

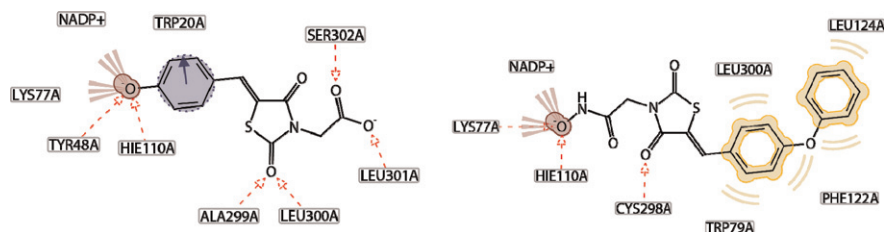
## Contents

### ARTICLES

#### Synthesis, induced-fit docking investigations, and in vitro aldose reductase inhibitory activity of non-carboxylic acid containing 2,4-thiazolidinedione derivatives

pp 5840–5852

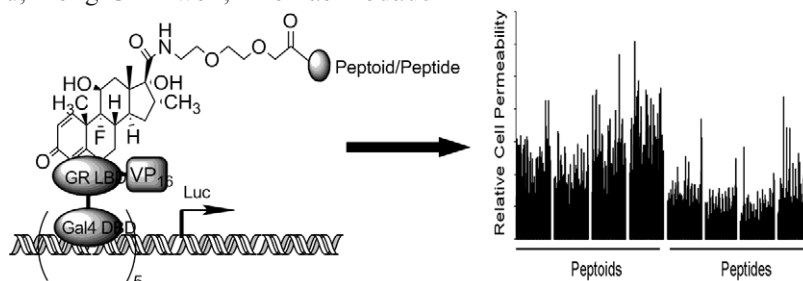
Rosanna Maccari\*, Rosaria Ottanà, Rosella Ciurleo, Dietmar Rakowitz, Barbara Matuszczak, Christian Laggner, Thierry Langer



#### High-throughput evaluation of relative cell permeability between peptoids and peptides

pp 5853–5861

Niclas C. Tan, Peng Yu, Yong-Uk Kwon, Thomas Kodadek\*



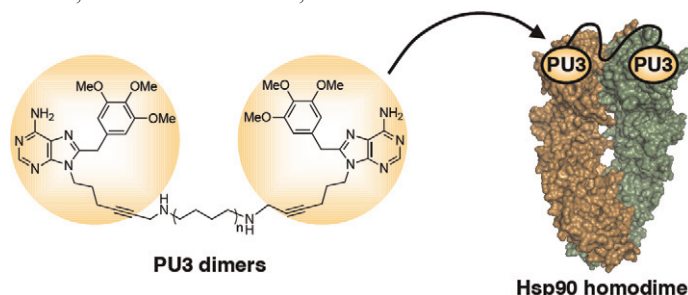
Physicochemical properties evaluation of peptoids and peptides to investigate the higher relative cell permeability of peptoids observed in high-throughput permeability assay.



#### Synthesis of Hsp90 inhibitor dimers as potential antitumor agents

pp 5862–5870

Kazuhiro Muranaka, Akiko Sano, Satoshi Ichikawa\*, Akira Matsuda\*



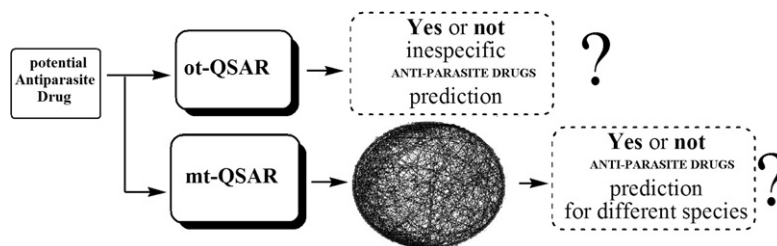
Structure-based drug design was used to systematically synthesize PU3-dimers. Their cytotoxic potency increased as the length of the bridging linker increased.



### Unified QSAR approach to antimicrobials. Part 3: First multi-tasking QSAR model for Input-Coded prediction, structural back-projection, and complex networks clustering of antiprotozoal compounds

pp 5871–5880

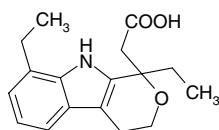
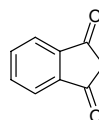
Francisco J. Prado-Prado, Humberto González-Díaz,\* Octavio Martinez de la Vega, Florencio M. Ubeira and Kuo-Chen Chou



### Towards the first inhibitors of trihydroxynaphthalene reductase from *Curvularia lunata*: Synthesis of artificial substrate, homology modelling and initial screening

pp 5881–5889

Mojca Brunskole, Bogdan Štefane, Karmen Zorko, Marko Anderluh, Jure Stojan, Tea Lanišnik Rižner and Stanislav Gobec\*

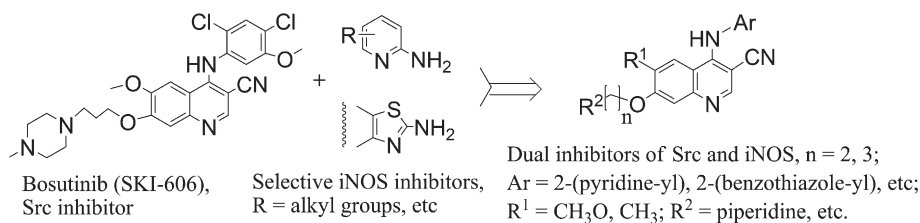
 $IC_{50} = 17 \mu M$  $IC_{50} = 66 \mu M$ 

A series of compounds were screened on trihydroxynaphthalene reductase from *Curvularia lunata*, a known plant pathogen and an opportunistic human pathogen, and several structurally diverse hits were obtained. Homology model of the enzyme was built to enable further structure-based design of new and improved inhibitors.

