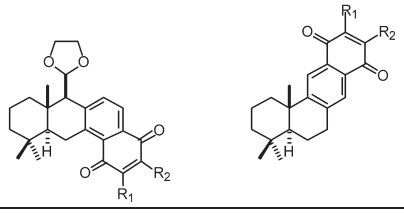
Synthesis and In Vitro Trypanocide Activity of Several Polycyclic Drimane-Quinone Derivatives

Bioorg. Med. Chem. 11 (2003) 2489

Mauricio A. Cuellar,[a] Cristian Salas,[a] Manuel J. Cortés,[a] Antonio Morello,[b] Juan Diego Maya[b] and Marcelo D. Preite[a,*]

[a]*Departamento de Química Orgánica, Facultad de Química, Pontificia Universidad Católica de Chile, Vicuña Mackenna 4860, Casilla 306, Correo 22, Santiago, Chile*
[b]*Facultad de Medicina, Programa de Farmacología Molecular y Clínica, ICBM, Universidad de Chile, Casilla 70086, Santiago 7, Chile*

Several drimane-derived naphtho- and anthraquinones were synthesized and their in vitro trypanocide activities were determined and compared with those of the current prescription drugs, nifurtimox and benznidazole. Two compounds showed a promisingly high bioactivity.



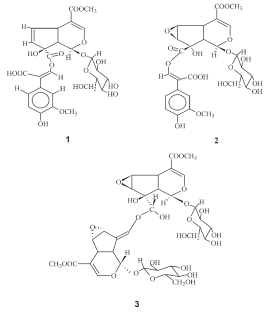
New Unusual Iridoids from the Leaves of Noni (*Morinda citrifolia* L.) Show Inhibitory Effect on Ultraviolet B-Induced Transcriptional Activator Protein-1 (AP-1) Activity

Bioorg. Med. Chem. 11 (2003) 2499

Shengmin Sang,[a,*] Guangming Liu,[b] Kan He,[c] Nanqun Zhu,[a] Zigang Dong,[b] Qunyi Zheng,[c] Robert T. Rosen[a] and Chi-Tang Ho[a]

[a]*Department of Food Science and Center for Advanced Food Technology, Rutgers University, 65 Dudley Road, New Brunswick, NJ 08901-8520, USA*
[b]*Hormel Institute, University of Minnesota, Austin, MN 55912, USA*
[c]*Pure World Botanicals, 375 Huyler Street, South Hackensack, NJ 07606, USA*

A novel iridoid dimer with two iridoid units connected by a rare ether group, together with two new unusual iridoids showing significant inhibition of UVB-induced Activator Protein-1 (AP-1) activity in cell cultures, have been isolated from the leaves of noni (*Morinda citrifolia* L.). Their structures were determined on the basis of detailed high-field 1D and 2D NMR spectral analysis. Their inhibitory effect on UVB-induced Activator Protein-1 (AP-1) activity are also discussed.



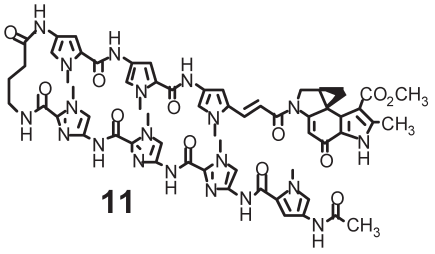
Specific Alkylation of Human Telomere Repeats by Hairpin Pyrrole-Imidazole Polyamide

Bioorg. Med. Chem. 11 (2003) 2503

Ryoko Takahashi, Toshikazu Bando and Hiroshi Sugiyama*

Division of Biofunctional Molecules, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, 2-3-10 Surugadai, Kanda, Chiyoda, Tokyo 101-0062, Japan

A novel hairpin polyamide-cyclopropapyrroloindole (CPI) conjugate PyImImIm-γ-PyPyPyLDu86 (conjugate **11**), which targets human telomere repeats $d(TTAGGG)_n$/$d(CCCTAA)_n$, was synthesized.



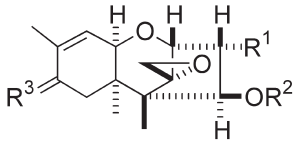
Cancer Preventive Potential of Trichothecenes from *Trichothecium roseum*

Bioorg. Med. Chem. 11 (2003) 2511

Kazuhide Konishi,[a] Akira Iida,[a,*] Masafumi Kaneko,[a] Kiyoshi Tomioka,[a] Harukuni Tokuda,[b] Hoyoku Nishino[b] and Yuko Kumeda[c]

[a]*Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan*
[b]*Department of Biochemistry, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto 602-0841, Japan*
[c]*Osaka Prefectural Institute of Public Health, Nakamichi, Osaka 537-0025, Japan*

Three new trichothecene sesquiterpenes, trichothecinols A–C (**1**–**3**), have been isolated from *Trichothecium roseum* together with three known analogues as chemopreventive agents.



