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# Bioorganic & Medicinal Chemistry

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## Bioorganic & Medicinal Chemistry Vol. 16, No. 24, 2008

### Contents

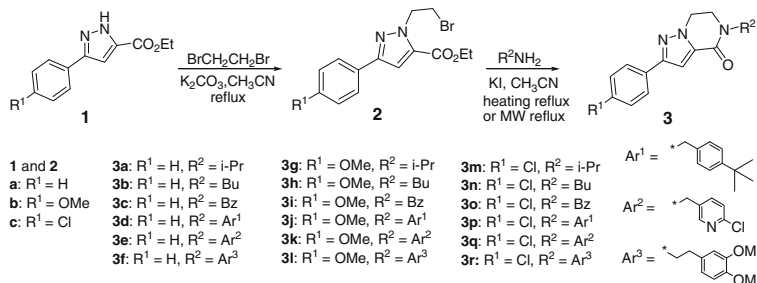
#### ARTICLES

#### Synthesis and preliminary biological evaluation of novel pyrazolo[1,5-*a*]pyrazin-4(5*H*)-one derivatives as potential agents against A549 lung cancer cells

pp 10165–10171

Jin-Hua Zhang, Chuan-Dong Fan, Bao-Xiang Zhao\*, Dong-Soo Shin, Wen-Liang Dong, Yong-Sheng Xie, Jun-Ying Miao\*

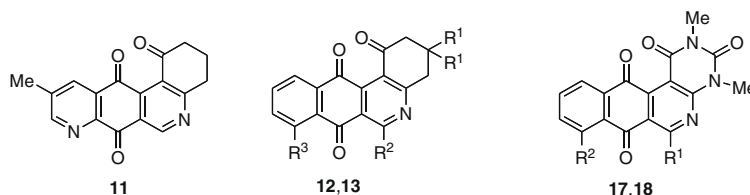
A series of novel pyrazolo[1,5-*a*]pyrazin-4(5*H*)-one derivatives were synthesized by the reaction of ethyl 3-aryl-1-(2-bromoethyl)-1*H*-pyrazole-5-carboxylate and amine in the general heating condition and microwave-assisted condition. Representative single-crystal structures were characterized by using X-ray diffraction analysis. Preliminary biological evaluation showed that the compounds could inhibit the growth of A549 cells in dosage- and time-dependent manners. Compound **3o** was the most effective small molecule in inhibiting A549 cell growth and might perform its action through modulating autophagy.



#### Studies on quinones. Part 44: Novel angucyclinone *N*-heterocyclic analogues endowed with antitumoral activity

pp 10172–10181

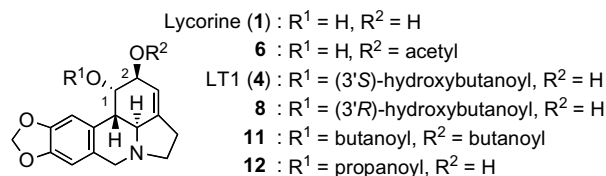
Jaime A. Valderrama\*, Pamela Colonelli, David Vásquez, M. Florencia González, Jaime A. Rodríguez, Cristina Theoduloz


A simple and flexible strategy for preparing angucyclinone aza-analogues **11–13**, **17**, **18** and their evaluation on normal fibroblast and four tumor cell lines is presented.

#### New lycorine-type alkaloid from *Lycoris traubii* and evaluation of antitrypanosomal and antimalarial activities of lycorine derivatives

pp 10182–10189

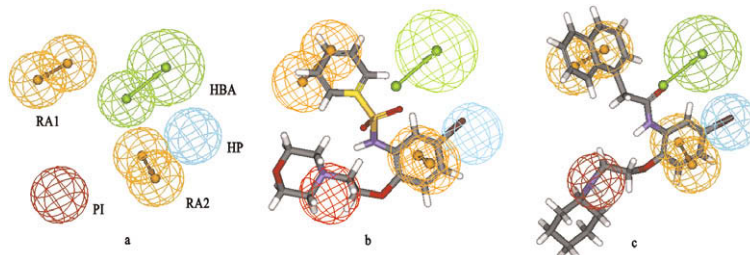
Yosuke Toriizuka, Eri Kinoshita, Noriyuki Kogure, Mariko Kitajima, Aki Ishiyama, Kazuhiko Otaguro, Haruki Yamada, Satoshi Ōmura, Hiromitsu Takayama\*


A new lycorine derivative LT1 (**4**) was isolated from the *Lycoris traubii* Hayward (Amaryllidaceae). Some lycorine ester derivatives were examined for their inhibitory activity against trypanosoma and against malaria in vitro. Among them, **6** showed potent activity against trypanosoma and **4**, **8**, **11**, and **12** showed significant activity against malaria.

