



European Journal of Medicinal Chemistry Vol 46, No 2, 2011

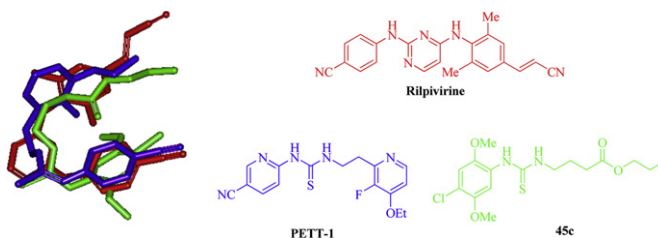
Contents

ORIGINAL ARTICLES

Structure–activity relationship studies of 1-(4-chloro-2,5-dimethoxyphenyl)-3-(3-propoxypropyl)thiourea, a non-nucleoside reverse transcriptase inhibitor of human immunodeficiency virus type-1

pp. 447–467

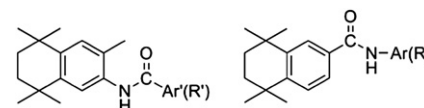
Michal Weitman, Ketzi Lerman, Abraham Nudelman*, Dan Thomas Major, Amnon Hizi* and Alon Herschhorn

**Synthesis and effects of some novel tetrahydronaphthalene derivatives on proliferation and nitric oxide production in lipopolysaccharide activated Raw 264.7 macrophages**

pp. 468–479

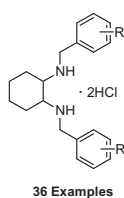
A. Selen Gurkan*, Arzu Z. Karabay, Zeliha Buyukbingol and Erdem Buyukbingol

Some novel retinoid derivatives were synthesized and evaluated for their nitric oxide inhibitory activity.

**Synthesis, antimicrobial activity and structure–activity relationship study of *N,N*-dibenzyl-cyclohexane-1,2-diamine derivatives**

pp. 480–487

Mukul Sharma, Penny Joshi, Nitin Kumar, Seema Joshi, Rajesh K. Rohilla, Nilanjan Roy and Diwan S. Rawat*

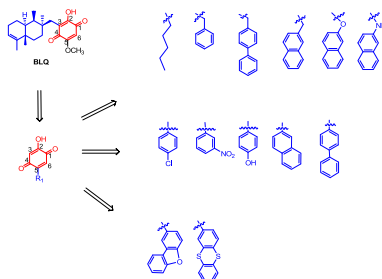


R-4	MIC (μg/mL)			
	<i>E. Coli</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>E. epidermidis</i>
Me	0.25	0.125	0.125	0.125
Et	0.008	0.004	0.008	0.008
<i>i</i> -Pr	0.004	0.0005	0.008	0.008
<i>n</i> -Bu	0.008	0.0005	0.008	0.008
<i>t</i> -Bu	0.008	0.0006	0.004	0.008

Structure-based design, synthesis and preliminary anti-inflammatory activity of bolinaquinone analogues

pp. 488–496

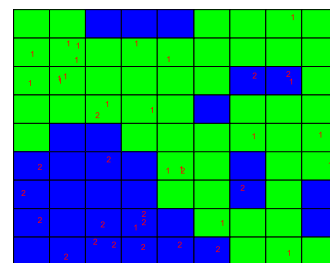
Carmen Petronzi, Rosanna Filosa*, Antonella Peduto, Maria Chiara Monti, Luigi Margarucci, Antonio Massa, Simona Francesca Ercolino, Valentina Bizzarro, Luca Parente, Raffaele Riccio and Paolo de Caprariis

**Ligand - based virtual screening procedure for the prediction and the identification of novel β -amyloid aggregation inhibitors using Kohonen maps and Counterpropagation Artificial Neural Networks**

pp. 497–508

Antreas Afantitis*, Georgia Melagraki*, Panayiotis A. Koutentis, Haralambos Sarimveis and George Kollias

In this work we have developed an *in silico* model to predict the inhibition of β -amyloid aggregation by small organic molecules. In particular we have explored the inhibitory activity of a series of 62 *N*-phenylanthranilic acids using Kohonen maps and Counterpropagation Artificial Neural Networks. The effects of various structural modifications on biological activity are investigated and novel structures are designed using the developed *in silico* model. More specifically a search for optimized pharmacophore patterns by insertions, substitutions, and ring fusions of pharmacophoric substituents of the main building block scaffolds is described. The detection of the domain of applicability defines compounds whose estimations can be accepted with confidence.



