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# Bioorganic & Medicinal Chemistry

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## Bioorganic & Medicinal Chemistry Vol. 16, No. 16, 2008

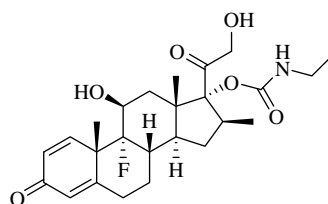
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##### Discovery of betamethasone 17 $\alpha$ -carbamates as dissociated glucocorticoid receptor modulators in the rat

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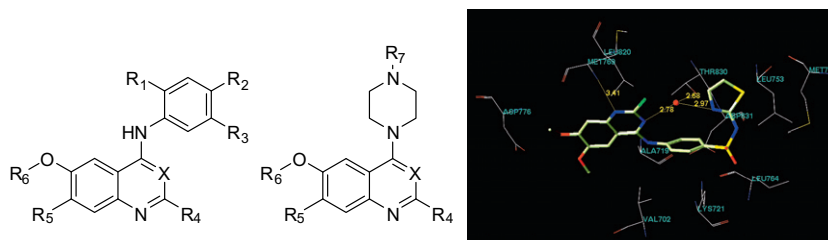
Amjad Ali\*, James M. Balkovec, Mark Greenlee, Milton L. Hammond, Greg Rouen, Gayle Taylor, Monica Einstein, Lan Ge, Georgianna Harris, Terri M. Kelly, Paul Mazur, Shilpa Pandit, Joseph Santoro, Ayesha Sitlani, Chuanlin Wang, Joann Williamson, Michael J. Forrest, Ester Carballo-Jane, Silvi Luell, Karen Lowitz, Denise Visco



##### Design, synthesis and in vitro antitumor activity of 4-aminoquinoline and 4-aminoquinazoline derivatives targeting EGFR tyrosine kinase

pp 7543–7551

Khaled Abouzid\*, Samia Shouman

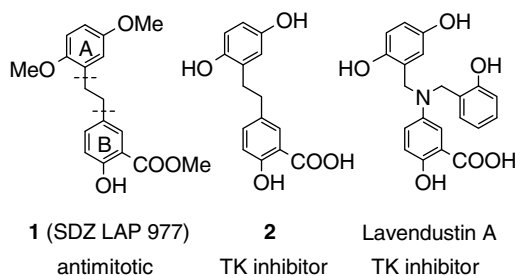


Compound **3b** in the ATP binding site of EGFR-TK

##### Structure–activity relationship studies on a novel class of antiproliferative agents derived from Lavendustin A. Part I: Ring A modifications

pp 7552–7560

Peter Nussbaumer\*, Anthony P. Winiski



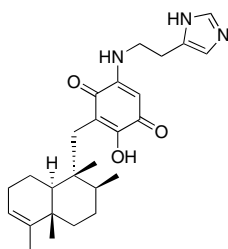
The SAR of A-ring modified analogues of a novel class of antiproliferative agents and studies on the mode of action of compound **1** are described and discussed.



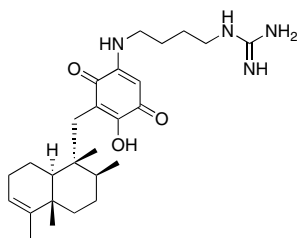
**Nakijiquinones G–I, new sesquiterpenoid quinones from marine sponge**

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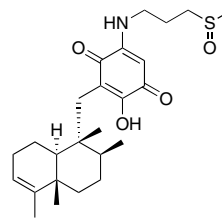
Yohei Takahashi, Takaaki Kubota, Junji Ito, Yuzuru Mikami, Jane Fromont, Jun'ichi Kobayashi\*



nakijiquinone G (1)



nakijiquinone H (2)



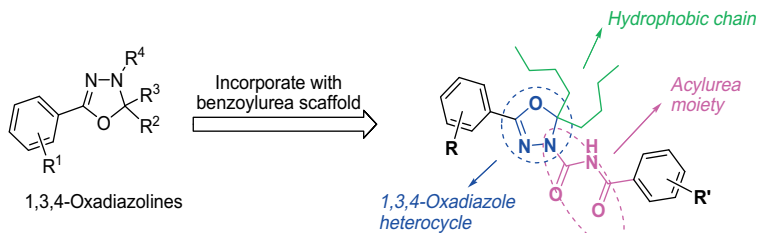
nakijiquinone I (3)

