

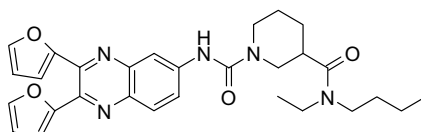
## Contents

### ARTICLES

#### Quinoxalinyurea derivatives as a novel class of JSP-1 inhibitors

pp 2118–2122

Li Zhang, Beiying Qiu, Bing Xiong, Xin Li, Jingya Li, Xin Wang, Jia Li\* and Jingkang Shen\*



Compound A17  $IC_{50} = 2.35 \pm 0.65 \mu M$

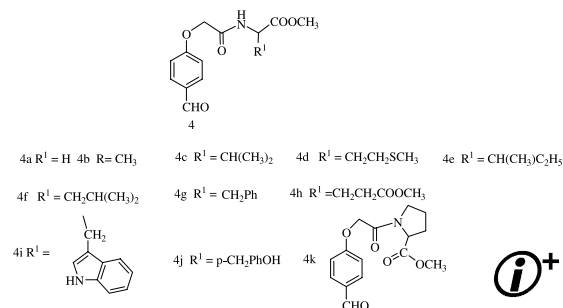
A series of quinoxalinyurea-based inhibitors are synthesized and shown to be the novel and potent inhibitors against JSP-1. Compound A17 showed the most potent activity to inhibit JSP-1.

#### Methyl 2-(2-(4-formylphenoxy)acetamido)-2-substituted acetate derivatives: A new class of acetylcholinesterase inhibitors

pp 2123–2125

Huan Wen, Yayao Zhou, Chonglan Lin, Hui Ge, Lin Ma, Zihou Wang, Wenlie Peng and Huacan Song\*

A new class of inhibitors of acetylcholinesterase (methyl 2-(2-(4-formylphenoxy)acetamido)-2-substituted acetate derivatives) is described. Compounds 4b and 4i were found to be more potent than galanthamine in inhibiting acetylcholinesterase.



#### Pharmacophore modeling and in silico screening for new KDR kinase inhibitors

pp 2126–2133

Hui Yu, Zhanli Wang, Liangren Zhang, Jufeng Zhang and Qian Huang\*

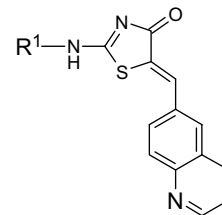
Three-dimensional pharmacophore hypothesis was built. The model was then employed as 3D search query to screen the database for other potential lead compounds.



### Synthesis and activity of quinolinyl-methylene-thiazolinones as potent and selective cyclin-dependent kinase 1 inhibitors pp 2134–2138

Shaoqing Chen,\* Li Chen, Nam T. Le, Chunlin Zhao, Achyutharao Sidduri, Jian Ping Lou, Christophe Michoud, Louis Portland, Nicole Jackson, Jin-Jun Liu, Fred Konzelmann, Feng Chi, Christian Tovar, Qing Xiang, Yingsi Chen, Yang Wen and Lyubomir T. Vassilev

A novel series of quinolinyl-methylene-thiazolinones has been identified as potent and selective CDK1 inhibitors, showing good antiproliferative activities on various human tumor cell lines.



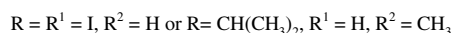
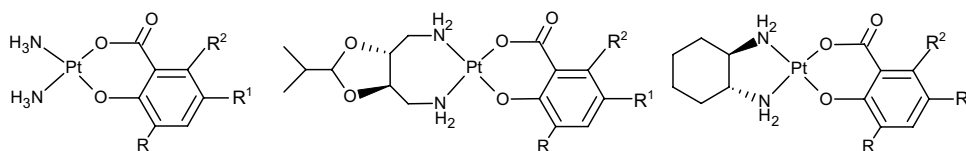
### A new platinum complex of triazine demonstrates G1 arrest with novel biological profile in human breast cancer cell line, MDA-MB-468 pp 2139–2145

Soma Mandal, Gervais Bérubé, Éric Asselin, Vernon J. Richardson, Jon G. Church, John Bridson, Tram N. Q. Pham, Saroj K. Pramanik and Sanat K. Mandal\*

A novel series of platinum derivatives was synthesized and biological response was evaluated in a human breast cancer cell line. S30 caused G1 arrest and apoptosis.

### Synthesis and in vitro cytotoxicity of novel lipophilic (diamine)platinum(II) complexes of salicylate derivatives pp 2146–2149

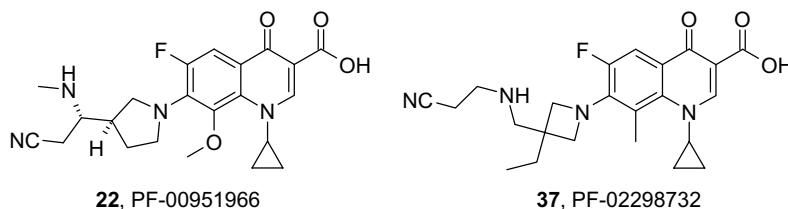
Qing-Song Ye, Li-Guang Lou, Wei-Ping Liu,\* Yao Yu, Xi-Zhu Chen, Shu-Qian Hou, Wen-Qui Gao and Yang Liu



Six novel (diamine)platinum(II) complexes of salicylate derivatives were prepared and their in vitro cytotoxicity as well as the liposolubility were determined. The results showed that the salicylate derivatives significantly enhanced both liposolubility and cytotoxicity of the platinum complexes.