### Design and synthesis of 7-alkoxy-4-heteroaryl-amino-3-quinolinecarbonitriles as dual inhibitors of $c$ -Src kinase and nitric oxide synthase

pp 5890–5898

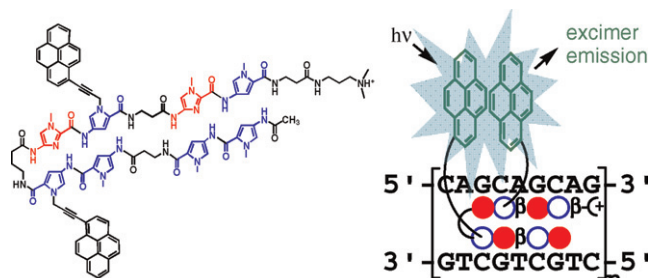
Xin Cao, Qi-Dong You,\* Zhi-Yu Li, Qing-Long Guo, Jing Shang, Ming Yan, Ji-Wang Chern and Men-Ling Chen



### Detection of triplet repeat sequences in the double-stranded DNA using pyrene-functionalized pyrrole-imidazole polyamides with rigid linkers

pp 5899–5907

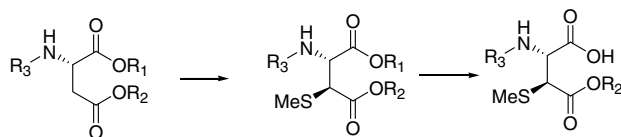
Jun Fujimoto, Toshikazu Bando,\* Masafumi Minoshima, Shinsuke Uchida, Makoto Iwasaki, Ken-ichi Shinohara and Hiroshi Sugiyama\*



**Synthesis of  $\beta$ -(S-methyl)thioaspartic acid and derivatives**

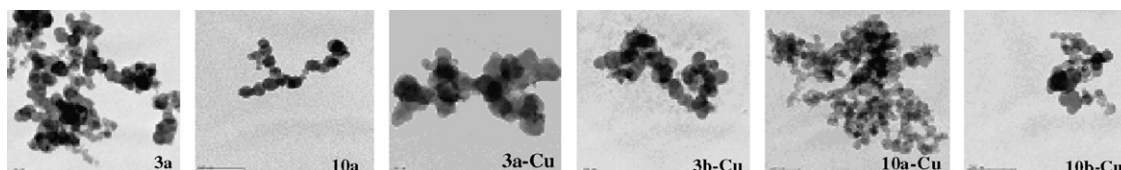
pp 5908–5913

Jorge Heredia-Moya and Kenneth L. Kirk\*

**Synthesis, nano-scale assembly, and in vivo anti-thrombotic activity of novel short peptides containing L-Arg and L-Asp or L-Glu**

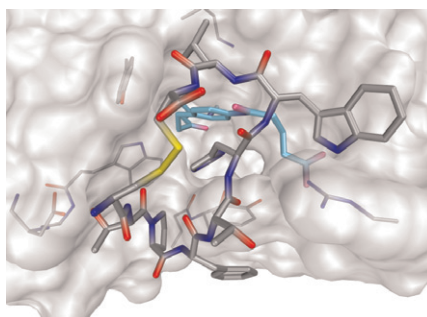
pp 5914–5925

Yu Chen, Guohui Cui, Ming Zhao,\* Chao Wang, Keduo Qian, Susan Morris-Natschke, Kuo-Hsiung Lee\* and Shiqi Peng\*

**Selection of phage-displayed peptides that bind to a particular ligand-bound antibody**

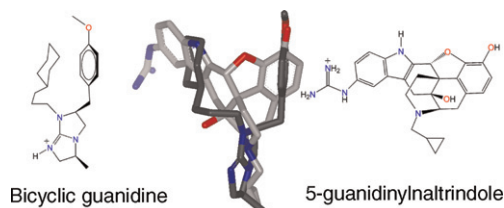
pp 5926–5931

Fujie Tanaka,\* Yunfeng Hu, Jori Sutton, Lily Asawapornmongkol, Roberta Fuller, Arthur J. Olson,\* Carlos F. Barbas, III\* and Richard A. Lerner

**Conformation-opioid activity relationships of bicyclic guanidines from 3D similarity analysis**

pp 5932–5938

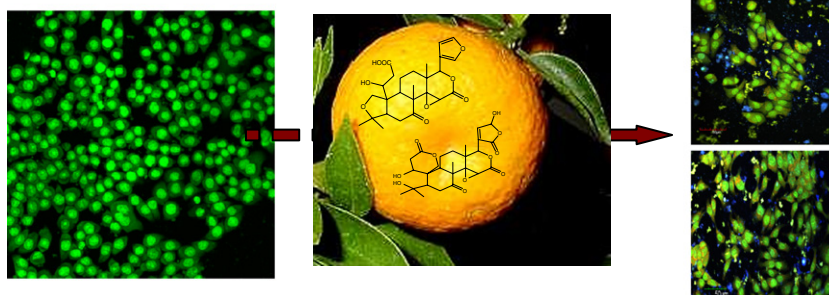
Karina Martínez-Mayorga,\* Jose L. Medina-Franco, Marc A. Giulianotti, Clemencia Pinilla, Colette T. Dooley, Jon R. Appel and Richard A. Houghten



