

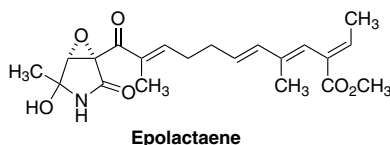
## Contents

### ARTICLES

#### Structure–activity relationships of epolactaene analogs as DNA polymerases inhibitors

pp 1983–1989

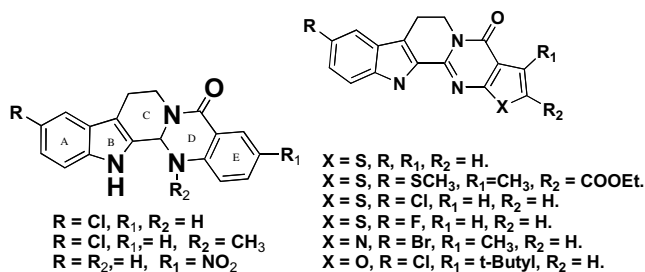
Kouji Kuramochi, Yoshiyuki Mizushina, Seigo Nagata, Fumio Sugawara, Kengo Sakaguchi and Susumu Kobayashi\*



#### Synthesis and cytotoxic activity of novel quinazolino- $\beta$ -carboline-5-one derivatives

pp 1991–1994

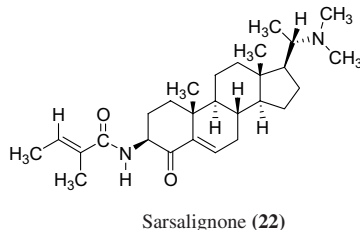
Bipul Baruah, Kavitha Dasu, Balasubramanian Vaitilingam, Premkumar Mamnoor, Prasanthi Penubaka Venkata, Sriram Rajagopal and Koteswar Rao Yeleswarapu\*



#### Kinetics and structure–activity relationship studies on pregnane-type steroidal alkaloids that inhibit cholinesterases

pp 1995–2003

Asaad Khalid, Zaheer-ul-Haq, Shazia Anjum, M. Riaz Khan, Atta-ur-Rahman and M. Iqbal Choudhary\*

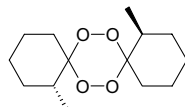


The mechanism of inhibition of acetyl-cholinesterase and butyrylcholinesterase enzymes by natural pregnane-type steroidal alkaloids isolated from *Sarcococca saligna* are discussed.

### Influence of stereoisomer of dispiro-1,2,4,5-tetraoxanes on their binding mode with heme and on antimalarial activity: molecular docking studies

pp 2005–2012

Somsak Tonmunphean,\* Atchara Wijitkosoom and Yuthana Tantirungrotechai

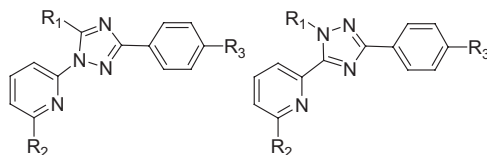


Quantum chemical calculations and automated molecular docking simulations of 13 dispiro-1,2,4,5-tetraoxane compounds were carried out to elucidate the most probable isomer(s) responsible for their antimalarial activity and to investigate an influence of stereoisomer on their binding mode with heme and on antimalarial activity.

### Design, synthesis, and biological evaluation of novel 2-pyridinyl-[1,2,4]triazoles as inhibitors of transforming growth factor $\beta$ 1 type 1 receptor

pp 2013–2020

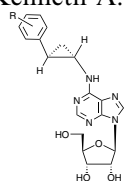
Dae-Kee Kim,\* Joonseop Kim and Hyun-Ju Park



### Exploring distal regions of the $A_3$ adenosine receptor binding site: sterically constrained $N^6$ -(2-phenylethyl)adenosine derivatives as potent ligands

pp 2021–2034

Susanna Tchilibon, Soo-Kyung Kim, Zhan-Guo Gao, Brian A. Harris, Joshua B. Blaustein, Ariel S. Gross, Heng T. Duong, Neli Melman and Kenneth A. Jacobson\*

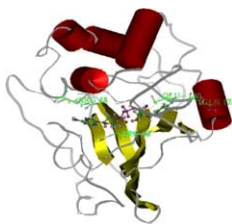


We have synthesized phenyl ring-substituted analogues of  $N^6$ -(1*S*,2*R*)-(2-phenyl-1-cyclopropyl)adenosine, which is highly potent in binding to the human  $A_3$ AR with a  $K_i$  value of 0.63 nM. The effects of these structural changes on affinity at human and rat adenosine receptors and on intrinsic efficacy at the human  $A_3$ AR were measured. A QSAR study of the  $N^6$ -region provided a model that was complementary to the putative  $A_3$ AR binding site in a rhodopsin-based homology model.

