

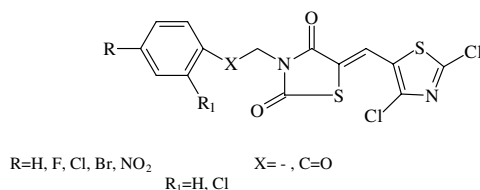
## Contents

### ARTICLES

#### Synthesis and antimicrobial activity of some new thiazolyl thiazolidine-2,4-dione derivatives

pp 6012–6017

Oya Bozdağ-Dündar,\* Özen Özgen, Arzu Menteşe, Nurten Altanlar, Onur Atlı, Engin Kendi and Rahmiye Ertan

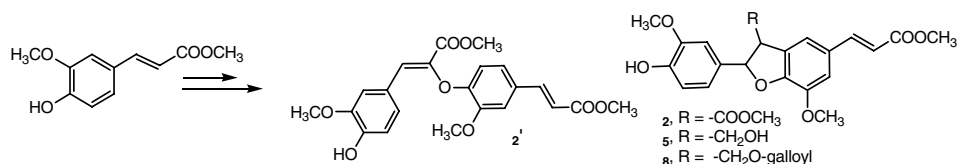


A new series of thiazolyl thiazolidine-2,4-diones were synthesized and tested for their in vitro antimicrobial activities.

#### Synthesis of ferulic ester dimers, functionalisation and biological evaluation as potential antiatherogenic and antiparasmodial agents

pp 6018–6026

D. L. A. Rakotondramanana, Mélanie Delomenède, Michel Baltas,\* Hubert Duran, Florence Bedos-Belval, Philippe Rasoanaivo, Anne Negre-Salvayre and Heinz Gornitzka



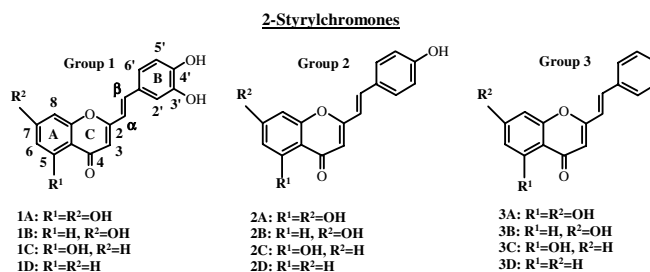
Feruloyl dimeric derivatives were synthesized and screened for their antiatherogenic and antiparasmodial activity.

#### 2-Styrylchromones: Novel strong scavengers of reactive oxygen and nitrogen species

pp 6027–6036

Ana Gomes, Eduarda Fernandes,\* Artur M. S. Silva, Clementina M. M. Santos, Diana C. G. A. Pinto, José A. S. Cavaleiro and José L. F. C. Lima

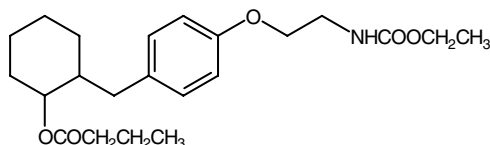
2-Styrylchromones were tested for their scavenging activity against ROS and RNS. Some of the studied compounds proved to be extremely efficient scavengers of the different ROS and RNS, showing, in some cases, IC<sub>50</sub>s under 1 μM.



**Insect pest control agents: Novel chiral butanoate esters (juvenogens)**

pp 6037–6042

Zdeněk Wimmer,\* Alexandra J. F. D. M. Floro, Marie Zarevúcka,  
Martina Wimmerová, Guido Sello and Fulvia Orsini

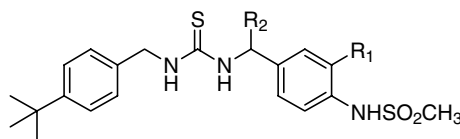


A chemoenzymic synthesis of all existing stereoisomers of ethyl *N*-{2-[4-(2-butanoyloxycyclohexyl)methyl]phenoxy}ethyl carbamate is presented.

