



Bioorganic & Medicinal Chemistry Letters Vol. 19, No. 5, 2009

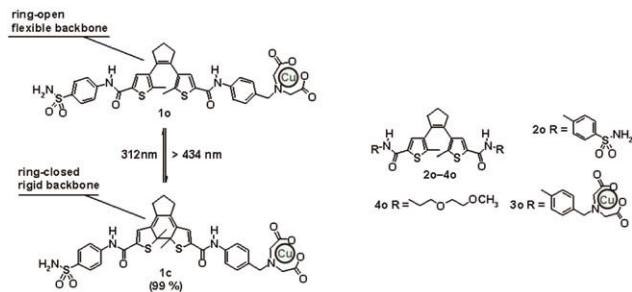
Contents

ARTICLES

Carbonic anhydrase inhibitors: Two-prong versus mono-prong inhibitors of isoforms I, II, IX, and XII exemplified by photochromic *cis*-1,2- α -dithienylethene derivatives

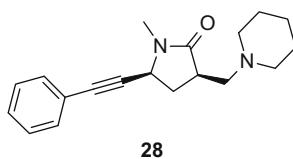
pp 1283–1286

Daniel Vomasta, Alessio Innocenti, Burkhard König, Claudiu T. Supuran *

Gamma-lactams—A novel scaffold for highly potent and selective $\alpha 7$ nicotinic acetylcholine receptor agonists

pp 1287–1291

Albert Enz, Dominik Feuerbach, Mathias U. Frederiksen *, Conrad Gentsch, Konstanze Hurth, Werner Müller, Joachim Nozulak, Bernard L. Roy *



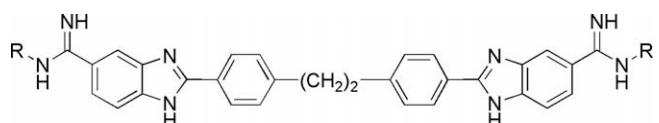
28

$\alpha 7$ pEC₅₀ = 8.0
 $\alpha 3\beta 4$ Selectivity ratio 126
 $\alpha 4\beta 2$ Selectivity ratio 820
 $\alpha 1\beta 1\gamma 8$ Selectivity ratio 1299
5HT₃ Selectivity ratio 126

Synthesis and in vitro activity of dicationic bis-benzimidazoles as a new class of anti-MRSA and anti-VRE agents

pp 1292–1295

Laixing Hu, Maureen L. Kully, David W. Boykin, Norman Abood *

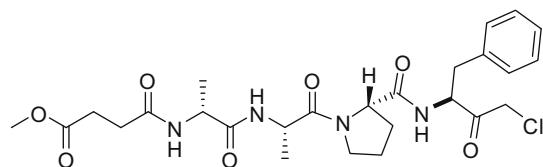


A new class of novel bis-benzimidazole diamidine compounds have been synthesized and evaluated for in vitro antibacterial activities, including MRSA and VRE bacterial strains.

Synthesis and application of MeOSuc-Ala-Ala-Pro-Phe-CH₂Cl as potent proteinase K inhibitor

pp 1296–1300

Anilkumar R. Kore*, Muthian Shanmugasundaram, Quoc Hoang, Mack Kuo, Laura M. Chapman, Helen H. Chen

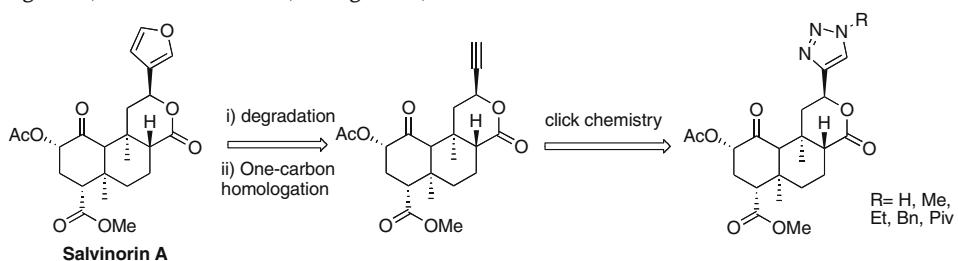


The synthesis and biological evaluation of MeOSuc-Ala-Ala-Pro-Phe-CH₂Cl as potent proteinase K inhibitor is reported.

Synthesis and biological evaluation of C-12 triazole and oxadiazole analogs of salvinorin A

pp 1301–1304

Lu Yang, Wei Xu, Feng Chen, Lee-Yuan Liu-Chen, Zhongze Ma, David Y. W. Lee*

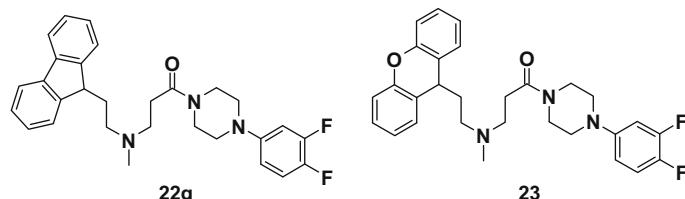


We have carried out the synthesis and biological evaluation of C-12 triazole and oxadiazole analogs of salvinorin A. SAR studies suggest that electronic factors that may affect either the electron density of hydrogen bond acceptor at C-12 or hydrophobic interactions between C-12 moiety and KOPR are critical to salvinorin A templated C-12 analog's affinity for KOPR.

**Discovery of novel non-peptidic β -alanine piperazine amide derivatives and their optimization to achiral, easily accessible, potent and selective somatostatin sst_1 receptor antagonists**

pp 1305–1309

Thomas Troxler*, Konstanze Hurth, Henri Mattes, Mahavir Prashad, Philippe Schoeffter, Daniel Langenegger, Albert Enz, Daniel Hoyer

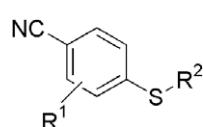


Pharmacophore considerations based on obeline and ergoline somatostatin sst_1 receptor antagonists led to the design of an achiral β -alanine piperazine amide derivative with largely retained sst_1 affinity and selectivity. Systematic optimization of this initial hit afforded highly potent and selective sst_1 receptor antagonists like fluorenyl derivative 22g or xanthenyl derivative 23. These achiral, non-peptidic compounds are easily prepared and show promising PK properties in rodents.