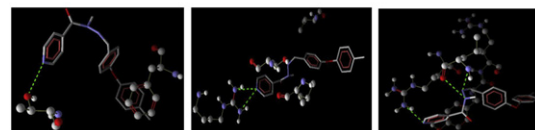
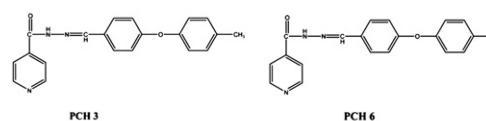
Class 1= active, Class 2= inactive

Design & synthesis of *N*-[substituted] pyridine-4-carbohydrazides as potential anticonvulsant agents

pp. 509–518

Laxmi Tripathi*, Ranjit Singh and James P. Stables

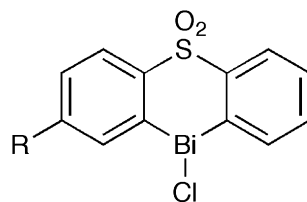
A series of *N*-[substituted] pyridine-4-carbohydrazides were designed, synthesized and evaluated for anticonvulsant activity and neurotoxicity. Computational study involving distance mapping, Log *P* calculation, prediction of pharmacokinetic properties and docking results were reported.

**Bismuth heterocycles based on a diphenyl sulfone scaffold: Synthesis and substituent effect on the antifungal activity against *Saccharomyces cerevisiae***

pp. 519–525

Toshihiro Murafuji*, Yudai Fujiwara, Daisuke Yoshimatsu, Isamu Miyakawa, Kouto Migita and Yuji Mikata

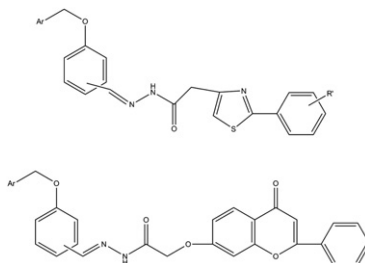
A series of heterocyclic organobismuth(III) compounds derived from diphenyl sulfones was synthesized. A clear structure–activity relationship between the antifungal activity and the lipophilicity was found for these compounds.

R = Me, Ph, OMe, Cl, H, *t*-Bu, CF₃, F, NMe₂

Synthesis and anti-inflammatory evaluation of some new acyl-hydrazones bearing 2-aryl-thiazole

pp. 526–534

Cristina Mariana Moldovan*, Ovidiu Oniga, Alina Pârvu, Brîndușa Tiperciuc, Philippe Verite, Adrian Pîrnău, Ovidiu Crișan, Marius Bojiță and Raluca Pop

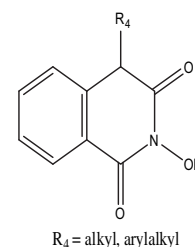


2-Hydroxyisoquinoline-1,3(2*H*,4*H*)-diones as inhibitors of HIV-1 integrase and reverse transcriptase RNase H domain: Influence of the alkylation of position 4

pp. 535–546

Muriel Billamboz, Fabrice Bailly*, Cédric Lion, Christina Calmels, Marie-Line Andréola, Myriam Witvrouw, Frauke Christ, Zeger Debyser, Laura De Luca, Alba Chimirri and Philippe Cotelte

A series of 2-hydroxyisoquinoline-1,3(2*H*,4*H*)-dione derivatives substituted on position 4 by alkyl and arylalkyl groups was synthesized. Their inhibitory properties of HIV-1 integrase and reverse transcriptase RNase H function were evaluated.

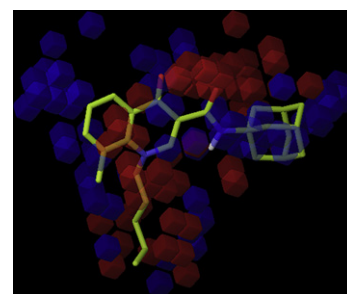


Three-dimensional quantitative structure–selectivity relationships analysis guided rational design of a highly selective ligand for the cannabinoid receptor 2

pp. 547–555

Simone Brogi, Federico Corelli, Vincenzo Di Marzo, Alessia Ligresti, Claudia Mugnaini, Serena Pasquini and Andrea Tafi*

A quantitative ligand-based selectivity model for CB2 receptor was developed, which was experimentally validated by the synthesis of a new extremely selective CB2 ligand. Such a prospective experimental validation lends support for the practicability of this kind of approaches as a valuable alternative to docking studies performed on homology receptor models.

