

European Journal of Medicinal Chemistry Vol 43, No 10, 2008

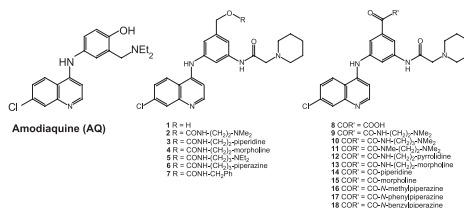
Contents

ORIGINAL ARTICLES

Synthesis and antimalarial activity of carbamate and amide derivatives of 4-anilinoquinoline

pp. 2045–2055

Sandrine Delarue-Cochin, Philippe Grellier, Louis Maes, Elisabeth Mouray, Christian Sergheraert and Patricia Melnyk*

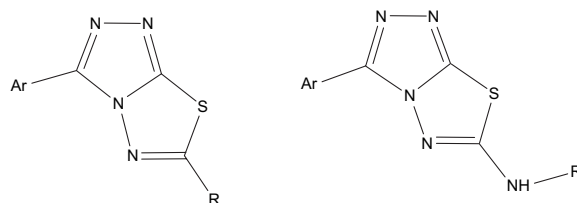


Condensed bridgehead nitrogen heterocyclic system: Synthesis and pharmacological activities of 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazole derivatives of ibuprofen and biphenyl-4-yloxy acetic acid

pp. 2056–2066

Mohd. Amir*, Harish Kumar and S.A. Javed

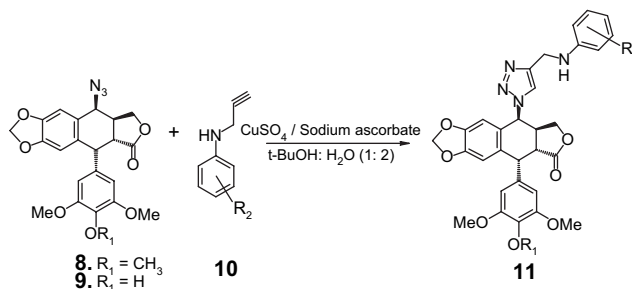
A series of 3,6-disubstituted-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazole derivatives of ibuprofen and biphenyl-4-yloxy acetic acid have been synthesized and evaluated for their anti-inflammatory, analgesic, ulcerogenic, lipid peroxidation and antimicrobial activities.



Studies on novel 4β-[(4-substituted)-1,2,3-triazol-1-yl] podophyllotoxins as potential anticancer agents

pp. 2067–2072

Bilal A. Bhat, P. Bhaskar Reddy, Satyam Kumar Agrawal, A.K. Saxena, H.M. Sampath Kumar* and G.N. Qazi

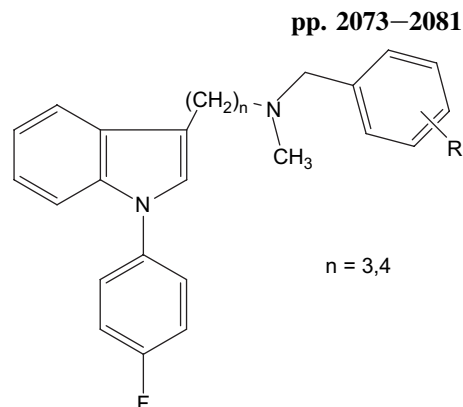


Substituted benzylaminoalkylindoles with preference for the σ_2 binding site

Maria Grazia Mamolo*, Daniele Zampieri, Caterina Zanette, Chiara Florio, Simona Collina, Mariangela Urbano, Ornella Azzolina and Luciano Vio

