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# Bioorganic & Medicinal Chemistry

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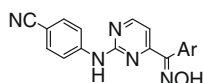
## Bioorganic & Medicinal Chemistry Volume 18, Issue 7, 2010

### Contents

#### ARTICLES

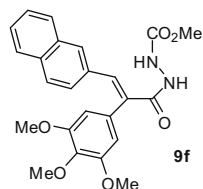
- Synthesis and biological evaluation of 4-(hydroxyimino)arylmethyl diarylpyrimidine analogues as potential non-nucleoside reverse transcriptase inhibitors against HIV** pp 2370–2374

Xiao-Qing Feng, Zhao-Sen Zeng, Yong-Hong Liang, Fen-Er Chen\*, Christophe Pannecouque, Jan Balzarini, Erik De Clercq



- Pyrazolone-fused combretastatins and their precursors: synthesis, cytotoxicity, antitubulin activity and molecular modeling studies** pp 2375–2387

Bojan Burja, Tamara Čimbora-Zovko, Sanja Tomić, Tihana Jelušić, Marijan Kočev, Slovenko Polanc\*, Maja Osmak\*

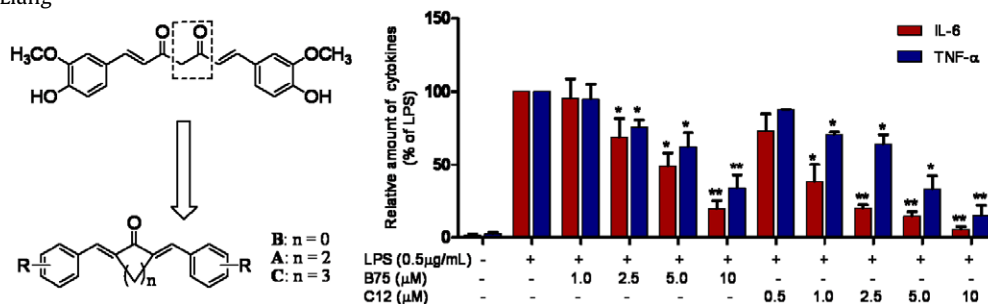


Hydrazide **9f** is highly cytotoxic against various tumor cells including cisplatin resistant cells. It binds to the colchicine binding site at the tubulin heterodimer and has a strong antitubulin potential.



- Synthesis of mono-carbonyl analogues of curcumin and their effects on inhibition of cytokine release in LPS-stimulated RAW 264.7 macrophages** pp 2388–2393

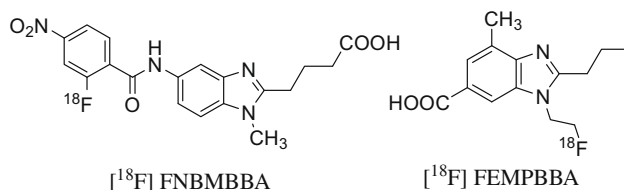
Chengguang Zhao, Ju Yang, Yi Wang, Donglou Liang, Xuyi Yang, Xiaoxia Li, Jianzhang Wu, Xiaoping Wu, Shulin Yang, Xiaokun Li, Guang Liang\*



### **<sup>18</sup>F Labeled benzimidazole derivatives as potential radiotracer for positron emission tomography (PET) tumor imaging**

pp 2394–2401

Shuting Zhang, Xiao Wang\*, Yong He, Rui Ding, Hang Liu, Jingli Xu, Man Feng, Guixia Li, Ming Wang, Cheng Peng, Chuanmin Qi\*

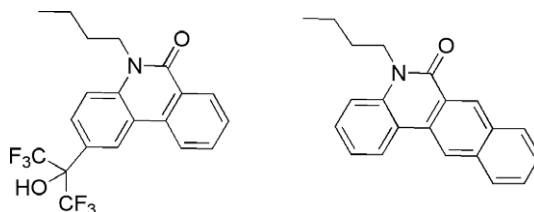


Two  $[^{18}\text{F}]$  labeled benzimidazole derivatives was synthesised.  $[^{18}\text{F}]$  FEMPBBBA has got an excellent result of biodistribution assay in S180 tumor bearing mice and has significant advantages in some aspects compared with L- $[^{18}\text{F}]$  FET and  $[^{18}\text{F}]$ -FDG in the same animal model, especially in tumor/brain uptake ratio.

### **Structural development studies of anti-hepatitis C virus agents with a phenanthridinone skeleton**

pp 2402–2411

Masahiko Nakamura, Atsushi Aoyama, Mohammed T. A. Salim, Mika Okamoto, Masanori Baba\*, Hiroyuki Miyachi, Yuichi Hashimoto, Hiroshi Aoyama\*

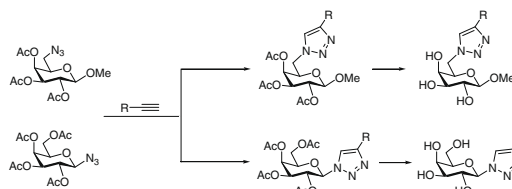


Substituted phenanthridinone skeleton was demonstrated to be useful as a scaffold to develop anti-HCV agents.

### **'Click chemistry' synthesis of a library of 1,2,3-triazole-substituted galactose derivatives and their evaluation against *Trypanosoma cruzi* and its cell surface *trans*-sialidase**

pp 2412–2427

Ivone Carvalho\*, Peterson Andrade, Vanessa L. Campo, Paulo M. M. Guedes, Renata Sesti-Costa, João S. Silva, Sergio Schenkman, Simone Dedola, Lionel Hill, Martin Rejzek, Sergey A. Nepogodiev, Robert A. Field\*



A 46-membered library of galactose-based triazoles was synthesized by 'click chemistry'. These compounds proved to be weak substrate analogue inhibitors of *Trypanosoma cruzi* *trans*-sialidase but some compounds showed selective trypanocidal activity whilst others showed selective toxicity towards mammalian cells.