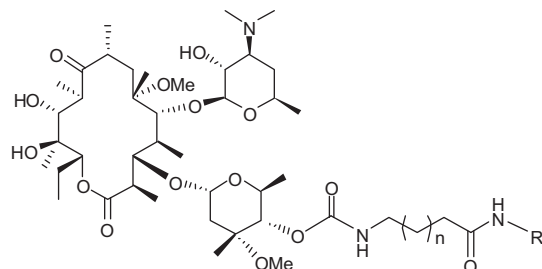


Synthesis and antibacterial evaluation of novel clarithromycin derivatives with C-4'' elongated arylalkyl groups against macrolide-resistant strains

pp. 556–566

Shutao Ma*, Bo Jiao, Yongjing Ju, Manjie Zheng, Ruixin Ma, Lin Liu, Ling Zhang, Xuecui Shen, Chenchen Ma, Ya Meng, Hui Wang, Yunkun Qi, Xiaodong Ma and Wenping Cui

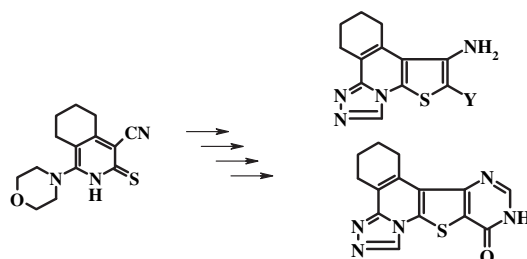
33 novel clarithromycin derivatives with elongated C-4'' side chains were synthesized and evaluated to probe the effect of different lengths of their C-4'' side chains on activity against resistant bacterial strains.



Synthesis and biological activity of pyrazolothienotetrahydroisoquinoline and [1,2,4]triazolo[3,4-a]thienotetrahydroisoquinoline derivatives

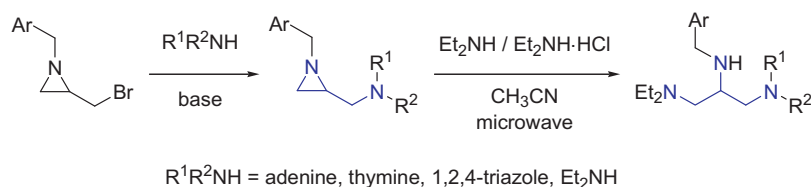
pp. 567–578

Adel M. Kamal, Shaban M. Radwan and Remon M. Zaki*

**Synthesis of 2-(aminomethyl)aziridines and their microwave-assisted ring opening to 1,2,3-triaminopropanes as novel antimalarial pharmacophores**

pp. 579–587

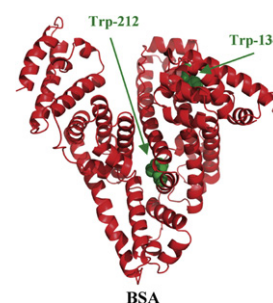
Matthias D'hooghe*, Sara Kenis, Karel Vervisch, Carmen Lategan, Peter J. Smith, Kelly Chibale and Norbert De Kimpe*

**Characterization of the baicalein–bovine serum albumin complex without or with Cu^{2+} or Fe^{3+} by spectroscopic approaches**

pp. 588–599

Daojin Li, Mei Zhu, Chen Xu and Baoming Ji*

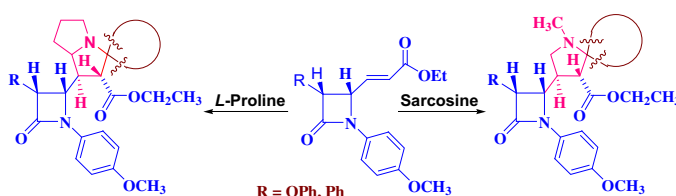
The binding of baicalein to bovine serum albumin (BSA) in aqueous solution has been studied by fluorescence, UV, CD and the three-dimensional (3D) fluorescence spectra.