 **$\alpha$ -Substituted *N*-(4-*tert*-butylbenzyl)-*N'*-[4-(methylsulfonylamino)-benzyl]thiourea analogues as potent and stereospecific TRPV1 antagonists**

pp 6043–6053

Jae-Uk Chung, Su Yeon Kim, Ju-Ok Lim, Hyun-Kyung Choi, Sang-Uk Kang, Hae-Seok Yoon,  
HyungChul Ryu, Dong Wook Kang, Jeewoo Lee,\* Bomi Kang, Sun Choi, Attila Toth,  
Larry V. Pearce, Vladimir A. Pavlyukovets, Daniel J. Lundberg and Peter M. Blumberg

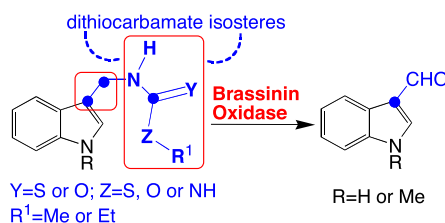


A series of  $\alpha$ -substituted *N*-(4-*tert*-butylbenzyl)-*N'*-[4-(methylsulfonylamino)benzyl]thiourea analogues have been investigated as TRPV1 receptor antagonists.

**Isosteric probes provide structural requirements essential for detoxification of the phytoalexin brassinin by the fungal pathogen *Leptosphaeria maculans***

pp 6054–6061

M. Soledade C. Pedras,\* Mukund Jha, Zoran Minic and Oladapo G. Okeola

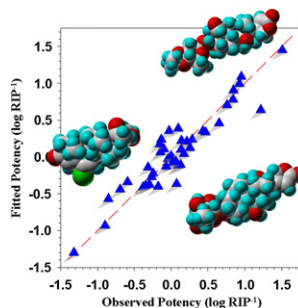


Essential structural features of substrates of brassinin oxidase: (i) –NH at the (mono/dithio)carbamate, urea or thiourea group; (ii) methylene bridge between indole and functional group; (iii) methyl or ethyl group attached to Z group.

**Identification and characterization of novel sodium/potassium-ATPase inhibitors by virtual screening of a compound database**

pp 6062–6070

David T. Stanton, Julie Ankenbauer, David Rothgeb, Matthew Draper and Stefan Paula\*

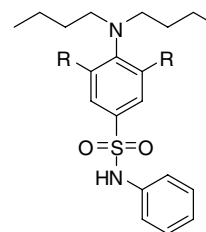


### Synthesis, biological evaluation, and molecular modeling of 3,5-substituted-*N*<sup>1</sup>-phenyl-*N*<sup>4</sup>,*N*<sup>4</sup>-di-*n*-butylsulfanilamides as antikinetoplastid antimicrotubule agents

pp 6071–6079

Tesmol G. George, Molla M. Endeshaw, Rachel E. Morgan, Kiran V. Mahasenan, Dawn A. Delfin, Mitali S. Mukherjee, Adam J. Yakovich, Jean Fotie, Chenglong Li and Karl A. Werbovetz\*

Analogues of antiparasitic antitubulin dinitroaniline sulfonamide **2b** have been prepared. Dicyano compound **5** displays biological activity comparable to **2b**.



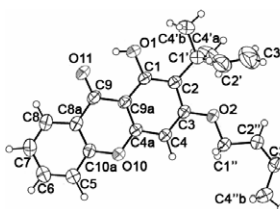
- 2b**: R = NO<sub>2</sub>  
**3**: R = NH<sub>2</sub>  
**4**: R = Cl  
**5**: R = CN  
**11**: R = COOCH<sub>3</sub>  
**12**: R = COOH  
**13**: R = CONH<sub>2</sub>  
**14**: R = COCH<sub>3</sub>



### Dihydroxyxanthenes prenylated derivatives: Synthesis, structure elucidation, and growth inhibitory activity on human tumor cell lines with improvement of selectivity for MCF-7

pp 6080–6088

Raquel A. P. Castanheiro, Madalena M. M. Pinto,\* Artur M. S. Silva, Sara M. M. Cravo, Luís Gales, Ana M. Damas, Naïr Nazareth, Maria S. J. Nascimento and Graham Eaton