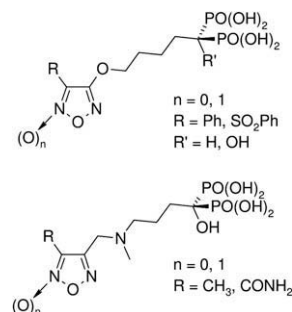


### **Synthesis and preliminary pharmacological characterisation of a new class of nitrogen-containing bisphosphonates (N-BPs)**

pp 2428–2438

Marco L. Lolli, Barbara Rolando, Paolo Tosco, Shilpi Chaurasia, Antonella Di Stilo, Loretta Lazzarato\*, Eva Gorassini, Riccardo Ferracini, Simonetta Oliaro-Bosso, Roberta Fruttero, Alberto Gasco

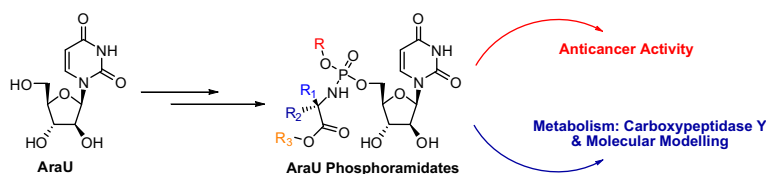
A new series of N-BPs able to inhibit osteoclastogenesis on RAW 246.7 and PBMC cells is presented. The most active compounds were tested for their ability to inhibit the mevalonate pathway.



### Phosphoramidates of 2'-β-D-arabinouridine (AraU) as phosphate prodrugs; design, synthesis, in vitro activity and metabolism

pp 2439–2446

Youcef Mehellou, Rocco Valente, Huw Mottram, Elisabeth Walsby, Kenneth I. Mills, Jan Balzarini, Christopher McGuigan\*



Herein, we describe the design, synthesis and anticancer activity of a series of AraU phosphoramidates. In addition, we report on the metabolism of these phosphoramidates by carboxypeptidase Y and molecular modelling studies investigating the possible cleavage of the P–N bond. Cell extract studies complement the modelling study.

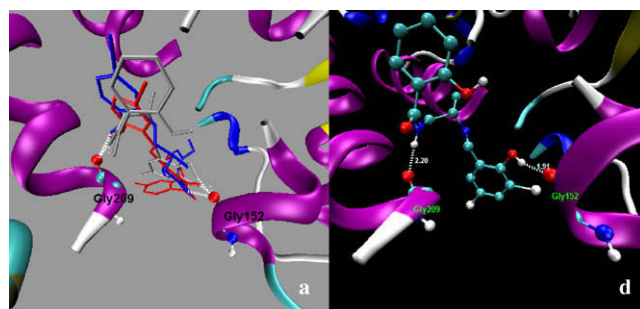


### Synthesis, molecular modeling and biological evaluation of PSB as targeted antibiotics

pp 2447–2455

Kui Cheng, Qing-Zhong Zheng, Jin Hou, Yang Zhou, Chang-Hong Liu\*, Jing Zhao\*, Hai-Liang Zhu\*

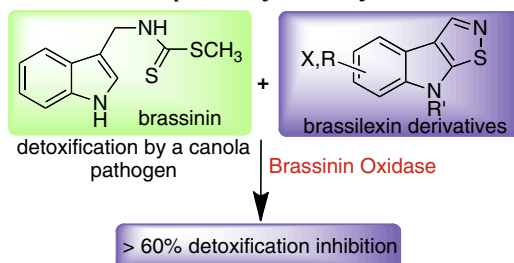
We described here the design, synthesis, molecular modeling, and biological evaluation of a series of peptide and Schiff bases (PSB) small molecules, inhibitors of *Escherichia coli* β-Ketoacyl-acyl carrier protein synthase III (ecKAS III). The initial lead compound was reported by us previously, we continued to carry out structure–activity relationship studies and optimize the lead structure to potent inhibitors in this research. The results demonstrated that both *N*-(2-(3,5-dichloro-2-hydroxybenzylideneamino)propyl)-2-hydroxybenzamide (**1f**) and 2-hydroxy-*N*-(2-(2-hydroxy-5-iodobenzylideneamino)propyl)-4-methylbenzamide (**3e**) were good ecKAS III inhibitory activity and well binding affinities by bonding Gly152/Gly209 of ecKAS III and fit into the mouth of the substrate tunnel, and can be as potential antibiotics agent, displaying minimal inhibitory concentration values in the range 0.20–3.13 μg/mL and 0.39–3.13 μg/mL against various bacteria.



### Discovery of inhibitors of brassinin oxidase based on the scaffolds of the phytoalexins brassilexin and wasalexin

pp 2456–2463

M. Soledade C. Pedras\*, Zoran Minic, Vijay K. Sarma-Mamillapalle, Mojmir Suchy



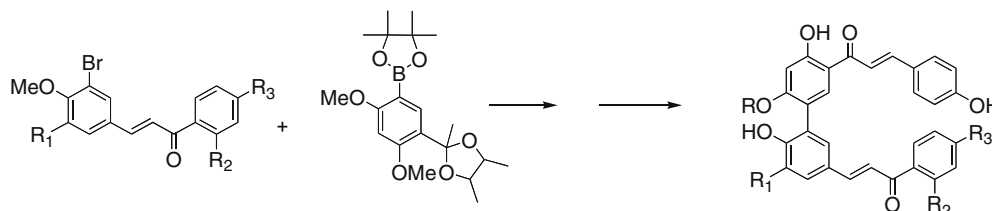
Brassinin oxidase, a unique detoxifying enzyme produced by the plant pathogen *Leptosphaeria maculans*, mediates the detoxification of the phytoalexin brassinin. Evaluation of different derivatives of the phytoalexins brassilexin and wasalexins A and B revealed 6-Cl-brassilexin to be the best competitive inhibitor discovered to date ( $K_i = 31 \mu\text{M}$ ).



