

## Contents

### REVIEW

#### A QSAR review on melanoma toxicity

pp 5508–5526

Rajeshwar P. Verma, Suresh B. Mekapati, Alka Kurup and Corwin Hansch\*

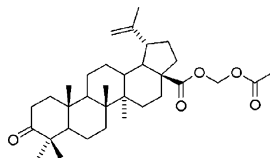
Quantitative structure–activity relationships have been performed for different sets of compounds with respect to their toxicities toward melanoma cells.

### ARTICLES

#### Influence of esterification and modification of A-ring in a group of lupane acids on their cytotoxicity

pp 5527–5535

Milan Urban, Jan Sarek,\* Iva Tislerova, Petr Dzubak and Marian Hajduch



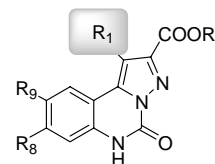
The aim of this work was to find an optimal ester group for preparation of lupane derivatives connecting high cytotoxicity with good chemical and pharmacological properties. Activities of methyl-, pivaloyloxymethyl- (Pom-), and acetoxymethyl- (Acm-) esters were compared with the activity of free acids. Although the methyl- and Pom-esters were generally less active than free acids, some Acm-esters had cytotoxicity similar to or even better than the starting compounds. Cytotoxic activity was measured in five cancer cell lines.

#### 1-Substituted pyrazolo[1,5-c]quinazolines as novel Gly/NMDA receptor antagonists:

pp 5536–5549

##### Synthesis, biological evaluation, and molecular modeling study

Flavia Varano,\* Daniela Catarzi, Vittoria Colotta, Francesca Romana Calabri, Ombretta Lenzi, Guido Filacchioni, Alessandro Galli, Chiara Costagli, Francesca Deflorian and Stefano Moro



The synthesis and Gly/NMDA, AMPA, and KA receptor binding affinity of a new set of 5,6-dihydro-pyrazolo[1,5-c]quinazoline-2-carboxylates bearing different substituents at position-1 are described. A molecular modeling study has been carried out to better understand receptor affinity and selectivity of these new pyrazolo-quinazoline derivatives.

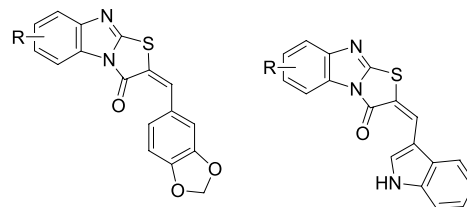
R<sub>1</sub> = COOEt, Cl, Br, CH<sub>3</sub>, COOH  
R<sub>2</sub> = Et, H  
R<sub>8</sub>, R<sub>9</sub> = H, Cl

### Synthesis and antitrichinellosis activity of some 2-substituted-[1,3]thiazolo[3,2-*a*]-benzimidazol-3(2*H*)-ones

pp 5550–5559

Anelia Ts. Mavrova,\* Kamelya K. Anichina, Dimitar I. Vuchev, Jordan A. Tsenov, Magdalena S. Kondeva and Mitka K. Micheva

Some new 2-arylden-thiazolo[3,2-*a*]benzimidazol-3(2*H*)-ones containing different substituents at the 6(7)-position were synthesized by using two methods. The structure and ratio of the 6- and 7-substituted isomers were established by spectral assignment and multiplet analysis of <sup>1</sup>H NMR spectra and the planar geometry of molecules was estimated through ab initio computations. The results of the pharmaco-therapeutic study showed remarkable activity of the compounds against the intestinal and muscle phases of *Trichinella spiralis* in white mice.

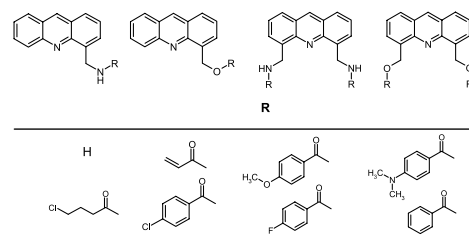


### Synthesis and antileishmanial activities of 4,5-di-substituted acridines as compared to their 4-mono-substituted homologues

pp 5560–5568

Di Giorgio Carole,\* De Méo Michel, Chiron Julien, Delmas Florence, Nikoyan Anna, Jean Séverine, Dumenil Gérard, Timon-David Pierre and Galy Jean-Pierre

