

European Journal of Medicinal Chemistry Vol 43, No 4, 2008

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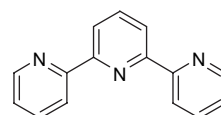
ORIGINAL ARTICLES

Synthesis of 2,6-diaryl-substituted pyridines and their antitumor activities

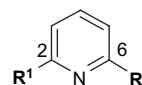
pp. 675–682

Jong-Keun Son, Long-Xuan Zhao, Arjun Basnet, Pritam Thapa, Radha Karki, Younghwa Na, Yurngdong Jahng, Tae Cheon Jeong, Byeong-Seon Jeong, Chong-Soon Lee and Eung-Seok Lee*

For the development of novel antitumor agents, we designed and synthesized 2,6-diaryl-substituted pyridine derivatives bearing three aryl groups, which are the bioisosteres of terpyridine, and evaluated their biological activities. Most of the 18 prepared compounds showed moderate cytotoxicity against several human cancer cell lines. From the structure–activity relationships we may conclude that the number of aryl groups employed would be critical for their biological activities.



α -Terpyridine



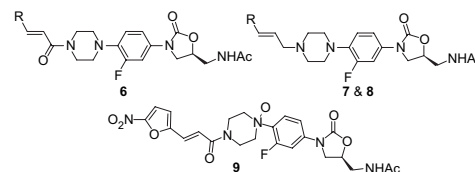
Bioisosteres of terpyridine
R¹, R²: phenyl, furyl, thienyl or pyridyl

Synthesis and *in vitro* antibacterial activities of novel oxazolidinones

pp. 683–693

Brijesh Kumar Srivastava*, Mukul R. Jain, Manish Solanki, Rina Soni, Darshan Valani, Sunil Gupta, Bhupendra Mishra, Vijay Takale, Prashant Kapadnis, Harilal Patel, Purvi Pandya, Jayendra Z. Patel and Pankaj R. Patel

A number of novel piperazinylarloxazolidinones possessing heteroaryl groups have been synthesized and their antibacterial activities were evaluated by MIC assay.

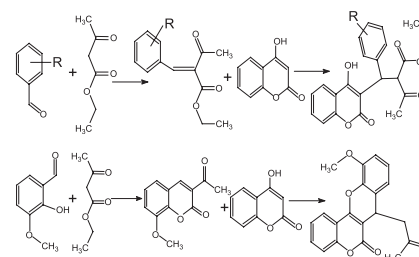


Synthesis, computational study and cytotoxic activity of new 4-hydroxycoumarin derivatives

pp. 694–706

Stanco Stanchev, Georgi Momekov, Frank Jensen and Ilia Manolov*

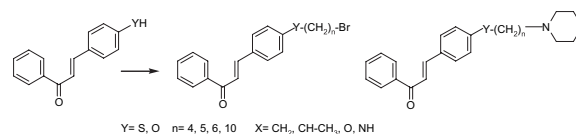
Six new coumarin derivatives have been synthesized. Their structure and properties are studied by computational method. They are tested for *in vitro* cytotoxic activity. The most active is ethyl 2-[(3,4-dihydroxyphenyl)(4-hydroxy-2-oxo-2*H*-chromen-3-yl)methyl]-3-oxobutanoate (SS-16).



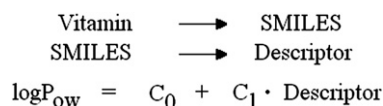
Synthesis, physicochemical properties and antimicrobial evaluation of new (*E*)-chalcones**pp. 707–713**

Z. Nowakowska*, B. Kędzia and G. Schroeder

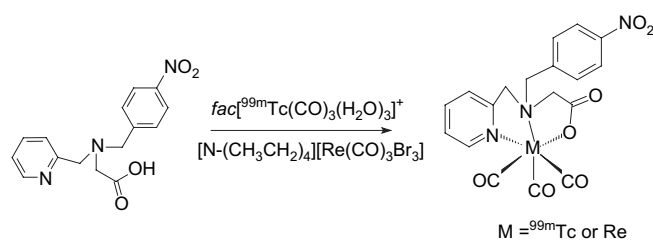
A series of 40 substituted chalcones have been synthesized and tested for their *in vitro* antibacterial and antifungal activities.

