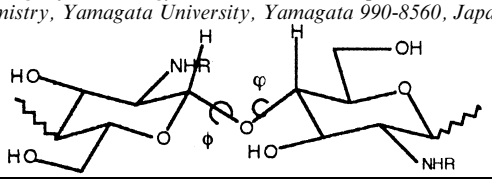
Graphical Abstracts

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]

[a]*Institute for Chemical Reaction Science, Tohoku University, Sendai 980-8577, Japan*
[b]*Institute of Development, Aging and Cancer, Tohoku Univeristy, Sendai 980-8575, Japan*
[c]*Yaizu Suisankagaku Industry Co., Ltd., Yaizu 425-8570, Japan*
[d]*Department of Applied Biochemistry, Shizuoka University, Shizuoka 422-8529, Japan*
[e]*Miyagi National College of Technology, Natori 981-1239, Japan*
[f]*Department 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]

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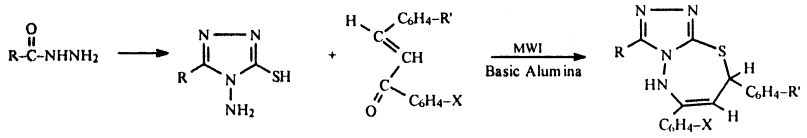
A novel synthesis and antimicrobial activity of 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazepines are described.



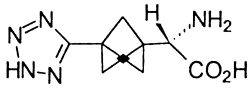
Synthesis and Biological Evaluation of 2-(3′-(1*H*-Tetrazol-5-yl) bicyclo[1.1.1]pent-1-yl)glycine (*S*-TBPG), a Novel mGlu1 Receptor Antagonist

Bioorg. Med. Chem. 9 (2001) 221

Gabriele Costantino,[a] Katiuscia Maltoni,[a] Maura Marinozzi,[a] Emidio Camaioni,[a]
Laurent Prezeau,[b] Jean-Philippe Pin[b] and Roberto Pellicciari[a]

[a]*Dipartimento di Chimica e Tecnologia del Farmaco. Università di Perugia, Via del Liceo 1, 06123 Perugia, Italy*
[b]*Centre 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.



S-TBPG
9

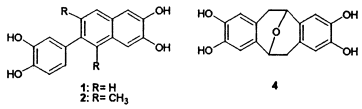
New Bis-Catechols 5-Lipoxygenase Inhibitors

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]

[a]*Laboratoire de Chimie Organique et Macromoléculaire, UPRESA CNRS 8009, USTL, 59655 Villeneuve d'Ascq, France*
[b]*Institut de Chimie Pharmaceutique Albert Lespagnol, Université de Lille 2, EA 2692, 3 rue J. Laguesse, 59006 Lille, France*
[c]*Laboratoire 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.



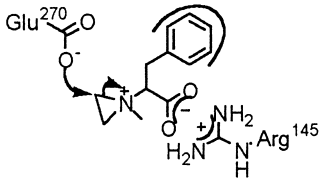
A New Inhibitor Design Strategy for Carboxypeptidase A as Exemplified by *N*-(2-Chloroethyl)-*N*-methylphenylalanine

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.

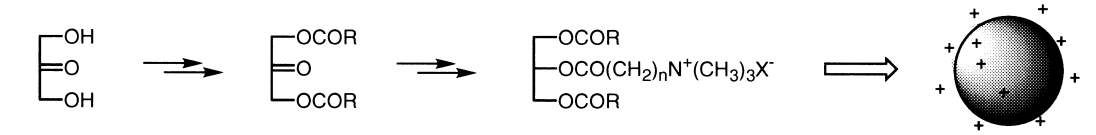


Symmetrical Cationic Triglycerides: An Efficient Synthesis and Application to Gene Transfer

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



1,3-dihydroxyacetone — symmetrical cationic triglycerides — cationic liposomes

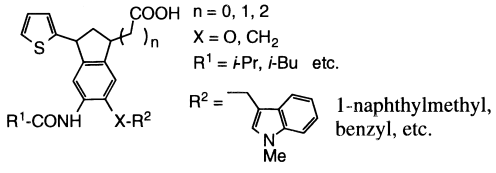
Design, Syntheses, and Structure–Activity Relationships of Indan Derivatives as Endothelin Antagonists; New Lead Generation of Non-peptidic Antagonist from Peptidic Leads

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 comformation of the linear peptide FR139317 by possible intramolecular hydrogen bonding.