**Novel triterpenoid from *Citrus aurantium* L. possesses chemopreventive properties against human colon cancer cells**

pp 5939–5951

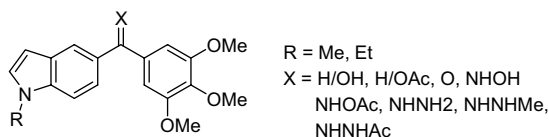
G. K. Jayaprakasha, K. K. Mandadi, S. M. Poullose, Y. Jadegoud, G. A. Nagana Gowda and Bhimanagouda S. Patil\*



**Diarylmethyloxime and hydrazone derivatives with 5-indolyl moieties as potent inhibitors of tubulin polymerization**

pp 5952–5961

Concepción Álvarez, Raquel Álvarez, Purificación Corchete, José Luis López, Concepción Pérez-Melero, Rafael Peláez\* and Manuel Medarde\*



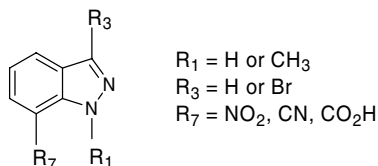
The synthesis and biological evaluation of indolylphenstatins, modified on the bridge, are described.



**Inhibitory effects of a series of 7-substituted-indazoles toward nitric oxide synthases: Particular potency of 1*H*-indazole-7-carbonitrile**

pp 5962–5973

Betty Cottyn, Francine Acher, Booma Ramassamy, Luke Alvey, Michel Lepoivre, Yves Frapart, Dennis Stuehr, Daniel Mansuy, Jean-Luc Boucher and Dominique Vichard\*

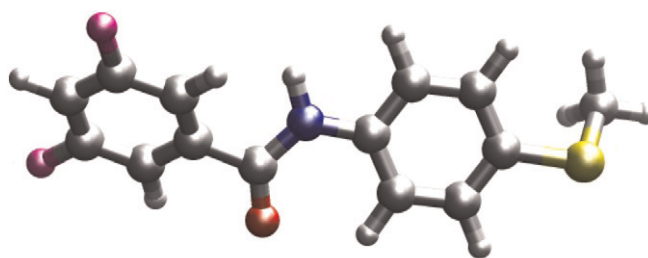


A series of new 7-monosubstituted and 3,7-disubstituted indazoles have been synthesized and tested as inhibitors of nitric oxide synthases.

**Benzanilides with spasmolytic activity: Chemistry, pharmacology, and SAR**

pp 5974–5981

Gerda Brunhofer, Norbert Handler, Klaus Leisser, Christian R. Studenik and Thomas Erker\*

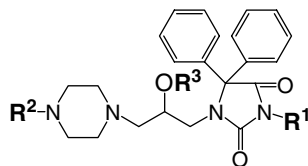


IC<sub>50</sub> 3.25 μM

### Synthesis, $\alpha_1$ -adrenoceptor antagonist activity, and SAR study of novel arylpiperazine derivatives of phenytoin

pp 5982–5998

Jadwiga Handzlik, Dorota Maciąg, Monika Kubačka, Szczepan Mogilski, Barbara Filipek, Katarzyna Stadnicka and Katarzyna Kieć-Kononowicz\*

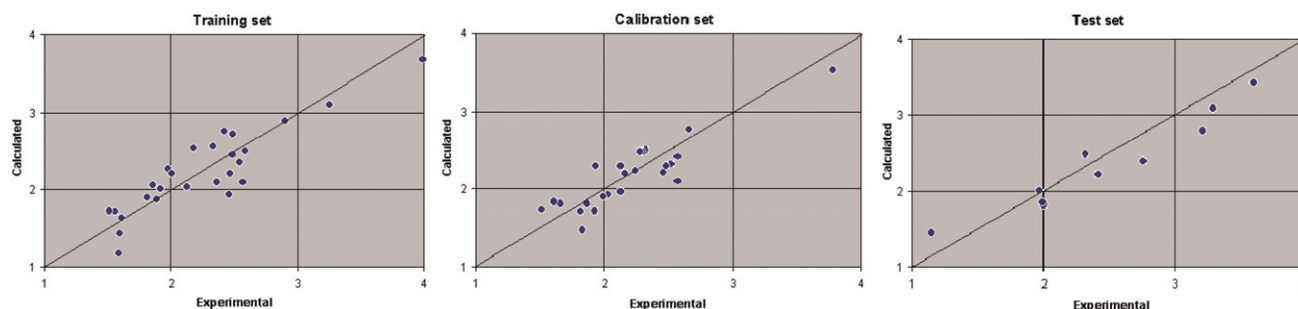


The preparation of series of 3-ethyl-1-[2-hydroxy-3-(4-phenylpiperazin-1-yl)-propyl]-2,4-dioxo-5,5-diphenylimidazolidine derivatives, as  $\alpha_1$ -adrenoceptors antagonists is described. Radioligand binding assays, functional bioassays and SAR study were carried out.

