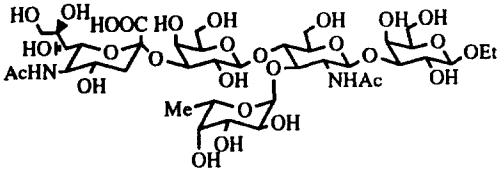
A Highly Practical Synthesis of Sialyl Lewis X Pentasaccharide and an Investigation of Binding to E-, P-, and L-Selectins

Bioorg. Med. Chem. **1996**, *4*, 1167

Takao Kiyoi,[a] Yoshiyuki Nakai,[a] Hirosato Kondo,[a,*] Hideharu Ishida,[b] Makoto Kiso[b] and Akira Hasegawa[b]
[a]Department of Medicinal Chemistry, Kanebo Ltd, New Drug Research Laboratories, 5-90 Tomobuchi-Cho, Miyakojima-Ku, Osaka 534, Japan and [b]Department of Applied Bioorganic Chemistry, Gifu University, Gifu 501-11, Japan

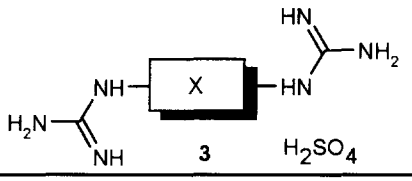
A practical chemical synthesis and a selectin blocking activity of a sialyl Lewis X pentasaccharide are described.



Synthesis and Pharmacology of Alkanediguanidinium Compounds that Block the Neuronal Nicotinic Acetylcholine Receptor

Bioorg. Med. Chem. **1996**, *4*, 1177

M. Villarroya,[a] L. Gandía,[a] M. G. López,[a] A. G. García,[a] S. Cueto,[b] J.-L. García-Navío[b] and J. Alvarez-Builla[b,*]
[a]Departamento de Farmacología, Facultad de Medicina, Universidad Autónoma de Madrid, Arzobispo Morcillo, 4, 28029 Madrid, Spain; [b]Departamento de Química Orgánica, Universidad de Alcalá de Henares, E-28871 Alcalá de Henares, Madrid, Spain

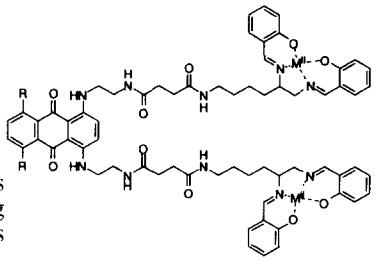


Salen–Anthraquinone Conjugates. Synthesis, DNA-Binding and Cleaving Properties, Effects on Topoisomerases and Cytotoxicity

Bioorg. Med. Chem. **1996**, *4*, 1185

Sylvain Routier,[a] Nicole Cotelle,[a] Jean-Pierre Catteau,[a] Jean-Luc Bernier,[a,*] Michael J. Waring,[b] Jean-François Riou[c] and Christian Bailly[d,*]
[a]Laboratoire de Chimie Organique Physique, URA CNRS 351, USTL Bât. C3, 59655 Villeneuve d'Ascq, France, [b]Department of Pharmacology, University of Cambridge, Cambridge CB2 1QJ, U.K. [c]Rhône-Poulenc Rorer, Centre de Recherche de Vitry-Alfortville, 94403 Vitry sur Seine, France, [d]Institut de Recherches sur le Cancer, INSERM U 124, Place de Verdun, 59045 Lille, France

A series of anthraquinone derivatives bearing either one or two salen moieties complexed with Cu^{II} or Ni^{II} have been synthesized. Their DNA-binding and cleaving properties and the effects of DNA cleavage mediated by topoisomerases as well as their cytotoxicity have been examined.

