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Contents

Publisher's Note

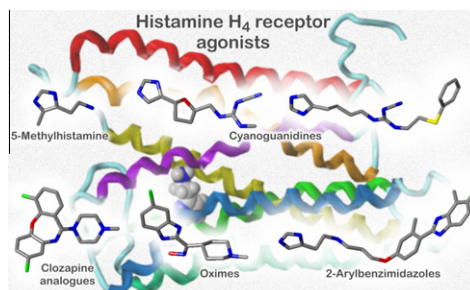
p 7190

BMCL DIGEST

Histamine H₄ receptor agonists

pp 7191–7199

Patrick Igel, Stefan Dove, Armin Buschauer*

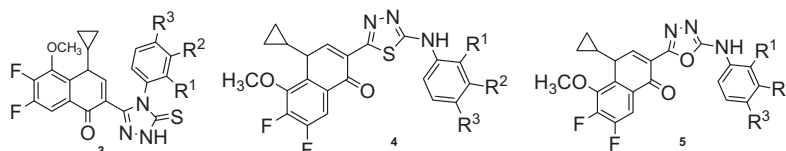


REGULAR ARTICLES

Green synthesis and biological evaluation of some novel azoles as antimicrobial agents

pp 7200–7204

Sharad Shelke*, Ganesh Mhaske, Sunil Gadakh, Charnsingh Gill



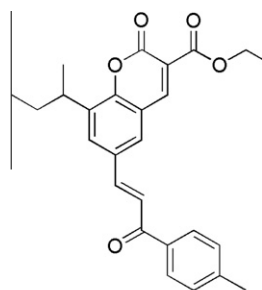
Triazoles **3**, thiadiazoles **4**, and oxadiazoles **5** have been synthesized by green techniques from thiosemicarbazides **2**. All products have been characterized by spectral study and screened for their antimicrobial activity.

Synthesis and in vitro evaluation of novel coumarin–chalcone hybrids as potential anticancer agents

pp 7205–7211

Koneni V. Sashidhara*, Abdhesh Kumar, Manoj Kumar, Jayanta Sarkar, Sudhir Sinha

A series of novel coumarin–chalcone hybrids have been synthesized and evaluated for their cytotoxicity. Compound **26** showed around 30-fold more selectivity towards C33A (cervical carcinoma) cells over normal fibroblast NIH3T3 cells.



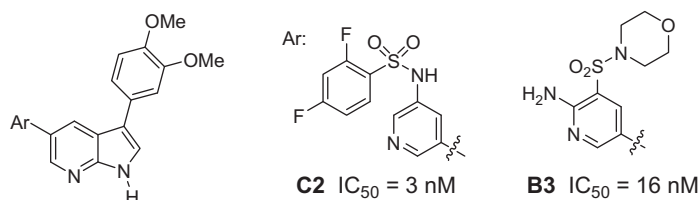
26 IC₅₀ = 3.59 μM



Discovery of new azaindole-based PI3K α inhibitors: Apoptotic and antiangiogenic effect on cancer cells

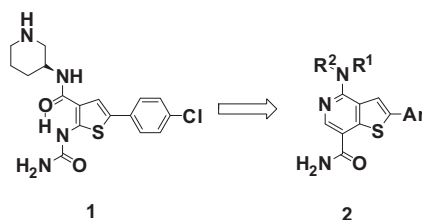
pp 7212–7215

Seunghye Hong, Soyoung Lee, Bomi Kim, Hyunseung Lee, Soon-Sun Hong*, Sungwoo Hong*

**Design, synthesis and SAR of thienopyridines as potent CHK1 inhibitors**

pp 7216–7221

Lianyun Zhao*, Yingxin Zhang, Chaoyang Dai, Timothy Guzi, Derek Wiswell, Wolfgang Seghezzi, David Parry, Thierry Fischmann, M. Arshad Siddiqui

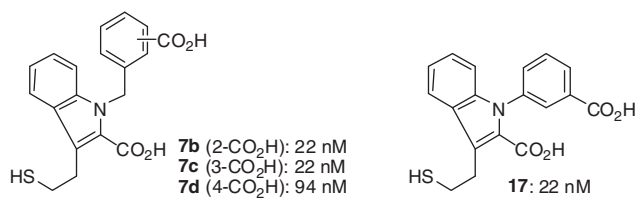


A novel series of CHK1 inhibitors based on thienopyridine template has been designed and synthesized. These inhibitors maintain critical hydrogen bonding with the hinge and conserved water in the ATP binding site. Several compounds show single digit nanomolar CHK1 activities. Compound **70** shows excellent enzymatic activity of 1 nM.

The discovery and structure–activity relationships of indole-based inhibitors of glutamate carboxypeptidase II

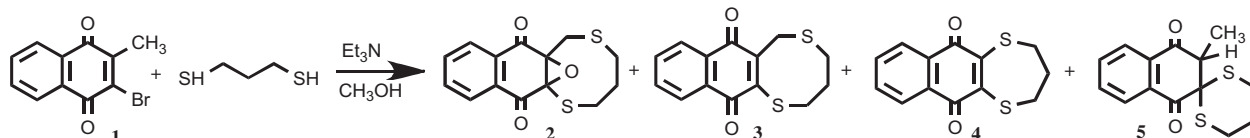
pp 7222–7225

Brian Grella, Jessica Adams, James F. Berry, Greg Delahanty, Dana V. Ferraris, Pavel Majer, Chiyong Ni, Krupa Shukla, Scott A. Shuler, Barbara S. Slusher, Marigo Stathis, Takashi Tsukamoto*

**Novel epoxide formation in the reaction of 2-bromo-3-methyl-1,4-naphthoquinone with 1,3-propanedithiol**

pp 7226–7229

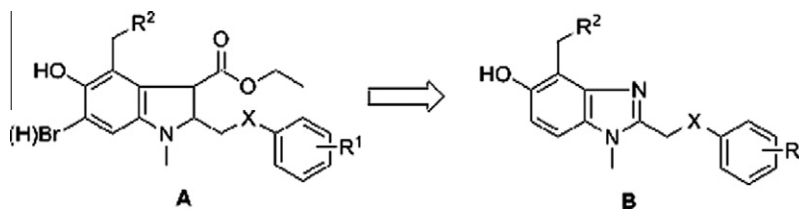
Tom M. Lam, Chain Lee, Katherine Katardjieff, Tetsuo Otsuki*



Synthesis and biological evaluation of 1*H*-benzimidazol-5-ols as potent HBV inhibitors

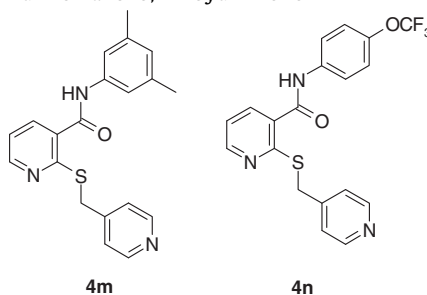
pp 7230–7233

Yanfeng Zhao, Yajing Liu, Dong Chen, Zengquan Wei, Wenzhao Liu, Ping Gong*

**Pyridylmethylthio derivatives as VEGF inhibitors. Part 1**

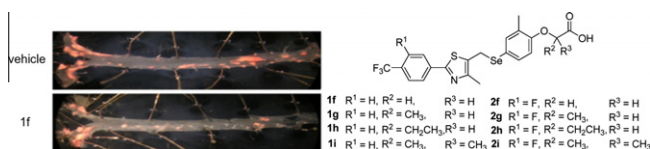
pp 7234–7238

Hisashi Tajima*, Takahiro Honda, Kenji Kawashima, Yoshimasa Sasabuchi, Minoru Yamamoto, Masakazu Ban, Kazuyoshi Okamoto, Kenji Inoue, Takaaki Inaba, Yuriko Takeno, Hiroyuki Aono

**Selective peroxisome proliferator-activated receptor δ isosteric selenium agonists as potent anti-atherogenic agents in vivo**

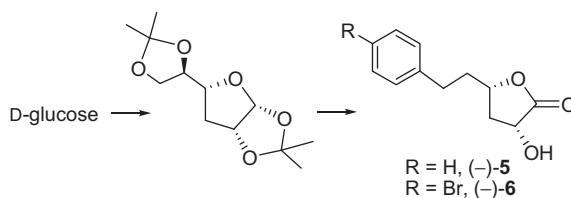
pp 7239–7242

Jungwook Chin, Jun Young Hong, Jaehwan Lee, Hoosang Hwang, Hyunsil Ko, Hyukjae Choi, Dongyup Hahn, Jaeyoung Ko, Sang-jip Nam, Jungae Tak, Jungyeob Ham, Heonjoong Kang*

**Design and synthesis of harzialactone analogues: Promising anticancer agents**

pp 7243–7245

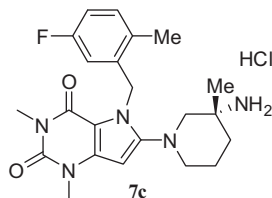
Vishwas U. Pawar, Sougata Ghosh, Balu A. Chopade, Vaishali S. Shinde*



Discovery of new chemotype dipeptidyl peptidase IV inhibitors having (R)-3-amino-3-methyl piperidine as a pharmacophore

pp 7246–7249

Yukihiro Nishio*, Hidenori Kimura, Shinya Tosaki, Eiji Sugaru, Mutsuko Sakai, Masakuni Horiguchi, Yumi Masui, Michiko Ono, Tsutomu Nakagawa, Hiroyuki Nakahira



The new chemotype DPP-IV inhibitors, such as compound **7c** (IC_{50} = 27 nM), is herein reported.