### QSAR modeling of acute toxicity by balance of correlations

pp 5999–6008

Andrey A. Toropov,\* Bakhtiyor F. Rasulev and Jerzy Leszczynski

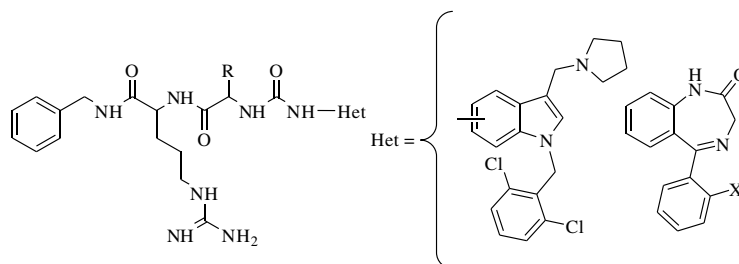


### Synthesis and pharmacological evaluation of peptide-mimetic protease-activated receptor-1 antagonists containing novel heterocyclic scaffolds

pp 6009–6020

Beatrice Severino, Ferdinando Fiorino, Elisa Perissutti, Francesco Frecentese, Giuseppe Cirino, Fiorentina Roviezzo, Vincenzo Santagada and Giuseppe Caliendo\*

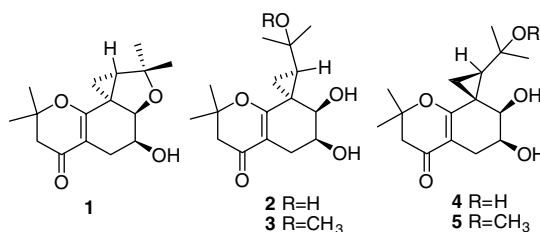
Here, we describe the synthesis and the pharmacological evaluation of novel PAR-1 peptide-mimetic antagonists characterized by the presence of new heterocyclic nuclei such as 2-methyl-indole (5- and 6-substituted) and 1,4-benzodiazepine moiety.



### Pestaloficiols A–E, bioactive cyclopropane derivatives from the plant endophytic fungus *Pestalotiopsis fici*

pp 6021–6026

Ling Liu, Renrong Tian, Shuchun Liu, Xulin Chen, Liangdong Guo and Yongsheng Che\*



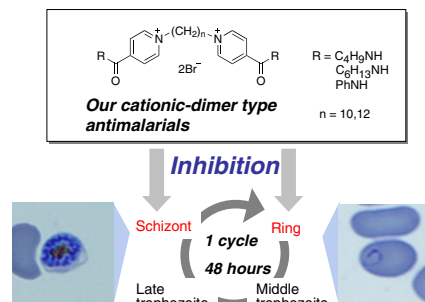
Pestaloficiols A–E (1–5), five new cyclopropane derivatives, have been isolated from the plant endophyte *Pestalotiopsis fici* and evaluated for anti-HIV-1 activity.

**Pyridinium cationic-dimer antimalarials, unlike chloroquine, act selectively between the schizont stage and the ring stage of *Plasmodium falciparum***

pp 6027–6033

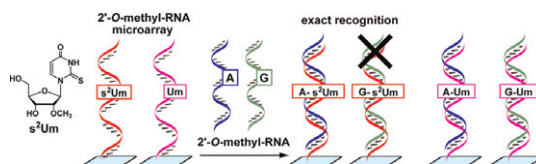
Mai Yoshikawa, Kazunori Motoshima, Kanji Fujimoto, Akihiro Tai, Hiroki Kakuta\* and Kenji Sasaki

Cationic-dimer type antimalarials of the MAP series act selectively between the schizont stage and the ring stage of *Plasmodium falciparum*.


**Study of the base discrimination ability of DNA and 2'-O-methylated RNA oligomers containing 2-thiouracil bases towards complementary RNA or DNA strands and their application to single base mismatch detection**

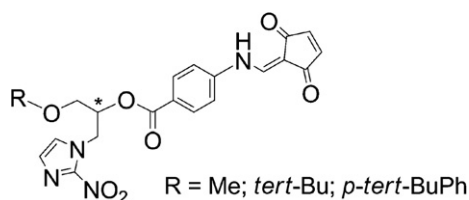
pp 6034–6041

Itaru Okamoto, Kohji Seio and Mitsuo Sekine\*


**Design of antiangiogenic hypoxic cell radiosensitizers: 2-Nitroimidazoles containing a 2-aminomethylene-4-cyclopentene-1,3-dione moiety**

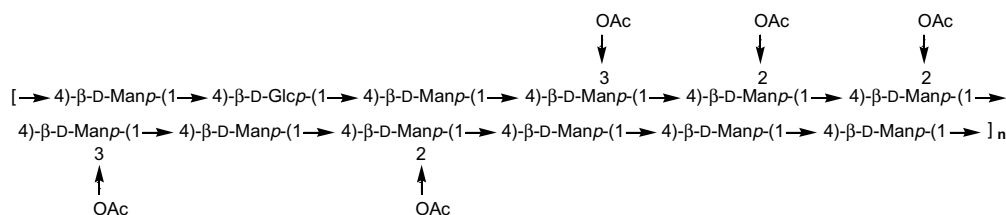
pp 6042–6053

Yoshihiro Uto, Hideko Nagasawa, Cheng-Zhe Jin, Shinichi Nakayama, Ayako Tanaka, Saori Kiyoi, Hitomi Nakashima, Mariko Shimamura, Seiichi Inayama, Tomoya Fujiwara, Yoshio Takeuchi, Yoshimasa Uehara, Kenneth L. Kirk, Eiji Nakata and Hitoshi Hori\*


