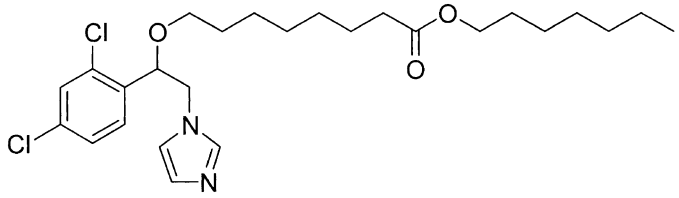
Design and Synthesis of Novel Imidazole Derivatives as Potent Inhibitors of Allene Oxide Synthase(CYP74)

Bioorg. Med. Chem. 10 (2002) 3707

Keimei Oh* and Noboru Murofushi

Department of Biotechnology, Akita Prefectural University, Shimoshinjo-Nakano, Akita-shi, Akita 010-0195, Japan

The first synthetic inhibitor of allene oxide synthase was reported.



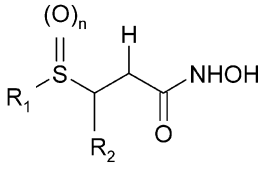
2D-QSAR in Hydroxamic Acid Derivatives as Peptide Deformylase Inhibitors and Antibacterial Agents

Bioorg. Med. Chem. 10 (2002) 3713

Manish K. Gupta, Pradeep Mishra, Philip Prathipati and Anil K. Saxena*

Medicinal Chemistry Division, Central Drug Research Institute, Lucknow 226001, India

Quantitative structure–activity relationship (QSAR) studies in a series of β-sulfonyl and β-sulfinyl hydroxamic acid derivatives against *Escherichia coli* DC2 and *Moraxella catarrhalis* RA21 are reported.



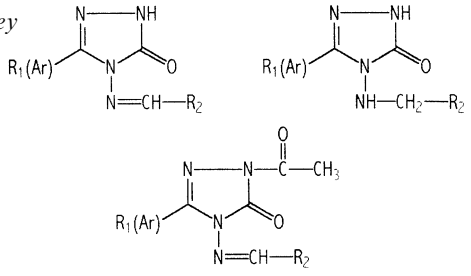
Synthesis of 3-Alkyl(aryl)-4-alkylidenamino-4,5-dihydro-1H-1,2,4-triazol-5-ones and 3-Alkyl-4-alkylamino-4,5-dihydro-1H-1,2,4-triazol-5-ones as Antitumor Agents

Bioorg. Med. Chem. 10 (2002) 3717

Neslihan Demirbaş,* Reyhan Ugurluoglu and Ahmet Demirbaş

Karadeniz Technical University, Department of Chemistry, 61080 Trabzon, Turkey

Synthesis, characterization and antitumor activities of some 1,2,4-triazole-5-ones derivatives have been described.



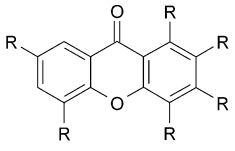
Xanthones as Inhibitors of Growth of Human Cancer Cell Lines and Their Effects on the Proliferation of Human Lymphocytes In Vitro

Bioorg. Med. Chem. 10 (2002) 3725

Madalena Pedro,[a] Fátima Cerqueira,[a] Maria Emília Sousa,[a,b] Maria São José Nascimento[a] and Madalena Pinto[a,*]

[a]*Centro de Estudos de Química Orgânica, Fitoquímica e Farmacologia da Universidade do Porto, Faculdade de Farmácia, Rua Aníbal Cunha, 164, 4050-047 Porto, Portugal*
[b]*Instituto Superior das Ciências da Saúde-Norte, Rua Central da Gandra, 1317, 4580 Gandra, Portugal*

The synthesis of 27 xanthones and their capacity to inhibit in vitro the growth of three human cancer cell lines, MCF-7 (breast cancer), TK-10 (renal cancer) and UACC-62 (melanoma) is described. The effect of these xanthones on the proliferation of human T-lymphocytes is also reported.



Bioorg. Med. Chem. 10 (2002) 3731

Design, Synthesis, Conformational Analysis, and Biological Studies of Urotensin-II Lactam Analogues

Paolo Grieco,[a] Alfonso Carotenuto,[b] Riccardo Patacchini,[c] Carlo A. Maggi,[c] Ettore Novellino[a] and Paolo Rovero[b,*]

[a]*Department of Pharmaceutical and Toxicological Chemistry, University of Naples 'Federico II', I-80131 Naples, Italy*
[b]*Department of Pharmaceutical Sciences, University of Salerno, I-84084 Fisciano, Italy*
[c]*Department of Pharmacology, Menarini Ricerche SpA, I-50131 Florence, Italy*

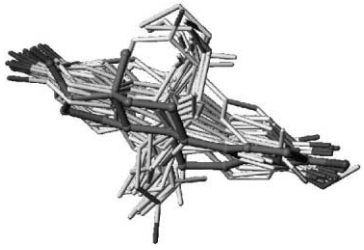
Bioorg. Med. Chem. 10 (2002) 3741

Binding Affinity Prediction of Novel Estrogen Receptor Ligands Using Receptor-Based 3-D QSAR Methods

Wolfgang Sippl*

Institute for Pharmaceutical Chemistry, Heinrich-Heine-Universität Düsseldorf, Universitätsstr. 1, D-40225 Düsseldorf, Germany

A combination of structure-based and 3-D QSAR methods was developed and applied for the binding affinity prediction of novel estrogen receptor ligands. The study shows that the receptor-based 3-D QSAR strategy is able to yield highly robust and predictive models ($q^2_{LOO} = 0.921$, SDEP = 0.345) which can be used for the development of novel bioactive ligands.



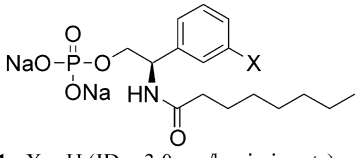
Bioorg. Med. Chem. 10 (2002) 3757

Highly Potent Inhibitors of TNF-α Production. Part I: Discovery of New Chemical Leads and Their Structure–Activity Relationships

Toshiaki Matsui,[a,*] Takashi Kondo,[b] Yoshitaka Nishita,[a] Satoshi Itadani,[b] Shingo Nakatani,[b] Nagashige Omawari,[c] Masaru Sakai,[b] Shuichi Nakazawa,[c] Akihito Ogata,[b] Hideaki Mori,[a] Kouichiro Terai,[b] Wataru Kamoshima,[b] Hiroyuki Ohno,[b] Takaaki Obata,[b] Hisao Nakai[b] and Masaaki Toda[b]

[a]*Fukui Research Institute, Ono Pharmaceutical Co., Ltd., Technoport, Yamagishi, Mikuni, Sakai, Fukui 913-8638, Japan*
[b]*Minase Research Institute, Ono Pharmaceutical Co., Ltd., Shimamoto, Mishima, Osaka 618-8585, Japan*
[c]*Headquarters, Ono Pharmaceutical Co., Ltd., Doshoumachi, Chuou, Osaka 541-8526, Japan*

Discovery of 2-(acylamino)-2-phenylethyl disodium phosphates **1** and **2** as structurally novel inhibitors for TNF-α production is reported. Structure–activity relationships (SARs) are also discussed and full details including the chemistry are reported.



