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Bioorganic & Medicinal Chemistry Volume 18, Issue 4, 2010

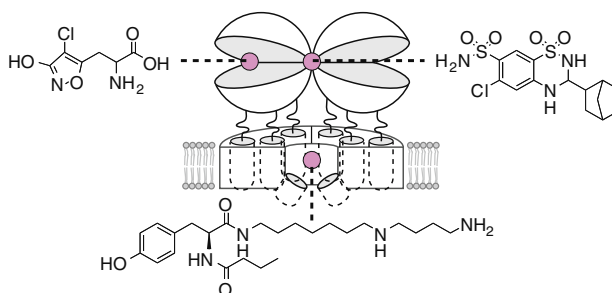
Contents

PERSPECTIVE

Developing a complete pharmacology for AMPA receptors: A perspective on subtype-selective ligands

pp 1381–1387

James J. Fleming, Pamela M. England*



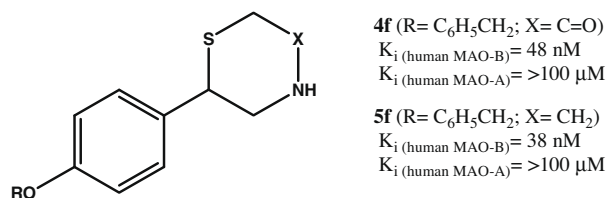
Several distinct ligand-binding sites exist on AMPA receptors and numerous classes of molecules have been identified that bind to them. Here we provide a perspective on ligands that are selective among the various AMPA receptor subtypes.

ARTICLES

2-Arylthiomorpholine derivatives as potent and selective monoamine oxidase B inhibitors

pp 1388–1395

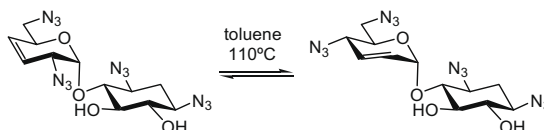
Susan Lühr, Marcelo Vilches-Herrera, Angélica Fierro, Rona R. Ramsay, Dale E. Edmondson, Miguel Reyes-Parada, Bruce K. Cassels, Patricio Iturriaga-Vásquez*



Synthesis of novel aminoglycosides via allylic azide rearrangement for investigating the significance of 2'-amino group

pp 1396–1405

Jianjun Zhang, Anthony Litke, Katherine Keller, Ravi Rai, Cheng-Wei Tom Chang*



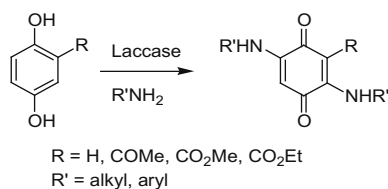
Using allylic azide rearrangement, a convenient method has been developed for the synthesis of 2',3'-dideoxyaminoglycosides that are, otherwise, difficult to be prepared. The antibacterial activity of these novel aminoglycosides also confirms the indispensable role of 2'-NH₂ group for both neomycin and kanamycin classes of aminoglycosides. A novel structural motif containing the hexylaminocarbonyl groups at O-5 and/or O-6 of 2',3'-dideoxyneamine could lead to the production of new aminoglycosides against resistant bacteria.



Diamination by N-coupling using a commercial laccase

pp 1406–1414

Kevin W. Wellington*, Paul Steenkamp, Dean Brady

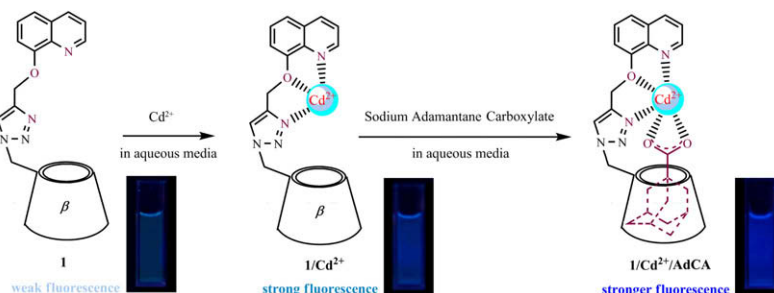


Nuclear diamination of *p*-hydrobenzoquinones with aromatic and aliphatic primary amines was catalysed by a commercial laccase, Denilite® II Base, from Novozymes. The amine and the *p*-hydrobenzoquinone was reacted under mild conditions (at room temperature and at 35 °C) in a reaction vessel open to air in the presence of laccase and a co-solvent to afford, exclusively, the diaminated *p*-benzoquinone. These compounds may have potential antiallergic, antibiotic, anticancer, antifungal, antiviral and/or 5-lipoxygenase inhibiting activity.