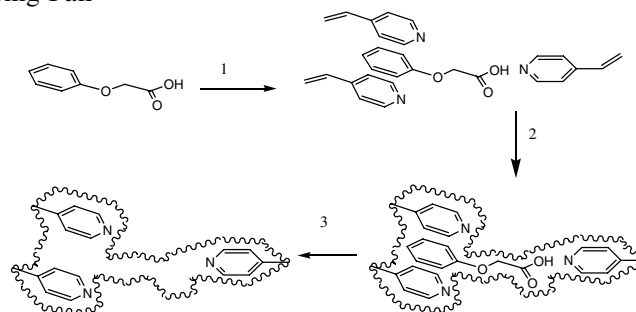


### Retention behavior of phenoxyacetic herbicides on a molecularly imprinted polymer with phenoxyacetic acid as a dummy template molecule

pp 6089–6095

Huiting Zhang, Tao Song, Wei Zhang, Wei Hua and Canping Pan\*

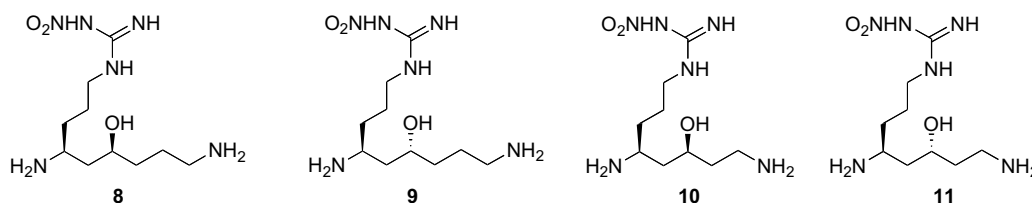
Molecularly imprinted polymers binding with phenoxyacetic acid as a dummy template molecule were synthesized in aqueous media. This material can selectively retain phenoxyacetic herbicides.



### Hydroxyethylene isosteres of selective neuronal nitric oxide synthase inhibitors

pp 6096–6108

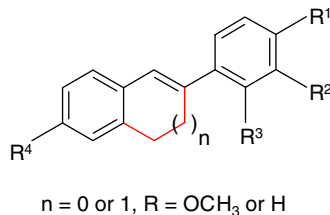
Erik P. Erdal, Pavel Martásek, Linda J. Roman and Richard B. Silverman\*



**'Bridged' stilbene derivatives as selective cyclooxygenase-1 inhibitors**

pp 6109–6118

Norbert Handler, Gerda Brunhofer, Christian Studenik, Klaus Leisser, Walter Jaeger, Stephanie Parth and Thomas Erker\*

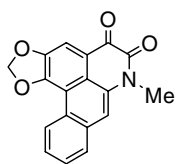


Modification of the resveratrol scaffold yielded in dihydronaphthalene and 1*H*-indene derivatives showing pronounced COX-1 inhibiting properties.

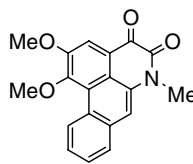
**Synthesis and biological evaluation of cepharadiones A and B and related dioxaporphines**

pp 6119–6125

Mark A. Elban, Jean C. Chapuis, Mei Li and Sidney M. Hecht\*



cepharadione A

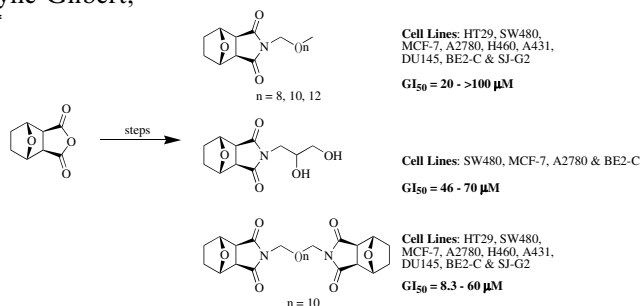


cepharadione B

**Norcantharimides, synthesis and anticancer activity: Synthesis of new norcantharidin analogues and their anticancer evaluation**

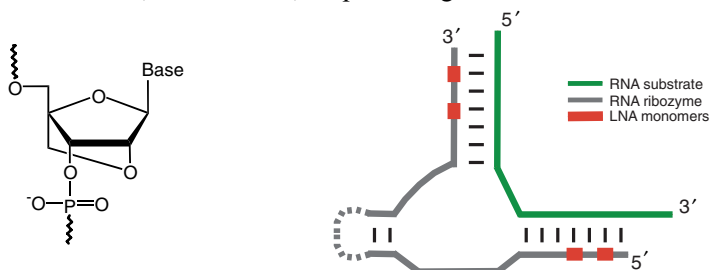
pp 6126–6134

Timothy A. Hill, Scott G. Stewart, Stephen P. Ackland, Jayne Gilbert, Benjamin Sauer, Jennette A. Sakoff and Adam McCluskey\*

**LNA nucleotides improve cleavage efficiency of singular and binary hammerhead ribozymes**

pp 6135–6143

Janne K. Christiansen, Sune Lobedanz, Khalil Arar, Jesper Wengel and Birte Vester\*



Insertion of LNA monomers into the substrate binding arms of hammerhead ribozymes allows these to be shortened and using LNA in the stem of helix II enabled separating the ribozyme into two short molecules to explore combinational possibilities.