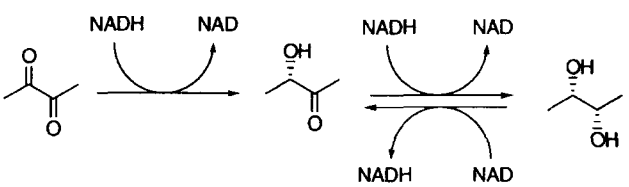


Properties of Diacetyl (Acetoin) Reductase from *Bacillus stearothermophilus*

Bioorg. Med. Chem. **1996**, *4*, 1197

P. Paolo Giovannini,[a] Alessandro Medici,[b] Carlo M. Bergamini,[a] and Mario Rippa[a,*]
[a]Department of Biochemistry and Molecular Biology and [b]Department of Chemistry, University of Ferrara, 44100 Ferrara, Italy

A reductase stereochemically catalysing the reaction reported here has been purified and partially characterised. The same enzyme also catalyses redox reactions on bicyclic octen and heptenols and could be used for the recycling of NAD and NADH in organic syntheses involving oxidoreductases.

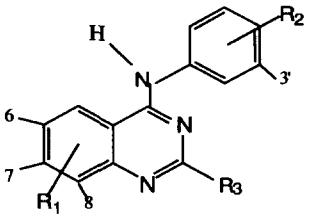


Tyrphostins IV—Highly Potent Inhibitors of EGF Receptor Kinase. Structure–Activity Relationship Study of 4-Anilidoquinazolines

Bioorg. Med. Chem. **1996**, *4*, 1203

Aviv Gazit,[a,b] Jeffrey Chen,[c] Harald App,[c] Gerald McMahon,[c] Peter Hirth,[c] Irit Chen[b] and Alexander Levitzki[b,*]
Departments of [a]Organic Chemistry and [b]Biological Chemistry, The Alexander Silverman Institute of Life Sciences, The Hebrew University of Jerusalem, Givat Ram, Jerusalem 91904, Israel. [c]SUGEN, Inc. 515 Galveston Drive, Redwood City, CA 94063-4720, U.S.A.

Potent 4-anilido substituted quinazolines which potently inhibit epidermal growth factor receptor (EGFR) kinase were prepared. Structure–activity relationship studies reveal high sensitivity to substitution at the aniline ring.

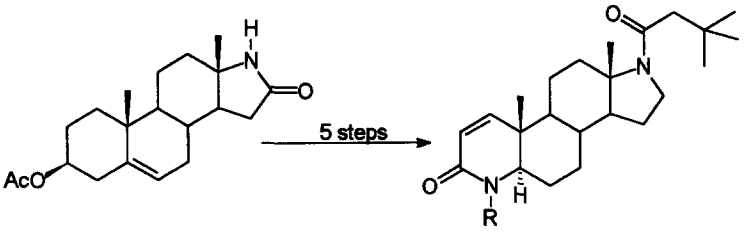


Synthesis of 4,17-Diazasteroid Inhibitors of Human 5α-Reductase

Bioorg. Med. Chem. **1996**, *4*, 1209

Jacek W. Morzycki,*[a,b] Zenon Łotowski,[a] Agnieszka Z. Wilczewska[a] and J. Darren Stuart[c]
[a]Institute of Chemistry, University of Warsaw, Białystok Branch, Piłsudskiego 11/4, 15-443 Białystok, Poland [b]Pharmaceutical Research Institute, Rydygiera 8, 01-793 Warszawa, Poland [c]Glaxo Inc. Research Institute, Five Moore Drive, Research Triangle Park, NC 27709, U.S.A.

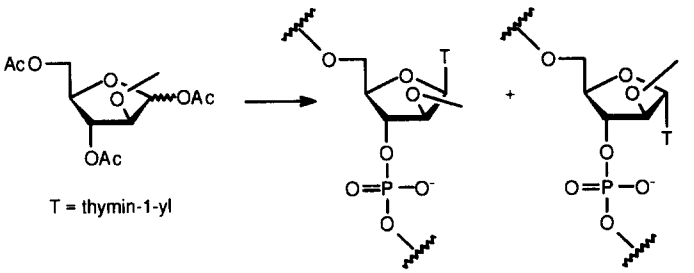
The synthesis of the 17-aza isomer of steroid 5α-reductase inhibitor, finasteride, is described. A series of 4,17-diazasteroids was assayed against the enzyme 5α-reductase.