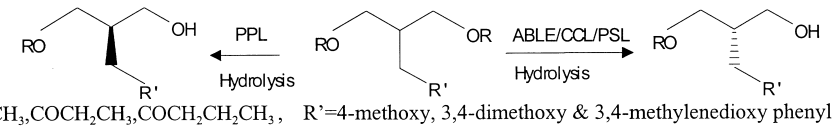


Purification and Characterisation of an Ester Hydrolase from a Strain of *Arthrobacter* Species: Its Application in Asymmetrisation of 2-Benzyl-1,3-propanediol Acylates

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



R=$COCH_3$,$COCH_2CH_3$,$COCH_2CH_2CH_3$, R'=4-methoxy, 3,4-dimethoxy & 3,4-methylenedioxy phenyl

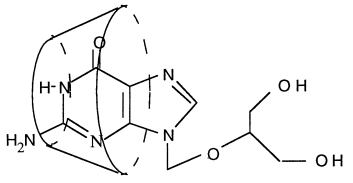
Effect of the Complexation with Cyclodextrins on the In Vitro Antiviral Activity of Ganciclovir Against Human Cytomegalovirus

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.

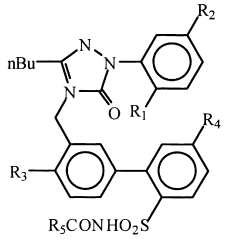
3-D QSAR Studies of Triazolinone Based Balanced AT_1/AT_2 Receptor Antagonists

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 AT_1 and AT_2 receptors have been identified using APEX-3-D expert system on 16 N^2-aryltriazolinone biphenyl sulphonamides.



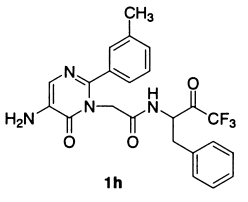
Non-Peptidic Inhibitors of Human Chymase. Synthesis, Structure–Activity Relationships, and Pharmacokinetic Profiles of a Series of 5-Amino-6-oxo-1,6-dihydropyrimidine-Containing Trifluoromethyl Ketones

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-CF_3 and found that compound **1h** has an inhibitory constant of 0.05063 μM toward human chymase—an activity superior in potency to that of the parent peptidic inhibitor—and good selectivity for chymase over other proteases.



1h

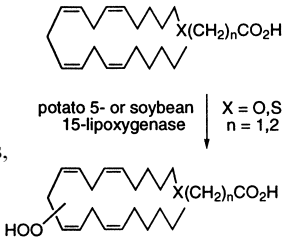
Oxidation of Oxa and Thia Fatty Acids and Related Compounds Catalysed by 5- and 15-Lipoxygenase

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]

[a]*Research School of Chemistry, Australian National University, Canberra, ACT 0200, Australia*
[b]*Peptech Ltd., Locked Bag 2053, North Ryde, NSW 2113, Australia*
[c]*Department 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.



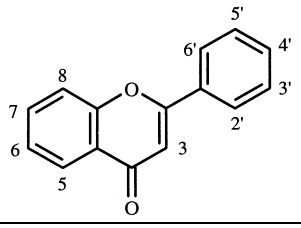
Molecular Modeling and QSAR Analysis of the Interaction of Flavone Derivatives with the Benzodiazepine Binding Site of the $GABA_A$ Receptor Complex

Bioorg. Med. Chem. 9 (2001) 323

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

[a]*Instituto de Química y Fisicoquímica Biológicas, Facultad de Farmacia y Bioquímica, Junín 956, (1113) Buenos Aires, Argentina*
[b]*CEQUINOR, Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, CC. 962, (1900) La Plata, Argentina*
[c]*Farmacoquímica, División Farmacia, Departamento de Ciencias Biológicas, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, CC. 243, (1900) La Plata, Argentina*
[d]*Instituto 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.



