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Bioorganic &
Medicinal
Chemistry

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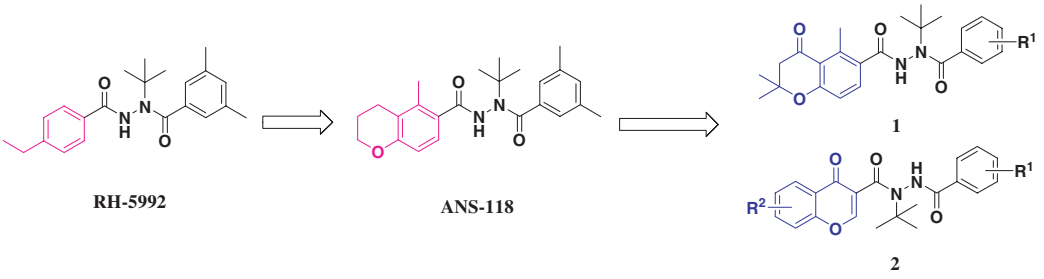
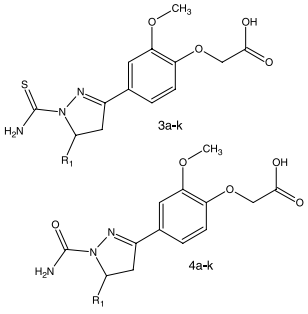
ARTICLES

Synthesis and insecticidal activity of chromanone and chromone analogues of diacylhydrazines **pp 1888–1895**
Pei-Liang Zhao, Jing Li and Guang-Fu Yang*

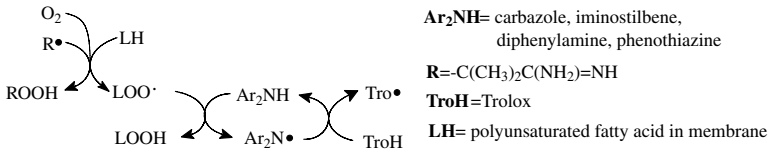


Discovery of novel phenoxyacetic acid derivatives as antimycobacterial agents **pp 1896–1902**
Mohamed Ashraf Ali and Mohammad Shaharyar*

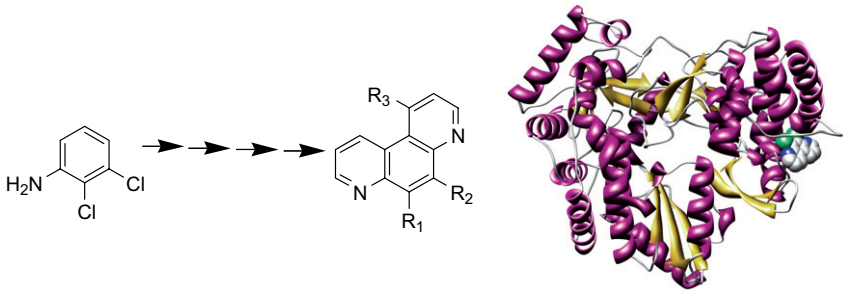
A series of 2-{4-[1-amino (thioxo) methyl-5-(substituted phenyl)-4,5-dihydro-1*H*-3-pyrazolyl]-2-methoxyphenoxy}acetic acid and 2-{4-[1-carbamoyl-5-(substituted phenyl)-4,5-dihydro-1*H*-3-pyrazolyl]-2-methoxyphenoxy}acetic acid were synthesized and the in vitro activity of the synthesized compounds against *Mycobacterium tuberculosis* H37Rv (MTB) and INH-resistant *M. tuberculosis* (INHR-MTB) was studied. Among the synthesized compounds, compound (**3f**) 2{-[4-(1-carbamoyl-5-(chloro phenyl)-4,5-dihydro-1*H*-3-pyrazolyl]-2-methoxyphenoxy} acetic acid was found to be the mostf active against *M. tuberculosis* H37Rv (MTB) and INH resistant *M. tuberculosis* (INHR-MTB) with minimum inhibitory concentration of 0.06 μg/ml.



