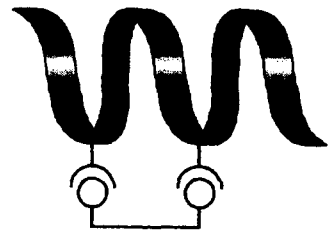
Design, Synthesis, and Evaluation of Synthetic Receptors for the Recognition of Aspartate Pairs in an α-Helical Conformation

Bioorg. Med. Chem. **1997**, *5*, 1455

Jeffrey S. Albert, Mark W. Peczuh and Andrew D. Hamilton*
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, U.S.A.

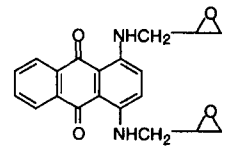


In this study, a series of zwitterionic, 16-mer peptides serve as models for the recognition of carboxylate pairs in proteins. A receptor is described that contains two guanidinium groups separated by 4–5 Å by a rigid bicyclo[3.3.0]-octane spacer. Studies employing circular dichroism spectroscopy demonstrated that the addition of the receptor to the $i+3$ peptide substrate caused a 23% enhancement of the helical structure in 15% water/methanol at 25 °C.

Antitumor Agents—CLXVII. Synthesis and Structure–Activity Correlations of the Cytotoxic Anthraquinone 1,4-Bis-(2,3-Epoxypropylamino)-9,10-Anthracenedione, and of Related Compounds

Bioorg. Med. Chem. **1997**, *5*, 1469

Mary G. Johnson,[a] Hiroshi Kiyokawa,[a] Shohei Tani,[a] Junko Koyama,[a] Susan L. Morris-Natschke,[a] Anthony Mauger,[b] Margaret M. Bowers-Daines,[c] Barry C. Lange[c] and Kuo-Hsiung Lee[a,*]
[a]*Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy CB#7360, University of North Carolina, Chapel Hill, NC 27599-7360, U.S.A.*
[b]*National Cancer Institute, Executive Plaza North Suite 831, 6130 Executive Boulevard MSC 7448, Rockville, MD 20892-7448, U.S.A.*
[c]*Research Laboratories, Rohm and Haas Company, 727 Norristown Road, Spring House, PA 19477, U.S.A.*



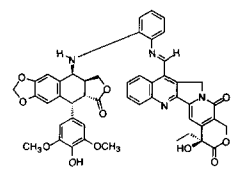
3

Synthesis and in vitro antineoplastic activity of derivatives of **3** with anthraquinone, naphthoquinone and quinone skeletons are described.

Antitumor Agents—CLXXIII. Synthesis and Evaluation of Camptothecin-4β-amino-4′-*O*-demethyl Epipodophyllotoxin Conjugates as Inhibitors of Mammalian DNA Topoisomerases and as Cytotoxic Agents

Bioorg. Med. Chem. **1997**, *5*, 1481

Kenneth F. Bastow,[a] Hui-Kang Wang,[a] Yung-Chi Cheng[b] and Kuo-Hsiung Lee[a,*]
[a]*Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599, U.S.A.*
[b]*Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510, U.S.A.*



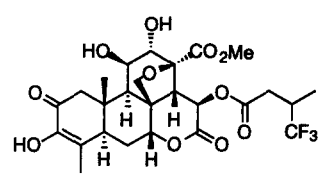
Conjugates of camptothecin and a 4′-*O*-demethyl epipodophyllotoxin derivative display dual target specificity against mammalian DNA topoisomerase I and II and a broad spectrum of cytotoxic activity against drug-resistant cells.

