

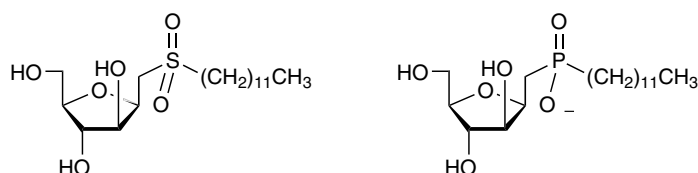
Contents

ARTICLES

Sulfone and phosphinic acid analogs of decaprenolphosphoarabinose as potential anti-tuberculosis agents

pp 5495–5503

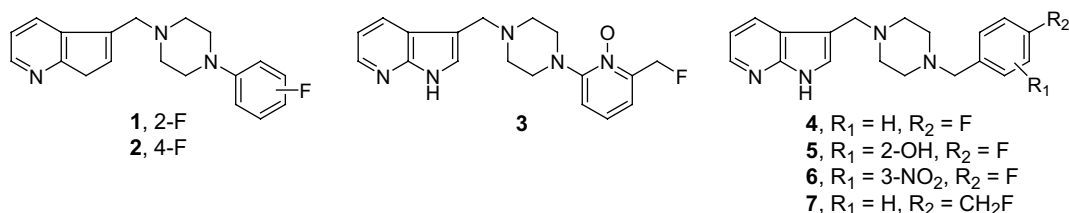
Charla A. Centrone and Todd L. Lowary*



Synthesis and evaluation of fluorine-substituted 1*H*-pyrrolo[2,3-*b*]pyridine derivatives for dopamine D₄ receptor imaging

pp 5505–5513

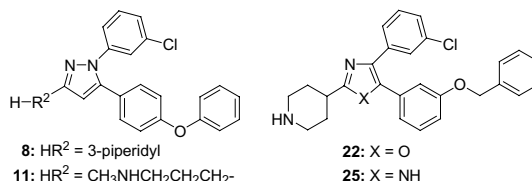
Seung-Jun Oh, Kyo Chul Lee, Sang-Yoon Lee, Eun Kyoung Ryu, Hideo Saji, Yearn Seong Choe,* Dae Yoon Chi,* Sang Eun Kim, Jeewoo Lee and Byung-Tae Kim



Synthesis and antibacterial activity of novel and potent DNA gyrase inhibitors with azole ring

pp 5515–5524

Akihiko Tanitame,* Yoshihiro Oyamada, Keiko Ofuji, Mika Fujimoto, Kenji Suzuki, Tomohiko Ueda, Hideo Terauchi, Motoji Kawasaki, Kazuo Nagai, Masaaki Wachi and Jun-ichi Yamagishi

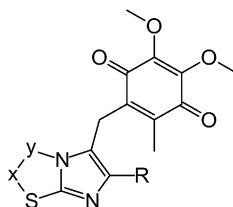


The pyrazole, oxazole and imidazole derivatives synthesized in this study exhibited potent antibacterial activity against multidrug resistant Gram-positive bacteria with minimal inhibitory concentration values equivalent to those against susceptible strains.

Effects of new ubiquinone-imidazo[2,1-*b*]thiazoles on mitochondrial complex I (NADH-ubiquinone reductase) and on mitochondrial permeability transition pore

pp 5525–5532

Aldo Andreani,* Massimiliano Granaola, Alberto Leoni, Alessandra Locatelli, Rita Morigi, Mirella Rambaldi, Maurizio Recanatini, Giorgio Lenaz, Romana Fato and Christian Bergamini