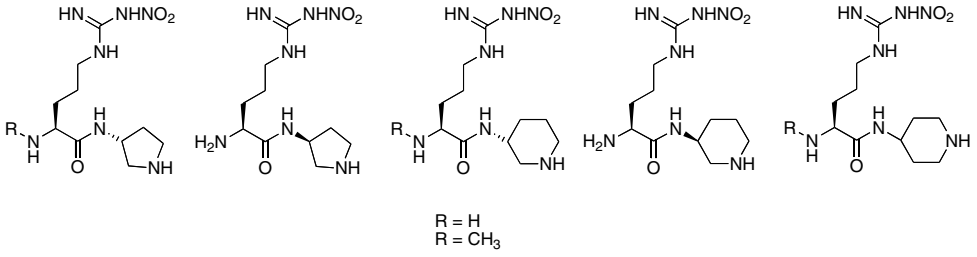
Free-radical-scavenging effect of carbazole derivatives on AAPH-induced hemolysis of human erythrocytes **pp 1903–1913**
You-Zhi Tang and Zai-Qun Liu*



Design, synthesis, and preliminary in vitro and in silico antiviral activity of [4,7]phenantrolines and 1-oxo-1,4-dihydro-[4,7]phenantrolines against single-stranded positive-sense RNA genome viruses **pp 1914–1927**
Antonio Carta,* Mario Loriga, Giuseppe Paglietti, Marco Ferrone, Maurizio Fermeglia, Sabrina Pricl, Tiziana Sanna, Cristina Ibba, Paolo La Colla* and Roberta Loddo



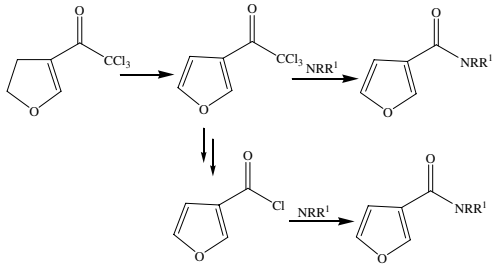
Selective L-nitroargininylaminopyrrolidine and L-nitroargininylaminopiperidine neuronal nitric oxide synthase inhibitors **pp 1928–1938**
Jiwon Seo, Pavel Martásek, Linda J. Roman and Richard B. Silverman*



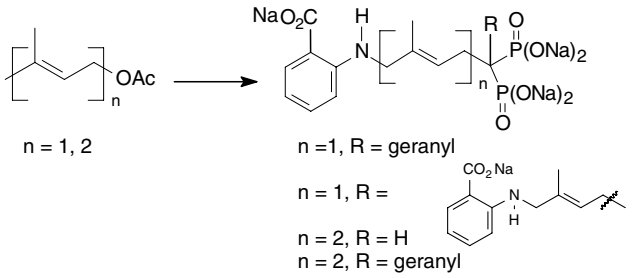
High-throughput assay for the identification of Hsp90 inhibitors based on Hsp90-dependent refolding of firefly luciferase **pp 1939–1946**
Lakshmi Galam, M. Kyle Hadden, Zeqiang Ma, Qi-Zhuang Ye, Bo-Geon Yun, Brian S. J. Blagg and Robert L. Matts*

An assay based on the Hsp90-dependent refolding of luciferase in reticulocyte lysate was optimized for high-throughput screening (av *Z*-factor = 0.62). Screening of ~20,000 compounds identified 120 potential Hsp90 inhibitors.

Synthesis, antimicrobial activity, and QSAR studies of furan-3-carboxamides **pp 1947–1958**
Nilo Zanatta,* Sydney H. Alves,* Helena S. Coelho, Deise M. Borchhardt, Pablo Machado, Kelen M. Flores, Fabio M. da Silva, Tatiana B. Spader, Jânio M. Santurio, Helio G. Bonacorso and Marcos A. P. Martins



Synthesis of fluorescently tagged isoprenoid bisphosphonates that inhibit protein geranylgeranylation **pp 1959–1966**
Mona A. Maalouf, Andrew J. Wiemer, Craig H. Kuder, Raymond J. Hohl and David F. Wiemer*

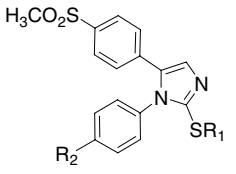


Modulating effects of a novel skin-lightening agent, α-lipoic acid derivative, on melanin production by the formation of DOPA conjugate products **pp 1967–1975**
Kentaro Tsuji-Naito,* Tomoko Hatani, Takeshi Okada and Takao Tehara

Melanin production is diverted or blocked by the effect of sodium zinc dihydrolipoylhistidinate on scavenging DOPAquinone to form a soluble lipoyl conjugates with L-DOPA.

