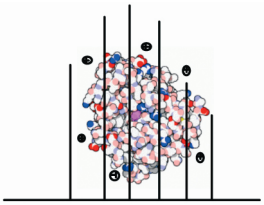
Bioorg. Med. Chem. 11 (2003) 311

Going Gently Into Flight: Analyzing Noncovalent Interactions by Mass Spectrometry

Bruce Ganem[a] and Jack D. Henion[b,*]

[a]*Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14853, USA*
[b]*Department of Population Medicine and Diagnostic Science, Cornell University, Ithaca, NY 14850, USA*

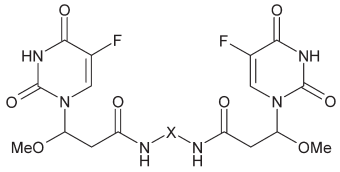


Bioorg. Med. Chem. 11 (2003) 315

Synthesis and Evaluation of New 5-Fluorouracil Antitumor Cell Differentiating Derivatives

José F. Domínguez,[a] Juan A. Marchal,[b] Antonio Correa,[a] Esmeralda Carrillo,[b] Houria Boulaiz,[c] Antonia Aránega,[c] Miguel A. Gallo[a] and Antonio Espinosa[a,*]

[a]*Departamento de Química Farmacéutica y Orgánica, Facultad de Farmacia, Universidad de Granada, Granada, Spain*
[b]*Departamento de Ciencias de la Salud, Universidad de Jaén, Jaén, Spain*
[c]*Departamento de Ciencias Morfologicas, Facultad de Medicina, Universidad de Granada, Granada, Spain*

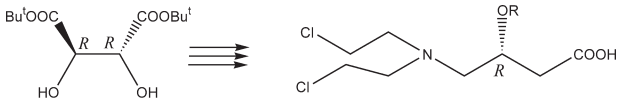


Bioorg. Med. Chem. 11 (2003) 325

New Nitrogen Mustards Structurally Related to (L)-Carnitine

Ludovic Faissat, Katja Martin, Claude Chavis, Jean-Louis Montéro and Marc Lucas*

ENSCM, Laboratoire de Chimie Biomoléculaire, UMR 5032, 8 Rue de l'Ecole Normale, 34296 Montpellier Cédex 05, France



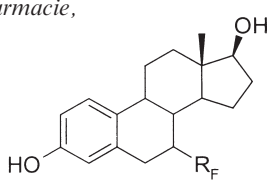
R = H, acetyl, propionyl, capryloyl, phenylacetyl and ROH = Chlorambucil

Bioorg. Med. Chem. 11 (2003) 335

Synthesis, Characterization and Biological Evaluation of 7α-Perfluoroalkylestradiol Derivatives

Jean-C1aude Blazejewski,[a,*] Martin P. Wilmshurst,[a] Matthew D. Popkin,[a] Claude Wakselman,[a] Guy Laurent,[b] Denis Nonclercq,[b] Anny Cleeren,[c] Yan Ma,[c] Hye-Sook Seo[c] and Guy Leclercq[c]

[a]*SIRCOB, ESA CNRS 8086, Université de Versailles, 45 Avenue des Etats-Unis, 78035 Versailles, France*
[b]*Service d'Histologie et de Cytologie Expérimentale, Faculté de Médecine et de Pharmacie, Université de Mons-Hainaut, 6 avenue du Champ de Mars, B 7000 Mons, Belgium*
[c]*Laboratoire J.-C. Heuson de Cancérologie Mammaire, Institut Jules Bordet, Service de Médecine, 1 rue Héger-Bordet, B1000 Brussels, Belgium*



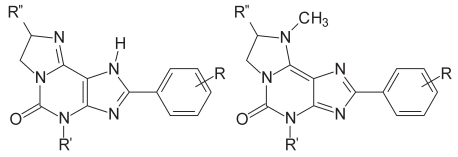
$R_F = CF_3, C_6F_{13}$

Bioorg. Med. Chem. 11 (2003) 347

2-Phenylimidazo[2,1-*i*]purin-5-ones: Structure–Activity Relationships and Characterization of Potent and Selective Inverse Agonists at Human A_3 Adenosine Receptors

Vita Ozola,[a] Mark Thorand,[a] Martina Diekmann,[a] Ramatullah Qurishi,[a] Britta Schumacher,[a] Kenneth A. Jacobson[b] and Christa E. Müller[a,*]

