

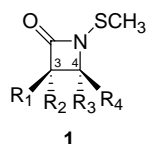
## Contents

### ARTICLES

***N*-Methylthio  $\beta$ -lactam antibacterials: Effects of the  $C_3/C_4$  ring substituents on anti-MRSA activity**

pp 6289–6308

Edward Turos,\* Cristina Coates, Jeung-Yeop Shim, Yang Wang, J. Michelle Leslie, Timothy E. Long, G. Suresh Kumar Reddy, Alex Ortiz, Marci Culbreath, Sonja Dickey, Daniel V. Lim, Eduardo Alonso and Javier Gonzalez

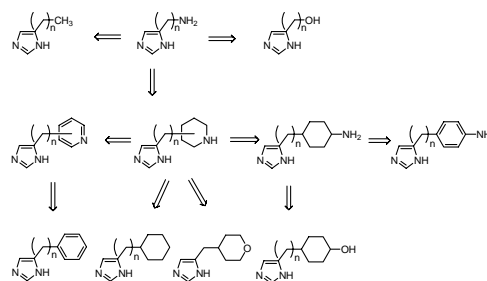


This report describes a study of the antibacterial properties of *N*-methylthio  $\beta$ -lactams **1** as a function of the  $C_3/C_4$  ring substituents  $R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$ .

**New high affinity  $H_3$  receptor agonists without a basic side chain**

pp 6309–6323

Ruengwit Kitbunnadaj, Marcel Hoffmann, Silvina A. Fratantoni, Gerold Bongers, Remko A. Bakker, Kerstin Wieland, Ahmed el Jilali, Iwan J. P. De Esch, Wiro M. P. B. Menge, Henk Timmerman and Rob Leurs\*

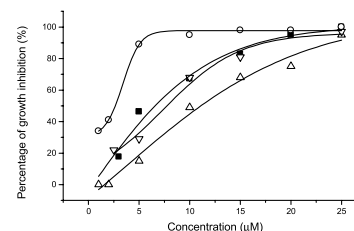
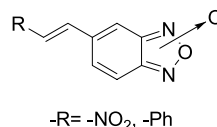


**Benzo[1,2-*c*]1,2,5-oxadiazole *N*-oxide derivatives as potential antitrypanosomal drugs. Part 3: Substituents-clustering methodology in the search for new active compounds**

pp 6324–6335

Gabriela Aguirre, Lucía Boiani, Hugo Cerecetto,\* Rossanna Di Maio,\* Mercedes González, Williams Porcal, Ana Denicola, Matías Möller, Leonor Thomson and Verónica Tórtora

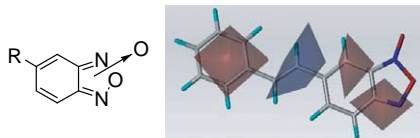
The results of a study on the use of Hansch's series design for the generation of new benzo[1,2-*c*]1,2,5-oxadiazole *N*-oxide derivatives as antitrypanosomal compounds are described. Benzofuroxans affect the mitochondrial electron chain, inhibiting parasite respiration.



### New potent 5-substituted benzofuroxans as inhibitors of *Trypanosoma cruzi* growth: Quantitative structure–activity relationship studies

pp 6336–6346

Gabriela Aguirre, Lucía Boiani, Mariana Boiani, Hugo Cerecetto,\*  
Rossanna Di Maio, Mercedes González,\* Williams Porcal, Ana Denicola,  
Oscar E. Piro, Eduardo E. Castellano, Carlos Mauricio R. Sant'Anna and  
Eliezer J. Barreiro



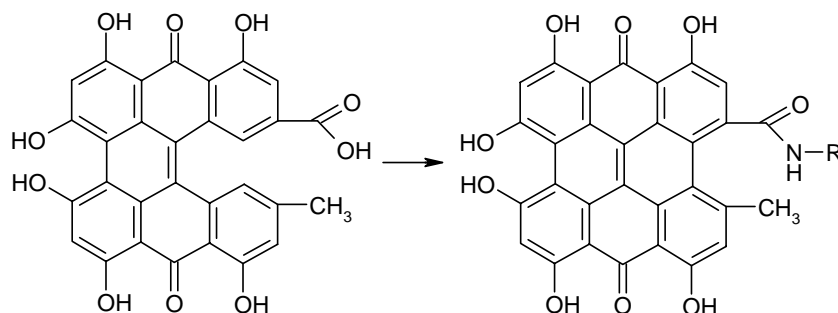
2D- and 3D-QSAR models of anti-*Trypanosoma cruzi* activity of benzofuroxans have been developed. New derivatives were synthesized and in vitro evaluated to complete the set of compounds.



