- AP Marseille), Laboratoire de Chimie Biomoléculaire, Faculté des Sciences de Luminy, case 907, 13288 Marseille Cedex 09, France*
[b]*Institut de Pharmacologie Moléculaire et Cellulaire du CNRS, UMR6097, 660 route des Lucioles, 06560 Valbonne, France*
[c]*LGPD Unité Mixte de Recherche 6545, Faculté des Sciences de Luminy, case 907, 13288 Marseille Cedex 09, France*
[d]*Laboratoire de Chimie Organique Biologique, UMR 7613, 4, place Jussieu, 75252 Paris Cedex 5, France*
[e]*Centre d'Immunologie de Marseille-Luminy, CNRS-INSERM- Univ. Méditerranée, Faculté des Sciences de Luminy, Case 906, 13288 Marseille Cedex 09, France*



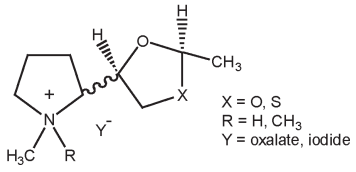
Bioorg. Med. Chem. 11 (2003) 3153

Synthesis and Cholinergic Affinity of Diastereomeric and Enantiomeric Isomers of 1-Methyl-2-(2-methyl-1,3-dioxolan-4-yl)pyrrolidine, 1-Methyl-2-(2-methyl-1,3-oxathiolan-5-yl)pyrrolidine and of Their Iodomethylates

Silvia Dei,[a] Cristina Bellucci,[a] Michela Buccioni,[b] Marta Ferraroni,[c] Fulvio Gualtieri,[a,*] Luca Guandalini,[a] Dina Manetti,[a] Rosanna Matucci,[d] Maria Novella Romanelli,[a] Serena Scapecchi[a] and Elisabetta Teodori[a]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Firenze, Via Gino Capponi 9, 50121 Firenze, Italy*
[b]*Dipartimento di Chimica, Università di Camerino,Via S.Agostino 1, 62032 Camerino (MC), Italy*
[c]*Dipartimento di Chimica, Università di Firenze, Via della Lastruccia 5, 50019 Sesto Fiorentino (FI), Italy*
[d]*Dipartimento di Farmacologia Preclinica e Clinica, Università di Firenze, Viale Pieraccini 6, 50139 Firenze, Italy*

Four out of the eight possible stereoisomers of 1-methyl-2-(2-methyl-1,3-dioxolan-4-yl)pyrrolidine, 1-methyl-2-(2-methyl-1,3-oxathiolan-5-yl)pyrrolidine and the corresponding iodomethylates have been synthesised. They were formally derived from hybridisation of potent though unselective agonists studied before, such as 1,3-dioxolane and 1,3-oxathiolane derivatives, with the structure of nicotine. In preliminary studies, their binding affinity has been evaluated on rat brain nicotinic and muscarinic receptors. While none of the compounds showed any nicotinic affinity up to the dose of 10 μM, most of the iodomethylates were endowed with promising affinity for the muscarinic receptors.



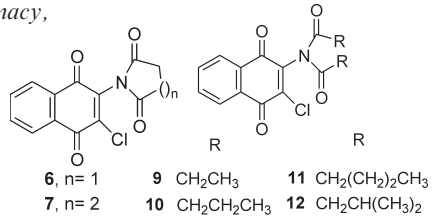
Bioorg. Med. Chem. 11 (2003) 3165

Synthesis and MEK1 Inhibitory Activities of Imido-Substituted 2-Chloro-1,4-naphthoquinones

Oladapo Bakare,[a,*] Curtis L. Ashendel,[b] Hairuo Peng,[c] Leon H. Zalkow[c] and Edward M. Burgess[c]

[a]*Department of Chemistry, Howard University, 525 College Street, Washington DC 20059, USA*
[b]*Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy, Purdue University, West Lafayette, IN 47907, USA*
[c]*School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA 30332, USA*

2-Chloro-3-(*N*-succinimidyl)-1,4-naphthoquinone **6** was found to be a selective inhibitor of MEK1 with an IC_{50} of 0.38 μM, while an open-chain homologue **10** showed selective cytotoxicity against renal cancer cell lines in the NCI in vitro tumor screening.



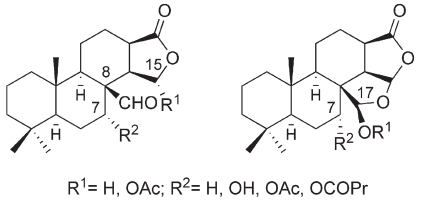
Bioorg. Med. Chem. 11 (2003) 3171

Synthesis and Cytotoxic Activity of Novel C7-Functionalized Spongiane Diterpenes

Manuel Arnó,[a] Liliana Betancur-Galvis,[b,*] Miguel A. González,[a,*] Jelver Sierra[b] and Ramón J. Zaragozá[a]

[a]*Departamento de Química Orgánica, Universidad de Valencia, E-46100 Burjassot, Valencia, Spain*
[b]*Grupo Infección y Cáncer, Universidad de Antioquia, A.A1226 Medellín, Colombia*

Based on two lead cytotoxic spongiane diterpenes, a new series of C7-oxygenated derivatives were synthesized and evaluated for their antitumor activity in vitro against the cancer cell lines HeLa and HEp-2. In general, introduction of either hydroxyl or acetoxy groups at C-7 did not improve the resultant cytotoxicity, while the presence of a butyrate ester led to more active compounds (CC_{50} = 4.0–9.5 μM).



