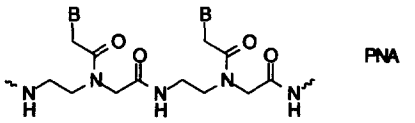
Bioorg. Med. Chem. **1996**, *4*, 5

Peptide Nucleic Acids (PNA): Synthesis, Properties and Potential Applications

Birgitte Hyrup[a] and Peter E. Nielsen[b]*
Center for Biomolecular Recognition, [a]Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen Ø, Denmark. [b]Department of Biochemistry B, The Panum Institute, Blegdamsvej 3, DK-2200 Copenhagen N, Denmark

This review summarizes our present knowledge about Peptide nucleic acids (PNA), a DNA mimic with a pseudopeptide backbone.

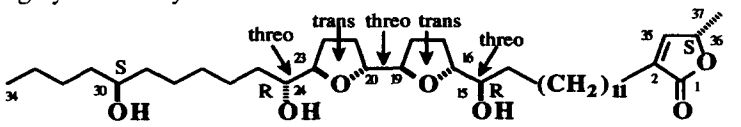


Bioorg. Med. Chem. **1996**, *4*, 25

The Absolute Configuration of Adjacent Bis-THF Acetogenins and Asiminocin, A Novel Highly Potent Asimicin Isomer from *Asimina triloba*

Geng-Xian Zhao, Jin-Feng Chao, Lu Zeng, Matthew J. Rieser, 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.

Asiminocin (**1**), a novel acetogenin isolated from *Asimina triloba*, was identified as 30*S*-hydroxy-4-deoxyasimicin. Compound **1** was highly inhibitory to three human solid tumor cell lines with over a billion times the potency of adriamycin.

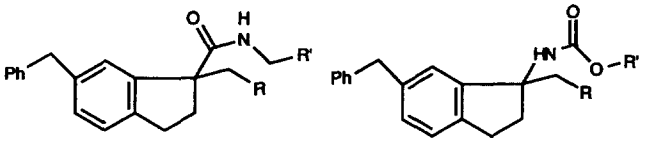


Bioorg. Med. Chem. **1996**, *4*, 33

The Design of Dipeptide Helical Mimetics: The Synthesis, Tachykinin Receptor Affinity and Conformational Analysis of 1,1,6-Trisubstituted Indanes

David C. Horwell, William Howson, Giles S. Ratcliffe and Henriëtte M. G. Willems*
Parke-Davis Neuroscience Research Centre, Addenbrookes Hospital Site, Hills Road, Cambridge CB2 2QB, U.K.

Six racemic and two homochiral dipeptide α-helix mimetics were synthesised and their affinity for the tachykinin NK_1, NK_2 and NK_3 receptors was evaluated.



R = C_6H_5 or 3-indole, R' = $C(CH_3)_3$ or $CH_2C_6H_5$

Bioorg. Med. Chem. **1996**, *4*, 43

Synthesis and In Vitro Antibacterial Activity of Spermidine-Based Mixed Catechol- and Hydroxamate-Containing Siderophore–Vancomycin Conjugates

Manuka Ghosh and Marvin J. Miller*
Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46556, U.S.A.

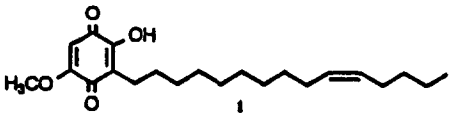
The first antibiotic conjugates of vancomycin (**1**) and siderophore (microbial iron transport agent) analogues containing spermidine-based catechol-ligands (conjugate **11**) as well as mixed catechol- and hydroxamate-ligands (conjugate **13**) are described.