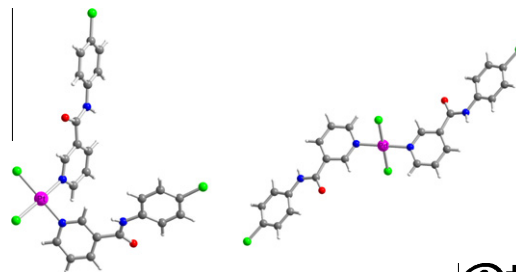


Synthesis, crystal structure, DNA-binding and cytotoxicity in vitro of novel *cis*-Pt(II) and *trans*-Pd(II) pyridine carboxamide complexes

pp 7250–7254

Chun-Yue Shi, En-Jun Gao, Shuang Ma, Mei-Lin Wang, Qi-Tao Liu*

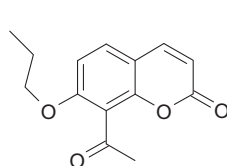
The synthesis, crystal structure, interaction with DNA and cytotoxic activity of two *cis*-platinum and *trans*-palladium complexes, (1) *cis*-[PtL₂Cl₂]-CH₃OH-DMF and (2) *trans*-[PdL₂Cl₂]-2DMF (where L = *N*-(4-chlorophenyl)-3-pyridinecarboxamide), are described. We have probed that the effect of solvent molecule on the network structure and activity of the resulting self-assembled products.



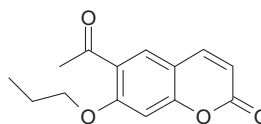
7,8-Disubstituted- but not 6,7-disubstituted coumarins selectively inhibit the transmembrane, tumor-associated carbonic anhydrase isoforms IX and XII over the cytosolic ones I and II in the low nanomolar/subnanomolar range

pp 7255–7258

Alfonso Maresca, Andrea Scozzafava, Claudiu T. Supuran*



K_i > 100 μ M (CA I and II)
 K_i = 56.7 nM (CA IX)
 K_i = 0.98 nM (CA XII)

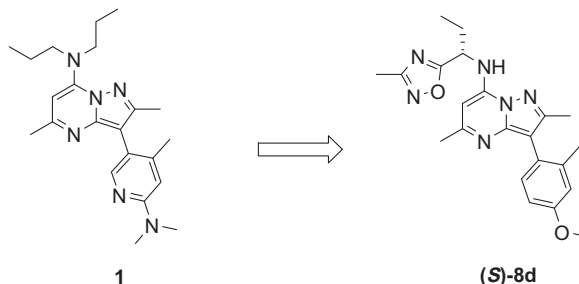


K_i < 100 μ M (CA I, II, XII)
 K_i = 7580 nM (CA IX)

Discovery of NBI-77860/GSK561679, a potent corticotropin-releasing factor (CRF₁) receptor antagonist with improved pharmacokinetic properties

pp 7259–7264

John E. Tellew, Marion Lanier, Manisha Moorjani, Emily Lin, Zhiyong Luo, Deborah H. Slee, Xiaohu Zhang, Sam R. J. Hoare, Dimitri E. Grigoriadis, Yves St. Denis, Romano Di Fabio, Enza Di Modugno, John Saunders, John P. Williams*

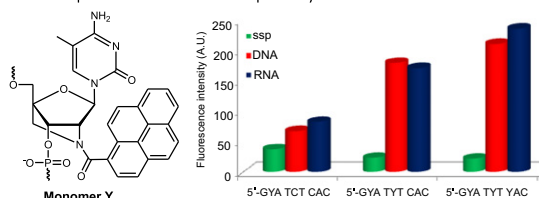


Novel insights into the use of Glowing LNA as nucleic acid detection probes—Influence of labeling density and nucleobases

pp 7265–7268

Michael E. Østergaard, Jyotirmoy Maity, B. Ravindra Babu, Jesper Wengel, Patrick J. Hrdlicka*

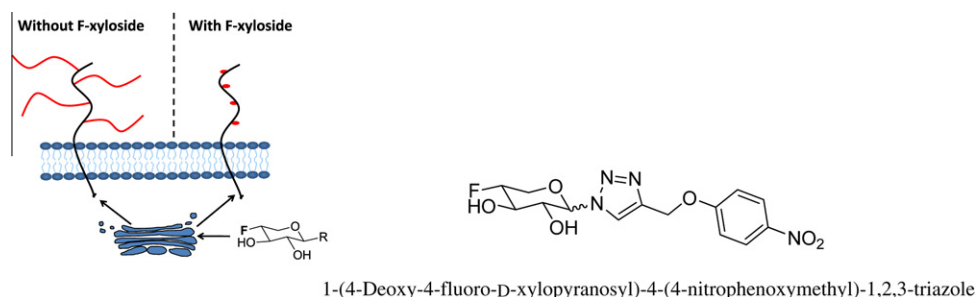
- Low single stranded probe (SSP) fluorescence
- Large hybridization-induced increases in fluorescence intensity
- High duplex fluorescence quantum yields (Φ_f 0.50–0.69)
- Improved thermal mismatch specificity



4-Deoxy-4-fluoro-xyloside derivatives as inhibitors of glycosaminoglycan biosynthesis

pp 7269–7273

Yasuhiro Tsuzuki, Thao Kim Nu Nguyen, Dinesh R. Garud, Balagurunathan Kuberan, Mamoru Koketsu*

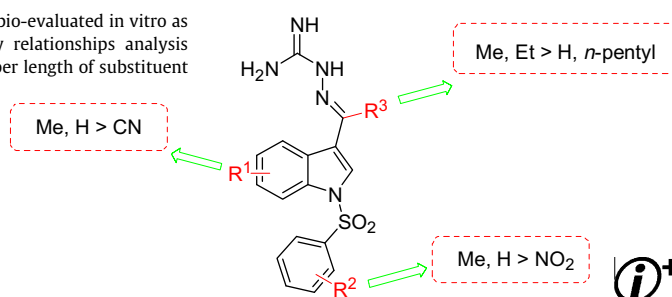


Antifungal agents. Part 5: Synthesis and antifungal activities of aminoguanidine derivatives of N-arylsulfonyl-3-acylindoles

pp 7274–7277

Hui Xu*, Yang-Yang Wang

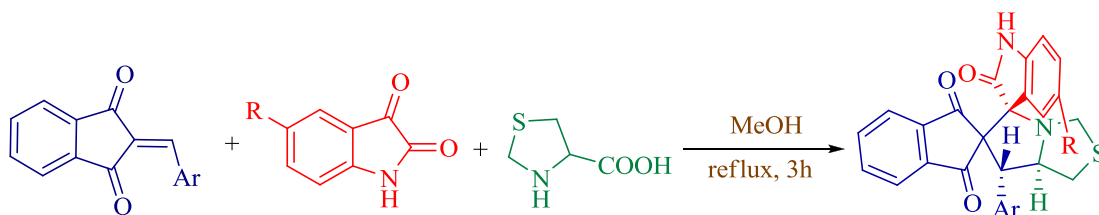
Eighteen Aminoguanidine derivatives of *N*-arylsulfonyl-3-acylindoles were prepared and bio-evaluated in vitro as antifungal agents against seven phytopathogenic fungi. Preliminary structure–activity relationships analysis demonstrated that introduction of electron-donating substituents R^1 and R^2 , and the proper length of substituent R^3 were very important for their antifungal activities.



