

Graphical Abstracts

The Conformational Study of Chitin and Chitosan Oligomers in Solution

Bioorg. Med. Chem. 9 (2001) 211

Hiroshi Sugiyama,^a Kanehiko Hisamichi,^b Kazuo Sakai,^c Taichi Usui,^d Jun-Ichi Ishiyama,^e Hideaki Kudo,^f Hiroki Ito^f and Yasuhisa Senda^f

^aInstitute for Chemical Reaction Science, Tohoku University, Sendai 980-8577, Japan

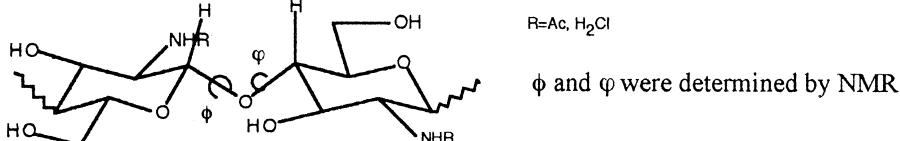
^bInstitute of Development, Aging and Cancer, Tohoku University, Sendai 980-8575, Japan

^cYaizu Suisankagaku Industry Co., Ltd., Yaizu 425-8570, Japan

^dDepartment of Applied Biochemistry, Shizuoka University, Shizuoka 422-8529, Japan

^eMiyagi National College of Technology, Natori 981-1239, Japan

^fDepartment of Chemistry, Yamagata University, Yamagata 990-8560, Japan



Microwave Assisted Solid Support Synthesis of Novel 1,2,4-Triazolo[3,4-b]-1,3,4-thiadiazepines as Potent Antimicrobial Agents

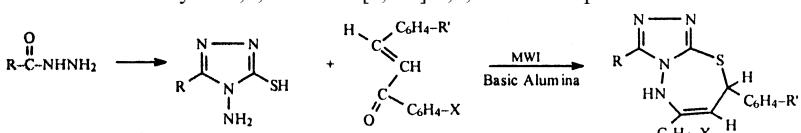
Bioorg. Med. Chem. 9 (2001) 217

M. Kidwai,^a P. Sapra,^a P. Misra,^a R. K. Saxena^b and M. Singh^b

^aDepartment of Chemistry, University of Delhi, Delhi-110007, India

^bDepartment of Microbiology, University of Delhi, South Campus, Delhi-110021, India

A novel synthesis and antimicrobial activity of 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazepines are described.



Synthesis and Biological Evaluation of 2-(3'-(1*H*-Tetrazol-5-yl)bicyclo[1.1.1]pent-1-yl)glycine (*S*-TBPG), a Novel mGlu1 Receptor Antagonist

Bioorg. Med. Chem. 9 (2001) 221

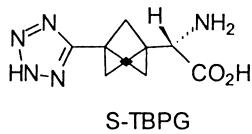
Gabriele Costantino,^a Katiuscia Maltoni,^a Maura Marzocchi,^a Emidio Cammaioni,^a

Laurent Prezeau,^b Jean-Philippe Pin^b and Roberto Pellicciari^a

^aDipartimento di Chimica e Tecnologia del Farmaco, Università di Perugia, Via del Liceo 1, 06123 Perugia, Italy

^bCentre National de la Recherche Scientifique, UPR 9023 — CCIPE, 141 Rue de la Cardonille, 34094 Montpellier, France

The novel amino acid **9**, *S*-TBPG, is synthesized and evaluated as potential mGluR ligand. *S*-TBPG (**9**) is shown to be a moderately potent and selective mGluR1 antagonist.



New Bis-Catechols 5-Lipoxygenase Inhibitors

Bioorg. Med. Chem. 9 (2001) 229

Romain Dupont,^a Jean-François Goossens,^b Nicole Cotelle,^a

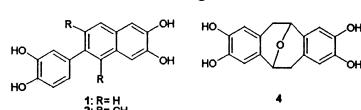
Laurence Vrielynck,^c Hervé Vezin,^a Jean-Pierre Hénichart^b and Philippe Cotelle^a

^aLaboratoire de Chimie Organique et Macromoléculaire, UPRESA CNRS 8009, USTL, 59655 Villeneuve d'Ascq, France

^bInstitut de Chimie Pharmaceutique Albert Lespagnol, Université de Lille 2, EA 2692, 3 rue J. Laguësse, 59006 Lille, France

^cLaboratoire de Spectrochimie Infra-Rouge et Raman, UMR CNRS 8516, USTL, 59655 Villeneuve d'Ascq, France

Three polyhydroxy-2-phenylnaphthalenes and the oxy analogue of tetrahydroxypavinan were prepared and evaluated for their antioxidant properties and inhibition of 5-lipoxygenase activity. Compounds **1** and **2** were found to be as potent 5-LO inhibitors as NDGA. The reliability of the 3-D structures with the 5-LO inhibition properties is discussed. Their antioxidant properties show that tested compounds are expected to act as redox inhibitors.