Quinolinotriazole- β -cyclodextrin and its adamantanecarboxylic acid complex as efficient water-soluble fluorescent Cd^{2+} sensors

pp 1415–1420

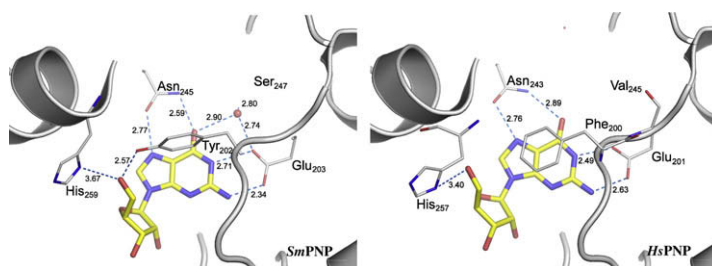
Ying-Ming Zhang, Yong Chen, Zhi-Qiang Li, Nan Li, Yu Liu*



Structural basis for selective inhibition of purine nucleoside phosphorylase from *Schistosoma mansoni*: Kinetic and structural studies

pp 1421–1427

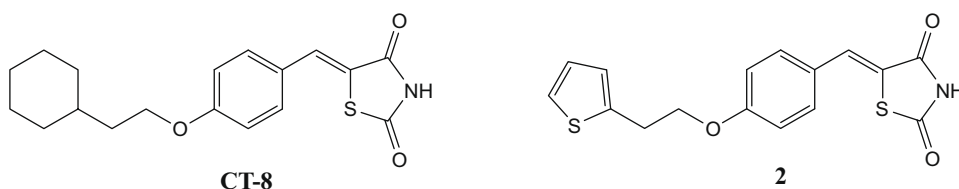
Marcelo S. Castilho*, Matheus P. Postigo, Humberto M. Pereira, Glaucius Oliva, Adriano D. Andricopulo*



Synthesis and SAR of thiazolidinedione derivatives as 15-PGDH inhibitors

pp 1428–1433

Ying Wu, Hsin-Hsiung Tai, Hoon Cho*



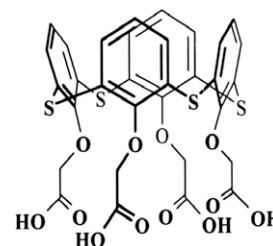
Replacement of the cyclohexylethyl group of **CT-8** with the hetero five-member ring increased the inhibitory potency. Compound **2** is a most potent 15-PGDH inhibitor that was effective in the nanomolar range.

Carboxylated calixarenes bind strongly to CD69 and protect CD69⁺ killer cells from suicidal cell death induced by tumor cell surface ligands

pp 1434–1440

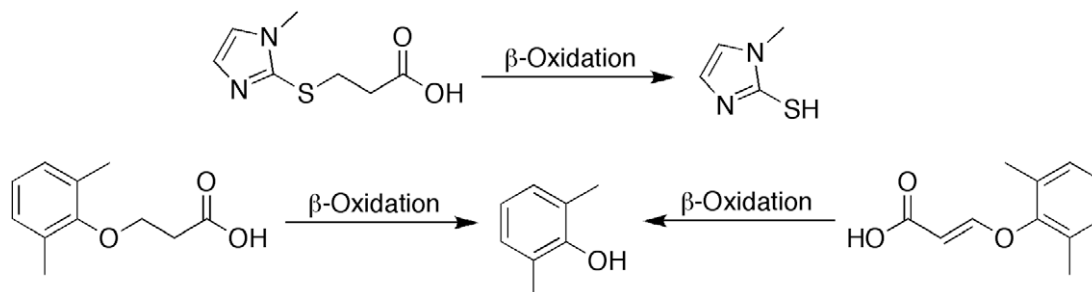
Karel Bezouška*, Renata Šnajdrová, Karel Křenek, Markéta Vančurová, Alan Kádek, David Adámek, Pavel Lhoták, Daniel Kavan, Kateřina Hofbauerová, Petr Man, Pavla Bojarová, Vladimír Křen

Carboxylated thiacalix[4]arenes proved to be highly specific antagonists for the leukocyte membrane antigen and important triggering receptor CD69. These compounds efficiently protect CD69^{high} lymphocytes from apoptosis induced by multivalent tumor surface ligands such as SiaTn, or by cross-linking using specific monoclonal antibodies. We are currently exploring such protective effects in animal tumor model under conditions in vivo.