### Total synthesis, antiprotozoal and cytotoxicity activities of rhuschalcone VI and analogs

pp 2464–2473

Shetonde O. Mihigo, Wendimagegn Mammo, Merhatibeb Bezabih, Kerstin Andrae-Marobela, Berhanu M. Abegaz\*

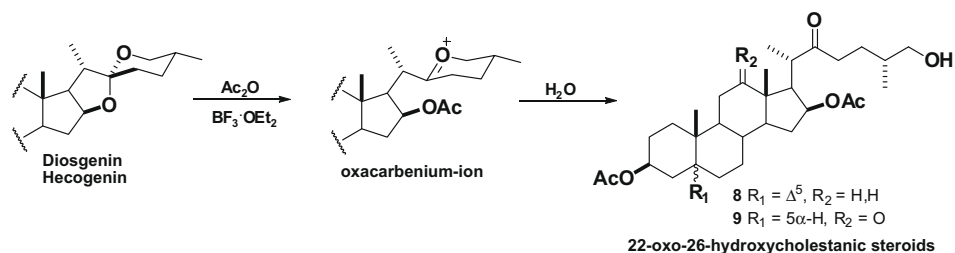


The total syntheses of natural product rhuschalcone VI and eight analogs employing the Suzuki–Miyaura reaction are reported together with antiprotozoal activities and cytotoxicity data for some of them.

### Synthesis of 26-hydroxy-22-oxocholestanic frameworks from diosgenin and hecogenin and their in vitro antiproliferative and apoptotic activity on human cervical cancer CaSki cells

pp 2474–2484

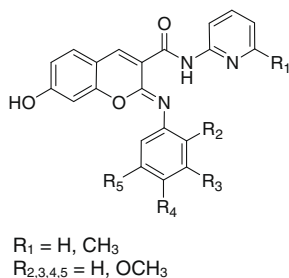
María A. Fernández-Herrera, Hugo López-Muñoz, José M. V. Hernández-Vázquez, Moisés López-Dávila, María L. Escobar-Sánchez, Luis Sánchez-Sánchez\*, B. Mario Pinto\*, Jesús Sandoval-Ramírez\*



### Chromene-3-carboxamide derivatives discovered from virtual screening as potent inhibitors of the tumour maker, AKR1B10

pp 2485–2490

Satoshi Endo\*, Toshiyuki Matsunaga, Kazuo Kuwata, Hai-Tao Zhao, Ossama El-Kabbani, Yukio Kitade, Akira Hara

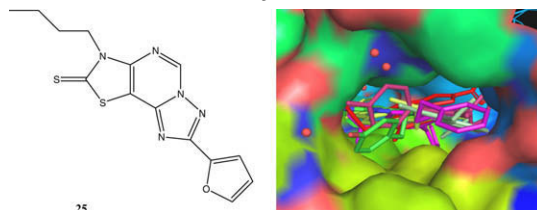


The chromene-3-carboxamide derivatives were found as potent inhibitors of AKR1B10.

### Novel 8-(furan-2-yl)-3-substituted thiazolo [5,4-e][1,2,4] triazolo[1,5-c] pyrimidine-2(3H)-thione derivatives as potential adenosine $A_{2A}$ receptor antagonists

pp 2491–2500

Chandra Bhushan Mishra, Sandeep Kumar Barodia, Amresh Prakash, J. B. Senthil Kumar, Pratibha Mehta Luthra\*



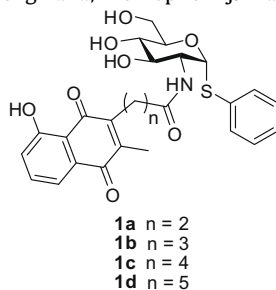
Novel thiazolotriazolopyrimidine derivatives were (**23–33**) designed and synthesized to evaluate their potential adenosine  $A_{2A}$  receptor ( $A_{2A}R$ ) antagonists activity. Docking simulation results showed that thiazolotriazolopyrimidine derivatives (**23–33**) and SCH58261, a standard  $A_{2A}R$  antagonist shared a similar binding motif inside the transmembrane (TM) region and extracellular loops of the human  $A_{2A}R$ . Our results showed that the compound **25** ( $R = C_4H_9$ ) possessed reasonably good affinity ( $K_i = 0.12$  nM) and high selectivity with  $A_{2A}$  receptor ( $A_{2A}/A_1 = 1288$ ).



### Conjugates of plumbagin and phenyl-2-amino-1-thioglucoiside inhibit MshB, a deacetylase involved in the biosynthesis of mycothiol

pp 2501–2514

David W. Gammon\*, Daniel J. Steenkamp, Vuyo Mavumengwana, Mohlopheni J. Marakalala, Theophilus T. Mudzungu, Roger Hunter, Muganza Munyololo

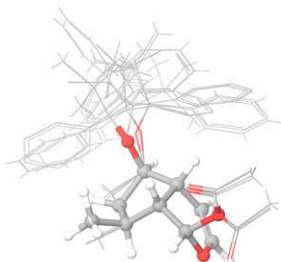


Compounds **1a–d** with plumbagin tethered to a phenyl-2-amino-thioglucoiside are potent inhibitors of the amidase mshB in the *Mycobacteria*.

**Enhancement of antiproliferative activity by molecular simplification of catalpol**

pp 2515–2523

Celina García\*, Leticia G. León, Carlos R. Pungitore, Carla Ríos-Luci, Antonio H. Daranas, Juan C. Montero, Atanasio Pandiella, Carlos E. Tonn, Víctor S. Martín\*, José M. Padrón\*



$$GI_{50} = 0.38\text{--}1.86 \mu\text{M}$$

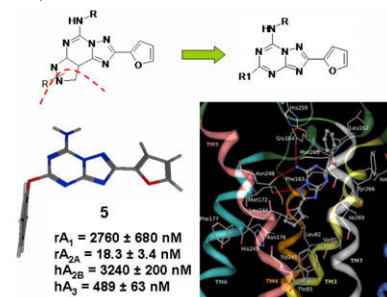
Molecular simplification of any given natural or synthetic template helps medicinal chemists designing shorten synthetic routes while keeping or enhancing the biological activity. This strategy is exemplified with simplified analogs of naturally occurring catalpol.

**Synthesis and pharmacological characterization of a new series of 5,7-disubstituted-[1,2,4]triazolo[1,5-a][1,3,5]-triazine derivatives as adenosine receptor antagonists: A preliminary inspection of ligand–receptor recognition process**

pp 2524–2536

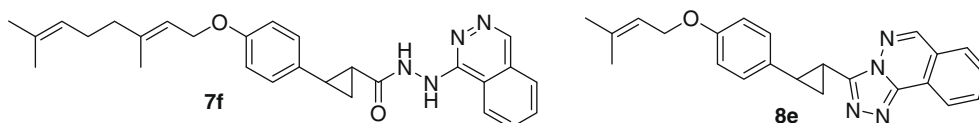
Giorgia Pastorin, Stephanie Federico, Silvia Paoletta, Marta Corradino, Francesca Cateni, Barbara Cacciari, Karl-Norbert Klotz, Zhan-Guo Gao, Kenneth A. Jacobson, Giampiero Spalluto\*, Stefano Moro\*

Using a molecular simplification approach, a novel series of triazolotriazine differently substituted at the C5 and N7 has been synthesized and pharmacologically characterized as adenosine receptor antagonists.