### Synthesis and structure–activity relationship study of cytotoxic germanicane- and lupane-type 3β-O-monodesmosidic saponins starting from betulin

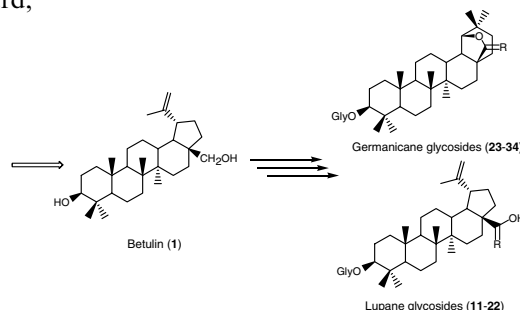
pp 6144–6157

Dominic Thibeault, Charles Gauthier, Jean Legault, Jimmy Bouchard, Philippe Dufour and André Pichette\*

Starting from betulin (**1**) isolated from the outer bark of *Betula papyrifera*, we successfully synthesized a library of 3-O-monodesmosidic saponins (**11–34**) in order to enhance the hydrosolubility and the cytotoxicity of germanicane- and lupane-type triterpenes.



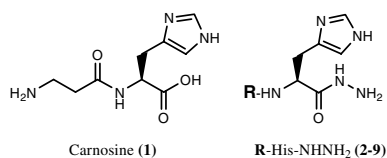
*Betula papyrifera*



### Malondialdehyde scavenging and aldose-derived Schiff bases' transglycation properties of synthetic histidyl-hydrazide carnosine analogs

pp 6158–6163

Andrea Guiotto,\* Paolo Ruzza, Mark A. Babizhayev and Andrea Calderan

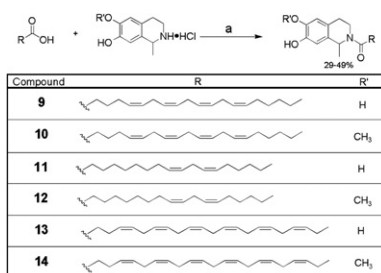


New carnosine analogs bearing the histidyl-hydrazide moiety have been synthesized and tested for their efficiency in scavenging malondialdehyde (MDA) derived from lipid peroxidation and for their ability to reverse the glycation process in the glucose–ethylamine Schiff base model.

### Fatty acyl amides of endogenous tetrahydroisoquinolines are active at the recombinant human TRPV1 receptor

pp 6164–6169

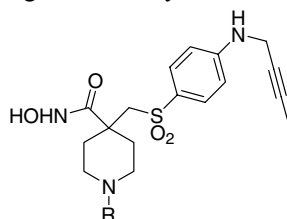
David K. O'Dell, Neta Rimmerman, Sarah R. Pickens and J. Michael Walker\*



### Structure-based design of TACE selective inhibitors: Manipulations in the S1'–S3' pocket

pp 6170–6181

Adrian Huang,\* Diane Joseph-McCarthy, Frank Lovering, Linhong Sun, Weiheng Wang, Weixin Xu, Yi Zhu, Junqing Cui, Yuhua Zhang and Jeremy I. Levin



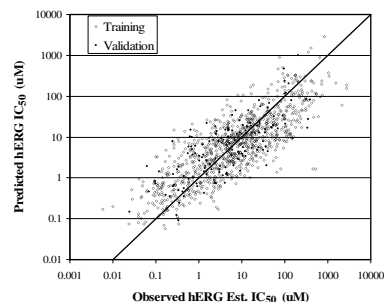
A series of β-sulfonyl hydroxamate TACE inhibitors, bearing a butynylamino P1' group, was designed and synthesized. Of the compounds investigated, **22** has excellent in vitro potency against isolated TACE enzyme, shows good selectivity over MMP-2 and MMP-13, and oral activity in an in vivo mouse model of TNF-α production.

