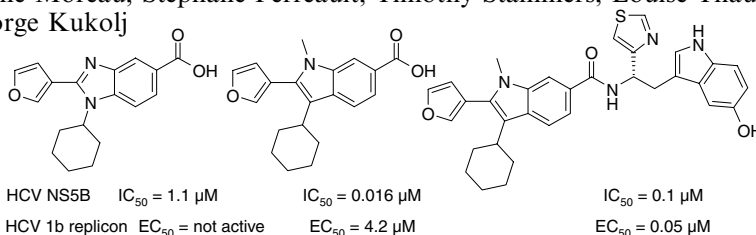


Contents

ARTICLES

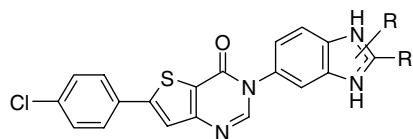
Improved replicon cellular activity of non-nucleoside allosteric inhibitors of HCV NS5B polymerase: From benzimidazole to indole scaffolds pp 4987–4993

Pierre L. Beaulieu,* James Gillard, Darren Bykowski, Christian Brochu, Nathalie Dansereau, Jean-Simon Duceppe, Bruno Haché, Araz Jakalian, Lisette Lagacé, Steven LaPlante, Ginette McKercher, Elaine Moreau, Stéphane Perreault, Timothy Stammers, Louise Thauvette, Jeff Warrington and George Kukolj



Novel benzimidazole-based MCH R1 antagonists pp 4994–5000

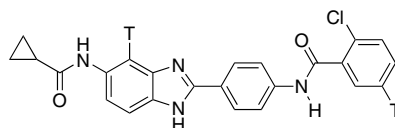
Andrew J. Carpenter,* Kamal A. Al-Barazanji, Kevin K. Barvian, Michael J. Bishop, Christy S. Britt, Joel P. Cooper, Aaron S. Goetz, Mary K. Grizzle, Donald L. Hertzog, Diane M. Ignar, Ronda O. Morgan, Gregory E. Peckham, Jason D. Speake and Will R. Swain



Structure–activity relationships and efforts to optimize pharmacokinetic properties of a class of benzimidazole-based MCH R1 antagonists are described.

Identification of potent agonists of photoreceptor-specific nuclear receptor (NR2E3) and preparation of a radioligand pp 5001–5004

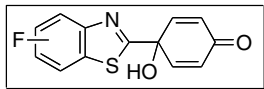
Scott E. Wolkenberg,* Zhijian Zhao, Marianna Kapitskaya, Andrea L. Webber, Konstantin Petrukhin, Yui Sing Tang, Dennis C. Dean, George D. Hartman and Craig W. Lindsley



NR2E3 β-lactamase EC₅₀, 141 nM

Antitumour properties of fluorinated benzothiazole-substituted hydroxycyclohexa-2,5-dienones ('quinols') pp 5005–5008

Cedric J. Lion, Charles S. Matthews, Geoffrey Wells, Tracey D. Bradshaw, Malcolm F. G. Stevens and Andrew D. Westwell*



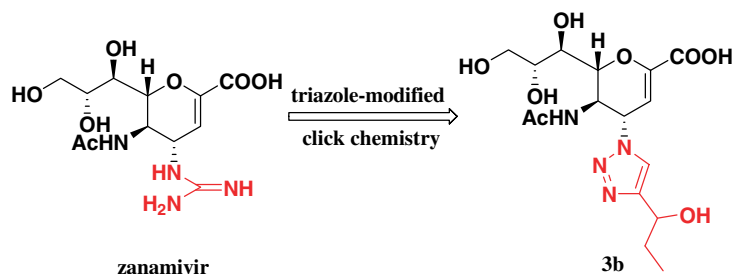
The synthesis and in vitro antitumour evaluation of a new series of fluorinated benzothiazole-substituted 4-hydroxycyclohexa-2,5-dienones ('quinols') is reported.

Syntheses of triazole-modified zanamivir analogues via click chemistry and anti-AIV activities

pp 5009–5013

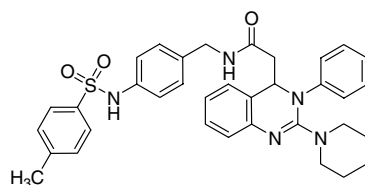
Jian Li, Mingyue Zheng, Wei Tang, Pei-Lan He, Weiliang Zhu, Tianxian Li, Jian-Ping Zuo,* Hong Liu* and Hualiang Jiang*

Compound **3b**, 4-triazole-modified zanamivir analogue, shows anti-AIV (H5N1) activity with EC_{50} of 6.4 μ M, which is very close to that of zanamivir (EC_{50} = 2.8 μ M).

**Growth inhibition of human cancer cells in vitro by T-type calcium channel blockers**

pp 5014–5017

Jae Yeol Lee,* Seong Jun Park, Sung Jun Park, Min Joo Lee, Hyewhon Rhim, Seon Hee Seo and Ki-Sun Kim

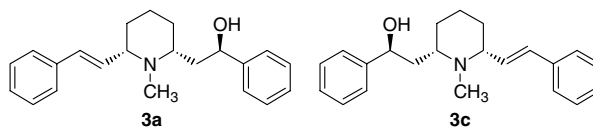


9c (KYS05041): GI_{50} = 2.70 ~ 3.06 μ M against human cancer cells

Des-keto lobeline analogs with increased potency and selectivity at dopamine and serotonin transporters

pp 5018–5021

Guangrong Zheng, David B. Horton, Agripina G. Deaciuc, Linda P. Dwoskin and Peter A. Crooks*

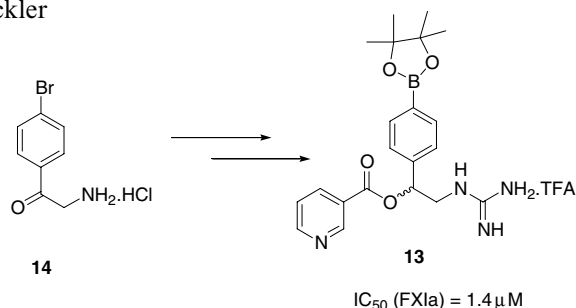


A series of *des*-keto lobeline analogs has been synthesized and evaluated for their ability to inhibit the dopamine transporter (DAT), the serotonin transporter (SERT) function and for their affinity for the synaptic vesicle monoamine transporter (VMAT2), as well as for $\alpha 4\beta 2$ and $\alpha 7$ neuronal nicotinic acetylcholine receptors (nAChRs). The enantiomers 8*R*-hydroxylobel-9-ene (**3a**) and 10*S*-hydroxylobel-7-ene (**3c**) exhibited high potency and selectivity at SERT and DAT, respectively.