### The synthesis and biological evaluation of novel series of nitrile-containing fluoroquinolones as antibacterial agents pp 2150–2155

Sean T. Murphy,\* Heather L. Case, Edmund Ellsworth, Susan Hagen, Michael Huband, Themis Joannides, Chris Limberakis, Keith R. Marotti, Amy M. Ottolini, Mark Rauckhorst, Jeremy Starr, Michael Stier, Clarke Taylor, Tong Zhu, Adrian Blaser, William A. Denny, Guo-Liang Lu, Jeff B. Smaill and Freddy Rivault



**3D-QSAR studies with the aid of molecular docking for a series of non-steroidal FXR agonists**

pp 2156–2160

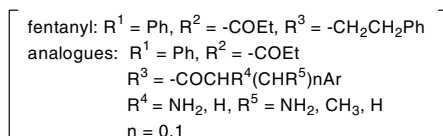
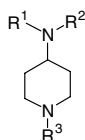
Tao Zhang, Jun-Hong Zhou, Liang-Wei Shi, Rui-Xin Zhu and Min-Bo Chen\*

We reported 3D-QSAR studies with the aid of molecular docking for a series of non-steroidal agonists of farnesoid x receptors. A proposal to design new agonists is discussed.

**Understanding the structural requirements of 4-anilidopiperidine analogues for biological activities at  $\mu$  and  $\delta$  opioid receptors**

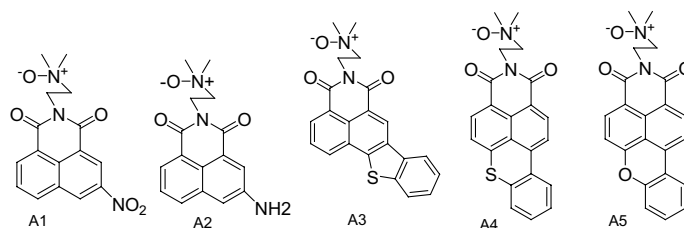
pp 2161–2165

Yeon Sun Lee, Joel Nyberg, Sharif Moye, Richard S. Agnes, Peg Davis, Shou-wu Ma, Josephine Lai, Frank Porreca, Ruben Vardanyan and Victor J. Hruby\*

**Novel *N*-oxide of naphthalimides as prodrug leads against hypoxic solid tumor: Synthesis and biological evaluation**

pp 2166–2170

Hong Yin, Yufang Xu,\* Xuhong Qian,\* Yuanli Li and Jianwen Liu

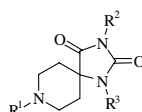


Novel potential anticancer agents against hypoxic solid tumor, aliphatic *N*-oxide of naphthalimides, were designed, synthesized, and evaluated in A375, V79 cells in vitro.

**Synthesis and structure–activity relationships of spirohydantoin-derived small-molecule antagonists of the melanin-concentrating hormone receptor-1 (MCH-R1)**

pp 2171–2178

Martin W. Rowbottom,\* Troy D. Vickers, Junko Tamiya, Mingzhu Zhang, Brian Dyck, Jonathan Grey, David Schwarz, Christopher E. Heise, Michael Hedrick, Jenny Wen, Hui Tang, Hua Wang, Andrew Fisher, Anna Aparicio, John Saunders and Val S. Goodfellow\*

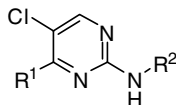


The design, synthesis, and SAR of a series of substituted spirohydantoins are described. Optimization of an in-house screening hit gave compounds that exhibited potent binding affinity and functional activity at MCH-R1.

### Synthesis and biological study of 2-amino-4-aryl-5-chloropyrimidine analogues as inhibitors of VEGFR-2 and cyclin dependent kinase 1 (CDK1)

pp 2179–2183

Shenlin Huang,\* Ronghua Li, Peter J. Connolly, Stuart Emanuel, Angel Fuentes-Pesquera, Mary Adams, Robert H. Gruninger, Javed Seraj, Steven A. Middleton, Jeremy M. Davis and David F. C. Moffat



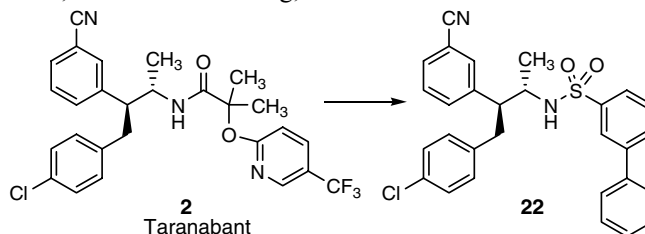
The novel series of 2-amino-4-aryl-5-chloropyrimidines was identified to be potent for both VEGFR-2 and CDK1. SAR at the 2- and 4-positions of the 5-chloropyrimidien core was studied, resulting in many potent analogues with (2-aminoethyl)phenylamino at the 2-position and cumylamino, indol-3-yl, or indol-6-yl at the 4-position. Several derivatives showed good bioavailability in rat PK study.