**Synthesis and antimicrobial activity of highly functionalised novel β -lactam grafted spiropyrrolidines and pyrrolizidines**

pp. 600–607

Natarajan Arumugam, Govindasami Periyasami, Raghavachary Raghunathan*, Subban Kamalraj and Johnpaul Muthumary

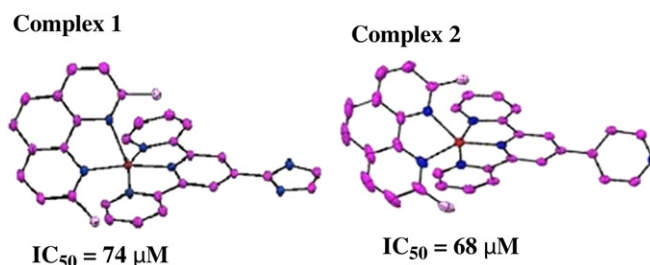
Synthesis of novel β -lactam grafted spiropyrrolidine/pyrrolizidines has been accomplished by intermolecular 1,3-dipolar cycloaddition reaction. These compounds showed good antimicrobial activity even at lower concentration.



Anomalous behavior of pentacoordinate copper complexes of dimethylphenanthroline and derivatives of terpyridine ligands: Studies on DNA binding, cleavage and apoptotic activity

pp. 608–617

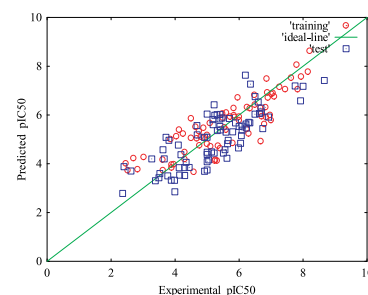
Subramaniyam Rajalakshmi, Thomas Weyhermüller, Allen J. Freddy, Hannah R. Vasanthi and Balachandran Unni Nair*

**Predicting hERG activities of compounds from their 3D structures: Development and evaluation of a global descriptors based QSAR model**

pp. 618–630

Nandita Sinha and Srikanta Sen*

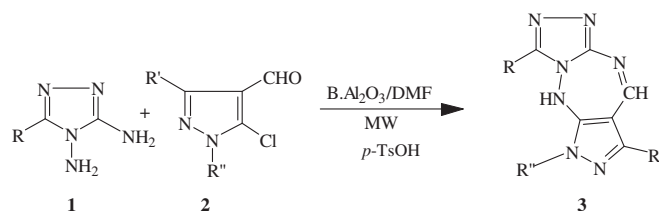
A predictive model of hERG activity was developed and evaluated. Statistical parameters and enrichment factor indicated the model's effectiveness. The test with randomized experimental data demonstrated its robustness.

**Efficient and novel one-pot synthesis of antifungal active 1-substituted-8-aryl-3-alkyl/aryl-4H-pyrazolo[4,5-*f*][1,2,4]triazolo[4,3-*b*][1,2,4]triazepines using solid support**

pp. 631–635

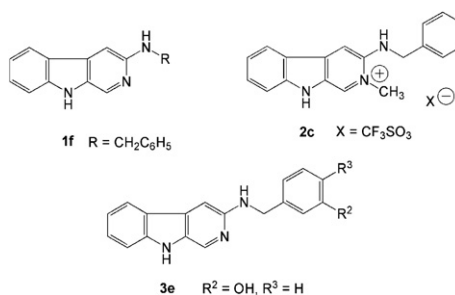
Monika Gupta*, Satya Paul and Rajive Gupta

A simple, efficient and environment-friendly procedure is developed for the synthesis of antifungal active 1-substituted-8-aryl-3-alkyl/aryl-4H-pyrazolo[4,5-*f*][1,2,4]triazolo[4,3-*b*][1,2,4]triazepines in the presence of *N,N*-dimethylformamide as an energy transfer medium, basic alumina as solid support and *p*-TsOH as catalyst under microwave irradiation.

**3-Benzylamino- β -carboline derivatives induce apoptosis through G₂/M arrest in human carcinoma cells HeLa S-3**

pp. 636–646

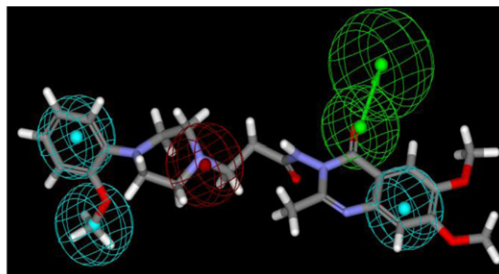
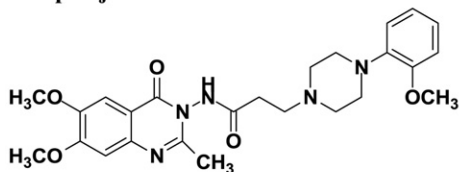
Reiko Ikeda, Toshie Iwaki, Tomoko Iida, Takasumi Okabayashi, Eishiro Nishi, Masaki Kurosawa, Norio Sakai and Takeo Konakahara*