4-(Alkylthio)- and 4-(arylthio)-benzonitrile derivatives as androgen receptor antagonists for the topical suppression of sebum production

pp 1310–1313

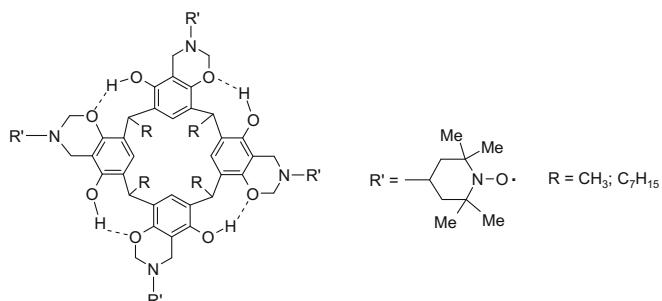
Lorna Mitchell*, Zhi Wang, Lain-Yen Hu, Catherine Kostlan, Matthew Carroll, Danielle Dettling, Daniel Du, David Pocallyko, Kimberly Wade



Antioxidant and antiradical activities of resorcinarene tetranitroxides

pp 1314–1317

Andriy I. Vovk*, Alexander M. Shivanyuk*, Roman V. Bugas, Oxana V. Muzychka, Andriy K. Melnyk

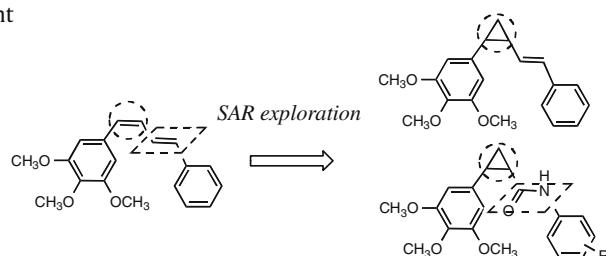


A resorcinarene oxazine bearing four TEMPO fragments at the wide rim exhibit a strong antiradical and antioxidant properties in model systems.

**Synthesis and biological evaluation of *cis*-locked vinylogous combretastatin-A4 analogues: Derivatives with a cyclopropyl-vinyl or a cyclopropyl-amide bridge**

pp 1318–1322

Nancy Ty, Julia Kaffy, Alban Arrault, Sylviane Thoret, Renée Pontikis*, Joelle Dubois, Luc Morin-Allory, Jean-Claude Florent

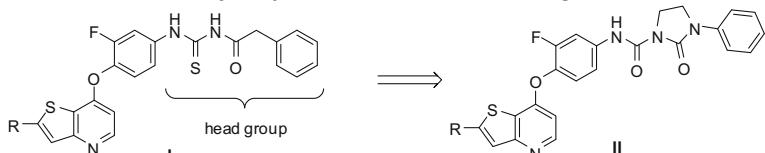


Docking of two representative compounds in the colchicine binding site of tubulin is reported.

**N-(3-fluoro-4-(2-arylthieno[3,2-*b*]pyridin-7-yloxy)phenyl)-2-oxo-3-phenylimidazolidine-1-carboxamides: A novel series of dual c-Met/VEGFR2 receptor tyrosine kinase inhibitors**

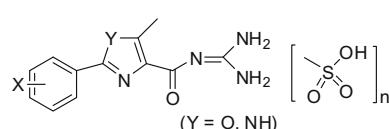
pp 1323–1328

Stéphane Raeppel*, Stephen Claridge, Oscar Saavedra, Frédéric Gaudette, Lijie Zhan, Michael Mannion, Nancy Zhou, Franck Raeppel, Marie-Claude Granger, Ljubomir Isakovic, Robert Déziel, Hannah Nguyen, Normand Beaulieu, Carole Beaulieu, Isabelle Dupont, Marie-France Robert, Sylvain Lefebvre, Marja Dubay, Jubrail Rahil, James Wang, Hélène Ste-Croix, A. Robert Macleod, Jeffrey Besterman, Arkadii Vaisburg

A series of *N*-(3-fluoro-4-(2-arylthieno[3,2-*b*]pyridin-7-yloxy)phenyl)-2-oxo-3-phenylimidazolidine-1-carboxamides (**II**) targeting c-Met and VEGFR2 tyrosine kinases, based on our previous acetylthiourea series (**I**), was designed and synthesized. The new compounds were potent against these two enzymes with IC₅₀ values in the low nanomolar range *in vitro*, possessed favorable pharmacokinetic profiles and showed high efficacy *in vivo* in several human tumor xenograft models in mice.**(2-Aryl-5-methylimidazol-4-ylcarbonyl)guanidines and (2-aryl-5-methyloxazol-4-ylcarbonyl)guanidines as NHE-1 inhibitors**

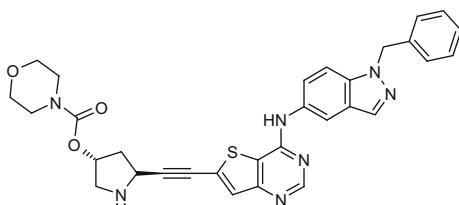
pp 1329–1331

Sunkyung Lee*, Kyu Yang Yi, Sung Jun Youn, Byung Ho Lee, Sung-eun Yoo



The synthesis and evaluation of (2-aryl-5-methylimidazol-4-ylcarbonyl)guanidines and (2-aryl-5-methyloxazol-4-ylcarbonyl)guanidines as NHE-1 inhibitors are described.

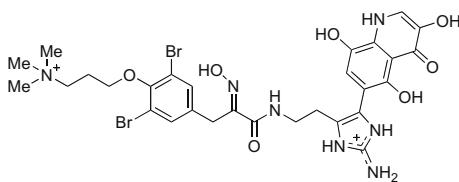
Synthesis and evaluation of aniline headgroups for alkynyl thienopyrimidine dual EGFR/ErbB-2 kinase inhibitors **pp 1332–1336**
 Alex G. Waterson*, Kimberly G. Petrov, Keith R. Hornberger, Robert D. Hubbard, Douglas M. Sammond, Stephon C. Smith, Hamilton D. Dickson, Thomas R. Caferro, Kevin W. Hinkle, Kirk L. Stevens, Scott H. Dickerson, David W. Rusnak, Glenn M. Spehar, Edgar R. Wood, Robert J. Griffin, David E. Uehling



Aniline 'headgroups' were synthesized and incorporated into an alkynyl thienopyrimidine series of EGFR and ErbB-2 inhibitors. Potent inhibition of enzyme activity and cellular proliferation was observed. In certain instances, protein binding was reduced and oral exposure was found to be somewhat improved relative to compounds containing the reference aniline.

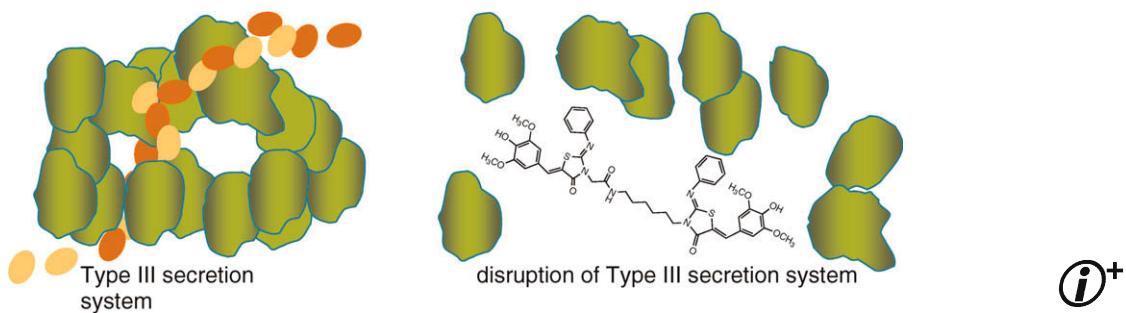
Tyrokeradines A and B, new bromotyrosine alkaloids with an imidazolyl-quinolinone moiety from a Verongid sponge **pp 1337–1339**

Hiroya Mukai, Takaaki Kubota, Kazuki Aoyama, Yuzuru Mikami, Jane Fromont, Jun'ichi Kobayashi*