**Synthesis and anticancer activity evaluation of 2(4-alkoxyphenyl)cyclopropyl hydrazides and triazolo phthalazines**

pp 2537–2548

Prithwiraj De, Michel Baltas\*, Delphine Lamoral-Theys, Céline Bruyère, Robert Kiss, Florence Bedos-Belval, Nathalie Saffon

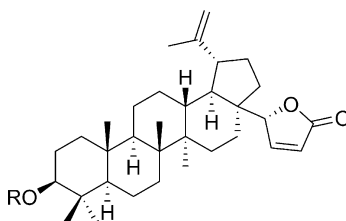


A series of new 2(4-alkoxyphenyl)cyclopropyl hydrazide- and triazolo-derivatives were synthesized and their in vitro anticancer activities have been evaluated. Compound **7f** and **8e** showed encouraging cytostatic activities particularly against apoptosis-resistant cancer cell lines.

**Synthesis and biological evaluation of antitumor-active  $\gamma$ -butyrolactone substituted betulin derivatives**

pp 2549–2558

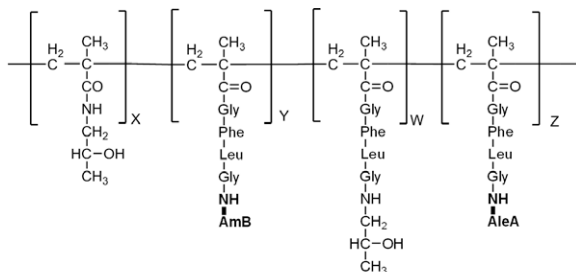
René Csuk\*, Alexander Barthel, Stefan Schwarz, Harish Kommera, Reinhard Paschke



### Water-soluble polymer–drug conjugates for combination chemotherapy against visceral leishmaniasis

pp 2559–2565

Salvatore Nicoletti, Karin Seifert, Ian H. Gilbert\*

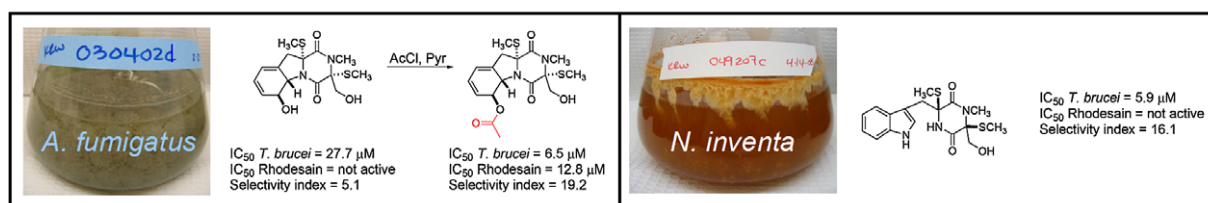


AleA = alendronic acid; AmB = amphotericin B

### Assessing the trypanocidal potential of natural and semi-synthetic diketopiperazines from two deep water marine-derived fungi

pp 2566–2574

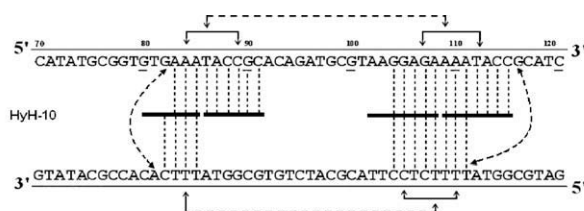
Katharine R. Watts, Joseline Ratnam, Kean-Hooi Ang, Karen Tenney, Jennifer E. Compton, James McKerrow, Phillip Crews\*



### Novel DNA–peptide interaction networks

pp 2575–2585

Jonathan T. B. Huang, Yen-Chung Chen, Jung-Cheng Chang, Kee-Ching G. Jeng, Karen K. L. Kao, Robin C. K. Yang, Lou-Sing Kan, Ming-Tsair Wey, Michael J. Waring, Chee-Shan Chen, Wei-Jyun Chien, Leung Sheli\*



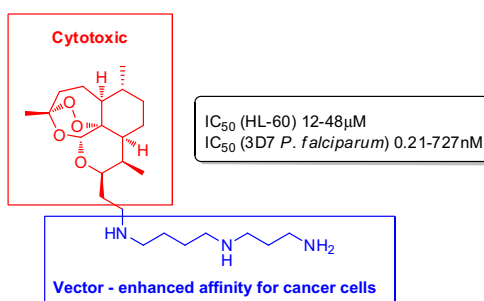
Recent footprinting and CD studies support the hypothesis of three types of DNA-peptide allosteric interaction networks.



### Design, synthesis and antimalarial/anticancer evaluation of spermidine linked artemisinin conjugates designed to exploit polyamine transporters in Plasmodium falciparum and HL-60 cancer cell lines

pp 2586–2597

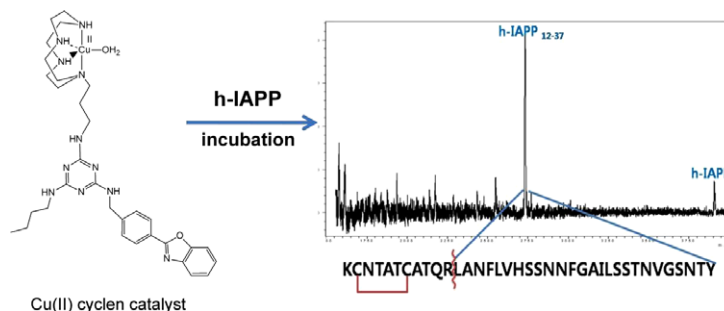
James Chadwick, Michael Jones, Amy E. Mercer, Paul A. Stocks, Stephen A. Ward, B. Kevin Park, Paul M. O'Neill\*