### Estimation of hERG inhibition of drug candidates using multivariate property and pharmacophore SAR

pp 6182–6192

Stephen R. Johnson,\* Hongwen Yue, Mary Lee Conder, Hong Shi, Arthur M. Doweyko, John Lloyd and Paul Levesque

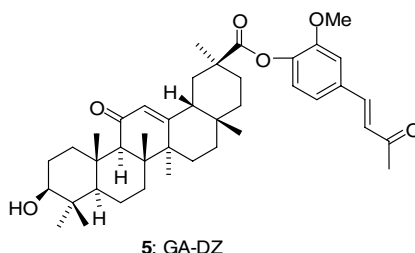
We describe the development and validation of an in silico model of hERG inhibition. The model includes several factors not previously reported for the estimation of hERG inhibition.



### Anti-tumor agents 255: Novel glycyrrhetic acid–dehydrozingerone conjugates as cytotoxic agents

pp 6193–6199

Jin Tatsuzaki, Masahiko Taniguchi, Kenneth F. Bastow, Kyoko Nakagawa-Goto, Susan L. Morris-Natschke, Hideji Itokawa, Kimiye Baba and Kuo-Hsiung Lee\*

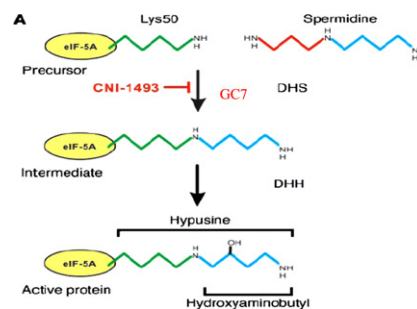


### Modification of eukaryotic initiation factor 5A from *Plasmodium vivax* by a truncated deoxyhypusine synthase from *Plasmodium falciparum*: An enzyme with dual enzymatic properties

pp 6200–6207

Annette Kaiser,\* Ina Hammels, Andrea Gottwald, Marwa Nassar, Mai Saad Zaghloul, Basma Abdal Motaal, Joachim Hauber and Achim Hoerauf

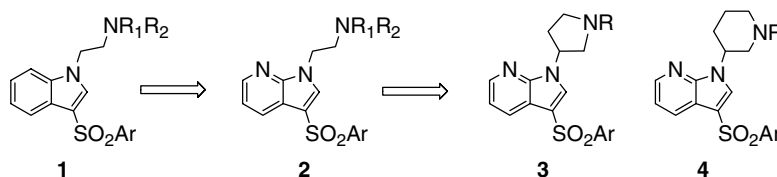
In the first step of hypusine biosynthesis deoxyhypusine synthase (DHS) catalyzes the transfer of the 4-aminobutyl moiety of spermidine to the  $\epsilon$ -amino group of one specific lysine residue in eIF-5A to form deoxyhypusine. In the second step this intermediate is subsequently hydroxylated by deoxyhypusine hydroxylase (DHH) to complete hypusine biosynthesis and thus eIF-5A maturation. CNI-1493 (former semapimod) and *N*-guanyl-1,7-diaminoheptane (GC7) are specific DHS inhibitors.



### Novel 1-(azacycyl)-3-arylsulfonyl-1*H*-pyrrolo[2,3-*b*]pyridines as 5-HT<sub>6</sub> agonists and antagonists

pp 6208–6226

Hassan Elokda,\* David Li, Geraldine McFarlane, Ronald C. Bernotas, Albert J. Robichaud, Ronald L. Magolda, Guo Ming Zhang, Deborah Smith and Lee E. Schechter

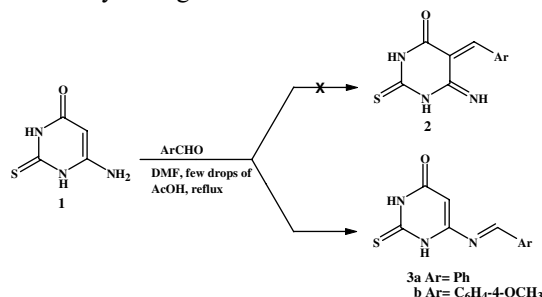


Indoles **1** are 5-HT<sub>6</sub> receptor ligands with modest 5-HT<sub>6</sub> functional activities. Azaindoles **2** have enhanced 5-HT<sub>6</sub> affinities and functional activities. Constraining the basic side chain provided 5-HT<sub>6</sub> ligands (**3** and **4**) with high binding affinities.