1 : X = H (ID_{50} 3.0 mg/kg, iv in rats)

2: X = OMe (ID_{50} 0.26 mg/kg, iv in rats)

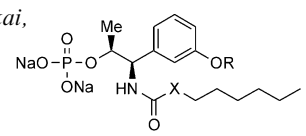
Bioorg. Med. Chem. 10 (2002) 3787

Highly Potent Inhibitors of TNF-α Production. Part II: Metabolic Stabilization of a Newly Found Chemical Lead and Conformational Analysis of an Active Diastereoisomer

Toshiaki Matsui,[a,*] Takashi Kondo,[b] Yoshitaka Nishita,[a] Satoshi Itadani,[b] Hiroshi Tsuruta,[b] Setsuko Fujita,[b] Nagashige Omawari,[c] Masaru Sakai,[b] Shuichi Nakazawa,[c] Akihito Ogata,[b] Hideaki Mori,[a] Wataru Kamoshima,[b] Kouichiro Terai,[b] Hiroyuki Ohno,[b] Takaaki Obata,[b] Hisao Nakai[b] and Masaaki Toda[b]

[a]*Fukui Research Institute, Ono Pharmaceutical Co., Ltd., Technoport, Yamagishi, Mikuni, Sakai, Fukui 913-8638, Japan*
[b]*Minase Research Institute, Ono Pharmaceutical Co., Ltd., Shimamoto, Mishima, Osaka 618-8585, Japan*
[c]*Headquarter, Ono Pharmaceutical Co., Ltd., Doshoumachi, Chuou, Osaka 541-8526, Japan*

Design and synthesis of metabolically stabilized inhibitors of TNF-α production, which could be new drug candidates, are reported.



2 : R = Me, X = CH_2, (ID_{50} 0.03 mg/kg, iv in rats)

3 : R = ^{i}Pr, X = CH_2, (ID_{50} 0.05 mg/kg, iv in rats)

4: R = Me, X = O, (ID_{50} 0.02 mg/kg, iv in rats)

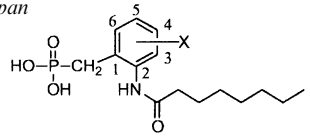
Bioorg. Med. Chem. 10 (2002) 3807

Discovery of Novel Phosphonic Acid Derivatives as New Chemical Leads for Inhibitors of TNF-α Production

Toshiaki Matsui,[a,*] Shinya Takahashi,[b] Naoki Matsunaga,[b] Kazunori Nakamura,[a] Nagashige Omawari,[c] Masaru Sakai,[b] Wataru Kamoshimo,[b] Kouichiro Terai,[c] Hiroyuki Ohno,[b] Takaaki Obata,[b] Hisao Nakai[b] and Masaaki Toda[b]

[a]*Fukui Research Institute, Ono Pharmaceutical Co., Ltd., Yamagishi, Mikuni, Sakai, Fukui 913-8638, Japan*
[b]*Minase Research Institute, Ono Pharmaceutical Co., Ltd., Shimamoto, Mishima, Osaka 618-8585, Japan*
[c]*Headquarters, Ono Pharmaceutical Co., Ltd., Doshoumachi, Chuou, Osaka 541-8526, Japan*

Discovery process of 2-(acylamino)benzylphosphonic acids **7**, **8**, **10** and **16** as another chemical leads of the inhibitors of TNF-α production is reported.



7: X = H; **8**: X = 3-Me; **10**: X = 5-Me; **16**: X = 4,5-OCH_2O-

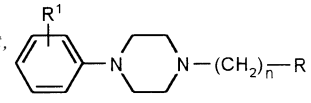
Bioorg. Med. Chem. 10 (2002) 3817

Synthesis and Pharmacological Evaluation of New Arylpiperazines. 3-{4-[4-(3-chlorophenyl)-1-piperazinyl]butyl}-quinazolidin-4-one — A Dual Serotonin $5\text{-}HT_{1A}/5\text{-}HT_{2A}$ Receptor Ligand with an Anxiolytic-Like Activity

Andrzej J. Bojarski,[a,*] Piotr Kowalski,[b] Teresa Kowalska,[b] Beata Duszyńska,[a] Sijka Charakchieva-Minol,[a] Ewa Tatarczyńska,[c] Aleksandra Kłodzińska[c] and Ewa Chojnacka-Wójcik[c]

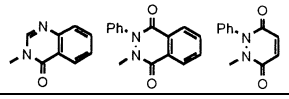
[a]*Department of Medicinal Chemistry Institute of Pharmacology, Polish Academy of Sciences, 12 Smętna Street, 31-343 Kraków, Poland*
[b]*Institute of Organic Chemistry and Technology, Cracow University of Technology, 24 Warszawska Street, 31-155 Kraków, Poland*
[c]*Department of New Drug Research, Institute of Pharmacology, Polish Academy of Sciences, 12 Smętna Street, 31-343 Kraków, Poland*

From among 12 new arylpiperazine derivatives studied as $5\text{-}HT_{1A}/5\text{-}HT_{2A}$ receptor ligands, 3-{4-[4-(3-chlorophenyl)-1-piperazinyl]butyl}-quinazolidin-4-one was preclinically tested as a potential anxiolytic agent.