**Mitochondrial biotransformation of ω-(phenoxy)alkanoic acids, 3-(phenoxy)acrylic acids, and ω-(1-methyl-1H-imidazol-2-ylthio)alkanoic acids: A prodrug strategy for targeting cytoprotective antioxidants to mitochondria**

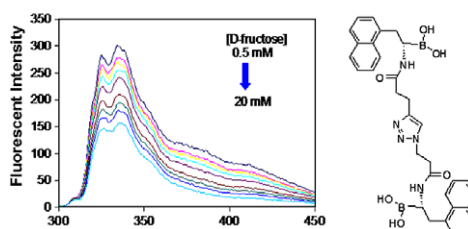
pp 1441–1448

Kurt S. Roser, Paul S. Brookes, Andrew P. Wojtovich, Leif P. Olson, Jalil Shojaie, Richard L. Parton, M. W. Anders*

**Synthesis and carbohydrate binding studies of fluorescent α-amidoboronic acids and the corresponding bisboronic acids**

pp 1449–1455

Shan Jin, Chunyuan Zhu, Yunfeng Cheng, Minyong Li, Binghe Wang*

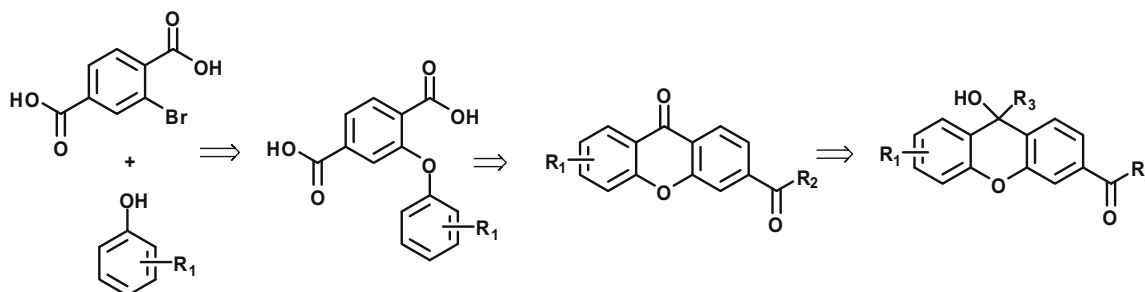


We describe a study of water soluble fluorescent bis-α-amidoboronic acids with significantly enhanced binding for oligosaccharides as compared to their monoboronic acid counterparts.

**Synthesis and cancer cell cytotoxicity of substituted xanthenes**

pp 1456–1463

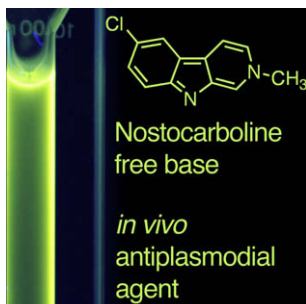
Rajan Giri, John R. Goodell, Chenguo Xing, Adam Benoit, Harneet Kaur, Hiroshi Hiasa, David M. Ferguson*



Antimalarial and antitubercular nostocarboline and eudistomin derivatives: Synthesis, in vitro and in vivo biological evaluation

pp 1464–1476

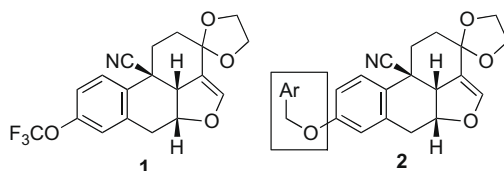
Simone Bonazzi, Damien Barbaras, Luc Patiny, Rosario Scopelliti, Patricia Schneider, Stewart T. Cole, Marcel Kaiser, Reto Brun, Karl Gademann*



Synthesis and anti-influenza virus activity of dihydrofuran-fused perhydrophenanthrenes with a benzyloxy-type side-chain

pp 1477–1481

Yuji Matsuya*, Nozomi Suzuki, Shin-ya Kobayashi, Tatsuro Miyahara, Hiroshi Ochiai, Hideo Nemoto

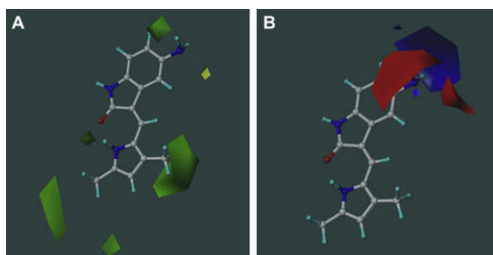


Novel dihydrofuran-fused tetracyclic compounds (2) with a benzyl-type ether side-chain were found to exhibit potent anti-influenza virus activity comparable to the previously reported derivative 1.

