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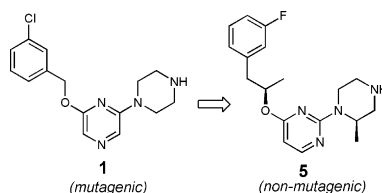
Bioorganic & Medicinal Chemistry Letters Vol. 19, No. 6, 2009

Contents

ARTICLES

- Biochemical basis for differences in metabolism-dependent genotoxicity by two diazinyloxy-piperazine-based 5-HT_{2C} receptor agonists** pp 1559–1563

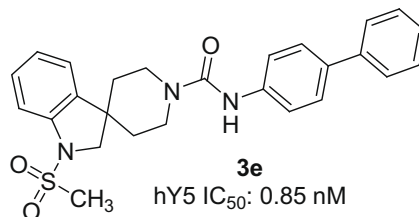
Amit S. Kalgutkar^{*}, Jonathan N. Bauman, Kim F. McClure, Jiri Aubrecht, Santo R. Cortina, Janvi Paralkar



A chemical strategy to abolish S9/NADPH-dependent mutagenicity of the 5-HT_{2C} receptor agonist **1** is examined.

- Identification of novel and orally active spiroindoline NPY Y5 receptor antagonists** pp 1564–1568

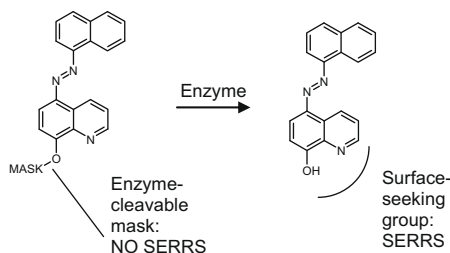
Toshihiro Sakamoto, Minoru Moriya, Yuji Haga, Toshiyuki Takahashi, Takunobu Shibata, Osamu Okamoto, Katsumasa Nonoshita, Hidefumi Kitazawa, Masayasu Hidaka, Akira Gomori, Hisashi Iwaasa, Akane Ishihara, Akio Kanatani, Takehiro Fukami^{*}, Ying-Duo Gao, Douglas J. MacNeil, Lihu Yang



A series of potent and orally active spiroindoline-3,4'-piperidine derivatives NPY Y5 receptor antagonists are described.

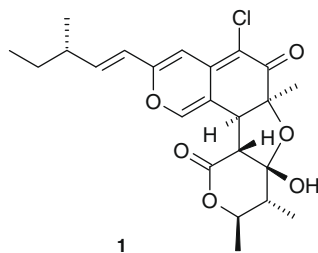
- Simultaneous detection of alkaline phosphatase and β -galactosidase activity using SERRS** pp 1569–1571

Andrew Ingram, Barry D. Moore, Duncan Graham^{*}



Bioactive metabolites produced by *Chaetomium globosum*, an endophytic fungus isolated from *Ginkgo biloba* pp 1572–1574

Jian-Chun Qin, Ya-Mei Zhang, Jin-Ming Gao*, Ming-Sheng Bai, Sheng-Xiang Yang, Hartmut Laatsch*, An-Ling Zhang

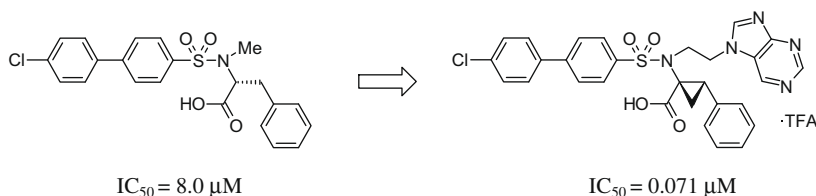


A novel chlorinated azaphilone analogue named chaetomugilin D (**1**) together with three known compounds **2–4** has been isolated from the cultures of *Chaetomium globosum*, an endophytic fungus present in *Ginkgo biloba*. The isolates displayed significant growth inhibitory activity against the brine shrimp and *Mucor miehei*.

Novel N-substituted 2-phenyl-1-sulfonylamino-cyclopropane carboxylates as selective ADAMTS-5 (Aggrecanase-2) inhibitors

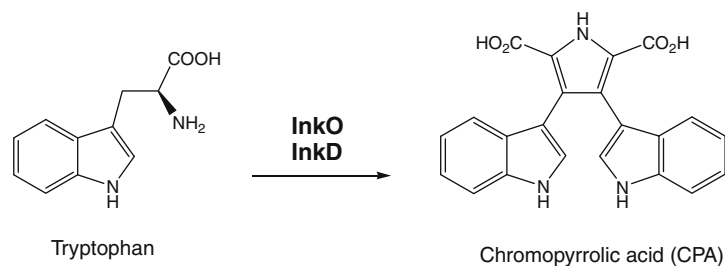
pp 1575–1580

Makoto Shiozaki*, Katsuya Maeda, Tomoya Miura, Yosuke Ogoshi, Julia Haas, Andrew M. Fryer, Ellen R. Laird, Nicole M. Littmann, Steven W. Andrews, John A. Josey, Takayuki Mimura, Yuichi Shinozaki, Hiromi Yoshiuchi, Takashi Inaba*

**Production of chromopyrrolic acid by coexpression of *inkOD* in a heterologous host *Streptomyces albus***

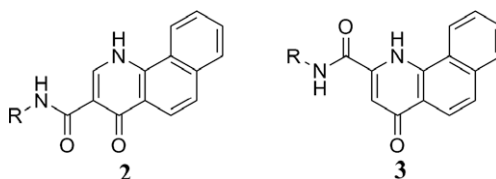
pp 1581–1583

Choong-Sik Chae, Jin-Soo Park, Soon-Chun Chung, Tae-Im Kim, So-Hyoung Lee, Kyung-Mi Yoon, Jongheon Shin*, Ki-Bong Oh*

**Benzo(h)quinoline derivatives as G-quadruplex binding agents**

pp 1584–1587

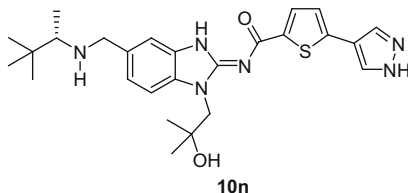
Hanumantharao Paritala, Steven M. Firestine*



5-Aminomethylbenzimidazoles as potent ITK antagonists

pp 1588–1591

Doris Riether*, Renée Zindell, Jennifer A. Kowalski, Brian N. Cook, Jörg Bentzien, Stéphane De Lombaert, David Thomson, Stanley Z. Kugler Jr., Donna Skow, Leslie S. Martin, Ernest L. Raymond, Hnin Hnin Khine, Kathy O'Shea, Joseph R. Woska Jr., Deborah Jeanfavre, Rosemarie Sellati, Kerry L. M. Ralph, Jennifer Ahlberg, Gabriel Labissiere, Mohammed A. Kashem, Steven S. Pullen, Hidenori Takahashi

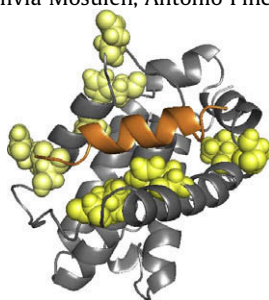


SAR studies around the 5-aminomethylbenzimidazoles and identification of tool compounds such as **10n** for proof-of-concept studies are described.