R^1 = *m*-Cl or *o*-OCH_3; n = 3, 4

R =

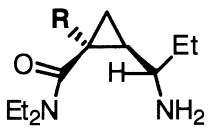


Bioorg. Med. Chem. 10 (2002) 3829

Synthesis of Derivatives of (1*S*,2*R*)-1-Phenyl-2-[(*S*)-1-aminopropyl]-*N*,*N*-diethylcyclopropanecarboxamide (PPDC) Modified at the 1-Aromatic Moiety as Novel NMDA Receptor Antagonists: the Aromatic Group is Essential for the Activity

Yuji Kazuta,[a] Ryuichi Tsujita,[b] Kanako Yamashita,[b] Shigeo Uchino,[c] Shinichi Kohsaka,[c] Akira Matsuda[a] and Satoshi Shuto[a,*]

[a]*Graduate School of Pharmaceutical Sciences, Hokkaido University, Kita-12, Nishi-6, Kita-ku, Sapporo 060-0812, Japan*
[b]*Institute for Life Science Research, Asahi Chemical Co., Ltd., Ohito-cho, Shizuoka 410-2321, Japan*
[c]*Department of Neurochemistry, National Institute of Neuroscience, 4-1-1 Ogawahigashi, Kodaira, Tokyo 187-8502, Japan*



R: Ph (PPDC)
H
o-, *m*-, *p*-F-Ph
o-, *m*-, *p*-F-Ph
1-, 2-naphthyl

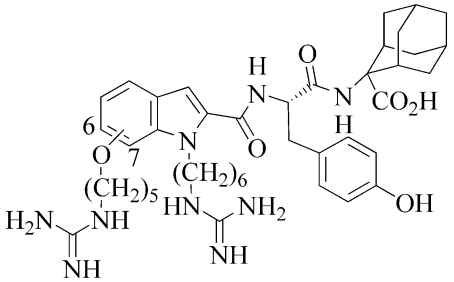
Bioorg. Med. Chem. 10 (2002) 3849

Synthesis and Biological Studies of Novel Neurotensin(8–13) Mimetics

Feng Hong[a,*], Javid Zaidi[a], Bernadette Cusack[b] and Elliott Richelson[b,*]

[a]*Neurochemistry Research, Mayo Clinic Jacksonville, 4500 San Pablo Road, Jacksonville, FL 32224, USA*
[b]*Neuropsychopharmarcology Research, Mayo Clinic Jacksonville, 4500 San Pablo Road, Jacksonville, FL 32224, USA*

Synthesis of novel potent neurotensin(8–13) (Arg^8-Arg^9-Pro^{10}-Tyr^{11}-Lle^{12}-Leu^{13}) mimetics **3**,**4** was reported.



3 at 6-position, **4** at 7-position

Bioorg. Med. Chem. 10 (2002) 3859

Synthesis, Conformation and T-Helper Cell Stimulation of an O-Linked Glycopeptide Epitope Containing Extended Carbohydrate Side-Chains

Mare Cudic, Hildegund C.J. Ertl and Laszlo Otvos, Jr.*

The Wistar Institute, 3601 Spruce Street, Philadelphia, PA 19104, USA

Glycosylated analogues of the T-helper cell epitope 31D were made and the influence of the carbohydrate on various biochemical properties was studied.

AVYT(**X**)RIMMNGGRLKR

X= Glc(α1-4)-Glc(α1-4)-Glc(β1-O) [Glc(α1-4)Glc]$_3$-Glc(β1-O)

X= Glc(α1-4)-Glc(β1-4)-GalNAc(α1-O) [Glc(α1-4)Glc]$_3$- GalNAc(α1-O)

Bioorg. Med. Chem. 10 (2002) 3871

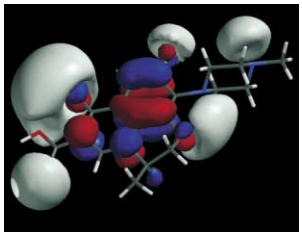
Combining Molecular Modeling with Experimental Methodologies: Mechanism of Membrane Permeation and Accumulation of Ofloxacin

Massimo Fresta,[a,*] Salvatore Guccione,[b] Andrea R. Beccari,[b] Pio M. Furneri[c] and Giovanni Puglisi[b]

[a]*Department of Pharmacobiological Sciences, University "Magna Græcia" of Catanzaro, Complesso "Ninì Barbieri", Roccelletta di Borgia (CZ), I-88021 Catanzaro, Italy*

[b]*Department of Pharmaceutical Sciences, University of Catania, Viale Andrea Doria 6, I-95125 Catania, Italy*

[c]*Department of Microbiological Sciences, University of Catania, Via Androne 31, I-95126 Catania, Italy*



The interaction between ofloxacin and biomembranes was examined as the possible initial step in a transmembrane diffusion process. The influence of environmental conditions and protonation on molecular physiochemical behavior, and hence on the membrane interaction, was investigated by differential scanning calorimetry (DSC). DSC experiments, which are in agreement with computational data, also showed that the complexing capability of ofloxacin with regard to Mg^{++} or Ca^{++} may govern the drug entrance into bacterial cells. Ofloxacin accumulation within *Escherichia coli* ATCC 25922 was measured as a function of time.

Bioorg. Med. Chem. 10 (2002) 3891

The Product of the Natural Reaction Catalyzed by 4-Oxalocrotonate Tautomerase Becomes an Affinity Label of Its Mutant

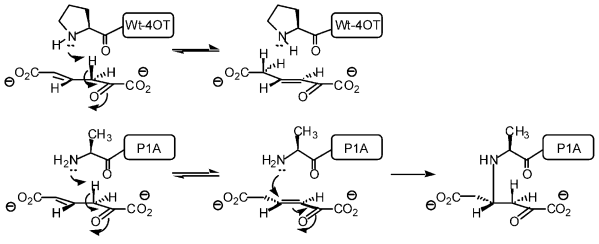
Ashraf Brik,[a,b,c] Philip E. Dawson[b,c,*] and Ehud Keinan[a,c,d,*]

[a]*Department of Molecular Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*

[b]*Departments of Cell Biology and Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*

[c]*The Skaggs Institute of Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA*

[d]*Department of Chemistry and Institute of Catalysis Science and Technology, Technion-Israel Institute of Technology, Technion City, Haifa 3200, Israel*



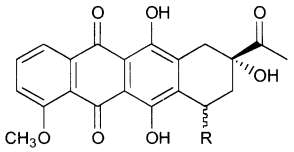
Highly evolved enzymes are optimized not only to catalyze a desired reaction but also to avoid undesired processes. As demonstrated here with 4-OT, even a minor change in the active site residues could result in a dramatic change in the delicately optimized balance of their chemical reactivity.