Synthesis of Cytotoxic Fluorinated Quassinoids

Bioorg. Med. Chem. **1997**, *5*, 1489

Nobuhiro Ohno,[a] Narihiko Fukamiya,[a] Masayoshi Okano,[a] Kiyoshi Tagahara,[b] and Kuo-Hsiung Lee[c,*]
[a]*Interdisciplinary Studies of Natural Environment, Faculty of Integrated Arts and Sciences, Hiroshima University, Higashi-Hiroshima 739, Japan*
[b]*Faculty of Pharmaceutical Sciences, Kobe Pharmaceutical University, Kobe 658, Japan*
[c]*School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599-7360, U.S.A.*

Synthesis and in vitro antineoplastic activity of four fluorinated quassinoid derivatives (**11-13**, and **17**).



17,

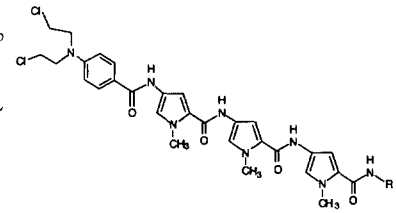
Bioorg. Med. Chem. **1997**, *5*, 1497

Structure–Activity Relationship of a Series of C-Terminus Modified Aminoalkyl, Diaminoalkyl- and Anilino-containing Analogues of the Benzoic Acid Mustard Distamycin Derivative Tallimustine: Synthesis, DNA Binding and Cytotoxicity Studies

Natalie Brooks,[a] John A. Hartley,[a] Jacob E. Simpson Jr.,[b] Stephen R. Wright,[b] Shirley Woo,[b] Sara Centioni,[b] Michael D. Fontaine,[b] Terry E. McIntyre,[b] and Moses Lee[b,*]

[a]*CRC Drug–DNA Interactions Research Group, Department of Oncology, UCL Medical School, 91 Riding House Street, London, W1P 8BT, U.K.*

[b]*Department of Chemistry, Furman University, Greenville, SC 29613, U.S.A.*



Bioorg. Med. Chem. **1997**, *5*, 1509

Isolation and Characterization of Novel Cytotoxic Saponins from *Archidendron ellipticum*

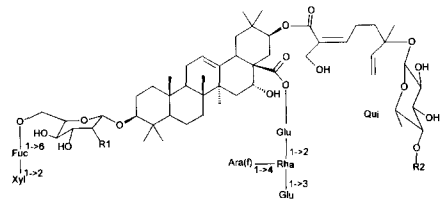
John A. Beutler,[a] Yoel Kashman,[b] Lewis K. Pannell,[c] John H. Cardellina II,[a] Mark R. A. Alexander,[d] Michael S. Balaschak,[d] Tanya R. Prather,[a] Robert H. Shoemaker,[a] and Michael R. Boyd[a,*]

[a]*Laboratory of Drug Discovery Research & Development, Developmental Therapeutics Program, Division of Cancer Treatment, Diagnosis, and Centers, National Cancer Institute, Frederick, MD 21702-1201, U.S.A.*

[b]*Department of Chemistry, Tel Aviv University, Tel Aviv, Israel*

[c]*Laboratory of Analytical Chemistry, National Institute of Diabetes, Digestive and Kidney Diseases, NIH, Bethesda, MD 20892, U.S.A.*

[d]*Science Application International Corporation, Frederick, MD 21702-1201*



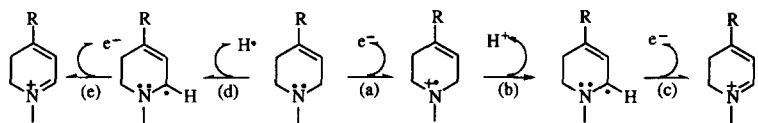
Elliptosides A–J, novel cytotoxic saponin esters, have been isolated from the tropical plant *Archidendron ellipticum*, identified and biologically evaluated.

Bioorg. Med. Chem. **1997**, *5*, 1519

Chemical Model Studies on the Monoamine Oxidase-B Catalyzed Oxidation of 4-Substituted 1-Methyl-1,2,3,6-tetrahydropyridines

Christelle Franot, Stéphane Mabic and Neal Castagnoli, Jr.*

Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, U.S.A.