### Identification of pharmacophore model, synthesis and biological evaluation of *N*-phenyl-1-arylamide and *N*-phenylbenzenesulfonamide derivatives as BACE 1 inhibitors

pp 10190–10197

Wenhai Huang, Haiping Yu, Rong Sheng, Jia Li, Yongzhou Hu\*

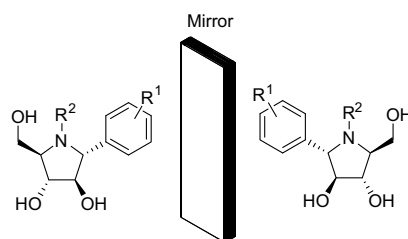


The pharmacophore model of arylpiperazine amide derivatives was built and the validation of the Hypo 1 was ascertained. Eleven *N*-phenyl-1-arylamide, *N*-phenylbenzenesulfonamide derivatives **26–28**, **33a–g** were selected, synthesized and tested the BACE 1 inhibitory activities.

### Synthesis and biological evaluation of a 2-aryl polyhydroxylated pyrrolidine alkaloid-based library

pp 10198–10204

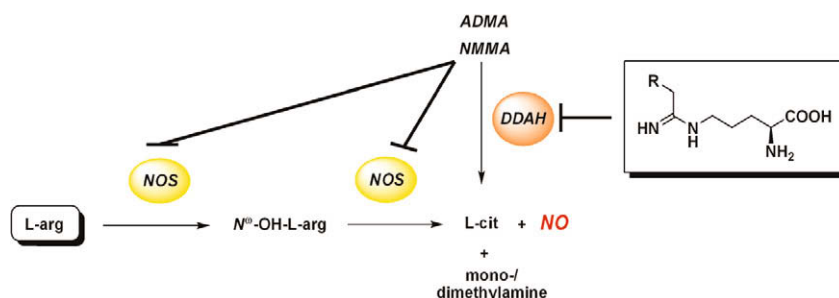
En-Lun Tsou, Sih-Yu Chen, Ming-Hsun Yang, Shih-Chi Wang, Ting-Ren Rachel Cheng\*, Wei-Chieh Cheng\*



### Structure–activity relationship of novel and known inhibitors of human dimethylarginine dimethylaminohydrolase-1: Alkenyl-amidines as new leads

pp 10205–10209

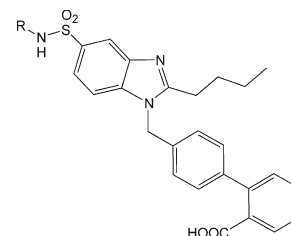
Jürke Kotthaus, Dennis Schade, Nikola Muschick, Eric Beitz, Bernd Clement\*



### Design, synthesis, and evaluation of 5-sulfamoyl benzimidazole derivatives as novel angiotensin II receptor antagonists

pp 10210–10215

Navneet Kaur, Amardeep Kaur, Yogita Bansal, Dhvanit I. Shah, Gulshan Bansal\*, Manjeet Singh

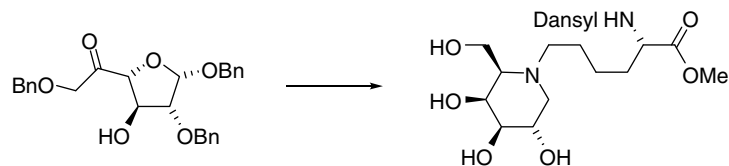


A series of 5-alkylsulfamoyl benzimidazole derivatives have been designed and synthesized as novel angiotensin II (Ang II) receptor antagonists. The compounds have been evaluated for in vitro Ang II antagonism and for in vivo antihypertensive activity on isolated rat aortic ring and desoxycortisone acetate induced hypertensive rats, respectively. The activity is found related to size of alkyl group. The maximum activity is observed with a compact and bulky alkyl group like *tert*-butyl and cyclohexyl. A receptor binding model is also proposed on the basis of structure–activity relationship in this study.

