Bioorg. Med. Chem. **1996**, *4*, 143

Solid Phase Synthesis of pp60^{src}-Related Phosphopeptides via 'Global' Phosphorylation and Their Use as Substrates for Enzymatic Phosphorylation by Casein Kinase-2

John W. Perich,*[a,b] Flavio Meggio[c] and Lorenzo A. Pinna[c]
[a]*Centre of Pharmacology–Endocrinology, CNRS-INSERM, Montpellier, France*
[b]*School of Chemistry, The University of Melbourne, Parkville 3052, Australia*
[c]*Department of Biological Chemistry, University of Padova, Padova, Italy*

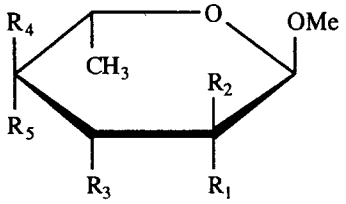
The seven phosphopeptides, NEY(*P*)SA, AEY(*P*)SA, ASY(*P*)SA, AS(*P*)YSA, ATY(*P*)SA, AT(*P*)YSA and AS(*P*)Y(*P*)SA, were prepared by the 'global' 'phosphite-triester' phosphorylation method. Their subsequent use in CK-2 studies showed that the Tyr(*P*) residue was the major site determinant and was able to direct phosphorylation to both the +1 and −1 position.

Bioorg. Med. Chem. **1996**, *4*, 151

Theoretical Study of Anthracycline Antibiotic Analogues — III. Conformational Analysis on Different 2,6-Dideoxy-2-halo-α-L-hexopyranoses by Molecular Mechanics and Semiempirical Methods

Redouan El Bergmi and José Molina Molina,*
Grupo de Modelización y Diseño Molecular, Instituto de Biotecnología, Campus Fuentenueva, Universidad de Granada, 18071-Granada, Spain

Molecular modeling studies, including solvation effects and electrostatic potential calculations, of compounds **1**–**11** were performed in an attempt to investigate the influence of the introduction of a halogen group at the C-2 position of the sugar moiety.



Bioorg. Med. Chem. **1996**, *4*, 165

Triazolines—XXVII. Δ^2-1,2,3-Triazoline Anticonvulsants: Novel 'Built-in' Heterocyclic Prodrugs with a Unique 'Dual-Action' Mechanism for Impairing Excitatory Amino Acid L-Glutamate Neurotransmission

P. K. Kadaba,[ab]* P. J. Stevenson,[c] I. P-Nnane[d] and L. A. Damani[d]
[a]*Division of Medicinal Chemistry and Pharmaceutics, College of Pharmacy, A. B. Chandler Medical Center, University of Kentucky, Lexington, KY 40536-0082, U.S.A.* [b]*K & K Biosciences Inc., 3411 Brookhaven Drive, Lexington, KY 40502, U.S.A.* [c]*Chelsea Department of Pharmacy, King's College London, London SW3 6LX, U.K. and* [d]*Department of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong*

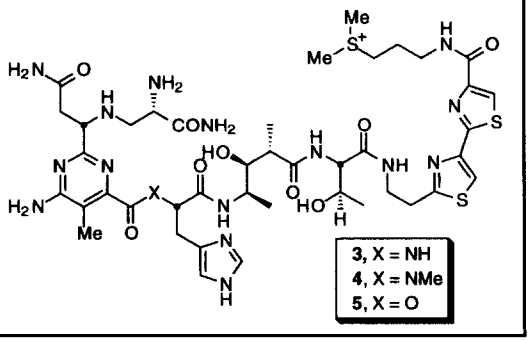
The metabolism and pharmacology of a unique triazoline anticonvulsant ADD17014 are reported and a mechanism of action proposed.

Bioorg. Med. Chem. **1996**, *4*, 179

Synthesis and Evaluation of Deglycobleomycin A_2 Analogues Containing a Tertiary N-Methyl Amide and Simple Ester Replacement for the L-Histidine Secondary Amide: Direct Functional Characterization of the Requirement for Secondary Amide Metal Complexation

Dale L. Boger,* Shuji Teramoto and Hui Cai
Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, CA 92037, U.S.A.