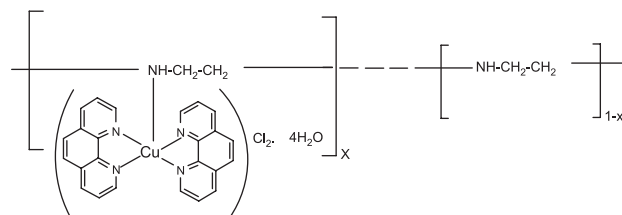
A series of substituted *N*-benzyl-3-[1-(4-fluorophenyl)-1*H*-indol-3-yl]-*N*-methylpropan-1-amines ($n = 3$) and *N*-benzyl-4-[1-(4-fluorophenyl)-1*H*-indol-3-yl]-*N*-methylbutan-1-amines ($n = 4$) have been synthesized and a preliminary evaluation of their affinity towards σ_1 and σ_2 receptors was performed by radioligand binding assay.

The results suggested that the phenyl substituents positively affected the ability to displace [3 H]-DTG from σ_2 sites, whereas the same substituents reduced the ability to displace [3 H]-(+)-pentazocine from σ_1 sites. For the most active compounds, K_i values were calculated from competitive binding experiments. Compounds with $n = 4$ displayed the greatest σ_2 over σ_1 receptor affinity. The butylene derivative with 2,4-dimethyl substitution on phenyl ring displayed the greatest σ_2 affinity ($\sigma_2 K_i = 5.9$ nM) and an appreciable σ_2 over σ_1 selectivity ($\sigma_1 K_i / \sigma_2 K_i = 22$).

**DNA binding and biological studies of some novel water-soluble polymer–copper(II)–phenanthroline complexes**

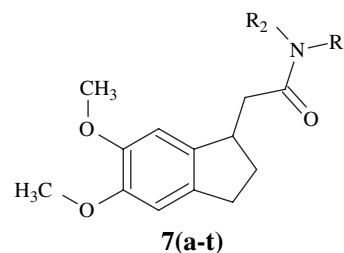
Rajendran Senthil Kumar, Sankaralingam Arunachalam*, Vaiyapuri Subbarayan Periasamy, Christo Paul Preethy, Anvarbatcha Riyasdeen and Mohammad Abdulkader Akbarsha

Some polymer–copper(II) complex samples (containing 1,10-phenanthroline ligand) with varying amounts of copper(II) complex content in the polymer chain were prepared and characterized. DNA binding properties of these samples have been found out using different physico-chemical methods.

**Synthesis and biological evaluation of amide derivatives of (5,6-dimethoxy-2,3-dihydro-1*H*-inden-1-yl) acetic acid as anti-inflammatory agents with reduced gastrointestinal ulcerogenicity**

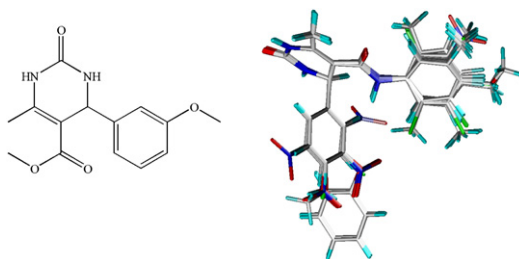
Meenakshi Sharma and S.M. Ray*

A series of (5,6-dimethoxy-2,3-dihydro-1*H*-inden-1-yl)acetic acid amides were synthesized and screened for their anti-inflammatory and related biological activities. The synthesized compounds showed long duration of anti-inflammatory activity and were free from ulcerogenicity liability of common NSAIDs.

**Synthesis, screening for antitubercular activity and 3D-QSAR studies of substituted *N*-phenyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamides**

Vijay Virsodia, Raghuvir R.S. Pissurlenkar, Dinesh Manvar, Chintan Dholakia, Priti Adlakha, Anamik Shah* and Evans C. Coutinho**

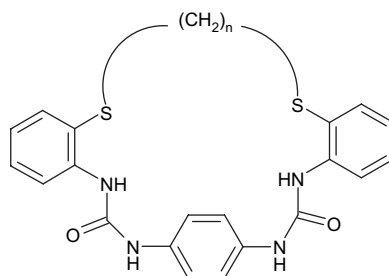
pp. 2103–2115



Facile synthesis of dithiatetraaza-macrocycles of potential anti-inflammatory activity