**1-Deoxygalactonojirimycin-lysine hybrids as potent D-galactosidase inhibitors**

pp 10216–10220

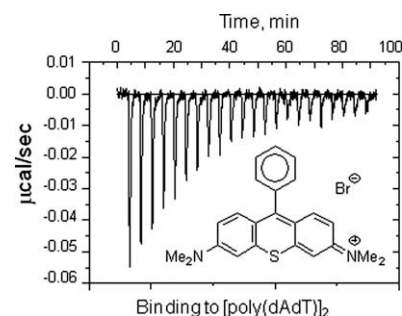
Andreas J. Steiner, Georg Schitter, Arnold E. Stütz\*, Tanja M. Wrodnigg, Chris A. Tarling, Stephen G. Withers, Katrin Fantur, Don Mahuran, Eduard Paschke, Michael Tropak

**Substituent control of DNA binding modes in a series of chalcogenoxanthylum photosensitizers as determined by isothermal titration calorimetry and topoisomerase I DNA unwinding assay**

pp 10221–10227

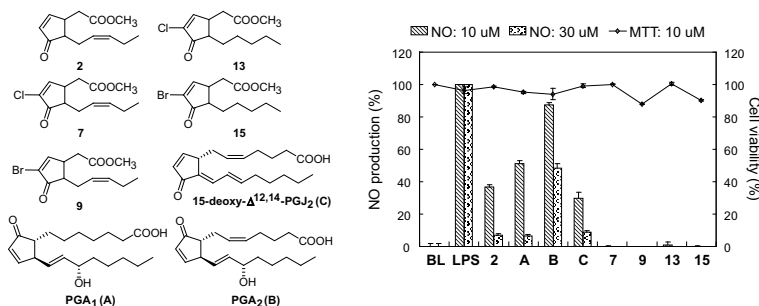
Ruel E. McKnight\*, Bilgehan Onogul, Shivani R. Polasani, Michael K. Gannon II, Michael R. Detty\*

The binding of a series of rhodamine-related chalcogenoxanthylum dyes to DNA was measured using isothermal titration calorimetry and a topoisomerase I DNA unwinding assay.

**New jasmonate analogues as potential anti-inflammatory agents**

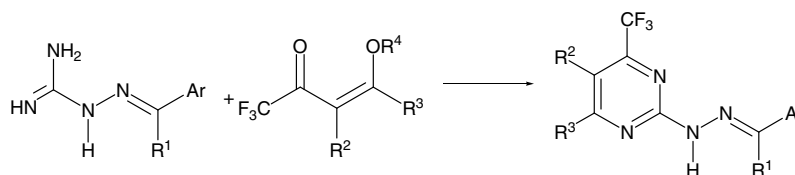
pp 10228–10235

Hung The Dang, Hye Ja Lee, Eun Sook Yoo, Jongki Hong, Baoquan Bao, Jae Sue Choi, Jee H. Jung\*

**Convergent synthesis and cruzain inhibitory activity of novel 2-(N'-benzylidenehydrazino)-4-trifluoromethyl-pyrimidines**

pp 10236–10243

Nilo Zanatta\*, Simone S. Amaral, Josiane M. dos Santos, Débora L. de Mello, Liana da S. Fernandes, Helio G. Bonacorso, Marcos A. P. Martins, Adriano D. Andricopulo, Deise M. Borchhardt

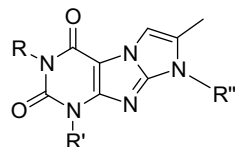
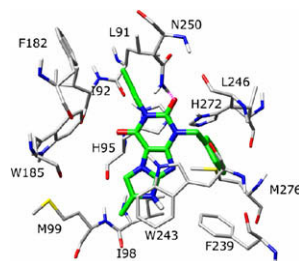




### Structure–activity relationship studies of a new series of imidazo[2,1-f]purinones as potent and selective A<sub>3</sub> adenosine receptor antagonists

pp 10281–10294

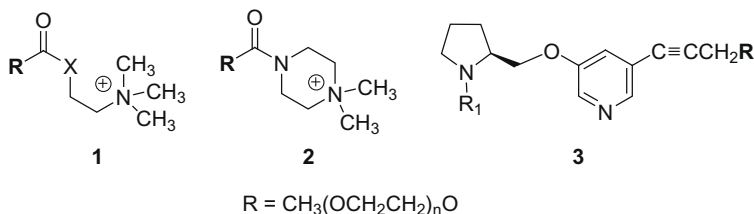
Pier Giovanni Baraldi\*, Delia Preti, Mojgan Aghazadeh Tabrizi, Romeo Romagnoli, Giulia Saponaro, Stefania Baraldi, Maurizio Botta, Cesare Bernardini, Andrea Tafi, Tiziano Tuccinardi, Adriano Martinelli, Katia Varani, Pier Andrea Borea