Synthesis, structure–activity relationship and crystallographic studies of 3-substituted indolin-2-one RET inhibitors

pp 1482–1496

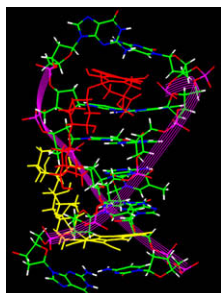
Luca Mologni*, Roberta Rostagno, Stefania Brussolo, Phillip P. Knowles, Svend Kjaer, Judith Murray-Rust, Enrico Rosso, Alfonso Zambon, Leonardo Scapozza, Neil Q. McDonald, Vittorio Lucchini, Carlo Gambacorti-Passerini



Interaction between double helix DNA fragments and the new antitumor agent sabarubicin, Men10755

pp 1497–1506

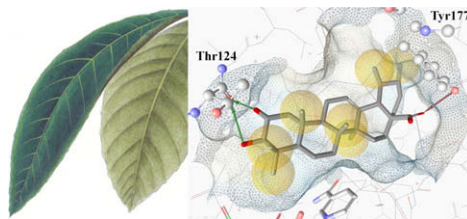
Stefania Mazzini*, Leonardo Scaglioni, Fabio Animati, Rosanna Mondelli*



11 β -Hydroxysteroid dehydrogenase 1 inhibiting constituents from *Eriobotrya japonica* revealed by bioactivity-guided isolation and computational approaches

pp 1507–1515

Judith M. Rollinger*, Denise V. Kratschmar, Daniela Schuster, Petra H. Pfisterer, Christel Gummy, Evelyne M. Aubry, Sarah Brandstötter, Hermann Stuppner, Gerhard Wolber, Alex Odermatt*

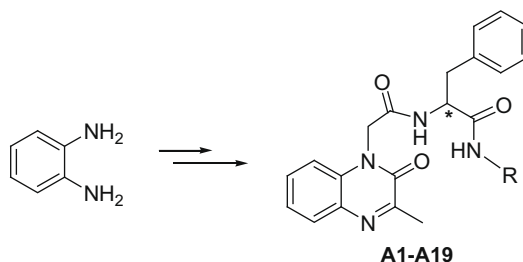


Predicted binding mode of the *Eriobotrya japonica* constituent corosolic acid in the binding site of 11 β -hydroxysteroid dehydrogenase 1.

Novel matrix metalloproteinase inhibitors derived from quinoxalinone scaffold (Part I)

pp 1516–1525

Yonggang Li, Jian Zhang, Wenfang Xu, Huawei Zhu, Xun Li*



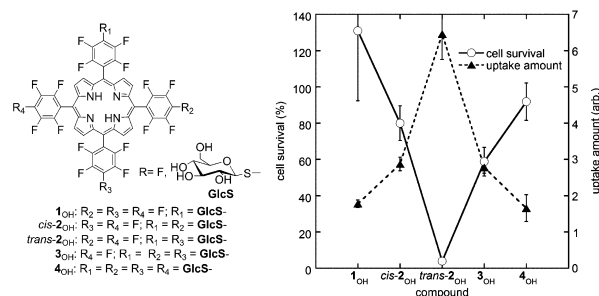
A series of novel quinoxalinone peptidomimetic derivatives (**A1–A19**) were synthesized and evaluated for their in vitro enzymatic inhibitory activities against aminopeptidase N (APN/CD13) and MMP-2.

Synthesis, photophysical properties and photocytotoxicity of mono-, di-, tri- and tetra-glucosylated fluorophenylporphyrins

pp 1526–1535

Shiho Hirohara*, Masataka Nishida, Kohei Sharyo, Makoto Obata, Tsuyoshi Ando, Masao Tanihara

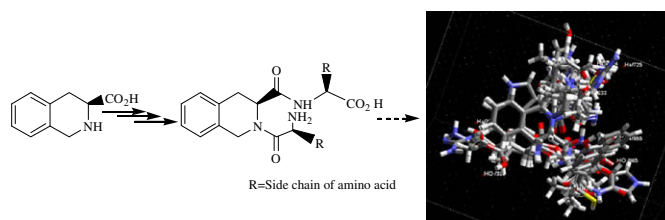
We synthesized five possible perfluorophenylporphyrins having 5-glucopyranosyl groups. The effect of the glycosylation patterns on the photocytotoxicity was discussed on the basis of photophysical properties as well as cellular uptake in HeLa cells.