### Homology modeling and molecular dynamics studies of a novel C3-like ADP-ribosyltransferase

pp 2035–2041

Jing-fa Xiao, Ze-sheng Li\* and Chia-chung Sun

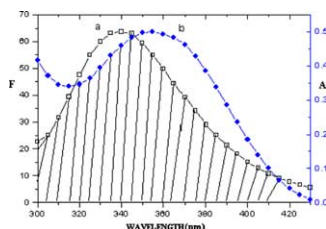


The  $NAD^+$ -enzyme complex is developed by molecular dynamics simulation, which indicates the key binding-site residues are Arg48, Glu180, Ser138, Asn134, Arg85, and Gln179.

**Study of the interactions between tetracycline analogues and lysozyme**

pp 2043–2047

Chong-qiu Jiang\* and Ting Wang

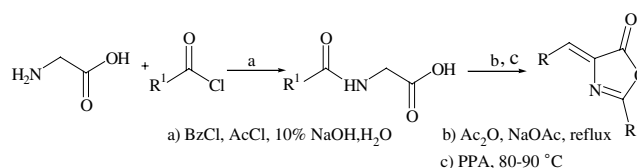


According to Förster dipole–dipole nonradiative energy transfer theory, we determined the energy transfer effect  $E$ , the critical distance  $R_0$ , and the distance between drugs and amino acid residue in LYSO  $r$ . This work shows that the energy transfer between the drugs and LYSO is nonradiative energy transfer. The main acting force between the drugs and LYSO is noncovalent bond action.

**Synthesis and immunomodulatory properties of selected oxazolone derivatives**

pp 2049–2057

Muhammad A. Mesaik, Shagufta Rahat, Khalid M. Khan,\* Zia-Ullah, Muhammad I. Choudhary, Shahnaz Murad, Zakiah Ismail, Atta-ur-Rahman and Aqeel Ahmad\*

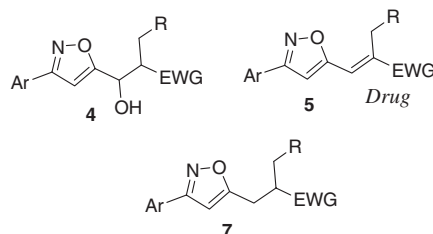


Eleven oxazolone derivatives were synthesized, characterized and screened for phagocyte chemiluminescence, neutrophil chemotaxis, T-cell proliferation, cytokine production from mononuclear cells and cytotoxicity.

**Baylis–Hillman reaction assisted parallel synthesis of 3,5-disubstituted isoxazoles and their in vivo bioevaluation as antithrombotic agents**

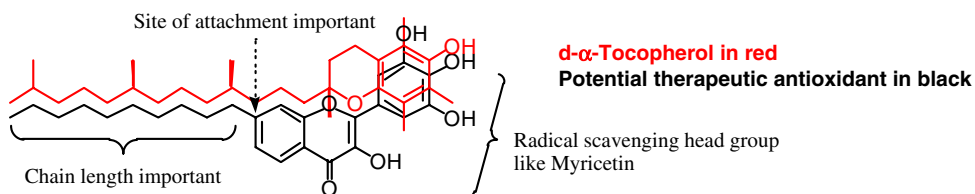
pp 2059–2077

S. Batra,\* A. K. Roy, A. Patra, A. P. Bhaduri, W. R. Surin, S. A. V. Raghavan, P. Sharma, K. Kapoor and M. Dikshit\*

**Potential therapeutic antioxidants that combine the radical scavenging ability of myricetin and the lipophilic chain of vitamin E to effectively inhibit microsomal lipid peroxidation**

pp 2079–2098

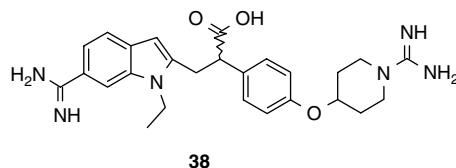
Christopher J. Bennett, Stuart T. Caldwell, Donald B. McPhail, Philip C. Morrice, Garry G. Duthie and Richard C. Hartley\*



**Design, synthesis and biological activity of amidinobicyclic compounds (derivatives of DX-9065a) as factor Xa inhibitors: SAR study of S1 and aryl binding sites**

pp 2099–2114

Satoshi Komoriya,\* Naoaki Kanaya, Takayasu Nagahara, Asako Yokoyama, Kazue Inamura, Yukio Yokoyama, Shin-ichi Katakura and Tsuyoshi Hara

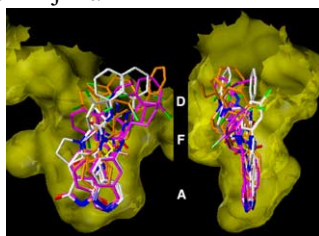


Compound **38** exhibited a high activity toward factor Xa and also showed prolongation of APTT after oral administration in rat.