**QSPR modeling of octanol/water partition coefficient for vitamins by optimal descriptors calculated with SMILES****pp. 714–740**

A.A. Toropov*, A.P. Toropova and I. Raska, Jr.

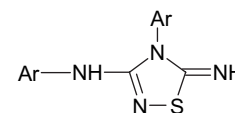
**Preparation and characterization of technetium and rhenium tricarbonyl complexes bearing the 4-nitrobenzyl moiety as potential bioreductive diagnostic radiopharmaceuticals. *In vitro* and *in vivo* studies****pp. 741–748**

Javier Giglio, Georgios Patsis, Ioannis Pirmettis, Minas Papadopoulos, Catherine Raptopoulou, Maria Pelecanou, Elsa León, Mercedes González, Hugo Cerecetto and Ana Rey*

**Synthesis and anticonvulsant activity of some novel 3-aryl amino/amino-4-aryl-5-imino-Δ²-1,2,4-thiadiazoline****pp. 749–754**

Arun Gupta, Pradeep Mishra, Sushil K. Kashaw*, Varsha Jatav and J.P. Stables

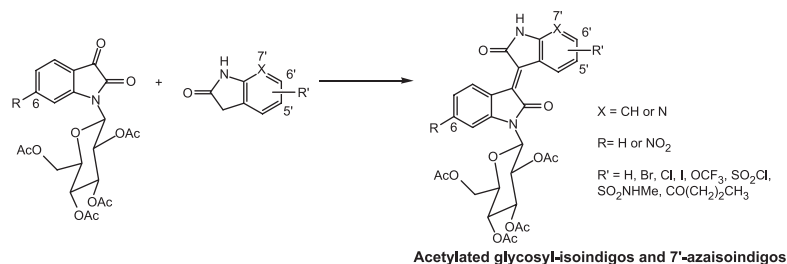
A series of 3-aryl amino/amino-4-aryl-5-imino-Δ²-1,2,4-thiadiazoline have been synthesized and evaluated for anticonvulsant activity and neurotoxicity by maximal electroshock induced seizures (MES) and subcutaneous pentylenetetrazole (ScPTZ) induced seizure models in mice. Almost all compounds showed protection against MES induced seizures whereas only **3b** was found to be active in ScPTZ test.



Synthesis and antiproliferative activities of isoindigo and azaisoindigo derivatives

pp. 755–762

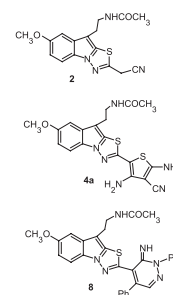
Fadoua Bouchikhi, Fabrice Anizon and Pascale Moreau*

**Synthesis and in vivo anti-mutagenic activity of novel melatonin derivatives**

pp. 763–770

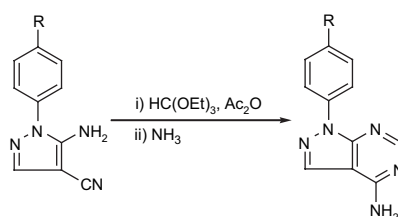
Gamal A. Elmegeed*, Wagdy K.B. Khalil, Amira Abdel Raouf and Mervat M. Abdelhalim

The purpose of this study was to evaluate the anti-mutagenic activity of the novel synthesized indole derivatives **2**, **4a**, and **8** in albino male mice in comparison with the parent melatonin. Efficacy of melatonin and its derivatives to influence cyclophosphamide (CP)-induced genotoxicity was tested using micronuclei (MN) formation in the bone marrow cells and determination of DNA, RNA and protein levels as well as cholinesterase and peroxidase activities in several organs of male mice. The present study suggests that compounds **4a**, **8** and melatonin were able to reduce the mutagenicity effect of CP in male mice. The ability of compounds **4a**, **8** and melatonin to reduce CP-related genotoxicity is possibly attributed to their antioxidant activity.