Bioorg. Med. Chem. 10 (2002) 3899

Design, Synthesis and Antitumor Activities of Novel 7-Arylseleno-7-deoxydaunomycinone Derivatives

Shu-Jia Zhang, Zheng-Ping Jia and Yan-Guang Wang*

Department of Chemistry, Zhejiang University, Hangzhou, 310027, China



3a~e : R=SeAr (7S) **7**: R=SPh (7S)

8: R=SPh (7R)

7-Arylseleno-7-deoxydaunomycinone derivatives **3a**–**e** and 7-thiophenyl-7-deoxydaunomycinones (**7** and **8**) were synthesized and the antitumor activities of them were evaluated against human stomach cancer SGC-7901 and human leukaemia HL60. The cytotoxic assay show that seleno daunomycinone derivatives are more active than thio analogues. 7-Deoxydaunomycinone **4** was obtained when selenophenols were used in excess and the possible mechanism was discussed.

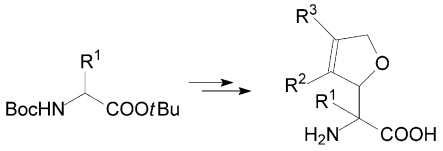
Bioorg. Med. Chem. 10 (2002) 3905

Straightforward Syntheses of Furanomycin Derivatives and their Biological Evaluation

Uli Kazmaier,[a,*] Saskia Pähler,[a] Rainer Endermann,[b] Dieter Häbich,[b] Hein-Peter Kroll[b] and Bernd Riedl[b]

[a]*Institut für Organische Chemie, Universität des Saarlandes, Im Stadtwald, Geb. 23.2, 66123 Saarbrücken, Germany*
[b]*Bayer AG, Pharma Research, 42096 Wuppertal, Germany*

Several types of furanomycin analogues were synthesized and investigated with respect to their antibacterial activity.



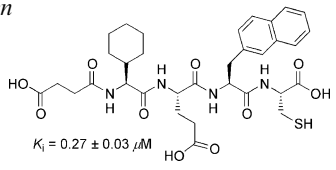
Bioorg. Med. Chem. 10 (2002) 3915

Tetrapeptides as Potent Protease Inhibitors of Hepatitis C Virus Full-Length NS3 (Protease-Helicase/NTPase)

Anja Johansson,[a] Anton Poliakov,[b] Eva Åkerblom,[a] Gunnar Lindeberg,[a] Susanne Winiwarter,[a] Bertil Samuelsson,[c] U. Helena Danielson[b] and Anders Hallberg[a,*]

[a]*Department of Medicinal Chemistry, Uppsala University, BMC, Box 574, SE-751 23 Uppsala, Sweden*
[b]*Department of Biochemistry, Uppsala University, BMC, Box 576, SE-751 23 Uppsala, Sweden*
[c]*Medivir AB, Lunastigen 7, SE-141 44 Huddinge, Sweden*

Potent protease inhibitors of Hepatitis C Virus full-length NS3 (protease-helicase/NTPase) were identified from a library of tetrapeptides. Potential binding interactions with the helicase domain are taken into consideration for the rationalization of the structure–activity relationship data obtained.



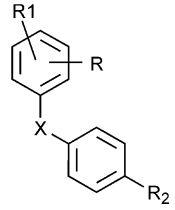
Bioorg. Med. Chem. 10 (2002) 3923

Nitrophenyl Derivatives as Aldose Reductase Inhibitors

Luca Costantino*, Anna Maria Ferrari, Maria Cristina Gamberini and Giulio Rastelli

Dipartimento di Scienze Farmaceutiche, Università di Modena e Reggio Emilia, Via Campi 183, 41100 Modena, Italy

A series of nitrophenyl derivatives and their carboxylic acid bioisosters were synthesized and tested as aldose reductase inhibitors. The results here obtained were compared with docking and molecular dynamics simulations, in order to clarify the binding mode of these compounds to the enzyme.

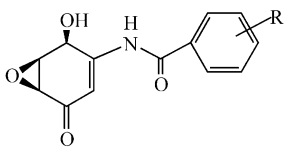


Bioorg. Med. Chem. 10 (2002) 3933

Synthesis and Structure–Activity Relationship of Dehydroxymethylepoxyquinomicin Analogues as Inhibitors of NF-κB Functions

Chanya Chaicharoenpong,[a] Kuniki Kato[b] and Kazuo Umezawa[a,*]

[a]*Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1Hiyoshi, Kohoku-ku, Yokohama 223-0061, Japan*
[b]*Research Laboratories, Pharmaceuticals Group, Nippon Kayaku Co. Ltd., 3-31 Shimo, Kita-ku, Tokyo 115-0042, Japan*



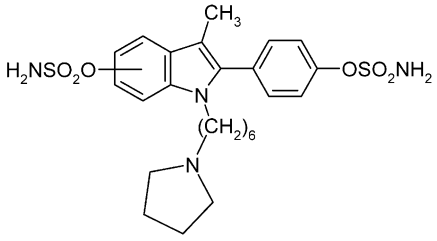
Bioorg. Med. Chem. 10 (2002) 3941

Sulfamoyloxy-Substituted 2-Phenylindoles: Antiestrogen-Based Inhibitors of the Steroid Sulfatase in Human Breast Cancer Cells

Thomas Golob, Renate Liebl and Erwin von Angerer*

Institut für Pharmazie, Universität Regensburg, D-93040 Regensburg, Germany

Nonsteroidal sulfamates derived from antiestrogens inhibit estrone sulfate-induced gene expression in breast cancer cells by a dual mode of action involving both the inhibition of steroid sulfatase and blockade of estrogen receptors.



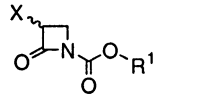
Bioorg. Med. Chem. 10 (2002) 3955

1-Alkoxycarbonyl-3-halogenoazetidin-2-ones as Elastase (PPE) Inhibitors

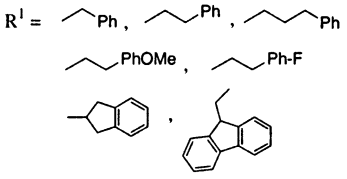
Stéphane Gérard, Gaëtan Nollet, Jennifer Vande Put and Jacqueline Marchand-Brynaert*

Unité de Chimie Organique et Médicinale, Université catholique de Louvain, Bâtiment Lavoisier, place Louis Pasteur 1, B-1348 Louvain-la-Neuve, Belgium

All compounds are reversible inhibitors of PPE (K_i ~2–150 μM).