**Cu(II) cyclen cleavage agent for human islet amyloid peptide**

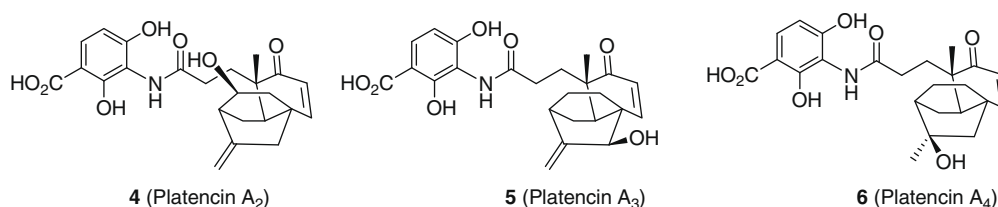
pp 2598–2601

Keunhong Jeong\*, Woo Young Chung, Young-Sik Kye, Dongwook Kim

**Isolation, structure and biological activities of platencin A<sub>2</sub>–A<sub>4</sub> from *Streptomyces platensis***

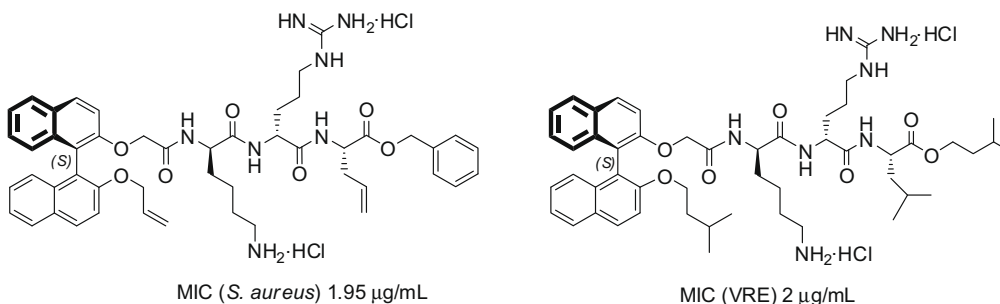
pp 2602–2610

Chaowei Zhang, John Ondeyka, Lisa Dietrich, Francis P. Gailliot, Michelle Hesse, Michael Lester, Karen Dorso, Mary Motyl, Sookhee N. Ha, Jun Wang, Sheo B. Singh\*

**Synthesis and antibacterial studies of binaphthyl-based tripeptides. Part 1**

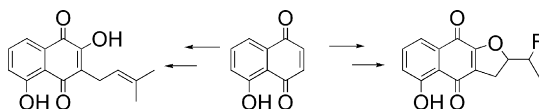
pp 2611–2620

John B. Bremner\*, Paul A. Keller\*, Stephen G. Pyne\*, Timothy P. Boyle, Zinka Brkic, Dorothy M. David, Mark Robertson, Kittiya Somphol, Dean Baylis, Jonathan A. Coates, John Deadman, Darshini Jeevarajah, David I. Rhodes

**Antiproliferative activity of synthetic naphthoquinones related to lapachol. First synthesis of 5-hydroxylapachol**

pp 2621–2630

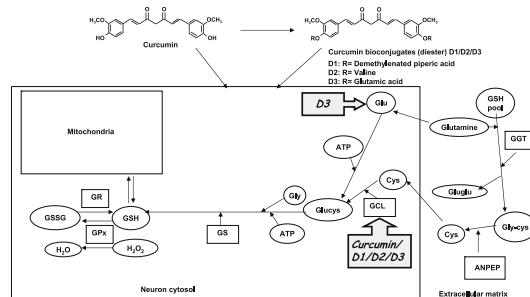
Evelyn L. Bonifazi, Carla Ríos-Luci, Leticia G. León, Gerardo Burton, José M. Padrón\*, Rosana I. Misico\*



## Bioconjugates of curcumin display improved protection against glutathione depletion mediated oxidative stress in a dopaminergic neuronal cell line: Implications for Parkinson's disease

pp 2631–2638

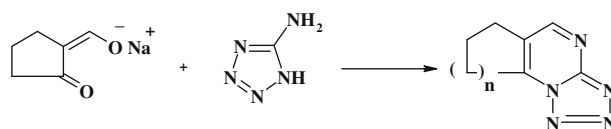
G. Harish, C. Venkateshappa, Rajeswara Babu Mythri, Shiv Kumar Dubey, Krishna Mishra, Neetu Singh, Shireen Vali, M. M. Srinivas Bharath\*



## Regioselective one-pot synthesis and anti-proliferative and apoptotic effects of some novel tetrazolo[1,5-a]pyrimidine derivatives

pp 2639–2644

Ahmed M. Hussein, Osama M. Ahmed\*

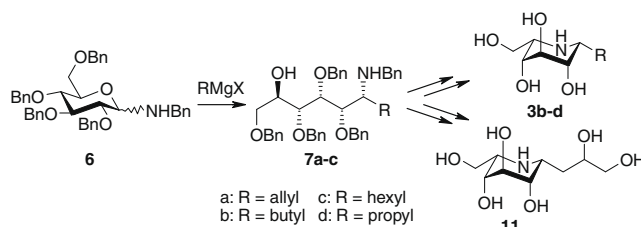


An easy and efficient route for the synthesis of tetrazolopyrimidines has been achieved by the reaction 5-amino-1H-tetrazole hydrate with the sodium formyl salts of cyclic ketones as a one-step reaction, afforded in a good yield the cycloalkane ring-fused tetrazolo[1,5-a]pyrimidines. The cyclohexane ring-fused tetrazolo[1,5-a]-pyrimidine derivative, 6,7,8,9-tetrahydrotetrazolo[1,5-a] quinazoline, exhibited potential and moderate anti-proliferative effects against EAC and HepG2, respectively. These anti-tumor activities may be mediated via induction of apoptosis and cell cycle arrest.