Molecular modeling study and synthesis of quinazolinone-aryl piperazine derivatives as α_1 -adrenoreceptor antagonists

pp. 647–658

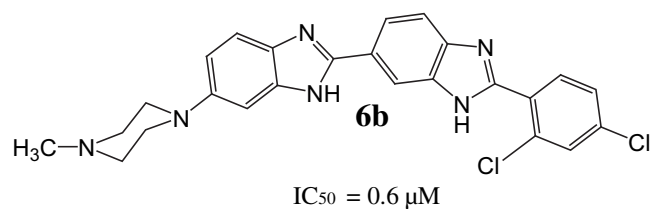
Sahar Mahmoud Abou-Seri, Khaled Abouzid* and Dalal A. Abou El Ella**

Comp 13j**Synthesis and biological activity of novel inhibitors of topoisomerase I: 2-Aryl-substituted 2-bis-1H-benzimidazoles**

pp. 659–669

Manish Singh and Vibha Tandon*

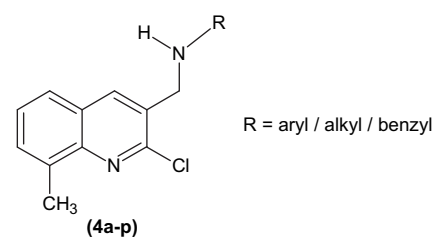
A series of 2-bisbenzimidazole derivatives were synthesized and evaluated as topoisomerase I inhibitors. Compound **6b** was found to be the most potent inhibitor.

**Synthesis, antidepressant and antifungal evaluation of novel 2-chloro-8-methylquinoline amine derivatives**

pp. 670–675

Suresh Kumar*, Sandhya Bawa**, Sushma Drabu, Himanshu Gupta, Lalit Machwal and Rajiv Kumar

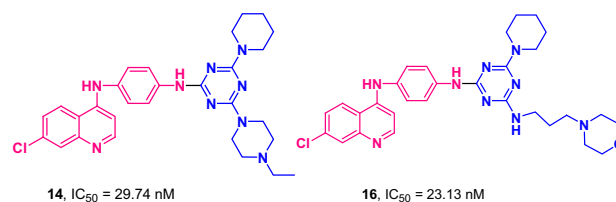
A series of heteroaryl amines containing 2-chloro-8-methylquinoline derivatives were synthesized and evaluated for antidepressant and antifungal activity.

**4-Anilinoquinoline triazines: A novel class of hybrid antimalarial agents**

pp. 676–690

Ashok Kumar, Kumkum Srivastava, S. Raja Kumar, M.I. Siddiqi, Sunil K. Puri, Jitendra K. Sexana and Prem M.S. Chauhan*

A series of novel hybrid class 4-anilinoquinoline triazines have been synthesized and screened for their antimalarial activity in in vitro and in vivo assay.

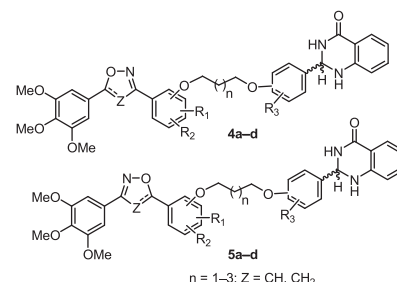


Synthesis and biological evaluation of 3,5-diaryl isoxazoline/isoxazole linked 2,3-dihydroquinazolinone hybrids as anticancer agents

pp. 691–703

Ahmed Kamal*, E. Vijaya Bharathi, J. Surendranadha Reddy, M. Janaki Ramaiah, D. Dastagiri, M. Kashi Reddy, A. Viswanath, T. Lakshminarayan Reddy, T. Basha Shaik, S.N.C.V.L. Pushpavalli and Manika Pal Bhadra*

New class of 3,5-diaryl isoxazoline/isoxazole linked 2,3-Dihydroquinazolinone hybrids were prepared and evaluated for anticancer activity. Some of the biological assays were also carried out for the most potent compound **4c**.