2,3-Diamino acid modifying 3S-tetrahydroisoquinoline-3-carboxylic acids: Leading to a class of novel agents with highly unfolded conformation, selective in vitro anti-platelet aggregation and potent in vivo anti-thrombotic activity

pp 1536–1554

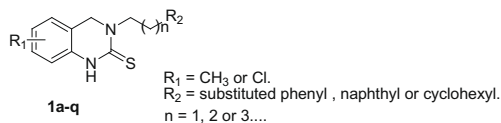
Xiaoyi Zhang, Wei Wang, Shenling Cheng, Ming Zhao*, Meiqing Zheng, Heng Wei Chang*, Jianhui Wu, Shiqi Peng*



Evaluation of 3,4-dihydroquinazoline-2(1H)-thiones as inhibitors of α -MSH-induced melanin production in melanoma B16 cells

pp 1555–1562

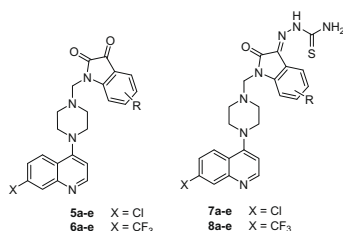
P. Thanigaimalai, Ki-Cheul Lee, Seong-Cheol Bang, Jee-Hyun Lee, Cheong-Yong Yun, Eunmiri Roh, Bang-Yeon Hwang, Youngsoo Kim, Sang-Hun Jung*



Design and synthesis of anti-breast cancer agents from 4-piperazinylquinoline: A hybrid pharmacophore approach

pp 1563–1572

V. Raja Solomon*, Changkun Hu, Hoyun Lee*

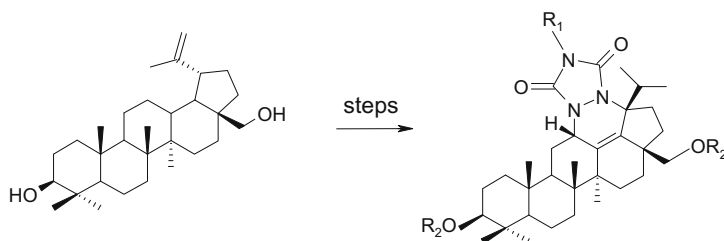


In the present study, synthesis of a new series of 4-piperazinylquinoline derivatives and evaluation of their cell killing activity on cancer and non-breast cancer cells are described.

Synthesis and anti-leishmanial activity of heterocyclic betulin derivatives

pp 1573–1582

Sami Alakurtti, Tuomo Heiska, Alexandros Kiriazis, Nina Sacerdoti-Sierra, Charles L. Jaffe, Jari Yli-Kauhahuoma*



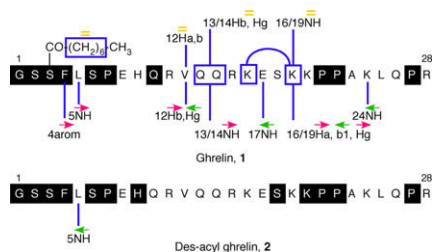
Birch bark extractive betulin was used as a starting material to synthesize new heterocyclic betulin derivatives that were screened against *Leishmania donovani* responsible for the neglected parasitic disease, visceral leishmaniasis.



Interaction between ghrelin and the ghrelin receptor (GHS-R1a), a NMR study using living cells

pp 1583–1590

Manuel Martín-Pastor, Antonia De Capua, Carlos J. P. Álvarez, M. Dolores Díaz-Hernández, Jesús Jiménez-Barbero, Felipe F. Casanueva, Yolanda Pazos*



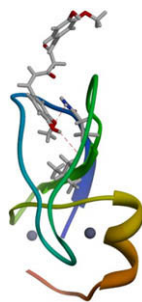
The evaluation of ^1H NMR spectra of GHS-R1a stably transfected cell lines and wild type cells has allowed the analysis of the behaviour of ghrelin (1) and des-acyl ghrelin (2) with the GHS-R1a receptor, under quasi-physiological conditions.