A facile 1,3-dipolar cycloaddition of azomethine ylides to 2-arylidene-1,3-indanediones: Synthesis of dispiro-oxindolpyrrolothiazoles and their antimycobacterial evaluation

pp 7278–7282

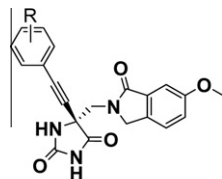
Shanmugavel Uma Maheswari, Kamaraj Balamurugan, Subbu Perumal*, Perumal Yogeewari, Dharmarajan Sriram



Novel TNF- α converting enzyme (TACE) inhibitors as potential treatment for inflammatory diseases

pp 7283–7287

Vinay M. Girijavallabhan*, Lei Chen, Chaoyang Dai, Robert J. Feltz, Luke Firmansjah, Dansu Li, Seong Heon Kim, Joseph A. Kozlowski, Brian J. Lavey, Aneta Kosinski, John J. Piwinski, Janeta Popovici-Muller, Razia Rizvi, Kristin E. Rosner, Banderpalle B. Shankar, Neng-Yang Shih, M. Arshad Siddiqui, Ling Tong, Michael K. C. Wong, De-yi Yang, Liping Yang, Wensheng Yu, Guowei Zhou, Zhuyan Guo, Peter Orth, Vincent Madison, Hong Bian, Daniel Lundell, Xiaoda Niu, Himanshu Shah, Jing Sun, Shelby Umland

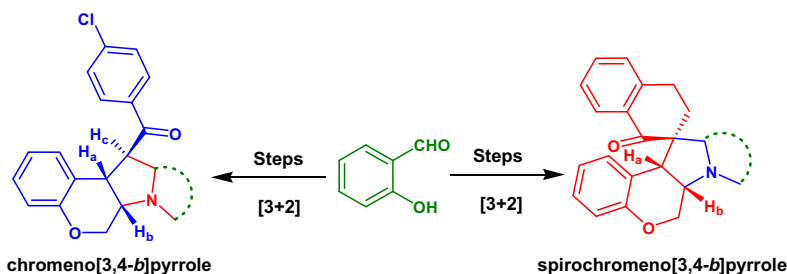


$K_i < 1$ nM
hWBA = < 250 nM

Stereoselective synthesis of hexahydro-3-methyl-1-arylchromeno[3,4-*b*]pyrrole and its annulated heterocycles as potent antimicrobial agents for human pathogens

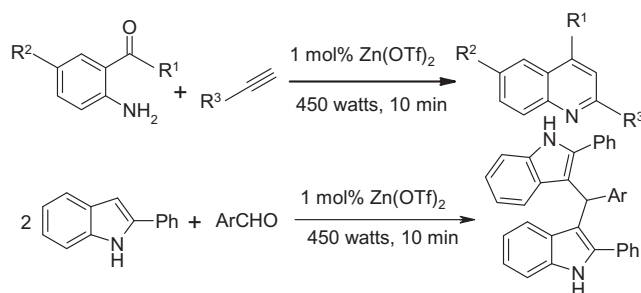
pp 7288–7291

S. Purushothaman, R. Prasanna, P. Niranjana, R. Raghunathan*, S. Nagaraj, R. Rengasamy

**Synthesis, antimicrobial and antioxidant evaluation of quinolines and bis(indolyl)methanes**

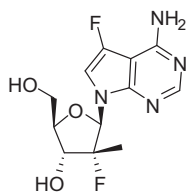
pp 7292–7296

C. Praveen, P. DheenKumar, D. Muralidharan, P. T. Perumal*

**Synthesis and anti-HCV activity of a new 2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogue**

pp 7297–7298

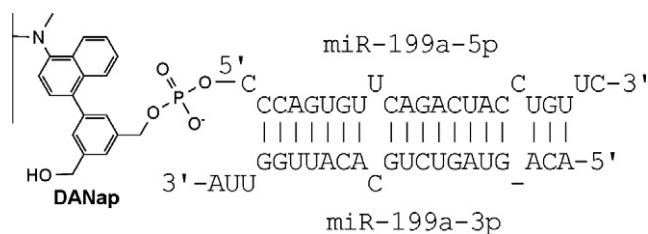
Weidong Hu, Ping'an Wang, Chuanjun Song*, Zhenliang Pan, Qiang Wang, Xiaohe Guo, Xuejun Yu, Zhenhua Shen, Shuyang Wang, Junbiao Chang*



Biaryl modification of the 5'-terminus of one strand of a microRNA duplex induces strand specificity

pp 7299–7302

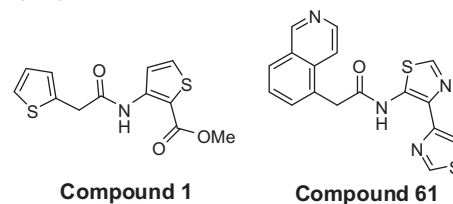
Aya Ogata, Chihiro Furukawa, Kouhei Sakurai, Hideo Iba, Yukio Kitade, Yoshihito Ueno*

**Design and synthesis of disubstituted thiophene and thiazole based inhibitors of JNK**

pp 7303–7307

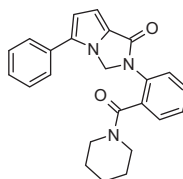
Roy K. Hom*, Simeon Bowers, Jennifer M. Sealy, Anh P. Truong, Gary D. Probst, Martin L. Neitzel, R. Jeffrey Neitz, Larry Fang, Louis Brogley, Jing Wu, Andrei W. Konradi, Hing L. Sham, Gergely Tóth, Hu Pan, Nanhua Yao, Dean R. Artis, Kevin Quinn, John-Michael Sauer, Kyle Powell, Zhao Ren, Frédérique Bard, Ted A. Yednock, Irene Griswold-Prenner

From high throughput screening, we discovered compound **1**, the prototype for a series of disubstituted thiophene inhibitors of JNK which is selective towards closely related MAP kinases p38 and Erk2. Herein we describe the evolution of these compounds to a novel class of thiophene and thiazole JNK inhibitors that retain favorable solubility, permeability, and P-gp properties for development as CNS agents for treatment of neurodegeneration. Compound **61** demonstrated JNK3 IC_{50} = 77 nM and retained the excellent broad kinase selectivity observed for the series.

**Synthesis and pharmacological characterization of 5-phenyl-2-[2-(1-piperidinylcarbonyl)phenyl]-2,3-dihydro-1H-pyrrolo[1,2-c]imidazol-1-ones: A new class of Neuropeptide S antagonists**

pp 7308–7311

Fabrizio Micheli*, Romano Di Fabio, Angelo Giacometti, Adelheid Roth, Elisa Moro, Giancarlo Merlo, Alfredo Paio, Emilio Merlo-Pich, Silvia Tomelleri, Federica Tonelli, Paola Zarantonello, Laura Zonzini, Anna Maria Capelli

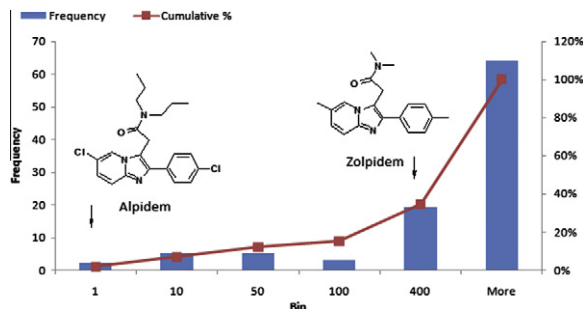


A new lead series was identified in the NPS antagonist field. The compound was prepared following up experimental observations rationalized with computational chemistry techniques and rational design.

Experimental solubility profiling of marketed CNS drugs, exploring solubility limit of CNS discovery candidate

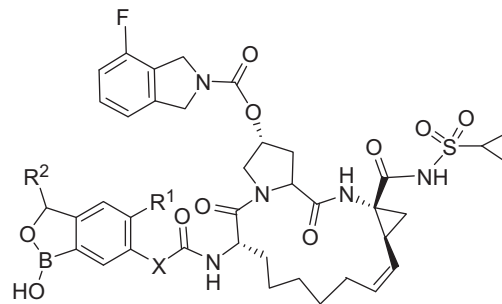
pp 7312–7316

Yun W. Alelyunas*, James R. Empfield, Dennis McCarthy, Russell C. Spreen, Khanh Bui, Luciana Pelosi-Kilby, Cindy Shen



Synthesis and biological evaluations of P4-benzoxaborole-substituted macrocyclic inhibitors of HCV NS3 protease pp 7317–7322

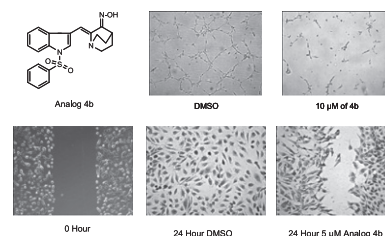
Charles Z. Ding*, Yong-Kang Zhang, Xianfeng Li, Yang Liu, Suoming Zhang, Yasheen Zhou, Jacob J. Plattner, Stephen J. Baker, Liang Liu, Maosheng Duan, Richard L. Jarvest, Jingjing Ji, Wieslaw M. Kazmierski, Matthew D. Tallant, Lois L. Wright, Gary K. Smith, Renae M. Crosby, Amy A. Wang, Zhi-Jie Ni, Wuxin Zou, Jon Wright