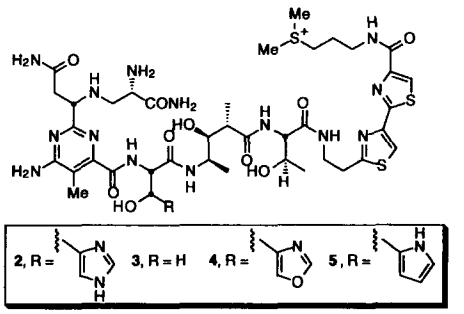
The preparation and comparative DNA cleavage properties of **3**–**5** are detailed.



Bioorg. Med. Chem. **1996**, *4*, 195

Synthesis and Evaluation of Potential N^{π} and N^{σ} Metal Chelation Sites within the β-Hydroxy-L-Histidine Subunit of Bleomycin A_2: Functional Characterization of Imidazole N^{π} Metal Complexation

Dale L. Boger,* Timothy M. Ramsey and Hui Cai
Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, CA 92037, U.S.A.



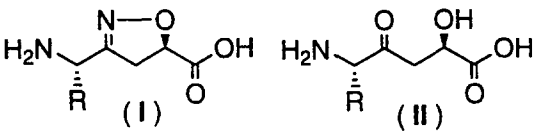
The synthesis and evaluation of **4** and **5**, functionalized deglycobleomycin A_2 (**2**) analogues incorporating an oxazole and pyrrole in place of metal chelating imidazole, are detailed.

Bioorg. Med. Chem. **1996**, *4*, 209

Synthesis of 2-Isoxazoline and α-Hydroxy Ketomethylene Dipeptide Isosteres

Yong Jun Chung, Eun Jung Ryu, Gyochang Keum and Byeang Hyean Kim*
Department of Chemistry, Pohang University of Science and Technology, Pohang, 790-784, Korea

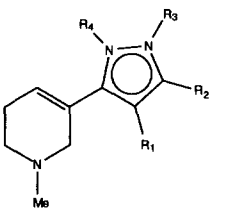
A simple and stereoselective method for synthesizing novel dipeptide isosteres [e.g., (**I**) and (**II**)] is reported.



Bioorg. Med. Chem. **1996**, *4*, 227

Synthesis and Muscarinic Activities of 3-(Pyrazolyl)-1,2,5,6-tetrahydropyridine Derivatives

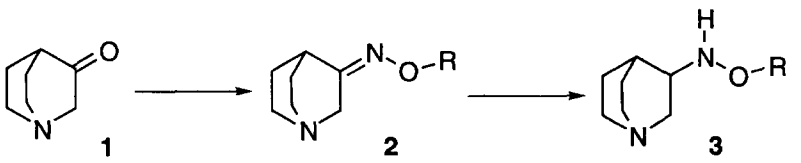
Ralf Plate,[a,*] Marc J. M. Plaum,[a] Thijs de Boer,[b] John S. Andrews,[b] Duncan R. Rae[c] and Sam Gibson[c]
[a]Department of Medicinal Chemistry and [b]Department of Neuropharmacology, Scientific Development Group N.V. Organon, P.O. Box 20, 5340 BH OSS, The Netherlands.
[c]Department of Medicinal Chemistry, Organon Laboratories, Ltd, Newhouse, Motherwell, U.K.



Bioorg. Med. Chem. **1996**, *4*, 239

Synthesis and Muscarinic M_3 Pharmacological Activities of 1-Azabicyclo[2.2.2]octan-3-one Oxime Derivatives

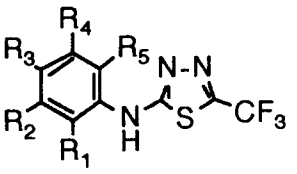
Ralf Plate,[*a] Marc J. M. Plaum,[a] Thijs de Boer[b] and John S. Andrews[b]
[a]Department of Medicinal Chemistry and [b]Department of Neuropharmacology, Scientific Development Group, N.V. Organon, P.O. Box 20, 5340 BH OSS, The Netherlands