### Substituted acyclic sulfonamides as human cannabinoid-1 receptor inverse agonists

pp 2184–2187

Helen E. Armstrong, Amy Galka, Linus S. Lin, Thomas J. Lanza, Jr., James P. Jewell, Shrenik K. Shah, Ravi Guthikonda, Quang Truong, Linda L. Chang, Grace Quaker, Vincent J. Colandrea, Xinchun Tong, Junying Wang, Sherry Xu, Tung M. Fong, Chun-Pyn Shen, Julie Lao, Jing Chen, Lauren P. Shearman, D. Sloan Stribling, Kimberly Rosko, Alison Strack, Sookhee Ha, Lex Van der Ploeg, Mark T. Goulet and William K. Hagmann\*

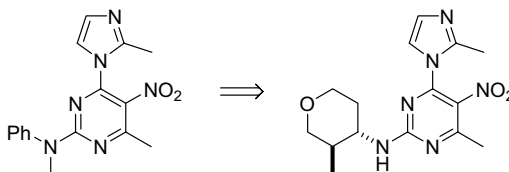
Sulfonamide analogues of the potent CB1R inverse agonist **2** (Taranabant) were optimized for CB1R activity.



### SAR studies on a novel series of human cytomegalovirus primase inhibitors

pp 2188–2192

X. Chen,\* J. Adrian, T. Cushing, H. DiMaio, L. Liang, V. Mayorga, S. Miao, M. G. Peterson, J. P. Powers, F. Spector, C. Stein, M. Wright, D. Xu, Q. Ye and J. Jaen

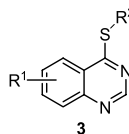


A novel series of imidazolylpyrimidines were found to possess inhibitory activity against the human CMV UL70 primase. Extensive SAR studies on an HTS lead led to potent, orally bioavailable compounds with anti-CMV IC<sub>50</sub> values of 150 nM in both viral yield and viral DNA replication assays and with a much reduced cytotoxicity compared to marketed treatments ganciclovir and cidofovir.

### Synthesis and bioactivity of 4-alkyl(aryl)thioquinazoline derivatives

pp 2193–2196

Song Yang, Zhi Li, Linhong Jin, Baoan Song,\* Gang Liu, Jiang Chen, Zhuo Chen, Deyu Hu, Wei Xue and Ruiqing Xu



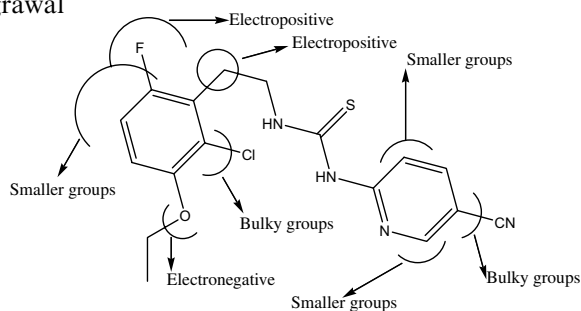
**3a:** R<sup>1</sup>=H, R<sup>2</sup>=5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-oxadiazol-2-yl; **3b:** R<sup>1</sup>=H, R<sup>2</sup>=3-methoxyphenyl; **3c:** R<sup>1</sup>=6, 7, 8-trimethoxyphenyl, R<sup>2</sup>=5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-oxadiazol-2-yl; **3d:** R<sup>1</sup>=6, 7, 8-trimethoxyphenyl, R<sup>2</sup>=3-methoxyphenyl; **3e:** R<sup>1</sup>=H, R<sup>2</sup>=5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-thiadiazol-2-yl; **3f:** R<sup>1</sup>=6, 7, 8-trimethoxyphenyl, R<sup>2</sup>=5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-thiadiazol-2-yl; **3g:** R<sup>1</sup>=H, R<sup>2</sup>=allyl; **3h:** R<sup>1</sup>=6-I, R<sup>2</sup>=Et; **3i:** R<sup>1</sup>=6-I, R<sup>2</sup>=n-Pr; **3j:** R<sup>1</sup>=6-I, R<sup>2</sup>=allyl; **3k:** R<sup>1</sup>=6-I, R<sup>2</sup>=n-Bu; **3l:** R<sup>1</sup>=6-I, R<sup>2</sup>=5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-oxadiazol-2-yl; **3m:** R<sup>1</sup>=6-I, R<sup>2</sup>=5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-thiadiazol-2-yl

A series of S'-substituted 4-alkyl(aryl)thioquinazoline derivatives were synthesized through thioetherification of 4-chloroquinazolines and thiol compounds refluxed in acetone in the presence of K<sub>2</sub>CO<sub>3</sub>. And their inhibitory activities against cancer cells were bioassayed.