**Structure and bioactivity of the polysaccharides in medicinal plant *Dendrobium huoshanense***

pp 6054–6068

Yves S.-Y. Hsieh, Cheng Chien, Sylvian K.-S. Liao, Shih-Fen Liao, Wei-Ting Hung, Wen-Bin Yang\*, Chih-Chien Lin, Ting-Jen Rachel Cheng, Chia-Chuan Chang, Jim-Min Fang\* and Chi-Huey Wong\*



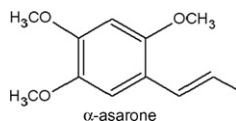
The glucomannan isolated from the mucilage of *Dendrobium huoshanense* with  $\beta$ -(1  $\rightarrow$  4) linkages and partial acetylation was found to induce the expression of G-CSF, IL-6, and other cytokines.



**Genotoxicity of  $\alpha$ -asarone analogues**

pp 6069–6074

Ewa Karwicka,\* Jadwiga Marczevska, Elżbieta Anuszevska,  
Bożena Łozowicka and Zdzisław Chilmonczyk

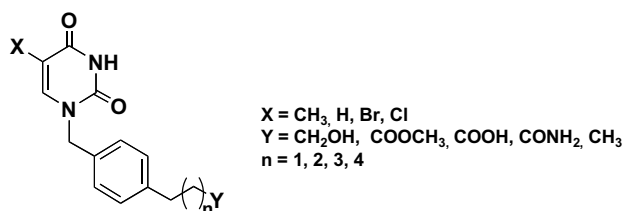


$\alpha$ -Asarone isolated from plants express hypolipidemic activity. In the present paper, we evaluated mutagenic and genotoxic activity of four  $\alpha$ -asarone isomers based on the reference Ames test and micronucleus test.

**Substituted benzyl-pyrimidines targeting thymidine monophosphate kinase of *Mycobacterium tuberculosis*: Synthesis and in vitro anti-mycobacterial activity**

pp 6075–6085

Cécile Gasse, Dominique Douguet, Valérie Huteau, Gilles Marchal, Hélène Munier-Lehmann and Sylvie Pochet\*

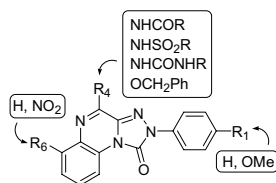


A series of *N*<sup>1</sup>-(4-substituted-benzyl)-pyrimidines as potential inhibitors of thymidine monophosphate kinase of *Mycobacterium tuberculosis* were synthesized and evaluated for their ability to inhibit recombinant enzyme and mycobacterial growth in vitro.

**Synthesis, ligand–receptor modeling studies and pharmacological evaluation of novel 4-modified-2-aryl-1,2,4-triazolo[4,3-*a*]quinoxalin-1-one derivatives as potent and selective human A<sub>3</sub> adenosine receptor antagonists**

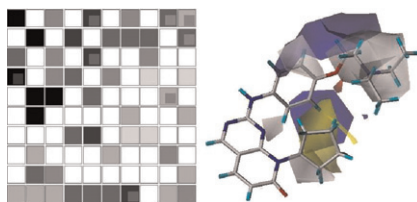
pp 6085–6102

Vittoria Colotta,\* Daniela Catarzi, Flavia Varano, Ombretta Lenzi, Guido Filacchioni, Claudia Martini, Letizia Trincavelli, Osele Ciampi, Chiara Traini, Anna Maria Pugliese, Felicita Pedata, Erika Morizzo and Stefano Moro

**Structural requirements of pyrido[2,3-*d*]pyrimidin-7-one as CDK4/D inhibitors: 2D autocorrelation, CoMFA and CoMSIA analyses**

pp 6103–6115

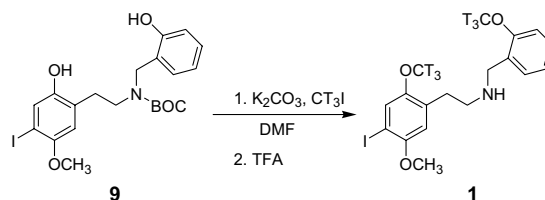
Julio Caballero,\* Michael Fernández and Fernando D. González-Nilo



### High specific activity tritium-labeled *N*-(2-methoxybenzyl)-2,5-dimethoxy-4-iodophenethylamine (INBMeO): A high-affinity 5-HT<sub>2A</sub> receptor-selective agonist radioligand

pp 6116–6123

David E. Nichols,\* Stewart P. Frescas, Benjamin R. Chemel, Kenneth S. Rehder, Desong Zhong and Anita H. Lewin

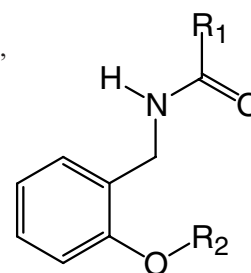


The title compound **1** was prepared in 99% radiochemical purity at a specific activity of 160 Ci/mmol. It had a  $K_d$  of 0.1–0.15 nM in two different heterologous cell lines stably expressing the human serotonin 5-HT<sub>2A</sub> receptor.