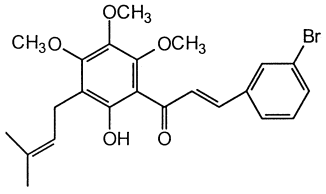
Synthetic and Biological Activity Evaluation Studies on Novel 1,3-Diarylpropenones

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]

[a]*Department of Chemistry, University of Delhi, Delhi-110 007, India*
[b]*Department of Biochemistry, VP Chest Institute, University of Delhi, Delhi-110 007, India*
[c]*Laboratory of Experimental Cancerology, Department of Radiotherapy, University Hospital, De Pintelaan 185, B-9000 Gent, Belgium*
[d]*Chemistry 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.



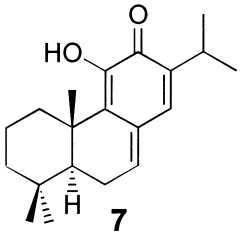
Synthesis of Variously Oxidized Abietane Diterpenes and Their Antibacterial Activities Against MRSA and VRE

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,*]

[a]*Laboratory of Bioorganic Chemistry, Tokyo University of Agriculture and Technology, Fuchu, Tokyo 183–8509, Japan*
[b]*Department 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 agianst 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.



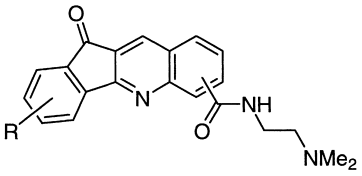
Bioorg. Med. Chem. 9 (2001) 445

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

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

[a]*Department of Chemistry, La Trobe University, Bundoora, Victoria, Australia 3083*
[b]*Auckland 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.

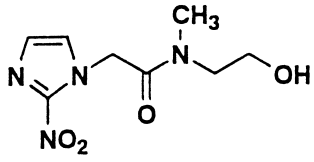


Bioorg. Med. Chem. 9 (2001) 453

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

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]

[a]*Department of Biological Science and Technology, Faculty of Engineering, The University of Tokushima, Minamijosanjimacho-2, Tokushima 770–8506, Japan*
[b]*Department of Radiology, Kochi Medical School, Kochi 783–0043, Japan*
[c]*Research & Development Center, Nagase & Co., Ltd., Hyogo 651–2241, Japan*
[d]*Institute of Oriental Medical Science, Tokyo 155–0032, Japan*
[e]*Keio University, School of Medicine, Tokyo 160–8582, Japan*



TX-1877

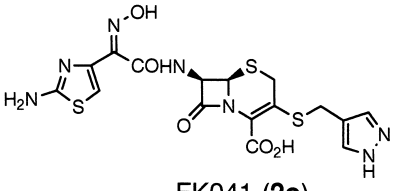
Bioorg. Med. Chem. 9 (2001) 465

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

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]

[a]*Medicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., 2-1-6, Kashima, Yodogawa-ku, Osaka 532–8514, Japan*
[b]*Medicinal 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.



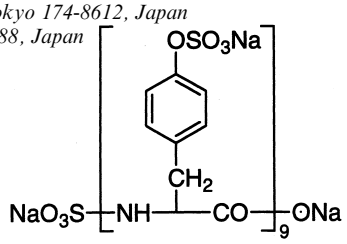
FK041 (**2o**)

Bioorg. Med. Chem. 9 (2001) 477

Synthesis and Anti-HIV Activity of Nonatyrosine *N*- and O^{1-9}-Decasulfate

Masaaki Ueki,[a] Shigeru Watanabe,[a] Yusuke Ishii,[a] Osamu Okunaka,[a] Keijiro Uchino,[b] Takeshi Saitoh,[c] Kyoichiro Higashi,[d] Hideki Nakashima,[e] Naoki Yamamoto[f] and Hiroshi Ogawara[d]