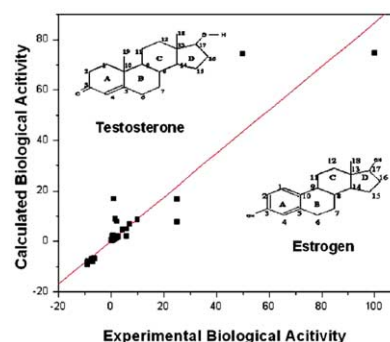


Electrophilicity index as a possible descriptor of biological activity

pp 5533–5543

R. Parthasarathi, V. Subramanian,* D. R. Roy and P. K. Chattaraj*

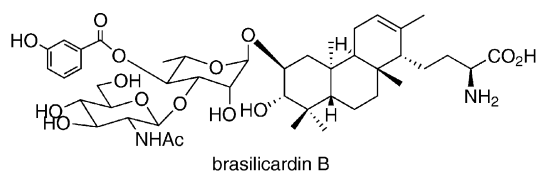
Development of generalized QSAR model is a mammoth task and in general a large number of descriptors are to be used to get a satisfactory correlation. In order to obtain a generalized model for QSAR, the structure–activity relationship has been developed for testosterone and estrogen derivatives with the help of a conceptually simpler single descriptor; namely the electrophilicity index. Results reinforce that electrophilicity index is suitable to effectively describe the biological activities.



Brasilicardins B–D, new tricyclic terpenoids from actinomycete *Nocardia brasiliensis*

pp 5545–5551

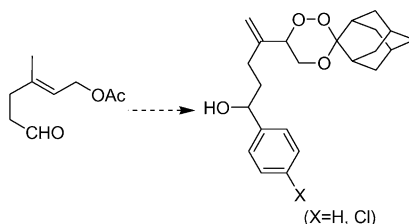
Kazusei Komatsu, Masashi Tsuda, Motoo Shiro, Yasushi Tanaka, Yuzuru Mikami and Jun'ichi Kobayashi*



Synthesis of new 6-alkylvinyl/arylalkylvinyl substituted 1,2,4-trioxanes active against multidrug-resistant malaria in mice

pp 5553–5562

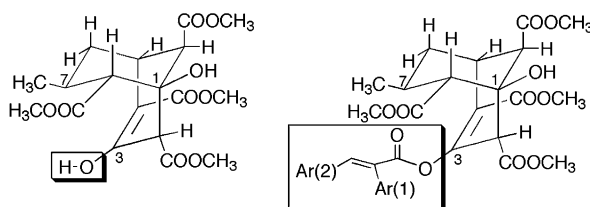
Chandan Singh,* Nitin Gupta and Sunil K. Puri



Synthesis and antitumor activity of bicyclo[3.3.1]nonenol derivatives

pp 5563–5569

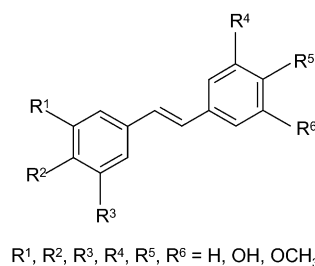
Jon K. F. Geirsson,* Stefan Jonsson and Jon Valgeirsson

**Resveratrol analogues as selective cyclooxygenase-2 inhibitors: synthesis and structure–activity relationship**

pp 5571–5578

Marek Murias, Norbert Handler, Thomas Erker, Karin Pleban, Gerhard Ecker, Philipp Saiko, Thomas Szekeres and Walter Jäger*

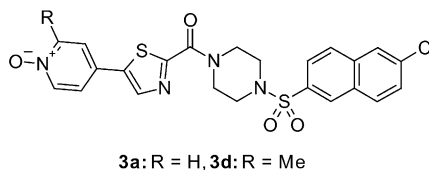
A series of hydroxylated and methoxylated *trans*-stilbenes were synthesized and evaluated for their ability to inhibit COX-1 and COX-2. Some of the hydroxylated derivatives are highly selective COX-2 inhibitor with potency comparable or better than clinically established drugs.