Antiangiogenic properties of substituted (Z)-(±)-2-(N-benzylindol-3-ylmethylene)quinuclidin-3-ol/one analogs and their derivatives pp 7323–7326

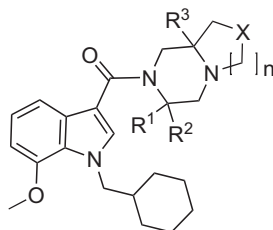
Amudhan Venkateswaran, Y. Thirupathi Reddy, Vijaykumar N. Sonar, Venkatraj Muthusamy, Peter A. Crooks, Michael L. Freeman, Konjeti R. Sekhar*

A series of substituted (Z)-(±)-2-(N-benzylindol-3-ylmethylene)quinuclidin-3-ols (**1a–1k**), (Z)-2-benzylindol-3-yl-methylene)quinuclidin-3-ones (**2a–2i**), (Z)-(±)-2-(1H/N-methyl-indol-3-ylmethylene)quinuclidin-3-ol (**3b**), and substituted (Z)-(±)-2-(N-benzenesulfonylindol-3-yl-methylene)quinuclidin-3-ols and their derivatives (**4a–4d**) that incorporate a variety of substituents in both the indole and N-benzyl/benzene sulfonyl moieties were evaluated for their antiangiogenic activity using Human Umbilical Vein Endothelial Cells (HUVECs). Eight analogs were identified as potent angiogenesis inhibitors at a non-toxic concentration of 10 μ M. The analog, **4b** was identified as the most potent antiangiogenic agent. The mechanism of inhibition is consistent with inhibition of ENOX activity.



Design, synthesis, and structure–activity relationship study of bicyclic piperazine analogs of indole-3-carboxamides as novel cannabinoid CB1 receptor agonists pp 7327–7330

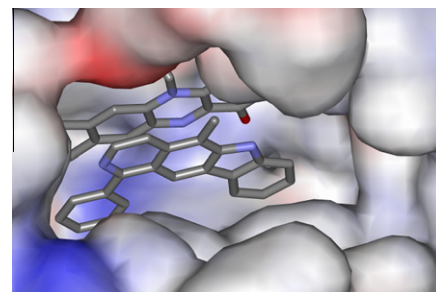
Elizabeth M. Moir, Kazuya Yoshiizumi, Jim Cairns, Phillip Cowley, Morag Ferguson, Fiona Jeremiah, Takao Kiyoi, Richard Morphy, Jason Tierney, Grant Wishart, Mark York, James Baker, Jean E. Cottney, Andrea K. Houghton, Petula McPhail, Andrew Osprey, Glenn Walker, Julia M. Adam*



In silico identification and biochemical evaluation of novel inhibitors of NRH:quinone oxidoreductase 2 (NQO2) pp 7331–7336

Karen A. Nolan, Mary C. Caraher, Matthew P. Humphries, Hoda Abdel-Aal Bettley, Richard A. Bryce, Ian J. Stratford*

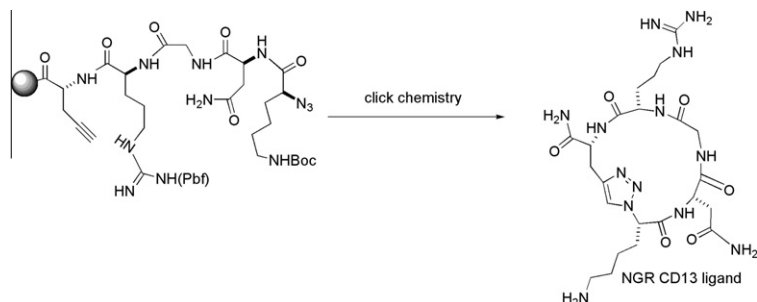
Virtual screening of the NCI Chemical database has revealed that diverse structural scaffolds can bind in the active site of NQO2. Many of these compounds are active in the micromolar range as enzyme inhibitors.



Synthesis of novel cyclic NGR/RGD peptide analogs via on resin click chemistry

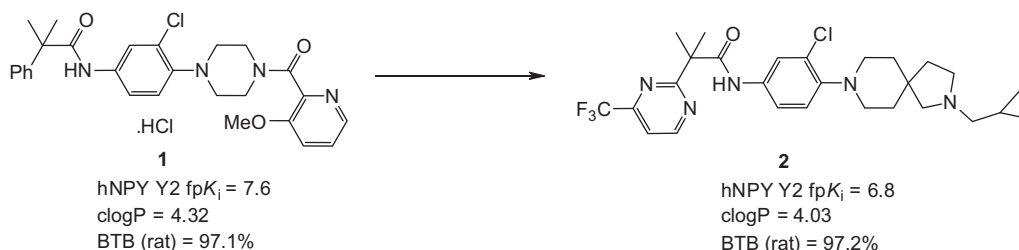
pp 7337–7340

Belhu B. Metaferia, Matthew Rittler, Jinesh S. Gheeya, Albert Lee, Heidi Hempel, Alberto Plaza, William G. Stetler-Stevenson, Carole A. Bewley, Javed Khan*

**The identification of a series of novel, soluble non-peptidic neuropeptide Y Y2 receptor antagonists**

pp 7341–7344

Gillian E. Lunniss*, Ashley A. Barnes, Nick Barton, Matteo Biagetti, Federica Bianchi, Stephen M. Blowers, Laura L. Caberlotto, Amanda Emmons, Ian P. Holmes, Dino Montanari, Roz Norris, Gemma V. Puckey, Dewi J. Walters, Steve P. Watson, John Willis

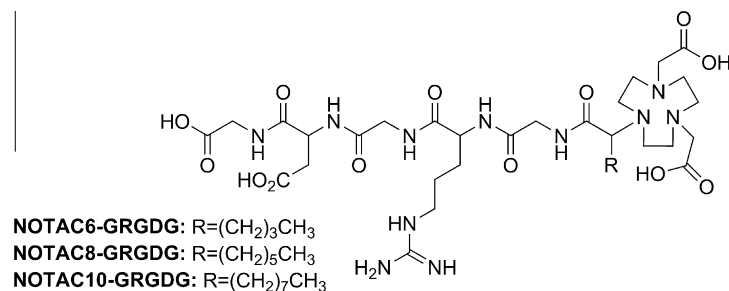


The optimisation of diamide **1** to amine **2**, a soluble and selective NPY Y2 receptor antagonist with enhanced CNS exposure is described.

Gallium labeled NOTA-based conjugates for peptide receptor-mediated medical imaging

pp 7345–7348

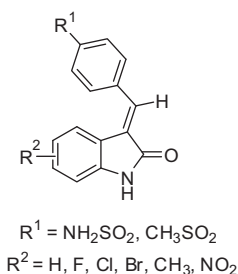
Arsénio de Sá, Áurea A. Matias, M. Isabel M. Prata, Carlos F. G. C. Geraldès, P. M. T. Ferreira, João P. André*

**Synthesis and biological evaluation of 3-[4-(amino/methylsulfonyl)phenyl]methylene-indolin-2-one derivatives as novel COX-1/2 and 5-LOX inhibitors**

pp 7349–7353

Yisheng Lai*, Lin Ma, Wenxing Huang, Xing Yu, Yihua Zhang, Hui Ji*, Jide Tian

A series of novel 3-[4-(amino/methylsulfonyl)phenyl]methylene-indolin-2-ones were synthesized. Some of them displayed potent inhibitory activities against COX-1/2 and 5-LOX in vitro, and strong anti-inflammatory and analgesic activities, and well gastric tolerability in vivo.

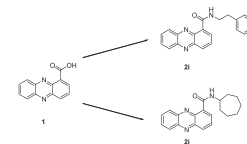


Phenazine-1-carboxylic acid derivatives: Design, synthesis and biological evaluation against *Rhizoctonia solani* Kuhn

pp 7369–7371

Long Ye, Hongyan Zhang, Hong Xu, Qi Zou, Chao Cheng, Dexian Dong, Yuquan Xu, Rongxiu Li*

Rhizoctonia solani Kuhn is the pathogen that causes sheath blight and results in significant yield reduction in rice and in nearly 50 other crops. In order to develop a new fungicide effective against this pathogen, a series of structurally diverse phenazine-1-carboxylic acid derivatives, **2a**, **2b**, **2c**, **2d**, **2e**, **2f**, **2g**, **2h**, **2i**, **2j**, and **2k**, were designed, synthesized and evaluated for their antifungal activity. The two most active compounds **2i** and **2j** were selected as lead compounds for further antifungal research.