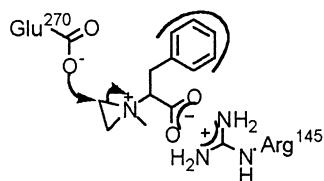
A New Inhibitor Design Strategy for Carboxypeptidase A as Exemplified by *N*-(2-Chloroethyl)-*N*-methylphenylalanine

Bioorg. Med. Chem. 9 (2001) 237

Jung Dae Park, Kyung Joo Lee and Dong H. Kim

Center for Biofunctional Molecules and Department of Chemistry, Pohang University of Science and Technology, San 31 Hyojadong, Pohang 790-784, South Korea

N-(2-Chloroethyl)-*N*-methylphenylalanine is a new class of mechanism-based inactivator for carboxypeptidase A, which has been designed rationally exploiting the chemistry that the chloroethylamine moiety readily undergoes an intramolecular S_N2 type reaction to generate an aziridinium ion.

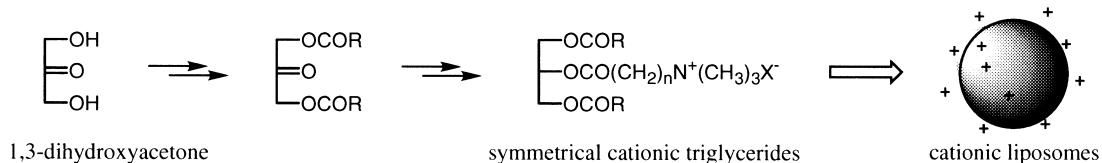


Symmetrical Cationic Triglycerides: An Efficient Synthesis and Application to Gene Transfer

Bioorg. Med. Chem. 9 (2001) 245

Satoshi Obika, Wei Yu, Atsuko Shimoyama, Takeshi Uneda, Kazuyuki Miyashita, Takefumi Doi and Takeshi Imanishi

Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan

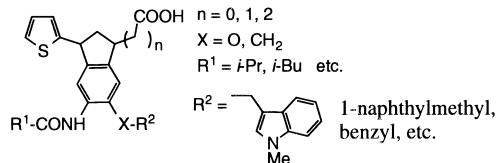


Design, Syntheses, and Structure–Activity Relationships of Indan Derivatives as Endothelin Antagonists; New Lead Generation of Non-peptidic Antagonist from Peptidic Leads

Bioorg. Med. Chem. 9 (2001) 255

Hiroshi Morimoto, Chiaki Fukushima, Rikako Yamauchi, Tomoko Hosino, Kohei Kikkawa, Kosuke Yasuda and Koichiro Yamada
Discovery Research Laboratory, Tanabe Seiyaku Co., Ltd, 2-2-50 Kawagishi, Toda-shi, Saitama 335-8505, Japan

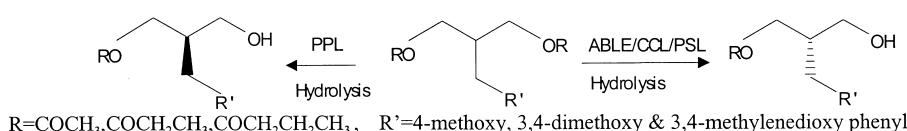
A new lead generation of non-peptidic antagonists from two peptidic ET_A-selective antagonists, BQ-123 and FR139317, was performed. A new series of indan derivatives was designed and synthesized according to a putative pharmacophore constructed from the superposition of the reported structure of cyclic peptide BQ-123 and a presumable B-turned active conformation of the linear peptide FR139317 by possible intramolecular hydrogen bonding.



Purification and Characterisation of an Ester Hydrolase from a Strain of *Arthrobacter* Species: Its Application in Asymmetrisation of 2-Benzyl-1,3-propanediol Acylates

Bioorg. Med. Chem. 9 (2001) 269

S. Johri, V. Verma, R. Parshad, S. Koul, S. C. Taneja and G. N. Qazi
Regional Research Laboratory (CSIR), Canal Road, Jammu-Tawi 180 001, India



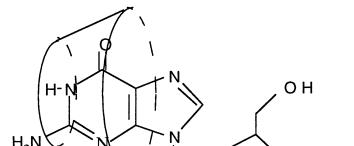
Effect of the Complexation with Cyclodextrins on the In Vitro Antiviral Activity of Ganciclovir Against Human Cytomegalovirus

Bioorg. Med. Chem. 9 (2001) 275

Céline Nicolazzi, Souad Abdou, Jocelyne Collomb, Alain Marsura and Chantal Finance*

Unité Mixte de Recherche Université-CNRS 7565, Structure et Réactivité des Systèmes Moléculaires Complexes, UHP, Nancy, France

The influence of the complexation of ganciclovir by cyclodextrins on its antiviral activity was studied.



Complex [ganciclovir: β -cyclodextrin]

Searching for Allosteric Effects Via QSARs

Bioorg. Med. Chem. 9 (2001) 283

Corwin Hansch, Rajni Garg and Alka Kurup

Department of Chemistry, Pomona College, Claremont, CA 91711, USA

A study of our database of 7,000 QSAR involving chemical–biological interaction uncovered 11 examples where the QSARs all contain inverted parabolas based on molecular refractivity. That is, biological activity first decreases with increase in MR and then increases. Two of the examples are for enzymes: cyclooxygenase and trypsin. The others are for various receptors. The results seem to be best rationalized by the larger compounds inducing a change in a receptor unit that allows for a new mode of interaction.