[a]*University of Bonn, Pharmaceutical Institute Poppelsdorf, Kreuzbergweg 26, D-53115 Bonn, Germany*
[b]*Laboratory of Bioorganic Chemistry, NIDDK, National Institutes of Health, Bethesda, Maryland, USA*

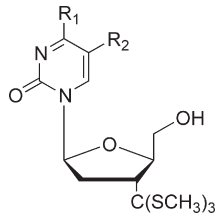


Bioorg. Med. Chem. 11 (2003) 357

Research on L-Nucleosides. Synthesis and Biological Evaluation of a Series of L- and D-2′,3′-Dideoxy-3′-[tris(methylthio)methyl]-β-pentofuranosyl Nucleosides

Claudia Mugnaini,[a] Maurizio Botta,[a,*] Massimo Coletta,[b] Federico Corelli,[a,*] Federico Focher,[c] Stefano Marini,[b] Michela Lucia Renzulli[a] and Annalisa Verri[c]

[a]*Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, via A. Moro, snc, I-53100 Siena, Italy*
[b]*Istituto di Genetica Molecolare, CNR, via Abbiategrasso 207, I-27100 Pavia, Italy*
[c]*Dipartimento di Medicina Sperimentale e Scienze Biochimiche, Università di Roma Tor Vergata, via Montpellier 1, I-00133 Rome, Italy*



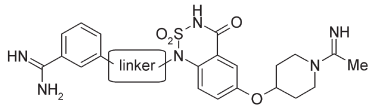
Bioorg. Med. Chem. 11 (2003) 367

Design, Synthesis and Biological Activity of YM-60828 Derivatives. Part 2: Potent and Orally-Bioavailable Factor Xa Inhibitors Based on Benzothiadiazine-4-one Template

Fukushi Hirayama,* Hiroyuki Koshio, Naoko Katayama, Tsukasa Ishihara, Hiroyuki Kaizawa, Yuta Taniuchi, Kazuo Sato, Yumiko Sakai-Moritani, Seiji Kaku, Hiroyuki Kurihara, Tomihisa Kawasaki, Yuzo Matsumoto, Shuichi Sakamoto and Shin-ichi Tsukamoto

Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., 21 Miyukigaoka, Tsukuba, Ibaraki 305-8585, Japan

Factor Xa inhibitors based on benzothiadiazine-4-one templates were prepared and evaluated for inhibitory activity against factor Xa in vitro and anticoagulant activity ex vivo.



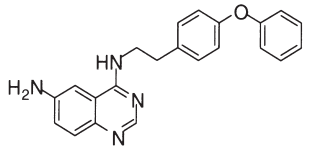
Bioorg. Med. Chem. 11 (2003) 383

Discovery of Quinazolines as a Novel Structural Class of Potent Inhibitors of NF-κB Activation

Masanori Tobe, Yoshiaki Isobe, Hideyuki Tomizawa, Takahiro Nagasaki, Hirotada Takahashi, Tominaga Fukazawa and Hideya Hayashi*

Pharmaceuticals and Biotechnology Laboratory, Japan Energy Corporation, Toda-shi, Saitama 335-8502, Japan

Compound **11q** exhibited a highly inhibitory activity toward NF-κB activation and also showed an anti-inflammatory effect.



11q

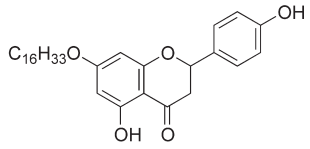
Bioorg. Med. Chem. 11 (2003) 393

Naringenin 7-*O*-cetyl Ether as Inhibitor of HMG-CoA Reductase and Modulator of Plasma and Hepatic Lipids in High Cholesterol-Fed Rats

Mi-Kyung Lee,[a] Surk-Sik Moon,[b] Seung-Eun Lee,[b] Song-Hae Bok,[c] Tae-Sook Jeong,[c] Yong Bok Park[d] and Myung-Sook Choi[a,*]

[a]*Department of Food Science and Nutrition, Kyungpook National University, 1370 Sank-Yuk Dong Puk-Ku, 702-701, Daegu, South Korea*
[b]*Department of Chemistry, Kongju National University, Kongju, South Korea*
[c]*Cardiovascular Research Laboratory, Korea Research Institute of Bioscience and Biotechnology, PO Box 115, Yusong, Daejon, South Korea*
[d]*Department of Genetic Engineering, Kyungpook National University, 1370 Sank-Yuk Dong Puk-Ku, 702-701, Daegu, South Korea*

This study to examine the lipid-lowering effect naringenin 7-*O*-cetyl ether in high cholesterol-fed rats. The supplementation of the compound was effective in altering lipid metabolism and lowering plasma and hepatic cholesterol level.