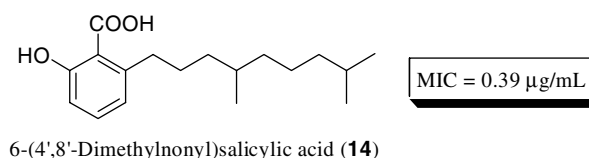
**Utility of 6-amino-2-thiouracil as a precursor for the synthesis of bioactive pyrimidine derivatives**

pp 6227–6235

 Nadia Ragab Mohamed,\* Manal Mohamed Talaat El-Saidi,  
 Yasser Mahmoud Ali and Mohamed Hilmy Elnagdi

**Molecular design of anti-MRSA agents based on the anacardic acid scaffold**

pp 6236–6241

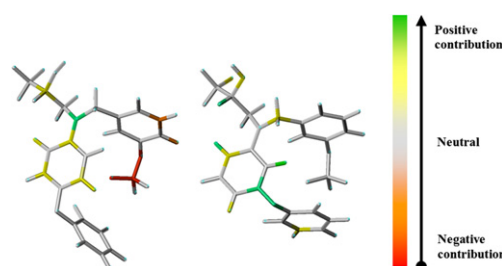
Ivan R. Green,\* Felismino E. Tocoli, Sang Hwa Lee, Ken-ichi Nihei and Isao Kubo\*


**2D Quantitative structure–activity relationship studies on a series of cholesteryl ester transfer protein inhibitors**

pp 6242–6252

Marcelo S. Castilho,\* Rafael V. C. Guido and Adriano D. Andricopulo

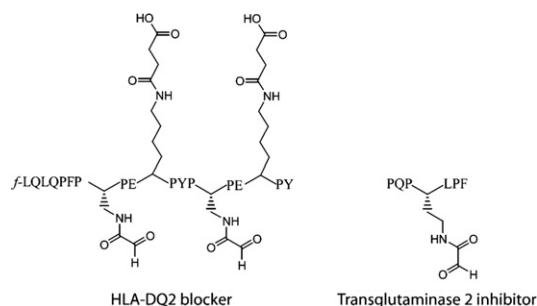
Classical 2D QSAR ( $r^2 = 0.76$ ,  $q^2 = 0.72$ ) and hologram QSAR ( $r^2 = 0.88$ ,  $q^2 = 0.70$ ) models were developed for a series of 85 CETP inhibitors (*N,N*-disubstituted trifluoro-3-amino-2-propanol derivatives). These models are complementary in nature and highlight important structural features for the design of novel CETP inhibitors with improved potency.


**Structure-based design of  $\alpha$ -amido aldehyde containing gluten peptide analogues as modulators of HLA-DQ2 and transglutaminase 2**

pp 6253–6261

Matthew Siegel, Jiang Xia and Chaitan Khosla\*

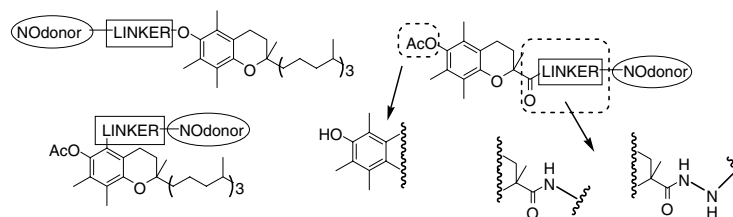
A series of aldehyde-functionalized gluten peptides were synthesized as inhibitors of HLA-DQ2 and transglutaminase 2, two human proteins that play a critical role in gluten induced pathogenesis of celiac sprue.



## Second generation of $\alpha$ -tocopherol analogs-nitric oxide donors: Synthesis, physicochemical, and biological characterization

pp 6262–6272

Gloria V. López, Fabiana Blanco, Paola Hernández, Ana Ferreira, Oscar E. Piro, Carlos Batthyány, Mercedes González, Homero Rubbo\* and Hugo Cerecetto\*



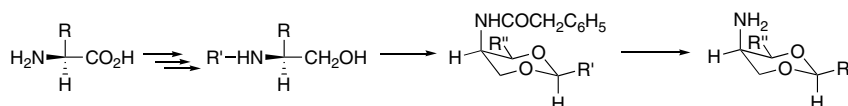
Synthesis, physicochemical, and biological characterization of second generation series of products obtained by coupling  $\alpha$ -tocopherol or analogs through appropriate spacers with the NO-donor either nitrooxy or furoxan moieties were described.