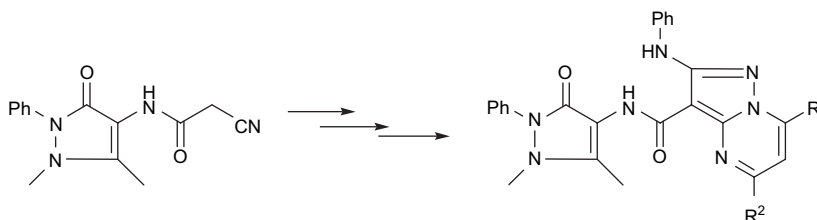
pp. 2116–2121

Adel S. Girgis*

**Synthesis and antimicrobial activity of some new heterocycles incorporating antipyrine moiety**

pp. 2122–2129

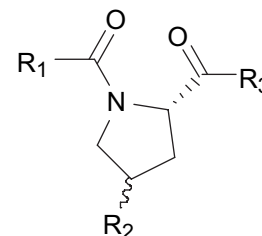
Samir Bondock*, Ramy Rabie, Hassan A. Etman and Ahmed A. Fadda

**Design, synthesis and preliminary evaluation of novel pyrrolidine derivatives as matrix metalloproteinase inhibitors**

pp. 2130–2139

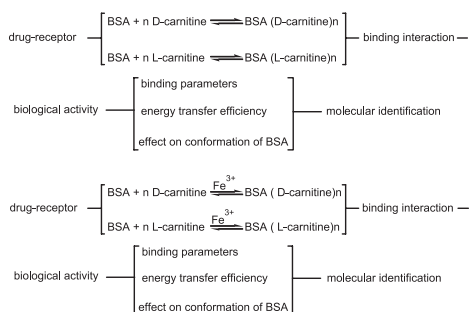
Xian-Chao Cheng, Qiang Wang, Hao Fang, Wei Tang and Wen-Fang Xu*

A series of novel pyrrolidine derivatives were designed, synthesized and assayed for their inhibitory activities on matrix metalloproteinase 2 (MMP-2) and aminopeptidase N (AP-N). The results showed that these pyrrolidine derivatives exhibited highly selective inhibition against MMP-2 as compared with AP-N. The hydroxamates **8a–c** were equally or more potent MMP-2 inhibitors than the positive control LY52. The binding mode of the most potent compound **8a** with MMP-2 was proposed. Structure–activity relationships were also briefly discussed.

**Study on the binding interaction between carnitine optical isomer and bovine serum albumin**

pp. 2140–2148

Ming Guo*, Wei-Jun Lü, Ming-Hui Li and Wei Wang

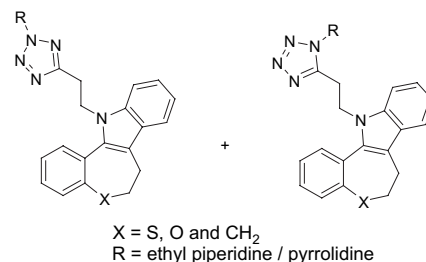


Synthesis and structure guided evaluation of estrogen agonist and antagonist activities of some new tetrazolyl indole derivatives

Uma Sharan Singh, Ravi Shankar, Gaya P Yadav, Geetika Kharkwal, Anila Dwivedi, Govind Keshri, M.M. Singh, P.R. Moulik and K. Hajela*

pp. 2149–2158

Several regioisomeric tetrazolyl indole derivatives with structurally modified alkyl substituents at the tetracyclic indole nitrogen containing *N*-ethyl amino tetrazole moiety have been synthesized and screened for their ER binding affinity, agonist (estrogenic), antagonist (antiestrogenic) and anti-implantation activities.



