



Bioorganic & Medicinal Chemistry Vol. 17, No. 19, 2009

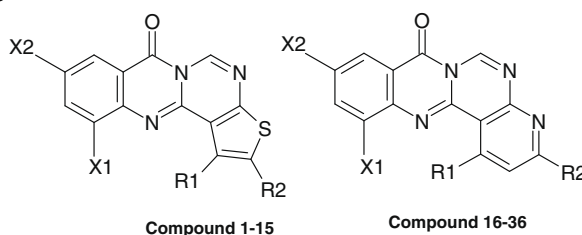
Contents

ARTICLES

A new therapeutic approach in Parkinson's disease: Some novel quinazoline derivatives as dual selective phosphodiesterase 1 inhibitors and anti-inflammatory agents

pp 6796–6802

Sachin S. Laddha^{*}, Satyendra P. Bhatnagar

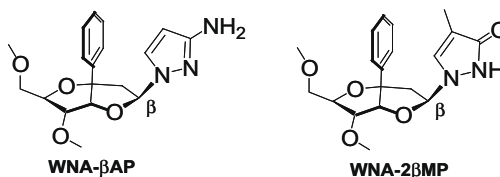


X1 and X2 = H, Br; R1 and R2 = alkyl and aryl

Recognition of CG interrupting site by W-shaped nucleoside analogs (WNA) having the pyrazole ring in an anti-parallel triplex DNA

pp 6803–6810

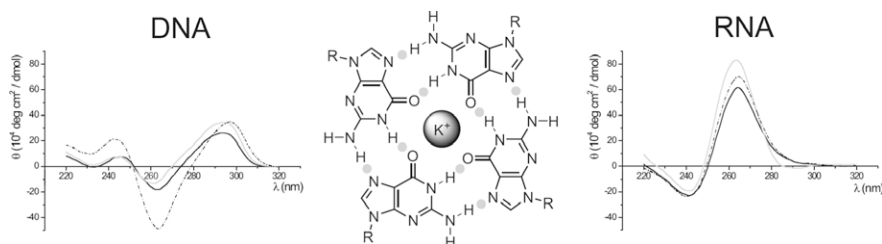
Yosuke Taniguchi, Yuko Uchida, Tomoko Takaki, Eriko Aoki, Shigeki Sasaki^{*}



A comparison of DNA and RNA quadruplex structures and stabilities

pp 6811–6815

Astrid Joachimi, Armin Benz, Jörg S. Hartig^{*}

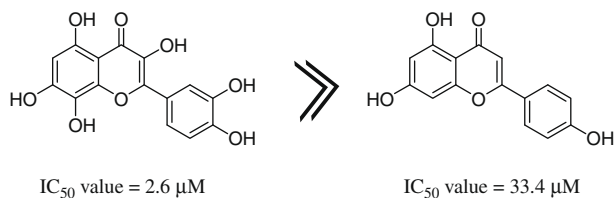


RNA quadruplexes are known to form four-stranded nucleic acid structures as well but few studies have investigated their properties. Here we compare the conformations and stabilities of quadruplex-forming DNA and RNA sequences.

Neuraminidase inhibitory activities of flavonols isolated from *Rhodiola rosea* roots and their in vitro anti-influenza viral activities

pp 6816–6823

Hyung Jae Jeong, Young Bae Ryu, Su-Jin Park, Jang Hoon Kim, Hyung-Jun Kwon, Jin Hyo Kim, Ki Hun Park, Mun-Chual Rho^{*}, Woo Song Lee^{*}



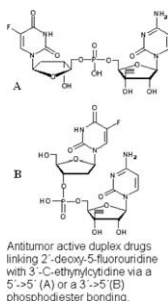
Neuraminidase activities depended on the position and number of hydroxy groups on the flavones backbone.