**Design, synthesis, and biological activity of non-amidine factor Xa inhibitors containing pyridine *N*-oxide and 2-carbamoylthiazole units**

pp 5579–5586

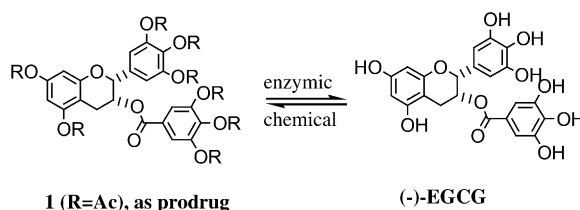
Noriyasu Haginoya,* Syozo Kobayashi, Satoshi Komoriya, Toshiharu Yoshino, Tsutomu Nagata, Yumiko Hirokawa and Takayasu Nagahara

To optimize the S4 binding element of a factor Xa inhibitor, a series of thiazol-5-ylpyridine *N*-oxides **3a–d** were synthesized. Among these compounds, 4-(thiazol-5-yl)pyridine *N*-oxides **3a** and **3d** had potent anti-fXa activities that excelled over the tetrahydrothiazolopyridine derivative **1b** in potency. 2-Methylpyridine *N*-oxide **3d** exhibited moderate selectivity over thrombin.

**A potential prodrug for a green tea polyphenol proteasome inhibitor: evaluation of the peracetate ester of (–)-epigallocatechin gallate [(–)-EGCG]**

pp 5587–5593

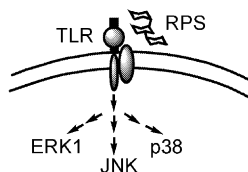
Wai Har Lam, Aslamuzzaman Kazi, Deborah J. Kuhn, Larry M. C. Chow, Albert S. C. Chan, Q. Ping Dou and Tak Hang Chan*



Studies on the immuno-modulating and anti-tumor activities of *Ganoderma lucidum* (Reishi) polysaccharides

pp 5595–5601

Hung-Sen Chen, Yow-Fu Tsai, Steven Lin, Chia-Ching Lin, Kay-Hooi Khoo, Chun-Hung Lin* and Chi-Huey Wong*



Isolation of Reishi polysaccharides for the study of their effect on cytokine expression in mouse splenocytes.

Polysaccharides of *Ganoderma lucidum* alter cell immunophenotypic expression and enhance CD56⁺ NK-cell cytotoxicity in cord blood

pp 5603–5609

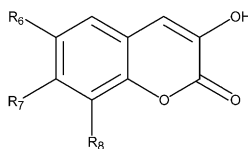
Chichen Michael Chien, Jing-Long Cheng, Wen-Teish Chang, Ming-Hsun Tien, Chien-Ming Tsao, Yung-Han Chang, Hwan-You Chang, Jung-Feng Hsieh, Chi-Huey Wong and Shui-Tein Chen*

Human umbilical cord blood MNCs were treated with polysaccharides of *Ganoderma lucidum* F3 and cultured for 7 days. Analysis of various subsets of UCB mononuclear cells revealed relative increments of macrophage, dendritic cells, and natural killer cells detected by flow cytometry after the culture period.

Antioxidant properties of 3-hydroxycoumarin derivatives

pp 5611–5618

Fabrice Bailly,* Cédric Maurin, Elisabeth Teissier, Hervé Vezin and Philippe Cotelle



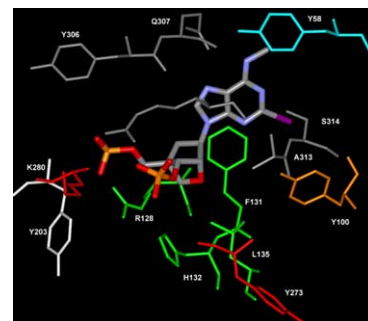
A series of hydroxylated 3-hydroxycoumarins was synthesised and evaluated for their antioxidant properties. The compounds substituted on the C-7 position were almost as antioxidant as quercetin or vitamin C. The antioxidant properties were related by an EPR study to their abilities to give stable semiquinonic or polyhydroxylated radicals.

