

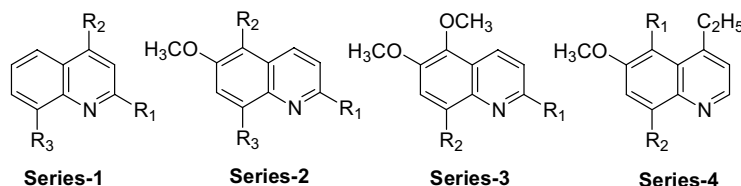
Contents

ARTICLES

Ring-substituted quinolines as potential anti-tuberculosis agents

pp 2501–2508

Suryanarayana Vangapandu, Meenakshi Jain, Rahul Jain,* Sukhraj Kaur and Prati Pal Singh

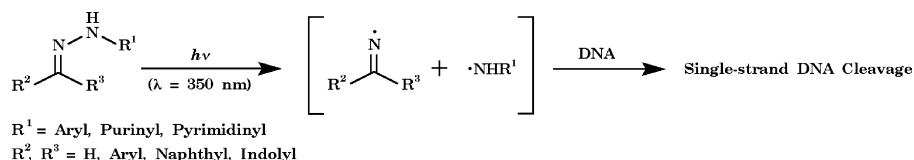


The anti-tuberculosis activities of ring-substituted quinolines (series 1–4) against drug-sensitive and drug-resistant *M. tuberculosis* H37Rv strains are described. The most effective analogues have exhibited potent efficacy (MIC = 1.0 µg/mL).

Aminyl and iminyl radicals from arylhydrazones in the photo-induced DNA cleavage

pp 2509–2515

Jih Ru Hwu,* Chun Chieh Lin, Shih Hsien Chuang, Ke Yung King, Tzu-Rong Su and Shwu-Chen Tsay

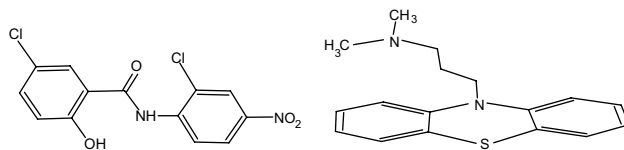


Old drugs as lead compounds for a new disease?

pp 2517–2521

Binding analysis of SARS coronavirus main proteinase with HIV, psychotic and parasite drugs

Xue Wu Zhang* and Yee Leng Yap

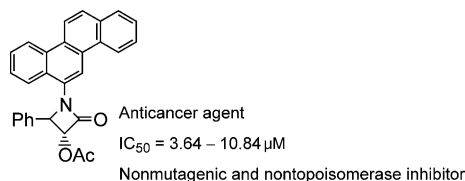


The binding analysis of SARS-CoV main proteinase with HIV, psychotic and parasite drugs (lopinavir, ritonavir, niclosamide and promazine) suggests that these existing drugs can be used as starting points for designing SARS-CoV proteinase inhibitors.

Synthesis of anticancer β -lactams: mechanism of action

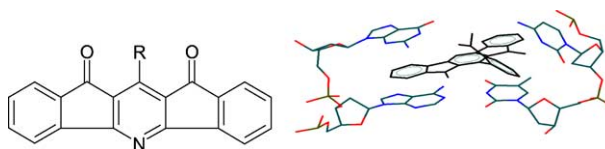
pp 2523–2528

Bimal K. Banik,* Frederick F. Becker and Indrani Banik

**Synthesis, cytotoxicity, QSAR, and intercalation study of new diindenopyridine derivatives**

pp 2529–2536

Ramin Miri,* Katayoun Javidnia, Bahram Hemmateenejad, Ali Azarpira and Zahra Amirghofran

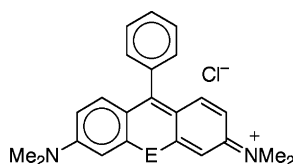


Several diindenopyridine derivatives were synthesized and evaluated for their antitumor activity on cell lines. Effect of structural parameters on the cytotoxicity was evaluated by QSAR analysis. The molecular modeling method was employed to study the DNA-intercalator complex.