Synthesis and in vitro biological evaluation of aryl boronic acids as potential inhibitors of factor XIa pp 5022–5027

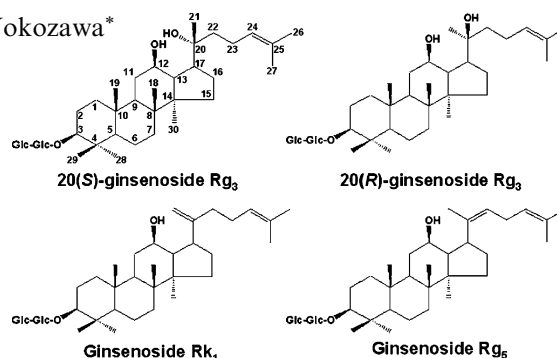
Tsvetelina I. Lazarova,* Lei Jin, Michael Rynkiewicz, Joan C. Gorga, Frank Bibbins, Harold V. Meyers, Robert Babine and James Strickler

A series of functionalized aryl boronic acids were synthesized and evaluated as potential inhibitors of factor XIa. Several of the compounds show a single digit micromolar inhibition against FXIa and selectivity against thrombin, trypsin, and FXa.

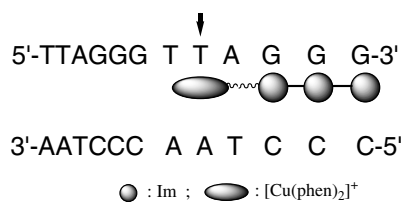
**Stereospecificity in hydroxyl radical scavenging activities of four ginsenosides produced by heat processing** pp 5028–5031

Ki Sung Kang, Hyun Young Kim, Noriko Yamabe and Takako Yokozawa*

The double bond at carbon-20(22) or the hydroxyl group (OH) at carbon-20 geometrically close to OH at carbon-12 is thought to increase the hydroxyl radical scavenging activity of ginsenosides.

**Site-Selective DNA cleavage by a novel complex of copper-conjugate of Phen and polyamide containing N-methylimidazole rings** pp 5032–5035

Dan Liu, Jiang Zhou, Huihui Li, Bo Zheng and Gu Yuan*

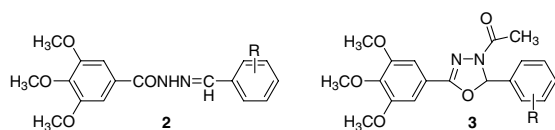


The binding mode and the cleavage site

A novel conjugate of 3-Clip-Phen and polyamide was synthesized for the targeting human telomeric repeat of 5'-TTAGGG-3', and the DNA cleaving activity and the sequence selectivity of this complex were confirmed by ESI-mass spectrometry.

Synthesis, structure, and bioactivity of N'-substituted benzylidene-3,4,5-trimethoxybenzohydrazide and 3-acetyl-2-substituted phenyl-5-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole derivatives pp 5036–5040

Linhong Jin, Jiang Chen, Baoan Song,* Zhuo Chen, Song Yang, Qianzhu Li, Deyu Hu and Ruiqing Xu



R= a: 2-F; b: 3-F; c: 4-F; d: 2-CF₃; e: 3-CF₃; f: 4-CF₃; g: 3,4-2Cl; h: 2,5-2OCH₃; i: 3,4-2F; j: 2,3-2OCH₃; k: 4-Cl-3-NO₂; l: 3,5-2Cl; m: 2,4-2OCH₃; n: 2,6-2Cl; o: 3,4,5-3OCH₃

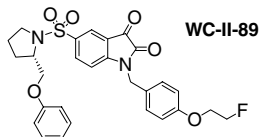
A series of 3-acetyl-2-substituted phenyl-5-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1,3,4-oxadiazole were synthesized through cyclization of N'-substituted benzylidene-3,4,5-trimethoxybenzohydrazide in acetic anhydride. And their inhibitory activities against cancer cells were performed.



Synthesis, radiolabeling, and in vivo evaluation of an ^{18}F -labeled isatin analog for imaging caspase-3 activation in apoptosis

pp 5041–5046

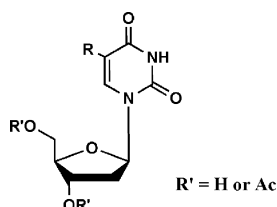
Dong Zhou, Wenhua Chu, Justin Rothfuss, Chenbo Zeng, Jinbin Xu, Lynne Jones, Michael J. Welch and Robert H. Mach*



Structurally diverse 5-substituted pyrimidine nucleosides as inhibitors of *Leishmania donovani* promastigotes in vitro

pp 5047–5051

Paul F. Torrence,* Xuesen Fan, Xinying Zhang and Philippe M. Loiseau

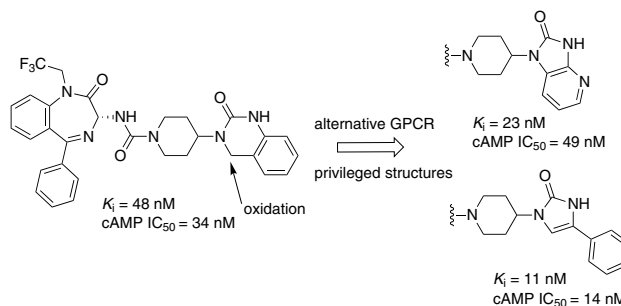


A series of 5-substituted pyrimidine nucleosides with R substituents ranging from formyl, to dicyanovinyl, to substituted chromenes, and including a pyrazolone, were all potent inhibitors of *Leishmania donovani* promastigotes.