**1,3,4-Oxadiazole-3(2H)-carboxamide derivatives as potential novel class of monoamine oxidase (MAO) inhibitors:**

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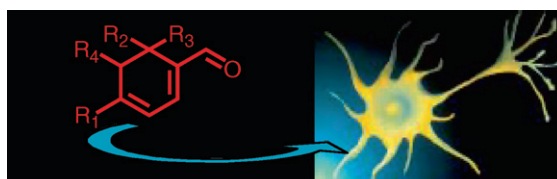
**Synthesis, evaluation, and role of urea moiety**

Shaoyong Ke, Zhong Li, Xuhong Qian\*

**Synthesis and cellular effects of cycloterpenals: Cyclohexadienal-based activators of neurite outgrowth**

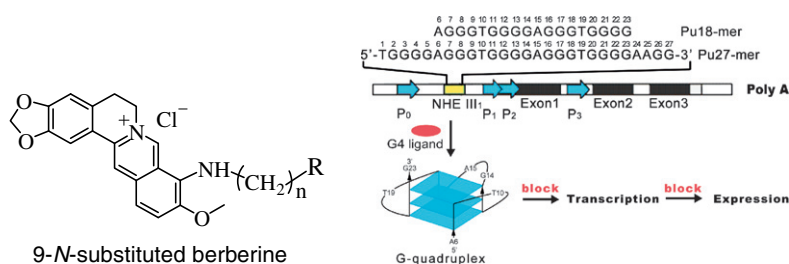
pp 7573–7581

Bennie J. Bench, Shane E. Tichy, Lisa M. Perez, Jenna Benson, Coran M. H. Watanabe\*

**CYCLOHEXADIENAL-BASED ACTIVATORS OF NEURITE OUTGROWTH****9-N-Substituted berberine derivatives: Stabilization of G-quadruplex DNA and down-regulation of oncogene c-myc**

pp 7582–7591

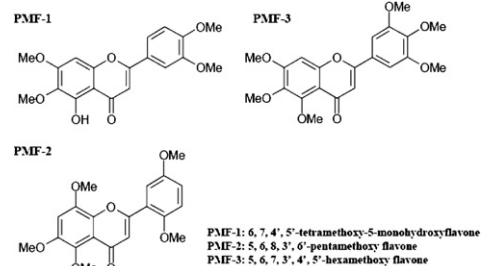
Yan Ma, Tian-Miao Ou, Jin-Qiang Hou, Yu-Jing Lu, Jia-Heng Tan, Lian-Quan Gu, Zhi-Shu Huang\*



### Inhibitory effects of polymethoxy flavones isolated from *Citrus reticulata* on degranulation in rat basophilic leukemia RBL-2H3: Enhanced inhibition by their combination

pp 7592–7598

Tomohiro Itoh\*, Kenji Ohguchi, Munekazu Iinuma, Yoshinori Nozawa, Yukihiro Akao

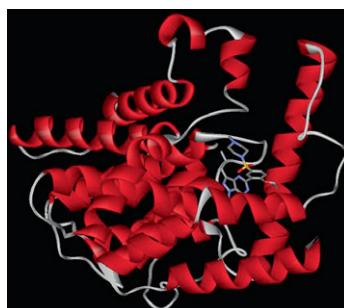


Polymethoxy flavones (PMFs) are present in fruit tissues of *Citrus* species. In this study, PMFs suppressed the antigen-induced degranulation in rat basophilic leukemia RBL-2H3 cells. Interestingly, the inactivation of Syk by PMF-combination treatment was enhanced compared with PMF-single treatment. But the inhibitory effect of degranulation by PMF-combination treatment was not associated with the suppression of  $\text{Ca}^{2+}$  influx.

### In silico prediction of novel phosphodiesterase type-5 inhibitors derived from Sildenafil, Vardenafil and Tadalafil

pp 7599–7606

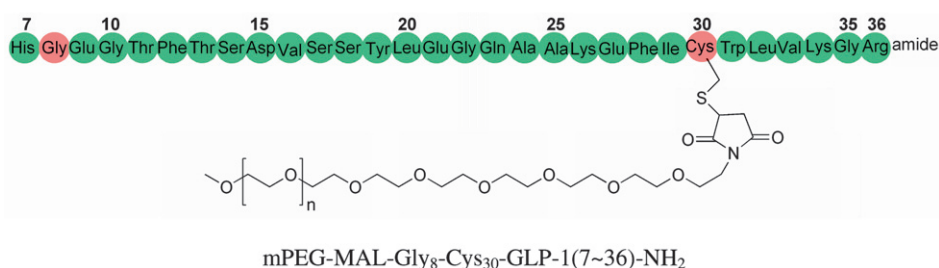
João E. Antunes, Matheus P. Freitas\*, Elaine F. F. da Cunha, Teodorico C. Ramalho, Roberto Rittner



