ANTITHROMBOTIC AGENTS : *FROM RGD TO PEPTIDE MIMETICS*

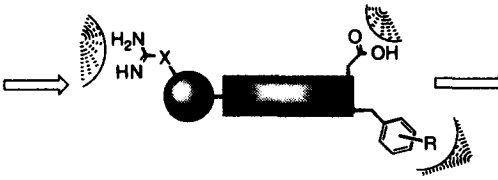
BioMed. Chem. **1995**, *3*, 337

Iwao Ojima*, Subrata Chakravarty and Qing Dong
Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY 11794-3400

This review covers the recent advances in the development of RGD peptides and their mimetics as potential therapeutic drugs for thrombosis related to cardiovascular and cerebrovascular diseases.

Glu-Cys-Glu-Ser-Gly-Pro-Cys-Cys-Arg-Asn^{10}-
Cys-Lys-Phe-Leu-Lys-Glu-Gly-Thr-Ile-Cys^{20}-
Lys-Arg-Ala-**Arg-Gly-Asp**-Asp-Met-Asp-Asp^{30}-
Tyr-Cys-Asn-Gly-Lys-Thr-Cys-Asp-Cys-Pro^{40}-
Arg-Asn-Pro-His-Lys-Gly-Pro-Ala-Thr^{49}

Echistatin (a snake venom)

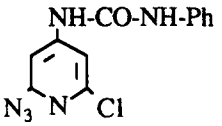


Peptide Mimetics

Synthesis, azido-tetrazole equilibrium studies and biological activity of 1-(2-azido-6-chloro-pyrid-4-yl)-3-phenylurea, a photoaffinity labeling reagent for cytokinin-binding proteins

BioMed. Chem. **1995**, *3*, 361

M. Dias[1], R. Mornet[1] and M. Laloue2
[1]*L.C.O.F.A., Faculté des Sciences, 2 Bd Lavoisier, 49045 Angers, France*
[2]*Laboratoire de Biologie Cellulaire, INRA, Route de St Cyr, 78028 Versailles, France*



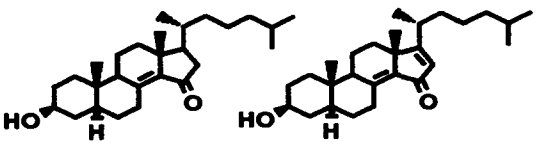
A 2-azidopyridine derivative was synthesised and its azido-tetrazole equilibrium was studied. It behaves as a cytokinin active compound and it is easily photolysable. Thus it appears to be a good candidate as a photoaffinitu labeling reagent for cytokinin-binding proteins, receptors in particular. A tritium-labeled derivative was synthesised.

CHEMICAL SYNTHESIS OF 15-KETOSTEROLS AND THEIR INHIBITIONS OF CHOLESTERYL ESTER TRANSFER PROTEIN

BioMed. Chem. **1995**, *3*, 367

H.-S. Kim*, S. H. Oh, D.-I. Kim, I.-C. Kim, K.-H. Cho#, Y. B. Park# Department of Industrial Chemistry and #Department of Genetic Engineering, Kyungpook National University, Taegu 702-701, Korea

The chemical synthesis of 15-ketosterols I and II and their inhibitory activity on cholesteryl ester transfer protein are described.

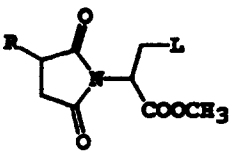


I II

Design, Synthesis and Biological Evaluation of Succinimide Derivatives as Potential Mechanism-Based Inhibitors of Human Leukocyte Elastase, Cathepsin G and Proteinase 3.

BioMed. Chem. **1995**, *3*, 375

W.C. Groutas*, M.J. Brubaker, L.S. Chong, R. Venkataraman, H. Huang, J.B. Epp, R. Kuang
Department of Chemistry, Wichita State University, Wichita, KS 67260
John R. Hoidal
School of Medicine, Division of Respiratory, Critical Care and Occupational Medicine, University of Utah Health Sciences Center, Salt Lake City, UT 84132



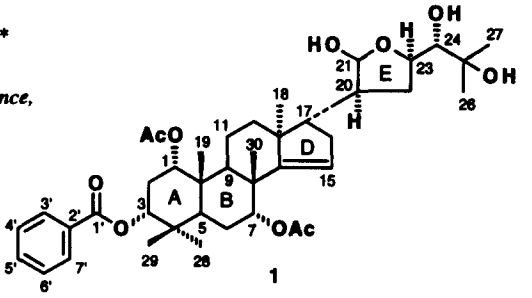
(I)

BioMed. Chem. **1995**, *3*, 383

MELIAVOLKENIN, A NEW BIOACTIVE TRITERPENOID FROM *MELIA VOLKENSII* (MELIACEAE)

Lu Zeng, Zhe-ming Gu, Ching-jer Chang, Karl V. Wood†, and Jerry L. McLaughlin*
Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, †Department of Chemistry, School of Science, Purdue University, West Lafayette, IN 47907, U. S. A.