Benzodiazepine calcitonin gene-related peptide (CGRP) receptor antagonists: Optimization of the 4-substituted piperidine

pp 5052–5056

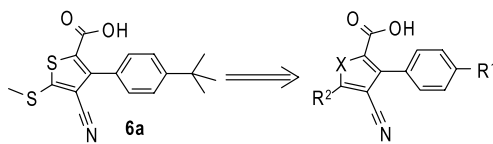
Christopher S. Burgey,* Craig A. Stump, Diem N. Nguyen, James Z. Deng, Amy G. Quigley, Beth R. Norton, Ian M. Bell, Scott D. Mosser, Christopher A. Salvatore, Ruth Z. Rutledge, Stefanie A. Kane, Kenneth S. Koblan, Joseph P. Vacca, Samuel L. Graham and Theresa M. Williams*



A novel class of AMPA receptor allosteric modulators. Part 1: Design, synthesis, and SAR of 3-aryl-4-cyano-5-substituted-heteroaryl-2-carboxylic acid derivatives

pp 5057–5061

Maria-Carmen Fernandez,* Ana Castaño, Esteban Dominguez, Ana Escibano, Delu Jiang, Alma Jimenez, Eric Hong, William J. Hornback, Eric S. Nisenbaum, Nancy Rankl, Eric Tromiczak, Grant Vaught, Hamideh Zarrinmayeh and Dennis M. Zimmerman



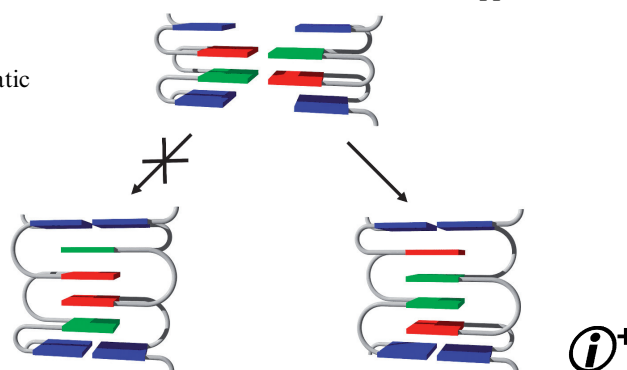
The synthesis and initial SAR studies of novel, highly potent positive allosteric modulators of AMPA receptors based on 3-(4-*tert*-butylphenyl)-4-cyano-5-methylsulfanyl-thiophene-2-carboxylic acid (**6a**) are described.

Selectivity in DNA interstrand-stacking

pp 5062–5065

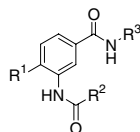
Simon M. Langenegger and Robert Häner*

Interstrand-stacking of different non-nucleosidic, polyaromatic compounds in DNA takes place with high selectivity.

**Solid-phase synthesis and structure–activity relationships of novel biarylethers as melanin-concentrating hormone receptor-1 antagonists**

pp 5066–5072

Vu Ma,* Anthony W. Bannon, Jamie Baumgartner, Clarence Hale, Faye Hsieh, Christopher Hulme, Kirk Rorrer, John Salon, Carlo van Staden and Paul Tempest

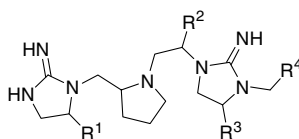


Solid-phase synthesis and structure–activity relationships of novel biarylethers as melanin-concentrating hormone receptor-1 antagonists are reported.

Pyrrolidine bis-cyclic guanidines with antimicrobial activity against drug-resistant Gram-positive pathogens identified from a mixture-based combinatorial library

pp 5073–5079

Mary E. Hensler, Gregory Bernstein, Victor Nizet and Adel Nefzi*

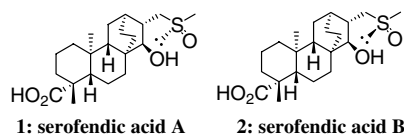


The solid-phase synthesis of a 738,192 member pyrrolidine bis-cyclic guanidine chemical library with four positions of diversity (R^1 – R^4) is reported. Screening this library yielded eight compound mixtures with bactericidal activity against methicillin-resistant *Staphylococcus aureus*. Thirty-six individual compounds from these mixtures exhibited potent bactericidal activity against important human pathogens.

Synthesis and neuroprotective effects of serofendic acid analogues

pp 5080–5083

Taro Terauchi,* Takashi Doko, Masahiro Yonaga, Akiharu Kajiwara, Tetsuhiro Niidome, Ryota Taguchi, Toshiaki Kume, Akinori Akaike and Hachiro Sugimoto

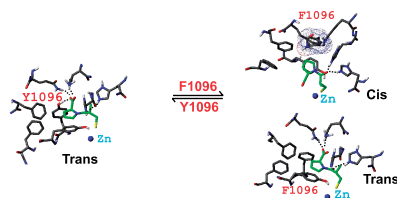


Analogues of serofendic acid were prepared and their protective effects against L-glutamate (Glu)-induced neurotoxicity were examined using primary cultures of rat cortical neurons.

The molecular basis for the selection of captopril *cis* and *trans* conformations by angiotensin I converting enzyme

pp 5084–5087

Andreas G. Tzakos, Nawazish Naqvi, Konstantinos Comporozos, Roberta Pierattelli, Vassiliki Theodorou, Ahsan Husain* and Ioannis P. Gerothanassis*



A combinatorial approach through NMR, flexible docking calculations, mutagenesis, and enzymatic studies rationalized the selectivity mechanism of the isomerization states of captopril from the ACE enzyme.