[a]*Department of Applied Chemistry, Science University of Tokyo, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan*
[b]*Central Laboratory, Nippon Flour Mills Co. Ltd., 5-1-3 Midorigaoka, Atsugi-Shi, Kanagawa 243-0041, Japan*
[c]*Institute for Consumer Healthcare, Yamanouchi Pharmaceutical Co., Ltd., 3-17-1 Hasune, Itabashi-ku, Tokyo 174-8612, Japan*
[d]*Department of Biochemistry, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose-Shi, Tokyo 204-8588, Japan*
[e]*Department of Microbiology and Immunology, Kagoshima University Dental School, 8-35-1 Sakuragaoka, Kagoshima-Shi, Kagoshima 890-8544, Japan*
[f]*Department of Microbiology, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan*

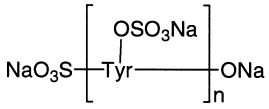


Synthesis and Chain Length–Anti-HIV Activity Relationship of Fully *N*- and *O*-Sulfated Homooligomers of Tyrosine

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]

[a]*Department of Applied Chemistry, Science University of Tokyo, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan*
[b]*Institute for Consumer Healthcare, Yamanouchi Pharmaceutical Co., Ltd., 3-17-1 Hasune, Itabashi-ku, Tokyo 174-8612, Japan*
[c]*Department of Microbiology and Immunology, Kagoshima University Dental School, 8-35-1 Sakuragaoka, Kagoshima-Shi, Kagoshima 890-8544, Japan*
[d]*Department of Microbiology, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan*
[e]*Department of Biochemistry, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose-Shi, Tokyo 204-8588, Japan*



(n = 8-19)

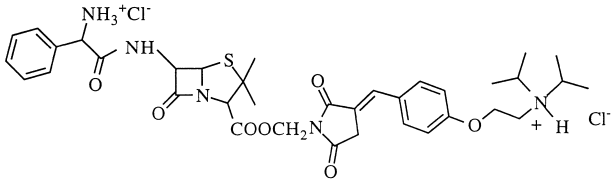
Syntheses and Hydrolysis of Basic and Dibasic Ampicillin Esters Tailored for Intracellular Accumulation

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]

[a]*Unité de Chimie Pharmaceutique et de Radiopharmacie, Université Catholique de Louvain, Avenue E. Mounier 73 p.b. 7340, B-1200 Bruxelles, Belgium*
[b]*Unité 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]

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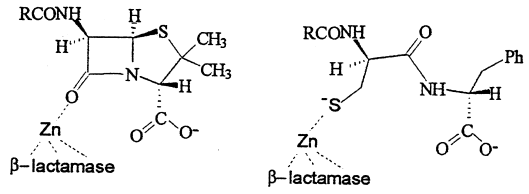
Several cysteinyl peptides have been synthesised and shown to be reversible competitive inhibitors of the *Bacillus cereus* metallo-β-lactamase. The pH dependence of pK_i indicates that the thiol anion displaces hydroxideion from the active site zinc(II). D,D-peptides bind to the enzyme better than other 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]

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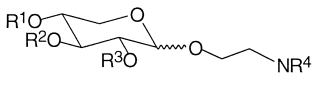

R^1, R^2, R^3 = Bn, CH_2COOH; R^4 various groups

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Highly Potent Cell Differentiation-Inducing Analogues of 1α,25-Dihydroxyvitamin D_3: Synthesis and Biological Activity of 2-Methyl-1,25-dihydroxyvitamin D_3 with Side-Chain Modifications

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

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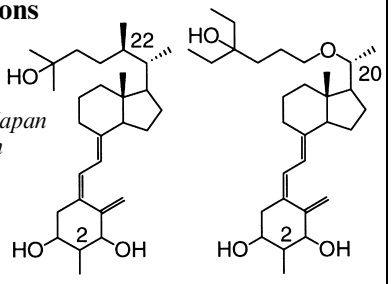

Bioorg. Med. Chem. 9 (2001) 537

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

Iain M. McLay, 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

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