### Microwave-assisted solid phase synthesis, PEGylation, and biological activity studies of glucagon-like peptide-1(7–36) amide

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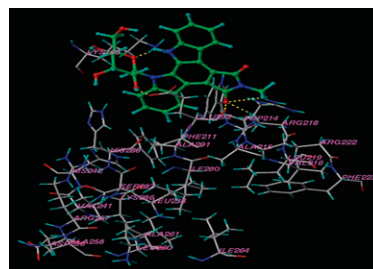
Yushi Chi, Huibin Zhang\*, Wenlong Huang\*, Jinpei Zhou, Yinghong Zhou, Hai Qian, Shuaijian Ni



### A concise approach to 1,11-didechloro-6-methyl-4'-O-demethyl rebeccamycin and its binding to human serum albumin: Fluorescence spectroscopy and molecular modeling method

pp 7615–7621

Fengling Cui\*, Lixia Qin, Guisheng Zhang\*, Xiaobing Liu, Xiaojun Yao, Beilei Lei

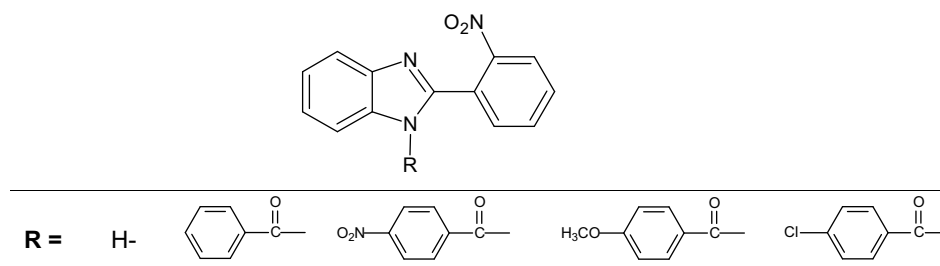


The tryptophan residue (Trp214) and the lysine residue (Lys195) of HSA are in close proximity to the pentenyl moiety of JDC-108, suggesting the existence of hydrophobic interaction between them.

**Determination and characterization of new benzimidazoles with activity against *Trypanosoma cruzi* by UV spectroscopy and HPLC**

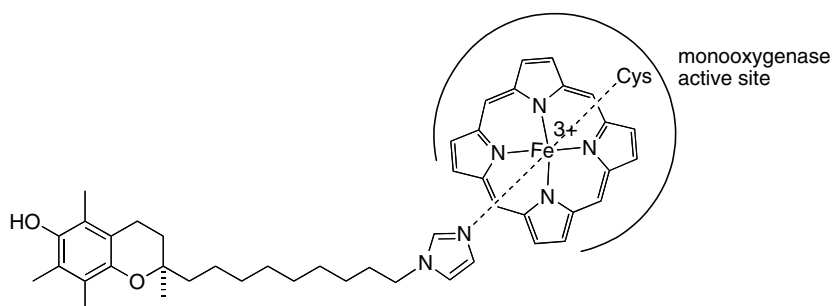
pp 7622–7630

Stephanie Brain-Isasi, Cristián Quezada, Hernán Pessoa, Antonio Morello, Marcelo J. Kogan, Alejandro Álvarez-Lueje\*


**Inhibition of oxidative metabolism of tocopherols with  $\omega$ -N-heterocyclic derivatives of vitamin E**

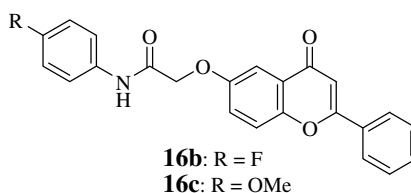
pp 7631–7638

Stephan Ohnmacht, Phillip Nava, Ryan West, Robert Parker, Jeffrey Atkinson\*


**Synthesis and antiproliferative evaluation of amide-containing flavone and isoflavone derivatives**

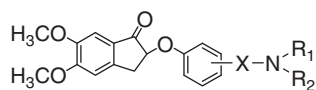
pp 7639–7645

I-Li Chen, Jhy-Yih Chen, Po-Chuen Shieh, Jih-Jung Chen, Choa-Hsun Lee, Shin-Hun Juang\*, Tai-Chi Wang\*