Synthesis and in vitro activities of new anticancer duplex drugs linking 2'-deoxy-5-fluorouridine (5-FdU) with 3'-C-ethynylcytidine (ECyd) via a phosphodiester bonding

pp 6824–6831

Herbert Schott^{*}, Sarah Schott, Reto A. Schwendener

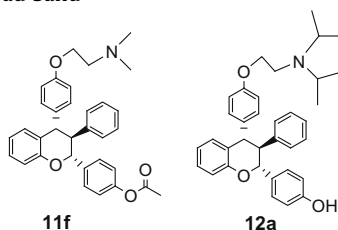


Antitumor active duplex drugs linking 2'-deoxy-5-fluorouridine with 3'-C-ethynylcytidine via a 5'→5' (A) or a 3'→5' (B) phosphodiester bonding.

Synthesis and biological evaluation of 2,3,4-triarylbenzopyran derivatives as SERM and therapeutic agent for breast cancer

pp 6832–6840

Shailesh Kumar, Shreekant Deshpande, Vishal Chandra, Shakti Kitchlu, Anila Dwivedi, Vadithe Lakshma Nayak, Rituraj Konwar, Yenamandra S. Prabhakar, Devi Prasad Sahu^{*}

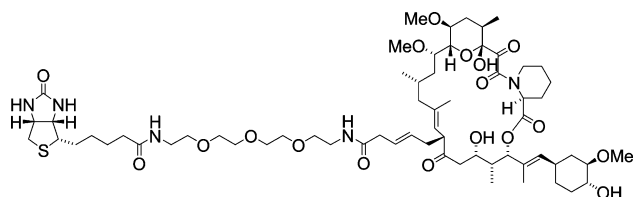


A library of novel 2,3,4-triarylbenzopyrans was synthesized and their SERM and anti-proliferative activities were evaluated. Compound **12a** showed the lowest IC₅₀ at 7 μM against MCF-7 and **11f** showed the lowest IC₅₀ value of 5.6 μM against MDA-MB-231 cell lines.

Rapid isolation of novel FK506 binding proteins from multiple organisms using gDNA and cDNA T7 phage display

pp 6841–6850

Andrew M. Piggott, Alison M. Krieger, Robert D. Willows, Peter Karuso^{*}

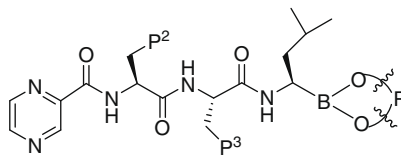


We describe the construction of the first prokaryotic T7 phage display libraries from randomly digested *Pseudomonas stutzeri* and *Vibrio fischeri* gDNA, and a plant cDNA library from *Arabidopsis thaliana*.



Design, synthesis and biological evaluation of tripeptide boronic acid proteasome inhibitors

pp 6851–6861

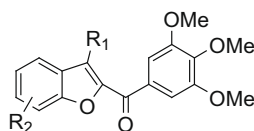
Yongqiang Zhu, Shuyang Yao, Bo Xu, Zemei Ge, Jingrong Cui^{*}, Tieming Cheng, Runtao Li^{*}

Series of tripeptide boronic acid proteasome inhibitors were designed and synthesized. The most active compound inhibited 20S proteasome with IC_{50} less than 0.1 nM and inhibited two hematologic cell lines with IC_{50} less than 10 nM.

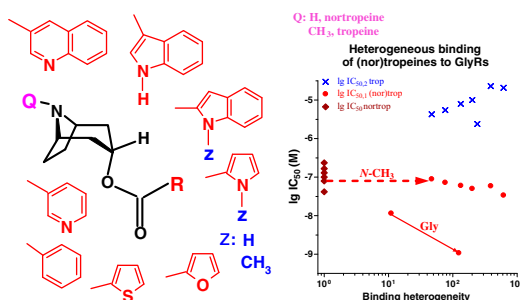
Design, synthesis and structure–activity relationship of 2-(3',4',5'-trimethoxybenzoyl)-benzo[b]furan derivatives as a novel class of inhibitors of tubulin polymerization

pp 6862–6871

Romeo Romagnoli^{*}, Pier Giovanni Baraldi^{*}, Maria Dora Carrion, Carlota Lopez Cara, Olga Cruz-Lopez, Manlio Tolomeo, Stefania Grimaudo, Antonietta Di Cristina, Maria Rosaria Pipitone, Jan Balzarini, Nicola Zonta, Andrea Brancale, Ernest Hamel