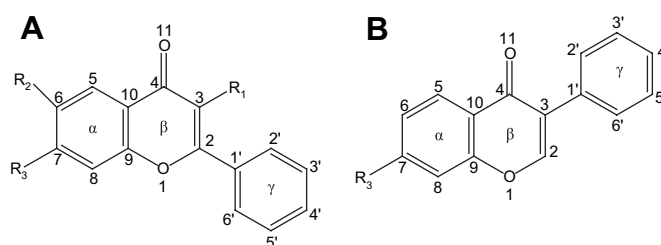
QSAR, action mechanism and molecular design of flavone and isoflavone derivatives with cytotoxicity against HeLa

Si Yan Liao, Jin Can Chen, Li Qian, Yong Shen and Kang Cheng Zheng*

pp. 2159–2170

A QSAR of flavone and isoflavone derivatives with cytotoxicity against HeLa has been studied by using DFT, MM2 and statistical methods. A simple and clear QSAR equation with excellent predictive ability was established. Five new compounds with higher cytotoxicity were theoretically designed.

Molecular structures of flavone (A) and isoflavone (B) derivatives.

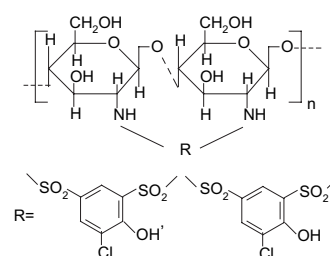


The antioxidant activity of 2-(4(or 2)-hydroxyl-5-chloride-1,3-benzene-di-sulfanamide)-chitosan

Zhimei Zhong, Rong Xing, Song Liu, Lin Wang, Shengbao Cai and Pengcheng Li*

pp. 2171–2177

New 2-(4(or 2)-hydroxyl-5-chloride-1,3-benzene-di-sulfanamide)-chitosan was synthesized and characterized. The antioxidant activities of the derivatives were investigated employing various established systems.

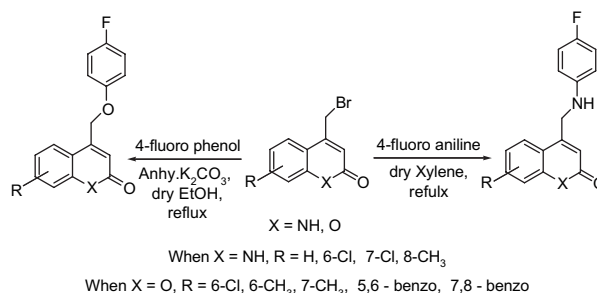


Synthesis and biological activities of some new fluorinated coumarins and 1-aza coumarins

Rajesh G. Kalkhambkar, Geeta M. Kulkarni*, Chandrappa M. Kamanavalli, N. Premkumar, S.M.B. Asdaq and Chung Ming Sun

pp. 2178–2188

A series of new fluorinated coumarins and 1-aza coumarins are synthesized and the effect of fluorine in the molecule on their anti-microbial, anti-inflammatory and analgesic activities is discussed. All the compounds are characterized by elemental analysis, IR, ¹H NMR, ¹³C NMR, ¹⁹F NMR, EI-MS and FAB-MS. ORTEP diagram of one of the compounds is reported herein.

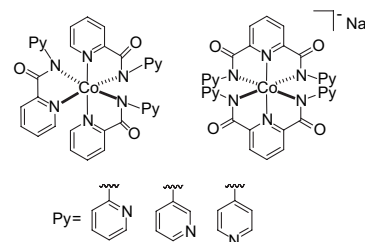


Synthesis, characterization and antibacterial activity of cobalt(III) complexes with pyridine–amide ligands

pp. 2189–2196

Anurag Mishra, Nagendra K. Kaushik, Akhilesh K. Verma and Rajeev Gupta*

Six cobalt(III) complexes with pyridine–amide-based ligands have been synthesized and characterized. These complexes show significant antibacterial activity (MIC: 2.7–375 µg/ml) and were found to be less cytotoxic than gentamycin.