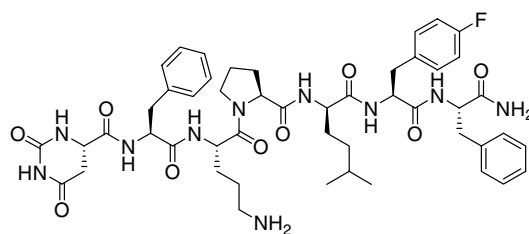


Peptidomimetic C5a receptor antagonists with hydrophobic substitutions at the C-terminus: Increased receptor specificity and in vivo activity

pp 5088–5092

Karsten Schnatbaum,* Elsa Locardi, Dirk Scharn, Uwe Richter, Heiko Hawlisch, Jochen Knolle and Thomas Polakowski

New C5a receptor antagonists characterized by C-terminal amino acids with hydrophobic substitutions are presented.



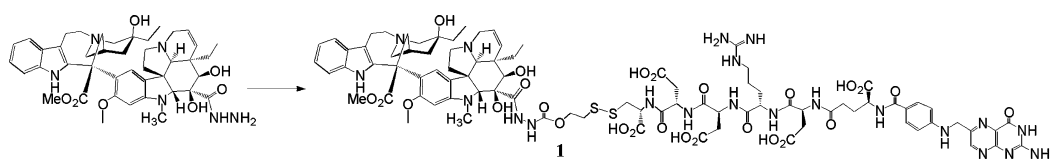
JPE1375 (36)



Design and regioselective synthesis of a new generation of targeted chemotherapeutics. Part 1: EC145, a folic acid conjugate of desacetylvinblastine monohydrazone

pp 5093–5096

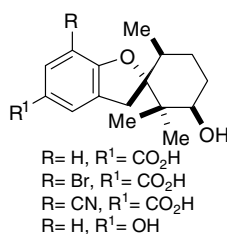
Iontcho R. Vlahov,* Hari Krishna R. Santhapuram, Paul J. Kleindl, Stephen J. Howard, Katheryn M. Stanford and Christopher P. Leamon



Synthesis of 3*H*-spiro[benzofuran-2,1'-cyclohexane] derivatives from naturally occurring filifolinol and their classical complement pathway inhibitory activity

pp 5097–5101

Mariana Useglio, Patricia M. Castellano, María A. Operto, René Torres and Teodoro S. Kaufman*



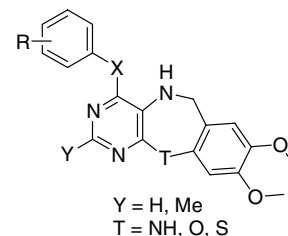
The synthesis of six filifolinol derivatives as classical complement pathway inhibitors is reported.

Novel tricyclic azepine derivatives: Biological evaluation of pyrimido[4,5-*b*]-1,4-benzoxazepines, thiazepines, and diazepines as inhibitors of the epidermal growth factor receptor tyrosine kinase

pp 5102–5106

Leon Smith, II,* Wai C. Wong, Alexander S. Kiselyov, Sabina Burdzovic-Wizemann, Yunyu Mao, Yongjiang Xu, Matthew A.J. Duncton, Ki Kim, Evgueni L. Piatnitski, Jacqueline F. Doody, Ying Wang, Robin L. Rosler, Daniel Milligan, John Columbus, Chris Balagtas, Sui Ping Lee, Andrey Kononov and Yaron R. Hadari

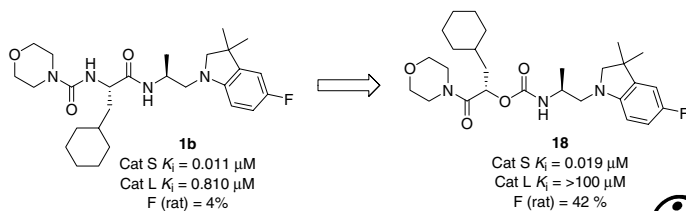
The synthesis and SAR studies of oxazepines, thiazepines, and diazepines as novel EGFR inhibitor classes are reported.

**Arylaminoethyl carbamates as a novel series of potent and selective cathepsin S inhibitors**

pp 5107–5111

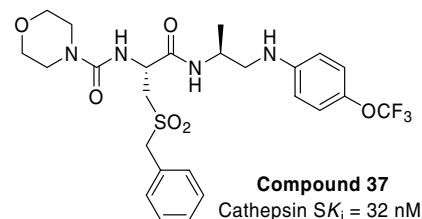
David C. Tully,* Hong Liu, Arnab K. Chatterjee, Phil B. Alper, Jennifer A. Williams, Michael J. Roberts, Daniel Mutnick, David H. Woodmansee, Thomas Hollenbeck, Perry Gordon, Jonathan Chang, Tove Tuntland, Christine Tumanut, Jun Li, Jennifer L. Harris and Donald S. Karanewsky

The synthesis and SAR of a novel series of arylaminoethyl carbamates is reported as potent, highly selective, and orally bioavailable noncovalent inhibitors of cathepsin S.