Deciphering the antitumoral activity of quinacrine: Binding to and inhibition of Bcl-xL

pp 1592–1595

Mar Orzáez, Laura Mondragón, Alicia García-Jareño, Silvia Mosulén, Antonio Pineda-Lucena, Enrique Pérez-Payá*

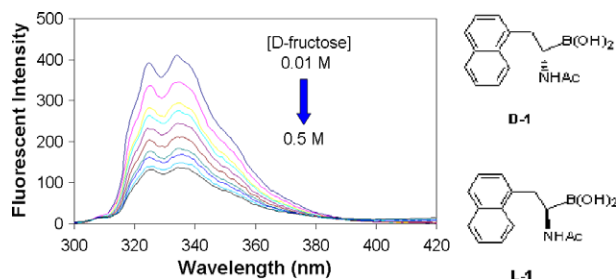


Bcl-xL residues undergoing chemical shift changes upon binding to quinacrine (yellow spheres) form a patch resembling the interaction reported between Bcl-xL (grey) and the BH3 domain (orange) of a Bak-derivative peptide.

**Identification of the first fluorescent α -amidoboronic acids that change fluorescent properties upon sugar binding**

pp 1596–1599

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

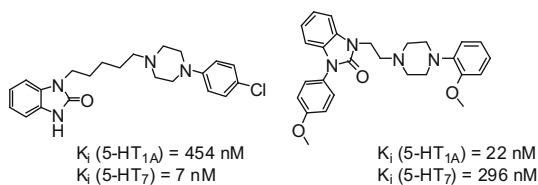


The first amidoboronic acids were identified that show significant fluorescent property changes upon binding with various carbohydrates.

Benzimidazolone-based serotonin 5-HT_{1A} or 5-HT₇R ligands: Synthesis and biological evaluation

pp 1600–1603

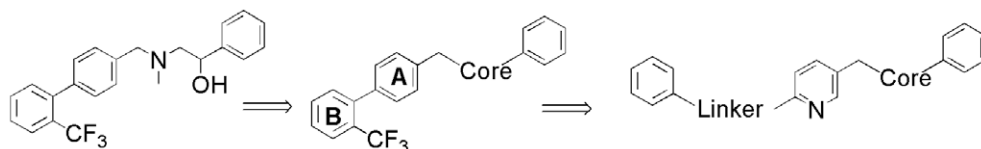
Eduard Badarau, Franck Suzenet*, Andrzej J. Bojarski, Adriana-Luminița Fînaru, Gérald Guillaumet



Morpholine containing CB2 selective agonists

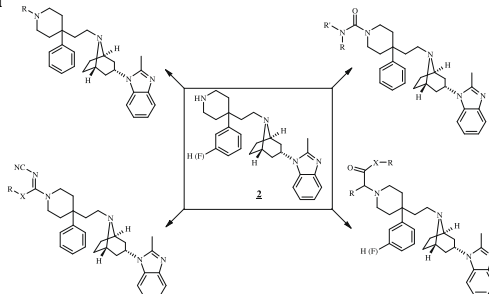
pp 1604–1609

Renée Zindell*, Doris Riether, Todd Bosanac, Angela Berry, Mark J. Gemkow, Andreas Ebnet, Sabine Löbbe, Ernest L. Raymond, Diane Thome, Daw-Tsun Shih, David Thomson

**[2-(4-Phenyl-4-piperidinyl)ethyl]amine based CCR5 antagonists: derivatizations at the N-terminal of the piperidine ring**

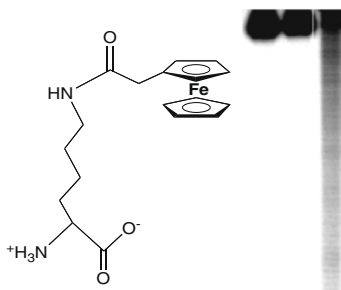
pp 1610–1613

Maosheng Duan*, Christopher Aquino, Robert Ferris, Wieslaw M. Kazmierski, Terry Kenakin, Cecilia Koble, Pat Wheelan, Chris Watson, Michael Youngman

**Enhancement of DNA cleavage activity of an unnatural ferrocene-amino acid conjugate**

pp 1614–1617

Pamela J. Higgins*, Amanda M. Gellett

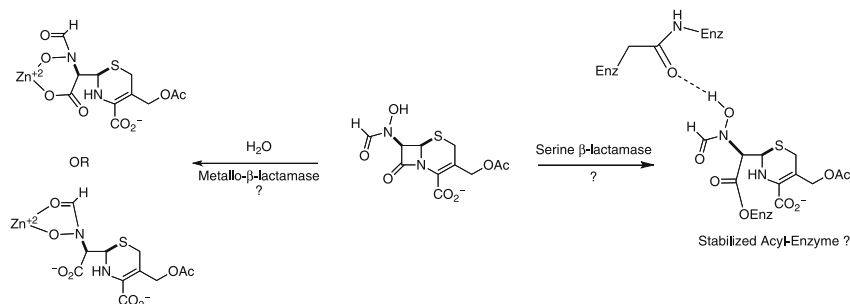


The nucleolytic activity exhibited by an unnatural ferrocenyl amino acid is non-specific along the DNA backbone and can be significantly enhanced under reducing and Fenton conditions.

Approaches to the simultaneous inactivation of metallo- and serine-β-lactamases

pp 1618–1622

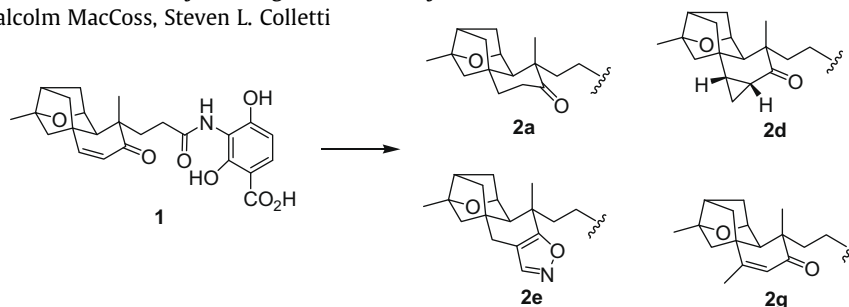
Sudhakar Reddy Ganta, Senthil Perumal, Sundar Ram Reddy Pagadala, Ørjan Samuelsen, James Spencer, R. F. Pratt, John D. Buynak*



Synthesis and biological evaluation of platensimycin analogs

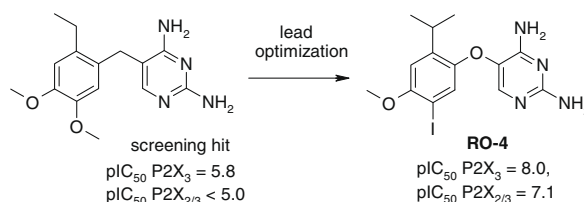
pp 1623–1627

Hong C. Shen*, Fa-Xiang Ding, Sheo B. Singh, Gopalakrishnan Parthasarathy, Stephen M. Soisson, Sookhee N. Ha, Xun Chen, Srinivas Kodali, Jun Wang, Karen Dorso, James R. Tata, Milton L. Hammond, Malcolm MacCoss, Steven L. Colletti