**Predicting anti-HIV activity of PETT derivatives: CoMFA approach**

pp 2197–2202

V. Ravichandran\* and R. K. Agrawal

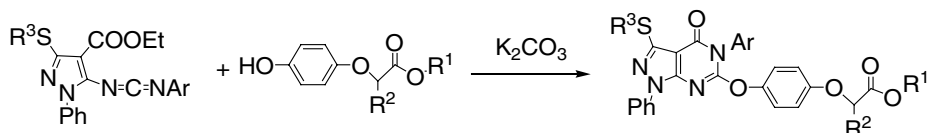


The parameters indicated in the substitution position of compound are responsible for anti-HIV activity.

**Synthesis and herbicidal activity of novel pyrazolo[3,4-*d*]pyrimidin-4-one derivatives containing aryloxyphenoxypionate moieties**

pp 2203–2209

Hui Liu, Hong-Qing Wang and Zhao-Jie Liu\*

**Phosph(on)ate as a zinc-binding group in metalloenzyme inhibitors: X-ray crystal structure of the antiviral drug foscarnet complexed to human carbonic anhydrase I**

pp 2210–2215

Claudia Temperini, Alessio Innocenti, Annalisa Guerri, Andrea Scozzafava, Stefano Rusconi and Claudiu T. Supuran\*

Phosph(on)ate as a zinc-binding group in metalloenzyme inhibitors: X-ray crystal structure of the antiviral drug foscarnet complexed to human carbonic anhydrase I.

**Structural requirements of HDAC inhibitors: SAHA analogs functionalized adjacent to the hydroxamic acid**

pp 2216–2219

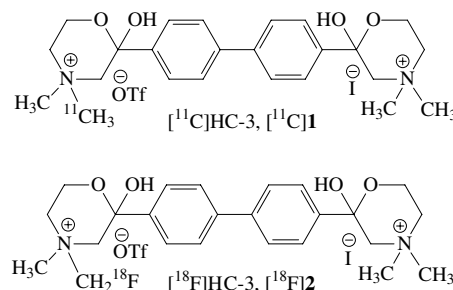
Anton V. Bieliauskas, Sujith V. W. Weerasinghe and Mary Kay H. Pflum\*

The synthesis and biological evaluation of a small library of C2-substituted SAHA analogs is reported.

### Synthesis and biodistribution of new radiolabeled high-affinity choline transporter inhibitors [<sup>11</sup>C]hemicholinium-3 and [<sup>18</sup>F]hemicholinium-3

pp 2220–2224

Qi-Huang Zheng,\* Mingzhang Gao, Bruce H. Mock, Shuyan Wang, Toshihiko Hara, Rachid Nazih, Michael A. Miller, Tim J. Receveur, John C. Lopshire, William J. Groh, Douglas P. Zipes, Gary D. Hutchins and Timothy R. DeGrado

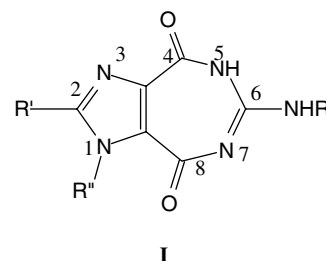


### Structure–activity relationship studies on anti-HCV activity of ring-expanded ('fat') nucleobase analogues containing the imidazo[4,5-*e*][1,3]diazepine-4,8-dione ring system

pp 2225–2228

Peng Zhang, Ning Zhang, Brent E. Korba and Ramachandra S. Hosmane\*

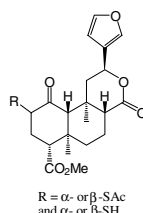
Continued SAR studies on anti-HCV activity of the title imidazo[4,5-*e*][1,3]diazepine ring system have been reported, focusing on hydrophobic substituents at the 2-position of the heterocycle.

i<sup>+</sup>

### Convenient synthesis and in vitro pharmacological activity of 2-thioanalogs of salvinorins A and B

pp 2229–2232

Ruslan V. Bikbulatov, Feng Yan, Bryan L. Roth and Jordan K. Zjawiony\*



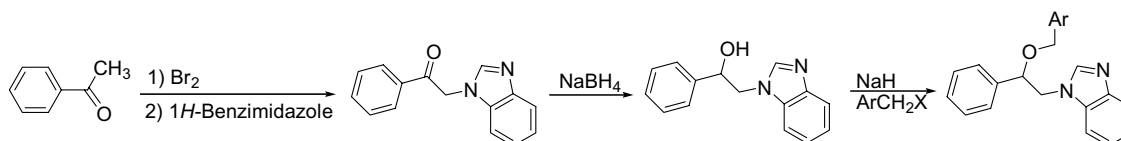
To study drug-receptor interactions, new thio-derivatives of salvinorin A, an extremely potent natural  $\kappa$ -opioid receptor agonist, were synthesized and examined for receptor binding affinity.