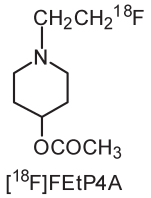
	R^1	R^2	R^3
1	OH	$COCH{=}CHCH_3$(*cis*)	O
2	H	$COCH{=}CHCH_3$(*cis*)	α-OH, β-H
3	OH	$COCH{=}CHCH_3$(*cis*)	α-OH, β-H

Bioorg. Med. Chem. 11 (2003) 2519

N-[^{18}F]fluoroethyl-4-piperidyl Acetate ([^{18}F]FEtP4A): A PET Tracer for Imaging Brain Acetylcholinesterase In Vivo

Ming-Rong Zhang,[a,b,*] Kenji Furutsuka,[a,b] Jun Maeda,[a,b] Tatsuya Kikuchi,[a,c] Takayo Kida,[a,b] Takashi Okauchi,[a,b] Toshiaki Irie[a] and Kazutoshi Suzuki[a]

[a]*Department of Medical Imaging, National Institute of Radiological Sciences, 4-9-1 Anagawa, Inage-ku, Chiba 263-8555, Japan*
[b]*SHI Accelerator Service Co. Ltd., 5-9-11, Kitashinagawa, Shinagawa-ku, Tokyo 141-8686, Japan*
[c]*Department of Pharmaceutical Sciences, Chiba University, 1-1-1 Yayoi, Inage-ku, Chiba 263-8522, Japan*



[^{18}F]FEtP4A

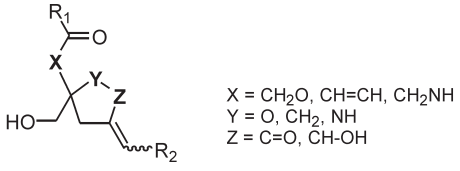
[^{18}F]FEtP4A, a potential PET tracer for imaging brain acetylcholinesterase (AchE) in vivo, was synthesized by the respective reaction of P4A with [^{18}F]FEtBr, [^{18}F]FEtBr/NaI and [^{18}F]FEtOTf. After iv injection of [^{18}F]FEtP4A into animals, ex vivo autoradiogram of rat brain and PET image of monkey brain displayed a significant radioactivity in the striatum, the region with the highest AchE activity in the brain.

Bioorg. Med. Chem. 11 (2003) 2529

Conformationally Constrained Analogues of Diacylglycerol (DAG). Effect on Protein Kinase C (PK-C) Binding by the Isosteric Replacement of Sn-1 and Sn-2 Esters in DAG-lactones

Ji-Hye Kang,[a] Hye-Eun Chung,[a] Su Yeon Kim,[a] Yerim Kim,[a] Jeewoo Lee,[a,*] Nancy E. Lewin,[b] Larry V. Pearce,[b] Peter M. Blumberg[b] and Victor E. Marquez[c]

[a]*Laboratory of Medicinal Chemistry, College of Pharmacy, Seoul National University, Seoul 151-742, South Korea*
[b]*Laboratory of Cellular Carcinogenesis and Tumor Promotion, NCI, NIH, Bethesda, MD 20892, USA*
[c]*Laboratory of Medicinal Chemistry, NCI, NIH, Frederick, MD 21701, USA*



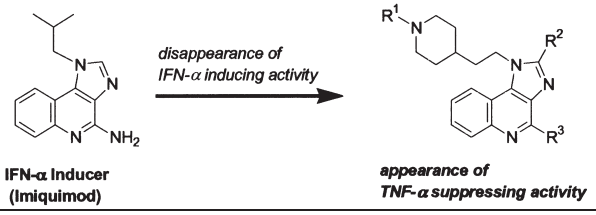
Bioorg. Med. Chem. 11 (2003) 2541

1*H*-Imidazo[4,5-*c*]quinoline Derivatives as Novel Potent TNF-α Suppressors: Synthesis and Structure–activity Relationship of 1-, 2-and 4-Substituted 1*H*-imidazo[4,5-*c*]quinolines or 1*H*-imidazo[4,5-*c*]pyridines

Tomoyuki Izumi,* Jun Sakaguchi, Makoto Takeshita, Harumi Tawara, Ken-ichi Kato, Hitomi Dose, Tomomi Tsujino, Yoshinari Watanabe and Hideo Kato

Research Division, R&D Headquarters, Hokuriku Seiyaku Co., Ltd., 37-1-1, Inokuchi, Katsuyama, Fukui, 911-8555, Japan

Structural modification of imiquimod, which is known as an interferon-α (IFN-α) inducer, for the aim of finding a novel and small-molecule tumor necrosis factor-α (TNF-α) suppressor and structure–activity relationship (SAR) are described.