Synthesis and Properties of α- and β-Oligodeoxynucleotides Containing α- and β-1-(2-*O*-Methyl-D-arabinofuranosyl)thymine

Bioorg. Med. Chem. **1996**, *4*, 1217

Charlotte H. Gotfredsen, Jens Peter Jacobsen and Jesper Wengel*
Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

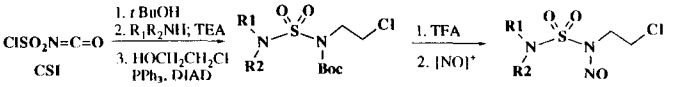


A New Family of Potential Oncostatics: 2-Chloroethylnitrososulfamides (CENS)—I. Synthesis, Structure, and Pharmacological Evaluation (Preliminary Results)

Bioorg. Med. Chem. **1996**, *4*, 1227

M. Abdaoui,[a] G. Dewynter,[a] N. Aouf,[a] G. Favre,[b] A. Morère[a] and J.-L. Montero [a,*]
[a]Laboratory of Biomolecular Chemistry, University of Montpellier-II, 34095 Montpellier, France; [b]Claudius-Regaud Institute for Medical Oncology, 31052 Toulouse, France

A new series of alkylating agents, 2-chloroethylnitrososulfamides (CENS), were developed on the model of 2-chloroethylnitrosoureas. Starting from chlorosulfonyl isocyanate, a four-step synthesis (carbamoylation–sulfamoylation, Mitsunobu alkylation, deprotection and nitrosation) gives the title compounds. The pharmacological evaluation shows a significant oncostatic activity.

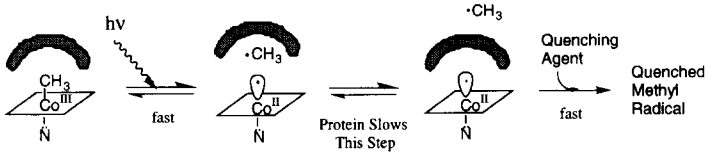


A Protein Radical Cage Slows Photolysis of Methylcobalamin in Methionine Synthase from *Escherichia coli*

Bioorg. Med. Chem. **1996**, *4*, 1237

Joseph T. Jarrett,[a] Catherine L. Drennan,[a,b] Mohan Amaratunga,[a] Jeffrey D. Scholten,[c] Martha L. Ludwig[a,b] and Rowena G. Matthews[a,b,*]

[a]*Biophysics Research Division and* [b]*Department of Biological Chemistry, University of Michigan, Ann Arbor, MI 48109, U.S.A.* [c]*Parke-Davis Research Division, Warner-Lambert Co., Ann Arbor, MI 48105, U.S.A.*



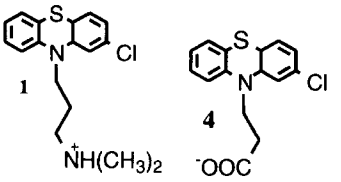
Charge is the Major Discriminating Factor for Glutathione Reductase Versus Trypanothione Reductase Inhibitors

Bioorg. Med. Chem. **1996**, *4*, 1247

Carlos H. Faerman,[a] Savvas N. Savvides,[a] Corey Strickland,[a] Mark A. Breidenbach,[a] James A. Ponasik,[b] Bruce Ganem,[b] Daniel Ripoll,[c] R. Luise Krauth-Siegel[d] and P. Andrew Karplus[a]

[a]*Department of Biochemistry, Molecular and Cell Biology* [b]*Department of Chemistry, Baker Laboratory and* [c]*Cornell Theory Center Cornell University, Ithaca, NY 14853-1301, U.S.A.* [d]*Institut für Biochemie II, Ruprecht-Karls-Universität, Heidelberg, Germany*

Compound **1** (net charge of +1) is a competitive inhibitor of trypanothione reductase ($K_i = 14$ μM), whereas compound **4** (net charge of −1) is a competitive inhibitor of human glutathione reductase ($K_i = 165$ μM). The selective inhibition of the two enzymes by phenothiazine derivatives is reported.