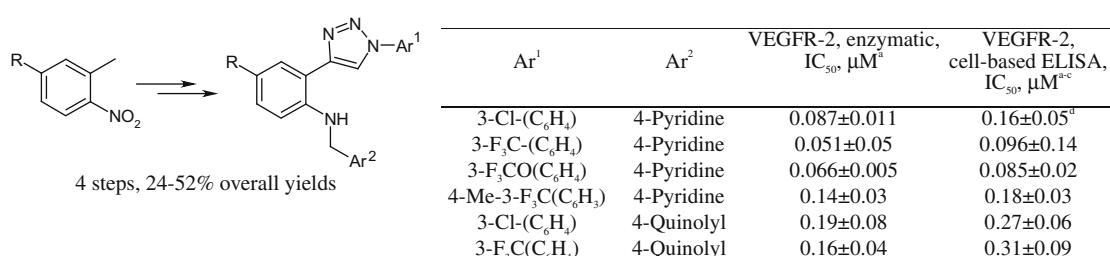


tyrokeradine A (1)

Tethered thiazolidinone dimers as inhibitors of the bacterial type III secretion system **pp 1340–1343**
 Toni Kline*, Kathleen C. Barry, Stona R. Jackson, Heather B. Felise, Hai V. Nguyen, Samuel I. Miller



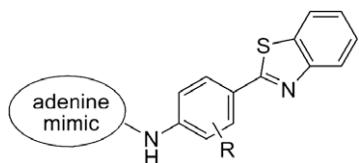
(1,2,3-Triazol-4-yl)benzenamines: Synthesis and activity against VEGF receptors 1 and 2 **pp 1344–1348**
 Alexander S. Kiselyov*, Marina Semenova, Victor V. Semenov



Both synthesis and activity of the novel derivatives of (1,2,3-triazol-4-yl)benzenamines are described. Selected molecules of these series are potent and selective inhibitors of vascular endothelial growth factor receptors I and II (VEGFR-1/2).

N-substituted 2'-(aminoaryl)benzothiazoles as kinase inhibitors: Hit identification and scaffold hopping
 Stefan Tasler, Oliver Müller, Tanja Wieber, Thomas Herz, Rolf Krauss ^{*}, Frank Totzke, Michael H. G. Kubbutat, Christoph Schächtele

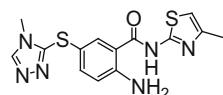
pp 1349–1356



Identification of novel and potent 2-amino benzamide derivatives as allosteric glucokinase activators

pp 1357–1360

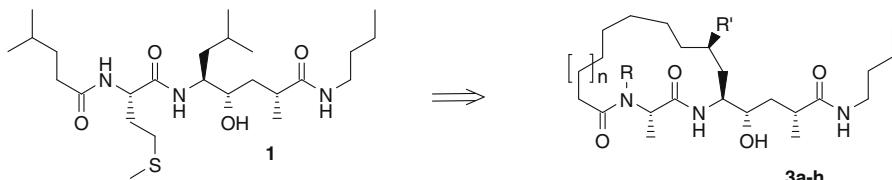
Teruyuki Nishimura ^{*}, Tomoharu Iino, Morihiro Mitsuya, Makoto Bamba, Hitomi Watanabe, Daisuke Tsukahara, Kenji Kamata, Kaori Sasaki, Sumika Ohyama, Hideka Hosaka, Mayumi Futamura, Yasufumi Nagata, Jun-ichi Eiki



The discovery and structure-activity-relationships of novel 2-amino benzamide glucokinase activators are described.

Structure-based design and synthesis of macrocyclic peptidomimetic β -secretase (BACE-1) inhibitors
 Rainer Machauer ^{*}, Siem Veenstra, Jean-Michel Rondeau, Marina Tintelnot-Blomley, Claudia Betschart, Ulf Neumann, Paolo Paganetti

pp 1361–1365



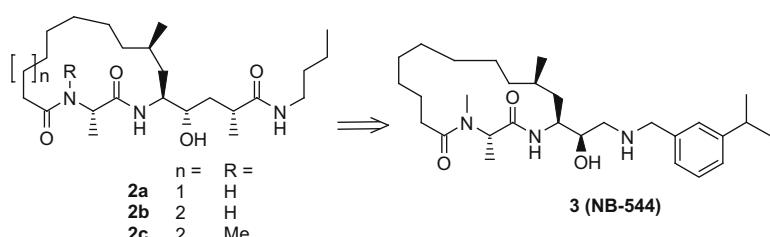
An X-ray co-crystal structure of **1** with BACE-1 allowed the design and syntheses of a series of macrocyclic analogues **3a–h**. These inhibitors show improved potency over their open-chain analogue.



Macrocyclic peptidomimetic β -secretase (BACE-1) inhibitors with activity in vivo

pp 1366–1370

Rainer Machauer ^{*}, Kurt Laumen, Siem Veenstra, Jean-Michel Rondeau, Marina Tintelnot-Blomley, Claudia Betschart, Anne-Lise Jaton, Sandrine Desrayaud, Matthias Staufenbiel, Sabine Rabe, Paolo Paganetti, Ulf Neumann



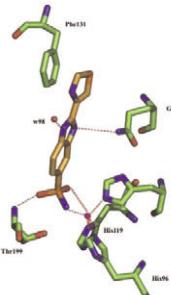
The macrocyclic peptidic BACE-1 inhibitors **2a–c** were optimized to the highly potent and selective inhibitor **3**. This compound shows inhibition of BACE-1 in the brain of APP51/16 transgenic mice, after intravenous application.



A thiabendazole sulfonamide shows potent inhibitory activity against mammalian and nematode α -carbonic anhydrases

pp 1371-1375

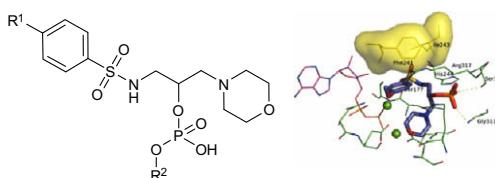
Letizia Crocetti, Alfonso Maresca, Claudia Temperini, Rebecca A. Hall, Andrea Scozzafava, Fritz A. Mühlischlegel, Claudiu T. Supuran*



Design and synthesis of new hydroxyethylamines as inhibitors of *D*-alanyl-*D*-lactate ligase (VanA) and *D*-alanyl-*D*-alanine ligase (DdlB)

pp 1376-1379

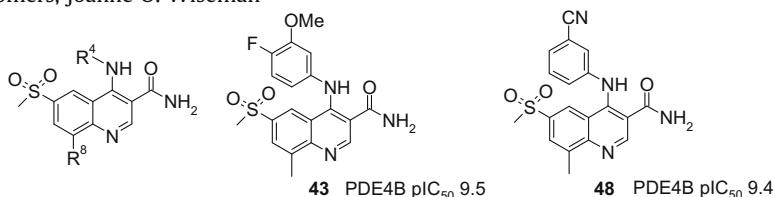
Matej Sova, Gašper Čadež, Samo Turk, Vita Majce, Slovenko Polanc, Sarah Batson, Adrian J. Lloyd, David I. Roper, Colin W. G. Fishwick, Stanislav Goehec*