**Identification and SAR of novel diaminopyrimidines. Part 1: The discovery of RO-4, a dual P2X₃/P2X_{2/3} antagonist for the treatment of pain**

pp 1628–1631

David S. Carter*, Muzaffar Alam, Haiying Cai, Michael P. Dillon, Anthony P. D. W. Ford, Joel R. Gever, Alam Jahangir, Clara Lin, Amy G. Moore, Paul J. Wagner, Yansheng Zhai

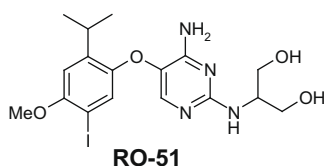


The discovery and structure–activity relationships of a novel series of diaminopyrimidine based dual P2X₃/P2X_{2/3} antagonists is described.

Identification and SAR of novel diaminopyrimidines. Part 2: The discovery of RO-51, a potent and selective, dual P2X₃/P2X_{2/3} antagonist for the treatment of pain

pp 1632–1635

Alam Jahangir*, Muzaffar Alam, David S. Carter, Michael P. Dillon, Daisy Joe Du Bois, Anthony P. D. W. Ford, Joel R. Gever, Clara Lin, Paul J. Wagner, Yansheng Zhai, Jeff Zira

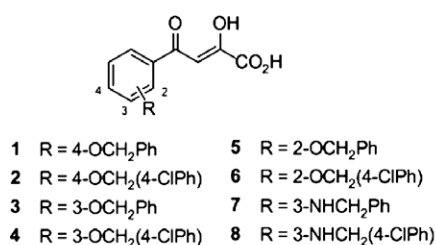


This paper describes the SAR and optimization of diaminopyrimidine template based P2X₃/P2X_{2/3} antagonists. Discovery and the synthesis a highly potent and drug-like dual P2X₃/P2X_{2/3} antagonists **RO-51** is presented.

Aryl diketoacids (ADK) selectively inhibit duplex DNA-unwinding activity of SARS coronavirus NTPase/helicase

pp 1636–1638

Chaewoon Lee, Jin Moo Lee, Na-Ra Lee, Bong-Suk Jin, Kyoung Jin Jang, Dong-Eun Kim, Yong-Joo Jeong*, Youhoon Chong*

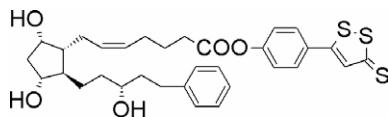


Compd	SCV Hel. IC ₅₀ (μM)	
	ATPase	Duplex DNA-Unwinding
1	41.3 ± 2.7	39.9 ± 0.5
2	> 50	> 50
3	> 50	> 50
4	24.4 ± 1.0	13.6 ± 0.3
5	> 50	> 50
6	> 50	28.7 ± 2.3
7	> 50	5.4 ± 0.1
8	> 50	11.0 ± 0.6

New prostaglandin derivative for glaucoma treatment

pp 1639–1642

Elena Perrino, Caterina Uliva, Cecilia Lanzi, Piero Del Soldato, Emanuela Masini, Anna Sparatore *

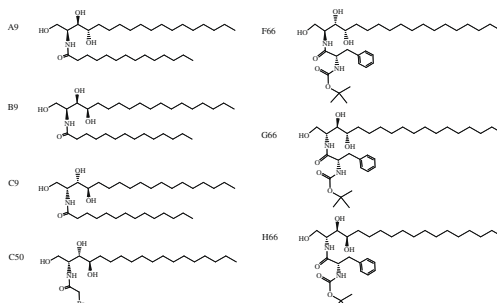
**ACS 67**

A hydrogen sulphide-releasing derivative of latanoprost acid (ACS 67) was synthesized and showed in rabbit a reduction of intraocular pressure and good tolerability.

Evaluation of synthetic sphingolipid analogs as ligands for peroxisome proliferator-activated receptors

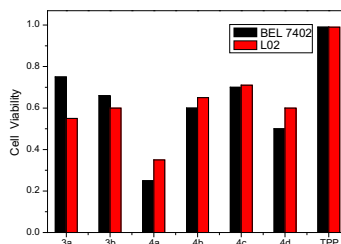
pp 1643–1646

Kiyomi Tsuji, Shigeru Satoh, Susumu Mitsutake, Itsuo Murakami, Jeong-Ju Park, Qian Li, Young-Tae Chang, Sung-Kee Chung, Yasuyuki Igarashi *

**Porphyrins containing nitric oxide donors: Synthesis and cancer cell-oriented NO release**

pp 1647–1649

Wukun Liu, Chaozhou Liu, Changjun Gong, Weiying Lin, Cancheng Guo *



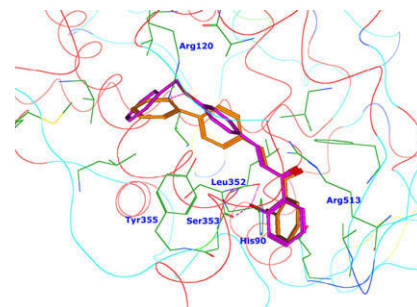
Four porphyrins with NO donors were synthesized, and the cancer cell-oriented accumulation and NO release from the porphyrins were found. The porphyrins with NO donor had more effective killing of BEL-7402 liver cancer cells than L-02 liver normal cells.

Inhibitory activity of prostaglandin E₂ production by the synthetic 2'-hydroxychalcone analogues: Synthesis and SAR study

pp 1650–1653

Thanh-Dao Tran *, Haeil Park, Hyun Pyo Kim, Gerhard F. Ecker, Khac-Minh Thai *

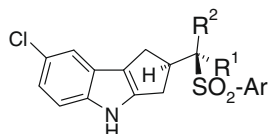
A series of 2'-hydroxychalcones has been synthesized and screened for their in vitro inhibitory activities of cyclooxygenase-2 catalyzed prostaglandin production from lipopolysaccharide-treated RAW 264.7 cells and docked into cyclooxygenase-2.



Discovery of tetrahydro-cyclopenta[b]indole as selective LXRs modulator

pp 1654–1657

Hassen Ratni*, Denise Blum-Kaelin, Henrietta Dehmlow, Peter Hartman, Philippe Jablonski, Raffaello Masciadri, Cyrille Maugeais, Angelique Patiny-Adam, Narendra Panday, Matthew Wright

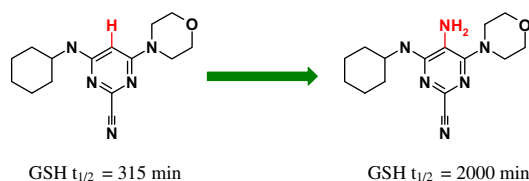


A novel series of selective LXRs modulator derived from a high throughput screening hit is reported.