**Design and synthesis of Rho kinase inhibitors (I)**

pp 2115–2137

Atsuya Takami, Masayuki Iwakubo, Yuji Okada, Takehisa Kawata, Hideharu Odai, Nobuaki Takahashi, Kazutoshi Shindo, Kaname Kimura, Yoshimichi Tagami, Mika Miyake, Kayoko Fukushima, Masaki Inagaki, Mutsuki Amano, Kozo Kaibuchi and Hiroshi Iijima\*

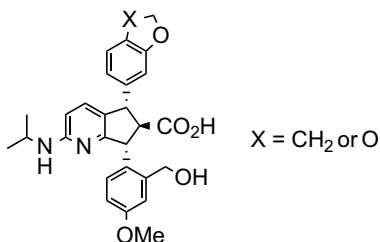


Structure-based design of several scaffolds of Rho kinase inhibitor was performed by using pharmacophore information obtained from a high-throughput screening and the enzyme homology model.

**Potent and orally active ET<sub>A</sub> selective antagonists with 5,7-diarylcyclopenteno[1,2-*b*]pyridine-6-carboxylic acid structures**

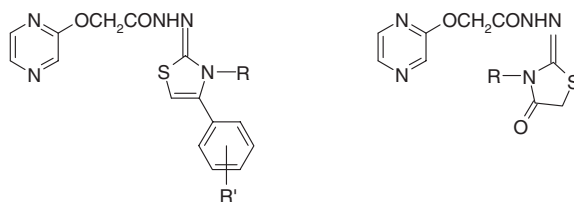
pp 2139–2150

Takashi Yoshizumi,\* Hirobumi Takahashi, Norikazu Ohtake, Hideki Jona, Yoshiyuki Sato, Hiroyuki Kishino, Toshihiro Sakamoto, Satoshi Ozaki, Hiroyuki Takahashi, Yoshihiro Shibata, Yasuyuki Ishii, Michiyasu Saito, Megumu Okada, Takashi Hayama and Masaru Nishikibe


**Synthesis and preliminary evaluation of some pyrazine containing thiazolines and thiazolidinones as antimicrobial agents**

pp 2151–2161

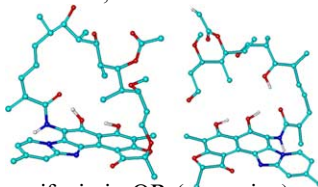
Chandrakant G. Bonde\* and Naresh J. Gaikwad



### Solution structure of rifaximin and its synthetic derivative rifaximin OR determined by experimental NMR and theoretical simulation methods

pp 2163–2172

Silvia Martini,\* Claudia Bonechi, Gianfranco Corbini, Alessandro Donati and Claudio Rossi



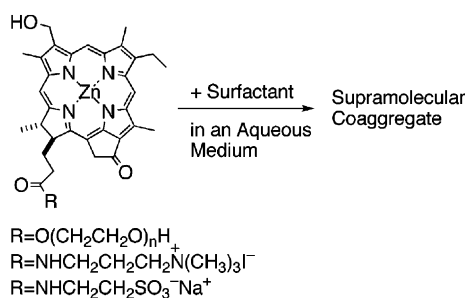
The solution structure of rifaximin and its derivative rifaximin OR (open ring) were determined by combining NMR experimental results, theoretical simulation of two-dimensional NMR spectra by complete relaxation matrix analysis (CORMA), and molecular dynamics calculations.

In this study the structural rearrangements due to the opening of the aliphatic chain of rifaximin after the reduction process to form rifaximin OR were investigated.