Quinolines as a novel structural class of potent and selective PDE4 inhibitors: Optimisation for oral administration

pp 1380-1385

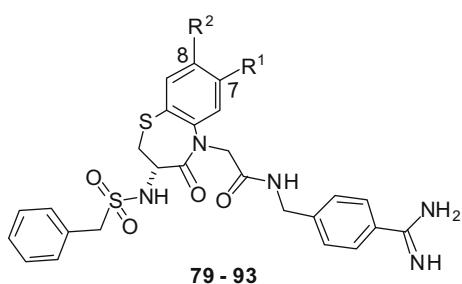
Christopher J. Lunniss*, Anthony W. J. Cooper, Colin D. Eldred, Michael Kranz, Mika Lindvall, Fiona S. Lucas, Margarette Neu, Alex G. S. Preston, Lisa E. Ranshaw, Alison J. Redgrave, J. Ed Robinson, Tracy J. Shipley, Yemisi E. Solanke, Don O. Somers, Joanne O. Wiseman



A series of quinoline-3-carboxamides has been identified as potent inhibitors of PDE4. The SAR has been explored and these studies have highlighted compounds **43** and **48** which show good potency, selectivity and rat PK suitable for oral dosing. The crystal structure of an example quinoline bound into the active site of PDE4 is also described.

Design, synthesis, and biological evaluation of 1,5-benzothiazepine-4-one derivatives targeting factor VIIa/tissue factor pp 1386–1391

Erwan Ayral, Philippe Gloanec*, Gilbert Bergé, Guillaume de Nanteuil, Philippe Mennecier, Alain Rupin, Tony L. Verbeuren, Pierre Fulcrand, Jean Martinez, Jean-François Hernandez*

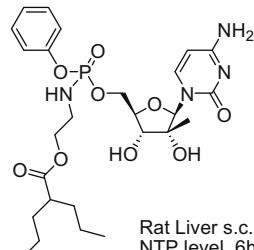


Synthesis and evaluation of novel phosphoramidate prodrugs of 2'-methyl cytidine as inhibitors of hepatitis c virus NS5B polymerase

pp 1392–1395

Monica Donghi*, Barbara Attenni, Cristina Gardelli, Annalise Di Marco, Fabrizio Fiore, Claudio Giuliano, Ralph Laufer, Joseph F. Leone, Vincenzo Pucci, Michael Rowley, Frank Narjes

The synthesis and SAR of phosphoramidate prodrugs of 2'-methyl cytidine as inhibitors of HCV NS5B polymerase is reported.

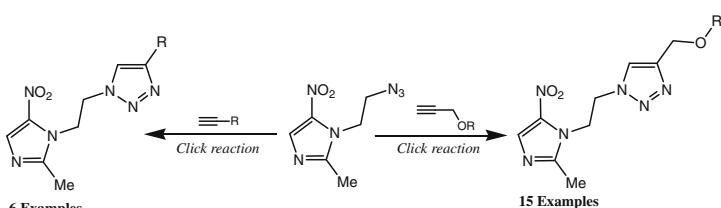


Rat Liver s.c. (1.5 μ mol/kg)
NTP level, 6h: 7.1 nmol/g

Synthesis and antibacterial activity evaluation of metronidazole–triazole conjugates

pp 1396–1398

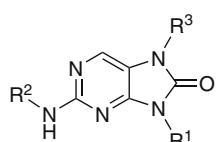
Beena, Nitin Kumar, Rajesh K. Rohilla, N. Roy, Diwan S. Rawat*



Synthesis and SAR studies of trisubstituted purinones as potent and selective adenosine A_{2A} receptor antagonists

pp 1399–1402

Yuefei Shao*, Andrew G. Cole, Marc-Raleigh Brescia, Lan-Ying Qin, Jingqi Duo, Tara M. Stauffer, Laura L. Rokosz, Brian F. McGuinness, Ian Henderson

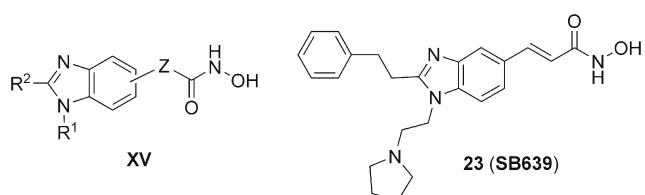


A series of trisubstituted purinones was synthesized and evaluated as A_{2A} receptor antagonists. The A_{2A} structure–activity relationships at the three substituted positions were studied and selectivity against the A₁ receptor was investigated.

N-Hydroxy-1,2-disubstituted-1H-benzimidazol-5-yl acrylamides as novel histone deacetylase inhibitors: Design, synthesis, SAR studies, and in vivo antitumor activity

pp 1403–1408

Haishan Wang*, Niefang Yu, Hongyan Song, Dizhong Chen, Yong Zou, Weiping Deng, Pek Ling Lye, Joyce Chang, Melvin Ng, Stéphanie Blanchard, Eric T. Sun, Kanda Sangthongpitag, Xukun Wang, Kee Chuan Goh, Xiaofeng Wu, Hwee Hoon Khng, Lijuan Fang, Siok Kun Goh, Wai Chung Ong, Zahid Bonday, Walter Stünkel, Anders Poulsen, Michael Entzeroth



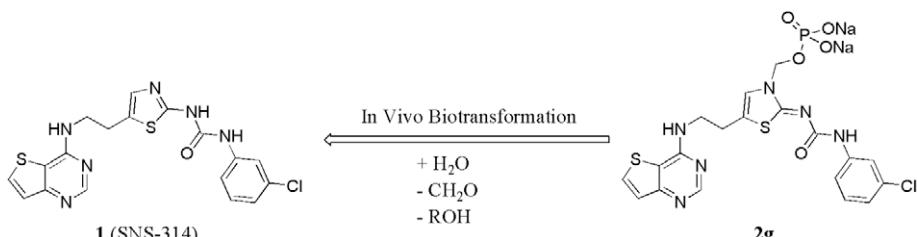
SAR has been established for R¹, R² and Z of benzimidazole-based HDAC inhibitors (XV). Compound 23 (SB639) is a promising lead for further optimization towards a clinical candidate.

Water-soluble prodrugs of an Aurora kinase inhibitor

pp 1409–1412

Johan D. Oslob*, Stacey A. Heumann, Chul H. Yu, Darin A. Allen, Subramanian Baskaran, Minna Bui, Erlie Delarosa, Amy D. Fung, Ahmad Hashash, Jonathan Hau, Sheryl Ivy, Jeffrey W. Jacobs, Willard Lew, Jack Maung, Robert S. McDowell, Sean Ritchie, Michael J. Romanowski, Jeffrey A. Silverman, Wenjin Yang, Min Zhong, Tarra Fuchs-Knotts

In vitro and in vivo properties of prodrug derivatives of the Aurora kinase inhibitor SNS-314 are described.