i<sup>+</sup>

### Synthesis and antimicrobial activity of some novel phenyl and benzimidazole substituted benzyl ethers

pp 2233–2236

Özden Özel Güven,\* Taner Erdoğan, Hakan Göker and Sulhiye Yıldız

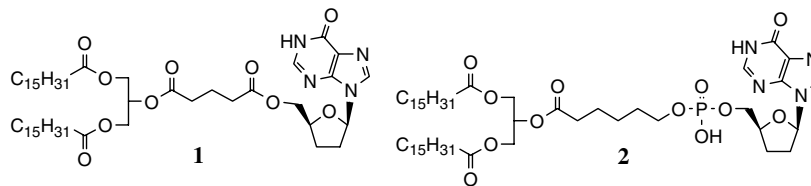


The synthesis and antibacterial effects of benzyl ethers were reported.

### Synthesis and biological evaluation of two glycerolipidic prodrugs of didanosine for direct lymphatic delivery against HIV

pp 2237–2240

Muriel Lalanne, Angelo Paci, Karine Andrieux, Nathalie Dereuddre-Bosquet, Pascal Clayette, Alain Deroussent, Micheline Ré, Gilles Vassal, Patrick Couvreur and Didier Desmaële\*

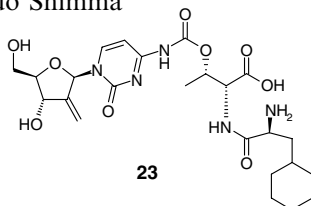


Glycerolipidic prodrugs of didanosine **1** and didanosine monophosphate **2** were synthesized and evaluated against HIV-1 in cell culture with no sign of toxicity.

### Design and synthesis of novel prodrugs of 2'-deoxy-2'-methylidenecytidine activated by membrane dipeptidase overexpressed in tumor tissues

pp 2241–2245

Yasunori Kohchi, Kazuo Hattori, Nobuhiro Oikawa, Eisaku Mizuguchi, Yoshiaki Isshiki, Kohsuke Aso, Kiyoshi Yoshinari, Haruyoshi Shirai, Masanori Miwa, Yukiko Inagaki, Masako Ura, Kotaroh Ogawa, Hisafumi Okabe, Hideo Ishitsuka and Nobuo Shimma\*



The novel prodrugs of DMDC including compound **23** that are activated by membrane dipeptidase preferentially in tumor tissue are designed and synthesized.

### A glycosylated complex of gadolinium, a new potential contrast agent for magnetic resonance angiography?

pp 2246–2249

G. Yu, M. Yamashita, K. Aoshima, M. Takahashi, T. Oshikawa, H. Takayanagi, S. Laurent,\* C. Burtea, L. Vander Elst and R. N. Muller

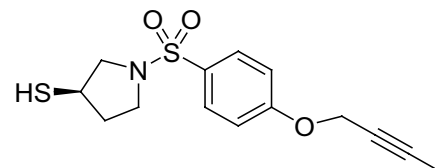
A new low-molecular weight dendrimer-like MRI contrast agent has been synthesized and characterized in vitro and in vivo in rats.

### Novel thiol-based TACE inhibitors: Rational design, synthesis, and SAR of thiol-containing aryl sulfonamides

pp 2250–2253

B. Govinda Rao,\* Upul K. Bandarage,\* Tiansheng Wang, Jon H. Come, Emanuele Perola, Yunyi Wei, Shi-Kai Tian and Jeffrey O. Saunders

A series of potent thiol-containing aryl sulfonamide TACE inhibitors was designed and synthesized. The SAR and MMP selectivity of the series were investigated. In particular, compound **4b** has shown excellent in vitro potency against the isolated TACE enzyme and good selectivity over MMP-2, -7, -8, -9, and -13.

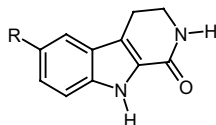


**4b** TACE  $K_i$  = 28 nM

**From pyrroles to 1-oxo-2,3,4,9-tetrahydro-1*H*- $\beta$ -carbolines: A new class of orally bioavailable mGluR1 antagonists**

pp 2254–2259

Romano Di Fabio,\* Fabrizio Micheli, Giuseppe Alvaro, Paolo Cavanni, Daniele Donati, Tatiana Gagliardi, Gabriele Fontana, Riccardo Giovannini, Micaela Maffei, Anna Mingardi, Maria Elvira Tranquillini and Giovanni Vitulli



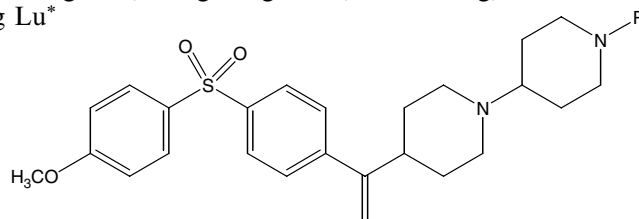
A new class of orally available mGluR1 antagonists was identified by replacement of the known pyrrole core with a  $\beta$ -carboline template suitably substituted at the position C-6.