Synthesis, properties, and photodynamic properties in vitro of heavy-chalcogen analogues of tetramethylrosamine

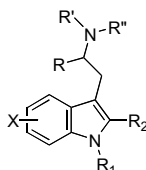
pp 2537–2544

Michael R. Detty,* Paras N. Prasad, David J. Donnelly, Tymish Ohulchanskyy, Scott L. Gibson and Russell Hilf

**TMR-O**, E = O, λ_{max} 552 nm, $\phi(^1O_2)$ 0.08**TMR-S**, E = S, λ_{max} 571 nm, $\phi(^1O_2)$ 0.21**TMR-Se**, E = Se, λ_{max} 582 nm, $\phi(^1O_2)$ 0.87**Binding of tryptamine analogs at $h5-HT_{1E}$ receptors: a structure–affinity investigation**

pp 2545–2552

Małgorzata Dukat, Carol Smith, Katharine Herrick-Davis, Milt Teitler and Richard A. Glennon*

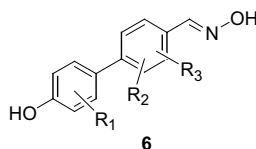


The binding of >40 tryptamine-related analogs at human 5-HT_{1E} receptors was examined for the purpose of formulating structure–affinity relationships (SAFIR). SAFIR and QSAR studies (CoMFA, QsarIS) implicated important roles for hydrogen bonding in the interaction of these ligands with the receptor.

ER β Ligands. Part 2: Synthesis and structure–activity relationships of a series of 4-hydroxy-biphenyl-carbaldehyde oxime derivatives

pp 2553–2570

Cuijian Yang, Richard Edsall, Jr., Heather A. Harris, Xiaochun Zhang, Eric S. Manas and Richard E. Mewshaw*



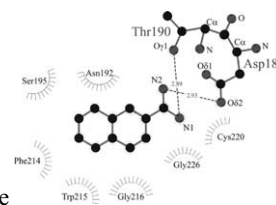
A series of biphenyl carbaldehyde oximes (**6**) was prepared and shown to have significant affinity and selectivity for ER β . SAR and modeling suggested the oxime moiety was mimicking the C-ring of genistein.

S1 subsite in snake venom thrombin-like enzymes: can S1 subsite lipophilicity be used to sort binding affinities of trypsin-like enzymes to small-molecule inhibitors?

pp 2571–2587

Floriano P. Silva, Jr. and Salvatore G. De-Simone*

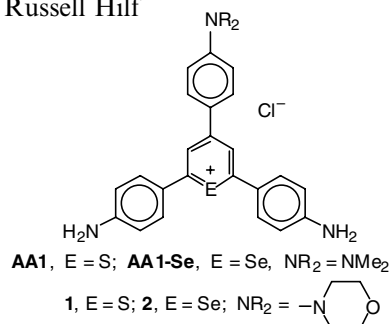
In addition to identifying the set of residues involved in molecular recognition of inhibitors bound to the S1 subsite of snake venom thrombin-like enzymes (SVTLEs), our calculations have indicated that nonpolar (van der Waals) intermolecular interactions and ligand's hydrophobicity are the most important factors affecting binding affinities to the S1 subsite of a SVTLE isolated from the venom of *Lachesis muta muta* (Lmm-TLE). Consequently, we have proposed that S1 subsite lipophilicity may be used to sort binding affinities of trypsin-like enzymes to small molecules by showing that the inhibitory potency of several S1-directed compounds follows subsite lipophilicity among Lmm-TLE and other three trypsin-like serine proteases. Noteworthy, in the course of our analyses we determined that thrombin's S1 subsite should, in fact, be considered less lipophilic than that of trypsin if we account for the presence of the sodium-controlled water channel communicating with the S1 subsite in the coagulant enzyme.