**Synthesis and SAR of arylaminoethyl amides as noncovalent inhibitors of cathepsin S: P3 cyclic ethers pp 5112–5117**

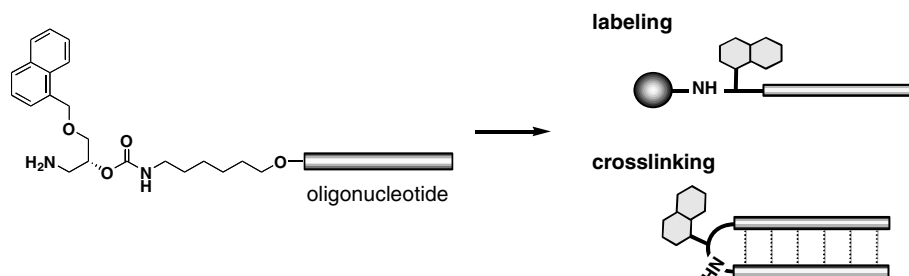
David C. Tully,* Hong Liu, Arnab K. Chatterjee, Phil B. Alper, Robert Epple, Jennifer A. Williams, Michael J. Roberts, David H. Woodmansee, Brian T. Masick, Christine Tumanut, Jun Li, Glen Spraggon, Michael Hornsby, Jonathan Chang, Tove Tuntland, Thomas Hollenbeck, Perry Gordon, Jennifer L. Harris and Donald S. Karanewsky

The synthesis and SAR a series of arylaminoethyl amide cathepsin S inhibitors are reported, focusing on the optimization of P3 and P2 subunits. An X-ray co-crystal structure of compound 37 bound to the active site of cathepsin S is also disclosed.

**Enhanced reactivity of amino-modified oligonucleotides by insertion of aromatic residue**

pp 5118–5121

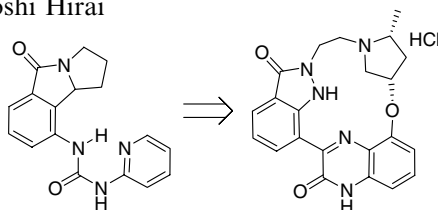
Naoshi Kojima, Maiko Sugino, Akiko Mikami, Ken Nonaka, Yumi Fujinawa, Isamu Muto, Kenichi Matsubara, Eiko Ohtsuka and Yasuo Komatsu*



Structure-based drug design of a highly potent CDK1,2,4,6 inhibitor with novel macrocyclic quinoxalin-2-one structure

pp 5122–5126

Nobuhiko Kawanishi,* Tetsuya Sugimoto, Jun Shibata, Kaori Nakamura, Kouta Masutani, Mari Ikuta and Hiroshi Hirai

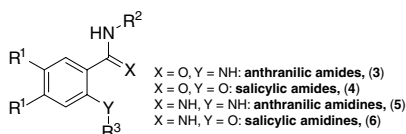


Identification of a novel series of CDK1,2,4,6 inhibitor with macrocyclic quinoxalin-2-one is reported. The structure-based designs and optimizations led to the potent CDK1,2,4,6 inhibitor that could be available as iv administration for in vivo studies from the lead compound with diarylurea scaffold.

Synthesis and biological evaluation of benzamides and benzamidines as selective inhibitors of VEGFR tyrosine kinases

pp 5127–5131

Hiroyuki Nakamura,* Yusuke Sasaki, Masaharu Uno, Tomohiro Yoshikawa, Toru Asano, Hyun Seung Ban, Hidesuke Fukazawa, Masabumi Shibuya and Yoshimasa Uehara

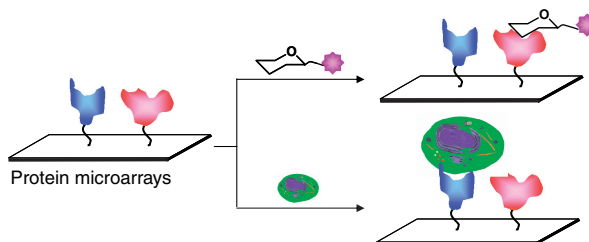


A series of benzamidines and benzamides was synthesized as selective inhibitors of vascular endothelial growth factor receptor (VEGFR) tyrosine kinases, and tested for inhibitory activity toward autophosphorylation by the enzyme assay.

Protein microarrays to study carbohydrate-recognition events

pp 5132–5135

Myung-ryul Lee, Sungjin Park and Injae Shin*



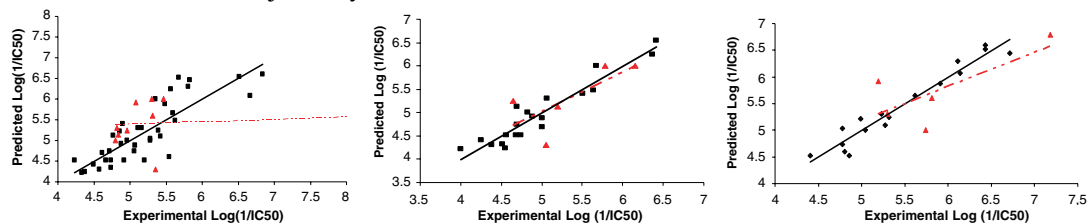
Protein microarrays are applied for studying carbohydrate-recognition events.



Cluster analysis and two-dimensional quantitative structure–activity relationship (2D-QSAR) of *Pseudomonas aeruginosa* deacetylase LpxC inhibitors

pp 5136–5143

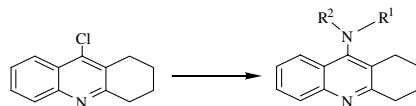
Rameshwar U. Kadam and Nilanjan Roy*



Conventional and cluster analysis based methods for QSAR development have been analysed and compared for their predictability on a set of *Pseudomonas aeruginosa* Deacetylase LpxC inhibitors. Cluster analysis based approach proved to be better than the conventional technique.

Search of antitubercular activities in tetrahydroacridines: Synthesis and biological evaluation

pp 5144–5147

R. P. Tripathi,* S. S. Verma, Jyoti Pandey, K. C. Agarwal, Vinita Chaturvedi,
Y. K. Manju, A. K. Srivastva, A. Gaikwad and S. Sinha

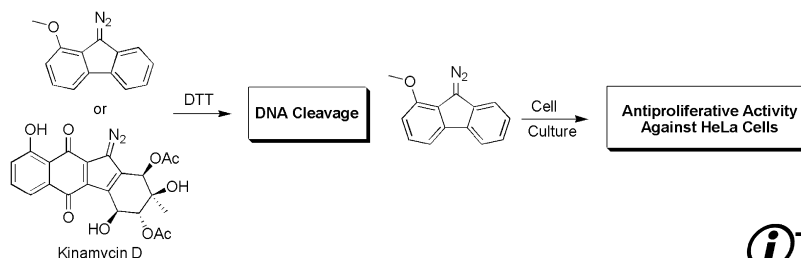
A series of 9-aminotetrahydroacridines were synthesized starting from anthranilic acid and cyclohexanone. Few of the compounds possess potent in vitro antitubercular activities with MIC as low as 0.78 $\mu\text{g/mL}$.