7 X=Br, **8** X=Cl, **9** X=I



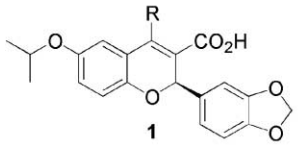
Bioorg. Med. Chem. 10 (2002) 3965

A Novel Class of Endothelin-A Receptor Antagonists, (*R*)-2-(benzo[1,3]dioxol-5-yl)-6-isopropyloxy-2*H*-chromene-3-carboxylic Acids (S-1255). Conformational Analysis of Basic Structure, Crucial for ET_A Antagonism, in Solution and Solid States

Natsuki Ishizuka,* Ken-ichi Matsumura, Junko Kikuchi and Hiroshi Nakai

Shionogi Research Laboratories, Shionogi & Co., Ltd., 12-4, Sagisu 5-chome, Fukushima-ku, Osaka 553-0002, Japan

Conformational analysis of ET_A receptor antagonists having a 2*H*-chromene skeleton was carried out using NMR and X-ray crystallography.



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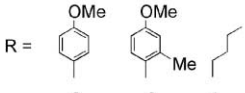
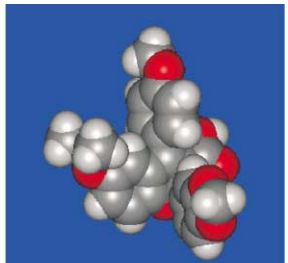


2 (S-1255) **3** **4**



Single-crystal X-ray structure of **2**

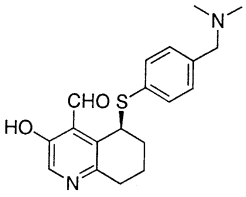
Bioorg. Med. Chem. 10 (2002) 3973

Stereoselectivity in Reactions of Amino Acids Catalyzed by Pyridoxal Derivatives Carrying Rigidly-Attached Chirally-Mounted Basic Groups—Transamination, Racemization, Decarboxylation, Retro-Aldol Reaction, and Aldol Condensation

Lei Liu, Mary Rozenman and Ronald Breslow*

Department of Chemistry, Columbia University, New York, NY 10027, USA

Amino acids are formed with enantioselectivity.



Bioorg. Med. Chem. 10 (2002) 3981

On the Topological Evidences for Modelling Lipophilicity

Vijay K. Agrawal,[a] Jyoti Singh[a] and Padmakar V. Khadikar[b,*]

[a]*QSAR and Chemical Laboratories, A.P.S. University, Rewa-486 003, India*
[b]*Research Division, Laxmi Fumigation and Pest Control Pvt. Ltd. 3 Khatipura, Indore-452 007, India*

Topological evidences for modelling lipophilicity of a large series of diversed compounds have been provided on the basis of distance-based topological indices. A pool of topological indices along with molecular descriptors related to the type of compounds present in the set of 140 compounds were used for this purpose. The results have shown that topology as well as the type of compounds are the responsible parameters for modelling lipophilicity.

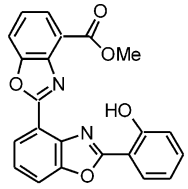
Bioorg. Med. Chem. 10 (2002) 3997

Synthesis and Evaluation of Anticancer Benzoxazoles and Benzimidazoles Related to UK-1

Devinder Kumar,[a] Melissa R. Jacob,[b] Michael B. Reynolds[a] and Sean M. Kerwin[a,*]

[a]*Division of Medicinal Chemistry and Institute of Cellular and Molecular Biology, College of Pharmacy, The University of Texas at Austin, Austin, TX 78712, USA*
[b]*National Center for Natural Products Research, School of Pharmacy, Thad Cochran Research Center, The University of Mississippi, University, MS 38677, USA*

Analogues of UK-1 were prepared and evaluated for anticancer and antibacterial activity. One analogue demonstrates selective anticancer activity characteristic of UK-1 and also binds Mg^{2+}-ions with affinity similar to UK-1.



UK-1

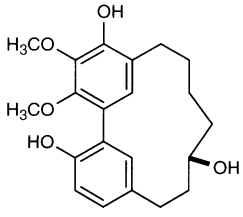
Bioorg. Med. Chem. 10 (2002) 4005

Inhibitors of Nitric Oxide Production from the Bark of *Myrica rubra*: Structures of New Biphenyl Type Diarylheptanoid Glycosides and Taraxerane Type Triterpene

Jing Tao, Toshio Morikawa, Iwao Toguchida, Shin Ando, Hisashi Matsuda and Masayuki Yoshikawa*

Kyoto Pharmaceutical University, Misasagi, Yamashina-ku, Kyoto 607-8412, Japan

Three new biphenyl type diarylheptanoid glycosides, myricanol 11-*O*-β-D-glucopyranoside, myricanone 5-*O*-β-D-glucopyranoside, and neomyricanone 5-*O*-β-D-glucopyranoside, and a new taraxerane type triterpene, myricetrione, were isolated from the bark of Chinese *Myrica rubra*. Their structures were elucidated on the basis of chemical and physicochemical evidence. Biphenyl type diarylheptanoids, triterpenes, and their polyphenols showed potent inhibitory effects on NO production in LPS-activated macrophages. Furthermore, diarylheptanoids, myricanol and myricanone, were found to inhibit induction of iNOS.



myricanol

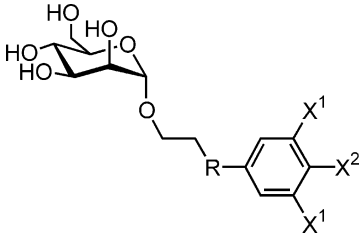
Bioorg. Med. Chem. 10 (2002) 4013

Facile Synthesis of Stable Lipid Analogues Possessing a Range of Alkyl Groups: Application to Artificial Glycolipids

Yasuo Azefu,[a] Hitoshi Tamiaki,[a,*] Reiko Sato[b] and Kazunori Toma[b]

[a]*Department of Bioscience and Biotechnology, Faculty of Science and Engineering, Ritsumeikan University, Kusatsu, Shiga 525-8577, Japan*
[b]*The Noguchi Institute, Itabashi, Tokyo 173-0003, Japan*

A series of novel glycolipid analogues were efficiently prepared from available benzoic acid derivatives. An α-mannosyl residue in the analogues showed high affinity for concanavalin A on an artificial membrane.