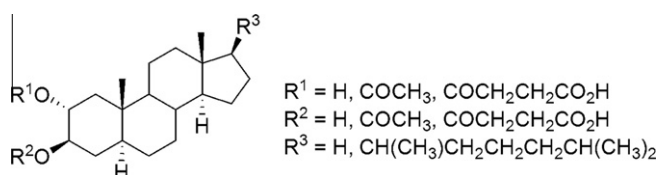
Antifungal evaluation of PCA derivatives	
Compound	<i>Rhizoctonia solani</i> Kuhn IC ₅₀ (μM)
1 (positive control)	0.068
2i	0.008
2j	0.003



Novel and efficient synthesis and antifungal evaluation of 2,3-functionalized cholestane and androstane derivatives

pp 7372–7375

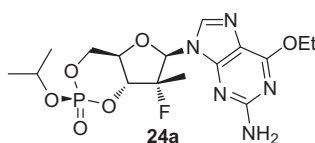
Branko S. Jursic, Sunil Kumar Upadhyay, Clinton C. Creech, Donna M. Neumann*



2'-Deoxy-2'-α-fluoro-2'-β-C-methyl 3',5'-cyclic phosphate nucleotide prodrug analogs as inhibitors of HCV NS5B polymerase: Discovery of PSI-352938

pp 7376–7380

P. Ganapati Reddy*, Donghui Bao, Wonsuk Chang, Byoung-Kwon Chun, Jinfa Du, Dhanapalan Nagarathnam, Suguna Rachakonda, Bruce S. Ross, Hai-Ren Zhang, Shalini Bansal, Christine L. Espiritu, Meg Keilman, Angela M. Lam, Congrong Niu, Holly Micolochick Steuer, Phillip A. Furman, Michael J. Otto, Michael J. Sofia



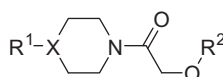
PSI-352938
EC₉₀ = 1.37 μM
CC₅₀ > 100 μM



4-Aryl piperazine and piperidine amides as novel mGluR5 positive allosteric modulators

pp 7381–7384

Hui Xiong*, Todd A. Brugel, Michael Balestra, Dean G. Brown, Kelly A. Brush, Caprice Hightower, Lindsay Hinkley, Valerie Hoesch, James Kang, Gerard M. Koether, John P. McCauley Jr., Francis M. McLaren, Laura M. Panko, Thomas R. Simpson, Reed W. Smith, James M. Woods, Becky Brockel, Vijay Chhajlani, Reto A. Gadiant, Nathan Spear, Linda A. Sygowski, Minli Zhang, Jalaj Arora, Nathalie Breyse, Julie M. Wilson, Methvin Isaac, Abdelmalik Slassi, Megan M. King

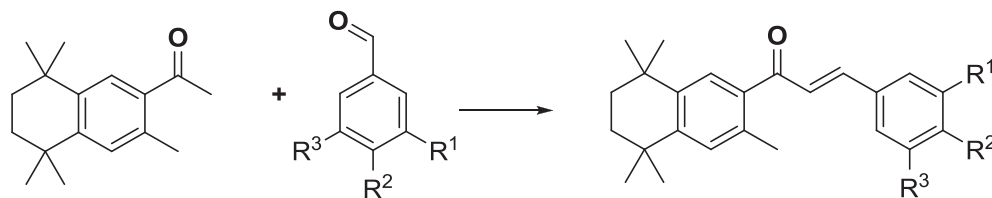


Positive allosteric modulation of metabotropic glutamate receptor 5 (mGluR5) is regarded as a potential novel treatment for schizophrenic patients. Herein we report the synthesis and SAR of 4-aryl piperazine and piperidine amides as potent mGluR5 positive allosteric modulators (PAMs). Several analogs have excellent activity and desired drug-like properties. Compound **2b** was further characterized as a PAM using several in vitro experiments, and produced robust activity in several preclinical animal models.

Synthesis and biological evaluation of retinoid-chalcones as inhibitors of colon cancer cell growth

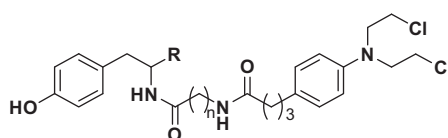
pp 7385–7387

Cassia S. Mizuno*, Shibby Paul, Nanjoo Suh, Agnes M. Rimando

**Synthesis of D- and L-tyrosine-chlorambucil analogs active against breast cancer cell lines**

pp 7388–7392

Caroline Descôteaux, Valérie Leblanc, Kevin Brasseur, Atul Gupta, Éric Asselin, Gervais Bérubé*

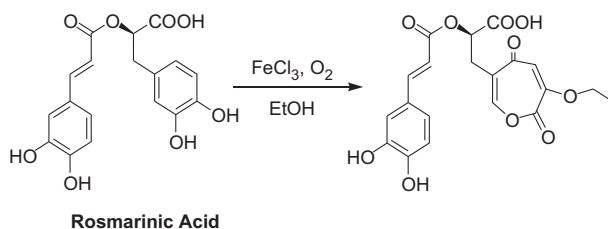
5, n = 5, 10; R = CO₂CH₃, CH₂OH

A series of D- and L-tyrosine-chlorambucil analogs is reported. The novel analogs showed significant in vitro anticancer activity when compared to chlorambucil on breast cancer cell lines. Some of the analogs showed selectivity towards MCF-7 (ER⁺) breast cancer cells.

A novel ring-expanded product with enhanced tyrosinase inhibitory activity from classical Fe-catalyzed oxidation of rosmarinic acid, a potent antioxidative Lamiaceae polyphenol

pp 7393–7396

Aya Fujimoto, Yoshimi Shingai, Mitsuhiro Nakamura, Tomomi Maekawa, Yoshiaki Sone, Toshiya Masuda*

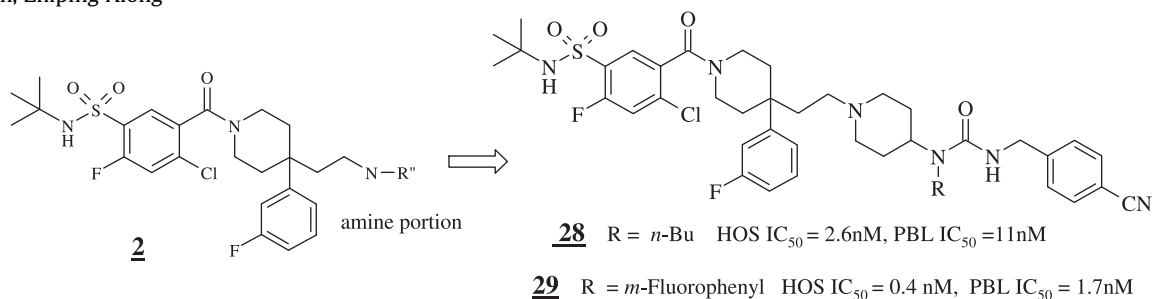


Rosmarinic Acid

Discovery of N-benzyl-N'-(4-pyridinyl)urea CCR5 antagonists as anti-HIV-1 agents (I): Optimization of the amine portion

pp 7397–7400

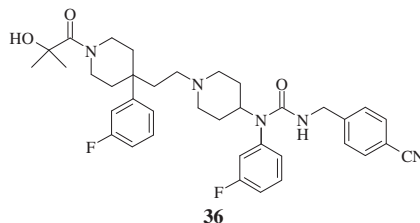
Maosheng Duan*, Jennifer Peckham, Mark Edelstein, Robert Ferris, Wieslaw M. Kazmierski, Andrew Spaltenstein, Pat Wheelan, Zhiping Xiong



Discovery of *N*-benzyl-*N'*-(4-pyridinyl)urea CCR5 antagonists as anti-HIV-1 agents (II): Modification of the acyl portion

pp 7401–7404

Maosheng Duan*, Jennifer Peckham, Mark Edelstein, Robert Ferris, Wieslaw M. Kazmierski, Andrew Spaltenstein, Pat Wheelan, Zhiping Xiong

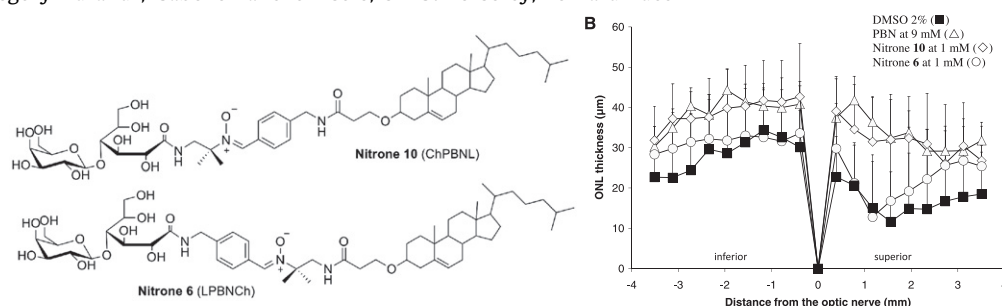
HOS IC₅₀: 8 nM PBL IC₅₀: 8.1 nM

F%: 53 (rat), 45(dog) and 14 (monkey)

Cholesterol-based α -phenyl-*N*-*tert*-butyl nitron derivatives as antioxidants against light-induced retinal degeneration

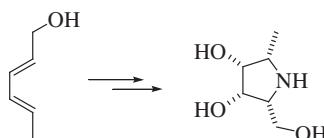
pp 7405–7409

Fanny Choteau, Grégory Durand*, Isabelle Ranchon-Cole, Christine Cercy, Bernard Pucci*

**Synthesis of *all-cis* 2,5-imino-2,5-dideoxy-fucitol and its evaluation as a potent fucosidase and galactosidase inhibitor**

pp 7410–7413

Azime Ak, Sandrine Prudent, Didier LeNouën, Albert Defoin*, Céline Tarnus

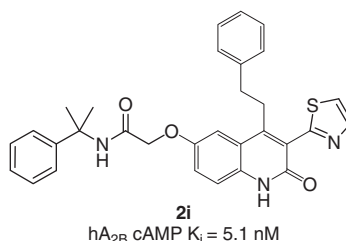


We describe the synthesis of the racemic aminofuranofucitol **3** from sorbic alcohol by nitroso-Diels–Alder as template for the synthesis of GDP-fucose analogues. Evaluation of this pyrrolidine as potent fucosidase and galactosidase inhibitor is discussed.