**Quantitative structure–selectivity relationship for M2 selectivity between M1 and M2 of piperidinyl piperidine derivatives as muscarinic antagonists**

pp 2260–2266

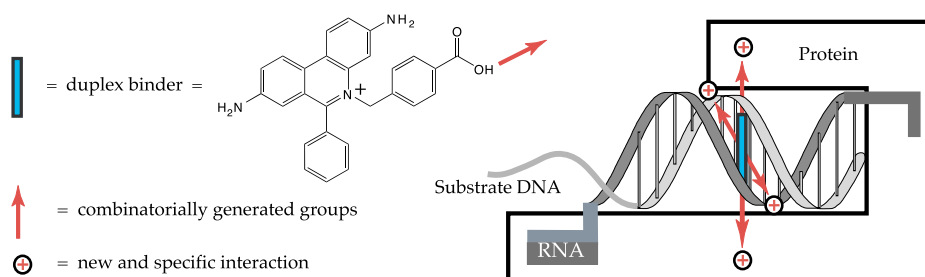
Yin-Yao Niu, Li-Min Yang, Ke-Min Deng, Jian-Hua Yao,\* Liang Zhu, Cong-Ying Chen, Min Zhang, Jin-E Zhou, Tian-Xiang Shen, Hong-Zhuan Chen and Yang Lu\*

A new M2/M1 quantitative structure–selectivity relationship (QSSR) model of piperidinyl piperidine derivatives as muscarinic M2 subtype receptor antagonists was constructed, discussed, and examined. This model could provide solid basis for designing novel molecules with higher antagonistic selectivity to muscarinic receptors.


**Design, synthesis, and evaluation of phenanthridine derivatives targeting the telomerase RNA/DNA heteroduplex**

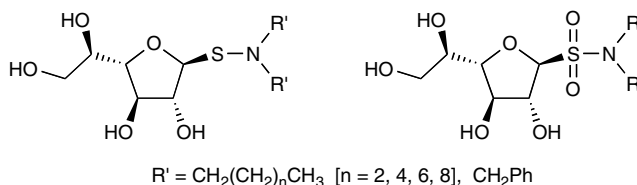
pp 2267–2273

Subhashree Rangarajan and Simon H. Friedman\*


**Synthesis and evaluation of galactofuranosyl *N,N*-dialkyl sulfenamides and sulfonamides as antimycobacterial agents**

pp 2274–2277

David J. Owen, Chris B. Davis, Regan D. Hartnell, Paul D. Mudge, Robin J. Thomson, Andrew K. J. Chong, Ross L. Coppel and Mark von Itzstein\*

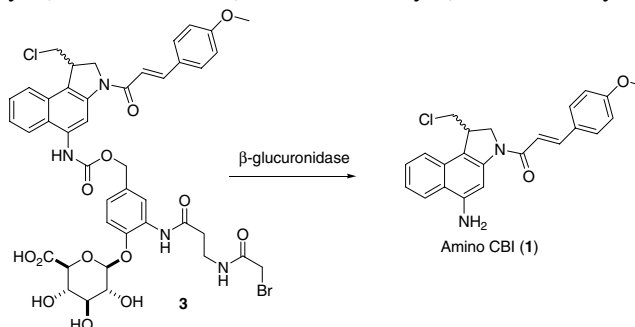




**Minor groove binder antibody conjugates employing a water soluble  $\beta$ -glucuronide linker**

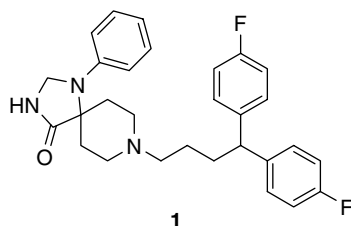
pp 2278–2280

Scott C. Jeffrey,\* Minh T. Nguyen, Ruth F. Moser, Damon L. Meyer, Jamie B. Miyamoto and Peter D. Senter

**Synthesis and structure–activity relationships of N-substituted spiropiperidines as nociceptin receptor ligands**

pp 2281–2284

John P. Caldwell,\* Julius J. Matasi, Hongtao Zhang, Ahmad Fawzi and Deen B. Tulshian

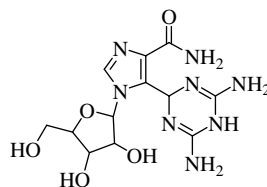


A series of N-substituted analogs based upon the spiropiperidine core of **1** was synthesized and exhibited high binding affinity to the nociceptin (NOP) receptor. The selectivities against other known opioid receptors were determined.