Bioorg. Med. Chem. **1996**, *4*, 49

Inhibition of Aldose Reductase by Maesanin and Related *p*-Benzoquinone Derivatives and Effects on Other Enzymes

Hiroyuki Haraguchi,*[a] Isao Ohmi[a] and Isao Kubo[b]
[a]*Faculty of Engineering, Fukuyama University, Gakuen-cho, Fukuyama 729-02, Japan*
[b]*Department of Environmental Science, Policy and Management, University of California, Berkeley, CA 94720-3112, U.S.A.*

Maesanin (**1**) and related *p*-benzoquinone derivatives inhibited porcine lens aldose reductase. 2,5-Dihydroxy-*p*-benzoquinone (**3**) was a potent inhibitor of aldose reductase and aldehyde reductase but had no effect on NADH oxidase.



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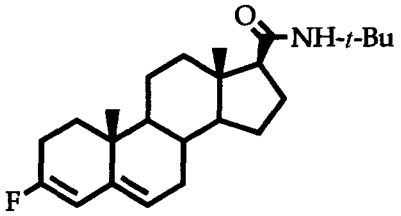
Bioorg. Med. Chem. **1996**, *4*, 55

Vinyl Fluoride as a Mimic of the 'Intermediate' Enol Form in the 5α-Reductase Transformation: Synthesis and In Vitro Activity of (*N*-1′,1′-Dimethylethyl)-3-haloandrost-3,5-diene-17β-carboxamides

Xun Li, Shankar M. Singh,* Van Luu-The, Jean Côté, Sylvie Laplante and Fernard Labrie
Medicinal Chemistry Division, Laboratory of Molecular Endocrinology, C.H.U.L. Research Center, Québec City, PQ G1V 4G2, Canada



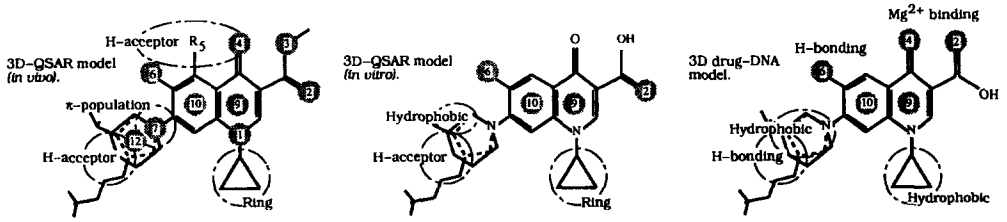
Ty. II, 5α-Re: IC_{50} = 480 nM

Synthesis and in vitro activity are described.

Bioorg. Med. Chem. **1996**, *4*, 61

Using SAR and QSAR Analysis to Model the Activity and Structure of the Quinolone–DNA Complex

Belsis Llorente, Fabrice Leclerc and Robert Cedergren*
Département de Biochimie, Université de Montréal, Montréal, PQ H3C 3J7, Canada

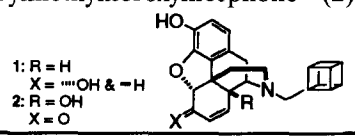


Bioorg. Med. Chem. **1996**, *4*, 73

N-Cubylmethyl Substituted Morphinoids as Novel Narcotic Antagonists

Chen-Yu Cheng,*[a] Ling-Wei Hsin,[a] Yen-Pin Lin,[a] Pao-Luh Tao[b] and Ting-Ting Jong[c]
[a]*School of Pharmacy, College of Medicine, National Taiwan University, Taipei, Taiwan.* [b]*Department of Pharmacology, National Defense Medical Center, Taipei, Taiwan.* [c]*Department of Chemistry, National Chunghsing University, Taichung, Taiwan*

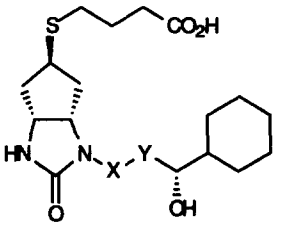
N-Cubylmethylnormorphine (**1**) and *N*-cubylmethylnoroxymorphone (**2**) have been synthesized and characterized as novel narcotic antagonists.