### Synthesis, in vitro cellular uptake and photo-induced antiproliferative effects of lipophilic hypericin acid derivatives

pp 6347–6353

Ivo Crnolatac, Ann Huygens, Arthur van Aerschot, Roger Busson, Jef Rozenski and Peter A.M. de Witte\*

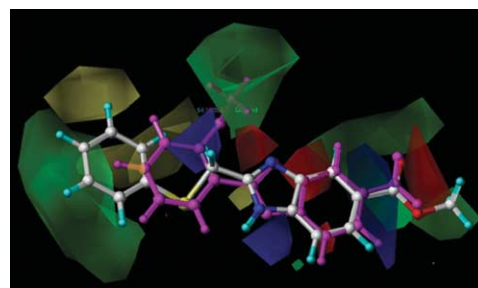


### 3D-QSAR analysis on benzazole derivatives as eukaryotic topoisomerase II inhibitors by using comparative molecular field analysis method

pp 6354–6359

Ozlem Temiz-Arpaci, Betul Tekiner-Gulbas, Ilkay Yildiz,\* Esin Aki-Sener and Ismail Yalcin

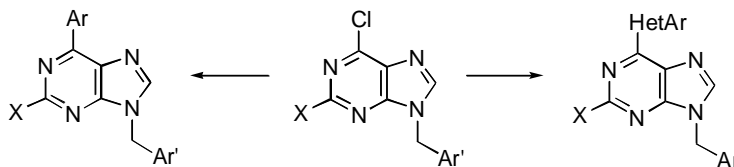
3D-QSAR analysis has been performed on a series of previously synthesized benzoxazole, benzimidazole, and oxazolo(4,5-b)pyridine derivatives, which are screened as eukaryotic topoisomerase II inhibitors, using CoMFA approaches. The contour plots provide many useful insights into relationships between structural features and inhibitory activity and also give a picture of the main chemical features responsible for the significant topoisomerase II inhibitory activity. These features could be used to design new lead compounds showing higher inhibitory activities.



### Selective anti-tubercular purines: Synthesis and chemotherapeutic properties of 6-aryl- and 6-heteroaryl-9-benzylpurines

pp 6360–6373

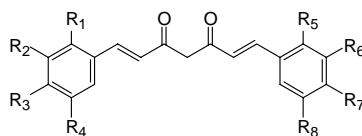
Morten Brændvang and Lise-Lotte Gundersen\*



**Synthesis and biological evaluation of polyhydroxycurcuminoids**

pp 6374–6380

Somepalli Venkateswarlu, Marellapudi S. Ramachandra and Gottumukkala V. Subbaraju\*

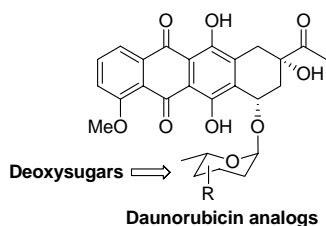


A series of curcumin analogs was prepared from the appropriately substituted benzaldehydes. These analogs have displayed strong antioxidative and potent tumor reducing activities.