**An analogue of AICAR with dual inhibitory activity against WNV and HCV NTPase/helicase: Synthesis and in vitro screening of 4-carbamoyl-5-(4,6-diamino-2,5-dihydro-1,3,5-triazin-2-yl)-imidazole-1- $\beta$ -D-ribofuranoside**

pp 2285–2288

Ravi K. Ujjanamatada, Andrea Baier, Peter Borowski and Ramachandra S. Hosmane\*

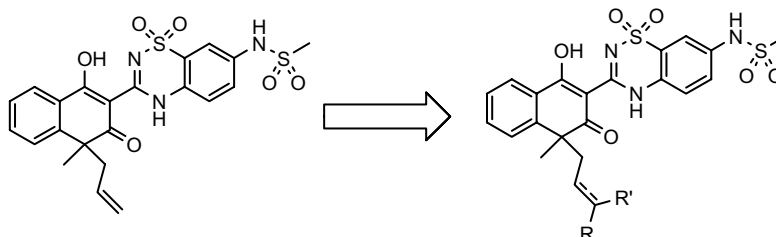


Synthesis and in vitro screening results of the title compound against *Flaviviridae* enzymes have been reported. The target compound exhibited anti-helicase activity against WNV and HCV NTPase/helicase with an  $IC_{50}$  of 23 and 37  $\mu$ M, respectively.

**Inhibitors of HCV NS5B polymerase: Synthesis and structure–activity relationships of unsymmetrical 1-hydroxy-4,4-dialkyl-3-oxo-3,4-dihydronaphthalene benzothiadiazine derivatives**

pp 2289–2292

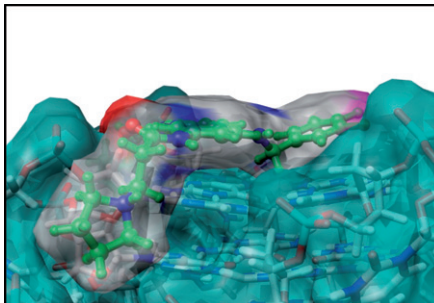
A. Chris Krueger,\* Darold L. Madigan, Brian E. Green, Douglas K. Hutchinson, Wen W. Jiang, Warren M. Kati, Yaya Liu, Clarence J. Maring, Sherie V. Masse, Keith F. McDaniel, Tim R. Middleton, Hongmei Mo, Akhteruzzaman Molla, Debra A. Montgomery, Teresa I. Ng and Dale J. Kempf



**Structure-based design of benzylamino-acridine compounds as G-quadruplex DNA telomere targeting agents**

pp 2293–2298

Cristina Martins, Mekala Gunaratnam, John Stuart, Vaidahi Makwana, Olga Greciano, Anthony P. Reszka, Lloyd R. Kelland and Stephen Neidle\*

**Discovery of novel 2,3-diarylfuro[2,3-*b*]pyridin-4-amines as potent and selective inhibitors of Lck: Synthesis, SAR, and pharmacokinetic properties**

pp 2299–2304

Matthew W. Martin,\* John Newcomb, Joseph J. Nunes, Jean E. Bemis, David C. McGowan, Ryan D. White, John L. Buchanan, Erin F. DiMauro, Christina Boucher, Theodore Faust, Faye Hsieh, Xin Huang, Josie H. Lee, Stephen Schneider, Susan M. Turci and Xiaotian Zhu

**Discovery of 4-amino-5,6-biaryl-furo[2,3-*d*]pyrimidines as inhibitors of Lck: Development of an expedient and divergent synthetic route and preliminary SAR**

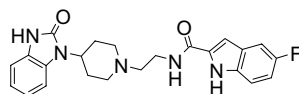
pp 2305–2309

Erin F. DiMauro,\* John Newcomb, Joseph J. Nunes, Jean E. Bemis, Christina Boucher, John L. Buchanan, William H. Buckner, Alan Cheng, Theodore Faust, Faye Hsieh, Xin Huang, Josie H. Lee, Teresa L. Marshall, Matthew W. Martin, David C. McGowan, Stephen Schneider, Susan M. Turci, Ryan D. White and Xiaotian Zhu

**Optimization of Halopemide for Phospholipase D2 inhibition**

pp 2310–2311

Lauren Monovich,\* Benjamin Mugrage, Elizabeth Quadros, Karen Toscano, Ruben Tommasi, Stacey LaVoie, Eugene Liu, Zhengming Du, Daniel LaSala, William Boyar and Paul Steed

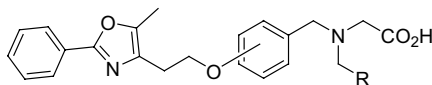


Halopemide, which was identified by HTS to inhibit phospholipase D2 (PLD2), provided the basis for an exploratory effort to identify potent inhibitors of PLD2 for use as inflammatory mediators. Parallel synthesis and purification were utilized to rapidly identify orally available amide analogs derived from indole 2-carboxylic acids with superior potency versus PLD2.