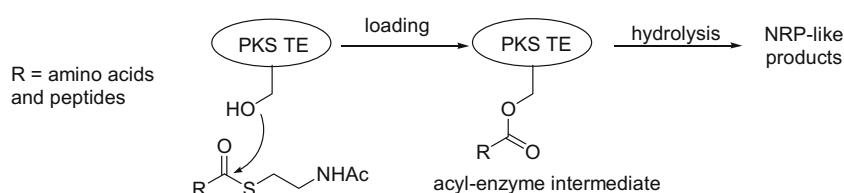
Aqueous Solubility: 0.014 mg/mL

Aqueous Solubility: 4.70 mg/mL

Polyketide synthase thioesterases catalyze rapid hydrolysis of peptidyl thioesters

pp 1413–1415

Meng Wang, Peter Opare, Christopher N. Boddy*

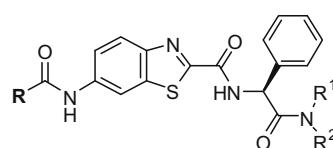


Polyketide synthase thioesterases hydrolyze non-ribosomal peptide-like substrates more rapidly than native polyketide-like substrates.

**Discovery of benzothiazole derivatives as efficacious and enterocyte-specific MTP inhibitors**

pp 1416–1420

Chi B. Vu*, Jill C. Milne, David P. Carney, Jeffrey Song, Wendy Choy, Philip D. Lambert, David J. Gagne, Michael Hirsch, Angela Cote, Meghan Davis, Elden Lainez, Nekeya Meade, Karl Normington, Michael R. Jirousek, Robert B. Perni



A series of benzothiazole derivatives is shown to be potent MTP inhibitors, with some showing oral activity in a mice diet-induced obesity model.

β-Lactam-based approach for the chemical programming of aldolase antibody 38C2

pp 1421–1424

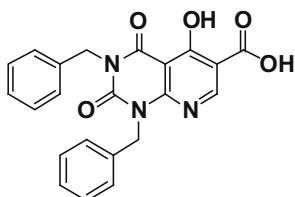
Julia I. Gavrilyuk, Ulrich Wuellner, Carlos F. Barbas III*



A heterocyclic molecule with significant activity against dengue virus

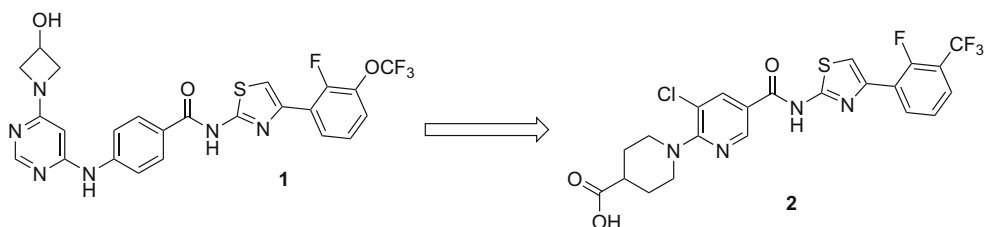
pp 1425–1427

Vasu Nair*, Guochen Chi, Qingning Shu, Justin Julander, Donald F. Smee

**The identification of orally bioavailable thrombopoietin agonists**

pp 1428–1430

Michael J. Munchhoff*, Amy S. Antipas, Laura C. Blumberg, William H. Brissette, Matthew F. Brown, Jeffrey M. Casavant, Jonathan L. Doty, James Driscoll, Thomas M. Harris, Lilli A. Wolf-Gouveia, Christopher S. Jones, Qifang Li, Robert G. Linde, Paul D. Lira, Anthony Marfat, Eric McElroy, Mark Mitton-Fry, Sandra P. McCurdy, Lawrence A. Reiter, Sharon L. Ripp, Andrei Shavnya, Lisa M. Thomasco, Kristen A. Trenova

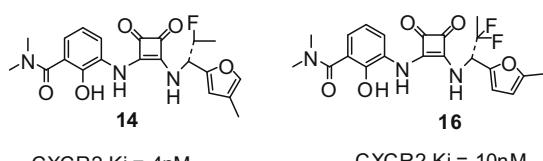


Progress towards the identification of bioavailable drug-like thrombopoietin agonist is reported.

Fluoroalkyl α side chain containing 3,4-diamino-cyclobutenediones as potent and orally bioavailable CXCR2–CXCR1 dual antagonists

pp 1431–1433

Purakkattel Biju*, Arthur G. Taveras, Michael P. Dwyer, Younong Yu, Jianhua Chao, R. William Hipkin, Xuedong Fan, Diane Rindgen, Jay Fine, Daniel Lundell

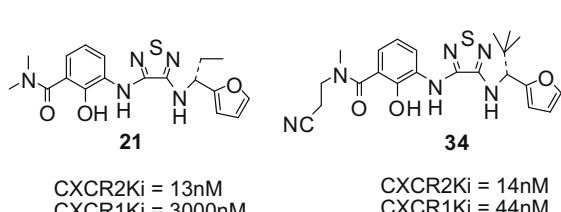


A series of potent and orally bioavailable 3,4-diaminocyclobutenediones with various fluoroalkyl groups as α side chain were prepared and found to show significant improvements in the binding affinities towards both CXCR2 and CXCR1 receptors.

3,4-Diamino-1,2,5-thiadiazole as potent and selective CXCR2 antagonists

pp 1434–1437

Purakkattel Biju*, Arthur G. Taveras, Younong Yu, Junying Zheng, R. William Hipkin, James Fossetta, Xuedong Fan, Jay Fine, Daniel Lundell

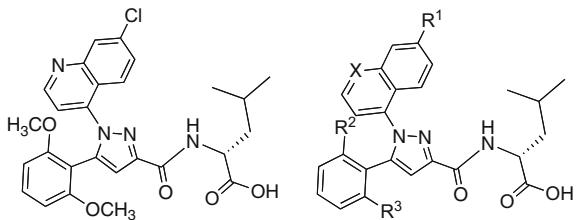


A novel series of potent and selective 3,4-diamino-1,2,5-thiadiazoles were prepared as CXCR2 receptor antagonists.

The identification of nonpeptide neurotensin receptor partial agonists from the potent antagonist SR48692 using a calcium mobilization assay

pp 1438–1441

James B. Thomas*, Hernán Navarro, Keith R. Warner, Brian Gilmour

Replacing 2-aminoadamantane-2-carboxylic acid in the antagonist SR48692 (**1a**) with the amino acid L-leucine provides partial agonists (**3a**) for the NTR1 receptor.

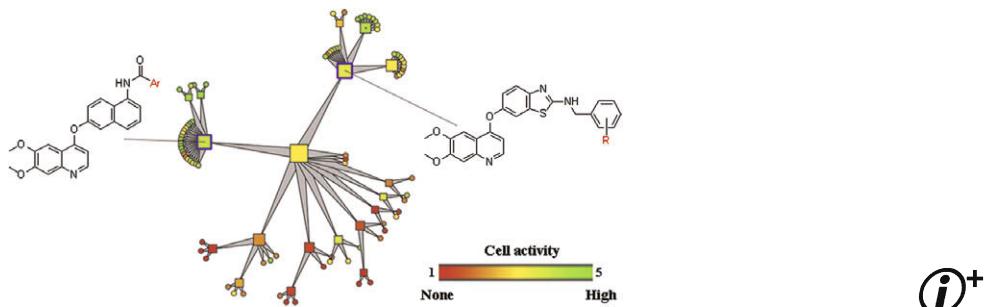
3a: NTR1 Partial agonist
 $EC_{50} = 67 \pm 26 \text{ nM}$
 $E_{\max} = 54\%$