### Coaggregate of amphiphilic zinc chlorins with synthetic surfactants in an aqueous medium to an artificial supramolecular light-harvesting system

pp 2173–2178

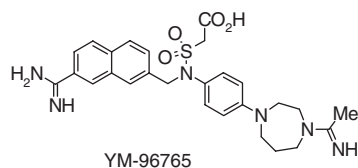
Tomohiro Miyatake,\* Hitoshi Tamiaki,\* Manabu Fujiwara and Takayuki Matsushita



### Synthesis and biological activity of novel 1,4-diazepane derivatives as factor Xa inhibitor with potent anticoagulant and antithrombotic activity

pp 2179–2191

Hiroyuki Koshio,\* Fukushi Hirayama, Tsukasa Ishihara, Yuta Taniuchi, Kazuo Sato, Yumiko Sakai-Moritani, Seiji Kaku, Tomihisa Kawasaki, Yuzo Matsumoto, Shuichi Sakamoto and Shin-ichi Tsukamoto



A series of fXa inhibitors based on a 1,4-diazepane template as the P4 moiety were prepared and evaluated for inhibitory activity against factor Xa in vitro and ex vivo. YM-96765 showed nanomolar potency in fXa inhibitory activity and had excellent oral anticoagulant activity. Moreover, this compound showed effective oral antithrombotic activity.

### Cytotoxicity of phenylpropanoid esters from the stems of *Hibiscus taiwanensis*

pp 2193–2197

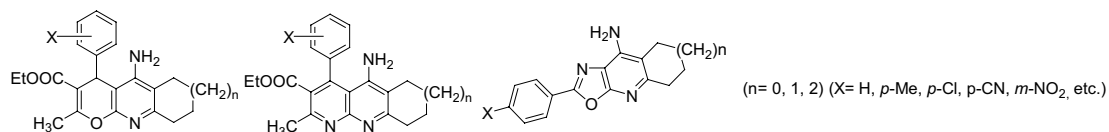
Pei-Lin Wu,\* Ta-Hsien Chuang, Cai-Xia He and Tian-Shung Wu\*

Three new phenylpropanoid esters, (7*S*,8*S*)-demethylcarolignan E (1), hibiscuwanin A (2), hibiscuwanin B (3), in addition to eight known ones were isolated from the stems of *Hibiscus taiwanensis*. Among those isolates, 9,9-*O*-feruloyl-(–)-secoisolaricinresinol (8) showed strong cytotoxic activity against human lung carcinoma and breast carcinoma cell lines with EC<sub>50</sub> values of 1.8 and 3.9 μg/mL, respectively.

**Synthesis, biological evaluation and molecular modelling of diversely functionalized heterocyclic derivatives as inhibitors of acetylcholinesterase/butyrylcholinesterase and modulators of  $\text{Ca}^{2+}$  channels and nicotinic receptors**

pp 2199–2218

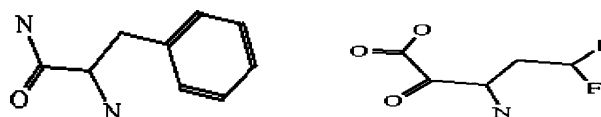
José L. Marco,\* Cristóbal de los Ríos, Antonio G. García, Mercedes Villarroja, M. Carmo Carreiras,\* Carla Martins, Ana Eleutério, Antonio Morreale, M. Orozco and F. Javier Luque



**Exploring the binding mechanism of the main proteinase in SARS-associated coronavirus and its implication to anti-SARS drug design**

pp 2219–2223

Xue Wu Zhang\* and Yee Leng Yap

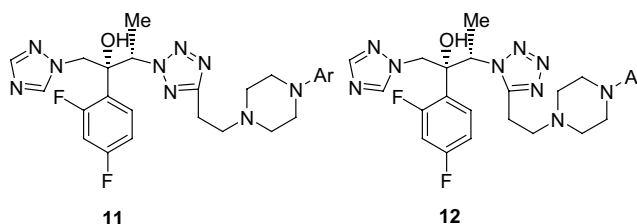


The structural similarities of SARS-CoV main proteinase with HAV 3c protease and HCV Ns3 protease suggest that the available inhibitors in these proteases could be useful for anti-SARS drug design.

**Optically active antifungal azoles: synthesis and antifungal activity of (2*R*,3*S*)-2-(2,4-difluorophenyl)-3-(5-{2-[4-aryl-piperazin-1-yl]-ethyl}-tetrazol-2-yl/1-yl)-1-[1,2,4]-triazol-1-yl-butan-2-ol**

pp 2225–2238

Ram Shankar Upadhayaya, Neelima Sinha, Sanjay Jain, Nawal Kishore, Ramesh Chandra and Sudershan K. Arora\*

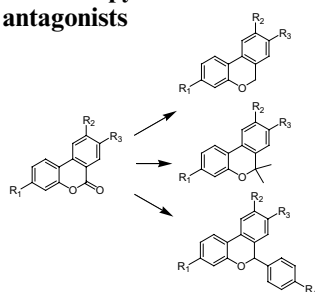


A series of (2*R*,3*S*)-2-(2,4-difluorophenyl)-3-(5-{2-[4-aryl-piperazin-1-yl]-ethyl}-tetrazol-2-yl/1-yl)-1-[1,2,4]-triazol-1-yl-butan-2-ol **11** and **12** has been synthesized and screened for their antifungal activity.