3-D QSAR Studies of Triazolinone Based Balanced AT₁/AT₂ Receptor Antagonists

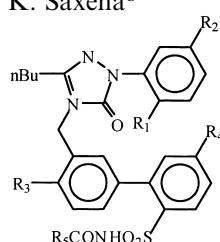
Bioorg. Med. Chem. 9 (2001) 291

Trupti Pandya,^a Suresh K. Pandey,^b Meena Tiwari,^a S. C. Chaturvedi^a and Anil K. Saxena^b

^a*Department of Pharmacy, S.G.S.I.T.S., Indore, India*

^b*Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow, India*

Essential structural and physicochemical requirements in terms of common biophoric sites (pharmacophore) and secondary sites for binding and interacting with AT₁ and AT₂ receptors have been identified using APEX-3-D expert system on 16 N²-aryltriazolinone biphenyl sulphonamides.



Non-Peptidic Inhibitors of Human Chymase. Synthesis, Structure–Activity Relationships, and Pharmacokinetic Profiles of a Series of 5-Amino-6-oxo-1,6-dihydropyrimidine-Containing Trifluoromethyl Ketones

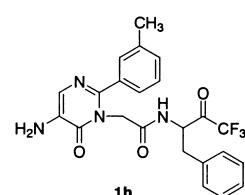
Bioorg. Med. Chem. 9 (2001) 301

Fumihiko Akahoshi,^a Atsuyuki Ashimori,^a Takuya Yoshimura,^a Teruaki Imada,^a Masahide Nakajima,^a Naoko Mitsutomi,^a Shigeki Kuwahara,^a Tatsuyuki Ohtsuka,^a Chikara Fukaya,^a Mizuo Miyazaki^b and Norifumi Nakamura^a

^a*Drug Discovery Laboratories, Welfide Corporation, 2-25-1 Shodai-Ohtani, Hirakata, Osaka 573-1153, Japan*

^b*Department of Pharmacology, Osaka Medical College, 2-7 Daigaku-cho, Takatsuki, Osaka 569-8686, Japan*

We designed non-peptidic inhibitors based on the predicted binding mode of the peptidic chymase inhibitor Val-Pro-Phe-CF₃ and found that compound **1h** has an inhibitory constant of 0.05063 μ M toward human chymase—an activity superior in potency to that of the parent peptidic inhibitor—and good selectivity for chymase over other proteases.



Oxidation of Oxa and Thia Fatty Acids and Related Compounds Catalysed by 5- and 15-Lipoxygenase

Bioorg. Med. Chem. 9 (2001) 317

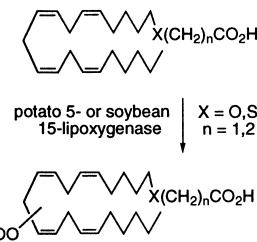
Christopher J. Easton,^a Thomas A. Robertson,^a Michael J. Pitt,^a Deborah A. Rathjen,^b Antonio Ferrante^c and Alfred Poulos^c

^aResearch School of Chemistry, Australian National University, Canberra, ACT 0200, Australia

^bPeptech Ltd., Locked Bag 2053, North Ryde, NSW 2113, Australia

^cDepartment of Immunopathology, Adelaide Women's and Children's Hospital, North Adelaide, SA 5006, Australia

Lipoxygenase-catalysed oxidations of nine modified fatty acids, including the illustrated reactions, have been investigated.



Molecular Modeling and QSAR Analysis of the Interaction of Flavone Derivatives with the Benzodiazepine Binding Site of the GABA_A Receptor Complex

Bioorg. Med. Chem. 9 (2001) 323

Mariel Marder,^a Guillermmina Estiú,^b Luis Bruno Blanch,^c Haydee Viola,^d Cristina Wasowski,^a Jorge H. Medina^d and Alejandro C. Paladini^a

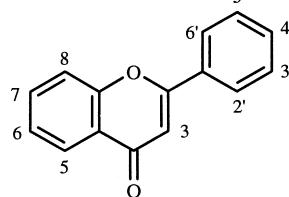
^aInstituto de Química y Fisicoquímica Biológicas, Facultad de Farmacia y Bioquímica, Junín 956, (1113) Buenos Aires, Argentina

^bCEQUINOR, Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, CC. 962, (1900) La Plata, Argentina

^cFarmacocinética, División Farmacia, Departamento de Ciencias Biológicas, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, CC. 243, (1900) La Plata, Argentina

^dInstituto de Biología Celular y Neurociencias, Facultad de Medicina, Paraguay 2155, (1121) Buenos Aires, Argentina

A receptor/pharmacophore model of flavone derivatives active on the GABA_A receptor has been established by superposition analysis of 120 natural or synthetic flavonoids and diazepam. QSAR regression analysis of interaction of parameters refines and supports the model.