**2-Phenoxy-indan-1-one derivatives as acetylcholinesterase inhibitors: A study on the importance of modifications at the side chain on the activity**

pp 7646–7653

Yanhong Shen, Rong Sheng, Jing Zhang, Qiaojun He, Bo Yang, Yongzhou Hu\*

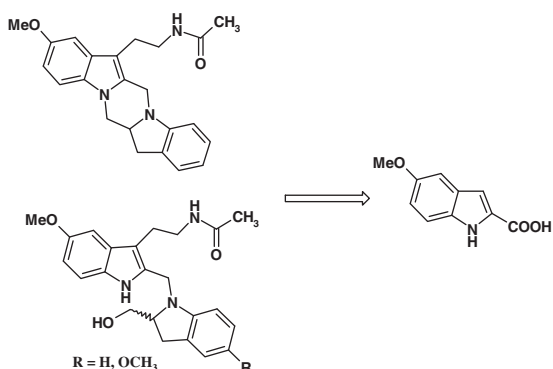


The design, synthesis and biological profile of a series of 2-phenoxy-indan-1-one derivatives as potent AChE inhibitors are described.

### Synthesis and pharmacological evaluation of pentacyclic 6a,7-dihydrodiindole and 2,3-dihydrodiindole derivatives as novel melatoninerigic ligands

pp 7654–7661

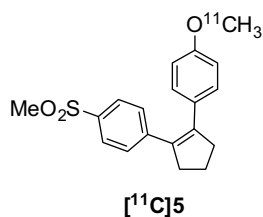
Mohamed I. Attia\*, Paula A. Witt-Enderby, Justin Julius



### Synthesis and evaluation in vitro and in vivo of a $^{11}\text{C}$ -labeled cyclooxygenase-2 (COX-2) inhibitor

pp 7662–7670

Frank Wuest\*, Torsten Kniess, Ralf Bergmann, Jens Pietzsch

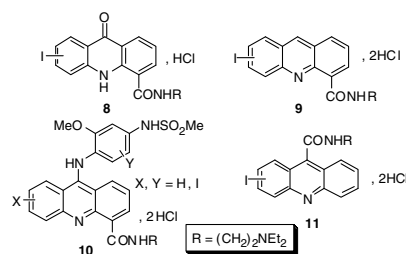


The radiosynthesis and radiopharmacological evaluation of 1- $[^{11}\text{C}]$ methoxy-4-(2-(4-(methanesulfonyl)phenyl)cyclopent-1-enyl)-benzene  $[^{11}\text{C}]5$  as novel PET radiotracer for imaging of COX-2 expression is described. Radiotracer  $[^{11}\text{C}]5$  was evaluated in vitro using various pro-inflammatory and tumor cell lines. Tumor uptake was demonstrated by dynamic small animal PET studies in a mouse tumor xenograft model.

### Design, synthesis and preliminary biological evaluation of acridine compounds as potential agents for a combined targeted chemo-radionuclide therapy approach to melanoma

pp 7671–7690

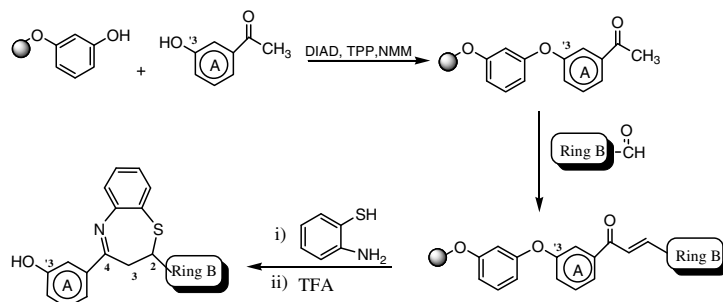
Nicolas Desbois, Maryline Gardette, Janine Papon, Pierre Labarre, Aurélie Maisonia, Philippe Auzeloux, Claire Lartigue, Bernadette Bouchon, Eric Debiton, Yves Blache, Olivier Chavignon, Jean-Claude Teulade, Jean Maublant, Jean-Claude Madelmont, Nicole Moins, Jean-Michel Chezal\*