**Mimicking the biological activity of diazobenzo[b]fluorene natural products with electronically tuned diazofluorene analogs**

pp 5148–5151

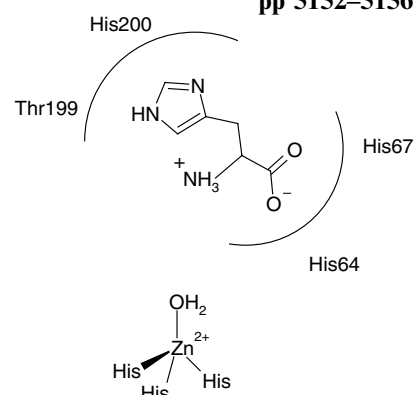
Wei Zeng, T. Eric Ballard, Alexander G. Tkachenko, Virginia A. Burns,
Daniel L. Feldheim and Christian Melander*

The synthesis, DNA cleaving, and anti-proliferative properties of electronically modulated diazofluorenes are reported.

**Carbonic anhydrase activators: The first X-ray crystallographic study of an adduct of isoform I**

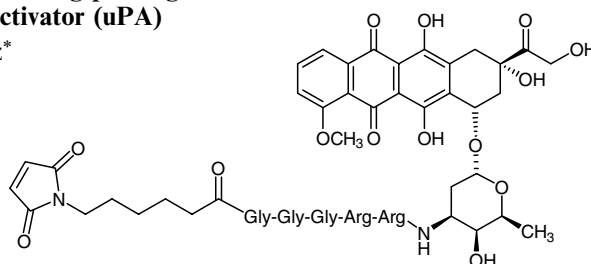
pp 5152–5156

Claudia Temperini, Andrea Scozzafava and Claudiu T. Supuran*

**Development of a novel albumin-binding prodrug that is cleaved by urokinase-type-plasminogen activator (uPA)**

pp 5157–5163

Da-Eun Chung and Felix Kratz*



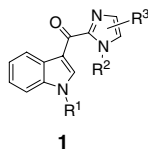
1

A water-soluble albumin-binding prodrug of doxorubicin (**1**) was developed that is cleaved specifically by the tumor-associated protease urokinase-type plasminogen activator (uPA).

Conjugated indole-imidazole derivatives displaying cytotoxicity against multidrug resistant cancer cell lines

pp 5164–5168

David A. James, Keizo Koya, Hao Li, Shoujun Chen, Zhiqiang Xia, Weiwen Ying, Yaming Wu and Lijun Sun*

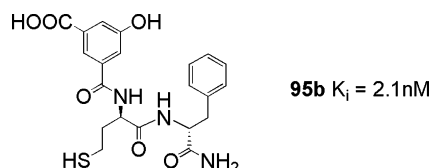


We report herein the SAR studies of a series of indole-imidazole compounds, that demonstrate substantial in vitro anti-proliferative activities against cancer cell lines, including multidrug resistance (MDR) phenotypes. The in vitro cytotoxic effects have been demonstrated across a wide array of tumor types, including hematologic and solid tumor cell lines of various origins (e.g., leukemia, breast, colon, and uterine).

Homo-cysteinyl peptide inhibitors of the L1 metallo- β -lactamase, and SAR as determined by combinatorial library synthesis

pp 5169–5175

Qin Sun, Andy Law, Michael W. Crowder and H. Mario Geysen*



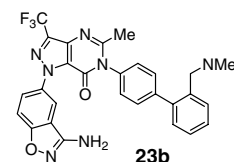
Homo-cysteinyl peptides library was synthesized and screened for their inhibitory activity toward L1 metallo- β -lactamase. The most active compound had a K_i of 2.1 nM.

Preparation of 1-(3-aminobenzo[d]isoxazol-5-yl)-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-ones as potent, selective, and efficacious inhibitors of coagulation factor Xa

pp 5176–5182

Yun-Long Li,* John M. Fevig,* Joseph Cacciola, Joseph Buriak, Jr., Karen A. Rossi, Janan Jona, Robert M. Knabb, Joseph M. Luettgen, Pancras C. Wong, Stephen A. Bai, Ruth R. Wexler and Patrick Y. S. Lam

Previously, potent factor Xa inhibitors were described based on the 1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one bicyclic core and a 4-methoxyphenyl P1 moiety. This letter describes the 1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one and related bicyclic cores with the 3-aminobenzoisoxazole P1 moiety. Many of these compounds are potent, selective, and efficacious inhibitors of coagulation factor Xa.

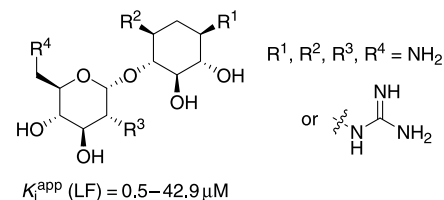


Selectively guanidinylated derivatives of neamine. Syntheses and inhibition of anthrax lethal factor protease

pp 5183–5189

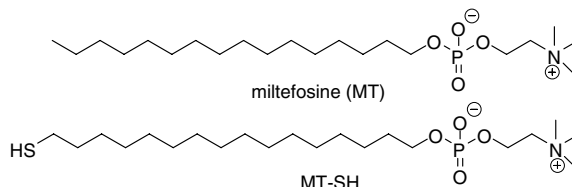
Guan-Sheng Jiao,* Ondrej Simo, Melissa Nagata, Sean O'Malley, Thomas Hemscheidt, Lynne Cregar, Sherri Z. Millis, Mark E. Goldman and Cho Tang

A series of mono-, di-, and tri-guanidinylated derivatives of neamine were prepared via selective guanidinylation of neamine. These molecules represent a novel scaffold as inhibitors of anthrax lethal factor zinc metalloprotease. Methods for the synthesis of these compounds are described, and structure–activity relationships among the series are analyzed. In addition, initial findings regarding the mechanism of LF inhibition for these molecules are presented.