## Synthesis of new $\beta$ -1-C-alkylated imino-1-iditols: A comparative study of their activity as $\beta$ -glucocerebrosidase inhibitors

pp 2645–2650

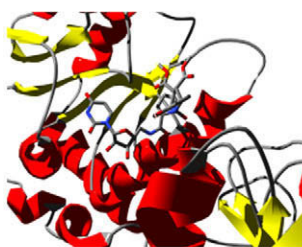
Wojciech Schönemann, Estelle Gallienne, Philippe Compain, Kyoko Ikeda, Naoki Asano, Olivier R. Martin\*



## Inhibition of *Escherichia coli* glycosyltransferase MurG and *Mycobacterium tuberculosis* Gal transferase by uridine-linked transition state mimics

pp 2651–2663

Amy E. Trunkfield, Sudagar S. Gurcha, Gurdial S. Besra, Timothy D. H. Bugg\*



Uridine-linked transition state analogue bound to *Escherichia coli* MurG

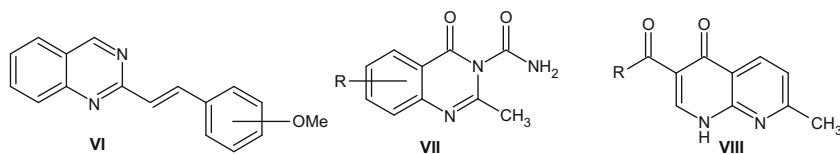




**Investigating the anti-proliferative activity of styrylanaphthalenes and azanaphthalenediones**

pp 2664–2671

Anna Mrozek-Wilczkiewicz, Danuta S. Kalinowski, Robert Musiol, Jacek Finster, Agnieszka Szurko, Katarzyna Serafin, Magdalena Knas, Sishir K. Kamalapuram, Zaklina Kovacevic, Josef Jampilek, Alicja Ratuszna, Joanna Rzeszowska-Wolny, Des R. Richardson\*, Jaroslaw Polanski\*

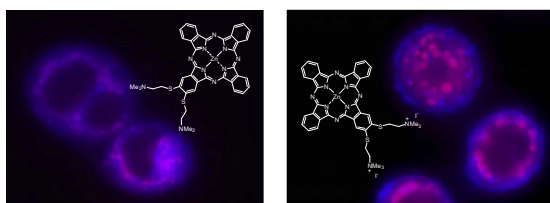


Several quinazolinone and styrylquinazoline analogues were found to have markedly greater anti-proliferative activity than desferoxamine and cis-platin.

**Preparation and in vitro photodynamic activity of amphiphilic zinc(II) phthalocyanines substituted with 2-(dimethylamino)ethylthio moieties and their N-alkylated derivatives**

pp 2672–2677

Wubiao Duan, Pui-Chi Lo, Lei Duan, Wing-Ping Fong, Dennis K. P. Ng\*



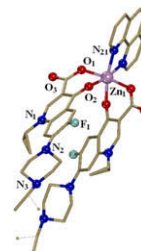
A new series of amphiphilic zinc(II) phthalocyanines containing amino or ammonium groups have been synthesized. In general, they exhibit high photocytotoxicity with IC<sub>50</sub> values as low as 0.08  $\mu$ M, and show high and selective affinity to the mitochondria or cell membrane of HT29 cells depending on the charge of the substituents.

**Zinc(II) complexes of the second-generation quinolone antibacterial drug enrofloxacin: Structure and DNA or albumin interaction**

pp 2678–2685

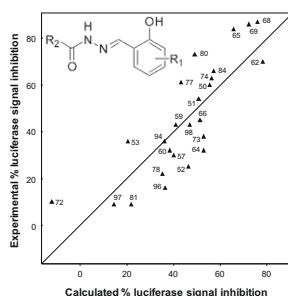
Alketa Tarushi, Catherine P. Raptopoulou, Vassilis Psycharis, Aris Terzis, George Psomas, Dimitris P. Kessissoglou\*

Zinc mononuclear complexes with the quinolone antibacterial drug enrofloxacin in the absence or presence of a nitrogen donor heterocyclic ligand 1,10-phenanthroline or 2,2'-bipyridine have been synthesized and structurally characterized. The interaction of the complexes with calf-thymus DNA, human and bovine serum albumin has also been evaluated.

**Statistical molecular design of a focused salicylidene acylhydrazide library and multivariate QSAR of inhibition of type III secretion in the Gram-negative bacterium *Yersinia***

pp 2686–2703

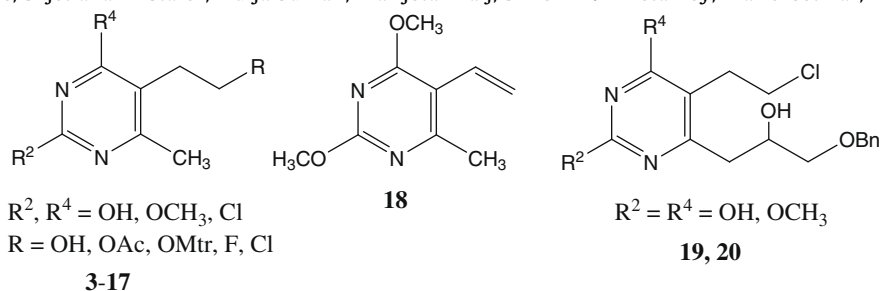
Markus K. Dahlgren, Caroline E. Zetterström, Åsa Gylfe, Anna Linusson, Mikael Elofsson\*



**Synthesis, X-ray crystal structure study and antitumoral evaluations of 5,6-disubstituted pyrimidine derivatives**

pp 2704–2712

Tatjana Gazivoda Kraljević, Svjetlana Krištafor, Lidija Šuman, Marijeta Kralj, Simon M. Ametamey, Mario Cetina\*, Silvana Raić-Malić\*

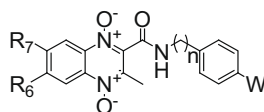


The present study deals with synthesis of 5,6-disubstituted pyrimidine derivatives and their cytostatic activities against human malignant cell lines. The structures of three compounds were determined by X-ray crystal structure analysis.