(a) $Fe^{+3}(Phen)_3(PF_6)_3^-$. (b) C_5H_5N(c) $Fe^{+3}(Phen)_3(PF_6)_3^-$(d) $(CH_3)_3CO^{\bullet}$. (e) Cu^{+2}.

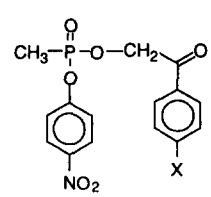
Bioorg. Med. Chem. **1997**, *5*, 1531

Modulation of Human α-Thrombin Activity with Phosphonate Ester Inhibitors

Edith J. Enyedy and Ildiko M. Kovach*

The Catholic University of America, Department of Chemistry, Washington, DC 20064, U.S.A.

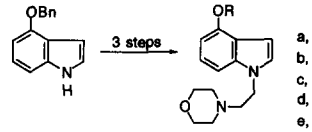
Enantiomers of 4-nitrophenyl 4-X-phenacyl methylphosphonate esters (X = H, PMN; CH_3; and CH_3O) inactivate human α-thrombin selectively and efficiently. The covalent attachement to thrombin is reversible due to a self-catalyzed intramolecular attack at phosphorus by the anion of the hydrated ketone. Pharmaceutical application of the concept is suggested.



Bioorg. Med. Chem. **1997**, 5, 1591

Synthesis, Pharmacology, and Molecular Modeling of Novel 4-Alkyloxy Indole Derivatives Related to Cannabimimetic Aminoalkyl Indoles (AAIs)

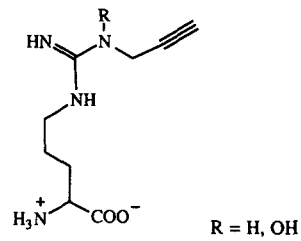
A. K. Dutta,[a] W. Ryan,[a] B. F. Thomas,[b] M. Singer,[a] D. R. Compton,[c] B. R. Martin,[c] and R. K. Razdan[a,*]
[a]*Organix Inc., 65 Cummings Park, Woburn, MA 01801, U.S.A*
[b]*Research Triangle Institute, Research Triangle Park, NC 27709, U.S.A.*
[c]*Medical College of Virginia, Richmond, VA 23298, U.S.A.*



Bioorg. Med. Chem. **1997**, 5, 1601

N^{ω}-Propargyl-L-arginine and N^{ω}-Hydroxy-N^{ω}-propargyl-L-arginine are Inhibitors, but not Inactivators, of Neuronal and Macrophage Nitric Oxide Synthases

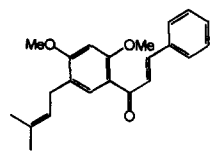
Walter Fast,[a] Marc E. Levsky,[a] Michael A. Marletta[b] and Richard B. Silverman*[,a]
[a]*Department of Chemistry and the Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, IL 60208-3113, U.S.A.*
[b]*Interdepartmental Program in Medicinal Chemistry, University of Michigan, Ann Arbor, MI 48109, U.S.A.*



Bioorg. Med. Chem. **1997**, 5, 1609

Anti-invasive Activity of Alkaloids and Polyphenolics in Vitro

Virinder S. Parmar,*[,a] Marc E. Bracke,[b] Jan Philippe,[c] Jesper Wengel,[d] Subhash C. Jain,[a] Carl E. Olsen,[e] Kirpal S. Bisht,[a] Nawal K. Sharma,[a] Andy Courtens,[b] Sunil K. Sharma,[d] Krist'l Vennekens,[b] Veerle Van Marck,[b] Sanjay K. Singh,[d] Naresh Kumar,[a] Ajay Kumar,[a] Sanjay Malhotra,[a] Rajesh Kumar,[a] Vivek K. Rajwanshi,[a] Rajni Jain[a] and Marc M. Mareel[b]
[a]*Department of Chemistry, University of Delhi, Delhi-110 007, India;* [b]*Laboratory of Experimental Cancerology, Department of Radiotherapy, Nuclear Medicine and Experimental Cancerology,* [c]*Department of Clinical Chemistry, University Hospital, De Pintelaan 185, B-9000 Gent, Belgium;* [d]*Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark;* [e]*Chemistry Department, Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Copenhagen, Denmark*