### Polyethylene glycol-based homologated ligands for nicotinic acetylcholine receptors

pp 10295–10300

Bradley A. Scates, Bethany L. Lashbrook, Benjamin C. Chastain, Kaoru Tominaga, Brandon T. Elliott, Nicholas J. Theising, Thomas A. Baker, Richard W. Fitch\*



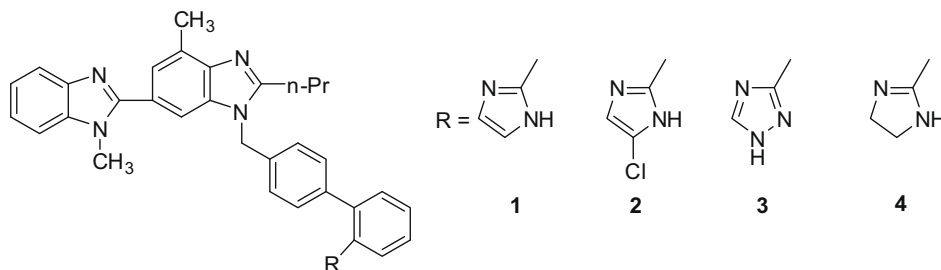
Three series of homologated ligands were synthesized and assessed for nicotinic receptor binding in rat cerebral cortex. Each series displayed affinity at nicotinic receptors that decreased slowly with increasing chain length.



### Synthesis and biological activities of novel nonpeptide angiotensin II receptor antagonists based on benzimidazole derivatives bearing a heterocyclic ring

pp 10301–10310

Xing-Zhou Guo, Lin Shi, Rui Wang, Xiao-Xiao Liu, Bo-Gang Li, Xiao-Xia Lu\*

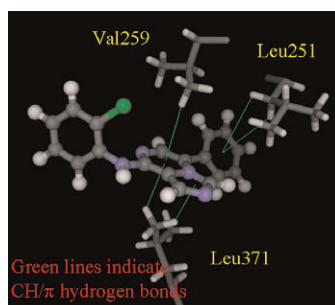


The synthesis and biological activities of a new series of benzimidazole derivatives bearing a heterocyclic ring as AT<sub>1</sub> receptor antagonists is described.

### The importance of CH/π hydrogen bonds in rational drug design: An ab initio fragment molecular orbital study to leukocyte-specific protein tyrosine (LCK) kinase

pp 10311–10318

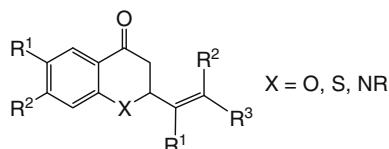
Tomonaga Ozawa\*, Eiichi Tsuji, Motoyasu Ozawa, Chiaki Handa, Harunobu Mukaiyama, Toshihiro Nishimura, Satoko Kobayashi, Kosuke Okazaki



### Synthesis and antimicrobial activity of 2-alkenylchroman-4-ones, 2-alkenylthiochroman-4-ones and 2-alkenylquinol-4-ones

pp 10319–10325

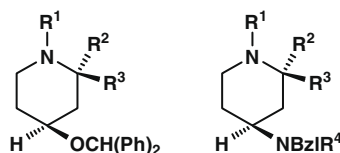
Nicole Hoettecke, Sven Rotzoll, Uwe Albrecht, Michael Lalk, Christine Fischer, Peter Langer\*



### Antimycobacterial and H<sub>1</sub>-antihistaminic activity of 2-substituted piperidine derivatives

pp 10326–10331

Robert Weis\*, Klaus Schweiger, Johanna Faist, Erich Rajkovic, Andreas J. Kungl, Walter M. F. Fabian, Walter Schunack, Werner Seebacher



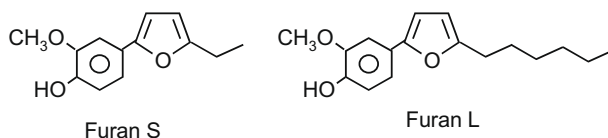
Piperidine derivatives with strong H<sub>1</sub>-antagonistic and antimycobacterial potencies were synthesized and investigated for a possible correlation between both activities.