Synthesis of 16-mercaptohexadecylphosphocholine, a miltefosine analog with leishmanicidal activity pp 5190–5193

Valentín Hornillos, José María Saugar, Beatriz G. de la Torre, David Andreu, Luis Rivas, A. Ulises Acuña* and Francisco Amat-Guerri*

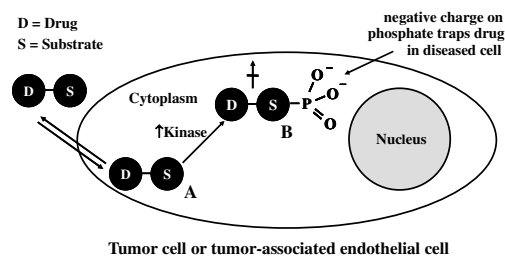


A miltefosine analog capped with a versatile terminal mercapto group presents the same very high leishmanicidal activity as the parent drug, opening new ways for the study of the unknown antiparasite mechanism of alkylphospholipids.

Kinase-mediated trapping of bi-functional conjugates of paclitaxel or vinblastine with thymidine in cancer cells pp 5194–5198

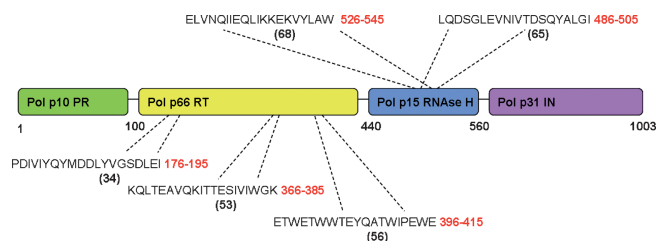
Simon E. Aspland,* Carlo Ballatore, Rosario Castillo, Joel Desharnais, Trisha Eustaquio, Philip Goelet, Zijian Guo, Qing Li, David Nelson, Chengzao Sun, Angelo J. Castellino and Michael J. Newman

In the present work, we explore the possibility of introducing selectivity to existing chemotherapeutics via the design of non-pro-drug, bi-functional molecules comprising a microtubule-binding agent and a substrate for a disease-associated kinase. The design, synthesis, and in vitro biological evaluation of paclitaxel–thymidine and vinblastine–thymidine bi-functional conjugates are reported here. This work provides the first account of ‘kinase-mediated trapping’ of cancer therapeutics.

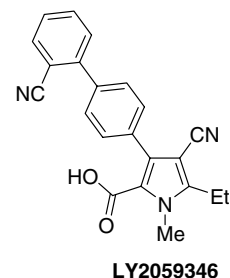
**Inhibition of HIV-1 integrase activity by synthetic peptides derived from the HIV-1 HXB2 Pol region of the viral genome** pp 5199–5202

Zahrah Zawahir and Nouri Neamati*

The five most potent peptides derive from different regions of the HIV-1 HXB2 Pol genome. Numbers adjacent to each peptide sequence indicate amino acid spans of the respective subunits on the Pol polypeptide (Numbering according to the HXB2 Numbering Engine nomenclature, Los Alamos National Laboratory). Numbers in parentheses indicate the number of the peptide (domains not drawn to scale).

**A novel class of positive allosteric modulators of AMPA receptors: Design, synthesis, and structure–activity relationships of 3-biphenyl-4-yl-4-cyano-5-ethyl-1-methyl-1H-pyrrole-2-carboxylic acid, LY2059346** pp 5203–5206

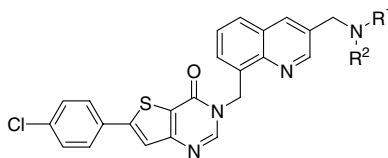
Hamideh Zarrinmayeh,* Eric Tromiczak, Dennis M. Zimmerman, Nancy Rankl, Ken H. Ho, Esteban Dominguez, Ana Castaño, Ana Escribano, Carmen Fernandez, Alma Jimenez, William J. Hornback and Eric S. Nisenbaum



Design and synthesis of substituted quinolines as novel and selective melanin concentrating hormone antagonists as anti-obesity agents

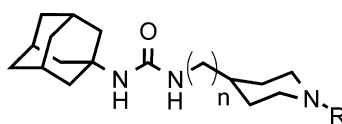
pp 5207–5211

Namal C. Warshakoon,* Justin Sheville, Ritu Tiku Bhatt, Wei Ji, Jose L. Mendez-Andino, Kenneth M. Meyers, Nick Kim, John A. Wos, Chrissy Mitchell, Jennifer L. Paris, Beth B. Pinney, Ofer Reizes and X. Eric Hu

**Synthesis and SAR of conformationally restricted inhibitors of soluble epoxide hydrolase**

pp 5212–5216

Paul D. Jones, Hsing-Ju Tsai, Zung N. Do, Christophe Morisseau and Bruce D. Hammock*

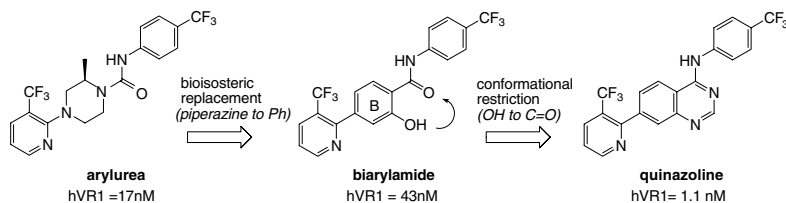


$n = 0, 1$
 $R = H, \text{ alkyl, acyl}$

**From arylureas to biarylamides to aminoquinazolines: Discovery of a novel, potent TRPV1 antagonist**

pp 5217–5221

Xiaozhang Zheng, Kevin J. Hodgetts, Harry Brielmann, Alan Hutchison, Frank Burkamp, A. Brian Jones, Peter Blurton, Robert Clarkson, Jayaraman Chandrasekhar, Rajagopal Bakthavatchalam, Stéphane De Lombaert, Marci Crandall, Daniel Cortright and Charles A. Blum*

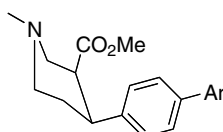


A novel VR1 antagonist template (4-aminoquinazoline) exhibits improved in vitro potency and oral bioavailability relative to the corresponding urea or carboxamide compounds.