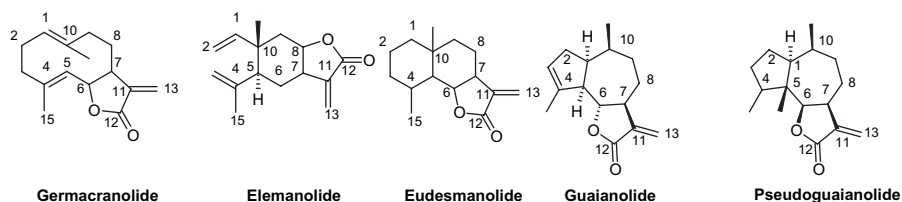


Use of self-organizing maps and molecular descriptors to predict the cytotoxic activity of sesquiterpene lactones

pp. 2197–2205

Mariane B. Fernandes, Marcus T. Scotti, Marcelo J.P. Ferreira and Vicente P. Emerenciano*

We investigate a set of 55 different sesquiterpene lactones, represented by 5 skeletons, using 3D molecular descriptors and Kohonen self-organizing maps to classify and predict the cytotoxic activity.

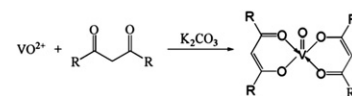
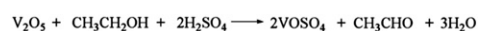


New diketone based vanadium complexes as insulin mimetics

pp. 2206–2210

A. Sheela, S. Mohana Roopan and R. Vijayaraghavan*

Two new complexes namely bisdimethylmalonatoovanadium(IV) [VO(DMM)₂] and bisdiethylmalonatoovanadium(IV) [VO(DEM)₂] have been synthesized and characterized. The antidiabetic activity of the complexes was proved by animal study.

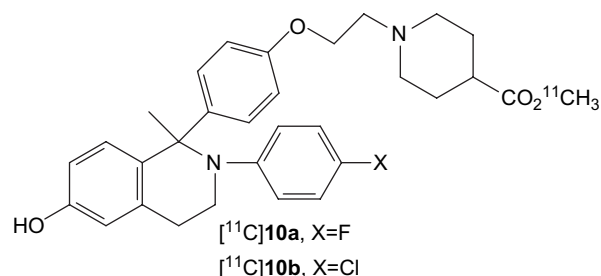


Synthesis and preliminary biological evaluation of new carbon-11 labeled tetrahydroisoquinoline derivatives as SERM radioligands for PET imaging of ER expression in breast cancer

pp. 2211–2219

Mingzhang Gao, Min Wang, Kathy D. Miller, George W. Sledge and Qi-Huang Zheng*

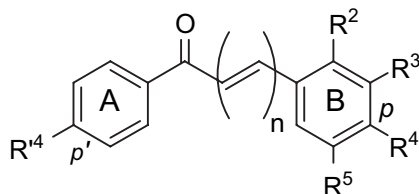
This paper reports the synthesis and preliminary biological evaluation of new carbon-11 labeled tetrahydroisoquinoline derivatives, potential SERM radioligands for PET imaging of ER expression in breast cancer.



Antifungal activity of chalcones: A mechanistic study using various yeast strains

pp. 2220–2228

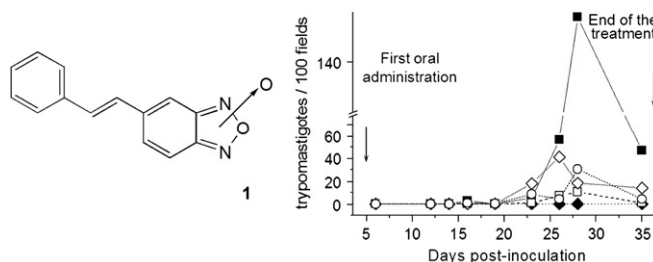
K.L. Lahtchev, D.I. Batovska*, St.P. Parushev, V.M. Ubivovk and A.A. Sibirny