**Synthesis and biological activities of some new dibenzopyranones and dibenzopyrans: search for potential oestrogen receptor agonists and antagonists**

pp 2239–2249

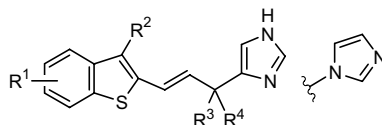
Jaya Pandey, Ashok K. Jha and K. Hajela\*



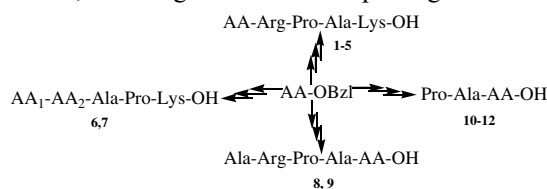
Some new tricyclic molecules namely substituted dibenzopyranones and dibenzopyrans bridged between the active molecules of 3,4-diaryl chroman and 2,3-diaryl benzopyrans have been synthesised and screened for their oestrogen receptor agonist and antagonist activities.

**C<sub>17,20</sub>-Lyase inhibitors I. Structure-based de novo design and SAR study of C<sub>17,20</sub>-lyase inhibitors** pp 2251–2273

Nobuyuki Matsunaga,\* Tomohiro Kaku, Fumio Itoh, Toshimasa Tanaka, Takahito Hara, Hiroshi Miki, Masahiko Iwasaki, Tetsuya Aono, Masuo Yamaoka, Masami Kusaka and Akihiro Tasaka

**The composition and sequence specificity of Pro-Ala-Lys-OH for the thrombolytic activities of P6A and related oligopeptides** pp 2275–2286

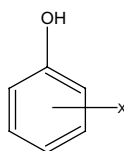
Ming Zhao, Chao Wang, Jiangyuan Liu, Kexiang Zhou and Shiqi Peng\*



In 1–5 AA=Ala (1), Gln (2), Gly (3), Lys (4), Arg (5), respectively; in 6 AA<sub>1</sub>=Ala, AA<sub>2</sub>=Arg; in 7 AA<sub>1</sub>, AA<sub>2</sub>, and Ala together=Ala; in 8 AA=*n*Leu; in 9 AA=Arg; in 10 AA=*n*Leu; in 11 AA=Arg; in 12 AA=Lys. Comparing with Ala-Arg-Pro-Ala-Lys-OH in the in vivo and in vivo thrombolytic assays the Pro-Ala-Lys-OH sequence containing peptides exhibited comparable or enhanced activity, and the non-Pro-Ala-Lys-OH peptides exhibited no activity.

**QSAR study on phenolic activity: need of positive hydrophobic term (log *P*) in QSAR** pp 2287–2293

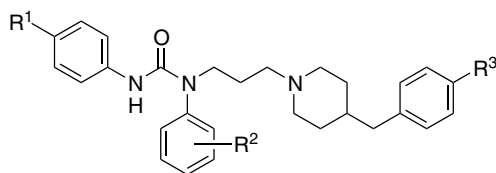
Mamta Thakur, Alok Agarwal, Abhilash Thakur and Padmakar V. Khadikar\*



The phenolic activity (log 1/*C*) of a large series of phenols against L1210 leukaemia cells was modelled using physicochemical parameters, other than conventional electronic and steric parameters. Attempts have also been made to examine need or otherwise of the hydrophobic parameter (log *P*), in such studies. The results have shown that contribution of log *P* in modelling log 1/*C* is favourable.