5-Aminopyrimidin-2-ynitriles as Cathepsin K inhibitors

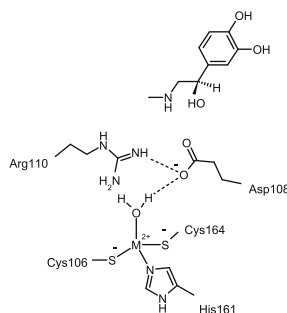
pp 1658–1661

Andrew D. Morley*, Peter W. Kenny*, Brenda Burton, Robert A. Heald, Philip A. MacFaul, Julia Mullett, Ken Page, Soraya S. Porres, Lyn Rosenbrier Ribeiro, Phil Smith, Stuart Ward, Tina J. Wilkinson

**Carbonic anhydrase activators: Activation of the β -carbonic anhydrase Nce103 from the yeast *Saccharomyces cerevisiae* with amines and amino acids**

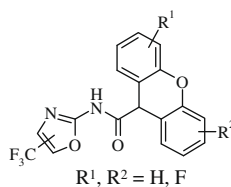
pp 1662–1665

Semra Isik, Feray Kockar, Meltem Aydin, Oktay Arslan, Ozen Ozensoy Guler, Alessio Innocenti, Andrea Scozzafava, Claudiu T. Supuran*

**Fluorinated 9H-xanthene-9-carboxylic acid oxazol-2-yl-amides as potent, orally available mGlu1 receptor enhancers**

pp 1666–1669

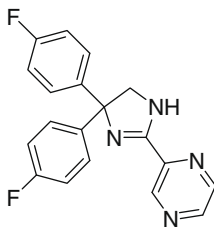
Eric Vieira*, Jörg Huwyler, Synèse Jolidon, Frédéric Knoflach, Vincent Mutel, Jürgen Wichmann



The synthesis of a new class of selectively fluorinated small molecule mGluR1 enhancers with improved pharmacokinetic properties is presented. Their potential use as pharmacological tools for the study of the physiological roles mediated by mGlu1 receptors is discussed.

Discovery of substituted 2,4,4-triarylimidazoline derivatives as potent and selective neuropeptide Y Y5 receptor antagonists pp 1670–1674

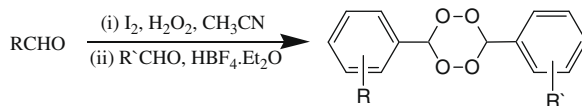
Nagaaki Sato*, Makoto Jitsuoka, Shiho Ishikawa, Keita Nagai, Hiroyasu Tsuge, Makoto Ando, Osamu Okamoto, Hisashi Iwaasa, Akira Gomori, Akane Ishihara, Akio Kanatani, Takehiro Fukami



Novel imidazoline derivatives were discovered to be potent neuropeptide Y Y5 receptor antagonists.

Iodine-catalyzed one-pot synthesis and antimalarial activity evaluation of symmetrically and asymmetrically substituted 3,6-diphenyl[1,2,4,5]tetraoxanes pp 1675–1677

Nitin Kumar, Shabana I. Khan, Mukul Sharma, Himanshu Atheaya, Diwan S. Rawat*



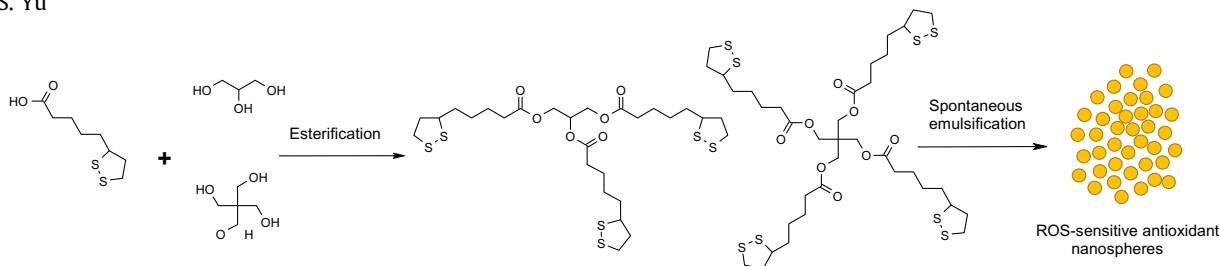
17 Examples

P. falciparum (D6 Clone); IC₅₀ = 0.38 - 3.79 μM

P. falciparum (W2 Clone); IC₅₀ = 0.45 - 6.01 μM

Preparation and characterization of antioxidant nanospheres from multiple α-lipoic acid-containing compounds pp 1678–1681

Bong Seop Lee, Xiangpeng Yuan, Qijin Xu, Fred S. McLafferty, Brian A. Petersen, Jeremy C. Collette, Keith L. Black, John S. Yu*

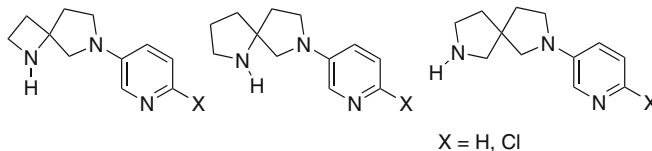


Reactive oxygen species (ROS)-sensitive antioxidant nanospheres were prepared from multiple α-lipoic acid-containing antioxidant compounds (mALAs) by using spontaneous emulsification.



Preparation and characterization of N-(3-pyridinyl) spirocyclic diamines as ligands for nicotinic acetylcholine receptors pp 1682–1685

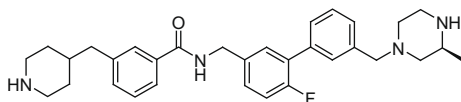
Kevin B. Sippy*, David J. Anderson, William H. Bunnelle, Charles W. Hutchins, Michael R. Schrimpf



M₃ muscarinic acetylcholine receptor antagonists: SAR and optimization of bi-aryl amines

pp 1686–1690

Brian Budzik*, Yonghui Wang*, Dongchuan Shi, Feng Wang, Haibo Xie, Zehong Wan, Chongye Zhu, James J. Foley, Parvathi Nuthulaganti, Lorena A. Kallal, Henry M. Sarau, Dwight M. Morrow, Michael L. Moore, Ralph A. Rivero, Michael Palovich, Michael Salmon, Kristen E. Belmonte, Dramane I. Laine, Jian Jin*



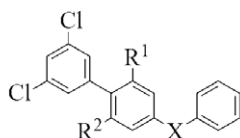
14, M₃ FLIPR pA₂ = 11.0

Exploration of multiple regions of a bi-aryl amine template led to the identification of highly potent M₃ muscarinic acetylcholine receptor antagonists such as **14** possessing good sub-type selectivity for M₃ over M₂. The structure–activity relationships and optimization of the bi-aryl amine series are described.