Synthetic and Biological Activity Evaluation Studies on Novel 1,3-Diarylpropenones

Bioorg. Med. Chem. 9 (2001) 337

Shubhasish Mukherjee,^a Vijayendra Kumar,^a Ashok K. Prasad,^a Hanumantharao G. Raj,^b Marc E. Bracke,^c Carl E. Olsen,^d Subhash C. Jain^a and Virinder S. Parmar^a

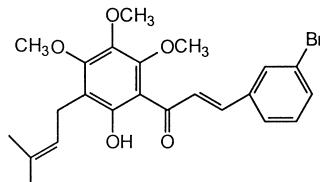
^aDepartment of Chemistry, University of Delhi, Delhi-110 007, India

^bDepartment of Biochemistry, VP Chest Institute, University of Delhi, Delhi-110 007, India

^cLaboratory of Experimental Cancerology, Department of Radiotherapy, University Hospital, De Pintelaan 185, B-9000 Gent, Belgium

^dChemistry Department, Royal Veterinary and Agricultural University, 40 Thorvaldsensvej, Frederiksberg C, DK-1871 Copenhagen, Denmark

Fourteen novel *C*-prenylated and *O*-allylated 1,3-diarylpropenones have been synthesized by Claisen-Schmidt condensation reaction and screened for their anti-invasive and antioxidant activities.



Synthesis of Variously Oxidized Abietane Diterpenes and Their Antibacterial Activities Against MRSA and VRE

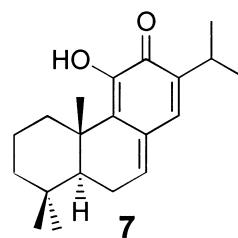
Bioorg. Med. Chem. 9 (2001) 347

Zhixiang Yang,^a Yoshikazu Kitano,^a Kazuhiro Chiba,^a Naohiro Shibata,^b Hiroshi Kurokawa,^b Yohei Doi,^b Yoshichika Arakawa^b and Masahiro Tada^{a,*}

^aLaboratory of Bioorganic Chemistry, Tokyo University of Agriculture and Technology, Fuchu, Tokyo 183-8509, Japan

^bDepartment of Bacterial and Blood Products, National Institute of Infectious Disease, Gakuen, Musashi-Murayama, Tokyo 208-0011, Japan

Variously oxidized 12 natural abietanes were synthesized via stereoselective cyclization of polyene. Antimicrobial activities of the synthesized diterpenes and their related compounds against MRSA and VRE were evaluated. Quinone methide, 11-hydroxy-12-oxo-7,9(11),13-abietatriene (7), showed the most potent antibacterial activity (0.5–1 µg/ml) against MRSA and VRE.



Rebeccamycin Analogues from Indolo[2,3-*c*]carbazole

Bioorg. Med. Chem. 9 (2001) 357

Aline Voldoire,^a Martine Sancelme,^a Michelle Prudhomme,^a Pierre Colson,^b Claude Houssier,^b Christian Bailly,^c Stéphane Léonce^d and Stéphanie Lambel^d

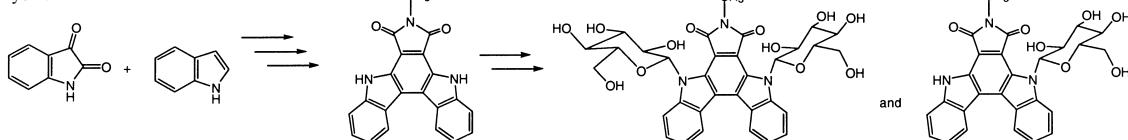
^aUniversité Blaise Pascal, Synthèse, Electrosynthèse et Etude de Systèmes à Intérêt Biologique, UMR 6504, 63177 Aubière, France

^bLaboratoire de Chimie Macromoléculaire et Chimie Physique, Université de Liège, Liège 4000, Belgium

^cCentre Oscar Lambret and INSERM U-524, IRCL, Place de Verdun, 59045 Lille, France

^dInstitut de Recherches SERVIER, 11 Rue des Moulinaux, 92150 Suresnes, France

The synthesis of rebeccamycin analogues containing an indolo[2,3-*c*]carbazole instead of indolo[2,3-*a*]carbazole is described. Their interaction with DNA with and without topoisomerase I, the antiproliferative activities against murine L1210 cells in vitro and the effects on the cell cycle are reported and compared with those of rebeccamycin.

**Synthesis of Sulfoquinovosylacylglycerols, Inhibitors of Eukaryotic DNA Polymerase α and β**

Bioorg. Med. Chem. 9 (2001) 367

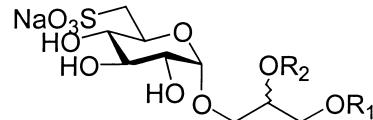
Shinya Hanashima,^a Yoshiyuki Mizushima,^a Takayuki Yamazaki,^a Keisuke Ohta,^a Syunya Takahashi,^b Hiroki Sahara,^c Kengo Sakaguchi^a and Fumio Sugawara^a

^aDepartment of Applied Biological Science, Science University of Tokyo, Noda, Chiba 278-8510, Japan

^bThe Institute of Physical and Chemical Research, Wako, Saitama 351-9800, Japan

^cMarine Biomedical Institute, Sapporo Medical University School of Medicine, Rishirifujii, Hokkaido 097-0101, Japan

Sulfoquinovosyldiacylglycerols (SQDGs) and sulfoquinovosylmonoacylglycerols (SQMGs), bearing diverse fatty acids, were synthesized from D-glucose, and were examined for enzymatic inhibitions of DNA polymerase α and β .