### Synthesis and activity on rat aorta rings and rat pancreatic $\beta$ -cells of ring-opened analogues of benzopyran-type potassium channel activators

pp 6124–6130

Smail Khelili, Xavier Florence, Mourad Bouhadja, Samia Abdelaziz, Nadia Mechouch, Yekhllef Mohamed, Pascal de Tullio, Philippe Lebrun and Bernard Pirotte\*

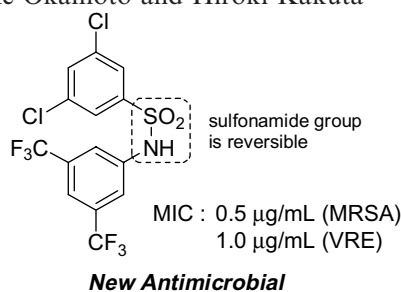


$R_1$  = alkyl or aryl (amide), NHR' (urea),  
 NHSO<sub>2</sub>Ar (sulfonylurea)  
 $R_2$  = Me, Et

### Design and synthesis of benzenesulfonanilides active against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*

pp 6131–6144

Kensuke Namba, Xiaoxia Zheng, Kazunori Motoshima, Hidetomo Kobayashi, Akihiro Tai, Eizo Takahashi, Kenji Sasaki, Keinosuke Okamoto and Hiroki Kakuta\*

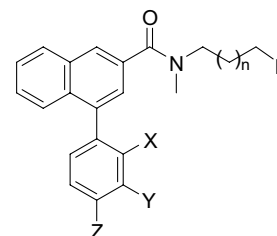


### Synthesis, fluorine-18 radiolabeling, and in vitro characterization of 1-iodophenyl-*N*-methyl-*N*-fluoroalkyl-3-isoquinoline carboxamide derivatives as potential PET radioligands for imaging peripheral benzodiazepine receptor

pp 6145–6155

Weiping Yu, Eric Wang, Ronald J. Voll, Andrew H. Miller and Mark M. Goodman\*

Four PK11195 analogues **9a–d** were synthesized and evaluated in vitro for the peripheral benzodiazepine receptor (PBR). 1-(2-Iodophenyl)-*N*-methyl-*N*-(3-fluoropropyl)-3-isoquinoline carboxamide (**9a**) was the most potent compound ( $K_i$  = 0.26 nM) of this series thus F-18 radiosynthesis of this ligand was developed for further PET studies.



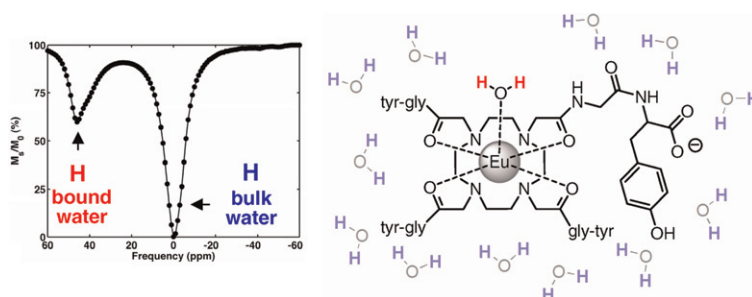
(**9a**) X=I, Y=Z=H, n=1  
 (**9b**) X=Z=H, Y=I, n=1  
 (**9c**) X=Y=H, Z=I, n=1  
 (**9d**) X=I, Y=Z=H, n=0



### Analogs of $\text{Eu}^{3+}$ DOTAM-Gly-Phe-OH and $\text{Tm}^{3+}$ DOTAM-Gly-Lys-OH: Synthesis and magnetic properties of potential PARACEST MRI contrast agents

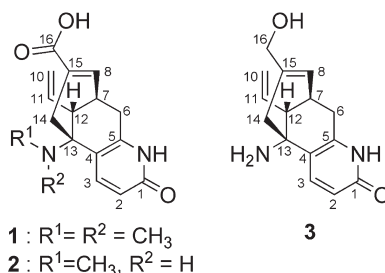
pp 6156–6166

Mojmír Suchý, Alex X. Li, Robert Bartha and Robert H. E. Hudson\*



### Lycoparins A–C, new alkaloids from *Lycopodium casuarinoides* inhibiting acetylcholinesterase

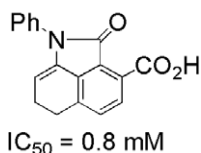
pp 6167–6171

Yusuke Hirasawa, Eri Kato, Jun'ichi Kobayashi, Nobuo Kawahara,  
Yukihiro Goda, Motoo Shiro and Hiroshi Morita\*

### Evaluation of novel Hyphodermin derivatives as Glycogen Phosphorylase a inhibitors

pp 6172–6178

Wendy A. Loughlin,\* Gregory K. Pierens, Maria J. Petersson, Luke C. Henderson and Peter C. Healy

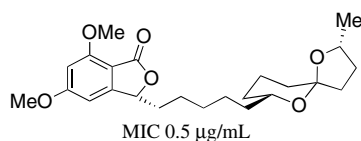


A series of Hyphodermin derivatives were evaluated as potential inhibitors of Glycogen Phosphorylase a, with  $\text{IC}_{50}$ 's of 0.8–11 mM being observed.