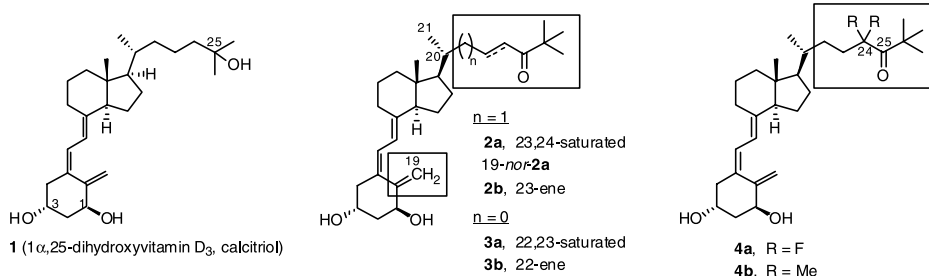
Newly synthesized 4,5-di-substituted acridines were assessed for in vitro antileishmanial activities as compared to those of their 4-mono-substituted homologues. Results led to the identification of a new class of promising acridine derivatives such as 4,5-bis(hydroxymethyl)acridine with a nonclassical mechanism of action based on inhibition of *Leishmania* internalization within macrophages.



### Highly antiproliferative, low-calcemic, side-chain ketone analogs of the hormone 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub>

pp 5569–5580

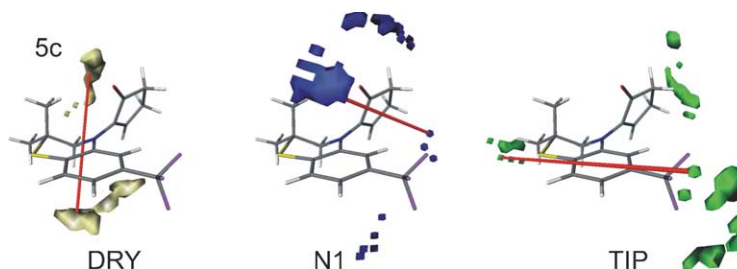
Gary H. Posner,\* Hyung Jin Kim, Mehmet Kahraman, Heung Bae Jeon, Byung Chul Suh, Hongbin Li, Patrick Dolan and Thomas W. Kensler



### Binding studies and GRIND/ALMOND-based 3D QSAR analysis of benzothiazine type K<sub>ATP</sub>-channel openers

pp 5581–5591

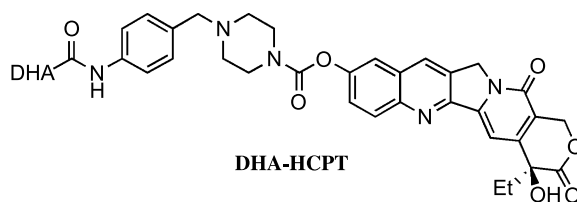
Emanuele Carosati, Horst Lemoine, Roberto Spogli, Dagmar Grittner, Raimund Mannhold, Oriana Tabarrini, Stefano Sabatini and Violetta Cecchetti\*



**Synthesis and evaluation of a DHA and 10-hydroxycamptothecin conjugate**

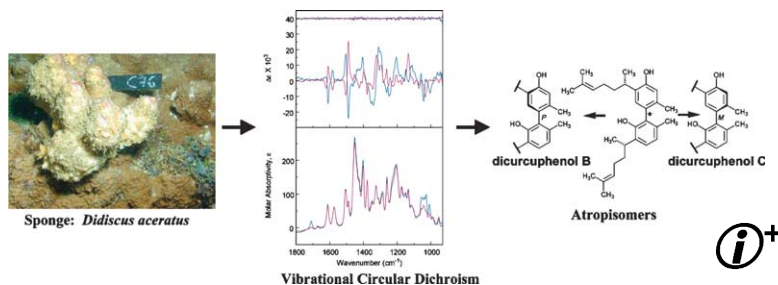
pp 5592–5599

Yuqiang Wang,\* Lianfa Li, Wei Jiang and James W. Larrick

**Stereochemical determination and bioactivity assessment of (*S*)-(+)-curcuphenol dimers isolated from the marine sponge *Didiscus aceratus* and synthesized through laccase biocatalysis**

