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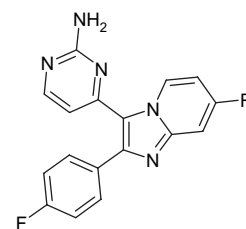
ORIGINAL ARTICLES

Synthesis and biological activity of imidazopyridine anticoccidial agents: Part II

pp. 1123–1151

Andrew Scribner*, Richard Dennis, Shuliang Lee, Gilles Ouvry, David Perrey, Michael Fisher, Matthew Wyvratt, Penny Leavitt, Paul Liberator, Anne Gurnett, Chris Brown, John Mathew, Donald Thompson, Dennis Schmatz and Tesfaye Biftu

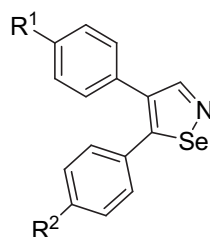
In this study, we present the synthesis and biological activity of imidazo[1,2-*a*]pyridine anticoccidial agents, whose antiparasitic activity against *Eimeria* is due to inhibition of a parasite specific cGMP-dependent protein kinase (PKG). From this series, several compounds showed subnanomolar in vitro activity and commercial levels of in vivo activity. However, the potential genotoxicity of these compounds precludes them from further development.



Investigations concerning the COX/5-LOX inhibiting and hydroxyl radical scavenging potencies of novel 4,5-diaryl isoselenazoles

pp. 1152–1159

Michael Scholz, Holger K. Ulbrich and Gerd Dannhardt*

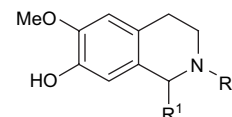


Syntheses of tetrahydroisoquinoline derivatives that inhibit NO production in activated BV-2 microglial cells

pp. 1160–1170

Jai Woong Seo, Ekaruth Srisook, Hyo Jin Son, Onyou Hwang**, Young-Nam Cha and Dae Yoon Chi*

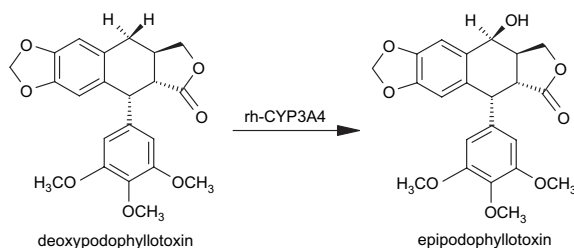
Seventeen tetrahydroisoquinoline derivatives have been synthesized and tested for their ability to inhibit NO synthesis.



Metabolic stereoselectivity of cytochrome P450 3A4 towards deoxypodophyllotoxin: *In silico* predictions and experimental validation

pp. 1171–1179

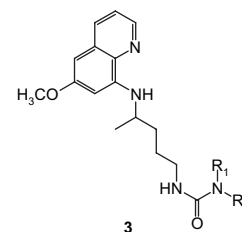
Mattijs K. Julsing, Nikolay P. Vasilev, Dina Schneidman-Duhovny, Remco Muntendam, Herman J. Woerdenbag, Wim J. Quax, Haim J. Wolfson, Iliana Ionkova and Oliver Kayser*


The novel primaquine derivatives of *N*-alkyl, cycloalkyl or aryl urea: Synthesis, cytostatic and antiviral activity evaluations

pp. 1180–1187

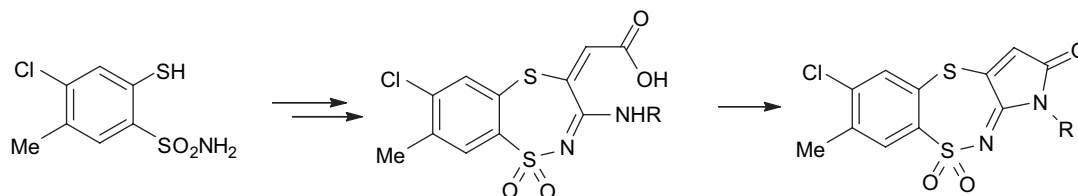
G. Džimbeg, B. Zorc*, M. Kralj, K. Ester, K. Pavelić, G. Andrei, R. Snoeck, J. Balzarini, E. De Clercq and M. Mintas**

Synthesis, cytostatic and antiviral activity evaluations of the urea derivatives of primaquine **3** are reported. Biological studies revealed that phenethyl and pyridine derivatives **3g** and **3h** possess selective inhibition against cytomegalovirus.