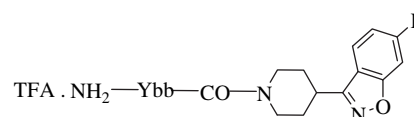


Synthesis of elastin based peptides conjugated to benzisoxazole as a new class of potent antimicrobials – A novel approach to enhance biocompatibility

pp. 704–711

R. Suhas, S. Chandrashekar and D. Channe Gowda*

A novel series of conjugates involving elastin peptide sequences and benzisoxazole derivative were synthesized and characterized. Most of the candidates of the series have exerted the highly potent activity against the human pathogens tested in the present study.



Ybb = Phe, Trp, Tyr, GGAP, GGIP, GGFP, GVGVP, GFGFP,

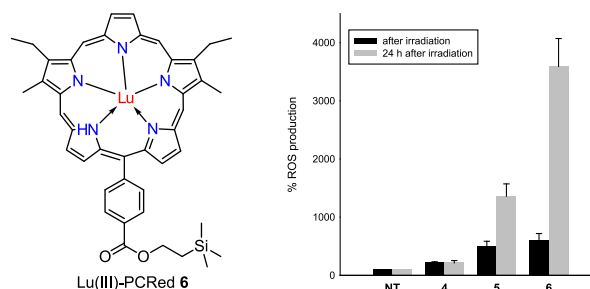
GEGFP GVGVP GVGVP GVGVP GFGFP GFGFP,

GEGFP GVGVP GVGFP GFGFP GVGVP GVGFP

Metallation of pentaphyrin with Lu(III) dramatically increases reactive-oxygen species production and cell phototoxicity

pp. 712–720

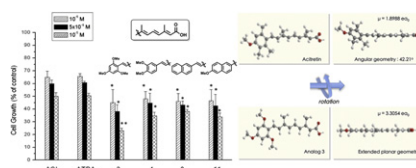
Maurizio Ballico, Valentina Rapozzi, Luigi E. Xodo** and Clara Comuzzi*



Syntheses, antiproliferative activity and theoretical characterization of acitretin-type retinoids with changes in the lipophilic part

pp. 721–737

George E. Magoulas, Stavros E. Bariamis, Constantinos M. Athanassopoulos, Anastasios Haskopoulos, Petros G. Dedes, Marios G. Krokidis, Nikos K. Karamanos, Dimitris Kleitsas, Dionissios Papaioannou* and George Maroulis**

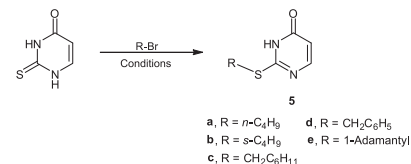


Synthesis and structure–activity relationship of 2-thiopyrimidine-4-one analogs as antimicrobial and anticancer agents

pp. 738–742

Supaluk Prachayasittikul*, Apilak Worachartcheewan, Chanin Nantasenamat, Maneekarn Chinworrungsee, Nirun Sornsongkhram, Somsak Ruchirawat and Virapong Prachayasittikul**

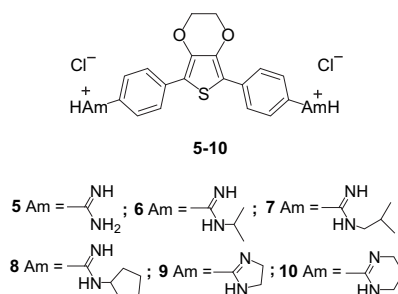
2-Thiopyrimidine-4-ones (**5a–e**) were synthesized to yield antimicrobial and potent cytotoxic activities. Their structure–activity relationships were described.



Synthesis, DNA/RNA affinity and antitumour activity of new aromatic diamidines linked by 3,4-ethylenedioxythiophene

pp. 743–755

Ivana Stolić, Katarina Mišković, Ivo Piantanida, Mirela Baus Lončar, Ljubica Glavaš-Obrovac* and Miroslav Bajić**

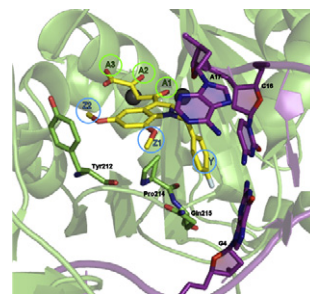


HIV-1 integrase strand-transfer inhibitors: Design, synthesis and molecular modeling investigation

pp. 756–764

Laura De Luca*, Sara De Grazia*, Stefania Ferro, Rosaria Gitto, Frauke Christ, Zeger Debyser and Alba Chimirri

A novel series of benzylindole derivatives, suggested by molecular modeling studies, was synthesized and evaluated for their anti-retroviral activity.