**New 3-methylquinoxaline-2-carboxamide 1,4-di-N-oxide derivatives as anti-*Mycobacterium tuberculosis* agents**

pp 2713–2719

Saioa Ancizu, Elsa Moreno, Beatriz Solano, Raquel Villar, Asunción Burguete, Enrique Torres, Silvia Pérez-Silanes\*, Ignacio Aldana, Antonio Monge

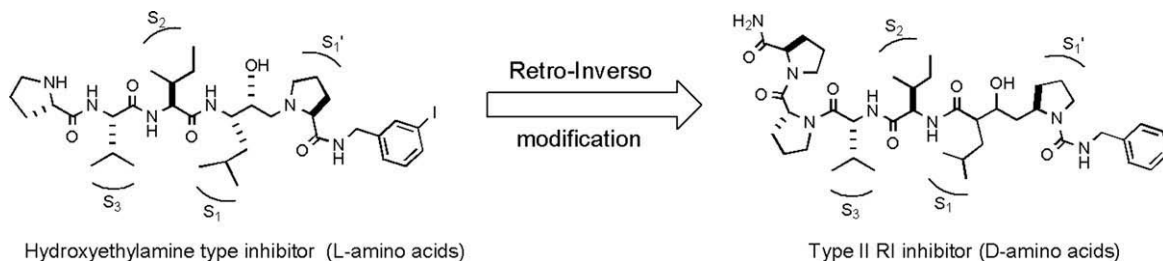


Thirty-six new amide quinoxaline 1,4-di-N-oxide derivatives have been synthesized and evaluated as potential anti-tubercular agents by the TAACF, obtaining biological values in the same order as the reference compound rifampin.

**Evaluation of retro-inverso modifications of HTLV-1 protease inhibitors containing a hydroxyethylamine isoster**

pp 2720–2727

Tadashi Tatsumi, Chiyuki Awahara, Hiromi Naka, Saburo Aimoto, Hiroyuki Konno, Kazuto Nosaka, Kenichi Akaji\*

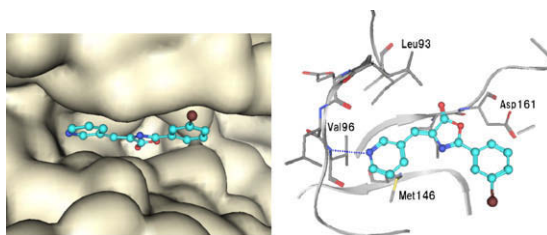


Retro-inverso (RI) modification of HTLV-1 protease inhibitors was effective without significantly influencing the inhibitory activity.

**Structure–activity relationship of novel DAPK inhibitors identified by structure-based virtual screening**

pp 2728–2734

Masako Okamoto\*, Kiyoshi Takayama, Tomoko Shimizu, Ayumu Muroya, Toshio Furuya



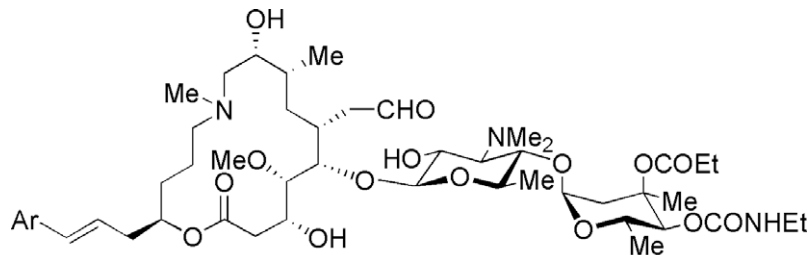
An in silico approach lead to the efficient discovery of novel potent and selective DAPK inhibitors.

### Novel azalides derived from 16-membered macrolides. III. Azalides modified at the C-15 and 4'' positions: Improved antibacterial activities

pp 2735–2747

Tomoaki Miura\*, Satomi Natsume, Kenichi Kanemoto, Eiki Shitara, Hideki Fushimi, Takuji Yoshida, Keiichi Ajito\*

The design and synthesis of 16-membered azalides modified at the C-15 and 4'' positions are described. 3-Hydroxyl azalides having an arylpropenyl and an ethylcarbamoyl group at the C-15 and C-4'' position, respectively, exhibited significant improvement in antibacterial activities against *erm*-resistant *Streptococcus pneumoniae*.

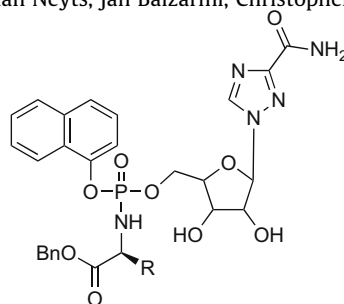


Ar = quinolin-3-yl, isoquinolin-4-yl, 1-aminoisoquinolin-4-yl

### Application of the phosphoramidate ProTide approach to the antiviral drug ribavirin

pp 2748–2755

Marco Derudas, Andrea Brancale, Lieve Naesens, Johan Neyts, Jan Balzarini, Christopher McGuigan\*



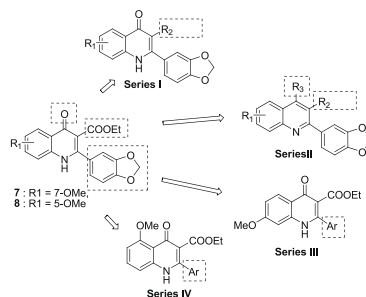
Phosphoramidate ProTides of ribavirin do not show in vitro antiviral enhancement despite apparent efficient ester cleavage in vitro. Poor amino acid cleavage in vitro is implicated.



### Synthesis and structure–activity relationships of antimalarial 4-oxo-3-carboxyl quinolones

pp 2756–2766

Yiqun Zhang, W. Armand Guiguemde, Martina Sigal, Fangyi Zhu, Michele C. Connelly, Solomon Nwaka, R. Kiplin Guy\*