Synthesis, anti-HIV-1 integrase, and cytotoxic activities of 4-chloro-*N*-(4-oxypyrimidin-2-yl)-2-mercaptobenzenesulfonamide derivatives

pp. 1188–1198

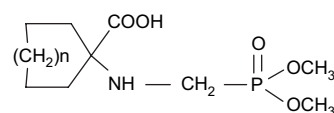
Zdzisław Brzozowski, Jarosław Sławiński, Franciszek Sączewski*, Tino Sanchez and Nouri Neamati


Novel *N*-(phosphonomethyl) glycine derivatives: Design, characterization and biological activity

pp. 1199–1205

Emilia D. Naydenova, Petar T. Todorov, Margarita N. Topashka-Ancheva, Georgi Ts. Momekov, Tsvetelina Z. Yordanova, Spiro M. Konstantinov and Kolio D. Troev*

A series of $C\alpha,\alpha$ -disubstituted cyclic derivatives of *N*-(phosphonomethyl) glycine have been synthesized and characterized. The results from this study unambiguously indicate that the new aminophosphonates exert antineoplastic potential, combined with low clastogenicity.

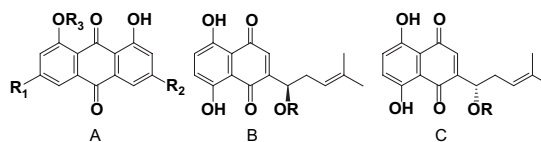


Comparison of the cytotoxic activities of naturally occurring hydroxyanthraquinones and hydroxynaphthoquinones

pp. 1206–1215

Xing-Ri Cui, Maiko Tsukada, Nao Suzuki, Takeshi Shimamura, Li Gao, Jyunichi Koyanagi, Fusao Komada and Setsuo Saito*

Hydroxyanthraquinones (A type compounds) were isolated from *Rheum palmatum* (Polygonaceae). B type hydroxynaphthoquinones were isolated from *Lithospermum erythrorhizon* Sieb. et Zucc. (Boraginaceae) and C type hydroxynaphthoquinones from *Macrotomia euchroma* (Royle) Pauls. (Boraginaceae). The cytotoxicities of these quinones on P-gp-underexpressing HCT 116 cells and P-gp-overexpressing Hep G2 cells were compared.

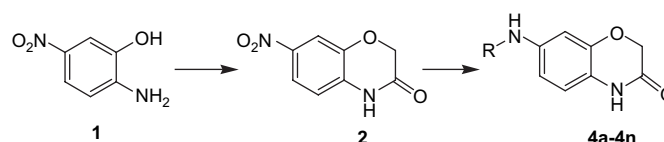


Synthesis of novel 7-benzylamino-2H-1,4-benzoxazin-3(4H)-ones as anticonvulsant agents

pp. 1216–1221

Zhong-Tai Piao, Li-Ping Guan, Li-Ming Zhao, Hu-Ri Piao and Zhe-Shan Quan*

A series of 7-benzylamino-2H-1,4-benzoxazin-3(4H)-ones was synthesized using 2-amino-5-nitrophenol as a starting material. Their anticonvulsant activities were evaluated by the maximal electroshock test (MES test) and their neurotoxicity was evaluated by the rotarod neurotoxicity test (Tox.).

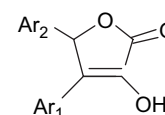


Synthesis and biological activities of a series of 4,5-diaryl-3-hydroxy-2(5H)-furanones

pp. 1222–1229

Fabrice Bailly*, Clémence Queffélec, Gladys Mbemba, Jean-François Mouscadet, Nicole Pommery, Jean Pommery, Jean-Pierre Hénichart and Philippe Cotelle

A series of thirteen 4,5-diaryl-3-hydroxy-2(5H)-furanones were synthesized. They were evaluated for their antioxidant potencies and inhibitory properties of 5-lipoxygenase, cyclooxygenases, HIV-1 integrase and PC3 cell proliferation. New hits were discovered either in the antiproliferation test or in the HIV anti-integrase test.