**In vivo studies of 5-arylethenylbenzofuroxans in acute murine models of Chagas' disease**

pp. 2229–2237

Lucía Boiani, Carolina Davies, Carolina Arredondo, Williams Porcal, Alicia Merlino, Alejandra Gerpe, Mariana Boiani, José Pedro Pacheco, Miguel Ángel Basombrío, Hugo Cerecetto* and Mercedes González*

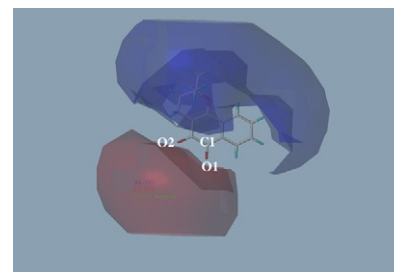
5-Arylethenylbenzofuroxans were studied *in vivo* using acute murine models of Chagas' disease. Compound **1** was the best for treating infection against the four studied strains.

**Studies of trypanocidal (inhibitory) power of naphthoquinones: Evaluation of quantum chemical molecular descriptors for structure–activity relationships**

pp. 2238–2246

M. Paulino*, E.M. Alvareda, P.A. Denis, E.J. Barreiro, G.M. Sperandio da Silva, M. Dubin, C. Gastellú, S. Aguilera and O. Tapia**

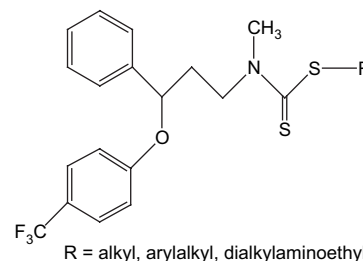
QSAR-2D and -3D treatments were made with a set of trypanocidal *ortho*- and *para*-naphthoquinones. The results indicate that the inhibitory activity of the tripanosomatids's growth is related to the semiquinone electronic state. The inhibitory activity increases as a function of the following factors: (i) a more negative value of the EHOMO; (ii) an increase of the negative charge of atoms O1 and O2 (red field) and of the positive charge QC1 (blue field) and (iii) with an increase in the electronegativity (χ).

**SHORT COMMUNICATIONS****Carbodithioic acid esters of fluoxetine, a novel class of dual-function spermicides**

pp. 2247–2256

S.T.V.S. Kiran Kumar, Lalit Kumar, Vishnu L. Sharma*, Ashish Jain, Rajeev K. Jain, Jagdamba P. Maikhuri, Manish Kumar, Praveen K. Shukla and Gopal Gupta

Carbodithioic acid esters of fluoxetine prepared by replacing the methylamino function in amino-propane chain with carbodithioic acid group and by adding various *S*-2-hydroxypropyl ester of dialkylamino carbodithioic acid at 3-methylamino group have shown good spermicidal, antifungal and anti-*Trichomonas* activities.

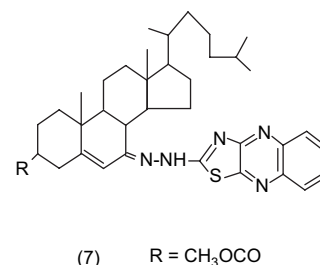


Synthesis, structure elucidation and antibacterial evaluation of new steroidal -5-en-7-thiazoloquinoxaline derivatives