Synthesis and monoamine transporter affinity of 2β-carbomethoxy-3β-(4'-p-substituted phenyl)-piperidine analogs of cocaine

pp 5222–5225

Frederic Bois, Ronald M. Baldwin, Nora S. Kula, Ross J. Baldessarini, M. Al Tikriti, Robert B. Innis and Gilles D. Tamagnan*

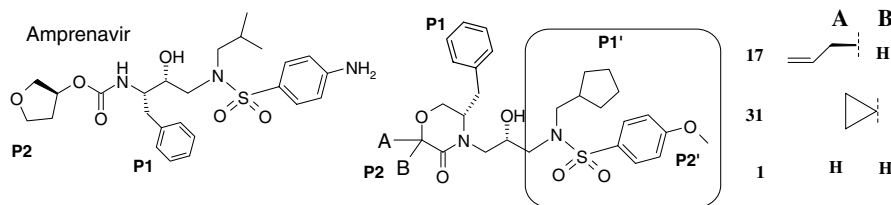


A series of novel piperidine based analogs of cocaine was synthesized and evaluated in vitro against the three monoamine transporters to develop new potential selective SERT radiotracers.

New, potent P1/P2-morpholinone-based HIV-protease inhibitors

pp 5226–5230

Wieslaw M. Kazmierski,* Eric Furfine, Andrew Spaltenstein and Lois L. Wright

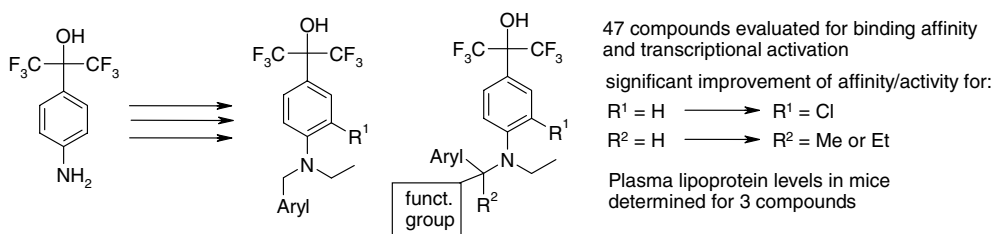


Morpholinone-based P1/P2 derivatives have been discovered to provide a new and promising scaffold toward potent mimetics of the HIV-1 protease inhibitor Amprenavir. In particular, allyl- and spiro-cyclopropyl—P2-substituted inhibitors **17** and **31** were found 500× more potent than the parent inhibitor **1**.

Synthesis and evaluation of anilinohexafluoroisopropanols as activators/modulators of LXRα and β

pp 5231–5237

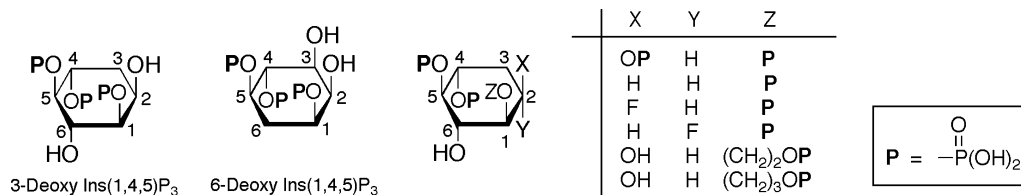
Narendra Panday,* Jörg Benz, Denise Blum-Kaelin, Vanessa Bourgeaux, Henrietta Dehmlow, Peter Hartman, Bernd Kuhn, Hassen Ratni, Xavier Warot and Matthew B. Wright



Convenient synthesis of 3- and 6-deoxy-D-myo-inositol phosphate analogues from (+)-*epi*- and (-)-*vibo*-quercitols

pp 5238–5243

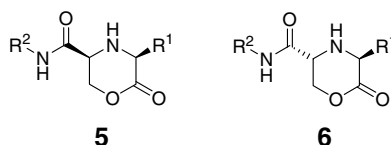
Seiichiro Ogawa* and Yoji Tezuka



Morpholin-2-one derivatives as novel selective T-type Ca²⁺ channel blockers

pp 5244–5248

Il Whea Ku, Sangwon Cho, Munikumar Reddy Doddareddy, Min Seok Jang, Gyochang Keum, Jung-Ha Lee, Bong Young Chung, Youseung Kim, Hyewhon Rhim* and Soon Bang Kang*



Morpholin-2-one-5-carboxamide derivatives were prepared by using a one-pot Ugi multicomponent reaction and showed potent and selective T-type calcium channel blocking activities.

OTHER CONTENTS**Summary of instructions to authors****p I**

*Corresponding author

①* Supplementary data available via ScienceDirect

COVER

View of the crystal structure of the DB819-d(CGCGAATTCGCG)₂ complex, looking down the minor groove of the DNA (see Campbell, N.H.; Evans, D.A.; Lee, M.P.H.; Parkinson, G.N.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 15). The DB819 molecule is shown in space-filling mode. Visualisation produced with the VMD program. [Humphrey, W.; Dalke, A.; Schulten, K. *J. Mol. Graphics* **1996**, *14*, 33.]

Available online at

www.sciencedirect.com

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



ELSEVIER

ISSN 0960-894X