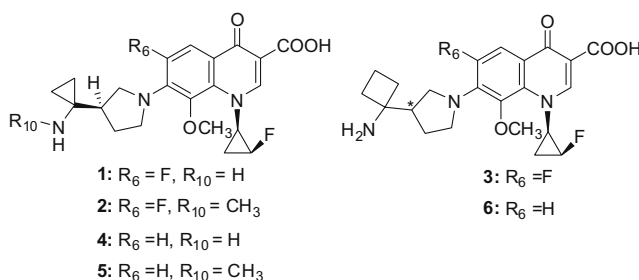
 $R_1 = H$ or Me $R_2 = H$, halogen, Me, OMe, OEt and OH**Synthesis of heteroaromatic tropeines and heterogeneous binding to glycine receptors**

pp 6872–6878

Gábor Maksay^{*}, Zoltán Vincze, Péter Nemes**Design, synthesis and biological evaluations of novel 7-[3-(1-aminocycloalkyl)pyrrolidin-1-yl]-6-desfluoro-8-methoxyquinolones with potent antibacterial activity against multi-drug resistant Gram-positive bacteria**

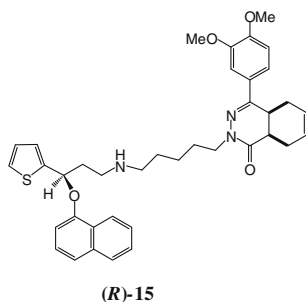
pp 6879–6889

Rie Miyauchi^{*}, Katsuhiro Kawakami, Masao Ito, Norikazu Matsushashi, Hitoshi Ohki, Hiroaki Inagaki, Hisashi Takahashi, Makoto Takemura



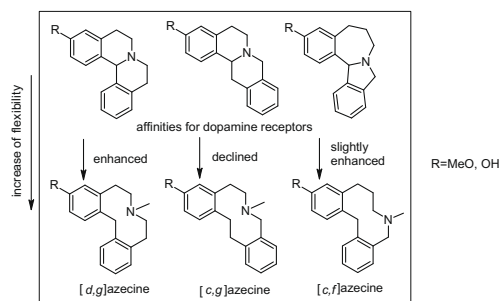
Inhibition of serotonin and norepinephrine reuptake and inhibition of phosphodiesterase by multi-target inhibitors as potential agents for depression

pp 6890–6897

John R. Cashman^{*}, Senait Ghirmai

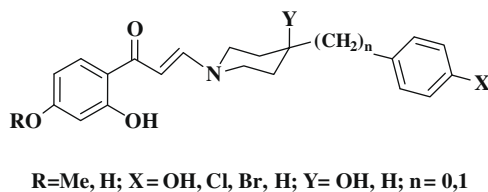
Dibenzazecine scaffold rebuilding—Is the flexibility always essential for high dopamine receptor affinities?

pp 6898–6907

Maria Schulze, Franziska K. U. Müller, Jennifer M. Mason, Helmar Görls, Jochen Lehmann, Christoph Enzensperger^{*}

Synthesis and dopaminergic activity of some *E*-3-(piperidin-1-yl)-1-(4-substituted phenyl)prop-2-en-1-one derivatives

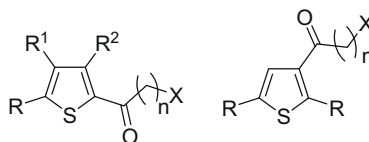
pp 6908–6913

Amirhossein Sakhteman, Alireza Foroumadi, Mohammad Sharifzadeh, Masoud Amanlou, Farhoush Rayatnia, Abbas Shafiee^{*}

A series of *E*-3-(piperidin-1-yl)-1-(4-substituted phenyl)prop-2-en-1-one derivatives have been synthesized and evaluated for dopaminergic activity in animal models.