pp. 2257–2261

Salman Ahmad Khan, Kishwar Saleem* and Zaheer Khan

Steroidal thiazolo[4,5-*b*]quinoxaline-2-yl-hydrazone derivatives, previously prepared from the reaction of cholest-5-en-7-one-thiosemicarbazones with 2,3-dichloroquinoxalines at 80 °C in high yield. The thiosemicarbazone derivatives were obtained by the condensation of the thiosemicarbazide with steroidal ketones. All the compounds have been characterized by means of elemental analyses, IR, ¹H NMR and mass spectroscopic data. The antibacterial activity was first tested in vitro by the disk diffusion assay against *Escherichia coli* and then the minimum inhibitory concentration (MIC) of active compounds was determined. The results showed that steroidal thiazoloquinoxaline derivatives are better growth inhibitors as compared to steroidal thiosemicarbazone of both types of bacteria (Gram-positive and Gram-negative). Compounds **7** and **8** are better antibacterial agents as compared to chloramphenicol.

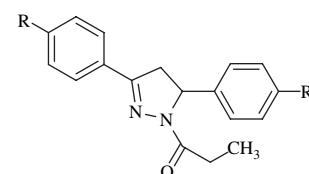


Synthesis, molecular modeling studies and selective inhibitory activity against MAO of N1-propanoyl-3,5-diphenyl-4,5-dihydro-(1H)-pyrazole derivatives

pp. 2262–2267

Franco Chimenti, Rossella Fioravanti*, Adriana Bolasco, Fedele Manna, Paola Chimenti, Daniela Secci, Francesca Rossi, Paola Turini, Francesco Ortuso, Stefano Alcaro and Maria Cristina Cardia

A series of N1-propanoyl-3,5-diphenyl-4,5-dihydro-(1H)-pyrazole derivatives were synthesized and assayed as inhibitors of MAO-A and MAO-B isoforms.

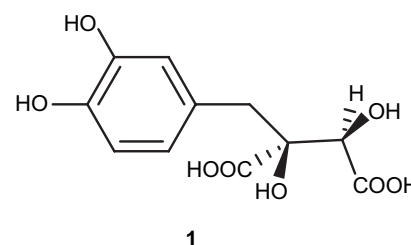


The total synthesis of fukiic acid, an HIV-1 integrase inhibitor

pp. 2268–2271

Clémence Queffélec, Fabrice Bailly, Gladys Mbemba, Jean-François Mouscadet, Zeger Debyser, Myriam Witvrouw and Philippe Cotelle*

A successful synthesis of fukiic acid is described in 7% overall yield (6 steps from veratraldehyde). *rac*-Fukiic acid was found to be a potent inhibitor of HIV-1 integrase but did not reveal antiviral activity in the MT-4 cells assay.

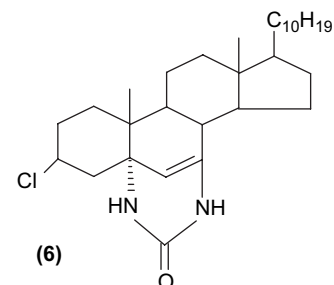


Synthesis, characterization and in vitro antibacterial activity of thiourea and urea derivatives of steroids

pp. 2272–2277

Salman Ahmad Khan, Neha Singh and Kishwar Saleem*

Some heterocyclic systems namely stigmest-6-en-7, 5α thiourea and stigmest-6-en-7, 5α urea derivatives of steroids were synthesized by the reaction of stigmest-5-en-7 one with thiourea/urea in the presence of a few drops of conc. HCl at 80 °C in high yield. All the compounds have been characterized by means of elemental analyses, IR, ¹H NMR, ¹³C NMR and mass spectroscopic data. The antibacterial activity of these compounds against two Gram-positive and two Gram-negative bacteria. The results showed that compounds **3** and **4** are better antibacterial agents as compared to standard drug chloramphenicol.



ERRATUM

Erratum to “Structural changes of benzylether derivatives of vesamicol and their influence on the binding selectivity to the vesicular acetylcholine transporter” pp. 2278–2278

Barbara Wenzel, Dietlind Sorger, Katrin Heinitz, Matthias Scheunemann, Reinhard Schliebs, Jörg Steinbach and Osama Sabri

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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