Bioorg. Med. Chem. **1996**, *4*, 81

Synthesis of Hexahydrocyclopentimidazol-2-(1*H*)-one Derivatives Displaying Selective DP-Receptor Agonist Properties

Paul Barraclough,*[a] Mary L. Bolofo,[b] Heather Giles,[b] Janet Gillam,[c] C. John Harris,[a] Michael G. Kelly,[a] Paul Leff,[b] Alan McNeill,[a] Alan D. Robertson,[a] Ray J. Stepney[a] and Brendan Whittle*[d]
Departments of [a]Medicinal Chemistry, [b]Biochemical Sciences, [c]Physical Sciences and [d]Pharmacology, Wellcome Research Laboratories, Langley Court, Beckenham, Kent, BR3 3BS, U.K.



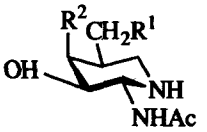
The rationale for, and the synthesis of, the selective DP-agonists **7–9** are described. X—Y = CH_2CH_2 (**7**), N=CH (**8**), $NHCH_2$ (**9**).

Bioorg. Med. Chem. **1996**, *4*, 91

Synthesis and Activity of 1-*N*-Iminosugar Inhibitors, Siastatin B Analogues for α-*N*-Acetylgalactosaminidase and β-*N*-Acetylglucosaminidase

Yoshio Nishimura,* Takahiko Satoh, Toshiaki Kudo, Shinichi Kondo and Tomio Takeuchi
Institute of Microbial Chemistry, 3-14-23 Kamiosaki, Shinagawa-ku, Tokyo 141, Japan

N-Acetylgalactosamine-based 1-*N*-iminosugars, new types of glycosidase inhibitor were synthesized and were proved to be potent inhibitors for α-*N*-acetylgalactosaminidase and/or β-*N*-acetylglucosaminidase.



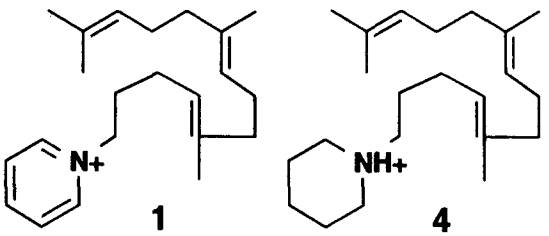
8: R^1=R^2=OH
9: R^1=N_3, R^2=OH
10: R^1=NH_2, R^2=OH
11: R^1=SCH_3, R^2=OH
12: R^1=$S(O)CH_3$, R^2=OH

Bioorg. Med. Chem. **1996**, *4*, 97

Design, Synthesis and In Vitro Evaluation of Pyridinium Ion Based Cyclase Inhibitors and Antifungal Agents

Ingo C. Rose,[a] Bradley A. Sharpe,[a] Roger C. Lee,[a] John H. Griffin,[a]* John O. Capobianco,[b] Dorothy Zakula[b] and Robert C. Goldman[b]
[a]Department of Chemistry, Stanford University, Stanford, CA 94305-5080, U.S.A. [b]Anti-Infective Research Division, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-3500, U.S.A.

N-Alkyl- and *N*-prenylpyridinium ions are potent and specific inhibitors of *Candida albicans* oxidosqualene–lanosterol cyclase and exhibit antifungal activity. Cation **1** inhibits the *C. albicans* cyclase at concentrations 100-fold lower than does the directly analogous piperidinium derivative **4**.

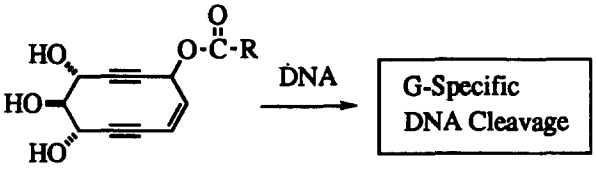


1 **4**

Bioorg. Med. Chem. **1996**, *4*, 105

Novel Designed Enediynes: Molecular Design, Chemical Synthesis, Mode of Cycloaromatization and Guanine-Specific DNA Cleavage