Design and synthesis of novel tri-aryl CB2 selective cannabinoid ligands

pp 1691–1693

Himanshu Bhattacharjee, Steven N. Gurley, Bob M. Moore II*



4 R¹ = OCH₃; R² = OCH₃; X = CHO

5 R¹ = OH; R² = OH; X = C=O

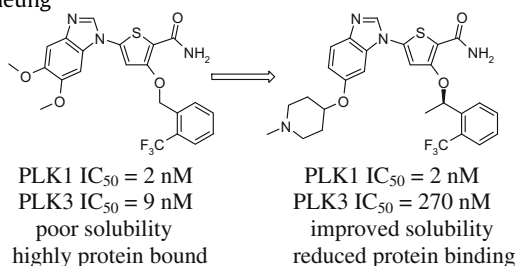
6 R¹ = OH; R² = OCH₃; X = C=O

7 R¹ = OH; R² = OH; X = C(CH₃)₂

Design of potent thiophene inhibitors of polo-like kinase 1 with improved solubility and reduced protein binding

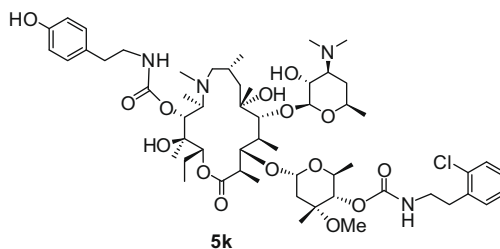
pp 1694–1697

Kyle A. Emmitte*, George M. Adjebang, C. Webb Andrews, Jennifer G. Badiang Alberti, Ramesh Bambal, Stanley D. Chamberlain, Ronda G. Davis-Ward, Hamilton D. Dickson, Daniel F. Hassler, Keith R. Hornberger, Jeffrey R. Jackson, Kevin W. Kuntz, Timothy J. Lansing, Robert A. Mook Jr., Kristen E. Nailor, Mark A. Pobanz, Stephon C. Smith, Chiu-Mei Sung, Mui Cheung

**Synthesis and antibacterial activity of 4,11-di-O-arylalkylcarbamoyl azithromycin derivatives**

pp 1698–1701

Shutao Ma*, Bo Jiao, Zhaopeng Liu, Hui Wang, Ruiqing Xian, Manjie Zheng, Hongxiang Lou*



5k
MIC = 0.06 µg/mL

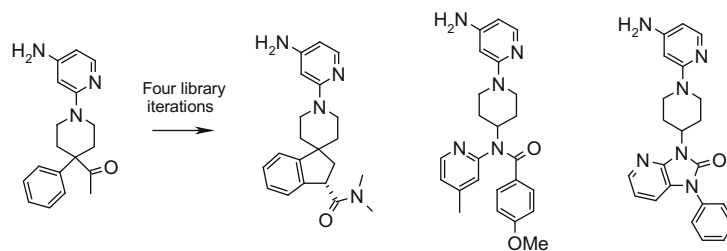
A series of new 4,11-di-O-arylalkylcarbamoyl azithromycin derivatives were designed, synthesized and evaluated for their in vitro antibacterial activities. Some derivatives exhibited greatly improved activity against erythromycin-resistant *Streptococcus pneumoniae* encoded by the *erm* or *mef* gene.



2,4-Diaminopyridine δ -opioid receptor agonists and their associated hERG pharmacology

pp 1702–1706

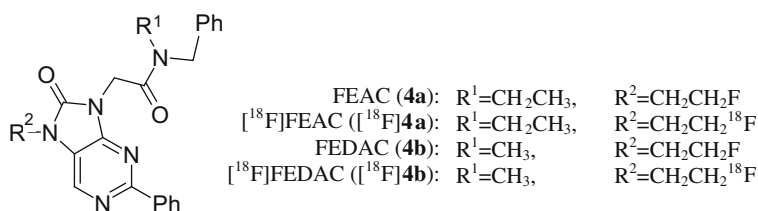
Dafydd R. Owen *, Margarita Rodriguez-Lens, Martin D. Corless, Steven M. Gaulier, Valerie A. Horne, Ross A. Kinloch, Graham N. Maw, David W. Pearce, Huw Rees, Tracy J. Ringer, Thomas Ryckmans, Blanda L. C. Stammen



A δ -opioid agonist hit was converted into potent and selective analogues using library chemistry.

[18 F]FEAC and [18 F]FEDAC: Two novel positron emission tomography ligands for peripheral-type benzodiazepine receptor in the brain

Kazuhiko Yanamoto, Katsushi Kumata, Tomoteru Yamasaki, Chika Odawara, Kazunori Kawamura, Joji Yui, Akiko Hatori, Kazutoshi Suzuki, Ming-Rong Zhang *

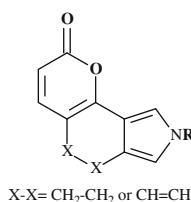


[^{18}F]FEAC ([^{18}F]**4a**) and [^{18}F]FEDAC ([^{18}F]**4b**), two potent PET ligands for peripheral-type benzodiazepine receptor, were synthesized and evaluated.

**Pyrano[2,3-*e*]isoindol-2-ones, new angelicin heteroanalogues**

pp 1711–1714

Paola Barraja, Virginia Spanò, Diana Patrizia, Anna Carbone, Girolamo Cirrincione *, Daniela Vedaldi, Alessia Salvador, Giampietro Viola, Francesco Dall'Acqua

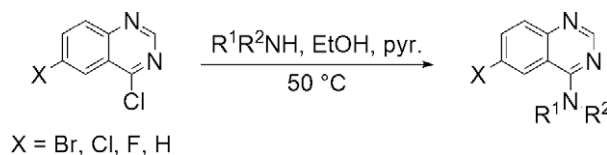


A versatile and convenient pathway for the synthesis of pyrano[2,3-*e*]isoindol-2-one derivatives and their photochemotherapeutic activity are reported.

**Potent inhibitors of Huntingtin protein aggregation in a cell-based assay**

pp 1715–1717

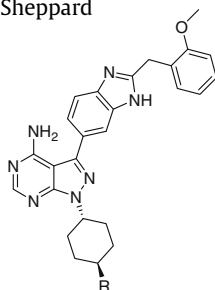
Alison Rinderspacher, Maria Laura Cremona, Yidong Liu, Shi-Xian Deng, Yuli Xie, Gangli Gong, Nathalie Aulner, Udo Többen, Katherine Myers, Caty Chung, Monique Andersen, Dušica Vidović, Stephan Schürer, Lars Brandén, Ai Yamamoto, Donald W. Landry *



Development of multitargeted inhibitors of both the insulin-like growth factor receptor (IGF-IR) and members of the epidermal growth factor family of receptor tyrosine kinases

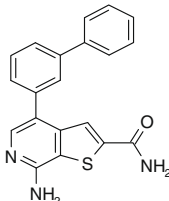
pp 1718–1721

Robert D. Hubbard*, Nwe Y. Bamaung, Steve D. Fidanze, Scott A. Erickson, Fabio Palazzo, Julie L. Wilsbacher, Qian Zhang, Lora A. Tucker, Xiaoming Hu, Peter Kovar, Donald J. Osterling, Eric F. Johnson, Jennifer Bouska, Jieyi Wang, Steven K. Davidsen, Randy L. Bell, George S. Sheppard

**Identification of a selective thieno[2,3-c]pyridine inhibitor of COT kinase and TNF- α production**

pp 1722–1725

Kevin Cusack*, Hamish Allen, Agnieszka Bischoff, Anca Clabbers, Richard Dixon, Shannon Fix-Stenzel, Michael Friedman, Yvette Gaumont, Dawn George, Thomas Gordon, Pintipa Grongsaard, Bernd Janssen, Yong Jia, Maria Moskey, Christopher Quinn, Andres Salmeron, Christine Thomas, Grier Wallace, Neil Wishart, Zhengtian Yu

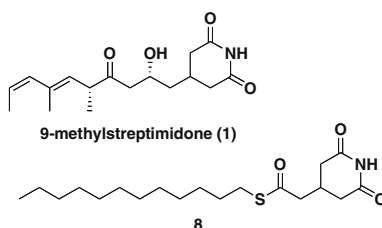


COT (Tpl2 in mice) is a serine/threonine MAP3 kinase that regulates production of TNF- α and other pro-inflammatory cytokines such as IL-1 β via the ERK/MAP kinase pathway. As TNF- α and IL-1 β are clinically validated targets for therapeutic intervention in rheumatoid arthritis (RA), blocking COT provides a potential avenue for amelioration of disease. Herein we describe identification of a cellular active selective small molecule inhibitor of COT kinase.