**Broad-Spectrum Antimicrobial Activity of Hemoglobin**

Bioorg. Med. Chem. 9 (2001) 377

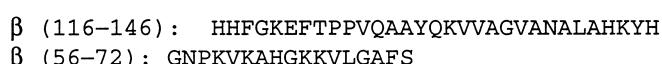
Craig A. Parish,^a Hong Jiang,^a Yoshi Tokiwa,^a Nina Berova,^a

Koji Nakanishi,^a Denise McCabe,^b Warren Zuckerman,^b Ming Ming Xia^b and Joëlle E. Gabay^b

^aDepartment of Chemistry, Columbia University, 3000 Broadway, New York, NY 10027, USA

^bDepartment of Microbiology, College of Physicians & Surgeons, 701 West 168th Street, New York, NY 10032, USA

Human hemoglobin, individual hemoglobin subunits, and synthetic peptides based on the sequence of the β subunit have novel antimicrobial activities against a wide range of microorganisms, including fungi, and gram-positive and gram-negative bacteria.

**N-Acy1-1,2,3,4a,5,10b-hexahydro-[1]benzopyrano[3,4-*b*][1,4]-oxazine-9-carbonitriles as Bladder-Selective Potassium Channel Openers**

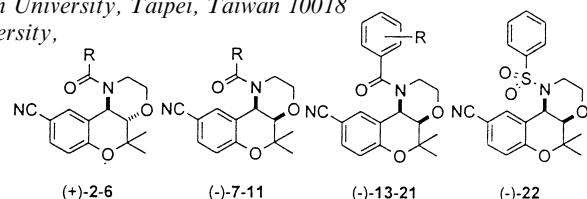
Bioorg. Med. Chem. 9 (2001) 383

Hsin-I. Chiu,^a Yen-Chung Lin,^a Chen-Yu Cheng,^a Ming-Cheng Tsai^b and Hon-Cheng Yu^c

^aInstitute of Pharmaceutical Sciences, College of Medicine, National Taiwan University, Taipei, Taiwan 10018

^bDepartment of Pharmacology, College of Medicine, National Taiwan University, Taipei, Taiwan 10018

^cDepartment of Urology, College of Medicine, National Taiwan University, Taipei, Taiwan 10018

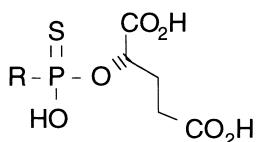


Stereoselective Inhibition of Glutamate Carboxypeptidase by Chiral Phosphonothioic Acids

Bioorg. Med. Chem. 9 (2001) 395

Haiyan Lu and Clifford E. Berkman

Department of Chemistry & Biochemistry, San Francisco State University, 1600 Holloway Avenue, San Francisco, CA 94132, USA



Synthesis and Evaluation of A-Ring Diastereomers of 1 α ,25-Dihydroxy-22-Oxavitamin D₃ (OCT)

Bioorg. Med. Chem. 9 (2001) 403

Susumi Hatakeyama,^a Toshio Okano,^b Junji Maeyama,^a Tomoyuki Esumi,^a Hiroko Hiyamizu,^a Yoshiharu Iwabuchi,^a Kimie Nakagawa,^b Keiichi Ozono,^c Akira Kawased^d and Noboru Kubodera^d

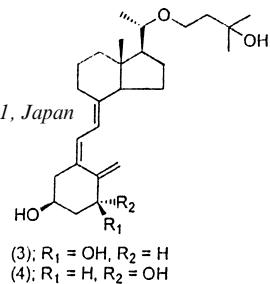
^a*Faculty of Pharmaceutical Sciences, Nagasaki University, Nagasaki 852-8521, Japan*

^b*Department of Hygienic Sciences, Kobe Pharmaceutical University, Kobe 658-8558, Japan*

^c*Department of Environmental Medicine, Osaka Medical Center for Material and Children Health, Osaka 594-1101, Japan*

^d*Chugai Pharmaceutical Co., Ltd., Tokyo 104-8301, Japan*

A-ring diastereomers of 1 α ,25-dihydroxy-22-oxavitamin D₃ (OCT) (**2**), 3-epi-1 α ,25-dihydroxy-22-oxavitamin D₃ (3-epiOCT) (**3**) and 1,3-diepi-1 α ,25-dihydroxy-22-oxavitamin D₃ (1,3-diepiOCT) (**4**) were synthesized by the convergent method. In vitro binding affinity for rat vitamin D binding protein and calf-thymus vitamin D receptor, differentiation-inducing activity on HL-60 cells, and transcriptional activity of 3-epiOCT (**3**) and 1,3-diepiOCT (**4**) were evaluated in comparison with OCT (**2**), 1-epi-1 α ,25-dihydroxy-22-oxavitamin D₃ (1-epiOCT) (**5**) and 1 α ,25-dihydroxyvitamin D₃ (**1**).