### Solid-phase synthesis and biological evaluation of a parallel library of 2,3-dihydro-1,5-benzothiazepines

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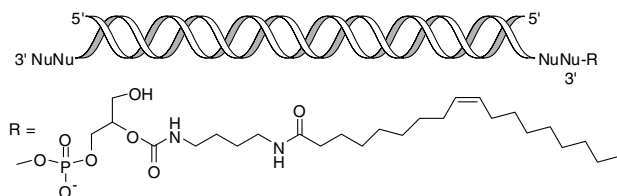
Farzana Latif Ansari\*, Fatima Iftikhar, Ihsan-ul-Haq, Bushra Mirza, Mohammad Baseer, Umer Rashid



**Synthesis and silencing properties of siRNAs possessing lipophilic groups at their 3'-termini**

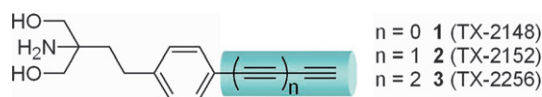
pp 7698–7704

Yoshihito Ueno\*, Koshi Kawada, Tomoharu Naito, Aya Shibata, Kayo Yoshikawa,  
Hye-Sook Kim, Yusuke Wataya, Yukio Kitade\*

**TX-2152: A conformationally rigid and electron-rich diyne analogue of FTY720 with in vivo antiangiogenic activity**

pp 7705–7714

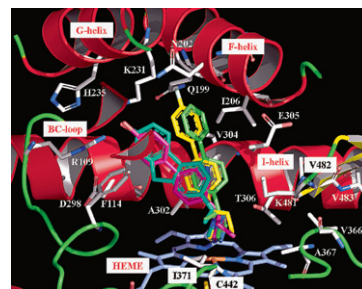
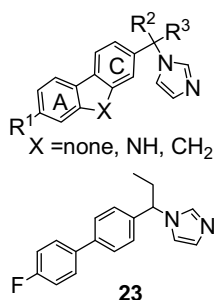
Shinichi Nakayama, Yoshihiro Uto, Kanako Tanimoto, Yasuhiro Okuno, Yuki Sasaki, Hideko Nagasawa, Eiji Nakata, Ken Arai,  
Kaori Momose, Tetsuro Fujita, Toshihiro Hashimoto, Yasuko Okamoto, Yoshinori Asakawa, Satoru Goto, Hitoshi Hori\*

**Synthesis, biological evaluation, and molecular modeling studies of methylene imidazole substituted biaryls as inhibitors of human 17 $\alpha$ -hydroxylase-17,20-lyase (CYP17)—Part II: Core rigidification and influence of substituents at the methylene bridge**

pp 7715–7727

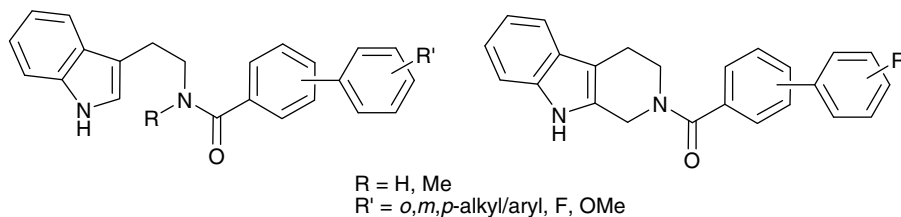
Qingzhong Hu, Matthias Negri, Kerstin Jahn-Hoffmann, Yan Zhuang,  
Sureyya Olgen, Marc Bartels, Ursula Müller-Vieira,  
Thomas Lauterbach, Rolf W. Hartmann\*

Novel substituted imidazolyl methylene biphenyls have been synthesized as CYP17 inhibitors. It turns out compound **23** (IC<sub>50</sub> = 345 nM) is more active in vivo, showed a longer plasma half-life (10 h) and a higher bioavailability compared to Abiraterone.

