

Anti-DNA Autoantibodies: the Other DNA-binding Proteins

Bioorg. Med. Chem. **1997**, 5, 467

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We review some common approaches that have been used to examine the specificity, affinity, and mode of binding of lupus anti-DNA for DNA antigens. We highlight the recent use of biophysical methods that have been used to study DNA-binding proteins, such as transcription factors, and demonstrate their utility when used in the study of lupus anti-DNA.

Combinatorial Chemistry in Drug Research from a New Vantage Point

Bioorg. Med. Chem. **1997**, 5, 473

Hubert Maehr

Roche Research Center, Hoffmann-La Roche Inc., Nutley, New Jersey 07110, U.S.A.

The application of set theory to combinatorial processes provides valuable tools for the planning, description, execution, and evaluation of combinatorial events.

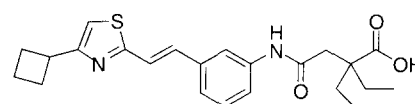
Structure Optimization of a Leukotriene D₄ Antagonist by Combinatorial Chemistry in Solution

Bioorg. Med. Chem. **1997**, 5, 493

Hubert Maehr* and Roxana Yang

Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ 07110, U.S.A.

The optimum structural features were deduced by the introduction of molecular diversity at three sites followed by the evaluation of a library containing 700 compounds.



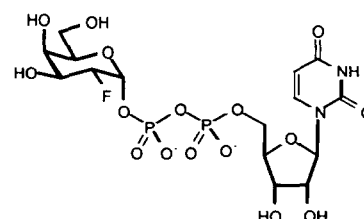
Ro24-5913

A Chemoenzymatic Synthesis of UDP-(2-deoxy-2-fluoro)-galactose and Evaluation of its Interaction with Galactosyltransferase

Bioorg. Med. Chem. **1997**, 5, 497

Takashi Hayashi, Brion W. Murray, Ruo Wang and Chi-Huey Wong*

Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, U.S.A.



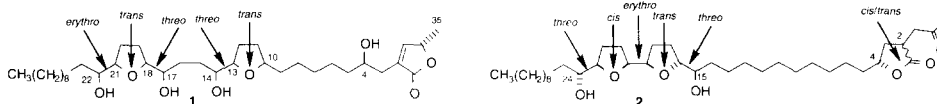
Additional Bioactive Annonaceous Acetogenins from *Asimina triloba* (Annonaceae)

Bioorg. Med. Chem. 1997, 5, 501

Kan He, Geng-Xian Zhao, Guoen Shi, Lu Zeng, Jin-Feng Chao, and Jerry L. McLaughlin*

Department of Medicinal Chemistry and Molecular Pharmacology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana 47907, U.S.A.

Trilobalicin (**1**), a new nonadjacent bis-THF ring Annonaceous acetogenin, 2,4-*cis*- (**2**) and 2,4-*trans*-trilobacinone (**3**), the ketolactones of trilobacin, an adjacent bis-THF ring acetogenin, were isolated from the stem bark of *Asimina triloba* (L.) Dunal (Annonaceae).



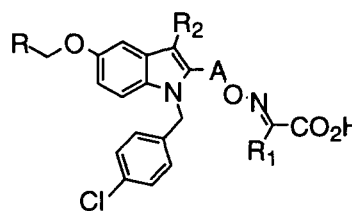
Synthesis of Indolylalkoxyiminoalkylcarboxylates as Leukotriene Biosynthesis Inhibitors

Bioorg. Med. Chem. 1997, 5, 507

Teodozj Kolasa,* Pramila Bhatia, Clint D. W. Brooks, Keren I. Hulkower, Jennifer B. Bouska, Richard R. Harris and Randy L. Bell

Immunoscience Research, D-47K, Abbott Laboratories, 100 Abbott Park, IL 60064-3500, U.S.A.

A series of quinolylmethoxyindolylalkyliminoxycarboxylates were synthesized and evaluated for inhibition of leukotriene biosynthesis.