**Syntheses and biological activities of daunorubicin analogs with uncommon sugars**

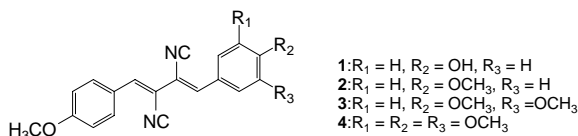
pp 6381–6387

Lizhi Zhu, Xianhua Cao, Wenlan Chen, Guisheng Zhang, Duxin Sun\* and Peng George Wang\*

**Xanthocillins as thrombopoietin mimetic small molecules**

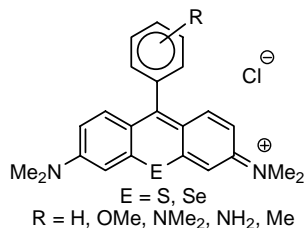
pp 6388–6393

Ryuichi Sakai,\* Takanori Nakamura, Taito Nishino, Masao Yamamoto, Atsushi Miyamura, Hisae Miyamoto, Norihisa Ishiwata, Norio Komatsu, Hisao Kamiya and Nobutomo Tsuruzoe

**Structure–activity studies of uptake and phototoxicity with heavy-chalcogen analogues of tetramethylrosamine in vitro in chemosensitive and multidrug-resistant cells**

pp 6394–6403

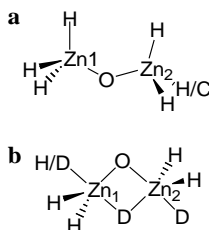
Scott L. Gibson, Jason J. Holt, Mao Ye, David J. Donnelly, Tymish Y. Ohulchanskyy, Youngjae You and Michael R. Detty\*



A series of substituted thio and seleno analogues of tetramethylrosamine were prepared and evaluated as photosensitizers against chemosensitive AUXB1 cells and multidrug-resistant CR1R12 cells.

### Homology modelling and active-site-mutagenesis study of the catalytic domain of the pneumococcal phosphorylcholine esterase pp 6404–6413

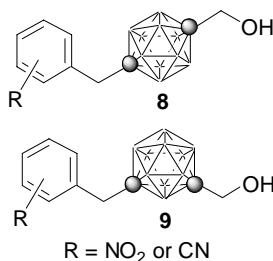
Nuria Eugenia Campillo,\* Juan Antonio Pérez, Laura Lagartera and Ana Gonzalez



Two models of pneumococcal phosphorylcholine esterase (Pce) with a binuclear Zn-binding site are proposed according to mutational studies.

### Design and synthesis of novel androgen receptor antagonists with sterically bulky icosahedral carboranes pp 6414–6424

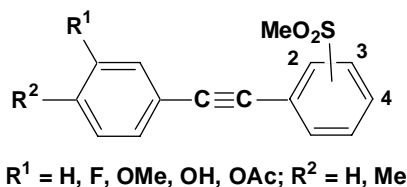
Tokuhiro Goto, Kiminori Ohta, Tomoharu Suzuki, Shigeru Ohta and Yasuyuki Endo\*



We designed and synthesized novel androgen receptor antagonists such as **8** or **9** bearing a carborane moiety.

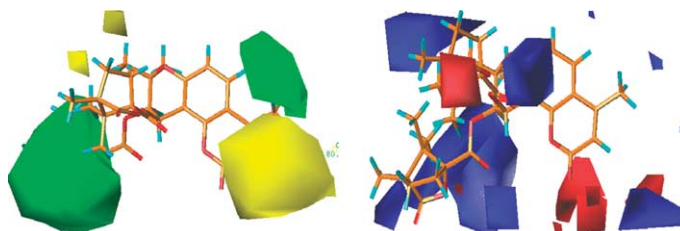
### Design, synthesis, and biological evaluation of linear 1-(4-, 3- or 2-methylsulfonylphenyl)-2-phenylacetylenes: A novel class of cyclooxygenase-2 inhibitors pp 6425–6434

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



### Molecular modeling, design, synthesis, and biological evaluation of novel 3',4'-dicamphanoyl-(+)-cis-khellactone (DCK) analogs as potent anti-HIV agents pp 6435–6449

Lan Xie,\* Chun-hong Zhao, Ting Zhou, Hai-feng Chen, Bo-tao Fan, Xian-hong Chen, Jian-zhou Ma, Jing-yun Li, Zhuo-yi Bao, Zhaowen Lo, Donglei Yu and Kuo-Hsiung Lee



**QSAR modeling of blood:air and tissue:air partition coefficients using theoretical descriptors**

pp 6450–6463

Alan R. Katritzky,\* Minati Kuanar, Dan C. Fara, Mati Karelson,  
William E. Acree, Jr., Vitaly P. Solov'ev and Alexandre Varnek\*

Human blood:air, human and rat tissue (fat, brain, liver, muscle, and kidney); air partition coefficients of a diverse set of organic compounds were correlated and predicted using structural descriptors by employing CODESSA-PRO and ISIDA programs.