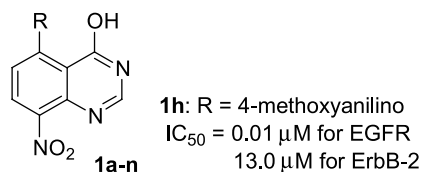
pp 5600–5612

Robert H. Cichewicz, Laura J. Clifford, Peter R. Lassen, Xiaolin Cao, Teresa B. Freedman, Laurence A. Nafie, Joshua D. Deschamps, Victor A. Kenyon, Jocelyn R. Flanary, Theodore R. Holman\* and Phillip Crews\*

**Synthesis and antitumor evaluation of novel 5-substituted-4-hydroxy-8-nitroquinazolines as EGFR signaling-targeted inhibitors**

pp 5613–5622

Yi Jin, Hui-Yuan Li, Li-Ping Lin, Jinzhi Tan, Jian Ding, Xiaomin Luo and Ya-Qiu Long\*

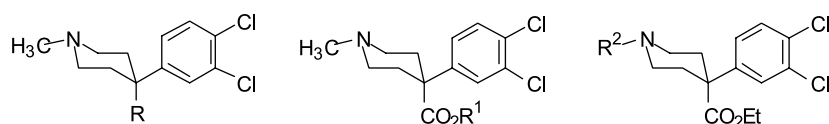


A series of novel 5-substituted-4-hydroxy-8-nitroquinazolines was synthesized and evaluated as inhibitors of EGFR/ErbB-2-overexpressing tumor cell lines proliferation, providing new promising templates for further development of potent inhibitors targeting both EGFR and ErbB-2.

**Structure–activity studies of 3′-4′-dichloro-meperidine analogues at dopamine and serotonin transporters**

pp 5623–5634

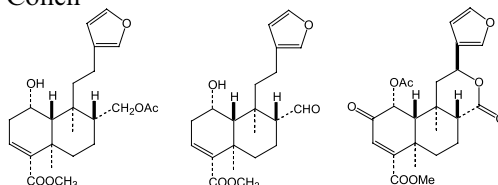
Jill B. Rhoden, Maud Bouvet, Sari Izenwasser, Dean Wade, Stacey A. Lomenzo and Mark L. Trudell\*



### New neoclerodane diterpenoids isolated from the leaves of *Salvia divinorum* and their binding affinities for human $\kappa$ opioid receptors

pp 5635–5639

David Y. W. Lee, Zhongze Ma, Lee-Yuan Liu-Chen, Yulin Wang, Yong Chen, William A. Carlezon, Jr. and Bruce Cohen\*

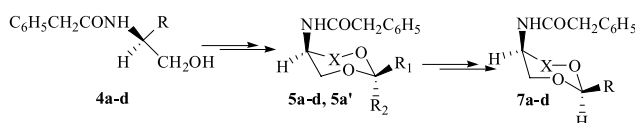


Three new neoclerodane diterpenoids—divinatorin D, divinatorin E, and salvinatorin G, along with 10 known terpenoids, were isolated from the leaves of *Salvia divinorum*. All these compounds were evaluated for their binding affinities to the human  $\kappa$  opioid receptors.

### Novel synthesis and anti-inflammatory activities of 2,5-disubstituted-dioxacycloalkanes

pp 5640–5646

Lanrong Bi, Yue Zhang, Ming Zhao,\* Chao Wang, Priscilla Chan, Jeffrey B.-H. Tok\* and Shiqi Peng\*