**CCR5 antagonists as anti-HIV-1 agents. Part 2: Synthesis and biological evaluation of *N*-[3-(4-benzylpiperidin-1-yl)propyl]-*N,N'*-diphenylureas** pp 2295–2306

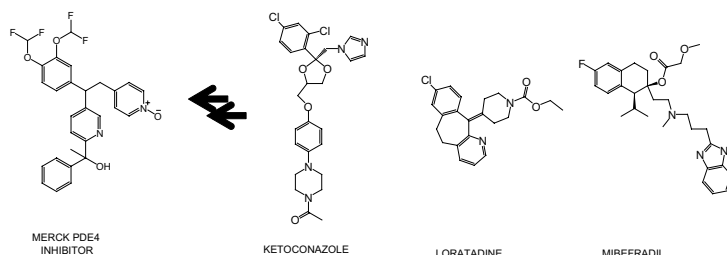
Shinichi Imamura,\* Osamu Kurasawa, Yoshi Nara, Takashi Ichikawa, Youichi Nishikawa, Takehiro Iida, Shohei Hashiguchi, Naoyuki Kanzaki, Yuji Iizawa, Masanori Baba and Yoshihiro Sugihara



**A model for identifying HERG K<sup>+</sup> channel blockers**

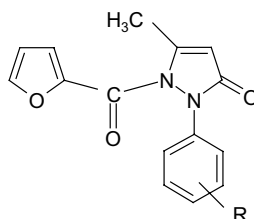
pp 2307–2315

Alex M. Aronov\* and Brian B. Goldman

**De novo design and synthesis of HIV-1 integrase inhibitors**

pp 2317–2333

Mahindra T. Makhija,\* Rajesh T. Kasliwal, Vithal M. Kulkarni and Nouri Neamati

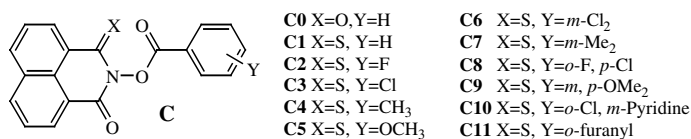


Novel HIV-1 integrase inhibitors were designed using a de novo design method LeapFrog, synthesized, and tested for in vitro inhibition of HIV-1 integrase.

***N*-Aroyloxylthioxo-naphthalimides as DNA photocleavers of aroyloxyl oxygen radicals: synthesis, evaluation, and substituents' effect**

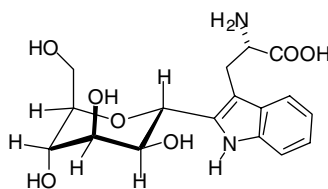
pp 2335–2341

Yufang Xu, Xiayu Huang, Xuhong Qian\* and Wei Yao

**α-*C*-Mannosyltryptophan is not recognized by conventional mannose-binding lectins**

pp 2343–2348

Toshio Nishikawa,\* Shigeo Kajii, Chihiro Sato, Zenta Yasukawa, Ken Kitajima and Minoru Isobe

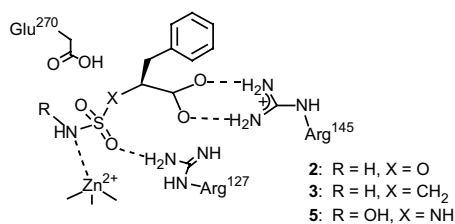




**Sulfamide derivatives as transition state analogue inhibitors for carboxypeptidase A**

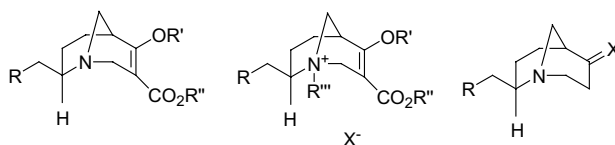
pp 2349–2356

Jung Dae Park and Dong H. Kim\*

**C(8)-Substituted 1-azabicyclo[3.3.1]non-3-enes: a novel scaffold for muscarinic receptor ligands**

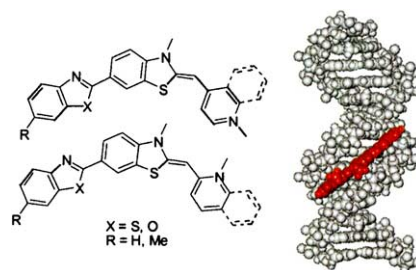
pp 2357–2367

Myoung Goo Kim, Erik T. Bodor, T. Kendall Harden\* and Harold Kohn\*

**Syntheses and DNA-binding studies of a series of unsymmetrical cyanine dyes: structural influence on the degree of minor groove binding to natural DNA**