**Synthesis of N-aryl-5-amino-4-cyanopyrazole derivatives as potent xanthine oxidase inhibitors**

pp. 771–780

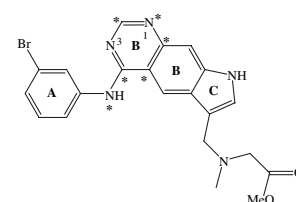
Sanjay Gupta, Lígia M. Rodrigues, Ana P. Esteves, Ana M.F. Oliveira-Campos*, M. São José Nascimento, N. Nazareth, Honorina Cidade, Marta P. Neves, Eduarda Fernandes, Madalena Pinto, Nuno M.F.S.A. Cerqueira and Natércia Brás

**Towards predictive inhibitor design for the EGFR autophosphorylation activity**

pp. 781–791

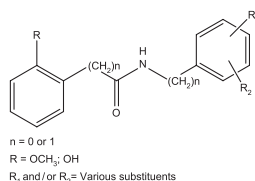
Amor A. San Juan*

In this study, a new alternative route is presented to control the aberrant EGFR by blocking the autophosphorylation activity. Based on 3D-QSAR studies the attachment of a bulky group on C-ring along with an electronegative group on B-ring and a hydrogen-bond donor on methyl formate opens a new avenue towards the optimization of novel chemical entities to develop potent inhibitors for EGFR autophosphorylation. The predictive power of this model stems from good validations obtained by predictive r^2 and complementary docking.



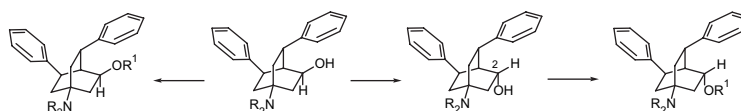
New amido derivatives as potential BKCa potassium channel activators. XI**pp. 792–799**

Vincenzo Calderone*, Francesca Lidia Fiamingo, Gabriella Amato, Irene Giorgi, Oreste Livi, Alma Martelli and Enrica Martinotti

**Epimers of bicyclo[2.2.2]octan-2-ol derivatives with antiprotozoal activity****pp. 800–807**

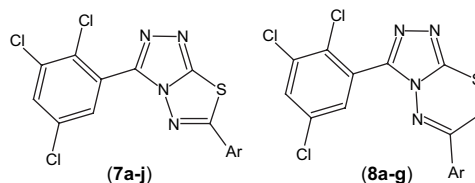
Christian Schlapper, Werner Seebacher, Marcel Kaiser, Reto Brun, Robert Saf and Robert Weis*

Epimerization of compounds with antiplasmodial and antitrypanosomal activity.

**Synthesis, antimicrobial and anti-inflammatory activities of some 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazoles and 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines bearing trichlorophenyl moiety****pp. 808–815**

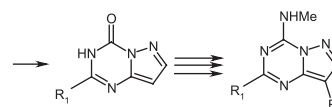
Prakash Karegoudar, D. Jagdeesh Prasad*, Mithun Ashok, Manjathuru Mahalinga, Boja Poojary and Bantwal Shivarama Holla

A series of 6-(substituted aryl)-3-(2,3,5-trichlorophenyl)-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazoles (**7a–j**) and 6-(substituted aryl)-3-(2,3,5-trichlorophenyl)-7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines (**8a–g**) have been synthesized by condensing the triazole (**6**) with various aromatic acids in presence of POCl_3 , and with various substituted phenacyl bromides. All the synthesized compounds have been screened for their antimicrobial and anti-inflammatory activities. Some of the compounds exhibited promising antimicrobial activities and moderate to good anti-inflammatory activity.

**Cyclic nucleotide phosphodiesterase type 4 inhibitors: Evaluation of pyrazolo[1,5-*a*]-1,3,5-triazine ring system as an adenine bioisostere****pp. 816–829**

Pierre Raboisson, Dominique Schultz, Christian Muller, Jean-Marie Reimund, Guillaume Pinna, Romain Mathieu, Philippe Bernard, Quoc-Tuan Do, Renee L. DesJarlais, Hélène Justiano, Claire Lugnier and Jean-Jacques Bourguignon*

Some derivatives belonging to the series of pyrazolo[1,5-*a*]-1,3,5 triazines act as adenine bioisosteres and present potent and selective PDE4 inhibitory properties.