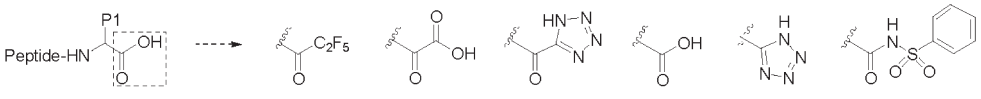


Bioorg. Med. Chem. 11 (2003) 2551

Acyl Sulfonamides as Potent Protease Inhibitors of the Hepatitis C Virus Full-Length NS3 (Protease-Helicase/NTPase). A Comparative Study of Different C-Terminals

Anja Johansson,[a] Anton Poliakov,[b] Eva Åkerblom,[a] Karin Wiklund,[a] Gunnar Lindeberg,[a] Susanne Winiwarter,[a] U. Helena Danielson,[b] Bertil Samuelsson[c] and Anders Hallberg[a,*]

[a]*Department of Medicinal Chemistry, Uppsala University, BMC, Box 574, SE-751 23 Uppsala, Sweden*
[b]*Department of Biochemistry, Uppsala University, BMC, Box 576, SE-751 23 Uppsala, Sweden*
[c]*Medivir AB, Lunastigen 7, SE-141 44 Huddinge, Sweden*



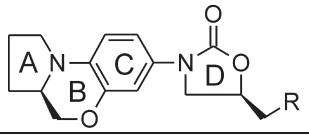
Bioorg. Med. Chem. 11 (2003) 2569

Three-Dimensional Quantitative Structure-Activity Relationship (3D-QSAR) Studies of Tricyclic Oxazolidinones as Antibacterial Agents

Bulusu Gopalakrishnan,[a,*] Akash Khandelwal,[a] Shaikh Abdul Rajjak,[a] Natesan Selvakumar,[b] Jagattaran Das,[b] Sanjay Trehan,[b] Javed Iqbal[c] and Magadi Sitaram Kumar[b]

[a]*Department of Molecular Modeling and Drug Design, Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India*
[b]*Antiinfectives Group, Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India*
[c]*Discovery Chemistry, Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India*

Robust QSAR models were obtained using CoMFA and CoMSIA methods that provide a guide to further modification of new tricyclic oxazolidinones.

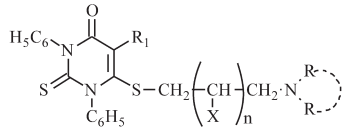


Bioorg. Med. Chem. 11 (2003) 2575

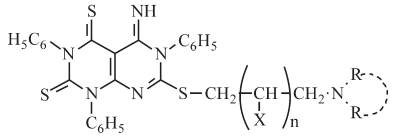
Synthesis and Antiproliferative Activity of Basic Thioanalogues of Merbarone

Angelo Ranise,[a,*] Andrea Spallarossa,[a] Silvia Schenone,[a] Olga Bruno,[a] Francesco Bondavalli,[a] Alessandra Pani,[b] Maria Elena Marongiu,[b] Valeria Mascia,[b] Paolo La Colla[b,*] and Roberta Loddo[b]

[a]*Dipartimento di Scienze Farmaceutiche, Università degli Studi di Genova, Viale Benedetto XV 3, 16132 Genova, Italy*
[b]*Dipartimento di Biologia Sperimentale, Università di Cagliari, Cittadella Universitaria di Monserrato, 09042 Monserrato, Cagliari, Italy*



$\mathbf{R_1}$ = $COOC_2H_5$, C_6H_5, $COCH_3$



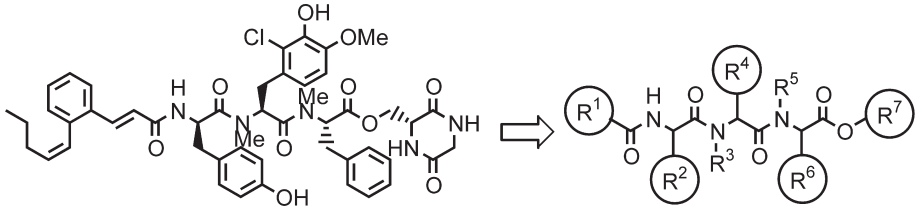
Bioorg. Med. Chem. 11 (2003) 2591

Solid Phase Synthesis of a Pepticinnamin E Library

Michael Thutewohl and Herbert Waldmann*

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

A library of analogues of the naturally occurring farnesyltransferase inhibitor pepticinnamin E is synthesized via different solid-phase routes.