Thienylhalomethylketones: Irreversible glycogen synthase kinase 3 inhibitors as useful pharmacological tools

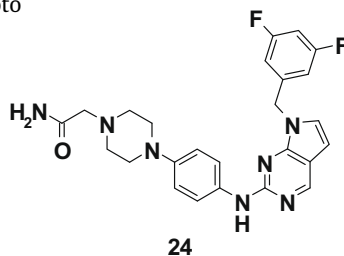
pp 6914–6925

Daniel I. Perez, Santiago Conde, Concepción Pérez, Carmen Gil, Diana Simon, Francisco Wandosell, Francisco J. Moreno, José L. Gelpí, Francisco J. Luque, Ana Martínez^{*}

Novel 7H-pyrrolo[2,3-d]pyrimidine derivatives as potent and orally active STAT6 inhibitors

pp 6926–6936

Shinya Nagashima *, Takeshi Hondo, Hiroshi Nagata, Takashi Ogiyama, Jun Maeda, Hiroaki Hoshii, Toru Kontani, Sadao Kuromitsu, Keiko Ohga, Masaya Orita, Kazuki Ohno, Ayako Moritomo, Koichi Shiozuka, Masako Furutani, Makoto Takeuchi, Mitsuaki Ohta, Shin-ichi Tsukamoto

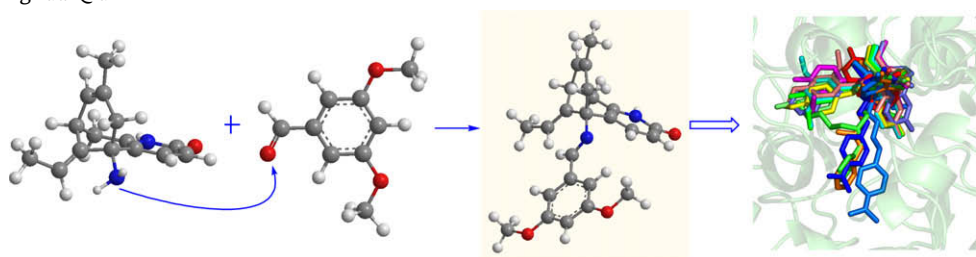


The novel 7H-pyrrolo[2,3-d]pyrimidine derivative **24** (AS1810722) inhibited STAT6 activation with an IC_{50} value of 1.9 nM and showed a good profile of CYP3A4 inhibition. Compound **24** also inhibited in vitro differentiation of Th2 cells and eosinophil infiltration in an antigen-induced mouse asthmatic model after oral administration.

Rational design and synthesis of highly potent anti-acetylcholinesterase activity huperzine A derivatives

pp 6937–6941

Jian Yan *, Lirong Sun, Guisheng Wu, Ping Yi, Fumei Yang, Lin Zhou, Xianmin Zhang, Zhongrong Li, Xiaosheng Yang, Huairong Luo, Minghua Qiu *

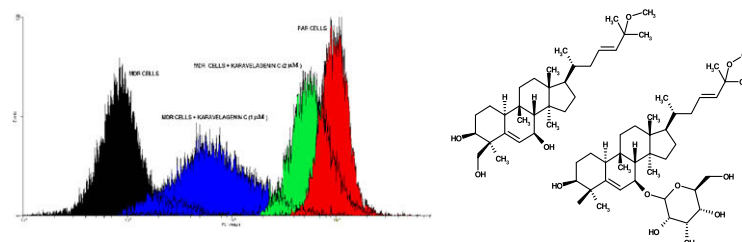


Hup A

compound **5** IC_{50} 0.02 nMcomplex compounds (**1-11**) with TcAChE**New potent P-glycoprotein modulators with the cucurbitane scaffold and their synergistic interaction with doxorubicin on resistant cancer cells**

pp 6942–6951

Cátia Ramalhete, Joseph Molnár, Silva Mulhovo, Virgílio E. Rosário, Maria-José U. Ferreira *