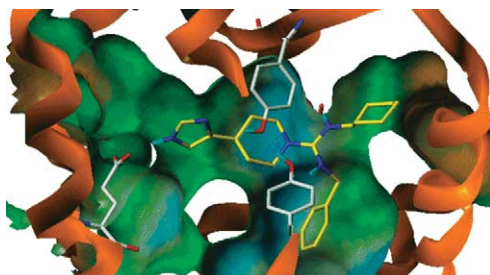


In **4a**: R = CH<sub>2</sub>OH; **4b**: R = CH(CH<sub>3</sub>)OH; **4c**: R = CH<sub>2</sub>CH<sub>2</sub>OH; **4d**: R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH; **5a**: X = CH<sub>2</sub>, R<sub>1</sub> = CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>, R<sub>2</sub> = H; **5a'**: X = CH<sub>2</sub>, R<sub>1</sub> = H, R<sub>2</sub> = CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>; **5b**: X = (S)-CHCH<sub>3</sub>, R<sub>1</sub> = CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>, R<sub>2</sub> = H; **5c**: X = CH<sub>2</sub>CH<sub>2</sub>, R<sub>1</sub> = CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>, R<sub>2</sub> = H; **5d**: X = CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, R<sub>1</sub> = CH<sub>2</sub>CH(OCH<sub>3</sub>)<sub>2</sub>, R<sub>2</sub> = H; **7a**: X = CH<sub>2</sub>, R = CH<sub>2</sub>CH(OCH<sub>3</sub>)OC<sub>2</sub>H<sub>5</sub>; **7b**: X = CH<sub>2</sub>, R = 1,3-dioxapentan-2-yl-methylene; **7c**: X = (S)-CHCH<sub>3</sub>, R = (2S,4S,5S)-4-methyl-5-phenylacetamino-1,3-dioxan-2-yl-methylene; **7d**: X = CH<sub>2</sub>CH<sub>2</sub>, R = (2S',5'S)-5-phenyl-acetamino-1,3-dioxacyclooctan-2-yl-methylene.

### Validation of a histamine H<sub>3</sub> receptor model through structure–activity relationships for classical H<sub>3</sub> antagonists

pp 5647–5657

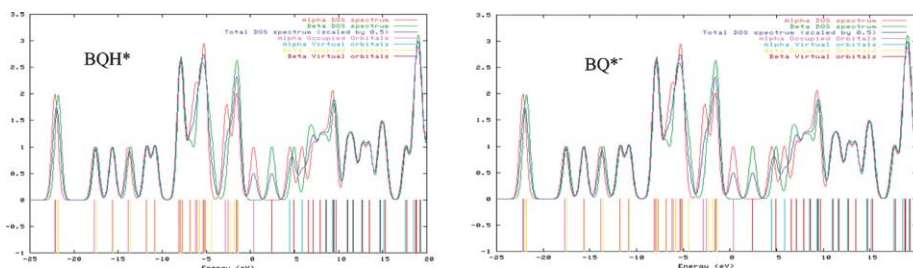
Simone Lorenzi, Marco Mor,\* Fabrizio Bordi, Silvia Rivara, Mirko Rivara, Giovanni Morini, Simona Bertoni, Vigilio Ballabeni, Elisabetta Barocelli and Pier Vincenzo Plazzi



### Density-functional theory and ab initio Hartree–Fork studies on the structural parameters and chemical activity of the free radicals generated by benzoquinone and hydroquinone

pp 5658–5667

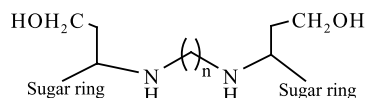
Yuanzhi Song, Jimin Xie,\* Huoming Shu, Ganqing Zhao, Xiaomeng Lv and Hongyan Cai



Occupied molecular orbital and unoccupied molecular orbital of BQH and BQ<sup>•</sup>.

**Synthesis and antitubercular activities of bis-glycosylated diamino alcohols****pp 5668–5679**

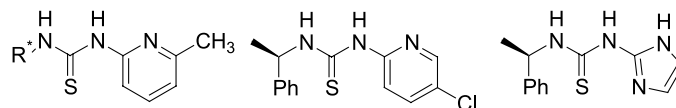
R. P. Tripathi,\* V. K. Tiwari, N. Tewari, D. Katiyar, N. Saxena, S. Sinha, A. Gaikwad,  
A. Srivastava, V. Chaturvedi, Y. K. Manju, R. Srivastava and B. S. Srivastava



A number of bis-glycosylated diamino-alcohols were synthesized and evaluated against *M. tuberculosis*, and many of them were found to have good in vitro activity.

**Thiourea-based non-nucleoside inhibitors of HIV reverse transcriptase as bifunctional organocatalysts in the asymmetric Strecker synthesis****pp 5680–5685**

Svetlana B. Tsogoeva,\* Martin J. Hateley, Denis A. Yalalov, Kathrin Meindl,  
Christoph Weckbecker and Klaus Huthmacher



The potential of novel and known pyridyl thiourea derivatives (non-nucleoside inhibitors of HIV reverse transcriptase) as bifunctional organic catalysts in the asymmetric Strecker synthesis was investigated.

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\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

2005: Human liver glycogen phosphorylase A (HLGPa) 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 HLGPa 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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