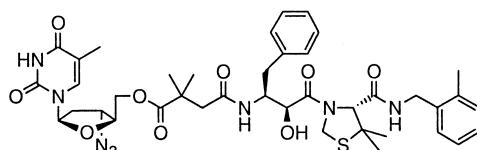
Synthesis and Biological Evaluation of Prodrug-Type Anti-HIV Agents: Ester Conjugates of Carboxylic Acid-Containing Dipeptide HIV Protease Inhibitors and a Reverse Transcriptase Inhibitor

Bioorg. Med. Chem. 9 (2001) 417

Hikaru Matsumoto, Takashi Matsuda, Shingo Nakata, Takatoshi Mitoguchi, Tooru Kimura, Yoshio Hayashi and Yoshiaki Kiso

Department of Medicinal Chemistry, Center for Frontier Research in Medicinal Science, Kyoto Pharmaceutical University, Yamashina-ku, Kyoto 607-8412, Japan

Prodrug-type conjugates of HIV protease inhibitors with a reverse transcriptase inhibitor were synthesized, which expressed excellent antiviral activity.



High Affinity Central Benzodiazepine Receptor Ligands. Part 2: Quantitative Structure-Activity Relationships and Comparative Molecular Field Analysis of Pyrazolo[4,3-*c*]quinolin-3-ones

Bioorg. Med. Chem. 9 (2001) 431

L. Savini,^b L. Chiasserini,^b C. Pellerano,^b G. Biggio,^c E. Maciocco,^c M. Serra,^c N. Cinone,^{a,d} A. Carrieri,^a C. Altomare^a and A. Carotti^a

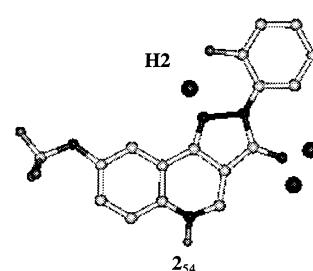
^a*Dipartimento Farmaco Chimico, Università degli Studi, via E. Orabona 4, I-70125 Bari, Italy*

^b*Dipartimento Farmaco Chimico Tecnologico, Università degli Studi, A. Moro, I-53100 Siena, Italy*

^c*Dipartimento di Biologia Sperimentale, via Palabanda 12, Università degli Studi, I-09123 Cagliari, Italy*

^d*Dipartimento di Scienze del Farmaco, Università degli Studi "G. D'Annunzio", via dei Vestini 31, I-66013 Chieti Scalo (CH), Italy*

Hansch and CoMFA analyses of a large series of pyrazolo-quinolines **2** allowed the identification of the key molecular determinants of high receptor binding affinity. The formation of a three-centred hydrogen bond (HB) at the HB donor site H₂ was studied by MEP calculation and comparison.



**Positioning of the Carboxamide Side Chain in
11-Oxo-11*H*-indeno[1,2-*b*]quinolinecarboxamide
Anticancer Agents: Effects on Cytotoxicity**

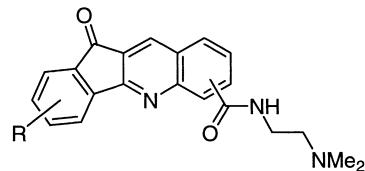
Bioorg. Med. Chem. 9 (2001) 445

Leslie W. Deady,^a José Desneves,^a Anthony J. Kaye,^a Graeme J. Finlay,^b Bruce C. Baguley^b and William A. Denny^b

^aDepartment of Chemistry, La Trobe University, Bundoora, Victoria, Australia 3083

^bAuckland Cancer Society Research Centre, Faculty of Medical and Health Science, The University of Auckland, Private Bag 92019, Auckland 1000, New Zealand

The cytotoxicity of 11-oxo-11*H*-indeno[1,2-*b*]quinolines bearing carboxamide-linked cationic side chains is heavily dependent on the position of the side chain on the chromophore.



**New Antimetastatic Hypoxic Cell Radiosensitizers:
Design, Synthesis, and Biological Activities of
2-Nitroimidazole-acetamide, TX-1877, and its Analogues**

Bioorg. Med. Chem. 9 (2001) 453

Soko Kasai,^a Hideko Nagasawa,^a Mao Yamashita,^a Mie Masui,^a Hideki Kuwasaka,^a Tomoko Oshodani,^a Yoshihiro Uto,^a Taisuke Inomata,^b Shigenori Oka,^c Seiichi Inayama^{d,e} and Hitoshi Hori^a

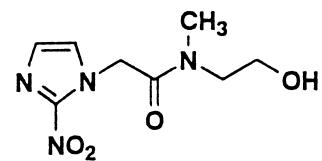
^aDepartment of Biological Science and Technology, Faculty of Engineering, The University of Tokushima, Minamijosanjimacho-2, Tokushima 770-8506, Japan