Design, synthesis, and biological evaluation of substituted 2-alkylthio-1,5-diarylimidazoles as selective COX-2 inhibitors **pp 1976–1982**
Latifeh Navidpour, Hooman Shadnia, Hamed Shafaroodi, Mohsen Amini, Ahmad Reza Dehpour and Abbas Shafiee*

Design, synthesis, and evaluation of a novel class of 1,5-diarylimidazole, possessing C-2 alkylthio (SMe or SEt) substituents as selective cyclooxygenase-2 inhibitors (**11a–j**) are described.



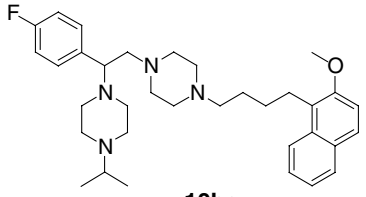
11a-j

R_1: Me, Et
R_2: H, F, Cl, Br, OMe

HSP90-like artificial chaperone activity based on indole β-cyclodextrin **pp 1983–1988**
Masaya Toda, Hideaki Itoh, Yoshihiko Kondo and Fumio Hamada*

Citrate synthase is converted from α-helix to the β-sheet by indole modified β-CyD under heating condition.

Structure–activity relationships of novel piperazines as antagonists for the melanocortin-4 receptor **pp 1989–2005**
Dai Nozawa,* Taketoshi Okubo, Takaaki Ishii, Hiroyuki Kakinuma, Shigeyuki Chaki, Shigeru Okuyama and Atsuro Nakazato



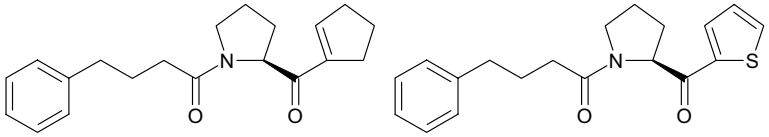
10bg

3D-QSAR and molecular docking studies of benzaldehyde thiosemicarbazone, benzaldehyde, benzoic acid, and their derivatives as phenoloxidase inhibitors **pp 2006–2015**
Chao-Bin Xue, Li Zhang, Wan-Chun Luo,* Xian-Ye Xie, Lin Jiang and Ting Xiao

Inhibitions of three classes compounds against phenoloxidase were investigated, and 3D-QSAR was performed. The interactions between compounds **N18** and phenoloxidase active site were also studied using FlexX docking.

Cell-penetrating autoantibody induces caspase-mediated apoptosis through catalytic hydrolysis of DNA **pp 2016–2023**
Eun-Jung Lee, Eun-Jung Jang, Eunhae Lee, Jaehoon Yu, Hee Yong Chung and Young-Ju Jang*

2(*S*)-(Cycloalk-1-enecarbonyl)-1-(4-phenyl-butanoyl)pyrrolidines and 2(*S*)-(aroyl)-1-(4-phenylbutanoyl) pyrrolidines as prolyl oligopeptidase inhibitors **pp 2024–2031**
Elina M. Jarho,* Jarkko I. Venäläinen, Sami Poutiainen, Harri Leskinen, Jouko Vepsäläinen, Johannes A. M. Christiaans, Markus M. Forsberg, Pekka T. Männistö and Erik A. A. Wallén