R = 2-quinolyl, 2-pyridyl, 4-thiazolyl, 2-benzothiazolyl; R₁ = H, CH₃; R₂ = H, S-tBu or S-2-quinolylmethyl; A = CH₂, CHR₃, CH₂C(Me₂)CH₂; R₃ = allyl, n-butyl, benzyl and cyclohexyl.

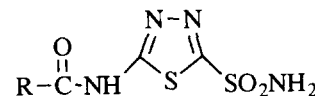
Synthesis and Investigation of Inhibition Effects of New Carbonic Anhydrase Inhibitors

Bioorg. Med. Chem. 1997, 5, 515

Oktay Arslan, Ö. İ. Küfrevioğlu and Barbaros Nalbantoğlu*

Department of Chemistry, Faculty of Science and Arts, Atatürk University, Erzurum, Turkey

Three new carbonic anhydrase (CA) inhibitors (**1**), (**2**) and (**3**) have been synthesized. The inhibition effect of (**1**) on CA II has shown that (**1**) is more a potent inhibitor than acetazolamide.



- (1) ClCH₂-CH₂-
- (2) Cl₂CH-
- (3) Ph-CH₂-CH₂-

Synthesis of Azasugars as Potent Inhibitors of Glycosidases

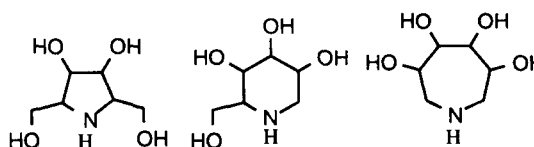
Bioorg. Med. Chem. 1997, 5, 519

Yves Le Merrer,* Lydie Poitout, Jean-Claude Depezay,^a Isabelle Dosbaa, Sabine Geoffroy and Marie-José Foglietti^b

^aUniversité René Descartes, Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, associé au CNRS, 45 rue des Saints-Pères, 75006 Paris Cedex 06, France

^bUniversité René Descartes, Laboratoire de Biochimie et de Glycobiologie, 4 avenue de l'Observatoire, 75006 Paris Cedex 06, France

A series of enantiomerically pure azasugars with a pyrrolidine, piperidine, or an azepane framework was synthesized from D-mannitol. Biological studies indicate, notably, that the polyhydroxylated azepanes are inhibitors of glycosidases with the K_i values in the low micromolar range.



Possible Ligand–Receptor Interactions for NK₁ Antagonists as Observed in their Crystal Structures

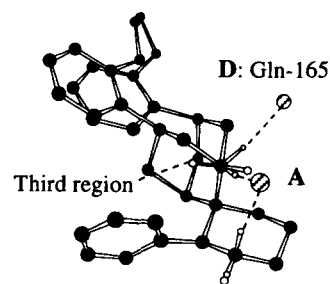
Bioorg. Med. Chem. 1997, 5, 535

Gertjan J. Boks,^{a,*} Jan P. Tollenaere^a and Jan Kroon^b

^aDepartment of Medicinal Chemistry, Utrecht Institute for Pharmaceutical Sciences, Universiteit Utrecht, Sorbonnelaan 16, NL-3584 CA Utrecht, The Netherlands

^bDepartment of Crystal and Structural Chemistry, Bijvoet Centre for Biomolecular Research, Universiteit Utrecht, Padualaan 8, NL-3584 CH Utrecht, The Netherlands

Interactions observed in small molecule crystal structures might well reflect interactions with a macromolecular receptor.