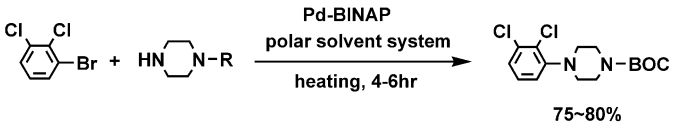


Bioorg. Med. Chem. 10 (2002) 4023

Progress in Arylpiperazine Synthesis by the Catalytic Amination Reaction

Yasuhiro Torisawa,* Takao Nishi and Jun-ichi Minamikawa

Process Research Laboratory, Second Tokushima Factory, Otsuka Pharmaceutical Co. Ltd., Kawauchi-cho, Tokushima 771-0182, Japan

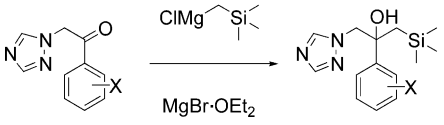


Bioorg. Med. Chem. 10 (2002) 4029

Synthesis of Silicon-Containing Azole Derivatives with Magnesium Bromide Diethyl Etherate, and an Investigation of Their Fungicidal Activities

Hiroyuki Itoh,[a,*] Hisaki Kajino,[a] Takahiro Tsukiyama,[a] Junzo Tobitsuka,[a] Hiroshi Ohta,[a] Yukiyoshi Takahi,[a] Mikio Tsuda[a] and Hideo Takeshiba[b]

[a]*Agroscience Research Laboratories, Sankyo Co., Ltd., Yasu, 1041, Yasu, Yasu-cho, Yasu-gun, Shiga-ken, 520-2342, Japan*
[b]*Medicinal Chemistry Research Laboratories, Sankyo Co., Ltd., 2-58, Hiromachi, 1-chome, Shinagawa-ku, Tokyo, 140-8710, Japan*



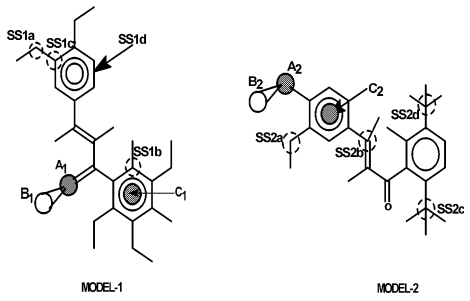
Bioorg. Med. Chem. 10 (2002) 4035

Development of 3D-QSAR Models for 5-Lipoxygenase Antagonists: Chalcones

M. Arockia Babu,[a] Neeraj Shakya,[b] Philip Prathipati,[b] S. G. Kaskhedikar[a] and Anil K. Saxena[b,*]

[a]*Department of Pharmacy, S.G.S.I.T.S., Indore 452003, India*
[b]*Medicinal Chemistry Division, Central Drug Research Institute, Lucknow 226001, India*

The 3D-QSAR models, quantifying the essential structural and physicochemical requirements in terms of common biophoric sites (pharmacophore) and secondary sites for binding and interacting with 5-lipoxygenase, have been developed for a series of chalcones using APEX-3D expert system.

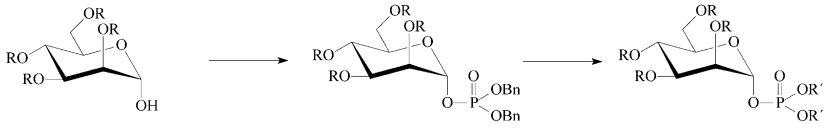


Bioorg. Med. Chem. 10 (2002) 4043

Membrane-Permeant Derivatives of Mannose-1-phosphate

Synke Rutschow,[a] Joachim Thiem,[a,*] Christian Kranz[b] and Thorsten Marquardt[b]

[a]*Institut für Organische Chemie, Universität Hamburg, Martin-Luther-King-Platz 6, D-20146 Hamburg, Germany*
[b]*Klinik und Poliklinik für Kinderheilkunde, Albert-Schweitzer-Str. 33, D-48129 Münster, Germany*



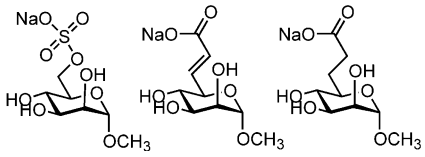
Bioorg. Med. Chem. 10 (2002) 4051

Synthesis and Biological Evaluation of New Mannose 6-Phosphate Analogues

Sébastien Vidal,[a] Marcel Garcia,[b] Jean-Louis Montero[a] and Alain Morère[a,*]

[a]*Laboratoire de Chimie Biomoléculaire (UMR 5032), Université Montpellier II, Ecole Nationale Supérieure de Chimie de Montpellier, 8 Rue de l'Ecole Normale, F-34296 Montpellier Cedex 05, France*
[b]*INSERM, Unité 540, EMCC, 60 Rue de Navacelles, F-34090 Montpellier, France*

Three new analogues of mannose 6-phosphate (M6P) have been synthesized and their affinity toward the M6P/IGFII receptor evaluated.

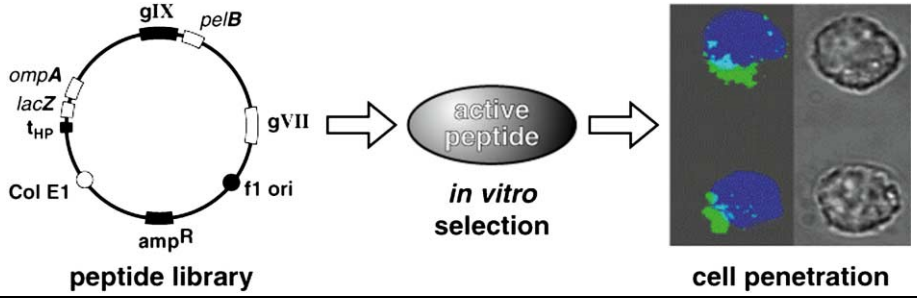


Bioorg. Med. Chem. 10 (2002) 4057

A Cell-penetrating Peptide from a Novel pVII–pIX Phage-Displayed Random Peptide Library

Changshou Gao,[a] Shenlan Mao,[a] Henrik J. Ditzel,[b] Lauge Farnaes,[b] Peter Wirsching,[a] Richard A. Lerner[a] and Kim D. Janda[a,*]

[a]*Department of Chemistry, The Scripps Research Institute and the Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA*
[b]*Department of Immunology, The Scripps Research Institute and the Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA*



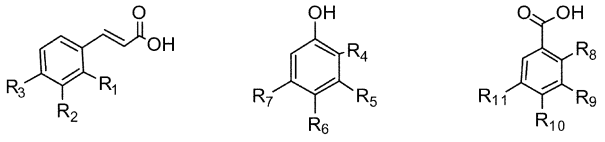
Bioorg. Med. Chem. 10 (2002) 4067

Study on the Multiple Mechanisms Underlying the Reaction Between Hydroxyl Radical and Phenolic Compounds by Qualitative Structure and Activity Relationship

Zhiyong Cheng, Jie Ren, Yuanzong Li,* Wenbao Chang and Zhida Chen

The Key Laboratory of Bioorganic and Molecular Engineering and Department of Chemical Biology, College of Chemistry and Molecular Engineering, Peking University, Beijing, China 100871

The rate constants of hydroxyl radical scavenging reaction were determined for assessing the antioxidant activities of selected phenolic compounds, and the related molecular mechanisms were elucidated in details with the aid of computed chemistry.