Bioorg. Med. Chem. **1996**, *4*, 247

Design and Synthesis of New Mitochondrial Cytotoxin *N*-Thiadiazolylanilines that Inhibit Tumor Cell Growth

Hitoshi Hori,[a]* Naoto Noguchi,[a] Hideakira Yokoyama,[a] Hirohiko Ise,[a] Cheng-Zhe Jin,[a] Soko Kasai,[a] Takatsugu Goto[a] and Zenei Taira[b]
[a]Department of Biological Science and Technology, Faculty of Engineering, The University of Tokushima, Minamijosanjimacho-2, Tokushima 770, Japan. [b]Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashirocho, Tokushima 770, Japan

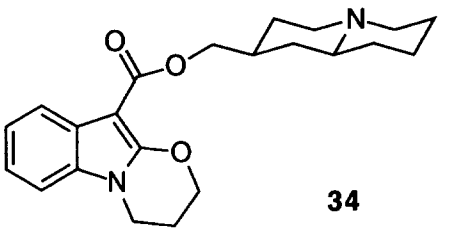


N-Thiadiazolylanilines TX-108 and TX-109, designed as mitochondrial cytotoxins, inhibited the growth of EMT6/KU mammary sarcoma cells at low micromolar levels.

Bioorg. Med. Chem. **1996**, *4*, 255

Azabicyclic Indole Esters as Potent 5-HT_4 Receptor Antagonists

P. A. Wyman,* L. M. Gaster, F. D. King, J. M. Sutton, E. S. Ellis, K. A. Wardle and T. J. Young
SmithKline Beecham Pharmaceuticals, Third Avenue, The Pinnacles, Harlow, Essex CM19 5AW, U.K.



34

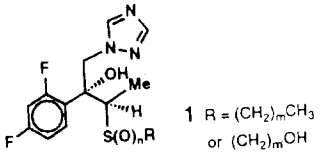
The synthesis and 5-HT_4 receptor antagonist potency of a series of azabicyclic indole esters is described. SAR studies identified the quinolizidinylmethyl side chain as optimum. This was incorporated with the oxazino[3,2-*a*]indole nucleus to afford **34** with pK_i of 10.0.

Bioorg. Med. Chem. **1996**, *4*, 263

Synthesis and Antifungal Activity of Alkylthio and Alkylsulfonyl Derivatives of SM-8668

Hiroshi Miyauchi,* Koichi Kozuki, Tomoharu Tanio and Naohito Ohashi
Research Center, Sumitomo Pharmaceuticals Co., Ltd, 1–98 Kasugadenaka 3-Chome, Konohana-ku, Osaka 554, Japan

Alkyl derivatives of sulfur-containing triazoles **1** were synthesized and estimated for their antifungal activities. Some of the compounds showed potent activities against both candidiasis and aspergillosis. The induction of hydroxyl group at the end of their alkyl chain made their activities stronger.

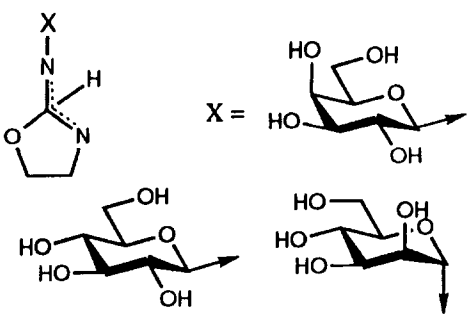


1 R = $(CH_2)_mCH_3$ or $(CH_2)_mOH$

Bioorg. Med. Chem. **1996**, *4*, 275

Synthesis and Inhibitory Activity of Glycosidase Inhibitors, Glycosylamino-Oxazolines

Chikara Uchida and Seiichiro Ogawa*
Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohuku-ku, Yokohama 223, Japan



Three glycosylamino-oxazolines with β-*galacto*, β-*gluco* and α-*manno* configurations, were synthesized and subjected to biological assay. The α-mannosyl compound was shown to be a moderate α-mannosidase (Jack beans) inhibitor.