^bDepartment of Radiology, Kochi Medical School, Kochi 783-0043, Japan

^cResearch & Development Center, Nagase & Co., Ltd., Hyogo 651-2241, Japan

^dInstitute of Oriental Medical Science, Tokyo 155-0032, Japan

^eKeio University, School of Medicine, Tokyo 160-8582, Japan



TX-1877

Orally Active Cephalosporins. Part 3: Synthesis, Structure–Activity Relationships and Oral Absorption of Novel C-3 Heteroarylmethylthio Cephalosporins

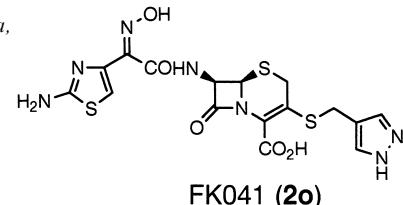
Bioorg. Med. Chem. 9 (2001) 465

Hirofumi Yamamoto,^a Takeshi Terasawa,^a Ayako Nakamura,^a Kohji Kawabata,^a Hisashi Takasugi,^a Hirokazu Tanaka,^a Satoru Matsumoto,^b Yoshimi Matsumoto^b and Shuichi Tawara^b

^aMedicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., 2-1-6, Kashima, Yodogawa-ku, Osaka 532-8514, Japan

^bMedicinal Biology Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., 2-1-6, Kashima, Yodogawa-ku, Osaka 532-8514, Japan

A series of cephalosporins having a C-3 heteroarylmethylthio side chain was synthesized and evaluated for antibacterial activity and oral absorption. Among them, FK041 (**2o**) exhibited potent activity against both Gram-positive and Gram-negative bacteria including *Haemophilus influenzae* and high oral absorption in rats.



Synthesis and Anti-HIV Activity of Nonatyrosine N- and O¹⁻⁹-Decasulfate

Bioorg. Med. Chem. 9 (2001) 477

Masaaki Ueki,^a Shigeru Watanabe,^a Yusuke Ishii,^a Osamu Okunaka,^a

Keiji Uchino,^b Takeshi Saitoh,^c Kyoichiro Higashi,^d Hideki Nakashima,^e Naoki Yamamoto^f and Hiroshi Ogawara^d

^aDepartment of Applied Chemistry, Science University of Tokyo, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan

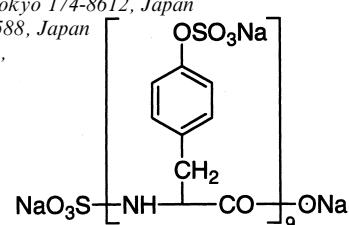
^bCentral Laboratory, Nippon Flour Mills Co. Ltd., 5-1-3 Midorigaoka, Atsugi-Shi, Kanagawa 243-0041, Japan

^cInstitute for Consumer Healthcare, Yamanouchi Pharmaceutical Co., Ltd., 3-17-1 Hasune, Itabashi-ku, Tokyo 174-8612, Japan

^dDepartment of Biochemistry, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose-Shi, Tokyo 204-8588, Japan

^eDepartment of Microbiology and Immunology, Kagoshima University Dental School, 8-35-1 Sakuragaoka, Kagoshima-Shi, Kagoshima 890-8544, Japan

^fDepartment of Microbiology, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan



Synthesis and Chain Length–Anti-HIV Activity Relationship of Fully *N*- and *O*-Sulfated Homooligomers of Tyrosine

Bioorg. Med. Chem. 9 (2001) 487

Masaaki Ueki,^a Shigeru Watanabe,^a Takeshi Saitoh,^b Hideki Nakashima,^c Naoki Yamamoto^d and Hiroshi Ogawara^e

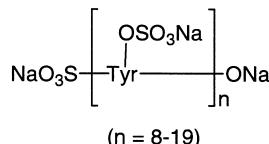
^aDepartment of Applied Chemistry, Science University of Tokyo, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan

^bInstitute for Consumer Healthcare, Yamanouchi Pharmaceutical Co., Ltd., 3-17-1 Hasune, Itabashi-ku, Tokyo 174-8612, Japan

^cDepartment of Microbiology and Immunology, Kagoshima University Dental School, 8-35-1 Sakuragaoka, Kagoshima-Shi, Kagoshima 890-8544, Japan

^dDepartment of Microbiology, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan

^eDepartment of Biochemistry, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose-Shi, Tokyo 204-8588, Japan



Syntheses and Hydrolysis of Basic and Dibasic Ampicillin Esters Tailored for Intracellular Accumulation

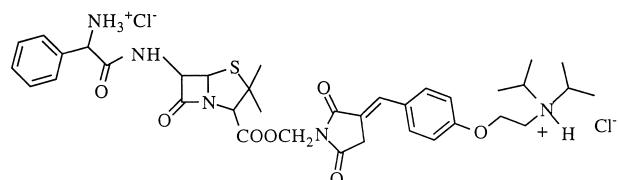
Bioorg. Med. Chem. 9 (2001) 493

Isabelle Paternotte,^{a,b} Hua Juan Fan,^a Pascal Scrève,^a Michel Claesen,^a Paul M. Tulkens^b and Etienne Sonveaux^a