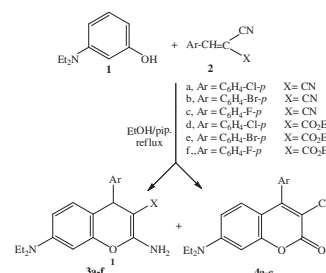


Synthesis of 4H-chromene, coumarin, 12H-chromeno[2,3-d]pyrimidine derivatives and some of their antimicrobial and cytotoxicity activities

pp. 765–772

Nermien M. Sabry, Hany M. Mohamed, Essam Shawky A.E.H. Khattab, Shymaa S. Motlaq and Ahmed M. El-Agrody*

Condensation of 3-*N,N*-diethylaminophenol (**1**) with various substituted α -cyanocinnamionitriles (**2a–c**) in ethanolic piperidine afforded **3a–c**, while condensation of 3-*N,N*-diethylaminophenol (**1**) with ethyl α -cyanocinnamate (**2d–f**) in ethanolic piperidine afforded in addition to ethyl 2-amino-4-(4-halophenyl)-7-(diethylamino)-4H-chromene-3-carboxylate (**3d–f**), the 4-(4-halophenyl)-7-(diethylamino)-coumarin-3-carbonitrile (**4a–c**).

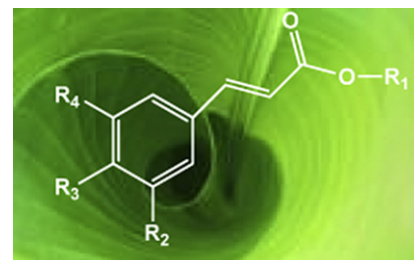


Synthesis and antioxidant activity of long chain alkyl hydroxycinnamates

pp. 773–777

Jose C.J.M.D.S. Menezes, Shrivallabh P. Kamat*, Jose A.S. Cavaleiro, Alexandra Gaspar, Jorge Garrido and Fernanda Borges*

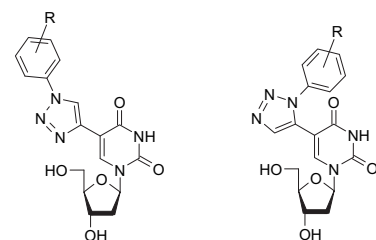
Long chain alkyl hydroxy cinnamates (8–21) were synthesized from the corresponding half esters of malonic acid (5–7) and benzaldehyde derivatives by Knoevenagel condensation. The antioxidant activity was highest for esters of caffeic acid followed by sinapic and ferulic esters. The parameters for drug-likeness of these hydroxycinnamyl esters were also evaluated.

**Synthesis of new C5-(1-substituted-1,2,3-triazol-4 or 5-yl)-2'-deoxyuridines and their antiviral evaluation**

pp. 778–786

Aurélien Montagu, Vincent Roy, Jan Balzarini, Robert Snoeck, Graciela Andrei and Luigi A. Agrofoglio*

Novel nucleosides were designed and synthesized by [3 + 2] cycloaddition, and showed moderate antiviral activities against several different DNA and RNA viruses. Some cytostatic activities against murine leukemia cells, human T-lymphocyte cells and cervix carcinoma cells were found.



Target compounds
(1,4-regioisomers)

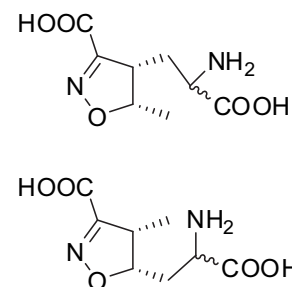
Target compounds
(1,5-regioisomers)

Synthesis of new isoxazoline-based acidic amino acids and investigation of their affinity and selectivity profile at ionotropic glutamate receptors

pp. 787–793

Andrea Pinto, Paola Conti*, Giovanni Grazioso, Lucia Tamborini, Ulf Madsen, Birgitte Nielsen and Carlo De Micheli

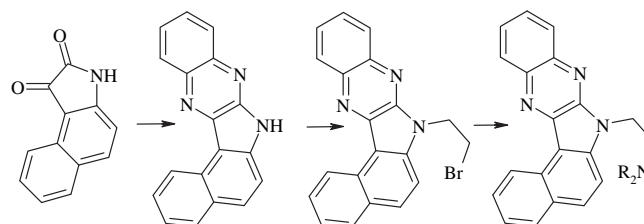
New isoxazoline-based acidic amino acids have been synthesized and tested at ionotropic glutamate receptors. Molecular modelling investigations have been carried out to rationalize the interaction with the NMDA receptors.