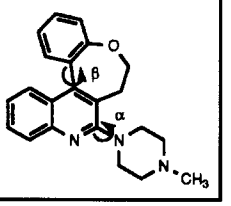
Molecular Structure and Dynamics of Some Potent 5-HT$_3$ Receptor Antagonists. Insight into the Interaction with the Receptor

Bioorg. Med. Chem. **1996**, *4*, 1255

Andrea Cappelli[a,*] Alessandro Donati,[b] Maurizio Anzini,[a] Salvatore Vomero,[a] Pier G. De Benedetti,[c] Maria Cristina Menziani[c] and Thierry Langer[d]

[a]*Dipartimento Farmaco Chimico Tecnologico, Università di Siena, Via Banchi di Sotto 55, 53100 Siena, Italy.* [b]*Dipartimento di Chimica, Università di Siena, Pian dei Mantellini, 53100 Siena, Italy.* [c]*Università degli Studi di Modena, Via Campi 183, 41100 Modena, Italy.* [d]*Institute of Pharmaceutical Chemistry, University of Innsbruck, Innrain 52A, A-6020 Innsbruck, Austria*

The molecular structure and the dynamic behaviour of some potent 5-HT$_3$ antagonists have been investigated by NMR spectroscopy and by computational methods in order to gain insight into the structure–activity relationships at a molecular level. A model of ligand–receptor interaction has been developed on the basis of molecular orbital calculation.



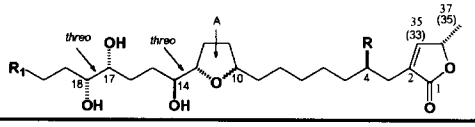
cis-Gigantrionenin and 4-Acetyl Gigantetrocin A, Two New Bioactive Annonaceous Acetogenins from *Goniothalamus giganteus*, and the Stereochemistries of Acetogenin 1,2,5-Triols

Bioorg. Med. Chem. **1996**, *4*, 1271

Lu Zeng, Yan Zhang, Qing Ye, Gouen Shi, Kan He and Jerry L. McLaughlin*

Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907, U.S.A.

Two novel acetogenins, *cis*-gigantrionenin (**1**) and 4-acetyl gigantetrocin A (**2**), were isolated from bark of *Goniothalamus giganteus* (Annonaceae). Compounds **1** and **2** showed significant bioactivities among six human solid tumor cell lines.



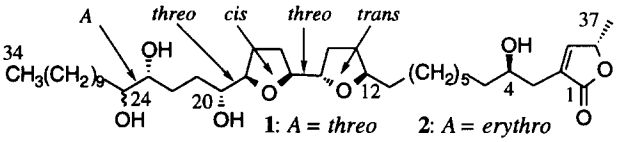
	A	R	R_1
1	*cis*	H	$CH_3(CH_2)_{11}CH{=}CH$-
2	*trans*	OAc	$CH_3(CH_2)_{11}$-

Bioorg. Med. Chem. **1996**, *4*, 1281

Applying Mosher's Method to Acetogenins Bearing Vicinal Diols. The Absolute Configurations of Muricatetrocin C and Rollidecins A and B, New Bioactive Acetogenins from *Rollinia mucosa*

G. Shi,[a] Z. Gu,[a] K. He,[a] K. V. Wood,[b] L. Zeng,[a] Q. Ye,[a] J. M. MacDougal[c] and J. L. McLaughlin[a,*]
[a]*Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN 47907, U.S.A.* [b]*Department of Chemistry, Purdue University, West Lafayette, IN 47907, U.S.A.* [c]*Division of Horticulture, Missouri Botanical Garden, P.O. Box 299, St. Louis, MO 63166, U.S.A.*

Muricatetrocin C, a new mono-THF acetogenin, and rollidecins A and B (**1**, **2**), new adjacent bis-THF acetogenins, were isolated and showed potent and selective cytotoxicities. Analyses of their per-Mosher esters determined their absolute configurations.