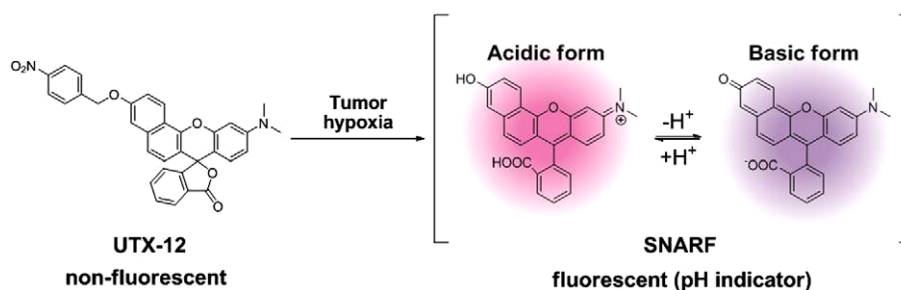


Discovery of new potent P-glycoprotein inhibitors, with the cucurbitane scaffold, on multidrug resistant cancer cells.

**Design of a bioreductively-activated fluorescent pH probe for tumor hypoxia imaging**

pp 6952–6958

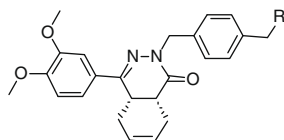
Eiji Nakata *, Yoshihiro Yukimachi, Hirokazu Kariyazono, Seongwang Im, Chiaki Abe, Yoshihiro Uto, Hiroshi Maezawa, Toshihiro Hashimoto, Yasuko Okamoto, Hitoshi Hori *



Synthesis and biological evaluation of novel phthalazinone derivatives as topically active phosphodiesterase 4 inhibitors

pp 6959–6970

Kohei Kagayama ^{*}, Tatsuya Morimoto, Seigo Nagata, Fumitaka Katoh, Xin Zhang, Naoki Inoue, Asami Hashino, Kiyoto Kageyama, Jiro Shikaura, Tomoko Niwa



A series of novel phthalazinones were synthesized as PDE4 inhibitors. The most potent of these, with IC₅₀ values in the subnanomolar range, had anti-inflammatory activity in a mouse dermatitis model.

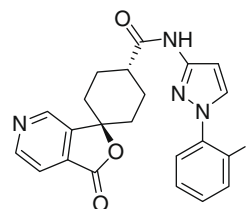


Discovery of *trans*-*N*-[1-(2-fluorophenyl)-3-pyrazolyl]-3-oxospiro[6-azaisobenzofuran-1(3*H*),1'-cyclohexane]-4'-carboxamide, a potent and orally active neuropeptide Y Y5 receptor antagonist

pp 6971–6982

Yuji Haga, Toshihiro Sakamoto, Takunobu Shibata, Katsumasa Nonoshita, Makoto Ishikawa, Takuya Suga, Hirobumi Takahashi, Toshiyuki Takahashi, Hidekazu Takahashi, Makoto Ando, Takashi Murai, Akira Gomori, Zenjun Oda, Hidefumi Kitazawa, Yuko Mitobe, Maki Kanesaka, Tomoyuki Ohe, Hisashi Iwaasa, Yasuyuki Ishii, Akane Ishihara, Akio Kanatani, Takehiro Fukami ^{*}

Compound **21j** showed high Y5 binding affinity, metabolic stability and brain and cerebrospinal fluid (CSF) penetration, and low susceptibility to P-glycoprotein transporters.