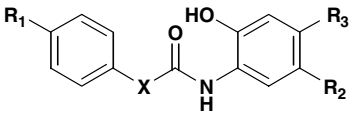


IC_{50} = 3.0 nM IC_{50} = 3.0 nM

Synthesis and biological evaluation of new *N*-(2-hydroxy-4(or 5)-nitro/aminophenyl)benzamides and phenylacetamides as antimicrobial agents **pp 2032–2044**

Tugba Ertan, Ilkay Yildiz,* Semiha Ozkan, Ozlem Temiz-Arpaci, Fatma Kaynak, Ismail Yalcin, Esin Aki-Sener and Ufuk Abbasoglu

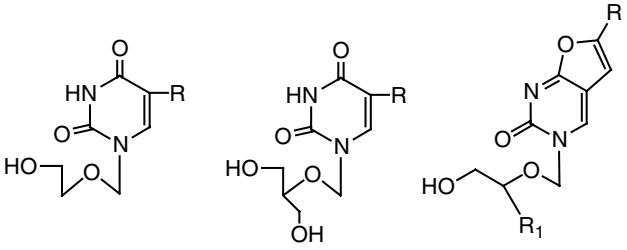
A new series of *N*-(2-hydroxy-4(or 5)-nitro/aminophenyl)benzamide and phenylacetamide derivatives (**1a**–**1n**, **2a**–**2n**) were synthesized and evaluated for antibacterial and antifungal activities against *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans*, and their drug-resistant isolates. Microbiological results indicated that the compounds possessed a broad spectrum of activity against the tested microorganisms at MIC values between 500 and 1.95 μg/ml. Benzamide derivative **1d** exhibited the greatest activity with MIC values of 1.95, 3.9, and 7.8 μg/ml against drug-resistant *B. subtilis*, *B. subtilis*, and *S. aureus*, respectively.



X = –, CH_2
R1 = H, F, Cl, Br, CH_3, C_2H_5, $C(CH_3)_3$
R2 = H, NO_2, NH_2
R3 = H, NO_2, NH_2

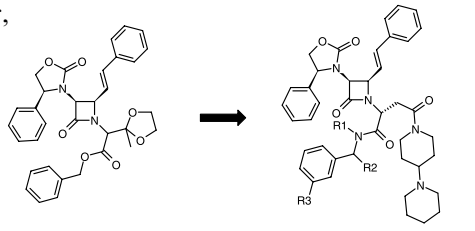
Studies on acyclic pyrimidines as inhibitors of mycobacteria **pp 2045–2053**

Naveen C. Srivastav, Tracey Manning, Dennis Y. Kunimoto and Rakesh Kumar*



Azetidinones as vasopressin V1a antagonists **pp 2054–2080**

Christophe D. Guillon,* Gary A. Koppel, Michael J. Brownstein, Michael O. Chaney, Craig F. Ferris, Shi-fang Lu, Karine M. Fabio, Marvin J. Miller, Ned D. Heindel, David C. Hunden, Robin D. G. Cooper, Stephen W. Kaldor, Jeffrey J. Skelton, Bruce A. Dressman, Michael P. Clay, Mitchell I. Steinberg, Robert F. Bruns and Neal G. Simon



1
hV1a IC_{50} = 45nM

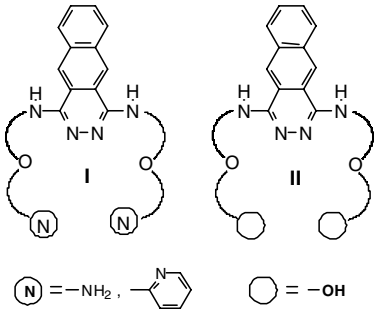
50
V1a K_i = 0.3 nM
R1 = H
R2 = (R)-methyl
R3 = H

51
V1a K_i = 0.66 nM
R1 = methyl
R2 = H
R3 = CF_3

1,4-Bis(alkylamino)benzo[*g*]phthalazines able to form dinuclear complexes of Cu(II) which as free ligands behave as SOD inhibitors and show efficient in vitro activity against *Trypanosoma cruzi* **pp 2081–2091**