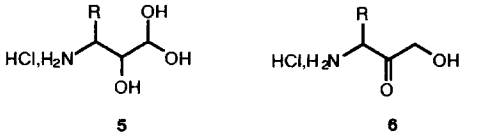


Bioorg. Med. Chem. **1996**, *4*, 1287

3-Amino-2-hydroxy-propionaldehyde and 3-Amino-1-hydroxy-propan-2-one Derivatives: New Classes of Aminopeptidase Inhibitors

Céline Tarnus, Jean-Marc Rémy and Hugues d'Orchymont*
Marion Merrell Research Institute, Strasbourg Center, 16 rue d'Ankara, 67080 Strasbourg Cedex, France

3-Amino-2-hydroxy-propionaldehydes (**5**) (characterized in their hydrated form) and the isomeric 3-amino-1-hydroxy-propan-2-ones (**6**) are micromolar inhibitors of aminopeptidase-M (AP-M, EC 3.4.11.2). In some cases, selective inhibition of AP-M was observed.

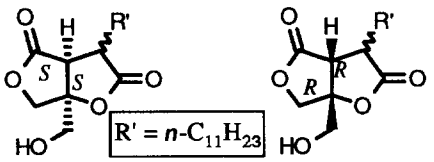


Bioorg. Med. Chem. **1996**, *4*, 1299

Synthesis of Bis-γ-Butyrolactones Containing Conformationally Constrained (*S*)- and (*R*)-Diacylglycerol Structures

Jeewoo Lee,[a] Nancy E. Lewin,[b] Peter M. Blumberg[b] and Victor E. Marquez[a,*]
Laboratories of [a]*Medicinal Chemistry and* [b]*Cellular Carcinogenesis and Tumor Promotion, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, U.S.A.*

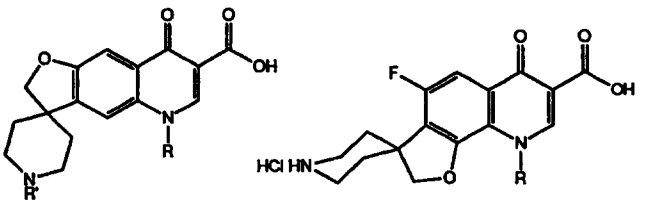
The synthesis of two sets of rigid diacylglycerol (DAG) analogues with both *R*- and *S*-enantiomers embedded into a bis-γ-butyrolactone template was accomplished stereoselectively from di-*O*-isopropylidene-α-D-apiose.



Bioorg. Med. Chem. **1996**, *4*, 1307

The Synthesis and In Vitro Antibacterial Activity of Conformationally Restricted Quinolone Antibacterial Agents

Curt S. Cooper,* Michael D. Tufano, Pamela K. Donner and Daniel T. W. Chu
Anti-infective Research Division, Abbott Laboratories, Abbott Park, IL 60064-3500, U.S.A.

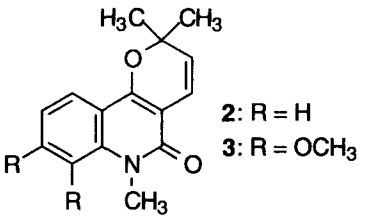


Bioorg. Med. Chem. **1996**, *4*, 1317

SRS-A Antagonist Pyranoquinolone Alkaloids from East African *Fagara* Plants and their Synthesis

Tadao Kamikawa,[a,*] Yasuyuki Hanaoka,[a] Satoru Fujie,[a] Ken Saito,[a] Yoshiro Yamagiwa,[a] Katsuya Fukuhara[b] and Isao Kubo[b,*]

[a]Department of Chemistry, Faculty of Science and Technology, Kinki University, Kowakae, Higashi-osaka-shi, Osaka 577, Japan and [b]Department of Environmental Science, Policy, and Management, University of California, Berkeley, CA 94720-3112, U.S.A.