**Discovery of novel quinolinone adenosine A_{2B} antagonists**

pp 7414–7420

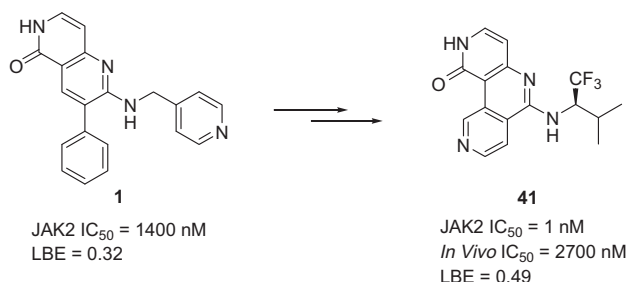
Brian F. McGuinness*, Koc-Kan Ho, Tara M. Stauffer, Laura L. Rokosz, Neelima Mannava, Steven G. Kultgen, Kurt Saionz, Anthony Klon, Weiqing Chen, Hema Desai, W. Lynn Rogers, Maria Webb, Juxing Yin, Yan Jiang, Tailong Li, Hao Yan, Konghua Jing, Shengting Zhang, Kanak Kanti Majumdar, Vikash Srivastava, Samiran Saha

hA_{2B} cAMP K_i = 5.1 nMThe synthesis and SAR of a novel series of A_{2B} receptor antagonists are reported.

The discovery of tricyclic pyridone JAK2 inhibitors. Part 1: Hit to lead

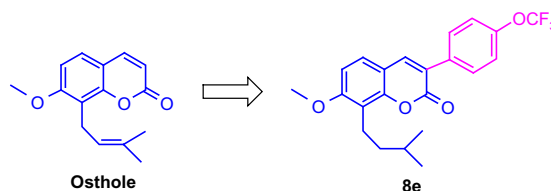
pp 7421–7425

Tony Siu*, Ekaterina S. Kozina, Joon Jung, Craig Rosenstein, Anjili Mathur, Michael D. Altman, Grace Chan, Lin Xu, Eric Bachman, Jan-Rung Mo, Melaney Bouthillette, Thomas Rush, Christopher J. Dinsmore, C. Gary Marshall, Jonathan R. Young

**Discovery of novel osthole derivatives as potential anti-breast cancer treatment**

pp 7426–7428

Lisha You*, Rui An, Xinhong Wang, Yimin Li

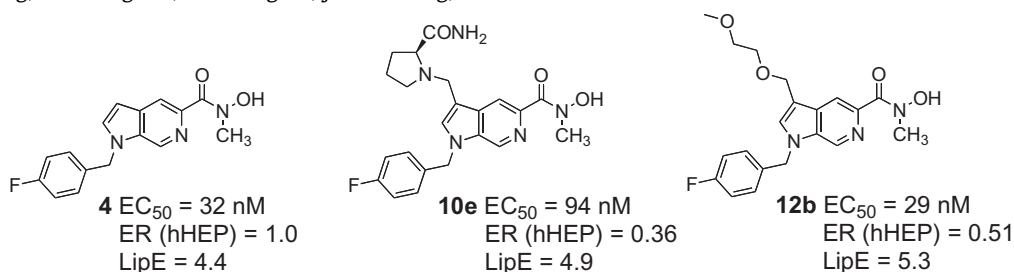


A series of osthole derivatives bearing aryl substituents at 3-position of coumarin, have been prepared and evaluated for their growth inhibitory activity against human breast cancer cell lines MCF-7 and MDA-MB-231. Compound **8e** was found to be the most potent compound with IC₅₀ values of 0.24 μM, 0.31 μM against MCF-7 and MDA-MB-231, respectively, which was improved more than 100-folds compared with its parent compound osthole.

**Azaindole *N*-methyl hydroxamic acids as HIV-1 integrase inhibitors-II. The impact of physicochemical properties on ADME and PK**

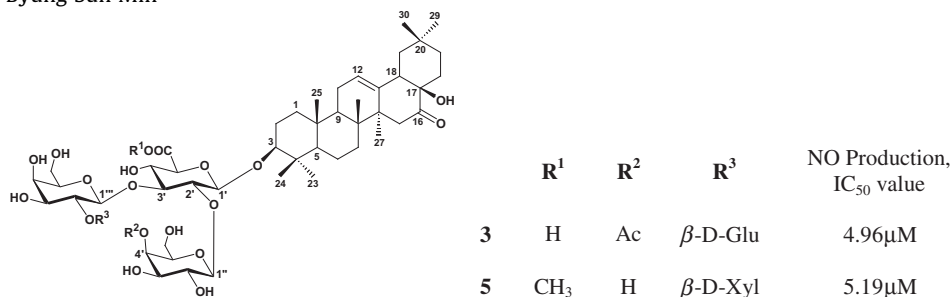
pp 7429–7434

Steven P. Tanis*, Michael B. Plewe*, Ted W. Johnson, Scott L. Butler, Deepak Dalvie, Dorothy DeLisle, Klaus R. Dress, Qiyue Hu, Buwen Huang, Jon E. Kuehler, Atsuo Kuki, Wen Liu, Qinghai Peng, Graham L. Smith, Jim Solowiej, Khanh T. Tran, Hai Wang, Anle Yang, Chunfeng Yin, Xiaoming Yu, Junhu Zhang, Huichun Zhu

**28-Nor-oleanane-type triterpene saponins from *Camellia japonica* and their inhibitory activity on LPS-induced NO production in macrophage RAW264.7 cells**

pp 7435–7439

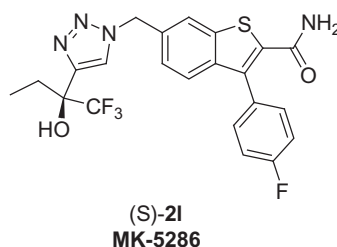
Nguyen Thi Phuong Thao, Tran Manh Hung, To Dao Cuong, Jin Cheol Kim, Eun Hee Kim, Seong Eun Jin, MinKyun Na, Young Mi Lee, Young Ho Kim, Jae Sue Choi, Byung Sun Min*



Potent and selective 5-LO inhibitor bearing benzothiophene pharmacophore: Discovery of MK-5286

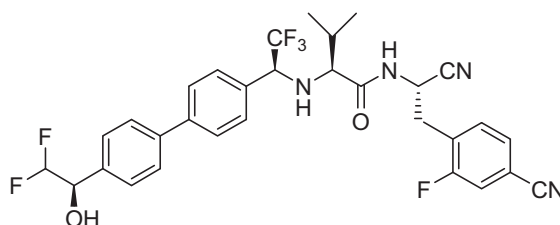
pp 7440–7443

Lianhai Li*, Carl Berthelette, Anne Chateaufneuf, Marc Ouellet, Claudio F. Sturino, Zhaoyin Wang

**Identification of potent and reversible cruzipain inhibitors for the treatment of Chagas disease**

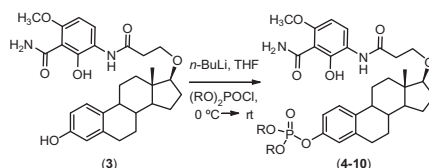
pp 7444–7449

Christian Beaulieu*, Elise Isabel, Angélique Fortier, Frédéric Massé, Christophe Mellon, Nathalie Méthot, Momar Ndao, Deborah Nicoll-Griffith, Doris Lee, Hyeram Park, W. Cameron Black

**3-O-Phosphate ester conjugates of 17-β-O-[1-[2-carboxy-(2-hydroxy-4-methoxy-3-carboxamido)-anilido]ethyl]1,3,5(10)-estratriene as novel bone-targeting agents**

pp 7450–7453

Shama Nasim, Ashish P. Vartak, William M. Pierce Jr., K. Grant Taylor, Ned Smith, Peter A. Crooks*

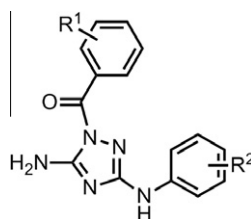


A series of 3-O-phosphorylated analogs (**4–10**) of a novel bone-targeted estradiol analog (**3**) were synthesized after a thorough study of the reaction of **3** with a selection of phosphoryl chlorides under a variety of reaction conditions. Evaluation of these novel phosphate analogs for affinity for hydroxyapatite revealed that they bind with equal or higher affinity when compared to the bone tissue accumulator, tetracycline.