Binding of curcumin and its long chain derivatives to the activator binding domain of novel protein kinase C

pp 1591–1598

Anjoy Majhi, Ghazi M. Rahman, Shyam Panchal, Joydip Das*

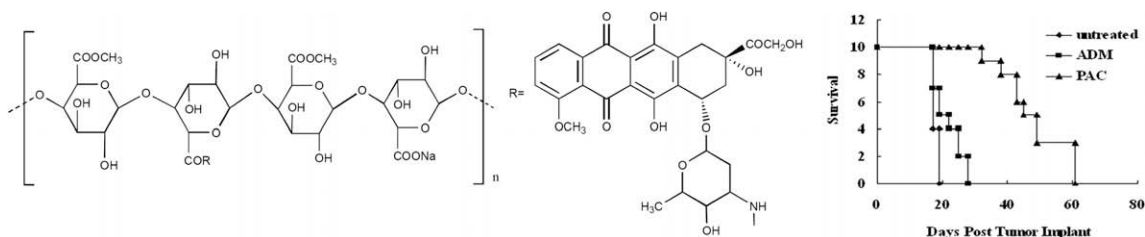


Binding of curcumin and PKC C1B.

Synthesis, characterization, and in vitro and in vivo evaluation of a novel pectin–adriamycin conjugate

pp 1599–1609

Xiao-Hai Tang*, Ping Xie, Yi Ding, Liang-Yin Chu, Jing-Ping Hou, Jin-Liang Yang, Xin Song, Yong-Mei Xie

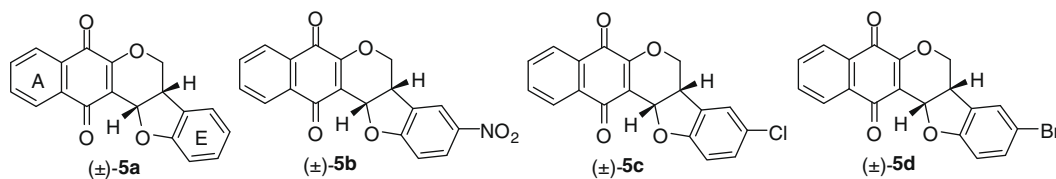


A novel pectin–adriamycin conjugate showed a good therapeutic effect on lung metastases of melanoma in C57BL/6 mice and resulted in a remarkably prolonged survival, which was up to twice as long as that of the mice treated with free ADM.

New pterocarpanquinones: Synthesis, antineoplastic activity on cultured human malignant cell lines and TNF- α modulation in human PBMC cells

pp 1610–1616

Chaquip D. Netto, Alcides J. M. da Silva, Eduardo J. S. Salustiano, Thiago S. Bacelar, Ingrid G. Riça, Moises C. M. Cavalcante, Vivian M. Rumjanek, Paulo R. R. Costa*

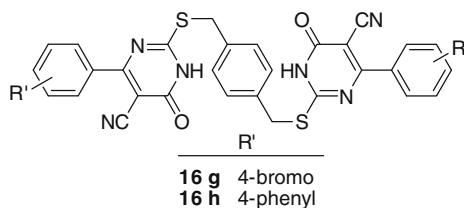


A new pterocarpanquinone (**5a**) was synthesized through a palladium catalyzed oxyarylation reaction and was transformed, through electrophilic substitution reaction, into derivatives **5b–d**. These compounds showed to be active against human leukemic cell lines and human lung cancer cell lines.

The first low μ M SecA inhibitors

pp 1617–1625

Weixuan Chen, Ying-ju Huang, Sushma Reddy Gundala, Hsiuchin Yang, Minyong Li, Phang C. Tai*, Binghe Wang*

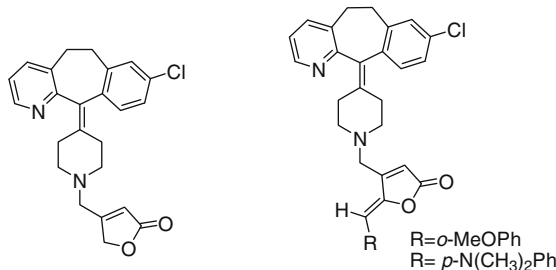


16 g 4-bromo
16 h 4-phenyl

Stereoselective synthesis of desloratadine derivatives as antagonist of histamine

pp 1626–1632

Gai-Zhi Liu, Hai-Wei Xu, Guang-Wei Chen, Peng Wang, Ya-Na Wang, Hong-Min Liu*, De-Quan Yu



A novel family of desloratadine derivatives as antagonist of histamine were prepared. Above three optimum structures display potent activity inhibiting histamine-induced effects.