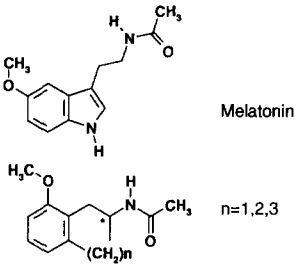
Bioorg. Med. Chem. **1996**, *4*, 1321

The High Affinity Melatonin Binding Site Probed with Conformationally Restricted Ligands—I. Pharmacophore and Minireceptor Models

J. M. Jansen,[a,†] S. Copinga,[a] G. Gruppen,[a] E. J. Molinari,[b] M. L. Dubocovich[b] and C. J. Grol[a,*]

[a]Department of Medicinal Chemistry, University Centre for Pharmacy, State University Groningen, Antonius Deusinglaan 1, NL-9713 AV Groningen, The Netherlands; [b]Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL 60611, U.S.A.

Affinity data of enantiomers of conformationally restricted melatonin analogues, together with analyses of their conformational behavior, automated pharmacophore searches, and minireceptor modeling led to conceptual models of the ML-1 binding site.



Bioorg. Med. Chem. **1996**, *4*, 1333

The High Affinity Melatonin Binding Site Probed with Conformationally Restricted Ligands—II. Homology Modeling of the Receptor

C. J. Grol* and J. M. Jansen

Department of Medicinal Chemistry, University Center of Pharmacy, State University Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, The Netherlands

Homology modeling study of the melatonin receptor ML-1 was performed based on a pharmacophore model of six melatonin agonists. With BacterioRhodopsine as a rough template, a ligand binding site was suggested with the serines from helix three and the histidine from helix five, forming hydrogen bonds with the amide and methoxy group of melatonin, respectively.

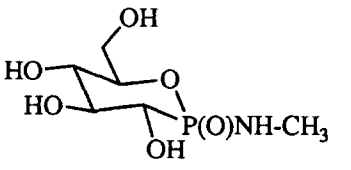
Bioorg. Med. Chem. **1996**, *4*, 1341

A Cyclic Phosphonamidate Analogue of Glucose as a Selective Inhibitor of Inverting Glycosidases

James W. Darrow and Dale G. Drueckhammer*

Department of Chemistry, Stanford University, Stanford, CA 94305, U.S.A.

A cyclic phosphonamidate analogue of glucose was prepared. This compound exhibited modest selective inhibition of glycosidases which proceed by inverting mechanisms.

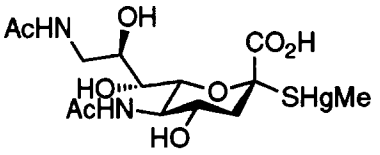


Synthesis and Inhibitory Properties of a Thiomethylmercuric Sialic Acid with Application to the X-ray Structure Determination of 9-*O*-Acetylsialic Acid Esterase from Influenza C Virus

Bioorg. Med. Chem. **1996**, *4*, 1349

Wolfgang Fitz,[a] Peter B. Rosenthal[b] and Chi-Huey Wong[a,*]
[a]Department of Chemistry, The Scripps Research Institute, La Jolla, CA 92037, U.S.A. [b]Department of Molecular and Cellular Biology and Committee on Higher Degrees in Biophysics, Harvard University, Cambridge, MA 02138, U.S.A.

2-α-Thiomethylmercuryl 9-acetamido-9-deoxy-sialoside was prepared and found to be an inhibitor of the 9-*O*-acetylsialic acid esterase from influenza C virus with a K_i of 4.2 ±0.5 mM. The inhibitor is being used in the X-ray determination of the crystal structure of the esterase.