Nucleotide analogues containing 2-oxa-bicyclo[2.2.1]heptane and L-α-threofuranosyl ring systems: interactions with P2Y receptors

pp 5619–5630

Michihiro Ohno, Stefano Costanzi, Hak Sung Kim, Veerle Kempeneers, Karen Vastmans, Piet Herdewijn, Savitri Maddileti, Zhan-Guo Gao, T. Kendall Harden and Kenneth A. Jacobson*

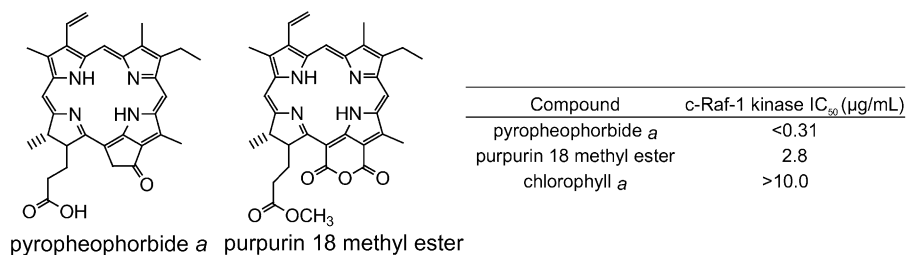
We have synthesized nucleotide analogues substituted with two novel ring systems and examined them as P2Y receptor ligands: (1) a (N) locked-carbocyclic (cLNA) derivative containing the oxabicyclo[2.2.1]heptane ring system and (2) L-α-threofuranosyl derivatives. We have also compared potencies and preferred conformations of these nucleotides with the known anhydrohexitol-containing P2Y₁ receptor antagonist MRS2283.



Using a kinase screen to investigate the constituents of the sponge *Stelletta clavosa* obtained from diverse habitats

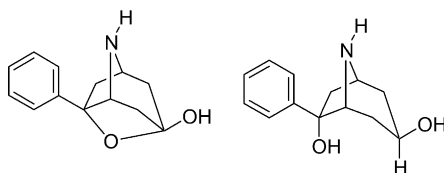
pp 5631–5637

Christopher J. Wegerski, Dennis France, Susan Cornell-Kennon and Phillip Crews*

**Synthesis and biological evaluation of bicyclic and tricyclic substituted nortropane derivatives: discovery of a novel selective α_{1D} -adrenergic receptor ligand**

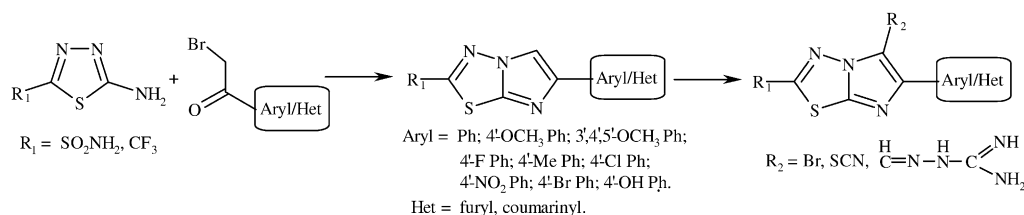
pp 5639–5650

Susan J. McGinty,* Angela Finch, Renate Griffith, Robert M. Graham and John B. Bremner

**Synthesis and anti-tubercular activity of a series of 2-sulfonamido/trifluoromethyl-6-substituted imidazo[2,1-*b*]-1,3,4-thiadiazole derivatives**

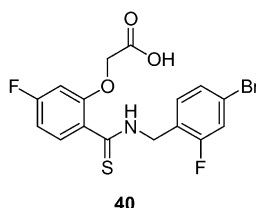
pp 5651–5659

Andanappa K. Gadad,* Malleappa N. Noolvi and Rajshekhar V. Karpoomath

**Design and synthesis of highly potent and selective (2-arylcarbamoyl-phenoxy)-acetic acid inhibitors of aldose reductase for treatment of chronic diabetic complications**

pp 5661–5675

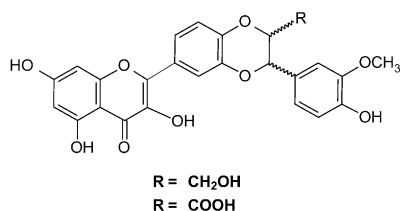
Michael C. Van Zandt,* Evelyn O. Sibley, Erin E. McCann, Kerry J. Combs, Brenda Flam, Diane R. Sawicki, Al Sabetta, Anne Carrington, Janet Sredy, Eduardo Howard, Andre Mitschler and Alberto D. Podjarny