### Characterization of novel furan compounds on the basis of their radical scavenging activity and cytoprotective effects against glutamate- and lipopolysaccharide-induced insults

pp 10332–10337

Keiko Nishio, Akiko Fukuhara, Yo Omata, Yoshiro Saito\*, Shuuhei Yamaguchi, Hisatoyo Kato, Yasukazu Yoshida, Etsuo Niki



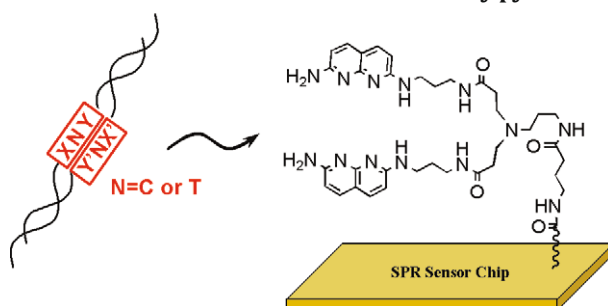
In the present study, we examined the radical scavenging activity and cytoprotective effects of novel furan compounds, which have potent inhibitory activity against oxygenases such as COX-1, COX-2 and 5-LOX.



### Dimer of 2,7-diamino-1,8-naphthyridine for the detection of mismatches formed by pyrimidine nucleotide bases

pp 10338–10344

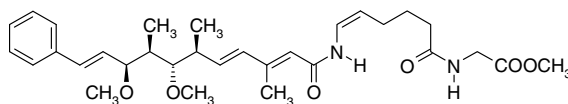
Akio Kobori, Kazuhiko Nakatani\*



We have developed a sensor for SPR assay system to detect C-C, C-T and T-T mismatch duplexes by employing a surface upon which mismatch-binding ligands (MBLs) are immobilized.

## The role of molecular modeling in the design of analogues of the fungicidal natural products crocacin A and D pp 10345–10355

Patrick J. Crowley\*, Edward A. Berry, Thomas Cromartie, Fevzi Daldal, Christopher R. A. Godfrey, Dong-Woo Lee, Janet E. Phillips, Anne Taylor, Russell Viner

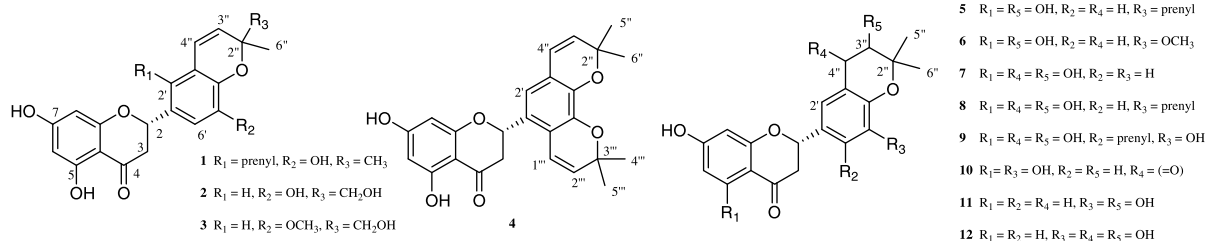


crocacin D

Molecular modeling was used to aid the designs of analogues of the natural products crocacin A and D which inhibited mitochondrial respiration and had activity against several plant pathogens on plants.

## Flavanones from the stem bark of *Erythrina abyssinica* pp 10356–10362

Long Cui, Phuong Thien Thuong, Hyun Sun Lee, Derek Tantoh Ndinteh, Joseph Tanyi Mbafor, Zacharias Tanee Fomum, Won Keun Oh\*



Twelve new flavanones bearing a 2,2-dimethylpyrano ring were isolated from a MeOH extract of the stem bark of *Erythrina abyssinica*. Compounds **1**, **3**, **5**, **6**, **8**, and **9** exhibited inhibitory effects on the enzyme activity of protein tyrosine phosphatase 1B (PTP1B) in an in vitro assay with IC<sub>50</sub> values ranging from  $13.9 \pm 2.1$  to  $19.0 \pm 1.8 \mu\text{M}$ . These results suggest that prenyl and methoxy groups on the B ring contribute to the inhibitory activity of flavanones against PTP1B.



### OTHER CONTENTS

#### Instructions to contributors

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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].

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