**Synthesis and biological evaluation on novel analogs of 9-methylstreptimidone, an inhibitor of NF- κ B**

pp 1726–1728

Yuichi Ishikawa, Miyuki Tachibana, Chino Matsui, Rika Obata, Kazuo Umezawa, Shigeru Nishiyama*



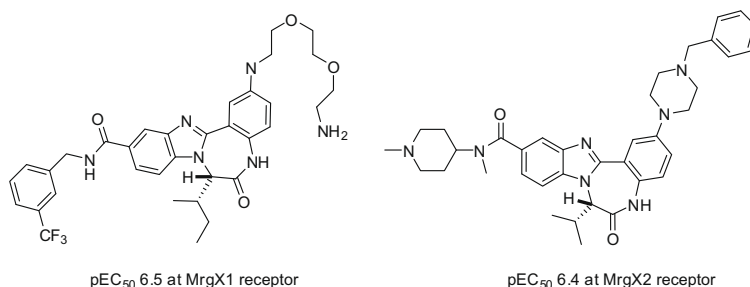
Synthesis and biological evaluation on analogs of 9-methylstreptimidone, an inhibitor of NF- κ B, are reported. Simplified compound **8** exhibited inhibitory activity against LPS-induced NO production comparable to that of 9-methylstreptimidone.

Discovery of non-peptidergic MrgX1 and MrgX2 receptor agonists and exploration of an initial SAR using solid-phase synthesis

pp 1729–1732

Leila Malik, Nicholas M. Kelly, Jian-Nong Ma, Erika A. Currier, Ethan S. Burstein, Roger Olsson*

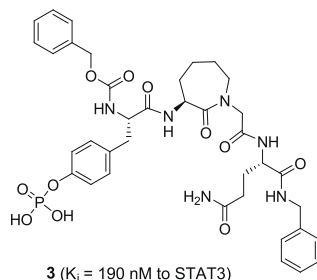
A class of small molecules displaying comparable activities with peptide ligands BAM22 and corticostatin-14 at both the human and rhesus monkey MrgX1 and MrgX2, respectively, receptors was discovered.

pEC₅₀ 6.5 at MrgX1 receptorpEC₅₀ 6.4 at MrgX2 receptor

Design, synthesis, and evaluation of peptidomimetics containing Freidinger lactams as STAT3 inhibitors

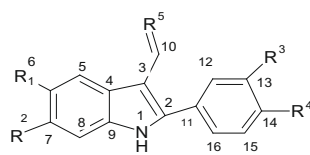
pp 1733–1736

Cindy Gomez, Longchuan Bai, Jian Zhang, Zaneta Nikolovska-Coleska, Jianyong Chen, Han Yi, Shaomeng Wang*

**Comparative QSAR modelling of 2-phenylindole-3-carbaldehyde derivatives as potential antimitotic agents**

pp 1737–1739

Amit Kumar Halder, Nilanjan Adhikari, Tarun Jha*

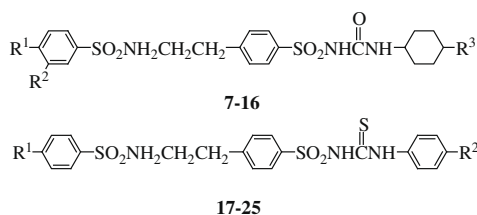


Comparative QSAR modelling was performed on 2-phenylindole-3-carbaldehydes to find more active antimitotic agents. Stepwise regression, FA-MLR, PVRA and PLS techniques were adopted for QSAR study.

**Synthesis and biological evaluation of sulfonylurea and thiourea derivatives substituted with benzenesulfonamide groups as potential hypoglycemic agents**

pp 1740–1744

Hui-bin Zhang, Ya-an Zhang, Guan-zhong Wu, Jin-pei Zhou*, Wen-long Huang*, Xiao-wen Hu

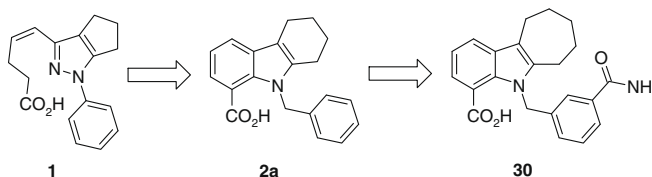


Compound **10** ($R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{CH}_3$) with excellent hypoglycemic and antithrombotic properties, might be useful in the treatment of diabetics with cardiovascular and nephropathy complications.

N-Benzyl-indolo carboxylic acids: Design and synthesis of potent and selective adipocyte fatty-acid binding protein (A-FABP) inhibitors

pp 1745–1748

Tjeerd Barf*, Fredrik Lehmann, Kristin Hammer, Saba Haile, Eva Axen, Carmen Medina, Jonas Uppenberg, Stefan Svensson, Lena Rondahl, Thomas Lundbäck

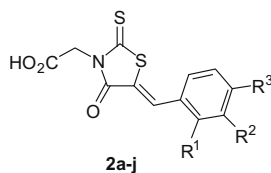


A novel class of hexahydrocyclohepta[b]indole-based A-FABP inhibitors have been synthesized and evaluated. The potency, selectivity profile, and structure–activity relationship trends of this class of compounds are discussed.

First small molecular inhibitors of *T. brucei* dolicholphosphate mannose synthase (DPMS), a validated drug target in African sleeping sickness

pp 1749–1752

Terry K. Smith, Benjamin L. Young, Helen Denton, David L. Hughes, Gerd K. Wagner*

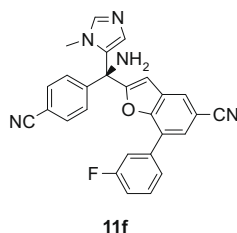


The development of thiazolidinones as dolicholphosphate mannose synthase (DPMS) inhibitors and novel trypanocidal agents (ED50 < 100 μ M) is reported.