### Anti-*Helicobacter pylori* activity of derivatives of the phthalide-containing antibacterial agents spiolaxine methyl ether, CJ-12,954, CJ-13,013, CJ-13,102, CJ-13,104, CJ-13,108 and CJ-13,015

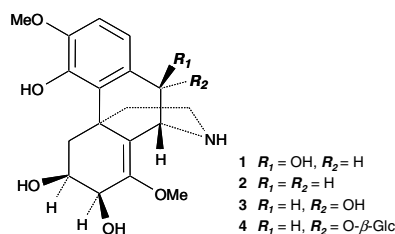
pp 6179–6185

Fiona J. Radcliff, John D. Fraser,\* Zoe E. Wilson, Amanda M. Heapy, James E. Robinson,  
Christina J. Bryant, Christopher L. Flowers and Margaret A. Brimble\*

**Isolation and antimalarial activity of new morphinan alkaloids on *Plasmodium yoelii* liver stage**

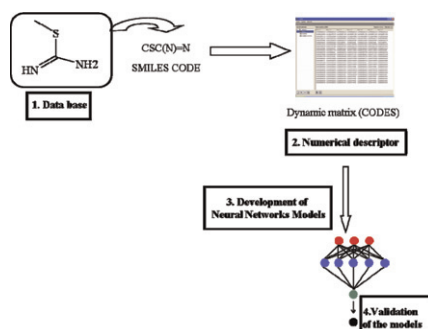
pp 6186–6192

Maëlle Carraz,\* Akino Jossang, Philippe Rasoanaivo, Dominique Mazier and François Frappier

**Design, synthesis, and evaluation of potential inhibitors of nitric oxide synthase**

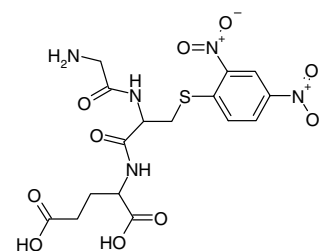
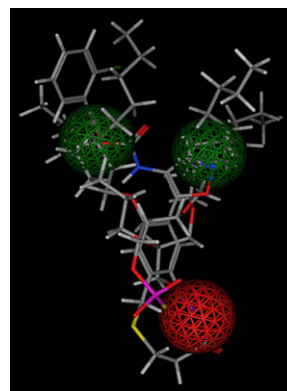
pp 6193–6206

Tania Castaño, Arantxa Encinas, Concepción Pérez, Ana Castro, Nuria E. Campillo\* and Carmen Gil\*

**Identification of non-lipid LPA<sub>3</sub> antagonists by virtual screening**

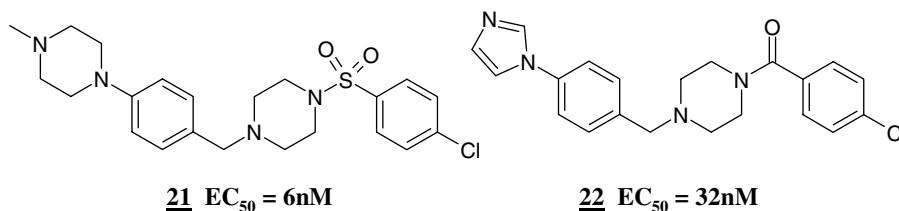
pp 6207–6217

James I. Fells, Ryoko Tsukahara, Yuko Fujiwara, Jianxiong Liu, Donna H. Perygin, Daniel A. Osborne, Gabor Tigyi and Abby L. Parrill\*

Using a structure-based pharmacophore for virtual screening, a non-lipid LPA<sub>3</sub>-selective antagonist was identified.**Design and evaluation of a novel series of 2,3-oxidosqualene cyclase inhibitors with low systemic exposure, relationship between pharmacokinetic properties and ocular toxicity**

pp 6218–6232

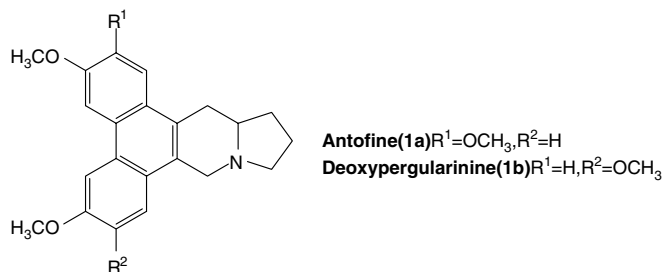
Marie-Hélène Fouchet,\* Frédéric Donche, Christelle Martin, Anne Bouillot, Christophe Junot, Anne-Bénédicte Boullay, Florent Potvain, Sylvie Demaria Magny, Hervé Coste, Max Walker, Marc Issandou and Nérina Dodic



**Total synthesis of phenanthroindolizidine alkaloids (±)-antofine, (±)-deoxypergularinine, and their dehydro congeners and evaluation of their cytotoxic activity**