**Codessa Approach:**

log human or rat (blood or tissue)  
partition coefficient = f(Whole molecular descriptors)

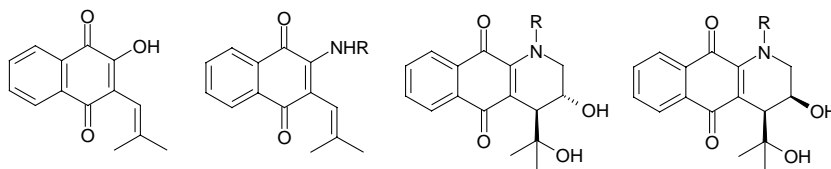
**ISIDA Approach:**

log human or rat (blood or tissue)  
partition coefficient = f (Fragment descriptors)

**New 1,2,3,4-tetrahydro-1-aza-anthraquinones and 2-aminoalkyl compounds from norlapachol with molluscicidal activity**

pp 6464–6469

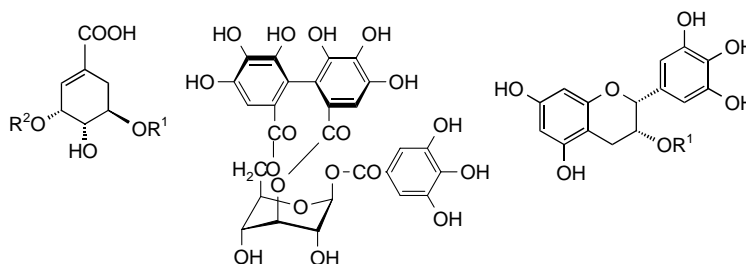
Ticiano P. Barbosa, Celso A. Camara,\* Tania M. S. Silva, Rodrigo M. Martins,  
Angelo C. Pinto and Maria D. Vargas\*

**Tannins and related compounds induce nitric oxide synthase and cytokines gene expressions in *Leishmania major*-infected macrophage-like RAW 264.7 cells**

pp 6470–6476

Herbert Kolodziej,\* Anne Burmeister, Weronika Trun, Oliver A. Radtke, Albrecht F. Kiderlen,  
Hideyuki Ito, Tsutomu Hatano, Takashi Yoshida and Lai Yeap Foo

Some polyphenol-containing extracts and polyphenolic constituents were studied for gene expressions of iNOS, IFN- $\alpha$ , IFN- $\gamma$ , TNF- $\alpha$ , IL-1, IL-10, IL-12, IL-18 in *Leishmania major*-infected RAW cells by RT-PCR, showing remarkable inducing potentials.

**Oxidation of liposomal membrane suppressed by flavonoids: Quantitative structure–activity relationship**

pp 6477–6484

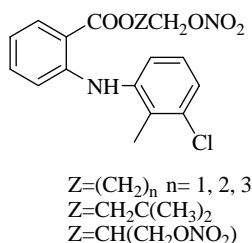
Lucia Rackova,\* Silvia Firakova, Daniela Kostalova, Milan Stefek, Ernest Sturdik and Magdalena Majekova

Antioxidant activity of the set of 12 flavonoids in liposomal membrane was correlated with 19 molecule parameters. The parameter of hydration energy  $E_{\text{HYDR}}$  was the best predictor of antioxidant activity ( $R = -0.747$ ).