Synthesis and structure–activity relationships of novel benzofuran farnesyltransferase inhibitors

pp 1753–1757

Kohsuke Asoh, Masami Kohchi, Ikumi Hyoudoh, Tatsuo Ohtsuka, Miyako Masubuchi, Kenichi Kawasaki, Hirosato Ebiiike, Yasuhiko Shiratori, Takaaki A. Fukami, Osamu Kondoh, Toshiyuki Tsukaguchi, Nobuya Ishii, Yuko Aoki, Nobuo Shimma, Masahiro Sakaitani*

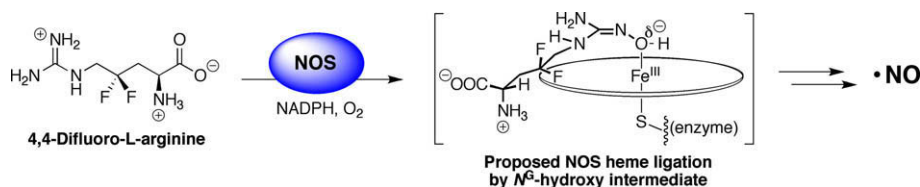


The synthesis and biological activity of benzofuran derivatives as farnesyltransferase inhibitor is described.

4,4-Difluorinated analogues of L-arginine and N^G-hydroxy-L-arginine as mechanistic probes for nitric oxide synthase

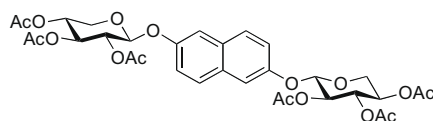
pp 1758–1762

Nathaniel I. Martin, Joshua J. Woodward, Michael B. Winter, Michael A. Marletta*

**Antiproliferative effects of peracetylated naphthoxylosides**

pp 1763–1766

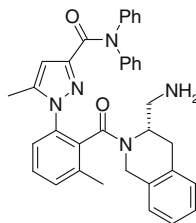
Ulrika Nilsson, Mårten Jacobsson, Richard Johnsson, Katrin Mani, Ulf Ellervik*



Atropisomeric small molecule Bcl-2 ligands: Determination of bioactive conformation

pp 1767–1772

John Porter*, Andrew Payne, Ian Whitcombe, Ben de Candole, Daniel Ford, Rachel Garlish, Adam Hold, Brian Hutchinson, Graham Trevitt, James Turner, Chloe Edwards, Clare Watkins, Jeremy Davis, Colin Stubberfield

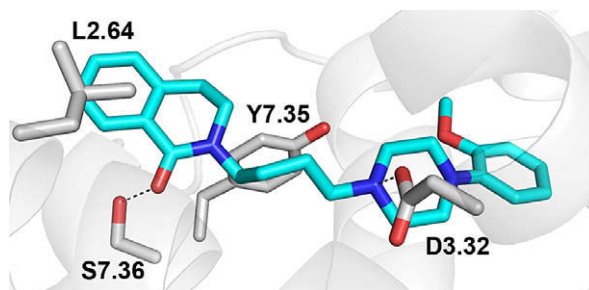


Determination of the bioactive conformation of a series of atropisomeric Bcl-2 inhibitors is reported.

Synthesis, binding affinity and SAR of new benzolactam derivatives as dopamine D₃ receptor ligands

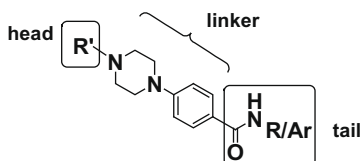
pp 1773–1778

Raquel Ortega, Enrique Raviña, Christian F. Masaguer*, Filipe Areias, José Brea, María I. Loza, Laura López, Jana Selent, Manuel Pastor, Ferran Sanz

**Synthesis and SAR of piperazinyl-N-phenylbenzamides as inhibitors of hepatitis C virus RNA replication in cell culture**

pp 1779–1783

Immacolata Conte*, Claudio Giuliano, Caterina Ercolani, Frank Narjes, Uwe Koch, Michael Rowley, Sergio Altamura, Raffaele De Francesco, Petra Neddermann, Giovanni Migliaccio, Ian Stansfield

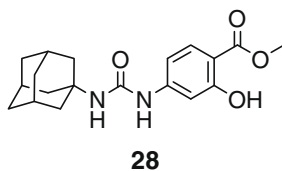


We report here synthesis and SAR of substituted piperazinyl-N-(aryl)benzamides as potent inhibitors of HCV replication exerted via modulation of the dimerization of NS5A.

Salicylate-urea-based soluble epoxide hydrolase inhibitors with high metabolic and chemical stabilities

pp 1784–1789

Takeo Kasagami, In-Hae Kim, Hsing-Ju Tsai, Kosuke Nishi, Bruce D. Hammock, Christophe Morisseau*



The methyl salicylate-based urea **28** was synthesized as a soluble epoxide hydrolase inhibitor. This compound had not only strong inhibitory activity but also relatively high metabolic and chemical stabilities.



Microbial biotransformation as a source of chemical diversity in cane toad steroid toxins

pp 1790–1792

R. Andrew Hayes, Andrew M. Piggott, Kristian Dalle, Robert J. Capon *

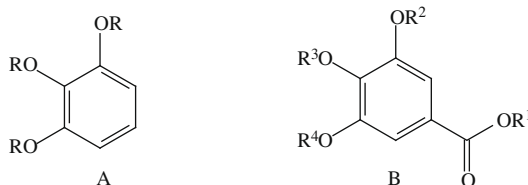


Bacteria isolated from the parotoid gland of the cane toad (*Bufo marinus*) have the ability to biotransform steroid toxins (bufadienolides), suggesting a possible new strategy for cane toad control.

**Relation between lipophilicity of alkyl gallates and antifungal activity against yeasts and filamentous fungi**

pp 1793–1796

P. C. Leal, A. Mascarello, M. Derita, F. Zuljan, R. J. Nunes, S. Zacchino, R. A. Yunes *

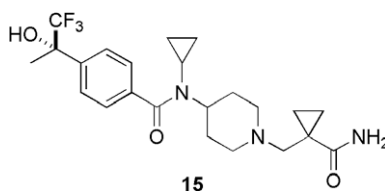


When the log *P* of each gallate was calculated and related to the different values of MIC against *Microsporium gypseum* it was observed that hexyl, heptyl, octyl and nonyl gallates exhibit a significant positive deviation from the curve corresponding to a polynomial equation obtained for the other gallates. This suggests that these compounds have a further mode of action besides their hydrophobicity, possibly the inhibition of some enzyme involved in ergosterol biosynthesis.

Discovery and optimization of piperidyl benzamide derivatives as a novel class of 11β-HSD1 inhibitors

pp 1797–1801

Yosup Rew *, Dustin L. McMinn, Zhulun Wang, Xiao He, Randall W. Hungate, Juan C. Jaen, Athena Sudom, Daqing Sun, Hua Tu, Stefania Ursu, Elisia Villemure, Nigel P. C. Walker, Xuelei Yan, Qiuping Ye, Jay P. Powers



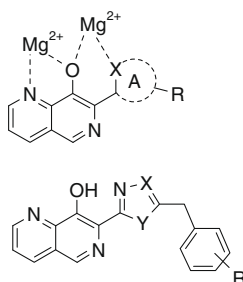
The discovery and optimization of a piperidyl benzamide series of 11β-HSD1 inhibitors is reported.