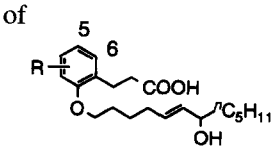
Among 100 alkaloids and flavonoids tested for anti-invasive activity, six compounds inhibited the invasion of human MCF-7/6 mammary carcinoma cells in confronting cultures with embryonic chick heart fragments at a concentration of 1 μM. Chalcones bearing prenyl group(s) have shown the best activity.

Bioorg. Med. Chem. **1997**, 5, 1621

Synthesis of Structural Analogues of Leukotriene B_4 and their Receptor Binding Activity

Mitoshi Konno, Takahiko Nakae, Shigeru Sakuyama, Minoru Nishizaki, Yoshihiko Odagaki, Hisao Nakai and Nobuyuki Hamanaka*
Department of Medicinal Chemistry, Minase Research Institute, Ono Pharmaceutical Co., Ltd, Shimamoto, Mishima, Osaka 618, Japan

Synthesis, SAR and the LTB_4 receptor binding assay of β-phenylpropionic acid derivatives are described.



28c R = 5-NHCO$(CH_2)_3$CONMe$_2$
38c R = 5-O$(CH_2)_4$COOH
52a R = 6-O$(CH_2)_4$COOH
52b R = 6-O$(CH_2)_4$CONMe$_2$

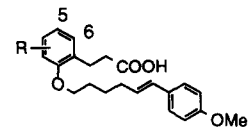
Bioorg. Med. Chem. **1997**, *5*, 1649

Trisubstituted Benzene Leukotriene B_4 Receptor Antagonists: Synthesis and Structure–Activity Relationships

Mitoshi Konno, Takahiko Nakae, Shigeru Sakuyama, Yoshihiko Odagaki, Hisao Nakai and Nobuyuki Hamanaka*

Department of Medicinal Chemistry, Minase Research Institute, Ono Pharmaceutical Ltd, Shimamoto, Mishima, Osaka 618, Japan

Synthesis, SAR, and the LTB_4 receptor antagonist activity of a series of β-phenylpropionic acid derivatives are described.



3b R = 6-O$(CH_2)_4$COOH
5c R = 5-NHCO$(CH_2)_3$CONMe$_2$

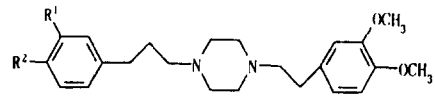
Bioorg. Med. Chem. **1997**, *5*, 1675

Synthesis, Structure, and Quantitative Structure–Activity Relationships of σ Receptor Ligands, 1-[2-(3,4-Dimethoxyphenyl)ethyl]-4-(3-phenylpropyl)piperazines

Ken-ichi Fujimura,[a,*] Junzo Matsumoto,[a] Masashi Niwa,[a] Tadayuki Kobayashi,[a] Yoichi Kawashima,[b] Yasuko In[c] and Toshimasa Ishida[c]

[a]Developmental Research Division, [b]Product Development Center, Santen Pharmaceutical Co., Ltd, 9–19 Shimoshinjo 3-chome, Higashiyodogawa-ku, Osaka 533, Japan, and [c]Osaka University of Pharmaceutical Sciences, 20-1 Nasahara 4-chome, Takatsuki, Osaka 569-11, Japan

Synthesis and X-ray analysis of σ-binding piperazines were reported. The activities were suggested to depend quantitatively on the electronic natures of R^1 and R^2.