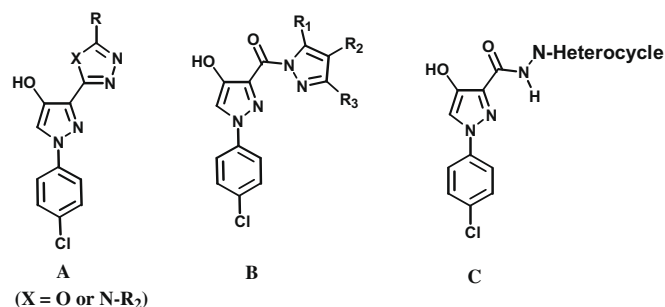


### Polysubstituted pyrazoles, part 6. Synthesis of some 1-(4-chlorophenyl)-4-hydroxy-1H-pyrazol-3-carbonyl derivatives linked to nitrogenous heterocyclic ring systems as potential antitumor agents

pp 2767–2776

Sherif A. F. Rostom\*

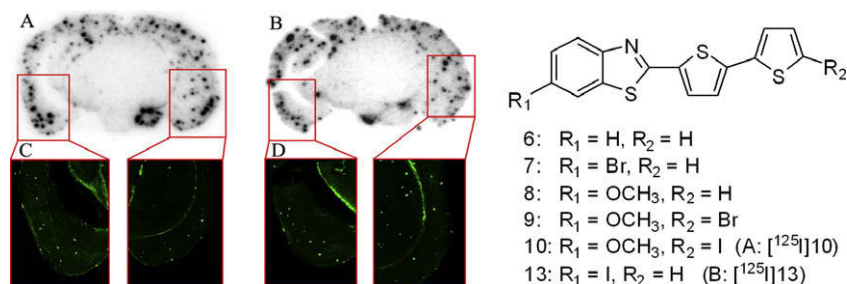
The synthesis of two novel series of 1-(4-chlorophenyl)-4-hydroxy-1H-pyrazoles linked to either polysubstituted 1H-pyrazole counterparts through a carbonyl bridge, or to some biologically-active nitrogenous heterocycles by an amide linker, is described. According to the National Cancer Institute (NCI) in vitro disease-oriented antitumor screening protocol, six compounds **2**, **3**, **6**, **7**, **13** and **14** revealed a significant broad spectrum of antitumor potential against most of the tested subpanel tumor cell lines at the GI<sub>50</sub> and TGI levels, together with a mild cytotoxic (LC<sub>50</sub>) activity. Compounds **13** and **14** proved to be the most active antitumor members identified in this study.

(X = O or N-R<sub>2</sub>)

### Synthesis and evaluation of novel benzothiazole derivatives based on the bithiophene structure as potential radiotracers for $\beta$ -amyloid plaques in Alzheimer's disease

pp 2777–2784

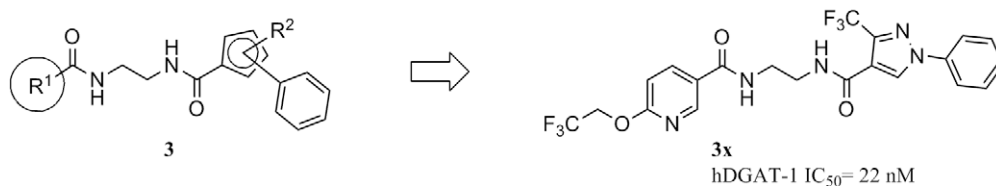
Meng-Chao Cui, Zi-Jing Li, Rui-Kun Tang, Bo-Li Liu\*



### Novel acyl coenzyme A (CoA): Diacylglycerol acyltransferase-1 inhibitors: Synthesis and biological activities of diacylthylenediamine derivatives

pp 2785–2795

Yoshihisa Nakada\*, Thomas D. Aicher, Yvan Le Huerou, Timothy Turner, Scott A. Pratt, Stephen S. Gonzales, Steve A. Boyd, Hiroshi Miki, Toshihiro Yamamoto, Hiroshi Yamaguchi, Koki Kato, Shuji Kitamura

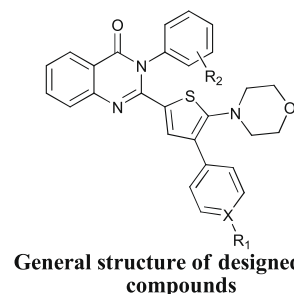


### Design, synthesis and evaluation of novel 2-thiophen-5-yl-3H-quinazolin-4-one analogues as inhibitors of transcription factors NF- $\kappa$ B and AP-1 mediated transcriptional activation: Their possible utilization as anti-inflammatory and anti-cancer agents

pp 2796–2808

Rajan S. Giri, Hardik M. Thaker, Tony Giordano, Jill Williams, Donna Rogers, Kamala K. Vasu\*, Vasudevan Sudarsanam

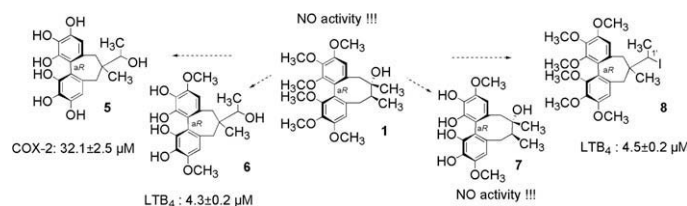
A series of 2-(2,3-disubstituted-thiophen-5-yl)-3H-quinazolin-4-one analogs was designed, synthesized and evaluated for its inhibitory activity towards transcription factors NF- $\kappa$ B and AP-1 mediated transcriptional activation. Their possible utilization as anti-inflammatory and anti-cancer agent has been discussed.




### Derivatives of schisandrin with increased inhibitory potential on prostaglandin $E_2$ and leukotriene $B_4$ formation in vitro

pp 2809–2815

Martina Blunder, Eva M. Pferschy-Wenzig, Walter M. F. Fabian, Antje Hufner, Olaf Kunert, Robert Saf, Wolfgang Schühly, Rudolf Bauer\*



\*Corresponding author

+ Supplementary data available via ScienceDirect

## COVER

Which conformation is the best for inhibitors of  $\beta$ -glucocerebrosidase?  ${}^4C_1$  conformation is the prevalent one for 1-C-alkylated iminosugars in the D-*gluco* series (upper structure),  ${}^1C_4$  the prevalent one in the L-*ido* series (lower structure), while both conformations occur in the D-*xylo* series (middle structures). This greater flexibility might be a good explanation for the very important affinity and selectivity of such compounds towards  $\beta$ -glucocerebrosidase. The figure was created using the three-dimensional structure of the enzyme including the modeled glucosylceramide substrate (in yellow) from the following publication: Futerman, A. H.; Sussman, J. L.; Horowitz, M.; Silman, I.; Zimran, A. *Trends Pharmacol. Sci.* **2004**, 25, 147–151. [Schönemann, W.; Gallienne, E.; Compain, P.; Ikeda, K.; Asano, N.; Martin, O. R. *Bioorg. Med. Chem.* **2010**, 18, 2645–2650.]

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