The use of oxadiazole and triazole substituted naphthyridines as HIV-1 integrase inhibitors.

pp 1802–1806

Part 1: Establishing the pharmacophore

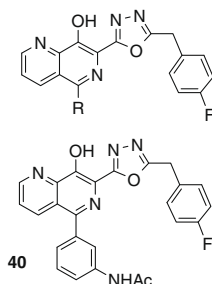
Brian A. Johns *, Jason G. Weatherhead, Scott H. Allen, James B. Thompson, Edward P. Garvey, Scott A. Foster, Jerry L. Jeffrey, Wayne H. Miller



1,3,4-Oxadiazole substituted naphthyridines as HIV-1 integrase inhibitors. Part 2: SAR of the C5 position

pp 1807–1810

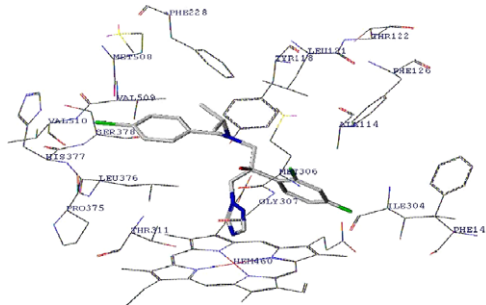
Brian A. Johns*, Jason G. Weatherhead, Scott H. Allen, James B. Thompson, Edward P. Garvey, Scott A. Foster, Jerry L. Jeffrey, Wayne H. Miller

**Design, synthesis, and biological evaluation of novel 1-(1*H*-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-substituted benzylamino-2-propanols**

pp 1811–1814

Xiaoyun Chai, Jun Zhang, Shichong Yu, Honggang Hu, Yan Zou, Qingjie Zhao, Zhigang Dan, Dazhi Zhang, Qiuye Wu*

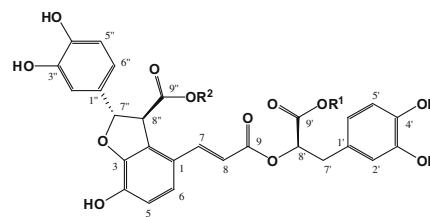
A number of novel triazole derivatives have been synthesized and studied with molecular docking to get the insight of structural requirements for better enzyme inhibition.

**Lithospermic acid derivatives from *Lithospermum erythrorhizon* increased expression of serine palmitoyltransferase in human HaCaT cells**

pp 1815–1817

Phuong Thien Thuong, Keon Wook Kang, Jeong Kee Kim, Dae Bang Seo, Sang Jun Lee, Sung Han Kim, Won Keun Oh*

Lithospermic acid (**1**) and two derivative esters, 9'-methyl lithospermate (**2**) and 9'-methyl lithospermate (**3**), isolated from *Lithospermum erythrorhizon*, were found to significantly increased the expressions of SPT mRNA and raised the level of SPT protein in HaCaT cells.

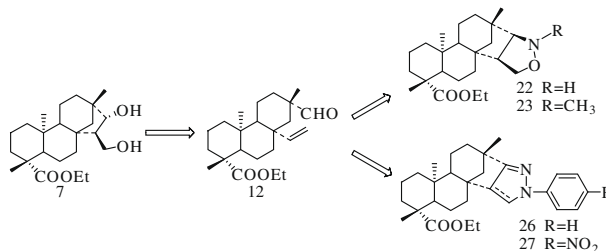


Lithospermic acid (**1**) $R^1 = R^2 = H$
 9'-Methyl lithospermate (**2**) $R^1 = H, R^2 = CH_3$
 9'-Methyl lithospermate (**3**) $R^1 = CH_3, R^2 = H$

**Stereoselective synthesis of 15- and 16-substituted isosteviol derivatives and their cytotoxic activities**

pp 1818–1821

Ya Wu, Gui-Fu Dai, Jing-Hua Yang, Yun-Xiao Zhang, Yu Zhu, Jing-Chao Tao*

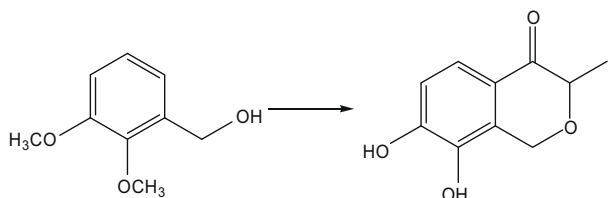


A novel series of 15- and 16-substituted isosteviol derivatives were designed and prepared. Within all compounds, **22** ($IC_{50} = 15 \mu M$) showed the most potent cytotoxic activities against B16-F10 melanoma cells.

Total synthesis and antihypertensive activity of (±)7,8-dihydroxy-3-methyl-isochromanone-4

pp 1822–1824

Jie Liu, Hao Ren, Jinyi Xu *, Renren Bai, Qi Yan, Wenlong Huang, Xiaoming Wu *, Jihua Fu, Qiujuan Wang, Qian Wu, Rong Fu



(±)7, 8-dihydroxy-3-methyl- isochromanone-4 (1)

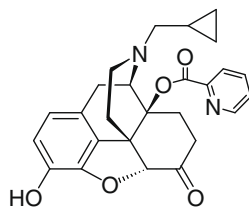
The total synthesis of (±)7,8-dihydroxy-3-methyl-isochromanone-4 (1) is described and this compound displays potent antihypertensive activity and moderate ACE inhibitory activity.

14-O-Heterocyclic-substituted naltrexone derivatives as non-peptide mu opioid receptor selective antagonists:

pp 1825–1829

Design, synthesis, and biological studies

Guo Li, Lindsey C. K. Aschenbach, Hengjun He, Dana E. Selley, Yan Zhang *



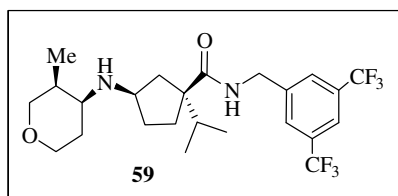
Compound 1

A series of 14-O-heterocyclic-substituted naltrexone derivatives were designed, synthesized, and evaluated. Among them, compound 1 showed binding affinity at subnanomolar level and highest selectivity for the mu opioid receptor.

**Design, synthesis, and structure–activity relationship of novel CCR2 antagonists**

pp 1830–1834

Shankaran Kothandaraman *, Karla L. Donnelly, Gabor Butora, Richard Jiao, Alexander Pasternak, Gregori J. Morriello, Stephen D. Goble, Changyou Zhou, Sander G. Mills, Malcolm MacCoss, Pasquale P. Vicario, Julia M. Ayala, Julie A. DeMartino, Mary Struthers, Margaret A. Cascieri, Lihu Yang *



Discovery of a novel series of 3-aminocyclopentanecarboxamide CCR2 receptor antagonists are presented herein. These compounds demonstrate high affinity and functional inhibition of hCCR2 receptors. A discussion on SAR along with the cross species PK profile for the best analog (59) is also included.

OTHER CONTENTS**Corrigenda**

pp 1835–1836

Instructions to contributors

p I

*Corresponding author

Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of **R-22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, 17, 5677.]

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