Oxidised derivatives of silybin and their antiradical and antioxidant activity

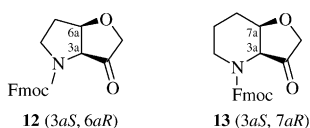
pp 5677–5687

Radek Gažák, Alena Svobodová, Jitka Psotová, Petr Sedmera, Věra Přikrylová,
Daniela Walterová and Vladimír Křen*

**Bicyclic peptidomimetic tetrahydrofuro[3,2-*b*]pyrrol-3-one and hexahydrofuro[3,2-*b*]pyridine-3-one based scaffolds: synthesis and cysteinyl proteinase inhibition**

pp 5689–5710

Martin Quibell,* Alex Benn, Nick Flinn, Tracy Monk, Manoj Ramjee,
Yikang Wang and John Watts

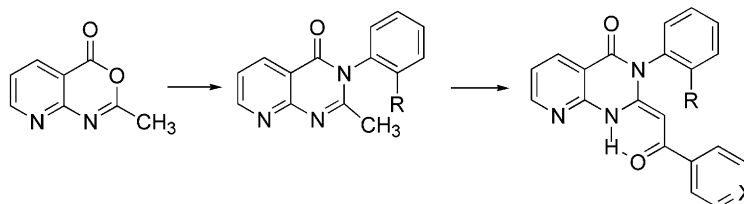


Fmoc protected 5,5 and 6,5-bicyclic ketones **12** and **13** were prepared through the corresponding diazomethylketone intermediates via a lithium chloride/acetic acid promoted carbene insertion reaction. Building blocks **12** and **13** were used in the solid phase synthesis of peptidomimetic inhibitors of a range of CAC1 cysteinyl proteinases. Compound **10**, a potent and selective inhibitor of cathepsin K exhibited promising activity in an in vitro cell-based human osteoclast assay of bone resorption.

Synthesis and anticonvulsant evaluation of some new 2-substituted-3-arylpyrido[2,3-*d*]pyrimidinones

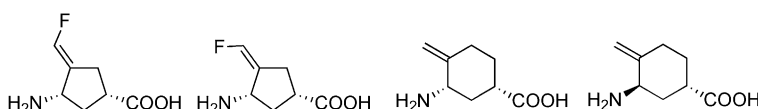
pp 5711–5717

David C. White, Thomas D. Greenwood, Aaron L. Downey, Jeffrey R. Bloomquist and
James F. Wolfe*

**Conformationally-restricted vigabatrin analogs as irreversible and reversible inhibitors of γ -aminobutyric acid aminotransferase**

pp 5719–5725

Yue Pan, Kristi Calvert and Richard B. Silverman*



OTHER CONTENTS

Contributors to this issue
Instructions to contributors

p I
pp III–VII

*Corresponding author

Ⓜ⁺ Supplementary data available via ScienceDirect

COVER

The front cover illustrates an example of a new *cis*-5,5-bicyclic scaffold for the design of potent inhibitors of CAC1 cysteinyl proteinases. Shown is a predicted binding conformation for *si* stereofacial thiolate addition to (3*aS*,6*aR*)-4-*tert*-butyl-*N*-[3-methyl-1-(3-oxo-hexahydrofuro[3,2-*b*]pyrrole-4-carbonyl)butyl]benzamide modelled in an active site slice of the cathepsin K crystal structure 1mem. [Quibell, M.; Benn, A.; Flinn, N.; Monk, T.; Ramjee, M.; Wang, Y.; Watts, J. *Bioorg. Med. Chem.* **2004**, *12*, 5689–5710].
© 2004 M. Quibell. Published by Elsevier Ltd.



Full text of this journal is available, on-line from **ScienceDirect**. Visit www.sciencedirect.com for more information.

CONTENTS
Direct

This journal is part of **ContentsDirect**, the *free* alerting service which sends tables of contents by e-mail for Elsevier books and journals. You can register for **ContentsDirect** online at: <http://contentsdirect.elsevier.com>

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE



ELSEVIER

ISSN 0968-0896