**Design, synthesis and biological evaluation of new tryptamine and tetrahydro- $\beta$ -carboline-based selective inhibitors of CDK4**

pp 7728–7739

Paul R. Jenkins\*, James Wilson, Daniel Emmerson, Marcos D. Garcia, Matthew R. Smith, Stephen J. Gray,  
Robert G. Britton, Sachin Mahale, Bhabatosh Chaudhuri

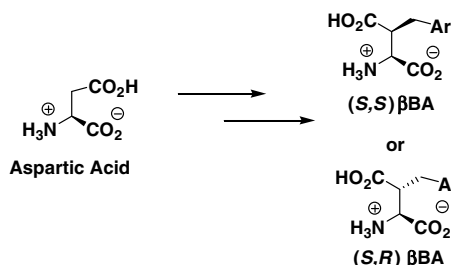


A library of selective inhibitors of CDK4 based on a tryptamine or  $\beta$ -carboline biphenyl carbonyl amides have been synthesised using the Suzuki–Miyaura cross-coupling reaction. The compounds were designed in view an observed  $\pi$ -stacking pocket within the active site of a CDK4 homology model.

### Synthesis and preliminary pharmacological evaluation of novel derivatives of L-β-threo-benzylaspartate as inhibitors of the neuronal glutamate transporter EAAT3

pp 7740–7748

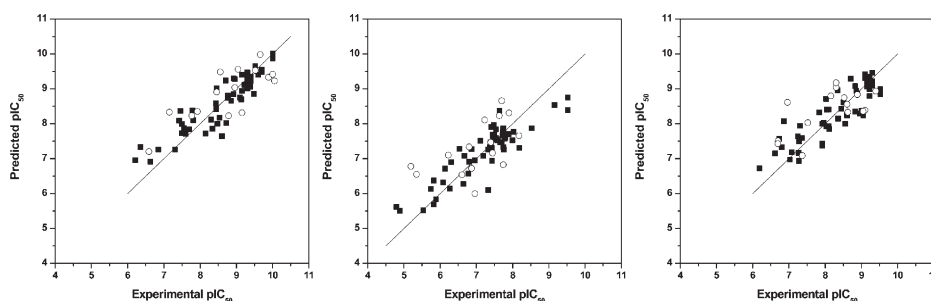
Terri L. Mavencamp, Joseph F. Rhoderick, Richard J. Bridges, C. Sean Esslinger\*



### Development of a receptor-based 3D-QSAR study for the analysis of MMP2, MMP3, and MMP9 inhibitors

pp 7749–7758

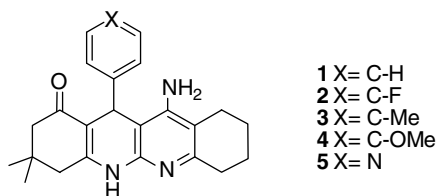
Tiziano Tuccinardi, Elisa Nuti, Gabriella Ortore, Armando Rossello, Stanislava I. Avramova, Adriano Martinelli\*



### New tacrine-dihydropyridine hybrids that inhibit acetylcholinesterase, calcium entry, and exhibit neuroprotection properties

pp 7759–7769

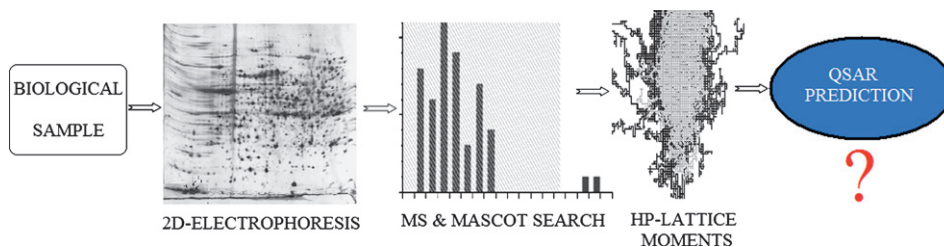
Rafael León\*, Cristóbal de los Ríos, José Marco-Contelles\*, Oscar Huertas, Xavier Barril, F. Javier Luque\*, Manuela G. López, Antonio G. García, Mercedes Villarroya\*



### HP-Lattice QSAR for dynein proteins: Experimental proteomics (2D-electrophoresis, mass spectrometry) and theoretic study of a *Leishmania infantum* sequence

pp 7770–7776

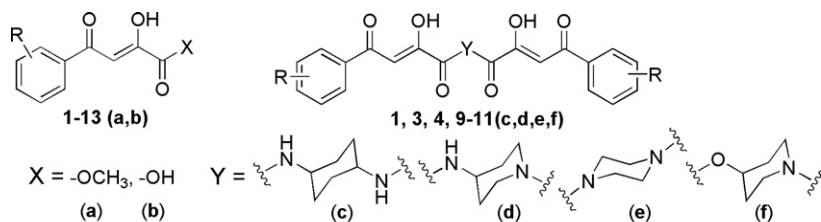
María Auxiliadora Dea-Ayuela, Yunierkis Pérez-Castillo, Alfredo Meneses-Marcel, Florencio M. Ubeira, Francisco Bolas-Fernández, Kuo-Chen Chou, Humberto González-Díaz\*