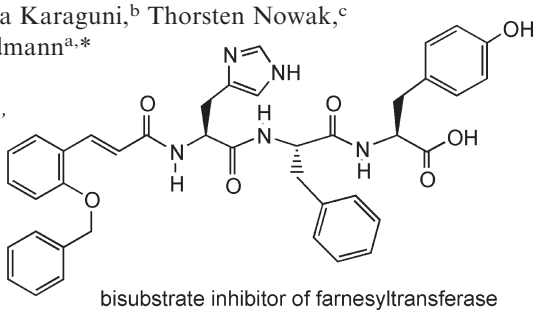


Bioorg. Med. Chem. 11 (2003) 2617

Identification of Mono- and Bisubstrate Inhibitors of Protein Farnesyltransferase and Inducers of Apoptosis from a Pepticinnamin E Library

Michael Thutewohl,[a] Lars Kissau,[a] Boriana Popkirova,[b] Ionna-Maria Karaguni,[b] Thorsten Nowak,[c] Michael Bate,[c] Jürgen Kuhlmann,[b] Oliver Müller[b] and Herbert Waldmann[a,*]

[a]*Max-Planck-Institut für molekulare Physiologie, Abt. Chemische Biologie, Otto-Hahn-Str. 11, D-44227 Dortmund und Fachbereich 3, Organische Chemie, Universität Dortmund, Germany*
[b]*Max-Planck-Institut für molekulare Physiologie, Abt. Strukturelle Biologie, Otto-Hahn-Str. 11, D-44227 Dortmund, Germany*
[c]*AstraZeneca, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG, UK*



bisubstrate inhibitor of farnesyltransferase

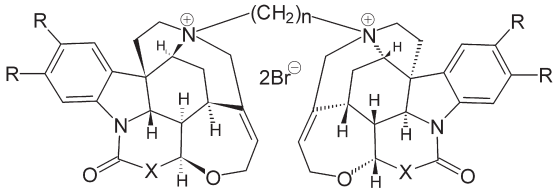
Bioorg. Med. Chem. 11 (2003) 2627

Bisquaternary Dimers of Strychnine and Brucine. A New Class of Potent Enhancers of Antagonist Binding to Muscarinic M_2 Receptors

D. P. Zlotos,[a,*] S. Buller,[b] U. Holzgrabe[a] and K. Mohr[b]

[a]*Pharmaceutical Institute, University of Würzburg, Am Hubland, 97074 Würzburg, Germany*
[b]*Department of Pharmacology and Toxicology, Institute of Pharmacy, University of Bonn, An der Immenburg 4, 53121 Bonn, Germany*

R = H, OCH_3; X = CH_2, C = N–OH; *n* = 6–8.

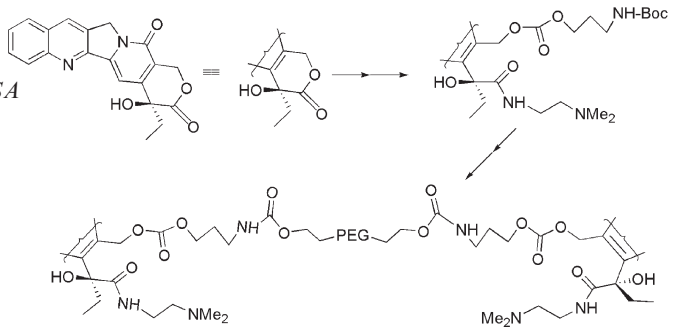


Bioorg. Med. Chem. 11 (2003) 2635

Tripartate Poly(ethylene Glycol) Prodrugs of the Open Lactone Form of Camptothecin

Richard B. Greenwald,* Hong Zhao and Jing Xia

Enzon Inc., 20 Kingsbridge Road, Piscataway, NJ 00854, USA

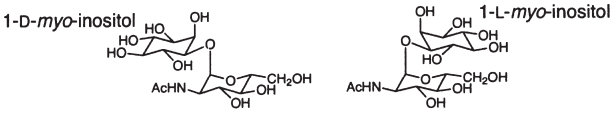


Bioorg. Med. Chem. 11 (2003) 2641

Synthesis of 1-D- and 1-L-*myo*-Inosityl 2-*N*-Acetamido-2-deoxy-α-D-glucopyranoside Establishes Substrate Specificity of the *Mycobacterium tuberculosis* Enzyme AcGI Deacetylase

Gillian M. Nicholas,[a] Lisa L. Eckman,[a] Pavol Kováč,[b] Sarah Otero-Quintero[a] and Carole A. Bewley[a,*]

[a]*Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892-0820, USA*
[b]*Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892-0820, USA*



Bioorg. Med. Chem. 11 (2003) 2649

Helical Templating of Oligopeptides by Cyclodextrin Dimers

David Wilson, Lisa Perlson and Ronald Breslow*

Department of Chemistry, Columbia University, New York, NY 10027, USA

A cyclodextrin dimer with the correct length can induce helical folding in a peptide carrying the hydrophobic L-*t*-butylphenylalanine unit in the i and i + 11 positions.