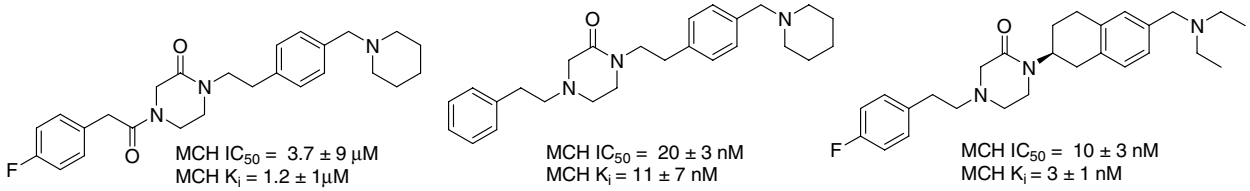
Marinela Rodríguez-Ciria, Ana M. Sanz, María J. R. Yunta, Fernando Gómez-Contreras,* Pilar Navarro, Manuel Sánchez-Moreno,* Samira Boutaleb-Charki, Antonio Osuna, Alfonso Castiñeiras, Mercedes Pardo, Carmen Cano and Lucrecia Campayo

The synthesis of a new series of benzo[*g*]phtalazine derivatives is reported. The complexating ability of these compounds towards Cu(II) might be connected with their SOD inhibitory activity in *Tripanosoma cruzi*.



The efficacy and cardiac evaluation of aminomethyl tetrahydronaphthalene ketopiperazines: A novel class of potent MCH-R1 antagonists pp 2092–2105

José L. Méndez-Andino,* Anny-Odile Colson, Kenneth M. Meyers, Maria C. Mitchell, Karen Hodge, Jeremy M. Howard, Nicholas Kim, David C. Ackley, Jerry K. Holbert, Scott W. Mittelstadt, Martin E. Dowty, Cindy M. Obringer, Paula Suchanek, Ofer Reizes, X. Eric Hu and John A. Wos

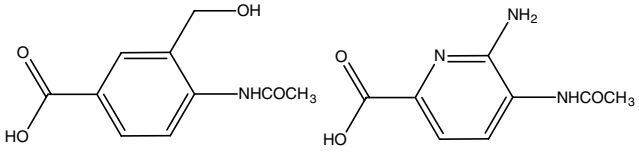


The design, synthesis, and biological studies of a novel class of MCH-R1 antagonists based on an aminotetrahydronaphthalene ketopiperazine scaffold are described.

Benzoic acid and pyridine derivatives as inhibitors of *Trypanosoma cruzi trans*-sialidase pp 2106–2119

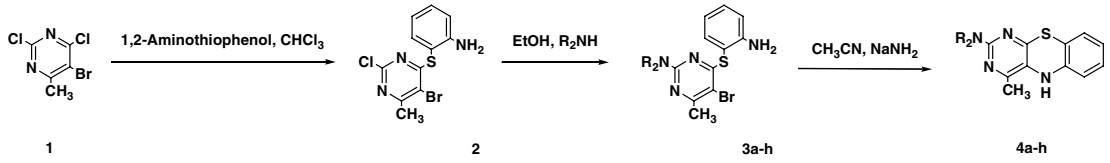
João Neres, Pascal Bonnet, Philip N. Edwards, Pravin L. Kotian, Alejandro Buschiazzo, Pedro M. Alzari, Richard A. Bryce and Kenneth T. Douglas*

Benzoic acid and pyridine-carboxylic acid derivatives inhibit *trans*-sialidase from *Trypanosoma cruzi* with I_{50} values between 0.4 and 1 mM. The strongest inhibitors in this structural family were:



Design and synthesis of pyrimido[4,5-*b*][1,4]benzothiazine derivatives, as potent 15-lipoxygenase inhibitors pp 2120–2126

M. Bakavoli,* M. Nikpour, M. Rahimizadeh, M. R. Saberi and H. Sadeghian



Substituted thiophene-anthranilamides as potent inhibitors of human factor Xa pp 2127–2146

Monica J. Kochanny,* Marc Adler, Janice Ewing, Brian D. Griedel, Elena Ho, Rushad Karanjawala, Wheeseong Lee, Dao Lentz, Amy M. Liang, Michael M. Morrissey, Gary B. Phillips, Joseph Post, Karna L. Sacchi, Steven T. Sakata, Babu Subramanyam, Ron Vergona, Janette Walters, Kathy A. White, Marc Whitlow, Bin Ye, Zuchun Zhao and Kenneth J. Shaw

A series of thiophene-anthranilamide fXa inhibitors is reported having subnanomolar inhibitory potency. The pharmacokinetic profile of compound **31** was evaluated in dogs. The X-ray crystal structure of this compound bound to factor Xa provides insight into the observed SAR for binding to factor Xa.