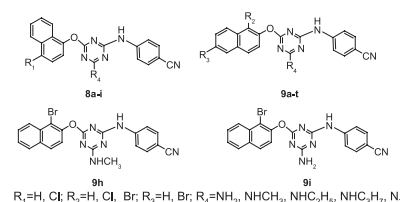


Non-nucleoside HIV-1 reverse transcriptase inhibitors. Part 11: Structural modulations of diaryltriazines with potent anti-HIV activity

pp. 1230–1236

Yuan-Zhen Xiong, Fen-Er Chen*, Jan Balzarini, Erik De Clercq and Christophe Pannecouque

A number of diaryltriazine derivatives (DATAs) **8a–i** and **9a–t** were prepared and evaluated for their anti-HIV activity. Among which **9h** and **9i** were the most potent compounds with noteworthy selectivity against HIV-1 RT.



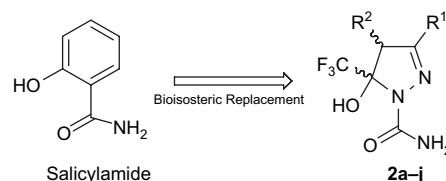
R₁=H, Cl R₂=H, Cl, Br R₃=H, Br R₄=NH₂, NHCH₃, NHC₂H₅, NHC₃H₇, N₃

Design and microwave-assisted synthesis of 5-trifluoromethyl-4,5-dihydro-1H-pyrazoles: Novel agents with analgesic and anti-inflammatory properties

pp. 1237–1247

Patricia D. Sauzem, Pablo Machado, Maribel A. Rubin, Gabriela da S. Sant'Anna, Henrique B. Faber, Alessandra H. de Souza, Carlos F. Mello, Paulo Beck, Robert A. Burrow, Helio G. Bonacorso, Nilo Zanatta and Marcos A.P. Martins*

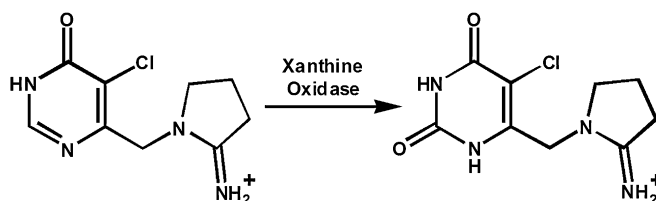
Exploring the hypothesis of bioisosteric replacement of benzene, present in the salicylamide, by a 5-trifluoromethyl-4,5-dihydro-1H-pyrazole scaffold, a series of 10 target compounds were synthesized by microwave induced techniques and screened with regard to their analgesic and anti-inflammatory properties.



Xanthine oxidase-activated prodrugs of thymidine phosphorylase inhibitors

pp. 1248–1260

Philip Reigan, Abdul Gbaj, Ian J. Stratford, Richard A. Bryce and Sally Freeman*

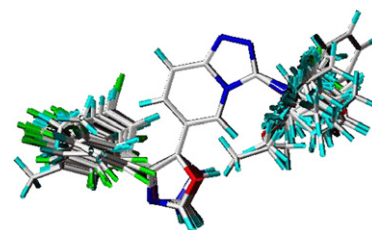


CoMFA and docking studies on triazolopyridine oxazole derivatives as p38 MAP kinase inhibitors

pp. 1261–1269

M. Ravi Shashi Nayana, Y. Nataraja Sekhar, N. Siva Kumari, S.K. Mahmood* and Muttineni Ravikumar

Three-dimensional quantitative structure–activity relationship (3D-QSAR) method, Comparative Molecular Field Analysis (CoMFA) and molecular docking studies using Glide were applied to a set of triazolopyridine oxazole derivatives as inhibitors of p38 MAP kinase.

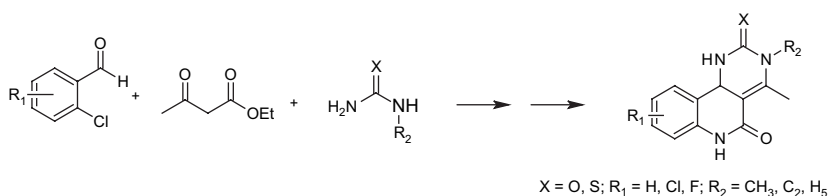


Synthesis and antioxidant activity evaluation of new hexahydropyrimido[5,4-c]quinoline-2,5-diones and 2-thioxohexahydropyrimido[5,4-c]quinoline-5-ones obtained by Biginelli reaction in two steps

pp. 1270–1275

Lhassane Ismaili, Arulraj Nadaradjane, Laurence Nicod, Catherine Guyon, Alain Xicluna, Jean-François Robert and Bernard Refouvet*

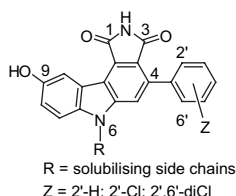
Several hexahydropyrimido[5,4-c] quinoline-2,5-diones and 2-thioxohexahydropyrimido[5,4-c] quinoline-5-ones were prepared and evaluated for their antioxidant properties.