### Nitric oxide releasing derivatives of tolfenamic acid with anti-inflammatory activity and safe gastrointestinal profile

pp 6485–6492

George N. Ziakas, Eleni A. Rekka,\* Antonios M. Gavalas, Phaedra T. Eleftheriou, Karyofillis C. Tsiakitzis and Panos N. Kourounakis

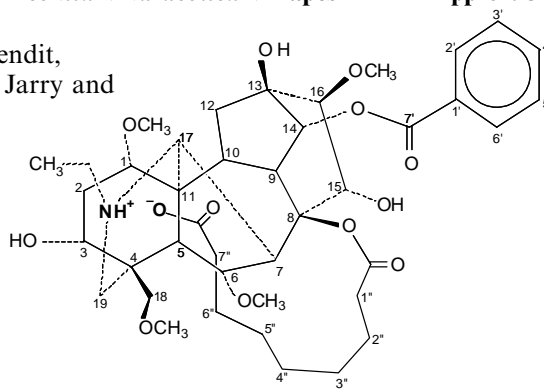


### 8-O-Azeloyl-14-benzoylaconine: A new alkaloid from the roots of *Aconitum karacolicum* Rapcs and its antiproliferative activities

pp 6493–6501

Ainura Chodoeva, Jean-Jacques Bosc, Jean Guillon, Alain Decendit, Michel Petraud, Christelle Absalon, Christiane Vitry, Christian Jarry and Jacques Robert\*

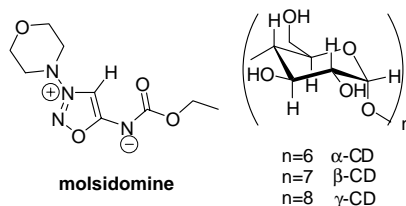
An original aconitine derivative, isolated from a Kirghiz plant, displays antiproliferative in vitro activity against three lines of human tumour cells in culture. It is characterised by the presence of an azeloyl substituent giving a zwitterionic structure to the molecule.



### Combined NMR-crystallographic and modelling investigation of the inclusion of molsidomine into $\alpha$ -, $\beta$ - and $\gamma$ -cyclodextrins

pp 6502–6512

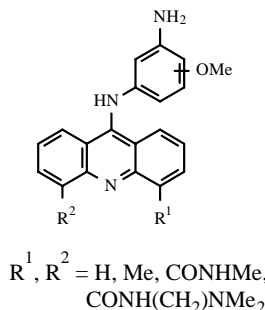
Gloria Uccello-Barretta,\* Federica Balzano, Donatella Paolino, Rebecca Ciaccio and Salvatore Guccione\*



### Synthesis and antitumor activity of 5-(9-acridinylamino)anisidine derivatives

pp 6513–6520

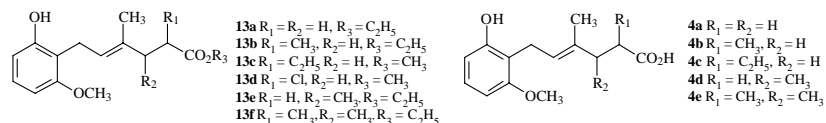
Valeriy A. Bacherikov, Jang-Yang Chang, Yi-Wen Lin, Ching-Huang Chen, Wen-Yu Pan, Huajin Dong, Rong-Zau Lee, Ting-Chao Chou and Tsann-Long Su\*



### Synthesis of some monocyclic analogues of mycophenolic acid via the Johnson ortho ester Claisen rearrangement

pp 6521–6528

Ma Elena Meza-Aviña, Mario Ordoñez, Mario Fernández-Zertuche,\* Lourdes Rodríguez-Fragoso, Jorge Reyes-Esparza and Abril A. Martínez de los Ríos-Corsino

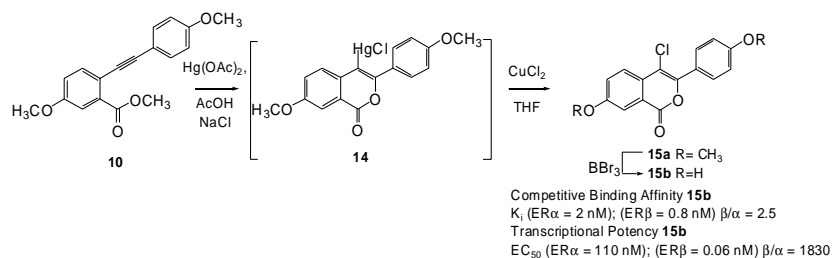


The synthetic methodology reported here allows the preparation of mycophenolic acid analogues bearing alkyl substituents at the  $\alpha$ - and  $\beta$ -positions on the side chain.