Enzymatic and cellular study of a serotonin *N*-acetyltransferase phosphopantetheine-based prodrug **pp 2147–2155**
Yousang Hwang, Surajit Ganguly, Anthony K. Ho, David C. Klein and Philip A. Cole*

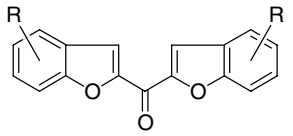
Crystal structure of the PXR–T1317 complex provides a scaffold to examine the potential for receptor antagonism **pp 2156–2166**
Yu Xue, Esther Chao, William J. Zuercher, Timothy M. Willson, Jon L. Collins and Matthew R. Redinbo*

The crystal structure of the nuclear xenobiotic receptor PXR in complex with T0901317 leads to the synthesis of agonists specific to PXR relative to the nuclear receptor LXR.

Development of selective inhibitors for anti-apoptotic Bcl-2 proteins from BHI-1 **pp 2167–2176**
Chengguo Xing,* Liangyou Wang, XiaoHu Tang and Yuk Y. Sham

Synthesis and antimycobacterial evaluation of benzofurobenzopyran analogues **pp 2177–2186**
Soizic Prado, Yves L. Janin,* Brigitte Saint-Joanis, Priscille Brodin, Sylvie Michel, Michel Koch, Stewart T. Cole, François Tillequin and Pierre-Etienne Bost

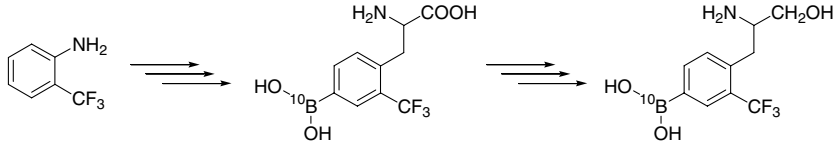
Inhibition of FLT3 and PDGFR tyrosine kinase activity by bis(benzo[*b*]furan-2-yl)methanones **pp 2187–2197**
Siavosh Mahboobi,* Andrea Uecker, Christophe Cénac, Andreas Sellmer, Emerich Eichhorn, Sigurd Elz, Frank-D. Böhmer and Stefan Dove*



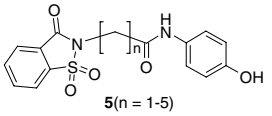
R = methoxy, hydroxy, nitro, amino

Disubstituted bisbenzofuranylmethanones were found to inhibit PDGFR and/or FLT3 autophosphorylation. Modeling studies suggest that conformational adaptation allows them to fit into the same binding site as the corresponding bisindolylmethanones.

Synthesis and evaluation as MRI probe of the trifluoromethylated *p*-boronophenylalanine and its alcohol derivative **pp 2198–2205**
Yoshihide Hattori, Hitoshi Yamamoto, Hideya Ando, Hirofumi Kondoh, Tomoyuki Asano, Mitsunori Kirihata, Yoshihiro Yamaguchi and Tateaki Wakamiya*



Synthesis and in vivo evaluation of non-hepatotoxic acetaminophen analogs **pp 2206–2215**
Anthony L. Vaccarino, Dennis Paul, Pranab K. Mukherjee, Elena B. Rodríguez de Turco, Victor L. Marcheselli, Liang Xu, Mark L. Trudell, J. M. Minguez, M. P. Matía, Carlos Sunkel, Julio Alvarez-Builla and Nicolas G. Bazan*



5(n = 1-5)

OTHER CONTENTS

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*Corresponding author
ⓘ+ 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].

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