Potent inhibitor scaffold against *Trypanosoma cruzi* trans-sialidase

pp 1633–1640

Shingo Arioka, Masahiro Sakagami, Rie Uematsu, Hiroto Yamaguchi, Hiroko Togame, Hiroshi Takemoto, Hiroshi Hinou, Shin-ichiro Nishimura*

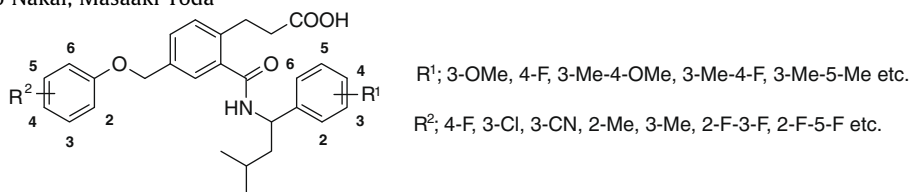
Novel inhibitors of *Trypanosoma cruzi* trans-sialidase, discovered from natural product library, are reported.

Structure	IC ₅₀ (μM)	
	<i>T. cruzi</i> trans-sialidase	Human Neu 2
	0.58	> 100
	78	570

**3-(2-Aminocarbonylphenyl)propanoic acid analogs as potent and selective EP3 receptor antagonists. Part 2: Optimization of the side chains to improve in vitro and in vivo potencies**

pp 1641–1658

Masaki Asada*, Maki Iwahashi, Tetsuo Obitsu, Atsushi Kinoshita, Yoshihiko Nakai, Takahiro Onoda, Toshihiko Nagase, Motoyuki Tanaka, Yoshiyuki Yamaura, Hiroya Takizawa, Ken Yoshikawa, Kazutoyo Sato, Masami Narita, Shuichi Ohuchida, Hisao Nakai, Masaaki Toda



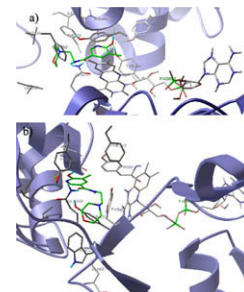
We identified a series of 3-[2-[(3-methyl-1-phenylbutyl)amino]carbonyl]-4-(phenoxy)methyl]phenyl]propanoic acid analogs as potent and selective EP3 receptor antagonists. Introduction of substituents into the two benzene nucleus resulted in the increased in vitro activities. Several compounds exhibited potent inhibitory effect against the PGE₂-induced uterine contraction in pregnant rats.

Design of novel nicotinamides as potent and selective monoamine oxidase a inhibitors

pp 1659–1664

Lei Shi, Ying Yang, Zi-Lin Li, Zhen-Wei Zhu, Chang-Hong Liu*, Hai-Liang Zhu*

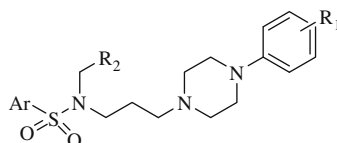
A series of nicotinamide derivatives (1–26) have been designed, synthesized and evaluated in vitro for their monoamine oxidase inhibitory activity and selectivity. Most of these synthesized compounds proved to be potent, and selective inhibitors of MAO-A rather than of MAO-B. 5-Chloro-6-hydroxy-N-(2-morpholinoethyl)nicotinamide (**13**) displayed the highest MAO-A inhibitory potency (IC₅₀ = 0.045 μM) and a good selectivity. 2-Bromo-N-(2-morpholinoethyl)nicotinamide (**3**) was the most potent MAO-B inhibitor with the IC₅₀ value of 0.32 μM, but it was not selective. Molecular dockings of compound **13** were performed in order to give structural insights regarding the MAO-A selectivity.