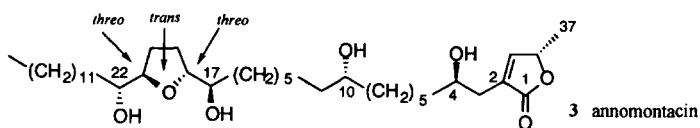
4-Deoxyannomontacin and (2,4-*cis* and *trans*)-Annomontacinone, New Bioactive Mono-tetrahydrofuran Annonaceous Acetogenins from *Goniothalamus giganteus*

Bioorg. Med. Chem. 1997, 5, 549

F. Alali, L. Zeng, Y. Zhang, Q. Ye, D. C. Hopp, J. T. Schwedler and J. L. McLaughlin*

Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN 47907, U.S.A.

Two biologically active annonaceous acetogenins are related to annomontacin (3).

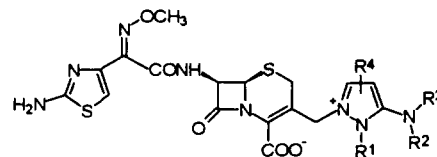


Studies on 3'-Quaternary Ammonium Cephalosporins—III. Synthesis and Antibacterial Activity of 3'-(3-Aminopyrazolium)cephalosporins

Bioorg. Med. Chem. 1997, 5, 557

Hidehori Ohki, Kohji Kawabata,* Yoshiko Inamoto, Shinya Okuda, Toshiaki Kamimura and Kazuo Sakane
New Drug Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., 2-1-6 Kashima, Yodogawa-ku, Osaka 532, Japan

The synthesis and in vitro antibacterial activity of 7β-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido] cephalosporins bearing *N*-mono or dialkyl and carbamoyl aminopyrazolium, and five- or six-membered rings fused to the 3-aminopyrazolium methyl groups at the 3-position, are described.



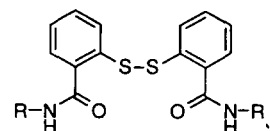
A New Class of Anti HIV-1 Agents Targeted Toward the Nucleocapsid Protein NCp7: The 2,2'-Dithiobisbenzamides

Bioorg. Med. Chem. 1997, 5, 569

J. M. Domagala,^{a,*} J. P. Bader,^b R. D. Gogliotti,^a J. P. Sanchez,^a M. A. Stier,^a Y. Song,^a J. V. N. Vara Prasad,^a P. J. Tummino,^a J. Scholten,^a P. Harvey,^a T. Holler,^a S. Gracheck,^a D. Hupe,^a W. G. Rice^c and R. Schultz^b

^aDepartments of Chemistry and Therapeutics, Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, 2800 Plymouth Road, Ann Arbor, MI 48105, U.S.A.; ^bAntiviral Evaluations Developmental Therapeutics Program, Bethesda, MD 20892, U.S.A.; ^cThe National Cancer Institute Antiviral Drug Mechanisms, SAIC, Frederick, MD 21702, U.S.A.

Certain 2,2'-dithiobisbenzamides have demonstrated good anti HIV-1 activity (2–10 μM, cytotoxicity >100 μM) and extrude Zn from the Zn-fingers of HIV-1 nucleocapsid protein (NCp7), the putative target. A broad SAR is presented. Optimal substituents on R are acids and amides.



Expanding the 43C9 Class of Catalytic Antibodies Using a Chain-shuffling Approach

Bioorg. Med. Chem. **1997**, *5*, 581

Grover Paul Miller,^a Bruce A. Posner^b and Stephen J. Benkovic^{a,*}

^aDepartment of Chemistry, Pennsylvania State University, University Park, PA 16802, U.S.A. and ^bPharmacology Department, University of Texas Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75235, U.S.A.

Crossing the 43C9 heavy-chain gene with a library of light-chains yields light-chain proteins sharing 92–96% sequence identity to 43C9. These clones attempt to broaden a class of 43C9-like antibodies, where the catalytic residues, His91 and Arg96, have been reproducibly selected. Similar catalytic properties between the 43C9-like antibodies suggests binding has been optimized, thus further maturation of the light chain would not lead to a better hydrolytic antibody.