### Novel dimeric aryldiketo containing inhibitors of HIV-1 integrase: Effects of the phenyl substituent and the linker orientation

pp 7777–7787

Li-Fan Zeng, Xiao-Hua Jiang, Tino Sanchez, Hu-Shan Zhang, Raveendra Dayam, Nouri Neamati\*, Ya-Qiu Long\*

1d, IC<sub>50</sub> = 23 and < 0.4 μM for 3'-processing and strand transfer, respectively

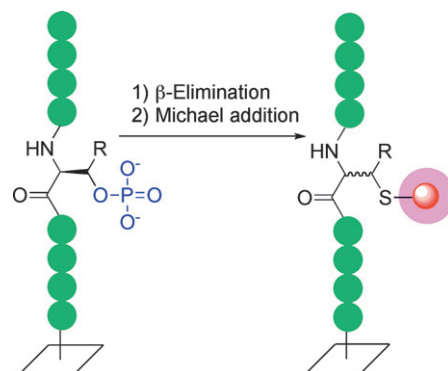
A new class of ADK dimer inhibitors of HIV-1 integrase was designed and synthesized by employing conformationally constrained diamine as linker. The substituent on the phenyl portion and the orientation of the linker were investigated with respect to the potency-enhancing effect.

### Array-based fluorescence assay for serine/threonine kinases using specific chemical reaction

pp 7788–7794

Shoji Akita, Naoki Umezawa\*, Nobuki Kato, Tsunehiko Higuchi\*

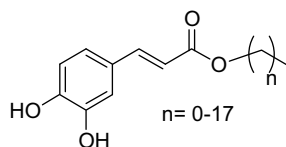
We report the development of an efficient fluorescence assay for serine/threonine kinases using a peptide array. Our approach is based on chemical reactions specific to phosphoserine and phosphothreonine residues.



### Inhibitory effect of the alkyl side chain of caffeic acid analogues on lipopolysaccharide-induced nitric oxide production in RAW264.7 macrophages

pp 7795–7803

Koji Uwai, Yuu Osanai\*, Takuma Imaizumi, Syu-ichi Kanno, Mitsuhiro Takeshita, Masaaki Ishikawa

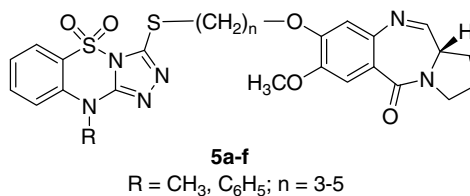


Caffeic acid ester derivatives were prepared and their inhibitory effects on NO production in murine macrophage RAW264.7 cells were tested.

### Synthesis, DNA-binding ability and evaluation of antitumour activity of triazolo[1,2,4]benzothiadiazine linked pyrrolo[2,1-c][1,4]benzodiazepine conjugates

pp 7804–7810

Ahmed Kamal\*, M. Naseer A. Khan, Y. V. V. Srikanth, K. Srinivasa Reddy, Aarti Juvekar, Subrata Sen, Nisha Kurian, Surekha Zingde

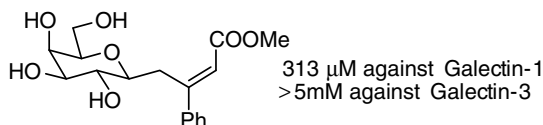


Novel triazolobenzothiadiazine-PBD conjugates were synthesized and exhibited significant anticancer activity against lung, breast, oral, colon, cervix, prostate and ovarian cancer cell lines.