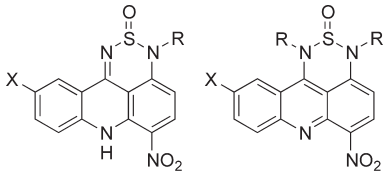
Bioorg. Med. Chem. 11 (2003) 399

Rational Design, Synthesis and Biological Evaluation of Thiadiazinoacridines: A New Class of Antitumor Agents

Ippolito Antonini,[a,*] Paolo Polucci,[a] Amelia Magnano,[a] Diego Cacciamani,[a] Marek T. Konieczny,[b] Jolanta Paradziej-Łukowicz[c] and Sante Martelli[a]

[a]*Department of Chemical Sciences, University of Camerino, Via S. Agostino 1, 62032 Camerino, Italy*
[b]*Department of Organic Chemistry, Faculty of Pharmacy, Medical University of Gdańsk, 80-416 Gdańsk, Poland*
[c]*Department of Pharmaceutical Technology and Biochemistry, Technical University of Gdańsk, 80-952 Gdańsk, Poland*

[1,2,6]Thiadiazino[3,4,5-*kl*]acridin-2-ones.



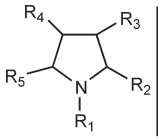
X = H, OMe, Me R = alkylaminoalkyl

Bioorg. Med. Chem. 11 (2003) 407

Synthesis, Antimicrobial and Antifungal Activity of a New Class of Spiro Pyrrolidines

A. Amal Raj,[a] R. Raghunathan,[a,*] M.R. SrideviKumari[b] and N. Raman[b]

[a]*Department of Organic Chemistry, Center for Advanced Studies in Botany, University of Madras, Guindy Campus, Chennai, India 600 025*
[b]*University of Madras, Guindy Campus, Chennai, India 600 025*



R_1 =CH_3, R_2 =H, R_3 =aryl, R_4 =2-spiro-1- cyclohexanone, R_5 =3-Spirooxindole

R_1 =CH_3, R_2 =H, R_3 =aryl, R_4 =2-spiro tetrahydronaphthalen-1-one, R_5 =3-spirooxindole

R_1 =CH_3, R_2 =H, R_3 =aryl, R_4 =2-Spiro arylidene-cyclohexanone, R_5 =3-spirooxindole

R_1 =CH_3, R_2 =H, R_3 =aryl, R_4 =2-spiro hexahydroindazole, R_5 =3-spirooxindole

R_1 =C_6H_{11}, R_2 =Benzoyl, R_3 = 3-spiro-5- phenyl-butenolide, R_4 =aryl, R_5 =phenyl

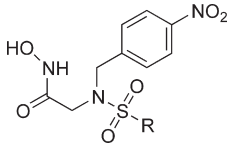
Bioorg. Med. Chem. 11 (2003) 421

A Quantitative Structure–Activity Relationship Study on Some Matrix Metalloproteinase and Collagenase Inhibitors

Dalip Kumar and S. P. Gupta*

Department of Chemistry, Birla Institute of Technology and Science, Pilani-333031, India

A quantitive structure–activity relationship study is performed on some hydroxamic acid-based inhibitors of matrix metalloproteinases and a bacterial collagenase using valence molecular connectivity and electropological state indices.



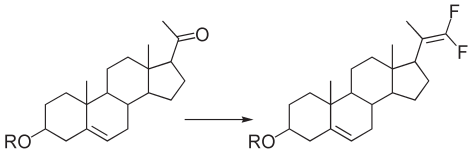
Bioorg. Med. Chem. 11 (2003) 427

Synthesis of 21,21-difluoro-3β-hydroxy-20-methylpregna-5,20-diene and 5,16,20-triene as Potential Inhibitors of Steroid $C_{17(20)}$ Lyase

Philip M. Weintraub,[a,*] Amy K. Holland,[b] Cynthia A. Gates,[c] William R. Moore,[d] Robert J. Resvick,[a] Philippe Bey[e] and Norton P. Peet[f,*]

[a]*Aventis Pharmaceuticals; Rte 202-206, PO Box 6800, Bridgewater, NJ 08807-0800, USA*
[b]*Vankel, 13000 Weston Parkway, Cary, NC 27513, USA*
[c]*Vertex Pharmaceuticals Inc., 130 Waverly St., Cambridge, MA 02139-4242, USA*
[d]*Locus Discoveries, Inc., 512 Township Line Rd, Blue Bell, PA 19422, USA*
[e]*ArQule, 19 Presidential Way, Woburn, MA 01801-5140, USA*
[f]*Aurigene Discovery Technologies, 8-A Preston Court, Bedford, MA 01730, USA*