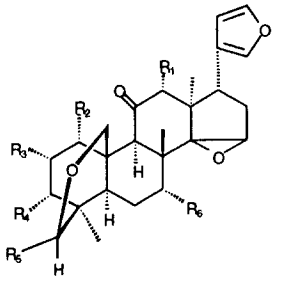


Cytotoxic Trichilin-Type Limonoids from *Melia azedarach*

Bioorg. Med. Chem. **1996**, *4*, 1355

Koichi Takeya, Zhi-Sheng Qiao, Chieko Hirobe and Hideji Itokawa*
Department of Natural Medicines, Tokyo University of Pharmacy & Life Science, Horinouchi 1432-1, Hachioji, Tokyo 192-03, Japan

Five new trichilin-type limonoids, 12-deacetyltrichilin I (**1**), 1-acetyltrichilin H (**2**), 3-deacetyltrichilin H (**3**), 1-acetyl-3-deacetyltrichilin H (**4**), 1-acetyl-2-deacetyltrichilin H (**5**), together with four known trichilins were isolated from the root bark of *Melia azedarach*. The structures were elucidated by spectroscopic means and their cytotoxic activities against P388 cells were tested by means of MTT assay.

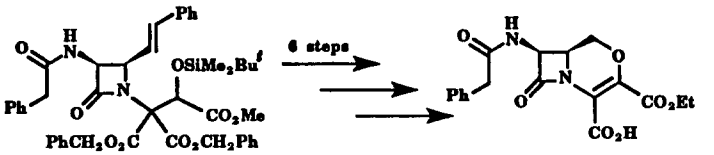


Synthesis and Biological Evaluation of an Electronically Activated Isooxacephem

Bioorg. Med. Chem. **1996**, *4*, 1361

Gholam H. Hakimelahi,[a,*] Shwu-Chen Tsay,[a] Hsi-Hwa Tso,[a] Zahra Ramezani[b] and Jih Ru Hwu[a,c,*]
[a]Organosilicon and Synthesis Laboratory, Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan 11529, R.O.C. [b]St Thomas Research Training Laboratory, Dominican International School, Tah Chih, Taipei, Taiwan 104, R.O.C. [c]Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 30043, R.O.C.

A new isooxacephem was synthesized and found to possess notable biological activities resulting from the electronic activation of the β-lactam moiety by an ester group.

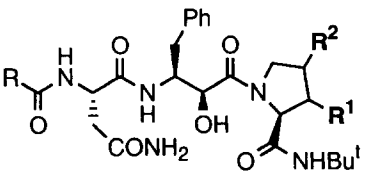


Structure–Activity Relationships of HIV-1 PR Inhibitors Containing AHPBA—II. Modification of Pyrrolidine Ring at P1′ Proline

Bioorg. Med. Chem. **1996**, *4*, 1365

T. Komai,[b] S. Higashida,[a] M. Sakurai,[a] T. Nitta,[a] A. Kasuya,[a] S. Miyamaoto,[a] R. Yagi,[b] Y. Ozawa,[b] H. Handa,[c] H. Mohri,[d] A. Yasuoka,[d] S. Oka,[d] T. Nishigaki,[b,*] S. Kimura,[d] K. Shimada[d] and Y. Yabe[a,*]; *[a]Exploratory Chemistry Research and [b]Biological Research Laboratories, Sankyo Co. Ltd, 1-2-58 Hiromachi, Shinagawa-ku, Tokyo 140, Japan; [c]Faculty of Bioscience and Biotechnology, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227, Japan; [d]Institute of Medical Science, University of Tokyo, Shiroganedai, Minato-ku, Tokyo 108, Japan*

Systematic replacement in the 3- or 4-position of the pyrrolidine ring at P1′ proline was carried out. Compound **26**, which has a Cl atom in the 4(*S*)-position was the most active among inhibitors substituted with other halogen atoms or other substituents. Furthermore, the replacement of the *Z* group in compound **26** with five- or six-membered fused aromatic heterocycle carbonyl groups produced more potent inhibitors. 7-Methoxybenzofuran-2-carbonyl derivative (**44**) was the best of these inhibitors.



Synthesis and Antitumor Activity of Duocarmycin Derivatives: A-Ring Pyrrole Analogues of Duocarmycin B2

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We describe the synthesis and antitumor activity of 8-substituted A-ring pyrrole analogues of duocarmycin B2.