**Synthesis of stable and selective inhibitors of human galectins-1 and -3**

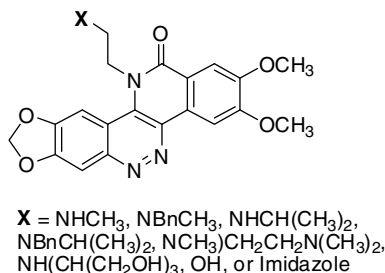
pp 7811–7823

Denis Giguère, Marc-André Bonin, Philippe Cloutier, Ramesh Patnam, Christian St-Pierre, Sachiko Sato, René Roy\*

**Syntheses and biological evaluation of topoisomerase I-targeting agents related to 11-[2-(*N,N*-dimethylamino)ethyl]-2,3-dimethoxy-8,9-methylenedioxy-11*H*-isoquino[4,3-*c*]cinnolin-12-one (ARC-31)**

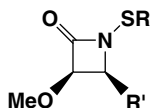
pp 7824–7831

Mavurapu Satyanarayana, Wei Feng, Liang Cheng, Angela A. Liu, Yuan-Chin Tsai, Leroy F. Liu, Edmond J. LaVoie\*

**Studies on the antifungal properties of *N*-thiolated  $\beta$ -lactams**

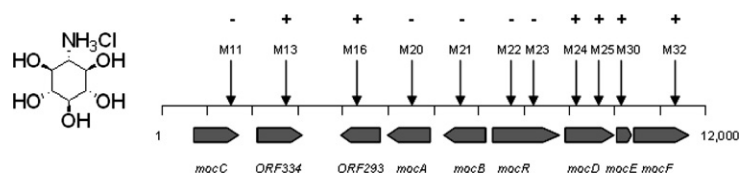
pp 7832–7837

Marci O'Driscoll, Kerriann Greenhalgh, Ashley Young, Edward Turos\*, Sonja Dickey, Daniel V. Lim

Investigations into the antifungal properties of *N*-thiolated  $\beta$ -lactams are described.**Chemical synthesis of *scyllo*-inosamine and catabolism studies in *Sinorhizobium meliloti***

pp 7838–7842

Elke Schoffers\*, Sing R. Gurung, Petra R. A. Kohler, Silvia Rossbach

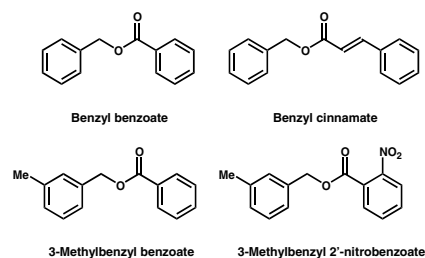
SIA was prepared from *myo*-inositol and fully characterized after 7 steps in 32% overall yield. Studies with bacterial mutant strains identified the *mocABCR* genes as essential for the catabolism of SIA.

### Inhibitory effects of benzyl benzoate and its derivatives on angiotensin II-induced hypertension

pp 7843–7852

Osamu Ohno, Mao Ye, Tomoyuki Koyama, Kazunaga Yazawa, Emi Mura, Hiroshi Matsumoto, Takao Ichino, Kaoru Yamada, Kazuhiko Nakamura, Tomohiro Ohno, Kohji Yamaguchi, Junji Ishida, Akiyoshi Fukamizu, Daisuke Uemura\*

We isolated benzyl benzoate and benzyl cinnamate from the resin of *Liquidambar styraciflua*, as antagonist-like compounds of angiotensin II (Ang II) receptors. Benzyl benzoate was shown to suppress Ang II-induced hypertension in mice. In addition, we found that the *meta*-methyl and 3-methylbenzyl 2'-nitrobenzoate derivatives showed about 10-fold higher activity than benzyl benzoate itself.

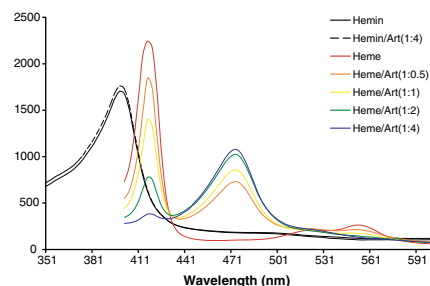


### Heme activates artemisinin more efficiently than hemin, inorganic iron, or hemoglobin

pp 7853–7861

Shiming Zhang\*, Glenn S. Gerhard\*

Artemisinin derivatives appear to mediate their anti-malarial effects through an initial redox-mediated reaction. Heme, inorganic iron, and hemoglobin have all been implicated as the key molecules that activate artemisinins. The reactions of artemisinin with different redox forms of heme, ferrous iron, and deoxygenated and oxygenated hemoglobin were analyzed under similar in vitro conditions. Heme reacted with artemisinin much more efficiently than the other iron-containing molecules, supporting the role of redox active heme as the primary activator of artemisinin.



#### OTHER CONTENTS

##### Erratum

##### Instructions to contributors

p 7862

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\*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].

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



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ISSN 0968-0896