Survey of Agonist SAR

Small molecules with potent osteogenic-inducing activity in osteoblast cells

pp 1442–1445

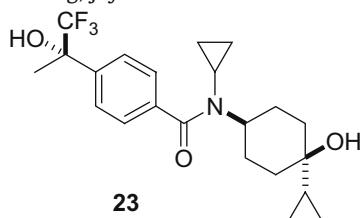
Chun-Ya E. Han, Youping Wang, Longchuan Yu, David Powers, Xiaoling Xiong, Violeta Yu, Yen Nguyen, David J. St. Jean Jr., Philip Babij*



Optimization of novel di-substituted cyclohexylbenzamide derivatives as potent 11 β -HSD1 inhibitors

pp 1446–1450

Dustin L. McMinn*, Yosup Rew, Athena Sudom, Seb Caille, Michael DeGraffenreid, Xiao He, Randall Hungate, Ben Jiang, Juan Jaen, Lisa D. Julian, Jacob Kaizerman, Perry Novak, Daqing Sun, Hua Tu, Stefania Ursu, Nigel P. C. Walker, Xuelei Yan, Qiuping Ye, Zhulun Wang, Jay P. Powers

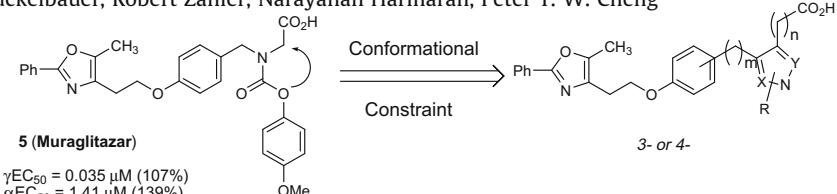


Novel 4,4-disubstituted cyclohexylbenzamide inhibitors of 11 β -HSD1 were optimized to account for liabilities relating to in vitro pharmacokinetics, cytotoxicity and protein related shifts in potency. A representative compound showing favorable in vivo pharmacokinetics was found to be an efficacious inhibitor of 11 β -HSD1 in a rat pharmacodynamic model ($ED_{50} = 10 \text{ mg/Kg}$).

Design, synthesis and structure–activity relationships of azole acids as novel, potent dual PPAR α/γ agonists

pp 1451–1456

Hao Zhang, Denis E. Ryono, Pratik Devasthale, Wei Wang, Kevin O’Malley, Dennis Farrelly, Liqun Gu, Thomas Harrity, Michael Cap, Cuixia Chu, Kenneth Locke, Litao Zhang, Jonathan Lippy, Lori Kunselman, Nathan Morgan, Neil Flynn, Lisa Moore, Vinayak Hosagrahara, Lisa Zhang, Pathanjali Kadiyala, Carrie Xu, Arthur M. Doweyko, Aneka Bell, Chiehying Chang, Jodi Muckelbauer, Robert Zahler, Narayanan Hariharan, Peter T. W. Cheng*

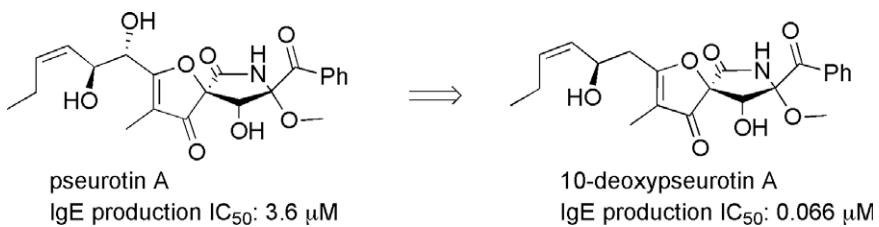


5 (Muraglitazar)
 $\gamma EC_{50} = 0.035 \mu\text{M} (107\%)$
 $\alpha EC_{50} = 1.41 \mu\text{M} (139\%)$

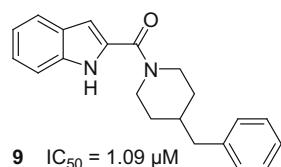
The design, synthesis and structure–activity relationships of a novel series of N-phenyl-substituted pyrrole, 1,2-pyrazole and 1,2,3-triazole acid analogs as PPAR α/γ ligands are outlined. The triazole acid analogs **3f** and **4f** were identified as potent dual PPAR α/γ agonists both in binding and functional assays in vitro. The 1,3-alkoxybenzyl triazole acetic acid analog **3f** showed excellent glucose and triglyceride lowering in diabetic *db/db* mice.

Pseurotin A and its analogues as inhibitors of immunoglobulin E production

pp 1457–1460

Minoru Ishikawa ^{*}, Tomohisa Ninomiya, Hirotomo Akabane, Nobuaki Kushida, Go Tsujiuchi, Makoto Ohyama, Shuichi Gomi, Keiko Shito, Takashi Murata**Investigations of SCIO-469-like compounds for the inhibition of p38 MAP kinase**

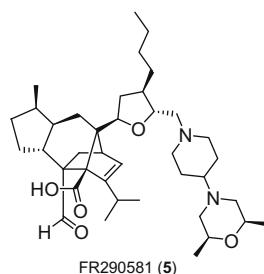
pp 1461–1464

Stefan Laufer ^{*}, Frank Lehmann

Heterocyclic 2-amides were identified as novel lead structures for p38 MAP kinase inhibition, and a SAR analysis of 25 compounds was executed.

**FR290581, a novel sordarin derivative: Synthesis and antifungal activity**

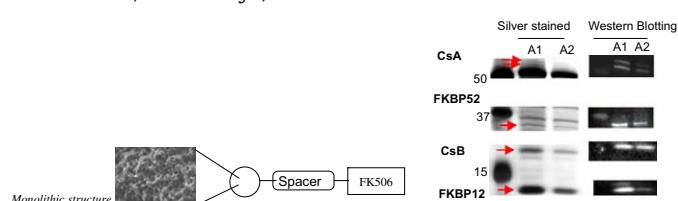
pp 1465–1468

Tadaatsu Hanadate ^{*}, Masaki Tomishima, Nobuyuki Shiraishi, Daisuke Tanabe, Hiroshi Morikawa, David Barrett, Satoru Matsumoto, Kazumi Ohtomo, Katsuyuki Maki

We have discovered the novel sordarin derivative FR290581, which exhibited superior activity, a good pharmacokinetic profile and good in vivo activity.

**Improvement of monolithic solid material by utilization of spacer for identification of the target using affinity resins**

pp 1469–1472

Emiko Iwaoka, Tomoko Mori, Tadashi Shimizu, Ken Hosoya, Akito Tanaka ^{*}

Introduction effects of spacer to monolithic solid material on identification of specific binding protein was analyzed using benzenesulfonamide as a bait, which exhibited introduction of ω -substituted heptanoic acid as spacer enabled affinity resins effectively to capture carbonic anhydrase type 2 from rat brain lysate with little amount of non-specific protein absorption. The same material with the optimized spacer bearing FK506 successfully captured FKBP52, calcineurin A and B at silver stained level as well, while that without spacer has failed.