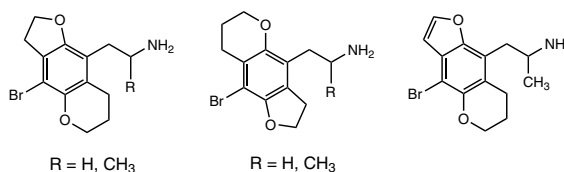
pp 6233–6241

Chung-Ren Su, Amooru G. Damu, Po-Cheng Chiang, Kenneth F. Bastow, Susan L. Morris-Natschke, Kuo-Hsiung Lee and Tian-Shung Wu\*

**'Hybrid' benzofuran–benzopyran congeners as rigid analogs of hallucinogenic phenethylamines**

pp 6242–6251

Danielle M. Schultz, Jennifer A. Prescher, Stephanie Kidd, Danuta Marona-Lewicka, David E. Nichols and Aaron Monte\*



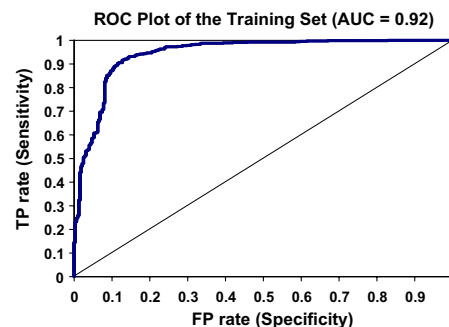
The synthesis and pharmacological characterization of a set of rigidified heterocyclic phenylalkylamine derivatives that have agonist activity at serotonin 5-HT<sub>2A</sub> receptors is reported. Affinity and functional potency were measured, and drug discrimination in rats was assessed for two of the most potent compounds.

**Support vector machines classification of hERG liabilities based on atom types**

pp 6252–6260

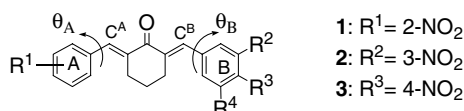
Lei Jia and Hongmao Sun\*

The receiver operating characteristic (ROC) curve of the SVM model built on the basis of the whole training set. Area under curve (AUC) of 0.92 indicates that the model is excellent.

***E,E*-2-Benzylidene-6-(nitrobenzylidene)cyclohexanones: Syntheses, cytotoxicity and an examination of some of their electronic, steric, and hydrophobic properties**

pp 6261–6268

Umashankar Das, Alireza Doroudi, Swagatika Das, Brian Bandy, Jan Balzarini, Erik De Clercq and Jonathan R. Dimmock\*

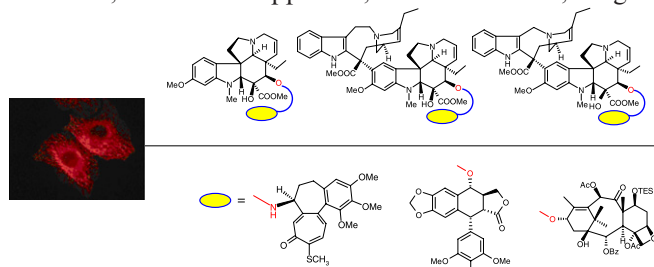


Three series of nitro compounds **1–3** were evaluated for cytotoxicity. The variation in potencies was explored by measuring the atomic charges on carbon atoms C<sup>A</sup> and C<sup>B</sup>, the torsion angle  $\theta_A$  and  $\theta_B$ , log *P* values and respiration in rat liver mitochondria.

### Inhibitors of tubulin polymerization: Synthesis and biological evaluation of hybrids of vindoline, anhydrovinblastine and vinorelbine with thiocolchicine, podophyllotoxin and baccatin III

pp 6269–6285

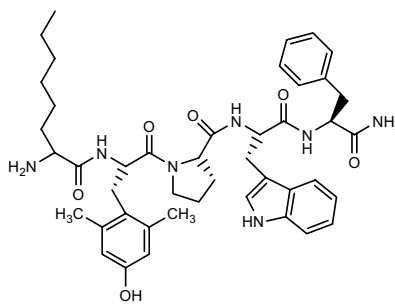
Daniele Passarella,\* Alessandra Giardini, Bruno Peretto, Gabriele Fontana, Alessandro Sacchetti, Alessandra Silvani, Cristina Ronchi, Graziella Cappelletti, Daniele Cartelli, Jurgen Borlak and Bruno Danieli



### Synthesis and in vitro evaluation of a library of modified endomorphin 1 peptides

pp 6286–6296

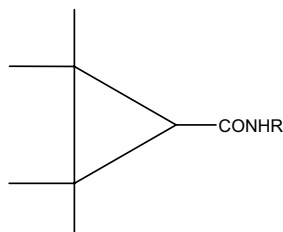
Yasuko Koda, Mark Del Borgo, Susanne T. Wessling, Lawrence H. Lazarus, Yoshio Okada, Istvan Toth and Joanne T. Blanchfield\*



### Synthesis and anticonvulsant activity of aromatic tetramethylcyclopropanecarboxamide derivatives

pp 6297–6305

Jakob Avi Shimshoni, Meir Bialer and Boris Yagen\*



A series of aromatic tetramethylcyclopropanecarboxamide derivatives were synthesized and some found to be active as anticonvulsants in the murine maximal electroshock and subcutaneous pentylenetetrazole seizure tests.

## OTHER CONTENTS

### Instructions to contributors

p I

\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, *102*, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, *61*(6), 355–360].

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