Meliavolkenin (1), a new triterpene with an apotirucallane skeleton, has been isolated from the root bark of *Melia volkensii* (Meliaceae) by bioactivity-directed fractionation using the brine shrimp lethality test. The structure has been elucidated using spectral and chemical data. 1 was bioactive in the brine shrimp lethality test and gave moderate cytotoxicities against three human solid tumor lines.



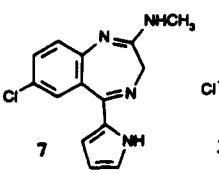
1

BioMed. Chem. **1995**, *3*, 391

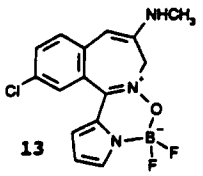
An Alternate Synthesis of the Tat-Antagonist 7-Chloro-N-methyl-5-(1*H*-pyrrol-2-yl)-3*H*-1,4-benzodiazepin-2-amine

H. Maehr, G. Zenchoff, and D. L. Coffen
Roche Research Center, Hoffmann La Roche Inc., Nutley, New Jersey 07110

Abstract: 7-Chloro-N-methyl-5-(1*H*-pyrrol-2-yl)-3*H*-1,4-benzodiazepin-2-amine (**7**), inhibits gene expression by HIV-1 at the level of transcriptional trans-activation by Tat and was synthesized. The related 13-chloro-5,5-difluoro-9-(methylamino)-5*H*-pyrrolo[1',2':3,4]-1,3,6,2-oxadiazabora[6,5-*d*]-8*H*-1,4-benzodiazepin-7-ium hydroxide inner salt (**13**) does not significantly inhibit Tat-mediated gene expression by HIV-1.



7

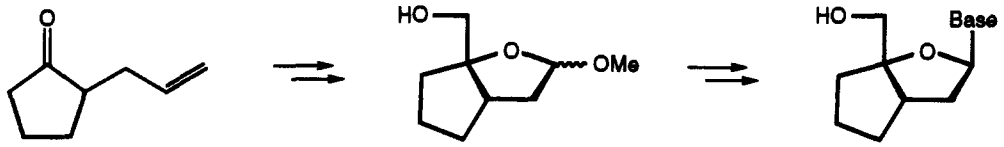


13

BioMed. Chem. **1995**, *3*, 397

SYNTHESIS AND CONFORMATIONAL ANALYSIS OF PYRIMIDINE NUCLEOSIDE ANALOGUES WITH A RIGID SUGAR MOIETY

Magnus Björsne, Thomas Szabó, Björn Classon, Bertil Samuelsson*, Dept. of Organic Chemistry,
Arrhenius Laboratories, Stockholm University, S-106 91 Sweden.



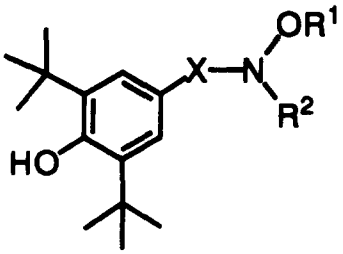
C1-exo conformation

BioMed. Chem. **1995**, *3*, 403

HYDROXYLAMINE ANALOGS OF 2,6 DI-*t*-BUTYLPHENOLS: DUAL INHIBITORS OF CYCLOOXYGENASE AND 5-LIPOXYGENASE OR SELECTIVE 5-LIPOXYGENASE INHIBITORS

James B. Kramer, Thomas Capiris, Jagadish C. Sircar, David T. Connor, Dirk A. Bornemeier, Richard D. Dyer, Paul J. Kuipers, John A. Kennedy, Clifford D. Wright, Godwin C. Okonkwo, Mark E. Lesch, Denis J. Schrier and Diane H. Boschelli*, *Parke Davis Pharmaceutical Research Division, Warner-Lambert Company 2800 Plymouth Rd., Ann Arbor, MI 48105*

The preparation of hydroxylamine analogs of 2,6-di-*tert*-butylphenols (DTBP) and the inhibition of cyclooxygenase (CO) and 5-lipoxygenase (5-LO) by these compounds is discussed.