Diamino-1,2,4-triazole derivatives are selective inhibitors of TYK2 and JAK1 over JAK2 and JAK3

pp 7454–7457

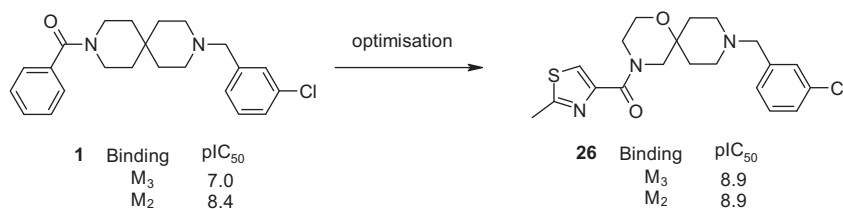
Jeremiah P. Malerich, Jennifer S. Lam, Barry Hart, Richard M. Fine, Boris Klebansky, Mary J. Tanga, Annalisa D'Andrea*



The discovery of new spirocyclic muscarinic M₃ antagonists

pp 7458–7461

Michael J. Stocks*, Lilian Alcaraz, Andrew Bailey, Keith Bowers, David Donald, Helen Edwards, Fraser Hunt, Nicholas Kindon, Garry Pairaudeau, Jill Theaker, Daniel J. Warner

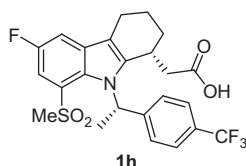


The optimisation of a new series of high potency muscarinic M₃ antagonists, derived from a high throughput screening library hit is described.

Potent and highly selective DP1 antagonists with 2,3,4,9-tetrahydro-1H-carbazole as pharmacophore

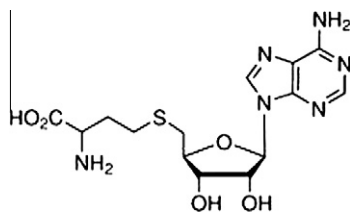
pp 7462–7465

Lianhai Li*, Christian Beaulieu, Marie-Claude Carriere, Danielle Denis, Gillian Greig, Daniel Guay, Gary O'Neill, Robert Zamboni, Zhaoyin Wang

**AdoHcy hydrolase of *Trichomonas vaginalis*: Studies of the effects of 5'-modified adenosine analogues and related 6-N-cyclopropyl derivatives**

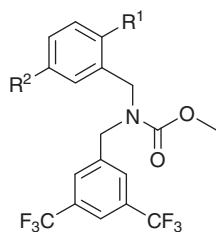
pp 7466–7468

Padraick J. Dornbush, Guillermo Vazquez-Anaya, Ajit Shokar, Saoly Benson, Magdalena Rapp, Stanislaw F. Wnuk, Lisa A. Wrischnik, Kirkwood M. Land*

**Design of a novel class of biphenyl CETP inhibitors**

pp 7469–7472

Zhijian Lu*, Joann B. Napolitano, Ashleigh Theberge, Amjad Ali, Milton L. Hammond, Eugene Tan, Xinchun Tong, Suoyu S. Xu, Melanie J. Latham, Laurence B. Peterson, Matt S. Anderson, Suzanne S. Eveland, Qiu Guo, Sheryl A. Hyland, Denise P. Milot, Ying Chen, Carl P. Sparrow, Samuel D. Wright, Peter J. Sinclair

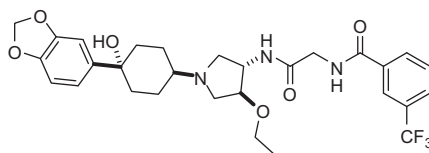


A new class of CETP inhibitors was designed and prepared. These compounds are potent both in vitro and in vivo. The most active compound (**12d**) has shown an ability to raise HDL significantly in transgenic mouse PD model.

Discovery of INCB3344, a potent, selective and orally bioavailable antagonist of human and murine CCR2

pp 7473–7478

Chu-Biao Xue*, Anlai Wang, David Meloni, Ke Zhang, Ling Kong, Hao Feng, Joseph Glenn, Taisheng Huang, Yingxin Zhang, Ganfeng Cao, Rajan Anand, Changsheng Zheng, Michael Xia, Qi Han, D. J. Robinson, Lou Storace, Lixin Shao, Mei Li, Carrie M. Brodmerkel, Maryanne Covington, Peggy Scherle, Sharon Diamond, Swamy Yeleswaram, Kris Vaddi, Robert Newton, Greg Hollis, Steven Friedman, Brian Metcalf



INCB3344

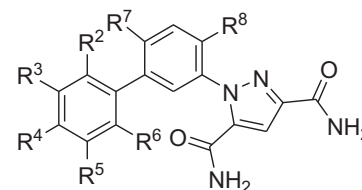
We report the discovery of a novel series of CCR2 antagonists through rational design based on a pharmacophore reported in the literature. SAR studies led to the identification of a potent human and murine CCR2 antagonist INCB3344 with high selectivity and good oral bioavailability in mice.

Discovery of a novel class of biphenyl pyrazole sodium channel blockers for treatment of neuropathic pain

pp 7479–7482

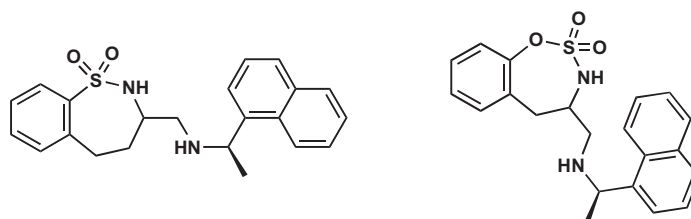
Sriram Tyagarajan*, Prasun K. Chakravarty, Bishan Zhou, Brett Taylor, Ronsar Eid, Michael H. Fisher, William H. Parsons, Mathew J. Wyvratt, Kathryn A. Lyons, Tracy Klatt, Xiaohua Li, Sanjeev Kumar, Brande Williams, John Felix, Birgit T. Priest, Richard M. Brochu, Vivien Warren, McHardy Smith, Maria Garcia, Gregory J. Kaczorowski, William J. Martin, Catherine Abbadie, Erin McGowan, Nina Jochowitz, Ann Weber, Joseph L. Duffy

A series of novel low molecular weight biaryl pyrazole dicarboxamides with good in vitro potency and in vivo efficacy were identified as sodium channel blockers. These state dependent sodium channel blockers were synthesized and evaluated for treatment of neuropathic pain. Compound **20** had outstanding efficacy in the Chung rat spinal nerve ligation (SNL) model of neuropathic pain.

**Design and synthesis of cyclic sulfonamides and sulfamates as new calcium sensing receptor agonists**

pp 7483–7487

Lionel Kiefer, Tatiana Gorjankina, Philippe Dauban, Hélène Faure, Martial Ruat, Robert H. Dodd*



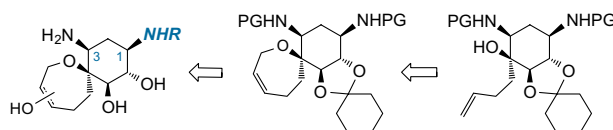
Cyclic sulfonamides and sulfamates as new calcimimetic agents

Cyclic sulfonamides and sulfamates as new calcimimetic agents.