Synthesis and structure–activity relationships of *N*-6 substituted analogues of 9-hydroxy-4-phenylpyrrolo[3,4-*c*]carbazole-1,3(2*H*,6*H*)-diones as inhibitors of Wee1 and Chk1 checkpoint kinases

pp. 1276–1296

Jeff B. Smaill*, Edward N. Baker, R. John Booth, Alexander J. Bridges, James M. Dickson, Ellen M. Dobrusin, Ivan Ivanovic, Alan J. Kraker, Ho H. Lee, Elizabeth A. Lunney, Daniel F. Ortwine, Brian D. Palmer, John Quin III, Christopher J. Squire, Andrew M. Thompson and William A. Denny

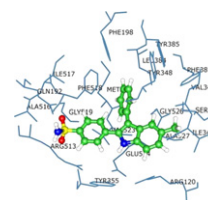


Exploration of physicochemical properties and molecular modelling studies of 2-sulfonyl-phenyl-3-phenyl-indole analogs as cyclooxygenase-2 inhibitors

pp. 1297–1303

Arun Kumar Gupta, Revathi A. Gupta, Love Kumar Soni and S.G. Kaskhedikar*

In the present work, modelling study has been performed to explore the physicochemical requirements of 2-sulfonyl-phenyl-3-phenyl-indole analogs as COX-2 enzyme inhibitors. QSAR analysis describes significance of descriptors like atomic van der Waals volume and atomic masses for COX-2 inhibition. Docking study suggested that phenyl sulfonamide moiety positioned in secondary pocket of enzyme which consists of amino acid residues Phe₅₁₈, Gln₁₉₂, Arg₅₁₃, Leu₃₅₂, Ser₃₅₃ and Val₅₂₃ is responsible for the selectivity. The unsubstituted phenyl ring positions in a hydrophobic cavity are lined by Tyr₃₈₅, Trp₃₈₇, Tyr₃₄₈, Leu₃₈₄ and Met₅₂₂. Interestingly, the indole C-5 CH₃-substituent is located in a hydrophobic region formed by Ile₃₄₅, Val₃₄₉, Ala₅₂₇, Leu₅₃₁ and Leu₅₃₄. The hydrophobic interactions of methyl group might be crucial for the potency of 2-sulfonyl-phenyl-3-phenyl-indole analogs. Distinguished descriptor might be helpful in identification of more potent analogs from the virtual library.

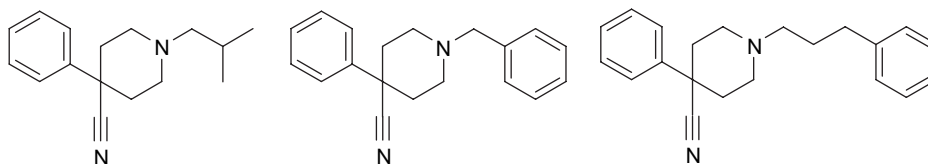


SHORT COMMUNICATIONS

Nitrile analogs of meperidine as high affinity and selective sigma-1 receptor ligands

pp. 1304–1308

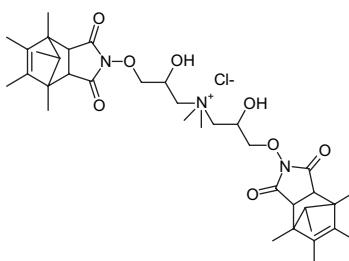
Susan L. Mercer, Jamaluddin Shaikh, John R. Traynor, Rae R. Matsumoto and Andrew Coop*



Synthesis and antibacterial activity of bis-[2-hydroxy-3-(1,7,8,9,10-pentamethyl-3,5-dioxo-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-4-yloxy)-propyl]-dimethyl-ammonium chloride

pp. 1309–1314

Marta Struga*, Jerzy Kossakowski, Joanna Stefańska, Andrzej Zimniak and Anna E. Koziol