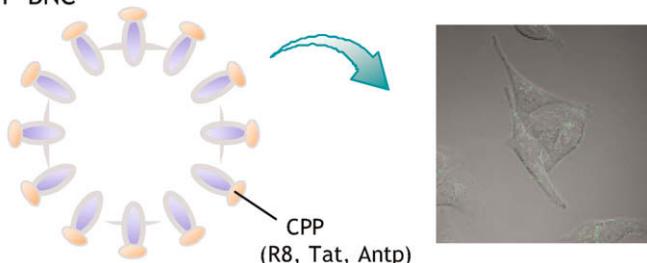


Construction of arginine-rich peptide displaying bionanocapsules

pp 1473–1476

Takuya Shishido, Daisaku Yonezawa, Kiyokazu Iwata, Tsutomu Tanaka, Chiaki Ogino, Hideki Fukuda, Akihiko Kondo *

CPP-BNC

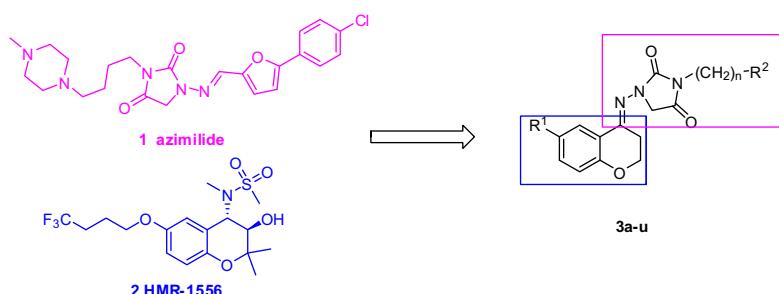


Bionanocapsules displaying cell-penetrating peptide (CPP-BNC) was constructed. CPP-BNC was efficiently internalized into various cell lines in a short time, compared with original BNC.

Molecular hybridization, synthesis, and biological evaluation of novel chroman I_{Kr} and I_{Ks} dual blockers

pp 1477–1480

Lupei Du, Minyong Li, Qian Yang, Yiqun Tang, Qidong You *, Lin Xia

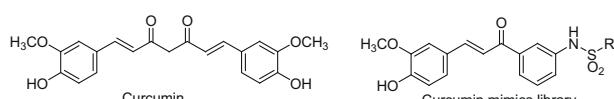


On the rationale of molecular hybridization of azimilide and HMR-1556, a novel series of I_{Kr} and I_{Ks} dual blockers were designed, synthesized and evaluated.

**Synthesis of sulfonyl curcumin mimics exerting a vasodilatation effect on the basilar artery of rabbits**

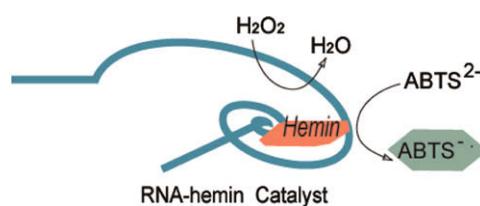
pp 1481–1483

Chan Mug Ahn, Byong-Gon Park, Ho Bum Woo, Jungyeob Ham, Woon-Seob Shin *, Seokjoon Lee *

**In vitro selection of hemin-binding catalytic RNA**

pp 1484–1487

Mingzhe Liu, Takuma Kagahara, Hiroshi Abe, Yoshihiro Ito *



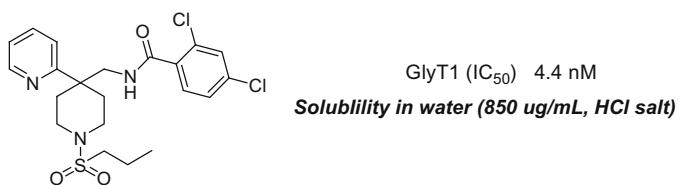
In vitro selection of catalytic RNA with peroxidase activity is reported.



Discovery of *N*-{[1-(propylsulfonyl)-4-pyridin-2-ylpiperidin-4-yl]methyl}benzamides as novel, selective and potent GlyT1 inhibitors

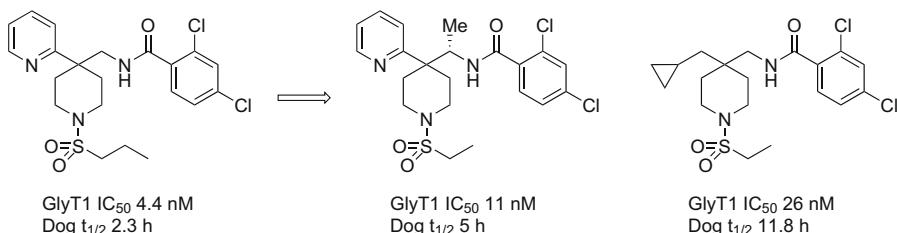
pp 1488–1491

Zhijian Zhao*, William H. Leister, Julie A. O'Brien, Wei Lemaire, David L. Williams Jr., Marlene A. Jacobson, Cyrille Sur, Gene G. Kinney, Doug J. Pettibone, Philip R. Tiller, Sheri Smith, George D. Hartman, Craig W. Lindsley, Scott E. Wolkenberg

**Discovery of GlyT1 inhibitors with improved pharmacokinetic properties**

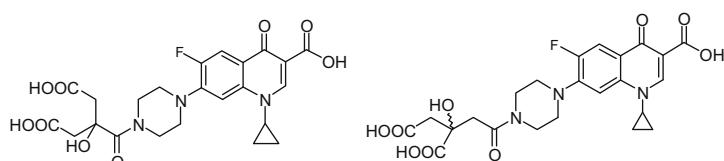
pp 1492–1495

Scott E. Wolkenberg*, Zhijian Zhao, David D. Wisnoski, William H. Leister, Julie O'Brien, Wei Lemaire, David L. Williams Jr., Marlene A. Jacobson, Cyrille Sur, Gene G. Kinney, Doug J. Pettibone, Philip R. Tiller, Sheri Smith, Christopher Gibson, Bennett K. Ma, Stacey L. Polksky-Fisher, Craig W. Lindsley, George D. Hartman

**Synthesis of citrate–ciprofloxacin conjugates**

pp 1496–1498

Siti R Md-Saleh, Emily C. Chilvers, Kevin G. Kerr, Stephen J. Milner, Anna M. Snelling, Jan P. Weber, Gavin H. Thomas, Anne-Kathrin Duhme-Klair*, Anne Routledge*

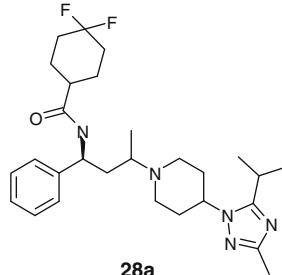


Citrate-functionalized ciprofloxacin conjugates have been synthesized and antimicrobial activities against clinically-relevant bacteria determined. Uptake mechanisms were investigated using wild-type and *ompF* deletion strains of *Escherichia coli* K-12.

1-Amido-1-phenyl-3-piperidinylbutanes – CCR5 antagonists for the treatment of HIV: Part 2

pp 1499–1503

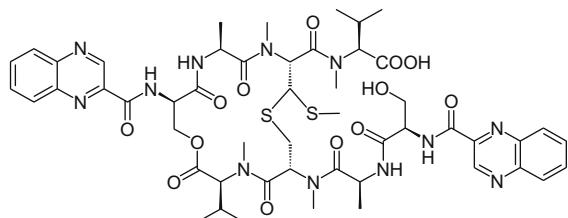
Christopher G. Barber*, David C. Blakemore, Jean-Yves Chiva, Rachel L. Eastwood, Donald S. Middleton, Kerry A. Paradowski



Optimisation of a series of compound 4-piperidinyltriazoles led to the identification of 28a which showed good whole cell antiviral activity, excellent selectivity over the hERG ion channel and complete oral absorption.