**SHORT COMMUNICATIONS****Synthesis and biological activity of 7H-benzo[4,5]indolo[2,3-b]-quinoxaline derivatives**

pp. 794–798

Marina O. Shibinskaya, Alexander S. Karpenko, Sergey A. Lyakhov*, Sergey A. Andronati, Nadezhda M. Zholobak, Nikolay Ya. Spivak, Natalia A. Samochina, Lev M. Shafran, Mykhail Ju. Zubritsky and Valerij F. Galat

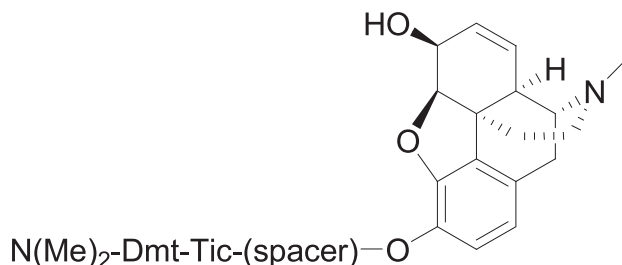
Synthesized 7-(2-aminoethyl)-7H-benzo[4,5]indolo[2,3-b]quinoxalines bind to DNA stronger ($\lg K_a = 6.23$ – 6.87) and exhibit significantly lower anti-viral and interferon inducing activities than 6-(2-aminoethyl)-6H-indolo[2,3-b]quinoxalines ($\lg K_a = 5.57$ – 5.89).



Opioid bifunctional ligands from morphine and the opioid pharmacophore Dmt-Tic

pp. 799–803

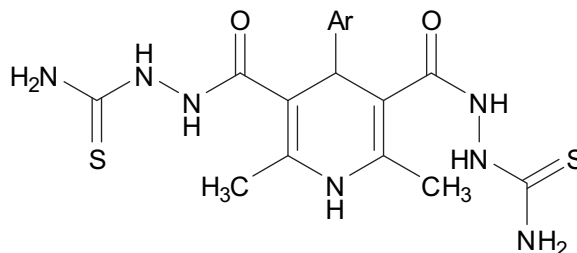
Gianfranco Balboni*, Severo Salvadori, Ewa D. Marczak, Brian I. Knapp, Jean M. Bidlack, Lawrence H. Lazarus, Xuemei Peng, Yu Gui Si and John L. Neumeyer**

**Synthesis and anticoagulant activity of a new series of 1,4-dihydropyridine derivatives**

pp. 804–810

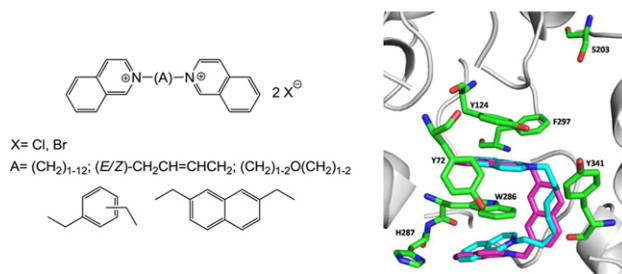
R. Surendra Kumar, A. Idhayadhulla, A. Jamal Abdul Nasser* and J. Selvin

Screening for anticoagulant activity of 1,4-dihydropyridine derivatives.

**Preparation and *in vitro* screening of symmetrical bis-isoquinolinium cholinesterase inhibitors bearing various connecting linkage – Implications for early Myasthenia gravis treatment**

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Kamil Musilek*, Marketa Komloova, Ondrej Holas, Martina Hrabanova, Miroslav Pohanka, Vlastimil Dohnal, Florian Nachon, Martin Dolezal and Kamil Kuca



COVER

An evaluation of hsp90 inhibitors chemical diversity has been performed. 2D-molecular descriptors, principal component analysis and fragment-based approach have been used to explore their chemical space. 45/5, P2000-2009 by Davide Audisio, Samir Messaoudi, Ismail Ijjaali, Elodie Dubus, François Petit, Jean-François Peyrat, Jean-Daniel Brion, Mouâd Alami © 2010 Published by Elsevier Masson SAS

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