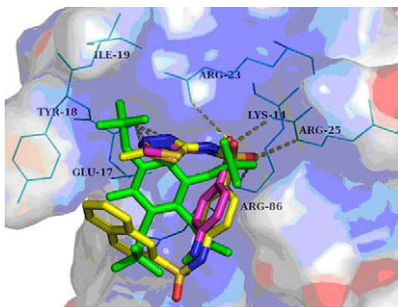
21j
hY5 IC₅₀: 1.3 nM



Computational modeling of novel inhibitors targeting the Akt pleckstrin homology domain

pp 6983–6992

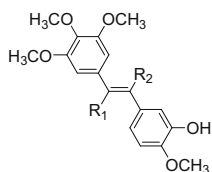
Lei Du-Cuny, Zuohe Song, Sylvester Moses, Garth Powis, Eugene A. Mash, Emmanuelle J. Meuillet, Shuxing Zhang ^{*}



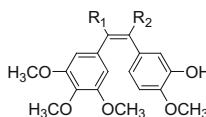
Application of the McMurry coupling reaction in the synthesis of tri- and tetra-arylethylene analogues as potential cancer chemotherapeutic agents

pp 6993–7001

Rajendra P. Tanpure, Amanda R. Harkrider, Tracy E. Strecker, Ernest Hamel, Mary Lynn Trawick, Kevin G. Pinney ^{*}



21: R₁ = Ph, R₂ = Me
23: R₁ = Ph, R₂ = Et
25: R₁ = R₂ = Ph
27: R₁ = Me, R₂ = Ph
29: R₁ = Et, R₂ = Ph

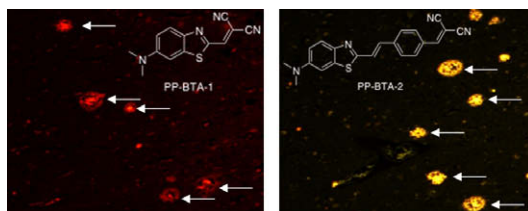


22: R₁ = Ph, R₂ = Me
24: R₁ = Ph, R₂ = Et
26: R₁ = R₂ = Ph
28: R₁ = Me, R₂ = Ph
30: R₁ = Et, R₂ = Ph

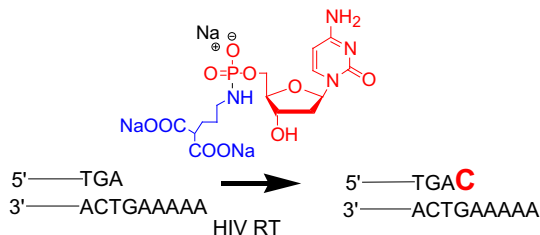


Push–pull benzothiazole derivatives as probes for detecting β -amyloid plaques in Alzheimer's brains

pp 7002–7007

Masahiro Ono ^{*}, Shun Hayashi, Hiroyuki Kimura, Hidekazu Kawashima, Morio Nakayama, Hideo Saji ^{*} **δ -Di-carboxybutyl phosphoramidate of 2'-deoxycytidine-5'-monophosphate as substrate for DNA polymerization by HIV-1 reverse transcriptase**

pp 7008–7014

Ivan Zlatev, Anne Giraut, François Morvan ^{*}, Piet Herdewijn, Jean-Jacques Vasseur

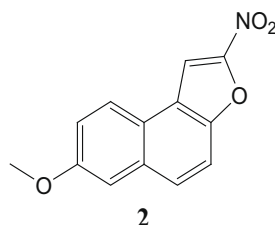
The replacement of the pyrophosphate moiety of 2'-deoxynucleoside triphosphates by non natural δ -dicarboxylic butyl amino acid allows incorporation of natural 2'-deoxycytidine into DNA using HIV-1 reverse transcriptase (RT) as enzyme. In contrast, 3'-deoxycytidine analog was not substrate of the HIV-1 RT.

**A SPR strategy for high-throughput ligand screenings based on synthetic peptides mimicking a selected subdomain of the target protein: A proof of concept on HER2 receptor**

pp 7015–7020

Luca Monfregola, Rosa Maria Vitale, Pietro Amodeo, Stefania De Luca ^{*}**Identification of small molecule regulators of the nuclear receptor HNF4 α based on naphthofuran scaffolds**