Design, Synthesis, and Biological Activity of Anti-angiogenic Hypoxic Cell Radiosensitizer Haloacetylcarbamoyl-2-nitroimidazoles

Bioorg. Med. Chem. **1997**, *5*, 591

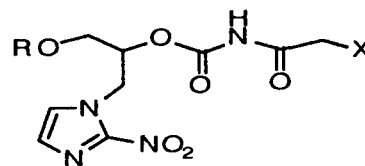
Hitoshi Hori,^{a,*} Cheng-Zhe Jin,^a Masatoshi Kiyono,^a Soko Kasai,^a Mariko Shimamura^b and Seiichi Inayama^{c,d}

^aDepartment of Biological Science and Technology, Faculty of Engineering, The University of Tokushima, Tokushima 770, Japan

^bDepartment of Cancer Therapeutics, The Tokyo Metropolitan Institute of Medical Sciences, Tokyo 113, Japan

^cPharmaceutical Institute, School of Medicine, Keio University, Tokyo 160, Japan

^dInstitute of Oriental Medical Science, Tokyo 155, Japan



Haloacetylcarbamoyl-2-nitroimidazoles

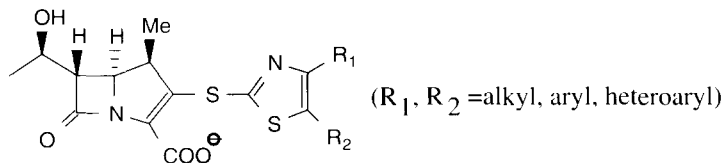
Synthesis and Biological Properties of a New Series of Anti-MRSA β -Lactams; 2-(Thiazol-2-ylthio)carbapenems

Bioorg. Med. Chem. **1997**, *5*, 601

Hisatoshi Shinagawa, Hiroshi Yamaga, Hitoshi Houchigai, Yoshihiro Sumita and Makoto Sunagawa*

Sumitomo Pharmaceuticals Research Center, 1-98 Kasugade naka 3 chome, Konohanaku, Osaka 554, Japan

Synthesis and biological properties of a series of 2-(thiazol-2-ylthio)carbapenems is described. Some of the compounds showed marked anti-MRSA activity with low HSA binding.



Studies on Duocarmycin SA and its Derivatives

Bioorg. Med. Chem. **1997**, *5*, 623

Satoru Nagamura,^{a,*} Akira Asai,^a Eiji Kobayashi,^b Katsushige Gomi^b and Hiromitsu Saito^b

^aTokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, 3-6-6, Asahi-machi, Machida-shi, Tokyo 194, Japan

^bPharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, 1188 Shimotogari, Nagaizumi, Sunto, Shizuoka 411, Japan

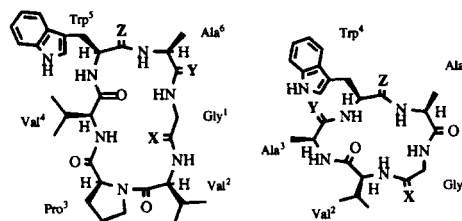
We describe the synthesis and antitumor activity of a new type of duocarmycin SA.

Thionation of Segetalins A and B, Cyclic Peptides with Estrogen-like Activity from Seeds of *Vaccaria segetalis*

Bioorg. Med. Chem. 1997, 5, 631

Hiroshi Morita,^a Young Sook Yun,^a Koichi Takeya,^a
Hideji Itokawa^{a,*} and Osamu Shiota^b

^aDepartment of Pharmacognosy, School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan and ^bDivision of Pharmacognosy and Phytochemistry, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158, Japan



segetalin A (1)	X=O	Y=O	Z=O	segetalin B (2)	X=O	Y=O	Z=O
thiosegetalin A1 (3)	X=S	Y=O	Z=S	thiosegetalin B1 (5)	X=S	Y=S	Z=O
thiosegetalin A2 (4)	X=S	Y=S	Z=O	thiosegetalin B2 (6)	X=S	Y=O	Z=S