Comparison of the dark and light-induced toxicity of thio and seleno analogues of the thiopyrylium dye AA1

pp 2589–2596

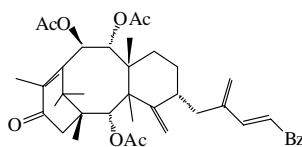
Michael R. Detty,* Scott L. Gibson and Russell Hilf



Taxol derivatives are selective inhibitors of DNA polymerase α

pp 2597–2601

Masahiko Oshige, Mika Takenouchi, Yasutaro Kato, Sinji Kamisuki, Toshifumi Takeuchi, Kouji Kuramochi, Isamu Shiina, Yoshihito Suenaga, Yo-ichi Kawakita, Kazufumi Kuroda, Noriyuki Sato, Susumu Kobayashi, Fumio Sugawara and Kengo Sakaguchi*



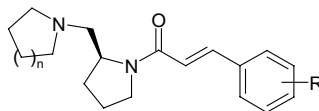
1 IC₅₀ = 27 and 36 μ M (pol. α and β)

Taxinine was found to selectively inhibit DNA polymerase α (pol. α) and β (pol. β) and Cephalomannine, and five intermediates synthesized chemically inhibited only the pol. α activity in vitro.

Cinnamic amides of (*S*)-2-(aminomethyl)pyrrolidines are potent H₃ antagonists

pp 2603–2616

Bernd Peschke,* Sonja Bak, Rolf Hohlweg, Ingrid Pettersson, Hanne Hoffmann Frølund Refsgaard, Dorte Viuff and Karin Rimvall

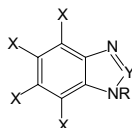


New imidazole-free H₃ antagonists have been found in a series of cinnamic amides of (*S*)-(aminomethyl)pyrrolidines. The influence of the substituent on the aromatic moiety on the potency and the inhibition of three cytochrome P450 subtypes are also described.

Synthesis and activity of 1*H*-benzimidazole and 1*H*-benzotriazole derivatives as inhibitors of *Acanthamoeba castellanii*

pp 2617–2624

Katarzyna Kopańska (née Zastąpiło), Andżelika Najda, Justyna Żebrowska, Lidia Chomicz, Janusz Piekarczyk, Przemysław Myjak and Maria Bretner*

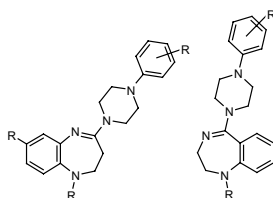


A number of chloro-, bromo- and methyl- analogues of 1*H*-benzimidazole and 1*H*-benzotriazole and their *N*-alkyl derivatives have been synthesized and tested in vitro against *Acanthamoeba castellanii*. Some compounds showed high inhibitory activity at tested concentrations.

Clozapine derived 2,3-dihydro-1*H*-1,4- and 1,5-benzodiazepines with D₄ receptor selectivity: synthesis and biological testing

pp 2625–2637

Thomas Hussenether, Harald Hübner, Peter Gmeiner and Reinhard Troschütz*

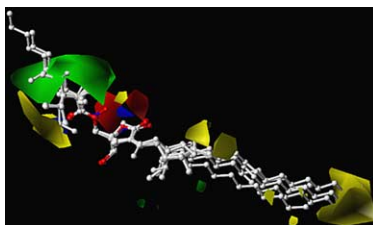


4-Arylpiperazinyl-1-yl-substituted 2,3-dihydro-1*H*-1,4- and 1,5-benzodiazepines and their aza-analogues were synthesized. Some of the title compounds show an impressively high selectivity for the dopamine D₄ receptor subtype. In a mitogenesis assay the most promising compounds showed partial agonistic effects.

3D-QSAR analysis of conformationally constrained diacylglycerol (DAG) analogues as potent protein kinase C (PK-C) ligands

pp 2639–2644

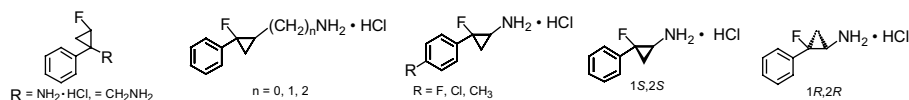
Su Yeon Kim and Jeewoo Lee*



Fluorinated phenylcyclopropylamines. Part 3: Inhibition of monoamine oxidase A and B

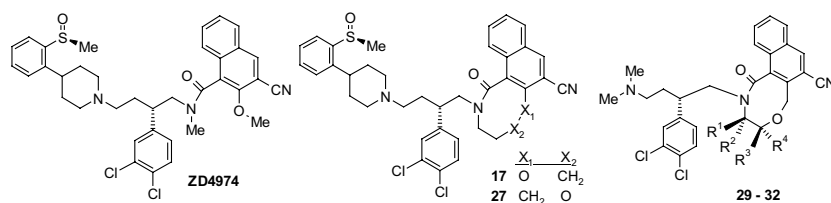
pp 2645–2652

Shinichi Yoshida,* Thomas C. Rosen, Oliver G. J. Meyer, Milton J. Sloan, Song Ye, Günter Haufe and Kenneth L. Kirk

**Naphtho[2,1-b][1,5] and [1,2-f][1,4]oxazocines as selective NK₁ antagonists**

pp 2653–2669

Cyrus J. Ohnmacht,* Jeffrey S. Albert, Peter R. Bernstein, William L. Rumsey, Brian B. Masek, Bruce T. Dembofsky, Gerard M. Koether, Donald W. Andisik and David Aharony

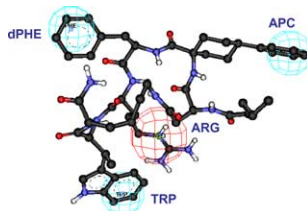


A series of stepwise structural modifications of the NK₁-selective ZD4974 enabled further refinement of a previously reported NK₁ pharmacophore model.

A predictive pharmacophore model of human melanocortin-4 receptor as derived from the solution structures of cyclic peptides

pp 2671–2677

Hongmao Sun,* David N. Greeley, Xin-Jie Chu, Adrian Cheung, Waleed Danho, Joseph Swistok, Yao Wang, Chunlin Zhao, Li Chen and David C. Fry

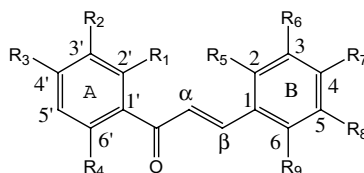


A predictive pharmacophore model of human melanocortin-4 receptor (hMC4R) was derived from the NMR structures of a series of rigidified MT-II related cyclic peptide agonists. The model successfully identified reported hMC4R small molecule ligands from a library of 1000 drug-like compounds.

Differential effects of synthesized 2'-oxygenated chalcone derivatives: modulation of human cell cycle phase distribution

pp 2679–2686

Yerra Koteswara Rao, Shih-Hua Fang and Yew-Min Tzeng*

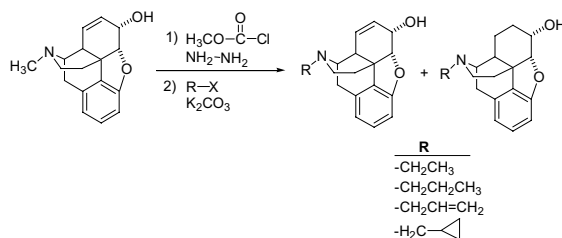


A series of 10 structurally related 2'-oxygenated chalcone derivatives, all of which bearing either hydroxyl and/or methoxy substituents on the A and B rings, were synthesized and evaluated for their cytotoxic activities against the human tumor cells such as Jurkat, U937 cells, and normal cells PHA stimulated PBMCs.

An investigation of the N-demethylation of 3-deoxymorphine and the affinity of the alkylation products to μ , δ , and κ receptors

pp 2687–2690

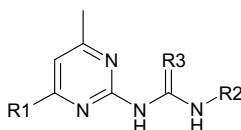
Csaba Csutoras, Ao Zhang, Jean M. Bidlack and John L. Neumeyer*



Synthesis and structure activity relationship of guanidines as NPY Y5 antagonists

pp 2691–2708

Christopher J. Aquino,* Joshi M. Ramanjulu, Dennis Heyer, Alejandro J. Daniels, Fabio Palazzo and Milana Dezube

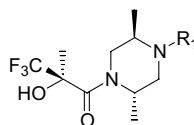


A series of bis-aryl substituted guanidines have been discovered as potent NPY Y5 antagonists. The SAR and in vitro metabolic stability of these compounds are discussed.

3D-QSAR studies of pyruvate dehydrogenase kinase inhibitors based on a divide and conquer strategy

pp 2709–2715

Teshome Leta Aboye, M. Elizabeth Sobhia and Prasad V. Bharatam*

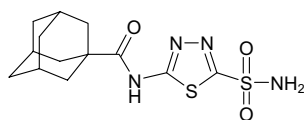


CoMFA study of pyruvate dehydrogenase kinase inhibitors based on a divide and conquer approach for alignment is reported.

Carbonic anhydrase inhibitors: aromatic and heterocyclic sulfonamides incorporating adamantyl moieties with strong anticonvulsant activity

pp 2717–2726

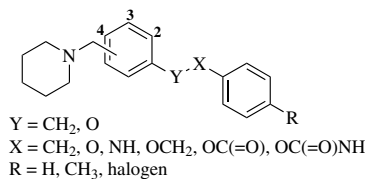
Marc A. Ilies, Bernard Masereel,* Stéphanie Rolin, Andrea Scozzafava, Gheorghe Câmpeanu, Valentin Cîmpeanu and Claudiu T. Supuran*



Structural variations of 1-(4-(phenoxyethyl)benzyl)piperidines as nonimidazole histamine H₃ receptor antagonists

pp 2727–2736

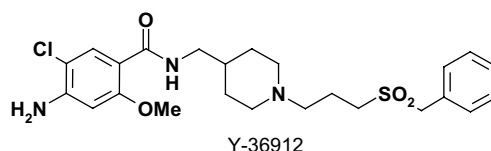
Tibor Mikó, Xavier Ligneau, Heinz H. Pertz, Jean-Michel Arrang, C. Robin Ganellin, Jean-Charles Schwartz, Walter Schunack and Holger Stark*



Synthesis and pharmacological properties of benzamide derivatives as selective serotonin 4 receptor agonists

pp 2737–2747

Shuji Sonda,* Kenichi Katayama, Toshio Kawahara, Noriko Sato and Kiyoshi Asano

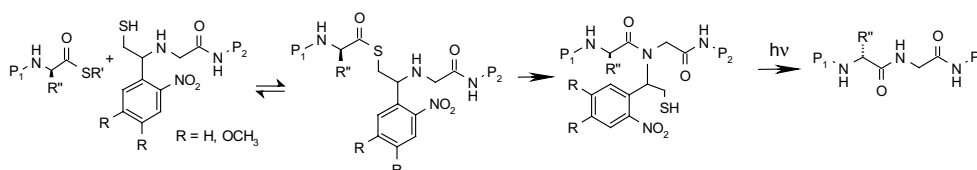


4-Amino-*N*-[1-[3-(benzylsulfonyl)propyl]piperidin-4-ylmethyl]-5-chloro-2-methoxybenzamide (**13a**, **Y-36912**) was a selective 5-HT₄ receptor agonist offering potential as a novel prokinetic agent with reduced side effects derived from 5-HT₃- and dopamine D₂ receptor-binding affinity. In the oral route of administration, this compound enhanced gastric emptying and defecation in mice, and has a possibility as a prokinetic agent, which is effective on both the upper and the lower gastrointestinal tract.

An *o*-nitrobenzyl scaffold for peptide ligation: synthesis and applications

pp 2749–2757

Chiara Marinzi,* John Offer, Renato Longhi and Philip E. Dawson

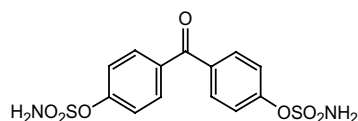


Two photolabile auxiliaries for extended ligation with thioester peptides are described. Post-ligation photolysis from the newly formed peptide bond liberates the native amide structure at the ligation junction. Synthesis of the auxiliaries, ligation properties, photolysis and compatibility with peptide sequence functionalities are reported.

Synthesis, in vitro and in vivo activity of benzophenone-based inhibitors of steroid sulfatase

pp 2759–2772

Hatem A. M. Hejaz, L. W. Lawrence Woo, Atul Purohit, Michael J. Reed and Barry V. L. Potter*

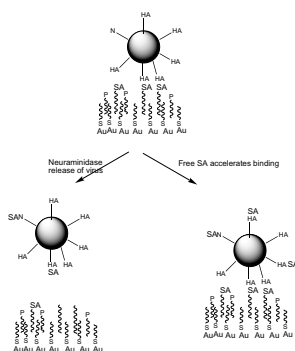


Benzophenone-4,4'-*O,O*-bis-sulfamate, is a potent nonsteroidal steroid sulfatase inhibitor with in vivo activity.

Binding of an influenza A virus to a neomembrane measured by surface plasmon resonance

pp 2773–2780

Peter Critchley* and Nigel J. Dimmock



Purification and partial amino acid sequences of the enzyme vinorine synthase involved in a crucial step of ajmaline biosynthesis

pp 2781–2786

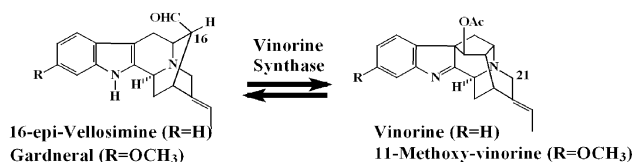
Irina Gerasimenko, Xueyan Ma, Yuri Sheludko, Reinhard Mentele, Friedrich Lottspeich and Joachim Stöckigt*

The isolation, enrichment, partial amino acid sequences and sequence comparison of vinorine synthase to other acetyltransferases from higher plants were reported.

Acetyltransfer in natural product biosynthesis—functional cloning and molecular analysis of vinorine synthase

pp 2787–2795

Anja Bayer, Xueyan Ma and Joachim Stöckigt*

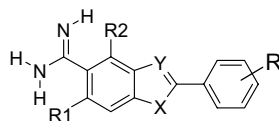


A cDNA clone encoding vinorine synthase was isolated from *Rauwolfia serpentina* and functionally expressed in *Escherichia coli*. The heterologously expressed enzyme was thoroughly characterized by molecular analysis, mainly by site-directed mutagenesis.

3D-QSAR CoMFA/CoMSIA studies on Urokinase plasminogen activator (uPA) inhibitors: a strategic design in novel anticancer agents

pp 2797–2805

B. A. Bhongade and A. K. Gadad*



Statistically significant 3D-QSAR CoMFA/CoMSIA models were generated for a series of indole/benzimidazole-5-carboxamides. The 3D-CoMFA, CoMSIA contour maps can be used as putative pharmacophore for the design of novel uPA inhibitors as cancer therapeutics.

OTHER CONTENTS

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*Corresponding author

COVER

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medicinal Chemistry* 2003, 11, 43–52.



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