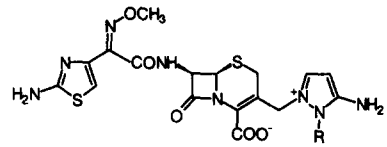
Bioorg. Med. Chem. **1997**, *5*, 1685

Studies on 3′-Quaternary Ammonium Cephalosporins—IV. Synthesis and Antibacterial Activity of 3′-(2-Alkyl-3-aminopyrazolium)cephalosporins Related to FK037

Hidenori 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 various 2-alkyl-3-aminopyrazoliomethyl groups at the 3-position are described. As a result we discovered FK037 which showed extremely potent broad-spectrum activity.



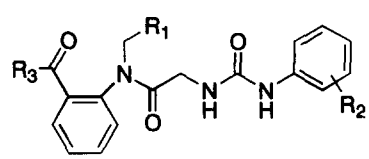
FK037: R=CH_2CH_2OH

Bioorg. Med. Chem. **1997**, *5*, 1695

Synthesis and Pharmacological Properties of Ureidomethylcarbamoylphenylketone Derivatives. A New Potent and Subtype-selective Nonpeptide CCK-B/gastrin Receptor Antagonist, S-0509

Sanji Hagishita,* Yasushi Murakami, Kaoru Seno, Susumu Kamata,* Nobuhiro Haga, Toshiro Konoike, Yasuhiko Kanda, Ryuichi Kiyama, Takeshi Shiota, Yasunobu Ishihara,* Michio Ishikawa, Mayumi Shimamura, Koji Abe and Koji Yoshimura

Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan



Bioorg. Med. Chem. **1997**, *5*, 1715

Anti-AIDS Agents—XXVI. Structure–Activity Correlations of Gomisin-G-Related Anti-HIV Lignans From *Kadsura interior* and of Related Synthetic Analogues

Dao-Feng Chen,[a,*] Shun-Xiang Zhang,[b] Lan Xie,[b] Jing-Xi Xie,[b] Ke Chen,[b] Yoshiki Kashiwada,[b] Bing-Nan Zhou,[c] Pei Wang,[a] L. Mark Cosentino[d] and Kuo-Hsiung Lee[b,*]

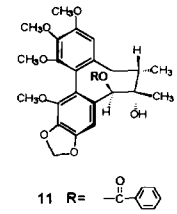
[a]*Department of Pharmacognosy, School of Pharmacy, Shanghai Medical University, Shanghai 200032, People's Republic of China*

[b]*Natural Products Laboratory, Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599, U.S.A.*

[c]*Shanghai Institute of Materia Medica, Academia Sinica, Shanghai 200031, People's Republic of China*

[d]*Biotech Research Laboratories, 3 Taft Court, Rockville, MD 20850, U.S.A.*

Twelve lignans from *Kadsura interior* and 10 related synthetic biphenyl derivatives were evaluated for anti-HIV activity. Gomisin-G (**11**) was the most active natural lignan.



11 R=

Bioorg. Med. Chem. **1997**, *5*, 1725

Comparison of Chemical Characteristics of the First and the Second Cysteine-Rich Domains of Protein Kinase Cγ

Kazuhiro Irie,[a,*] Yoshiaki Yanai,[a] Kentaro Oie,[a] Junya Ishizawa,[a] Yu Nakagawa,[a] Hajime Ohigashi,[a] Paul A. Wender[b,*] and Ushio Kikkawa[c]

[a]*Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Kyoto 606, Japan*

[b]*Department of Chemistry, Stanford University, Stanford, CA 94305, U.S.A.*

[c]*Biosignal Research Center, Kobe University, Kobe 657, Japan*

γ-CRD1: H_2N-HKFTARFFKQPTFCSHCTDFIWGIGKQGLQCQVCSFVVHRRCHEFVTFECPG-COOH

γ-CRD2: H_2N-HKFRLHSYSSPTFCDHCGSLLYGLVHQGMKCSCCEMNVHRRCVRSVPSLCG-COOH