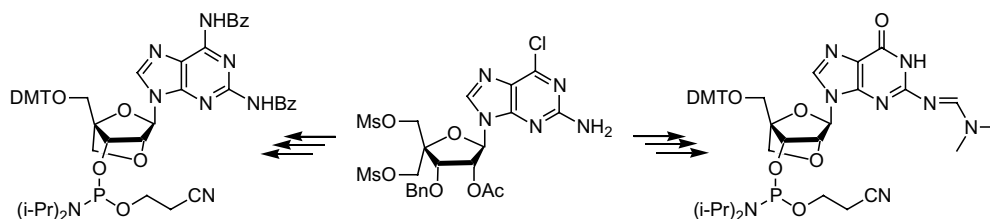
pp 2369–2384

H. Jonas Karlsson,\* Mattias H. Bergqvist, Per Lincoln and Gunnar Westman\*

**LNA guanine and 2,6-diaminopurine. Synthesis, characterization and hybridization properties of LNA 2,6-diaminopurine containing oligonucleotides**

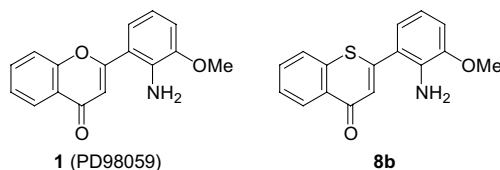
pp 2385–2396

Christoph Rosenbohm, Daniel Sejer Pedersen, Miriam Frieden, Flemming R. Jensen, Susan Arent, Sine Larsen and Troels Koch\*



## Synthesis and structure–activity relationships of thioflavone derivatives as specific inhibitors of the ERK-MAP kinase signaling pathway pp 2397–2407

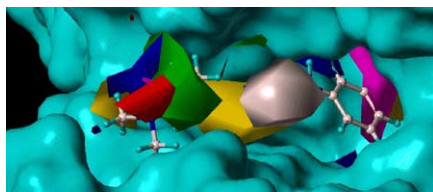
Tadashi Kataoka,\* Shin-ichi Watanabe, Eiji Mori, Ryoji Kadomoto, Susumu Tanimura and Michiaki Kohno\*



In a cell-based assay, 2-(2'-amino-3'-methoxyphenyl)-4*H*-1-benzothiopyran-4-one (**8b**) showed a more potent inhibitory effect than the corresponding oxygen compound (PD98059, **1**) on the Raf-induced activation of the ERK-MAP kinase pathway as well as cell proliferation.

## Elucidating inhibitory models of the inhibitors of epidermal growth factor receptor by docking and 3D-QSAR pp 2409–2417

Gang Chen, Xiaomin Luo,\* Weiliang Zhu, Cheng Luo, Hong Liu, Chum Mok Puah, Kaixian Chen and Hualiang Jiang\*

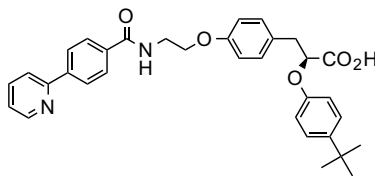


One hundred and twenty four EGFR PTK's inhibitors with different scaffolds were used in CoMFA and CoMSIA studies. Highly reliable and predictive 3D-QSAR models were derived, which reveal how steric, electrostatic, and hydrophobic interactions contribute to inhibitors' bioactivities.



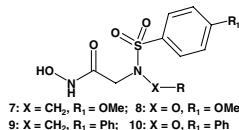
## Synthesis and biological activity of novel $\alpha$ -substituted $\beta$ -phenylpropionic acids having pyridin-2-ylphenyl moiety as antihyperglycemic agents pp 2419–2439

Makoto Takamura,\* Mitsuya Sakurai, Eriko Yamada, Sachie Fujita, Makoto Yachi, Toshiyuki Takagi, Aya Isobe, Yuka Hagsawa, Toshihiko Fujiwara and Hiroaki Yanagisawa



## New *N*-arylsulfonyl-*N*-alkoxyaminoacetohydroxamic acids as selective inhibitors of gelatinase A (MMP-2) pp 2441–2450

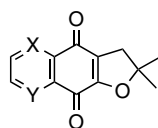
Armando Rossello,\* Elisa Nuti, Elisabetta Orlandini, Paolo Carelli, Simona Rapposelli, Marco Macchia, Filippo Minutolo, Laura Carbonaro, Adriana Albini, Roberto Benelli, Giovanni Cercignani, Gillian Murphy and Aldo Balsamo



New *N*-arylsulfonyl-substituted alkoxyaminoacetohydroxamic acid derivatives of types **8** and **10** were synthesized and tested for their inhibitory activities on some matrix metalloproteinases. The combination of a biphenylsulfonamide group with oxyamino oxygen in the pharmacophoric central skeleton of sulfonamide-based MMPi obtained in the new sulfonamides **10** seems to be able to give selectivity for MMP-2 over MMP-1. The most potent derivative of this type shows anti-invasive properties in an in vitro model of invasion on matrigel, carried out on cellular lines of fibrosarcoma HT1080.