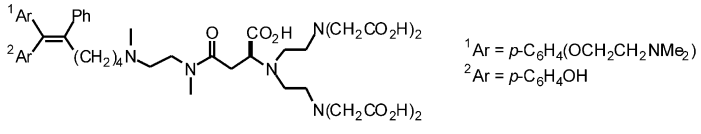


Bioorg. Med. Chem. 10 (2002) 4075

Synthesis and Estrogen Receptor Affinity of a 4-Hydroxytamoxifen-Labeled Ligand for Diagnostic Imaging

Matthew R. Lashley,[a] Edmund J. Niedzinski,[a] Jane M. Rogers,[b] Michael S. Denison[b] and Michael H. Nantz[a,*]

[a]*Department of Chemistry, University of California, Davis, CA 95616, USA*
[b]*Department of Environmental Toxicology, University of California, Davis, CA 95616, USA*



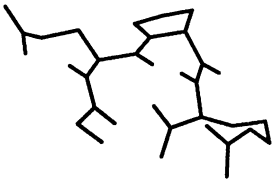
Bioorg. Med. Chem. 10 (2002) 4083

Folded Conformation of an Immunostimulating Tetrapeptide Rigin: High Temperature Molecular Dynamics Simulation Study

Ashish and R. Kishore*

Institute of Microbial Technology, Sector 39-A, Chandigarh, 160 036, India

High temperature unrestrained molecular dynamics simulation study of a phagocytosis stimulating peptide: H-Gly-Gin-Pro-Arg-OH, revealed its strong preferences for an overall tightly folded, i.e., a *distorted* type III β-turn, conformation stabilised by an effective *salt bridge*, i.e., Gly $H_3N^+ \cdots C^{\alpha}OO^-$ Arg interaction.



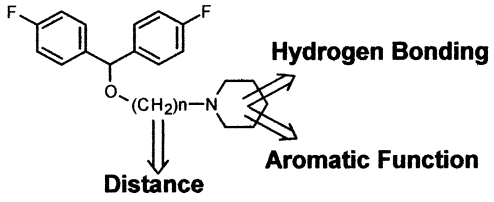
Bioorg. Med. Chem. 10 (2002) 4091

Novel (Bisarylmethoxy)butylpiperidine Analogues as Neurotransmitter Transporter Inhibitors with Activity at Dopamine Receptor Sites

Sung-Woon Choi,[a] David R. Elmaleh,[a] Robert N. Hanson,[b] Timothy M. Shoup[a] and Alan J. Fischman[a,*]

[a]*Division of Nuclear Medicine, Department of Radiology, Massachusetts General Hospital, Boston, MA 02114, USA*
[b]*Department of Chemistry, Northeastern University, Boston, MA 02115, USA*

New (bisarylmethoxy)alkylpiperidine derivatives having dual activities at the dopamine transporter and dopamine receptor sites were prepared as potential cocaine antagonists. Most of the compounds showed dual activities and attenuated hyperlocomotion induced by cocaine. The design and structure–activity relationships of these compounds are described.



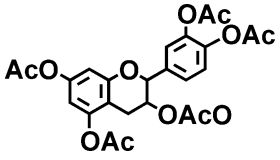
Bioorg. Med. Chem. 10 (2002) 4103

Mechanism of Biochemical Action of Substituted 4-Methylbenzopyran-2-ones. Part 9: Comparison of Acetoxy 4-Methylcoumarins and Other Polyphenolic Acetates Reveal the Specificity to Acetoxy Drug: Protein Transacetylase for Pyran Carbonyl Group in Proximity to the Oxygen Heteroatom

Ishwar Singh,[a] Ekta Kohli,[b] Hanumantharao G. Raj,[b] Kapil Gyanda,[a] Sapan K. Jain,[a] Yogesh K. Tyagi,[b] Garima Gupta,[b] Ranju Kumari,[b] Ajit Kumar,[b] Giridhari Pal,[b] Ashok K. Prasad,[a] Ramesh C. Rastogi,[a] Carl E. Olsen,[c] Subhash C. Jain[a] and Virinder S. Parmar[a,*]

[a]*Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007, India*
[b]*Department of Biochemistry, V. P. Chest Institute, University of Dehli, Delhi-110 007, India*
[c]*Chemistry Department, Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Copenhagen, Denmark*

The absolute requirement of carbonyl group in the pyran ring in the benzopyran-based polyphenolic acetates for the transacetylase (TA) activity was established by the observation that the TA activity was hardly discernible when catechin pentacetate and 7-acetoxy-3,4-dihydro-2,2-dimethylbenzopyran (both lacking the pyran carbonyl group) were used as the substrates. The TA activity with acetoxyflavonoids was remarkably lower than that with acetoxycoumarins, thus suggesting the specificity for pyran carbonyl group in proximity to the oxygen heteroatom.

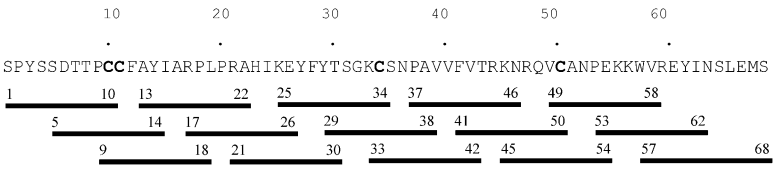


Bioorg. Med. Chem. 10 (2002) 4113

Anti-HIV-1 Peptides Derived from Partial Amino Acid Sequences of CC-Chemokine RANTES

Yasuhiro Nishiyama,[a,*] Tsutomu Murakami,[b] Suguru Shikama,[c] Keisuke Kurita[c] and Naoki Yamamoto[b]

[a]*Chemical Immunology and Therapeutics Research Center, Department of Pathology and Laboratory Medicine, University of Texas-Houston Medical School, 6431 Fannin, Houston, Texas 77030, USA*
[b]*Department of Molecular Virology, Tokyo Medical and Dental University School of Medicine, Bunkyo-ku, Tokyo 113-8519, Japan*
[c]*Department of Applied Chemistry, Faculty of Engineering, Seikei University, Musashino-shi, Tokyo 180-8633, Japan*



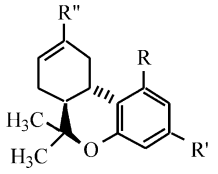
Bioorg. Med. Chem. 10 (2002) 4119

1-Methoxy-, 1-Deoxy-11-hydroxy- and 11-Hydroxy-1-methoxy-Δ^8-tetrahydrocannabinols: New Selective Ligands for the CB_2 Receptor

John W. Huffman,[a,*] Simon M. Bushell,[a] John R. A. Miller,[a] Jenny L. Wiley[b] and Billy R. Martin[b]

[a]*Howard L. Hunter Laboratory, Clemson University, Clemson, SC 29634-1905, USA*
[b]*Department of Pharmacology and Toxicology, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, VA 23298-0613, USA*

The synthesis and pharmacology of three series of CB_2 receptor ligands are described. R = H, OCH_3; R′ = 1,1-dimethylethyl to 1,1-dimethylheptyl; R″ = CH_3, CH_2OH.