## Toward the development of chemoprevention agents. Part II: Chemo-enzymatic synthesis and anti-inflammatory activities of a new class of 5-amino-2-substitutedphenyl-1,3-dioxacycloalkanes

pp 6273–6290

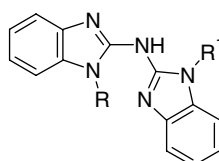
Keli Gu, Lanrong Bi, Ming Zhao,\* Chao Wang, Jingfang Ju\* and Shiqi Peng\*



## Synthesis and antitrichinellosis activity of some bis(benzimidazol-2-yl)amines

pp 6291–6297

Anelia Ts. Mavrova,\* Pavletta Denkova, Yordan A. Tsenov, Kameliya K. Anichina and Dimitar I. Vutchev

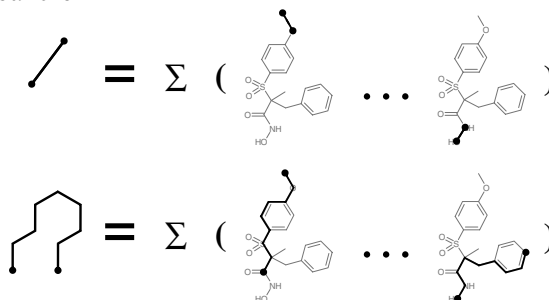


New derivatives of 2-aminobenzimidazole were synthesized using two methods and studied for antitrichinellosis activity. The in vitro and in vivo screening of the intestinal phase of *Trichinella spiralis* exhibited significant effectiveness of the investigated compounds.

## QSAR modeling of matrix metalloproteinase inhibition by *N*-hydroxy- $\alpha$ -phenylsulfonfylacetamide derivatives

pp 6298–6310

Michael Fernández and Julio Caballero\*

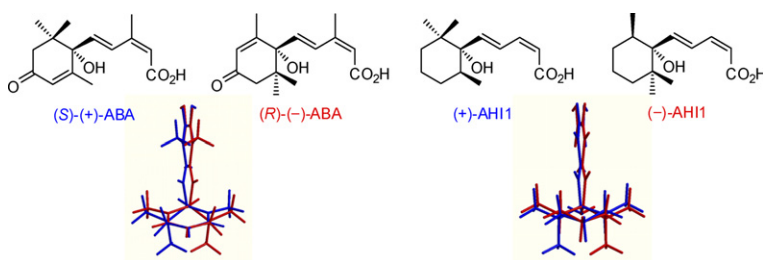




**Asymmetrical ligand binding by abscisic acid 8'-hydroxylase**

pp 6311–6322

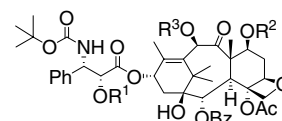
Kotomi Ueno, Hidetaka Yoneyama, Masaharu Mizutani, Nobuhiro Hirai and Yasushi Todoroki\*

**Synthesis and evaluation of water-soluble docetaxel prodrugs-docetaxel esters of malic acid**

pp 6323–6330

Wenting Du, Lan Hong, Tongwei Yao, Xiaochun Yang, Qiaojun He, Bo Yang and Yongzhou Hu\*

The synthesis and evaluation of docetaxel esters of malic acid is reported. 2'-MalyI docetaxel and their sodium salts behave as prodrugs, and compound **3a** demonstrated enhanced antitumor activity in vitro when compared to docetaxel and showed the inhibitory effect on tumor growth in vivo.



- 2a** R<sup>1</sup> = DL-malyI, R<sup>2</sup> = H, R<sup>3</sup> = H      **3a** sodium salt of **2a**  
**2b** R<sup>1</sup> = L-malyI, R<sup>2</sup> = H, R<sup>3</sup> = H      **3b** sodium salt of **2b**  
**2c** R<sup>1</sup> = D-malyI, R<sup>2</sup> = H, R<sup>3</sup> = H      **3c** sodium salt of **2c**  
**4** R<sup>1</sup> = DL-malyI, R<sup>2</sup> = DL-malyI, R<sup>3</sup> = DL-malyI  
**5** R<sup>1</sup> = H, R<sup>2</sup> = DL-malyI, R<sup>3</sup> = H

**OTHER CONTENTS****Summary of instructions to authors**

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\*Corresponding author

i<sup>+</sup> Supplementary data available via ScienceDirect**COVER**

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's "Induced Fit Docking" technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem.* **2006**, *14*, 3160–3173].

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