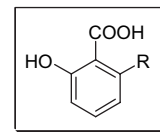


Design and evaluation of anacardic acid derivatives as anticavity agents

pp. 1315–1320

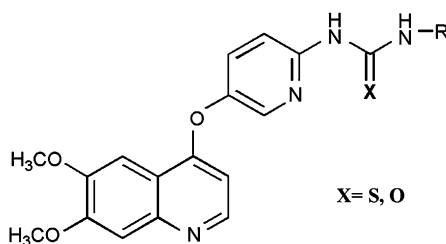
Ivan R. Green*, Felismino E. Tocoli, Sang Hwa Lee,
Ken-ichi Nihei and Isao Kubo**

On the basis of antibacterial anacardic acids, 6-pentadecenylsalicylic acids, isolated from the cashew apple, *Anacardium occidentale* L. (Anacardiaceae), a series of 6-alk(en)ylsalicylic acids were synthesized and tested for their antibacterial activity against *Streptococcus mutans* ATCC 25175. Among them, 6-(4',8'-dimethylnonyl)salicylic acid was found to exhibit the most potent antibacterial activity against this cariogenic bacterium with the minimum inhibition concentration (MIC) of 0.78 µg/ml.

**Structure activity relationships of quinoline-containing c-Met inhibitors**

pp. 1321–1329

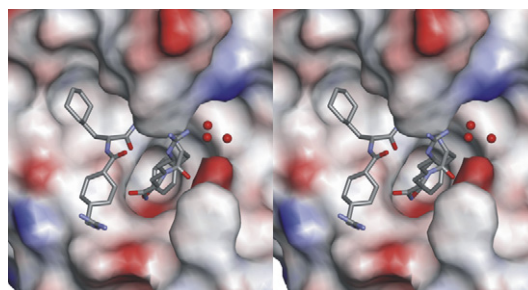
Pei-Pei Kung*, Lee Funk, Jerry Meng, Gordon Alton, Ellen Padrique and Barbara Mroczkowski

**Structure of a novel thrombin inhibitor with an uncharged D-amino acid as P1 residue**

pp. 1330–1335

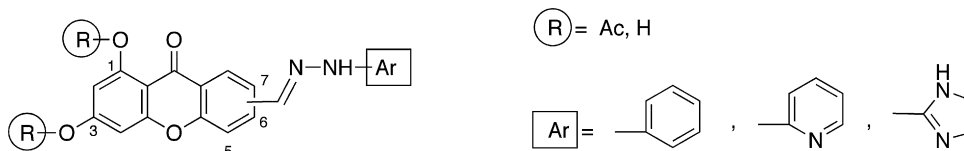
Rainer Friedrich, Daniel Riester, Peter Göttig, Marcel Thürk, Andreas Schwienhorst and Wolfram Bode*

The first crystal structure of a thrombin–inhibitor (discovered by a computer-assisted multiparameter optimization process, CADDIS®) complex, where an uncharged inhibitor residue makes hydrogen bonds within the thrombin S1 pocket.

**PRELIMINARY COMMUNICATIONS****Synthesis and antiproliferative activity of aryl- and heteroaryl-hydrazones derived from xanthone carbaldehydes**

pp. 1336–1343

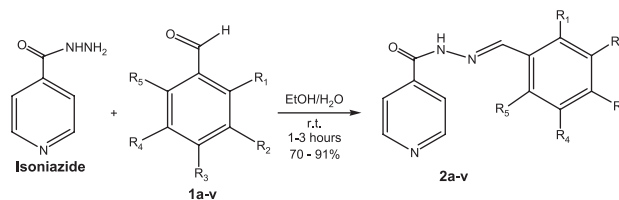
Martine Varache-Lembège, Stéphane Moreau, Stéphane Larrouture, Danièle Montaudon, Jacques Robert and Alain Nuhric*



Synthesis and anti-mycobacterial activity of (*E*)-*N'*-(monosubstituted-benzylidene)isonicotinohydrazide pp. 1344–1347 derivatives

Maria Cristina da Silva Lourenço, Marcelle de Lima Ferreira, Marcus Vinícius Nora de Souza*,
Mônica Amado Peralta, Thatyana Rocha Alves Vasconcelos and Maria das Graças M.O. Henriques

A series of 22 *N'*-[(*E*)-(monosubstituted-phenyl)methylidene]isonicotinohydrazide derivatives (**2a–v**) have been synthesized and evaluated for their in vitro antibacterial activity against *Mycobacterium tuberculosis* H₃₇Rv using the Alamar Blue susceptibility test.



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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