### Isocoumarins as estrogen receptor beta selective ligands: Isomers of isoflavone phytoestrogens and their metabolites

pp 6529–6542

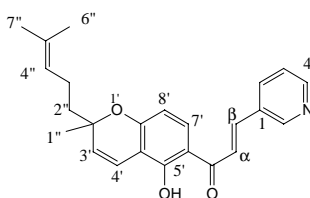
Meri De Angelis, Fabio Stossi, Michael Waibel, Benita S. Katzenellenbogen and John A. Katzenellenbogen\*



### Synthesis of chromenochalcones and evaluation of their in vitro antileishmanial activity

pp 6543–6550

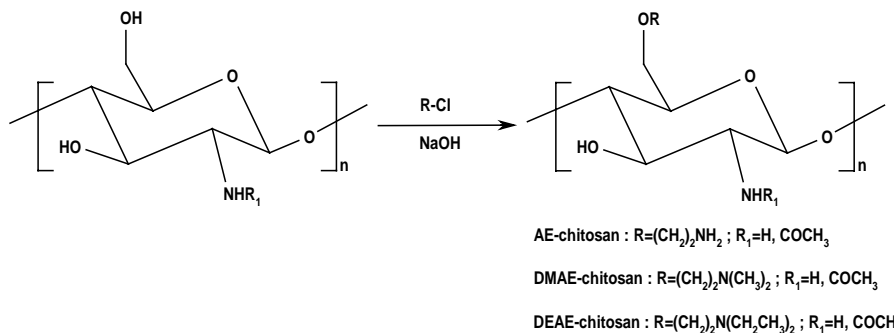
Tadigoppula Narender,\* Tanvir Khaliq, Shweta, Nishi, Neena Goyal and Suman Gupta



### Water-soluble chitosan derivatives as a BACE1 inhibitor

pp 6551–6555

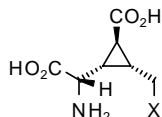
Jae-Young Je and Se-Kwon Kim\*



**C3'-*cis*-Substituted carboxycyclopropyl glycines as metabotropic glutamate 2/3 receptor agonists: Synthesis and SAR studies**

pp 6556–6570

Rosario González,\* Iván Collado, Beatriz López de Uralde, Alicia Marcos, Luisa M. Martín-Cabrejas, Concepción Pedregal, Jaime Blanco-Urgoiti, Javier Pérez-Castells, M. Alejandro Fernández, Sherri L. Andis, Bryan G. Johnson, Rebecca A. Wright, Darryle D. Schoepp and James A. Monn

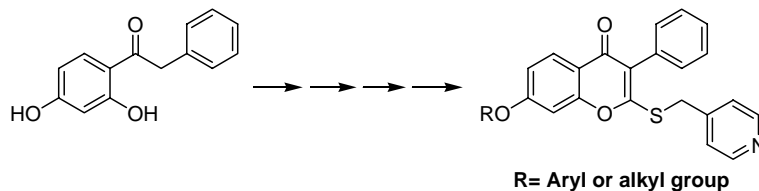


The synthesis of a series of C3'-*cis*-substituted carboxycyclopropyl glycines bearing a wide variety of functional groups is described, and the structure–activity relationship for this series as agonists of group II metabotropic glutamate receptors is reported.

**Lead optimization of 7-benzyloxy 2-(4'-pyridylmethyl)thio isoflavone aromatase inhibitors**

pp 6571–6577

Bin Su, John C Hackett, Edgar S. Díaz-Cruz, Young-Woo Kim and Robert W. Brueggemeier\*

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p II

\*Corresponding author

i\* Supplementary data available via ScienceDirect

**COVER**

2005: Human liver glycogen phosphorylase A (HLGP<sub>a</sub>) 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 HLGP<sub>a</sub> 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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