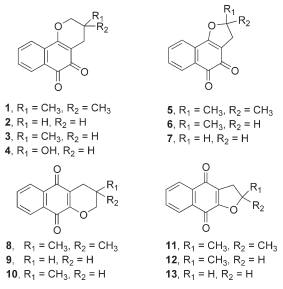
Bioorg. Med. Chem. 11 (2003) 3179

Potent Antitumor Activity of Synthetic 1,2-Naphthoquinones and 1,4-Naphthoquinones

Ngampong Kongkathip,[a,*] Boonsong Kongkathip,[a] Pongpun Siripong,[b] Chak Sangma,[a] Suwaporn Luangkamin,[a] Momad Niyomdecha,[a] Suppachai Pattanapa,[a] Suratsawadee Piyaviriyagul[b] and Palangpon Kongsaeree[c]

[a]*Natural Products and Organic Synthesis Research Unit, Department of Chemistry, Faculty of Science, Kasetsart University, Bangkok 10900, Thailand*
[b]*Natural Products Research Section, Research Division, National Cancer Institute, Bangkok 10400, Thailand*
[c]*Department of Chemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*

Thirteen 1,2- and 1,4-naphthoquinones (**1**–**13**) with mostly showed potent cytotoxicity were synthesized in high yields.



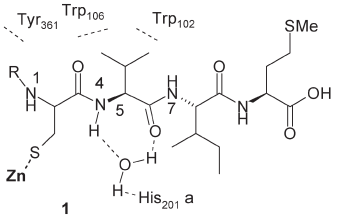
Bioorg. Med. Chem. 11 (2003) 3193

Parallel Liquid Synthesis of *N*,*N*′-Disubstituted 3-Amino Azepin-2-ones as Potent and Specific Farnesyl Transferase Inhibitors

Thierry Le Diguarher,[a] Jean-Claude Ortuno,[a] Gilbert Dorey,[a] David Shanks,[a] Nicolas Guilbaud,[b] Alain Pierré,[b] Jean-Luc Fauchère,[a] John A. Hickman,[b] Gordon C. Tucker[b] and Patrick J. Casara[a,*]

[a]*Department of Medicinal Chemistry, Institut de Recherches Servier, 125 chemin de Ronde, 78290 Croissy sur Seine, France*
[b]*Department of Experimental Oncology, Institut de Recherches Servier, 125 chemin de Ronde, 78290 Croissy sur Seine, France*

A rapid structure–activity study was performed by parallel liquid synthesis on *N*,*N*′-disubstitution of 3-amino azepin-2-one to afford potent and specific farnesyl transferase inhibitors with low nM enzymatic and cellular activities. The activities of the selected compounds were validated in vivo, and compounds **41a** and **44a** presented significant antitumour activity.



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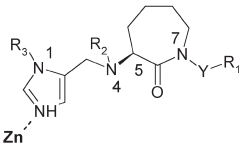


2

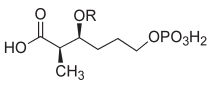
Bioorg. Med. Chem. 11 (2003) 3205

Synthesis and Biological Evaluation of Substrate-Based Inhibitors of 6-Phosphogluconate Dehydrogenase as Potential Drugs against African Trypanosomiasis

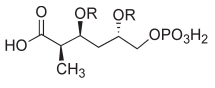
Christophe Dardonville,[a] Eliana Rinaldi,[b] Stefania Hanau,[b] Michael P. Barrett,[c] Reto Brun[d] and Ian H. Gilbert[a,*]

[a]*Welsh School of Pharmacy, Redwood building, Cardiff University, King Edward VII Avenue, Cardiff CF10 3XF, UK;* [b]*Dipartimento di Biochimica e Biologia Molecolare, Universita' di Ferrara, Via Luigi Borsari 46, 44100 Ferrara, Italy;* [c]*IBLS, Division of Infection & Immunity, University of Glasgow, Glasgow G12 8QQ, UK;* [d]*Swiss Tropical Institute, Socinstrasse 57, CH-4002 Basel, Switzerland*

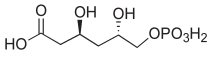
The synthesis and biological evaluation of three series of 6-phosphogluconate (6PG) analogues is described. These compounds were tested as inhibitors of 6-phosphogluconate dehydrogenase (6PGDH) from sheep liver and also *Trypanosoma brucei* where the enzyme is a validated drug target. The trypanocidal effect of the compounds was also evaluated in vitro against *T. brucei rhodesiense* as well as other related trypanosomatid parasites (i.e., *Trypanosoma cruzi* and *Leishmania donovani*).



(2*R*)-2-methyl-4,5-dideoxy analogues



(2*R*)-2-methyl-4-deoxy analogues



2,4-dideoxy analogue

Bioorg. Med. Chem. 11 (2003) 3215

Synthesis, Resolution, and Determination of the Absolute Configuration of the Enantiomers of *cis*-4,5-dihydroxy-1,2-dithiane 1,1-dioxide, an HIV-1 NCp7 Inhibitor

Anand Mayasundari,[a] William G. Rice,[b] Jonathan B. Diminnie[a] and David C. Baker[a,*]

[a]*Department of Chemistry, The University of Tennessee, Knoxville, Knoxville, TN 37996-1600, USA*
[b]*Laboratory of Antiviral Drug Mechanisms, National Cancer Institute-FCRDC, SAIC Frederick, Frederick, MD 21702-1201, USA*

The more bioactive enantiomer: