

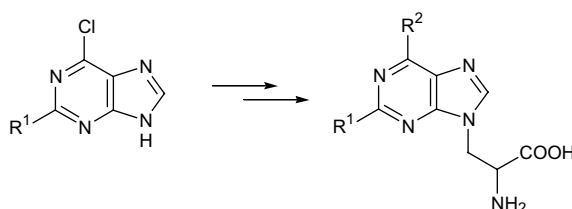
Contents

ARTICLES

Synthesis and immunobiological activity of base substituted 2-amino-3-(purin-9-yl)-propanoic acid derivatives

pp 2349–2354

Petra Doláková,* Antonín Holý, Zdeněk Zídek, Milena Masojídková and Eva Kmoníčková



A comparison between two polarizability parameters in chemical–biological interactions

pp 2355–2372

Rajeshwar P. Verma* and Corwin Hansch

A comparative study on the two polarizability parameters, that is, NVE (sum of the valence electrons) and CMR (calculated molar refractivity) has been undertaken by QSAR analyses in chemical–biological interactions, where α is the polarizability of the molecules.

$$\alpha = a(\text{NVE}) \pm \text{constant} \quad (\text{i})$$

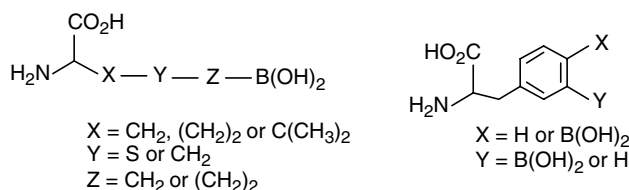
$$\alpha = b(\text{CMR}) \pm \text{constant} \quad (\text{ii})$$

$$\text{NVE} = c(\text{CMR}) \pm \text{constant} \quad (\text{iii})$$

Synthesis and evaluation of new ω -borono- α -amino acids as rat liver arginase inhibitors

pp 2373–2379

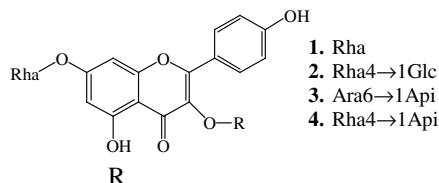
Olivier Busnel, François Carreaux, Bertrand Carboni, Stephanie Pethe, Sandrine Vadon-Le Goff, Daniel Mansuy and Jean-Luc Boucher*



New ω -borono- α -amino acids analogues of the previously known arginase inhibitors *S*-(2-boronoethyl)-L-cysteine and 2-amino-6-boronohexanoic acid have been synthesized and tested as inhibitors of purified rat liver arginase.

Inhibitory effects of flavonol glycosides from *Cinnamomum osmophloeum* on inflammatory mediators in LPS/IFN- γ -activated murine macrophages pp 2381–2388

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

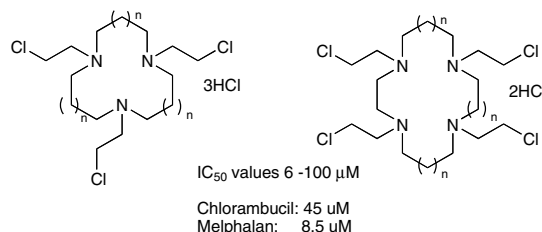


Four kaempferol glycosides were isolated from the leaves of *Cinnamomum osmophloeum*. The compound, kaempferol 3-*O*- β -D-glucopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-7-*O*- α -L-rhamnopyranoside (**2**), was established by spectral analyses and acid hydrolysis. Compounds **1–4** were evaluated for their inhibitory effects on production of nitric oxide (NO) and cytokines (TNF- α and IL-12), in LPS/IFN- γ -activated macrophages.

Synthesis of novel DNA cross-linking antitumour agents based on polyazamacrocycles pp 2389–2395

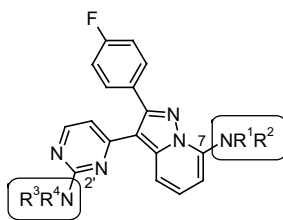
Laurie L. Parker, Fiona M. Anderson, C. Caroline O'Hare, Stephen M. Lacy, John P. Bingham, David J. Robins* and John A. Hartley

Novel azamacrocyclic nitrogen mustards were highly efficient at cross-linking DNA ($XL_{50} \ll 10$ nM)—up to 10^4 times better than chlorambucil (XL_{50} 100 μ M).



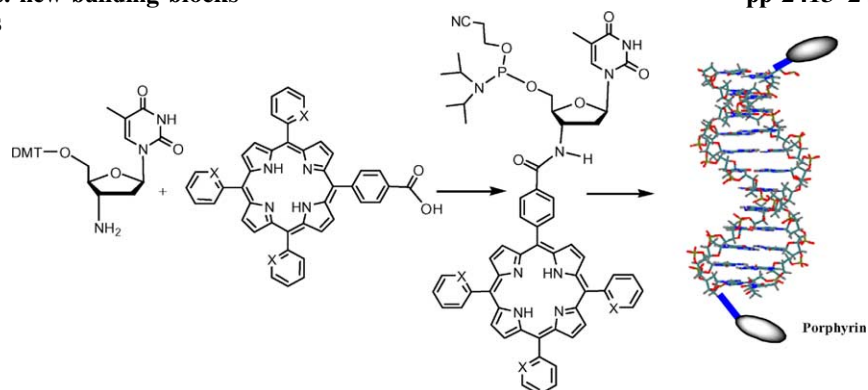
Pyrazolopyridine antiherpetics: SAR of C2' and C7 amine substituents pp 2397–2411

Brian A. Johns,* Kristjan S. Gudmundsson, Elizabeth M. Turner, Scott H. Allen, Vicente A. Samano, John A. Ray, George A. Freeman, F. Leslie Boyd, Jr., Connie J. Sexton, Dean W. Selleseth, Katrina L. Creech and Kelly R. Moniri



Porphyrin substituted phosphoramidites: new building blocks for porphyrin–oligonucleotide syntheses pp 2413–2421

Milan Balaz, Andrea E. Holmes, Michele Benedetti, Gloria Proni and Nina Berova*

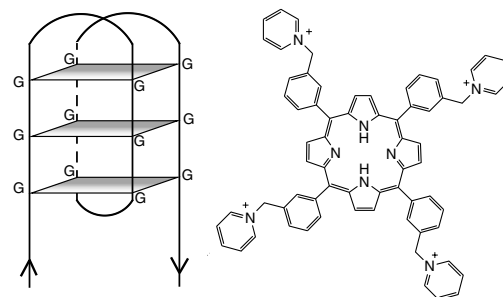


Stabilization of guanine quadruplex DNA by the binding of porphyrins with cationic side arms

pp 2423–2430

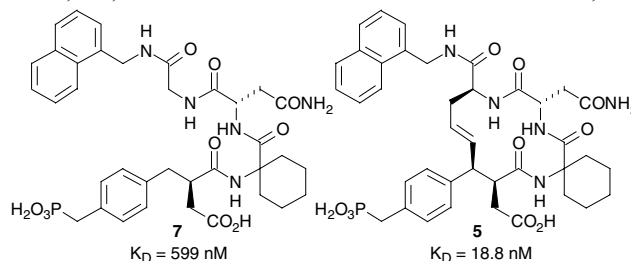
Takeshi Yamashita, Tadayuki Uno and Yoshinobu Ishikawa*

We synthesized novel quadruplex-interacting porphyrins with cationic pyridinium and trimethylammonium arms at *para*- or *meta*-position of all phenyl groups of tetratolyl porphyrin. The *meta*-isomers stabilized an antiparallel quadruplex structure more greatly than the *para*-isomers and well-studied TMPyP4.

**Evaluation of macrocyclic Grb2 SH2 domain-binding peptide mimetics prepared by ring-closing metathesis of C-terminal allylglycines with an N-terminal β -vinyl-substituted phosphotyrosyl mimetic**

pp 2431–2438

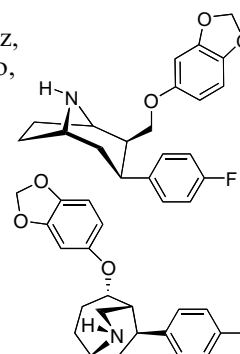
Shinya Oishi, Rajeshri G. Karki, Zhen-Dan Shi, Karen M. Worthy, Lakshman Bindu, Oleg Chertov, Dominic Esposito, Peter Frank, William K. Gillette, Melissa Maderia, James Hartley, Marc C. Nicklaus, Joseph J. Barchi, Jr., Robert J. Fisher and Terrence R. Burke, Jr.*

**Synthesis, structural identification, and ligand binding of tropane ring analogs of paroxetine and an unexpected aza-bicyclo[3.2.2]nonane rearrangement product**

pp 2439–2449

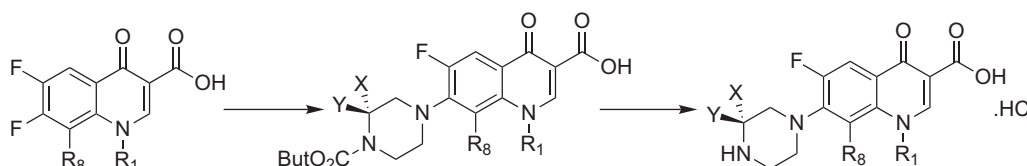
Scott P. Runyon, Jason P. Burgess, Philip Abraham, Kathryn I. Keverline-Frantz, Judy Flippen-Anderson, Jeffrey Deschamps, Anita H. Lewin, Hernán A. Navarro, John W. Boja, Michael J. Kuhar and F. Ivy Carroll*

Tropane-derived analogs of paroxetine were designed and synthesized as potential inhibitors of serotonin reuptake based on the structural and biological similarity between the two classes of compounds. The greater flexibility of paroxetine permits conformational heterogeneity thereby allowing paroxetine to adopt a conformation favored by the 5-HTT, which cannot be achieved by the structurally-rigid tropane ring analogs.

**Syntheses of quinolone hydrochloride enantiomers from synthons (*R*)- and (*S*)-2-methylpiperazine**

pp 2451–2458

Bo Liu, Chun-Hao Yang, Guang-Yu Xu, Yong-Hong Zhu, Jing-Rong Cui, Xi-Han Wu* and Yu-Yuan Xie*

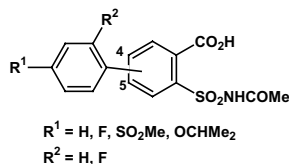


A series of chiral quinolone hydrochloride was synthesized from synthons (*R*)- and (*S*)-2-methylpiperazine in high yield and tested for their antibacterial activity to explore the steric influence on biological activities.

Design, synthesis, and biological evaluation of *N*-acetyl-2-carboxybenzenesulfonamides: a novel class of cyclooxygenase-2 (COX-2) inhibitors

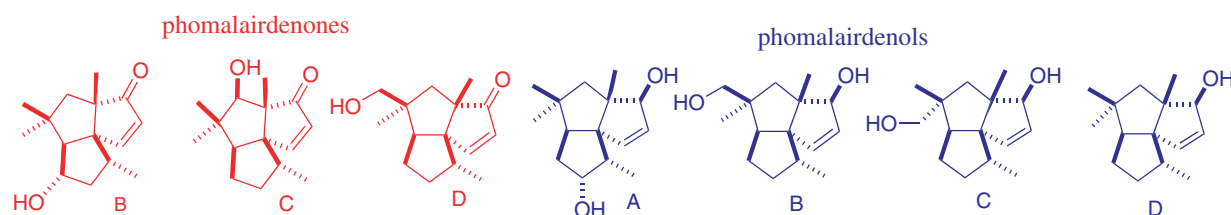
pp 2459–2468

Qiao-Hong Chen, P. N. Praveen Rao and Edward E. Knaus*


New sesquiterpenic phytotoxins establish unprecedented relationship between different groups of blackleg fungal isolates

pp 2469–2475

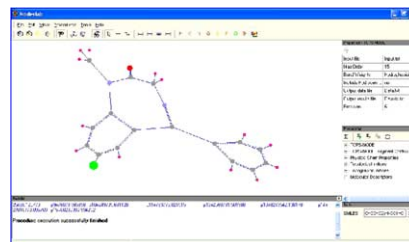
M. Soledade C. Pedras,* Paulos B. Chumala and Uppala Venkatesham


A topological substructural approach applied to the computational prediction of rodent carcinogenicity

pp 2477–2488

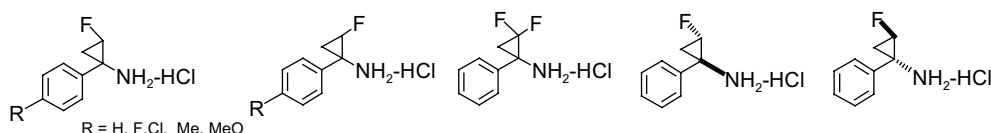
Aliuska Morales Helguera, Miguel Angel Cabrera Pérez,* Maykel Pérez González, Reinaldo Molina Ruiz and Humberto González Díaz

The rodent carcinogenic activity was investigated by using a topological substructural molecular design approach (TOPS-MODE). The *in silico* model obtained explained more than 76% of variance and it was successfully validated. This methodology evidenced the role of hydrophobicity and the dipole moment of the molecules in the prediction of carcinogenicity.


Fluorinated phenylcyclopropylamines. Part 4: Effects of aryl substituents and stereochemistry on the inhibition of monoamine oxidases by 1-aryl-2-fluoro-cyclopropylamines

pp 2489–2499

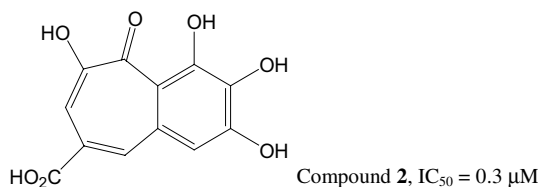
Song Ye, Shinichi Yoshida, Roland Fröhlich, Günter Haufe and Kenneth L. Kirk*



Benzotropolone inhibitors of estradiol methylation: kinetics and in silico modeling studies

pp 2501–2507

Joshua D. Lambert, Dapeng Chen, Ching Y. Wang, Ni Ai, Shengmin Sang,
Chi-Tang Ho, William J. Welsh and Chung S. Yang*

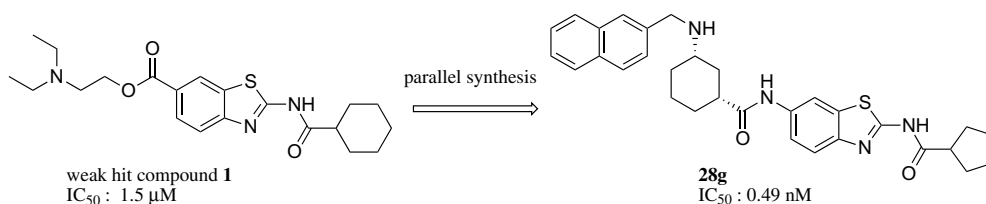


Benzotropolone compounds were assessed in vitro and in silico for their ability to inhibit hydroxyestradiol methylation by human catechol-*O*-methyltransferase (COMT).

Synthesis of potent and selective inhibitors of *Candida albicans* *N*-myristoyltransferase based on the benzothiazole structure

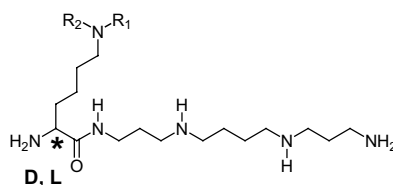
pp 2509–2522

Kazuo Yamazaki,* Yasushi Kaneko, Kie Suwa, Shinji Ebara, Kyoko Nakazawa
and Kazuhiro Yasuno

**Lysine–spermine conjugates: hydrophobic polyamine amides as potent lipopolysaccharide sequestrants**

pp 2523–2536

Mark R. Burns, Stewart J. Wood, Kelly A. Miller, Thuan Nguyen, Jens R. Cromer and Sunil A. David*

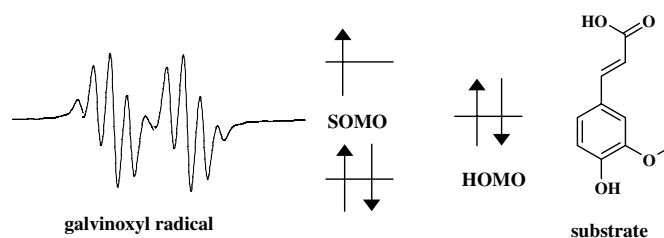


Lysine–spermine conjugates with a long-chain aliphatic (C_{16} – C_{20}) substituent at R_1 bind and neutralize bacterial lipopolysaccharides. These compounds reduce lethality in a murine model of lipopolysaccharide-induced shock, and may serve as novel leads for developing novel anti-lipopolysaccharide agents for the therapy of Gram-negative sepsis.

Structural modification of phenylpropanoid-derived compounds and the effects on their participation in redox processes

pp 2537–2546

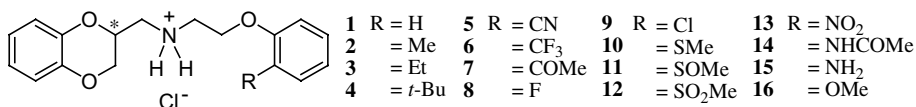
Wendy R. Russell,* Lorraine Scobbie and Andrew Chesson



QSAR study for a novel series of *ortho* monosubstituted phenoxy analogues of α_1 -adrenoceptor antagonist WB4101

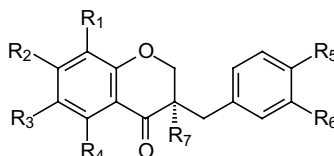
pp 2547–2559

Laura Fumagalli, Cristiano Bolchi, Simona Colleoni, Marco Gobbi, Barbara Moroni, Marco Pallavicini, Alessandro Pedretti, Luigi Villa, Giulio Vistoli and Ermanno Valoti*


Anti-inflammatory activity and QSAR studies of compounds isolated from Hyacinthaceae species and *Tachiadenus longiflorus* Griseb. (Gentianaceae)

pp 2561–2568

Karen du Toit, Esameldin E. Elgorashi, Sarel F. Malan, Siegfried E. Drewes, Johannes van Staden, Neil R. Crouch and Dulcie A. Mulholland*

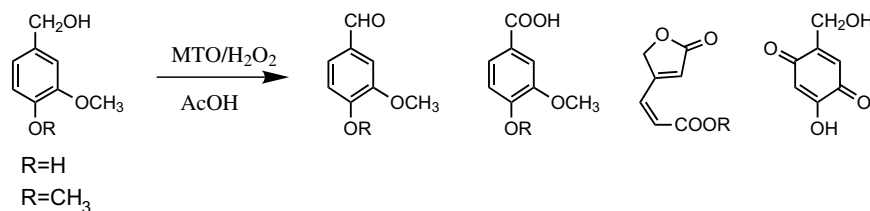


Twenty-two homoisoflavanones and structurally related compounds of natural and synthetic origin were screened for anti-inflammatory activity. A QSAR study yielded three equations with significant prediction values for the anti-inflammatory activity of the compounds investigated.

Methyltrioxorhenium: a new catalyst for the activation of hydrogen peroxide to the oxidation of lignin and lignin model compounds

pp 2569–2578

Claudia Crestini,* Paola Pro, Veronica Neri and Raffaele Saladino*



Methyltrioxorhenium was found a powerful and promising catalyst for the oxidation of lignins and lignin model compounds by use of hydrogen peroxide as primary oxidant.

Bridge-linked bis-quaternary ammonium anti-microbial agents: relationship between cytotoxicity and anti-bacterial activity of 5,5'-[2,2'-(tetramethylenedicarbonyldioxy)-diethyl]bis(3-alkyl-4-methylthiazonium iodide)s

pp 2579–2587

Kazuto Ohkura, Akiko Sueno, Hideaki Nagamune and Hiroki Kourai*

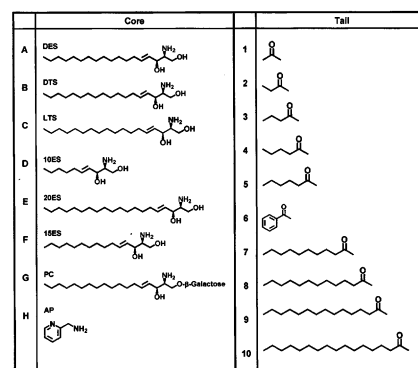
We synthesized five types of bridge-linked bis-quaternary ammonium compounds (bis-QACs), and we examined the relationship between the cytotoxicity and the anti-bacterial activity against *E. coli* of these bis-QACs. 5DEBT-4,8 should be a significant useful compound tested in the present study.

Inhibitory activity of a ceramide library on interleukin-4 production from activated T cells

pp 2589–2595

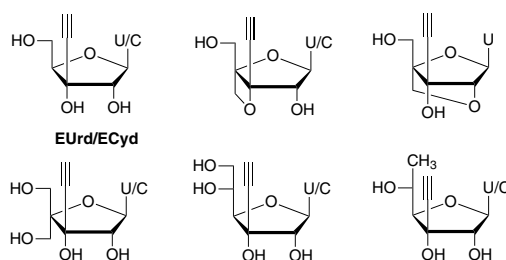
Jin Park, Qian Li, Young-Tae Chang and Tae Sung Kim*

Interleukin-4 is a critical factor closely associated with the development of allergic diseases. In this study we investigated the inhibitory activity of IL-4 production in activated T cells by screening ceramide derivatives prepared by solid phase combinatorial chemistry.

**Synthesis and biological evaluation of branched and conformationally restricted analogs of the anticancer compounds 3'-C-ethynyluridine (EUrd) and 3'-C-ethynylecytidine (ECyd)**

pp 2597–2621

Patrick J. Hrdlicka, Nicolai K. Andersen, Jan S. Jepsen, Flemming G. Hansen, Kim F. Haselmann, Claus Nielsen and Jesper Wengel*

**Synthesis and characterization of novel 6-fluoro-4-piperidinyl-1,2-benzisoxazole amides and 6-fluoro-chroman-2-carboxamides: antimicrobial studies**

pp 2623–2628

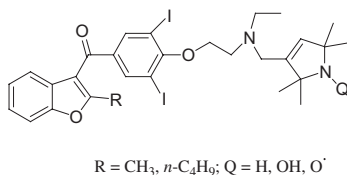
B. S. Priya, Basappa, S. Nanjunda Swamy and Kanchugarakoppal S. Rangappa*

Novel derivatives of 6-fluoro-4-piperidinyl-1,2-benzisoxazole amides **4(I–VI)** were obtained by the condensation of different acid chlorides with 6-fluoro-3-piperidin-4-yl-benzof[d]isoxazole. Also, 6-fluoro-chroman-2-carboxamides **6(I–III)** were synthesized by using nebolic acid chloride with different amines in presence of triethylamine as acid scavenger and dichloroethane as solvent. The synthesized compounds were characterized by IR, ¹H NMR, and CHN analysis. These molecules were evaluated for their efficacy as antimicrobials in vitro by disc diffusion and microdilution method against pathogenic strains such as *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas fluorescens*, *Xanthomonas campestris pvs*, *X. oryzae*, *Aspergillus niger*, *A. flavus*, *Fusarium oxysporum*, *Trichoderma* species, *F. monaliforme*, and *Penicillium* species. Compounds **4I**, **4IV**, **4V**, **6I**, **6II** and **6III** showed better inhibitory activity than compared to standard drugs. Among these compounds, **4IV** and **6III** showed potent inhibitory activity against all the strains and found to be nonstrain dependent. The title compounds represent a novel class of potent antimicrobial agents.

Synthesis and evaluation of the permeability transition inhibitory characteristics of paramagnetic and diamagnetic amiodarone derivatives

pp 2629–2636

Tamás Kálai, Gábor Várbiro, Zita Bognár, Anita Pálfi, Katalin Hantó, Balázs Bognár, Erzsébet Ösz, Balázs Sümegi and Kálmán Hideg*

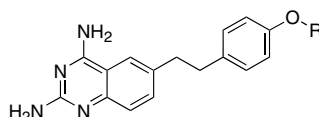


Several new amiodarone analogues were synthesized with introducing pyrroline and 1,2,3,6-tetrahydropyridine nitroxides into phenolether side chain. Their toxicity and transition inhibitory effect was studied.

Design, synthesis and evaluation of 2,4-diaminoquinazolines as inhibitors of trypanosomal and leishmanial dihydrofolate reductase

pp 2637–2649

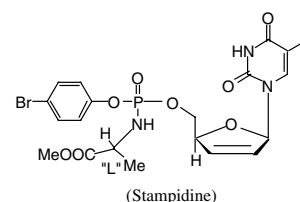
Soghra Khabnadideh, Didier Pez, Alexander Musso, Reto Brun, Luis M. Ruiz Pérez, Dolores González-Pacanowska and Ian H. Gilbert*


Enzymatic hydrolysis of stampidine and other stavudine phosphoramidates in the presence of mammalian proteases

pp 2651–2655

T. K. Venkatachalam, P. Samuel and F. M. Uckun*

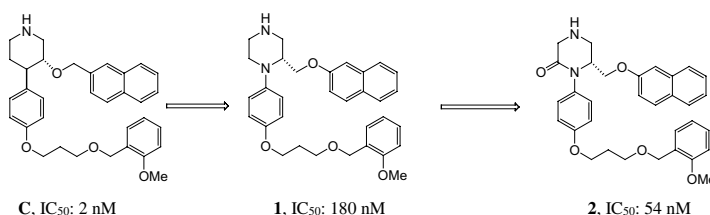
Mammalian proteases have not been implicated in the metabolism of any nucleoside phosphoramidate prodrug. The results presented herein provide unprecedented and conclusive experimental evidence that mammalian proteases are capable of hydrolyzing stavudine phosphoramidates. Specifically, cathepsin B and proteinase K are able to metabolize stampidine and other phosphoramidate derivatives of stavudine. Additionally, cathepsin B exhibits chiral selectivity at the phosphorus center. The elucidation of the metabolic pathways leading to activation of stampidine may provide the basis for pharmacologic interventions aimed at modulating the metabolism and thereby improving the therapeutic window of stampidine as an anti-HIV agent.


Discovery of novel non-peptidic ketopiperazine-based renin inhibitors

pp 2657–2664

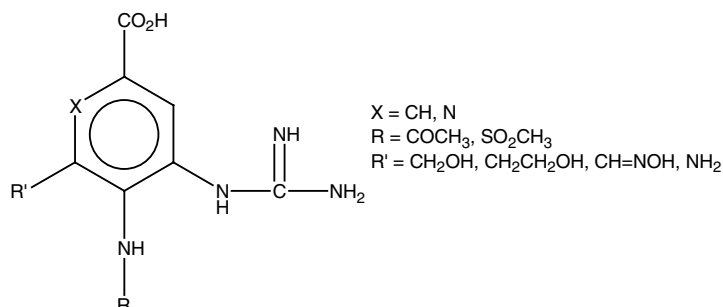
Daniel D. Holsworth,* Noel A. Powell, Dennis M. Downing, Cuiman Cai, Wayne L. Cody, J. Michael Ryan, Robert Ostroski, Mehran Jalaie, John W. Bryant and Jeremy J. Edmunds

Ketopiperazine **2** was designed from a previously published analog. Compound **2** was shown to be a novel, potent inhibitor of renin that, when administered orally, lowered blood pressure in a hypertensive double transgenic (human renin and angiotensinogen) mouse model. Compound **2** was further optimized to sub-nanomolar potency by designing an analog that addressed the S3 sub-pocket of the renin enzyme.


Synthesis and inhibitory activity of benzoic acid and pyridine derivatives on influenza neuraminidase

pp 2665–2678

Pooran Chand,* Pravin L. Kotian,* Philip E. Morris, Shanta Bantia, David A. Walsh and Yarlagadda S. Babu

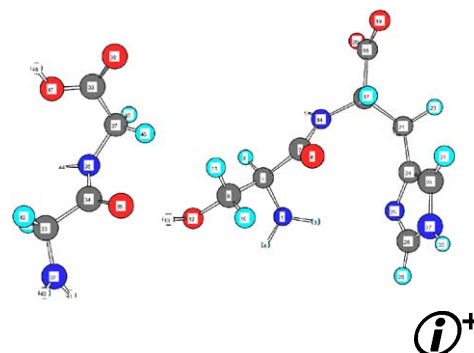


The study on the interaction between seryl-histidine dipeptide and proteins by circular dichroism and molecular modeling

pp 2679–2689

Qing Zeng, Qiang Yin and Yufen Zhao*


We find that the distance is remarkably 3.37 Å between the oxygen atom of the hydroxyl group of seryl-histidine dipeptide (O₁₂) and the carbon atom of the amide bond (C₃₄). It can be inferred that the nucleophilic attack on C₃₄ by O₁₂ causes the breakage of the hydrogen bonds of β-sheets.

**OTHER CONTENTS**

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*Corresponding author

 Supplementary data available via ScienceDirect
COVER

2005: Human liver glycogen phosphorylase A (HLGPa) is an attractive target enzyme for discovering anti-type 2 diabetes drugs. This picture shows the interaction model for a series of indole-2-carboxamides to HLGPa derived from molecular docking simulations [Liu, G.; Zhang, Z.; Luo, X.; Shen, J.; Liu, H.; Shen, X.; Chen, K.; Jiang, H. *Bioorg. Med. Chem.* **2004**, *12*, 4147–4157].



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