^aUnité de Chimie Pharmaceutique et de Radiopharmacie, Université Catholique de Louvain, Avenue E. Mounier 73 p.b. 7340, B-1200 Bruxelles, Belgium

^bUnité de Pharmacologie Cellulaire et Moléculaire, Université Catholique de Louvain, Avenue E. Mounier 73 p.b. 7340, B-1200 Bruxelles, Belgium

Synthesis and hydrolysis of basic and dibasic ampicillin esters tailored for intracellular accumulation



Cysteinyl Peptide Inhibitors of *Bacillus cereus* Zinc β -Lactamase

Bioorg. Med. Chem. 9 (2001) 503

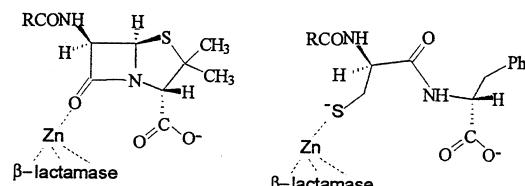
Sakina Bounaga,^a Moreno Galleni,^b Andrew P. Laws^a and Michael I. Page^a

^aDepartment of Chemical and Biological Sciences, University of Huddersfield, Queensgate, Huddersfield, HD1 3DH, UK

^bUniversité de Liège, Centre d'Ingenierie des Protéines, Institut de Chimie B6, Sart Tilman B4000, Liège 1, Belgique

Several cysteinyl peptides have been synthesised and shown to be reversible competitive inhibitors of the *Bacillus cereus* metallo- β -lactamase. The pH dependence of pK_i indicates that the thiol anion displaces hydroxide ion from the active site zinc(II).

D,D-peptides bind to the enzyme better than other diastereoisomers which is compatible with the predicted stereochemistry of the active site.



Design, Synthesis and Preliminary Biological Evaluation of a Focused Combinatorial Library of Stereodiverse Carbohydrate-Scaffold-Based Peptidomimetics

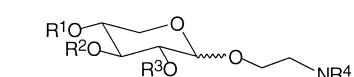
Bioorg. Med. Chem. 9 (2001) 511

Nicolas Moitessier,^a Sylvie Dufour,^c Françoise Chrétien,^a Jean Paul Thiery,^c Bernard Maigret^b and Yves Chapleur^a

^aGroupe SUCRES, Groupe de Biochimie Théorique, Unité Mixte 7565 CNRS-Université Henri Poincaré-Nancy 1, BP 239, F-54506 Nancy-Vandoeuvre, France

^bGroupe de Biochimie Théorique, Unité Mixte 7565 CNRS-Université Henri Poincaré-Nancy 1, BP 239, F-54506 Nancy-Vandoeuvre, France

^cUnité Mixte 144, CNRS-Institut Curie, 24 Rue d'Ulm, F-75000 Paris, France



R₁, R₂, R₃ = Bn, CH₂COOH; R₄ various groups

**Highly Potent Cell Differentiation-Inducing Analogues of
1 α ,25-Dihydroxyvitamin D₃: Synthesis and Biological
Activity of 2-Methyl-1,25-dihydroxyvitamin D₃ with Side-Chain Modifications**

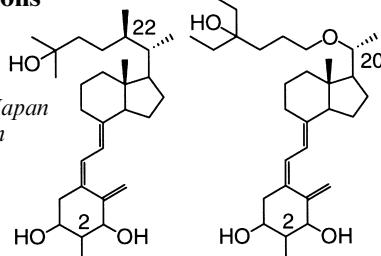
Bioorg. Med. Chem. 9 (2001) 525

Toshie Fujishima,^a Liu Zhaopeng,^a Katsuhiro Konno,^a Kimie Nakagawa,^b
Toshio Okano,^b Kentaro Yamaguchi^c and Hiroaki Takayama^a

^aFaculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-0195, Japan

^bDepartment of Hygienic Sciences, Kobe Pharmaceutical University, Kobe 658-8558, Japan

^cChemical Analytical Center, Chiba University, Inage-ku, Chiba 263-8522, Japan



**The Discovery of RPR 200765A, a p38 MAP Kinase Inhibitor
Displaying a Good Oral Anti-Arthritic Efficacy**

Bioorg. Med. Chem. 9 (2001) 537

Iain M. McLean, Frank Halley,* John E. Souness, Jeffrey McKenna, Veronique Benning, Mark Birrell,
Brenda Burton, Maria Belvisi, Alan Collis, Alex Constan, Martyn Foster, David Hele, Zaid Jayyosi, Mike Kelley,
Chris Maslen, Glen Miller, Marie-Claude Ouldelhkim, Kenneth Page, Simon Phipps, Kenneth Pollock,
Barry Porter, Andrew J. Ratcliffe, Elisabeth J. Redford, Stephen Webber,
Bryan Slater, Veronique Thybaud and Nicola Wilsher

Aventis, Dagenham Research Centre, Rainham Road South, Dagenham,
Essex, RM10 7XS, UK