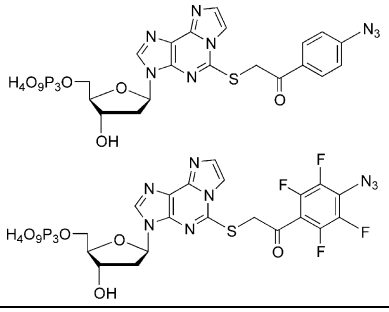


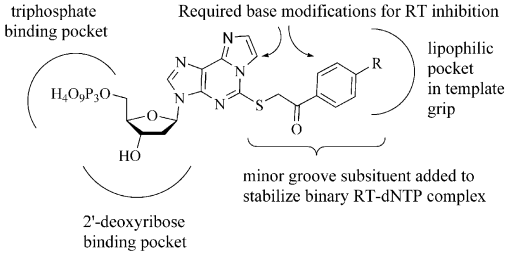
Bioorg. Med. Chem. 10 (2002) 4131

Characterization of a Binding Site for Template Competitive Inhibitors of HIV-1 Reverse Transcriptase Using Photolabeling Derivatives

Weiying Lin,[a] Ke Li[a] and Michael B. Doughty[a,b,*]

[b]*Department of Medicinal Chemistry, The University of Kansas, Lawrence, KS 66045, USA*
[a]*Department of Chemistry and Physics, Southeastern Louisiana University, Hammond, LA, USA*





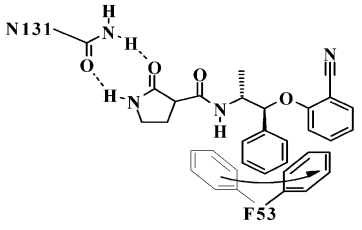
Bioorg. Med. Chem. 10 (2002) 4143

Design of Inhibitors of Scytalone Dehydratase: Probing Interactions with an Asparagine Carboxamide

Gregory S. Basarab,[a,*] Douglas B. Jordan,[b] Troy C. Gehret[a] and Rand S. Schwartz[c]

[a]*DuPont Central Research & Development, Experimental Station, Wilmington, DE 19880, USA*
[b]*DuPont Pharmaceuticals Company, Experimental Station, Wilmington, DE 19880, USA*
[c]*DuPont Agricultural Products, Experimental Station, Wilmington, DE 19880, USA*

Inhibitors of scytalone dehydratase as fungicides were designed by positioning a carbonyl for formation of a hydrogen bond with a key asparagine residue seen in models derived by X-ray diffraction. To achieve a good orientation for hydrogen bonding, the inhibitors incorporate a phenyl substituent that displaces a phenylalanine residue away from the five- or six-membered rings.



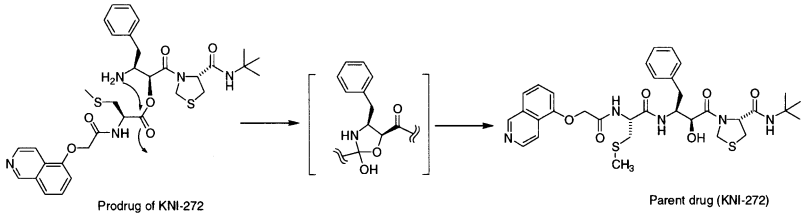
Bioorg. Med. Chem. 10 (2002) 4155

New Water-Soluble Prodrugs of HIV Protease Inhibitors Based on *O→N* Intramolecular Acyl Migration

Yoshio Hamada, Jun Ohtake, Youhei Sohma, 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

These prodrugs were stable in a strongly acidic solution, and could be converted to the parent compounds promptly via *O→N* acyl migration reaction in the aqueous condition from slightly acidic to basic pH.



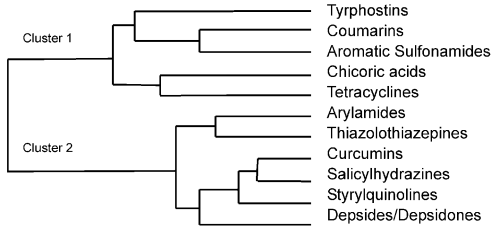
QSAR Studies of HIV-1 Integrase Inhibition

Bioorg. Med. Chem. 10 (2002) 4169

Hongbin Yuan and Abby L. Parrill*

Department of Chemistry, University of Memphis, Memphis, TN 38152, USA

QSAR models have been developed for HIV-1 integrase inhibitors that were assigned into two clusters on the basis of structural descriptors. Different pharmacophores were recognized for each cluster of inhibitors. The results showed that the inhibitors in two clusters have different modes of binding to the enzyme.



Cluster Analysis of HIV-1 Integrase Inhibitors

Mapping of the Active Site of Rat Kidney γ-glutamyl Transpeptidase Using Activated Esters and Their Amide Derivatives

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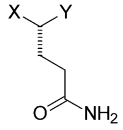
Glutamine analogues were synthesized and evaluated for their ability to inhibit a colorimetric reaction of γ-glutamyl transpeptidase in order to probe their donor substrate binding site affinity.



X = H	**Y = H**	**K_i = n/o**	**no inhibition**
X = H	**Y = COO^-**	**K_i = 12.6 mM**	**mixed non-competitive**
X = NH_3^+	**Y = H**	**K_i = 23.2 mM**	**uncompetitive**
X = NH_3^+	**Y = COO^-**	**K_i = 3.4 mM**	**competitive**
X = NH_3^+	**Y = $CONH_2$**	**K_i = 14.6 mM**	**competitive**
X = NH_3^+	**Y = $COOCH_3$**	**K_i = 5.0 mM**	**competitive**