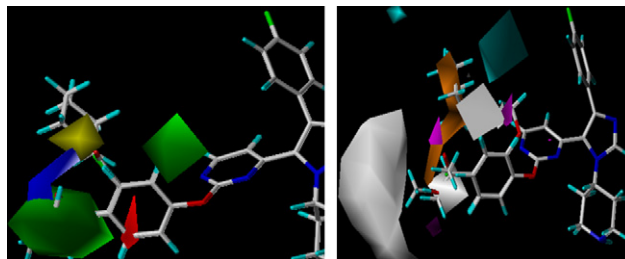


Molecular modeling studies of phenoxypyrimidinyl imidazoles as p38 kinase inhibitors using QSAR and docking

pp. 830–838

G.K. Ravindra, G. Achaiah* and G.N. Sastry**

A series of p38 kinase inhibitors of phenoxypyrimidinyl imidazole analogues were studied with molecular docking and 3D-QSAR approaches to get the insight of structural requirements for better enzyme inhibition.

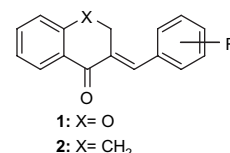


Design, synthesis and antiproliferative activity of some 3-benzylidene-2,3-dihydro-1-benzopyran-4-ones which display selective toxicity for malignant cells

pp. 839–845

Pal Perjesi*, Umashankar Das, Erik De Clercq, Jan Balzarini, Masame Kawase, Hiroshi Sakagami, James P. Stables, Tamas Lorand, Zsuzsanna Rozmer and Jonathan R. Dimmock**

The differences in cytotoxicity between series **1** and **2** are likely influenced by variation in physicochemical properties. Series **1** displayed greater cytotoxicity towards certain neoplasms than various normal cells.

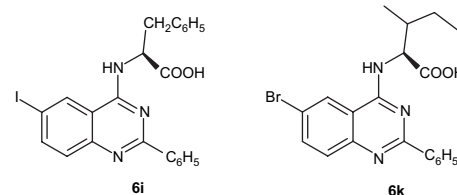


Synthesis of novel 4,6-disubstituted quinazoline derivatives, their anti-inflammatory and anti-cancer activity (cytotoxic) against U937 leukemia cell lines

pp. 846–852

P. Mani Chandrika, T. Yakaiah, A. Raghu Ram Rao*, B. Narsaiah*, N. Chakra Reddy, V. Sridhar and J. Venkateshwara Rao

A series of novel quinazoline derivatives have been synthesized and subjected to anti-inflammatory and anti-cancer (cytotoxic) activities. Compounds **6i** and **6k** showed promising anti-cancer activity.

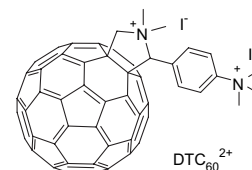


Synthesis, properties and photodynamic inactivation of *Escherichia coli* by novel cationic fullerene C₆₀ derivatives

pp. 853–861

Mariana B. Spesia, M. Elisa Milanese and Edgardo N. Durantini*

Dicationic fullerene derivative, DTC₆₀²⁺, bearing the two charged groups on a side of the C₆₀ sphere, is an interesting agent with potential applications in photodynamic inactivation of bacteria.

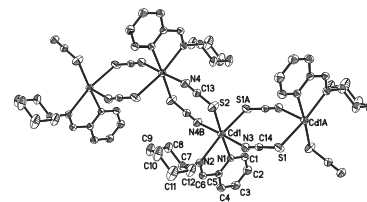


Schiff base transition metal complexes as novel inhibitors of xanthine oxidase

pp. 862–871

Zhong-Lu You, Da-Hua Shi, Chen Xu, Qiang Zhang and Hai-Liang Zhu*

Twenty transition metal complexes with Schiff bases were evaluated for their inhibitory activities on xanthine oxidase (XO), of which 11 were newly synthesized and characterized by X-ray single crystal diffraction. It was found that 9 of the 20 complexes showed the potent inhibitory activities against XO near to the standard inhibitor allopurinol. Cadmium complex $[\text{Cd}(\text{C}_{12}\text{H}_{16}\text{N}_2)(\mu\text{-NCS})_2]$ (**8**) possessed the most potent inhibitory activity with the IC_{50} value of $2.16 \mu\text{M}$.