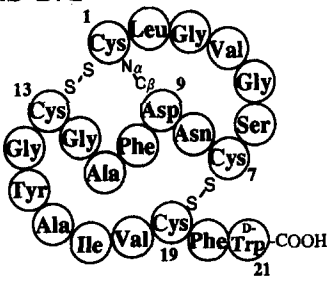
Kazunobu Toshima,* Kazumi Ohta, Takaaki Kano, Takatsugu Nakamura, Masaya Nakata, Mitsuhiro Kinoshita and Shuichi Matsumura
Department of Applied Chemistry, Keio University, Hiyoshi, Kohuku-ku, Yokohama 223, Japan



MS-271, A Novel Inhibitor of Calmodulin-Activated Myosin Light Chain Kinase from *Streptomyces* sp.—I. Isolation, Structural Determination and Biological Properties of MS-271

Bioorg. Med. Chem. **1996**, *4*, 115

Keiichi Yano, Shinichiro Toki, Satoshi Nakanishi, Keiko Ochiai, Katsuhiko Ando, Mayumi Yoshida, Yuzuru Matsuda and Motoo Yamasaki*
Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd, Machida-shi, Tokyo 194, Japan

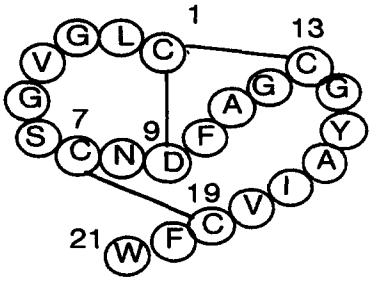


A novel cyclic peptide, MS-271, was isolated from the culture broth of an actinomycete, *Streptomyces* sp. M-271 as an inhibitor of smooth muscle myosin light chain kinase (MLCK). MS-271 inhibited the MLCK from chicken gizzard with an IC_{50} value of 8 μM, MS-271 did not inhibit cyclic AMP-dependent protein kinase, protein kinase C or calcium/calmodulin-dependent cyclic nucleotide phosphodiesterase at concentrations up to 400 μM. The primary structure of MS-271 was identical to that of siamycin I, an anti-HIV peptide isolated from a microbial source.

MS-271, A Novel Inhibitor of Calmodulin-Activated Myosin Light Chain Kinase from *Streptomyces* sp.—II. Solution Structure of MS-271: Characteristic Features of the 'Lasso' Structure

Bioorg. Med. Chem. **1996**, *4*, 121

Ritsuko Katahira, Motoo Yamasaki, Yuzuru Matsuda and Mayumi Yoshida*
Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd, 3-6-6 Asahimachi, Machida-shi, Tokyo 194, Japan

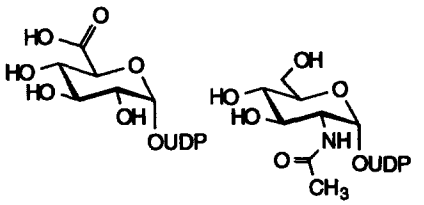


The three-dimensional structure of the myosin light chain kinase (MLCK) inhibitor MS-271 was determined by ^1H NMR in deuterated dimethyl sulphoxide. The structural calculations involved the combined use of distance geometry and simulated annealing. The results indicated that MS-271 undergoes an extraordinary folding, i.e., the 'tail' (Phe10–Trp21) passes through the 'ring' region (Cys1–Asp9) ('lasso' structure). Several characteristic features of the 'lasso' structures are indicated.

Overexpression, One-Step Purification and Characterization of UDP-Glucose Dehydrogenase and UDP-*N*-Acetylglucosamine Pyrophosphorylase

Bioorg. Med. Chem. **1996**, *4*, 131

Claudio De Luca,[a,b] Manfred Lansing,[b] Fabiana Crescenzi,[b] Irene Martini,[b] Gwo-Jenn Shen,[a] Michael O'Regan[b] and Chi-Huey Wong*[a]
[a]*Department of Chemistry, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, CA 92037, U.S.A.* [b]*Fidia Advanced Biopolymers, Via Ponte della Fabbrica 3/a, 35031 Abano Terme, Italy*



The two enzymes were overexpressed and used in the synthesis of Hyaluronic Acid.