Novel 21,21-difluorovinyl steroids, designed as difluorinated $C_{20(21)}$ enol mimics of pregnenolone, were targeted as potential mechanism-based inhibitors of $C_{17(20)}$ lyase, a crucial enzyme in the biosynthesis of testosterone. Addition of (difluoromethyl)diphenylphosphine oxide reagent to 17-acetyl steroids was the approach chosen for the construction of these compounds. Of particular interest were the abnormal Wittig products which formed during attempted preparation of the triene **9**. The target difluoroolefin **3** was found to be a moderately potent, time-dependent inhibitor of the enzyme.



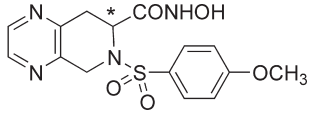
Bioorg. Med. Chem. 11 (2003) 433

Synthesis and Structure–Activity Relationships of 5,6,7,8-Tetrahydropyrido[3,4-*b*]pyrazine-based Hydroxamic Acids as HB-EGF Shedding Inhibitors

Kazuya Yoshiizumi, Minoru Yamamoto, Tomohiro Miyasaka, Yasuko Ito, Hiroshi Kumihara, Masaaki Sawa, Takao Kiyoi, Takeshi Yamamoto, Fumio Nakajima, Ryoichi Hirayama, Hirosato Kondo, Etsuko Ishibushi, Hiroshi Ohmoto, Yoshimasa Inoue and Kohichiro Yoshino

R&D Laboratories, Nippon Organon K.K., 1-5-90, Tomobuchi-cho, Miyakojima-ku, Osaka 534-0016, Japan

The structure–activity relationships of tetrahydropyrido[3,4-*b*]pyrazine-based hydroxamic acids as novel HB-EGF shedding inhibitors are described.

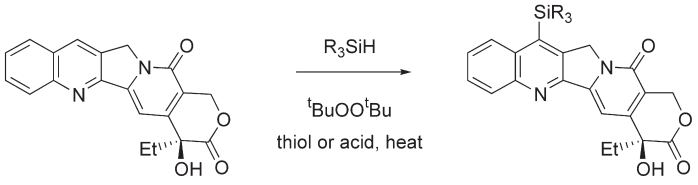


Bioorg. Med. Chem. 11 (2003) 451

Semisynthesis of DB-67 and Other Silatecans from Camptothecin by Thiol-Promoted Addition of Silyl Radicals

Wu Du,[a] Bashir Kaskar,[b] Peter Blumbergs,[b] P.-K. Subramanian[b] and Dennis P. Curran[a,*]

[a]*Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260 USA*
[b]*Ash Stevens Inc., Detroit, MI, 48202, USA*



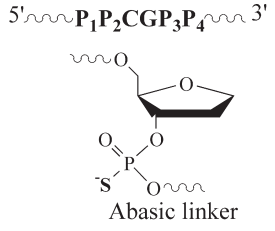
Bioorg. Med. Chem. 11 (2003) 459

Requirement of Nucleobase Proximal to CpG Dinucleotide for Immunostimulatory Activity of Synthetic CpG DNA

Dong Yu, Ekambar R. Kandimalla, Qiuyan Zhao, Lakshmi Bhagat, Yanping Cong and Sudhir Agrawal*

Hybridon, Inc., 345 Vassar Street, Cambridge, MA 02139, USA

Substitution of an abasic linker at C, G, P_3 or P_4 position of CpG DNA resulted in loss of immunostimulatory activity. An abasic nucleoside is permitted at either P_1 or P_2 depending on the neighboring base.



Bioorg. Med. Chem. 11 (2003) 465

Novel Strategies for the Solid Phase Synthesis of Substituted Indolines and Indoles

K. C. Nicolaou,[a,b,*] A. J. Roecker,[a] Robert Hughes,[a] Ruben van Summeren,[a] Jeffrey A. Pfefferkorn[a] and Nicolas Winssinger[a,b]

[a]*Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.* [b]*Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA*

Four classes of nitrogen-containing heterocycles were synthesized on solid support utilizing a polymer-bound selenenyl bromide resin. A number of small combinatorial libraries of compounds reminiscent of certain designed ligands of biological and medicinal interest were constructed demonstrating the potential utility of the developed methodology to chemical biology studies and the drug discovery process.