**Antimycobacterial activity of diphenylpyraline derivatives**

pp. 872–879

Robert Weis*, Johanna Faist, Ulrike di Vora, Klaus Schweiger, Barbara Brandner, Andreas J. Kungl and Werner Seebacher

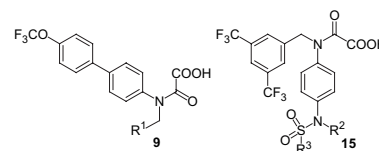
Synthesis and antimycobacterial activity of derivatives of *diphenylpyraline* and their 1-phenyl and 1-phenethyl analogues are reported.

**SHORT COMMUNICATION*****In vitro* PAI-1 inhibitory activity of oxalamide derivatives**

pp. 880–884

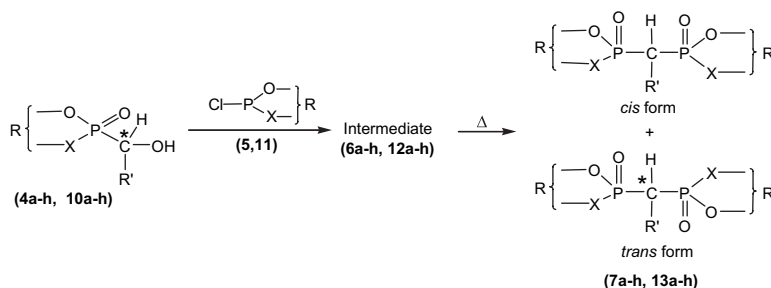
Mukul R. Jain*, Shankar Shetty, Ganes Chakrabarti, Vrajesh Pandya, Ajay Sharma, Bhavesh Parmar, Soma Srivastava, Mehul Raviya, Hitesh Soni and Pankaj R. Patel

A number of oxalamide derivatives have been synthesized and evaluated for PAI-1 inhibitory activity. *In vitro* PAI-1 inhibitory activities of oxalamide derivatives are evaluated by chromogenic assay. Few compounds have shown significant PAI-1 inhibitory activity.

**PRELIMINARY COMMUNICATION****Synthesis and anticancer activity of new class of bisphosphonates/phosphanamidates**

pp. 885–892

Y.B. Kiran, C. Devendranath Reddy*, D. Gunasekar, C. Suresh Reddy, Annette Leon and Luiz C.A. Barbosa

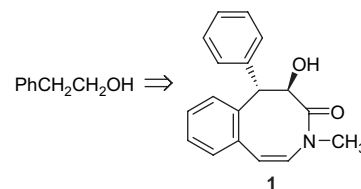


LABORATORY NOTE**An elegant synthesis of Zetaclausenamide**

Nianchun Ma*, Kemei Wu and Liang Huang

pp. 893–896

Zetaclausenamide **1** with hepatoprotective activity was prepared from 2-phenylethanol via six steps.



COVER

Overlay of the experimental and docked conformations of the ligand fluorescein in complex with an anti-fluorescein 4-4-20 Fab fragment (PDB code 1flr, 1.85 Å). The top-scoring conformation (purple) selected by the HINT force field, among the 255 poses generated by AutoDock, nearly overlays the crystallographic structure (yellow), while the conformation selected by the AutoDock scoring function (green) reverses the positions of the carbonyl and hydroxyl groups.

Image provided by Francesca Spyraakis, Alessio Amadasi, Micaela Fornabaio, Donald J. Abraham, Andrea Mozzarelli, Glen E. Kellogg, Pietro Cozzini. © 2008. Published by Elsevier Masson SAS

* Corresponding authors.



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