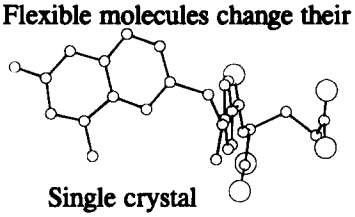
Conformational Changes of Small Molecules Binding to Proteins

BioMed. Chem. **1995**, *3*, 411

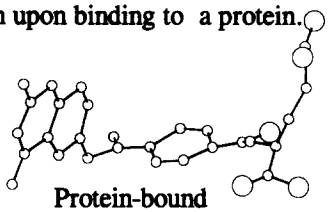
Marc C. Nicklaus, Shaomeng Wang, John S. Driscoll and George W. A. Milne

Laboratory of Medicinal Chemistry, DTP, DCT, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-4255, USA

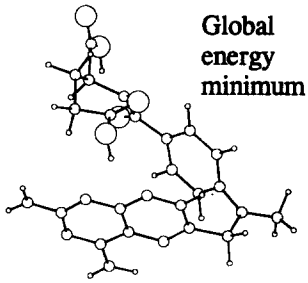
Flexible molecules change their conformation upon binding to a protein.



Single crystal



Protein-bound



Global energy minimum

On the Conformation of Phe78 of a Chromoprotein Antibiotic, Neocarzinostatin

BioMed. Chem. **1995**, *3*, 429

Seiichi Imajo, Masaji Ishiguro,* Toshiyuki Tanaka,† Masahiro Hirama,† and Alexei Teplyakov‡

Suntory Institute for Biomedical Research, Shimamoto, Osaka 618 †Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980-77 Japan, ‡EMBL, c/o DESY, Hamburg, Germany

A model of neocarzinostatin from NMR and X-ray crystallographic data suggested a flexible conformation of the Phe78 residue in solution.

Targeting Peptide Nucleic Acid-Protein Conjugates to Structural Features Within Duplex DNA

BioMed. Chem. **1995**, *3*, 437

James C. Norton, John H. Waggenspack, Elana Varnum, and David R. Corey, Howard Hughes Medical Institute, Dept. of Pharmacology, Univ. of Texas Southwestern Medical Center, Dallas, TX 75235, USA.

Nuclease-SH + PNA-SH ⟶ **Nuclease-SS-PNA**

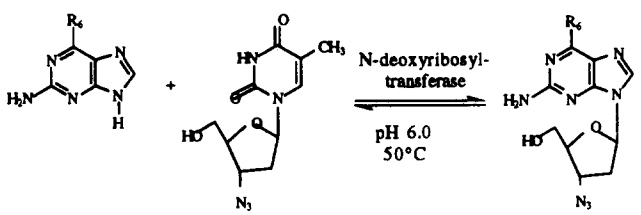
Duplex DNA ⟶ **Selective Hydrolysis at Targeted Inverted Repeats**

A convenient small scale PNA synthesis strategy has been developed and used to afford PNAs for attachment to staphylococcal nuclease. Affinity cleavage reveals conjugates hybridize at inverted repeats within ds DNA

2-Amino-9-(3-Azido-2,3-Dideoxy-β-D-erythro-Pentofuranosyl)-6-Substituted-9H-Purines: Synthesis and Anti-HIV Activity

BioMed. Chem. **1995**, *3*, 447

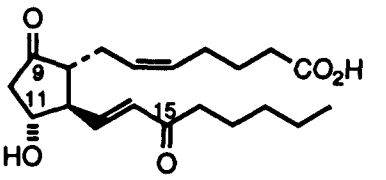
G. A. Freeman*=, S. R. Shaver=, J. L. Rideout=, and S. A. Short≠, *Burroughs Wellcome Co., =Division of Organic Chemistry and ≠Division of Experimental Therapy, 3030 Cornwallis Rd. RTP, N. C. 27709*



FTIR Spectral Study of Intramolecular Hydrogen Bonding in E-type of 15-Keto-prostaglandins in Dilute CCl_4 Solution: Structure-Activity Relationships

Mamoru Takasuka and Masumi Yamakawa
Shionogi Research Laboratories, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553, Japan

BioMed. Chem. **1995**, *3*, 459



On the basis of formation ratio of the intramolecular hydrogen bond in CCl_4, we examined the structure-activity relationships of the α- and ω-side chains for prostaglandins.