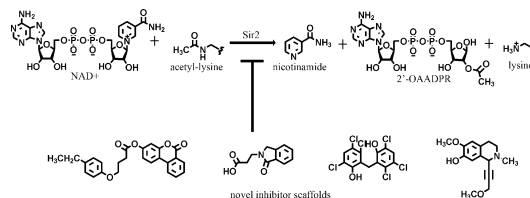
pp 7021–7030

Rémy Le Guével, Frédéric Oger, Aurélien Lecorgne, Zuzana Dudasova, Soizic Chevance, Arnaud Bondon, Peter Barath, Gérard Simonneaux, Gilles Salbert ^{*}

Identification and characterization of novel sirtuin inhibitor scaffolds

pp 7031–7041

Brandi D. Sanders, Brittany Jackson, Michael Brent, Alexander M. Taylor, Weiwei Dang, Shelley L. Berger, Stuart L. Schreiber, Konrad Howitz, Ronen Marmorstein



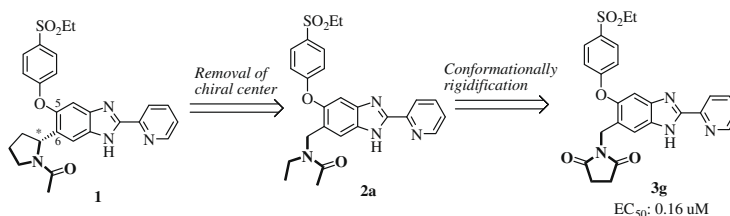
Sir2 enzymes catalyze the reaction between NAD⁺ and acetyl-lysine to form the products nicotinamide, 2'-O-acetyl-ADP-ribose, and lysine. Here, we identified and characterized four novel inhibitor scaffolds of this enzyme family with low micromolar potency through high throughput in vitro screening against the sirtuin homologue, yeast Hst2.



The design and optimization of a series of 2-(pyridin-2-yl)-1H-benzimidazole compounds as allosteric glucokinase activators

pp 7042–7051

Keiji Takahashi *, Noriaki Hashimoto, Chisato Nakama, Kenji Kamata, Kaori Sasaki, Riki Yoshimoto, Sumika Ohyama, Hideka Hosaka, Hiroko Maruki, Yasufumi Nagata, Jun-ichi Eiki, Teruyuki Nishimura

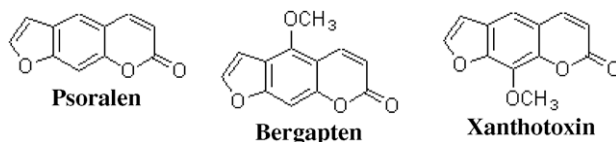


Novel benzimidazole GKAs, exemplified by **3g**, were designed and synthesized by removing the chiral center of lead **1**, followed by conformational rigidification. Rat OGTT and X-ray crystallographic analysis were also conducted.

Furanocoumarins: Novel topoisomerase I inhibitors from *Ruta graveolens* L.

pp 7052–7055

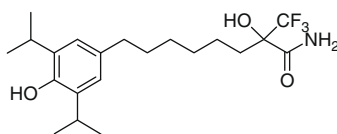
Renuka Diwan, Nutan Malpathak *



Comparative molecular field analysis and synthetic validation of a hydroxyamide-propofol binding and functional block of neuronal voltage-dependent sodium channels

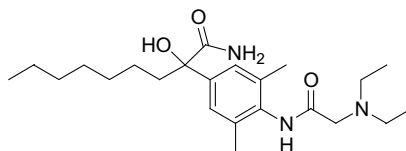
pp 7056–7063

Milton L. Brown *, Hilary A. Eidam, Mikell Paige, Paulianda J. Jones, Manoj K. Patel




Ligand-based design and synthesis of novel sodium channel blockers from a combined phenytoin–lidocaine pharmacophore**pp 7064–7072**

Yuesheng Wang, Paulianda J. Jones, Timothy W. Batts, Victoria Landry, Manoj K. Patel, Milton L. Brown *

**OTHER CONTENTS****Erratum****p 7073****Instructions to contributors****p I**

*Corresponding author

 Supplementary data available via ScienceDirect**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

Available online at

 **ScienceDirect**
www.sciencedirect.com

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE

**ELSEVIER**

ISSN 0968-0896