Second generation analogs of rigid 6,7-spiro scaffolds targeting the bacterial ribosome

pp 7488–7492

Christos I. Stathakis, Ioannis Mavridis, Georgia Kythreoti, Athanasios Papakyriakou, Ioannis A. Katsoulis, Thomas Cottin, Panoula Anastasopoulou, Dionisios Vourloumis*



PG= carbamate type protective group

pp 7493–7497

Chemical structures of compounds 17 and 20 are shown. Compound 17 is a complex molecule featuring a cyclopentyl ester, a piperidine ring, a fluorenyl group, and a boronic acid moiety. Compound 20 is a complex molecule featuring a fluorenyl group, a piperidine ring, a sulfonamide group, and a boronic acid moiety.

pp 7498–7502

COc1ccc(cc1)-c2nc(C(=O)NN=C(C)c3cc(OC)c(OC)cc3)cn2

SKI-178

Herein, we report the identification of a novel sphingosine kinase 1-specific small-molecule inhibitor, SKI-178, that is active *in vitro* and *in vivo*.

pp 7503–7506

Oc1cc(Cl)cc(N2C(=O)Nc3ccc(R)cc32)c1

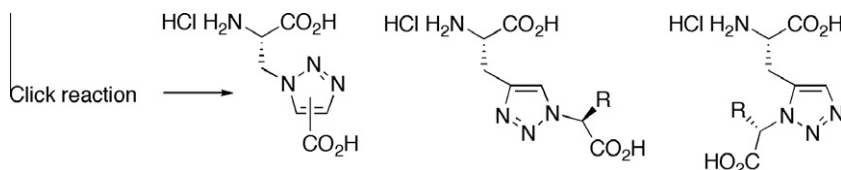
pp 7507–7511

Chemical reaction scheme showing the synthesis of 2-(benzyloxy)-3-(2-hydroxy-3-oxo-4-phenyl-2H-chromen-6-yl)-2H-chromene. The reaction involves 2-phenylacetaldehyde, 2-hydroxy-3-oxo-4-phenyl-2H-chromene-6-carbaldehyde, and 2H-chromene reacting in the presence of InCl_3 at 120°C to form the product.

1,2,3-Triazolyl amino acids as AMPA receptor ligands

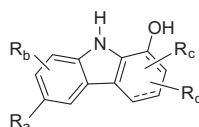
pp 7512–7515

N. J. Stanley, D. Sejer Pedersen, B. Nielsen, T. Kvist, J. M. Mathiesen, H. Bräuner-Osborne, D. K. Taylor, A. D. Abell*

**Synthesis of potent, substituted carbazoles as selective androgen receptor modulators (SARMs)**

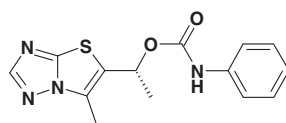
pp 7516–7520

Chris P. Miller*, Pushpal Bhaket, Nagarajan Muthukaman, C. Richard Lyttle, Maysoun Shomali, Kyla Gallacher, Connie Slocum, Gary Hattersley

**The identification of novel orally active mGluR5 antagonist GSK2210875**

pp 7521–7524

Maria Pilla, Michela Andreoli, Michela Tessari, Sonia Delle-Fratte, Adelheid Roth, Sharon Butler, Fiona Brown, Parita Shah, Ezio Bettini, Palmina Cavallini, Roberto Benedetti, Doug Minick, Paul Smith, Ben Tehan, Pier D'Alessandro, Olivier Lorthioir, Catherine Ball, Vincenzo Garzya, Caroline Goodacre, Stephen Watson*



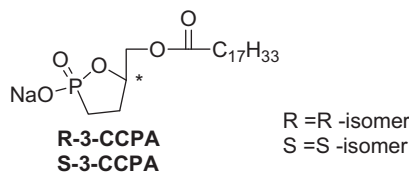
GSK2210875
mGluR5 pIC₅₀ = 7.4
mouse neophobia MED = 5mg/kg p.o.

The identification of the novel orally active mGluR5 antagonist GSK2210875 is described. This MPEP competitive chemotype was identified via HTS and demonstrates intriguing and complex SAR distinct from known mGluR5 ligands. Notably a focus on polar compounds of modest potency but high free brain exposure afforded a compound with oral activity.

Synthesis and pharmacological evaluation of the stereoisomers of 3-carba cyclic-phosphatidic acid

pp 7525–7528

Renuka Gupte, Anjaih Siddam, Yan Lu, Wei Li, Yuko Fujiwara, Nattapon Panupinthu, Truc-Chi Pham, Daniel L. Baker, Abby L. Parrill, Mari Gotoh, Kimiko Murakami-Murofushi, Susumu Kobayashi, Gordon B. Mills, Gabor Tigyi, Duane D. Miller*

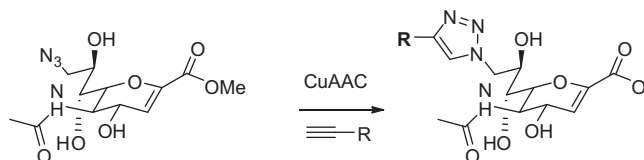


The first stereochemical synthesis and pharmacological evaluation of 18:1 3CCPA is described.

Inhibition of human neuraminidase 3 (NEU3) by C9-triazole derivatives of 2,3-didehydro-*N*-acetyl-neuraminic acid

pp 7529–7533

Yao Zou, Amgad Albohy, Mahendra Sandbhor, Christopher W. Cairo*



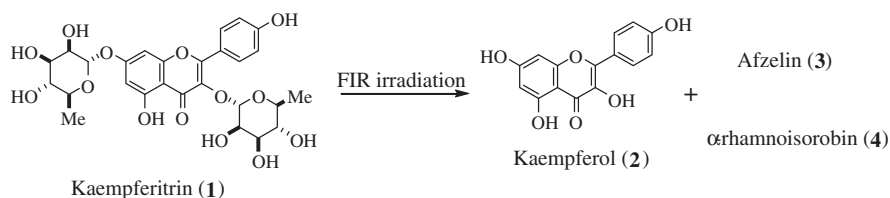
Synthetic inhibitors were used to test the tolerance of the NEU3 active site for modifications of DANA; three potent inhibitors were identified.



Changes in flavonoid content and tyrosinase inhibitory activity in kenaf leaf extract after far-infrared treatment

pp 7534–7536

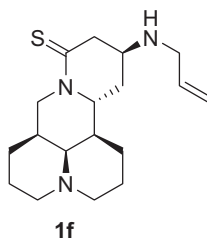
Ho Sik Rho*, Soo Mi Ahn, Bum Chun Lee, Myung Kyoo Kim, Amal Kumar Ghimeray, Cheng Wu Jin, Dong Ha Cho*



Synthesis and in vitro inhibitory activity of matrine derivatives towards pro-inflammatory cytokines

pp 7537–7539

Honggang Hu, Shaozhan Wang, Chunmei Zhang, Liang Wang, Li Ding, Junping Zhang*, Qiuye Wu*

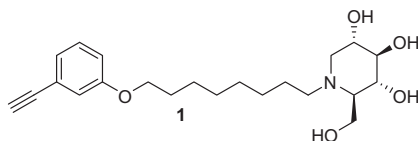


A series of matrine derivatives were synthesized and evaluated for their inhibitory effect on pro-inflammatory cytokines. Compound **1f** was found to be the most potent compound.

N-(8-(3-Ethynylphenoxy)octyl)-1-deoxynojirimycin suppresses growth and migration of human lung cancer cells

pp 7540–7543

Yunxue Zhao*, Wenjia Liu, Ying Zhou, Xiumei Zhang, Paul V. Murphy*

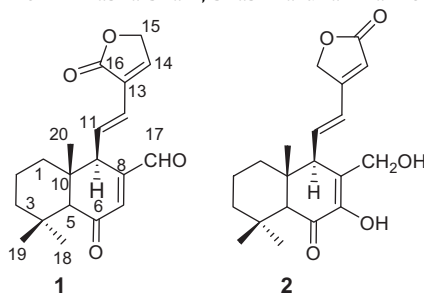


The DNJ derivative **1** inhibits lung cancer cell growth, migration and promotes apoptosis

Two new cytotoxic labdane diterpenes from the rhizomes of *Hedychium coronarium*

pp 7544–7548

G. Suresh, P. Prabhakar Reddy, K. Suresh Babu*, Thokhir Basha Shaik, Shasi Vardhan Kalivendi

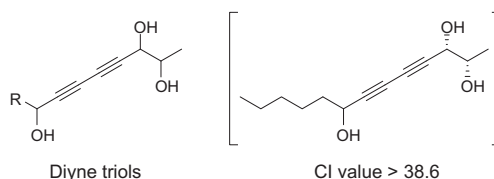


Phytochemical investigation on *Hedychium coronarium* rhizomes yielded two new labdane diterpenes (**1** and **2**) along with 10 known compounds (**3–12**). Cytotoxic activity of the isolates were studied against A-549 (human lung carcinoma) SK-N-SH (human neuroblastoma), MCF-7 (breast cancer) and HeLa (cervical cancer) cell lines.

SAR studies of gymnasterkoreayne derivatives with cancer chemopreventive activities

pp 7549–7552

Dongyun Shin*, Jung-Eun Yang, Saet Byoul Lee, Chu Won Nho



We synthesized diyne triols, derivatives of gymnasterkoreayne and evaluated their cancer chemopreventive activities by chemopreventive index (CI) to reveal structure–activity relationship, and discovered more active compounds than natural diynes.

OTHER CONTENTS**Corrigenda**

pp 7553–7555

*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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