Structure–activity studies of echinomycin antibiotics against drug-resistant and biofilm-forming *Staphylococcus aureus* and *Enterococcus faecalis* **pp 1504–1507**

Aaron M. Socha, Kerry L. LaPlante, David J. Russell, David C. Rowley *



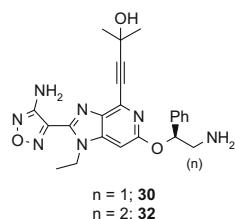
Four echinomycin antibiotics, including the new compound depsiechinoserine, were evaluated against antibiotic-resistant and biofilm-forming strains of *Staphylococcus aureus* and *Enterococcus faecalis*. Structure–activity relationships are presented.



Aminofurazans as potent inhibitors of AKT kinase

Meagan B. Rouse *, Mark A. Seefeld, Jack D. Leber, Kenneth C. McNulty, Lihui Sun, William H. Miller, ShuYun Zhang, Elisabeth A. Minthorn, Nestor O. Concha, Anthony E. Choudhry, Michael D. Schaber, Dirk A. Heerding

pp 1508–1511



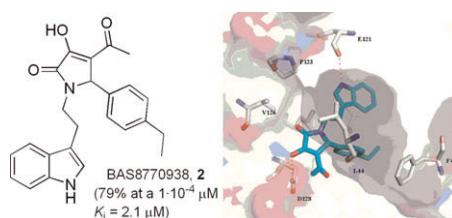
AKT inhibitors containing an imidazopyridine aminofurazan scaffold have been optimized. We have previously disclosed identification of the AKT inhibitor GSK690693, which has been evaluated in clinical trials in cancer patients. Herein we describe recent efforts focusing on investigating a distinct region of this scaffold that have afforded compounds (**30** and **32**) with comparable activity profiles to that of GSK690693.



Indolyl-pyrrolone as a new scaffold for Pim1 inhibitors

Stefania Olla, Fabrizio Manetti, Emmanuele Crespan, Giovanni Maga, Adriano Angelucci, Silvia Schenone, Mauro Bologna, Maurizio Botta *

pp 1512–1516



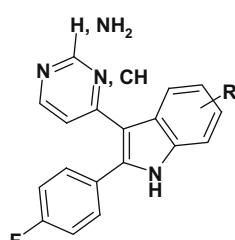
Indolyl-pyrrolone derivatives identified by structure-based pharmacophore models were found to inhibit activity of Pim1 in an enzymatic assay, leading to the identification of a new scaffold for Pim1 inhibition.



Synthesis and biological activity of anticoccidial agents: 2,3-diaryllindoles

Andrew Scribner *, Joseph A. Moore III, Gilles Ouvry, Michael Fisher, Matthew Wyvrott, Penny Leavitt, Paul Liberator, Anne Gurnett, Chris Brown, John Mathew, Donald Thompson, Dennis Schmaltz, Tesfaye Biftu

pp 1517–1521

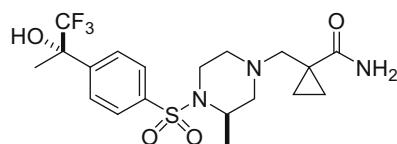


In this study, we present the synthesis and biological activity of 2,3-diaryllindoles, whose antiparasitic activity against *Eimeria* is due to inhibition of a parasite specific cGMP-dependent protein kinase (PKG). From this series, several compounds showed subnanomolar in vitro activity and significant in vivo activity.

Synthesis and optimization of arylsulfonylpiperazines as a novel class of inhibitors of 11 β -hydroxysteroid dehydrogenase type 1 (11 β -HSD1)

pp 1522–1527

Daqing Sun*, Zhulun Wang, Mario Cardozo, Rebekah Choi, Michael DeGraffenreid, Yongmei Di, Xiao He, Juan C. Jaen, Marc Labelle, Jinsong Liu, Ji Ma, Shichang Miao, Athena Sudom, Liang Tang, Hua Tu, Stefania Ursu, Nigel Walker, Xuelei Yan, Qiuping Ye, Jay P. Powers



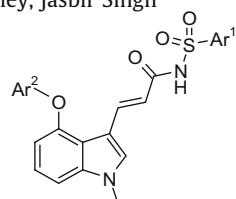
(S)-28

The synthesis and SAR of a series of arylsulfonylpiperazine inhibitors of 11 β -HSD1 are described. Optimization rapidly led to potent, selective, and orally bioavailable inhibitors demonstrating efficacy in a cynomolgus monkey ex vivo enzyme inhibition model.

3-Acrylamide-4-aryloxyindoles: Synthesis, biological evaluation and metabolic stability of potent and selective EP₃ receptor antagonists

pp 1528–1531

Nian Zhou, Wayne Zeller, Jun Zhang, Emmanuel Onua, Alex S. Kiselyov, Jose Ramirez, Guðrún Palsdóttir, Guðrún Halldorsdóttir, Þorkell Andrésson, Mark E. Gurney, Jasbir Singh*

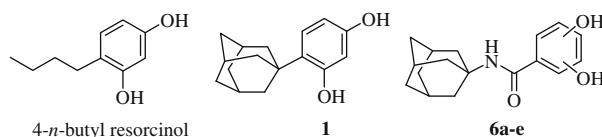


A series of potent and selective EP₃ receptor antagonists are described. Utilizing a pharmacophore model developed for the EP₃ receptor, a series of 3,4-disubstituted indoles were found to be efficient ligands for this target. These compounds showed high selectivity over IP, FP and other EP receptors. An optimized molecule **7c** featured a sound profile and potency in the functional rat and human platelet aggregation assays.

Studies on depigmenting activities of dihydroxyl benzamide derivatives containing adamantine moiety

pp 1532–1533

Ho Sik Rho*, Heung Soo Baek, Soo Mi Ahn, Jae Won Yoo, Duck Hee Kim, Han Gon Kim



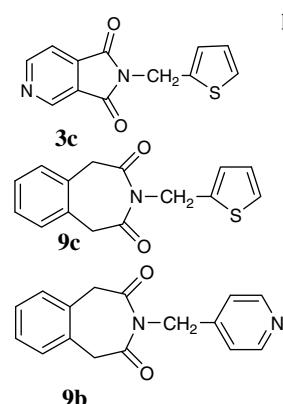
Dihydroxyl benzamide derivatives **6a–e** significantly suppressed the cellular melanin formation without tyrosinase inhibitory activities.

Microwave-assisted synthesis of N-substituted cyclic imides and their evaluation for anticancer and anti-inflammatory activities

pp 1534–1538

Sham M. Sondhi*, Reshma Rani, Partha Roy, S. K. Agrawal, A. K. Saxena

A number of N-substituted cyclic imides have been synthesized and screened for anticancer. **9c** exhibited good anticancer activity against colon (COLO-205) cancer and **9b** exhibited good anti-inflammatory activity.



OTHER CONTENTS

Corrigendum**p 1539****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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