## Synthesis of dihydronaphthofurandiones and dihydrofuroquinolinediones with trypanocidal activity and analysis of their stereoelectronic properties pp 2451–2458

Ricardo A. Tapia,\* Cristian Salas, Antonio Morello, Juan Diego Maya and Alejandro Toro-Labbé

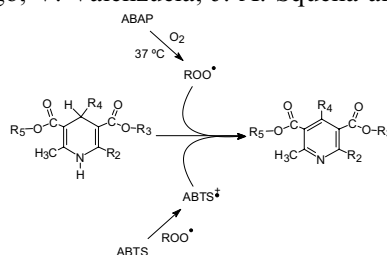


**10** X = C, Y = N  
**11** X = N, Y = C

The synthesis and trypanocidal activity of some dihydronaphthofurandiones and dihydrofuroquinolinediones is described. Compounds **10** and **11** have shown potent trypanocidal activity. Relationships between the stereoelectronic properties and the trypanocidal activity of these heterocyclic quinones are discussed.

## Structural effects on the reactivity 1,4-dihydropyridines with alkylperoxyl radicals and ABTS radical cation pp 2459–2468

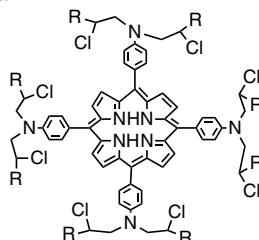
C. Yáñez, C. López-Alarcón, C. Camargo, V. Valenzuela, J. A. Squella and L. J. Núñez-Vergara\*



A series of eight commercial C-4 substituted 1,4-dihydropyridines and other synthesized related compounds were tested for direct potential scavenger effect towards alkylperoxyl radicals and ABTS radical cation in aqueous Britton–Robinson buffer pH 7.4. The pyridine derivative was confirmed by GC/MS technique as the final product of reaction.

## Chloroalkyl piperazine and nitrogen mustard porphyrins: synthesis and anticancer activity pp 2469–2475

Can-Cheng Guo,\* Rong-Biao Tong and Ke-Lai Li

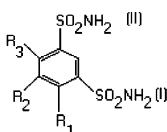


R = H, CH<sub>3</sub>, CH<sub>2</sub>Cl

Fifteen new chloroalkyl piperazine and nitrogen mustard porphyrins have been synthesized. Most of the synthetic porphyrins had good anticancer activity toward bel-7404 liver cancer cell in the absence of light. They might have potential applications in medicine.

## QSAR study on CA inhibitory activity of disulfonamides: effect of halogen substitution pp 2477–2482

Mona Jaiswal, Padmakar V. Khadikar\* and Claudiu T. Supuran

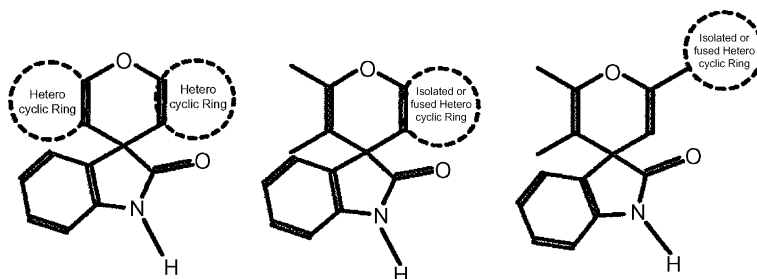


The paper deals with quantitative structure–activity relationship (QSAR) study on CA inhibitory activity (log IC<sub>50</sub>) of disulfonamides using a large series of distance-based topological indices. The study discusses effect due to halogen-substitution nearer (*o*-position) to –SO<sub>2</sub>NH<sub>2</sub> groups. The results have shown that halogen substitution at R<sub>3</sub> has pronounced effect on the inhibitory activity. Predictive power of the proposed models is discussed on the basis of regression data and cross-validation parameters.

**Synthesis and evaluation of some new spiro indoline-based heterocycles as potentially active antimicrobial agents**

pp 2483–2488

A. H. Abdel-Rahman,\* E. M. Keshk, M. A. Hanna and Sh. M. El-Bady

**OTHER CONTENTS**

Corrigendum

Contributors to this issue

Instructions to contributors

p 2489

p I–II

pp III–VII

\*Corresponding author

①\* Supplementary data available via ScienceDirect

**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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