Synthesis and biological evaluation of (phenylpiperazinyl-propyl)arylsulfonamides as selective 5-HT_{2A} receptor antagonists

pp 1665–1675

Euna Yoo, Juhee Yoon, Ae Nim Pae, Hyewhon Rhim, Woo-Kyu Park, Jae Yang Kong, Hea-Young Park Choo*

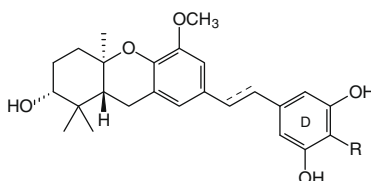


11-24

Structural analogues of schweinfurthin F: Probing the steric, electronic, and hydrophobic properties of the D-ring substructure

pp 1676–1683

Natalie C. Ulrich, John G. Kodet, Nolan R. Mente, Craig H. Kuder, John A. Beutler, Raymond J. Hohl, David F. Wiemer*

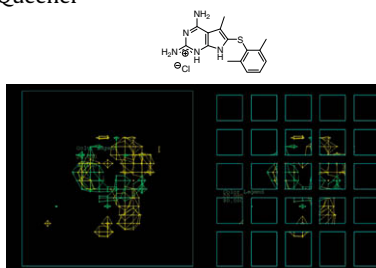


Synthesis of a set of schweinfurthin analogues varied in the D-ring alkyl substituent and stilbene moiety has been accomplished, and the activity of these compounds has been measured in a two-cell line screen. The most potent analogue and a much less active compound also were tested in the NCI 60-cell line assay, and showed comparable potency in that more extensive screen.

**CoMFA analysis of tgDHFR and rIDHFR based on antifolates with 6–5 fused ring system using the all-orientation search (AOS) routine and a modified cross-validated r²-guided region selection (q²-GRS) routine and its initial application**

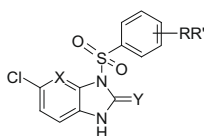
pp 1684–1701

Aleem Gangjee*, Xin Lin, Lisa R. Biondo, Sherry F. Queener

**Novel 1,3-dihydro-benzimidazol-2-ones and their analogues as potent non-nucleoside HIV-1 reverse transcriptase inhibitors**

pp 1702–1710

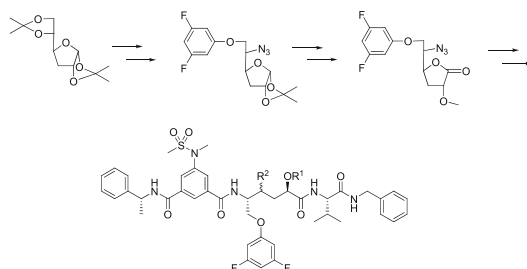
Anna-Maria Monforte*, Patrizia Logoteta, Laura De Luca, Nunzio Iraci, Stefania Ferro, Giovanni Maga, Erik De Clercq, Christophe Pannecouque, Alba Chimirri



Discovery of potent BACE-1 inhibitors containing a new hydroxyethylene (HE) Scaffold: Exploration of P1' alkoxy residues and an aminoethylene (AE) central core

pp 1711–1723

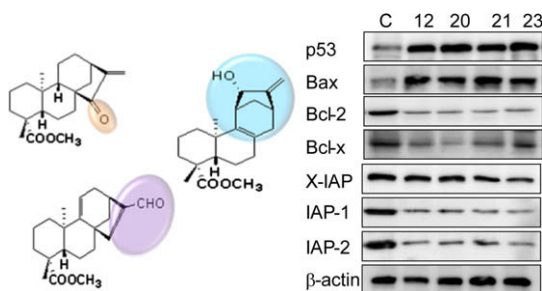
Catarina Björklund, Hans Adolfsson, Katarina Jansson, Jimmy Lindberg, Lotta Vrang, Anders Hallberg, Åsa Rosenquist, Bertil Samuelsson*



Synthesis and induction of apoptosis signaling pathway of *ent*-kaurane derivatives

pp 1724–1735

Idaira Hueso-Falcón, Natalia Girón, Pilar Velasco, Juan M. Amaro-Luis, Angel G. Ravelo, Beatriz de las Heras*, Sonsoles Hortelano*, Ana Estevez-Braun*



OTHER CONTENTS

Bioorganic & Medicinal Chemistry Reviews and Perspectives

pp 1736–1738

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Cyanobacteria produce natural products that are inhibiting the growth of competing phototrophs. These algicidal allelochemicals can display powerful antiplasmodial activity, as they might be targeting the apicoplast, an organelle of algal origin in Plasmodium. Nostocarboline is an unusual chlorinated freshwater metabolite and is active in an in vivo *P. berghei* mouse model. Screening allelochemicals from cyanobacteria might thus constitute an ecological rationale for the identification of novel antimalarial agents. [Bonazzi, S.; Barbaras, D.; Patiny, L.; Scopelliti, R.; Schneider, P.; Cole, S. T.; Kaiser, M.; Brun, R.; Gademann, K. *Bioorg. Med. Chem.* **2010**, *18*, 1464.]

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