**Discovery of tertiary aminoacids as dual PPAR $\alpha$ / $\gamma$  agonists-I**

pp 2312–2316

Pratik V. Devasthale,\* Sean Chen, Yoon Jeon, Fucheng Qu, Denis E. Ryono, Wei Wang, Hao Zhang, Lin Cheng, Dennis Farrelly, Rajasree Golla, Gary Grover, Zhengping Ma, Lisa Moore, Ramakrishna Seethala, Wei Sun, Arthur M. Doweiko, Gamini Chandrasena, Paul Sleph, Narayanan Hariharan and Peter T. W. Cheng\*



1,3- and 1,4-Alkoxybenzylglycines

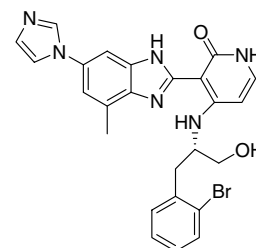
A novel series of potent dual agonists of PPAR $\alpha$  and PPAR $\gamma$ , the oxybenzylglycines, were identified and explored using a solution-phase library approach. The synthesis and structure–activity relationships of this series of dual PPAR $\alpha$ / $\gamma$  agonists are described.

**Discovery and initial SAR of 3-(1*H*-benzo[d]imidazol-2-yl)pyridin-2(1*H*)-ones as inhibitors of insulin-like growth factor 1-receptor (IGF-1R)**

pp 2317–2321

Upender Velaparthi,\* Mark Wittman, Peiying Liu, Karen Stoffan, Kurt Zimmermann, Xiaopeng Sang, Joan Carboni, Aixin Li, Ricardo Attar, Marco Gottardis, Ann Greer, ChiehYing Y. Chang, Bruce L. Jacobsen, John S. Sack, Yax Sun, David R. Langley, Balu Balasubramanian and Dolatrai Vyas

The discovery and synthesis of 3-(1*H*-benzo[d]imidazol-2-yl)pyridin-2(1*H*)-one inhibitors of insulin-like growth factor receptor-1 (IGF-1R) are presented. Installing amine containing side chains at the 4-position of pyridone ring significantly improved the enzyme potency. SAR and biological activity of these compounds are presented.

IGF1R IC<sub>50</sub> = 0.29  $\mu$ M**Estrogen receptor ligands. Part 16: 2-Aryl indoles as highly subtype selective ligands for ER $\alpha$** 

pp 2322–2328

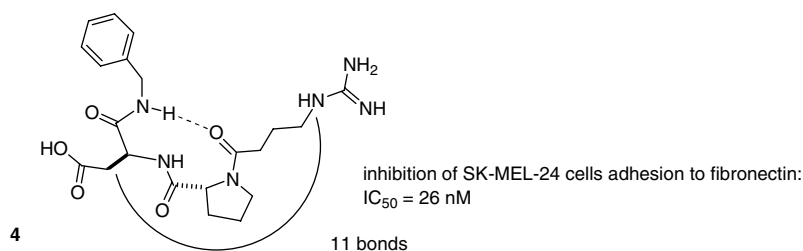
Kevin D. Dykstra,\* Liangqin Guo, Elizabeth T. Birzin, Wanda Chan, Yi Tien Yang, Edward C. Hayes, Carolyn A. DaSilva, Lee-Yuh Pai, Ralph T. Mosley, Bryan Kraker, Paula M. D. Fitzgerald, Frank DiNinno, Susan P. Rohrer, James M. Schaeffer and Milton L. Hammond

A novel class of indole ligands for estrogen receptor  $\alpha$  have been discovered which exhibit potent affinity and high selectivity. Substitution of the bazedoxifene skeleton to the linker present in the HTS lead **1a** provided **22b** which was found to be 130-fold  $\alpha$ -selective and acted as an antagonist of estradiol activity in uterine tissue and MCF-7 cancer cells.

**Inhibition of cancer cell adhesion by heterochiral Pro-containing RGD mimetics**

pp 2329–2333

Luca Gentilucci,\* Giuliana Cardillo, Federico Squassabia, Alessandra Tolomelli, Santi Spampinato, Antonino Sparta and Monica Baiula



**Design of antimicrobial compounds based on peptide structures**

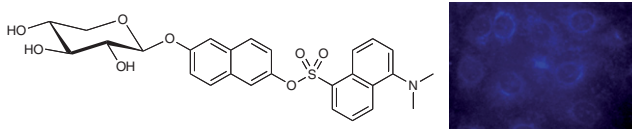
pp 2334–2337

Christian Appelt, Anna K. Schrey, J. Arvid Söderhäll and Peter Schmieder\*

**Evaluation of fluorescently labeled xylopyranosides as probes for proteoglycan biosynthesis**

pp 2338–2341

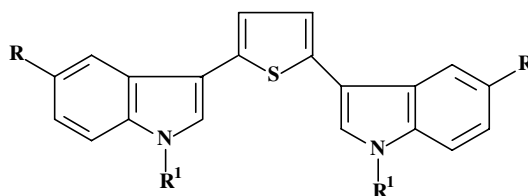
Richard Johnsson, Katrin Mani and Ulf Ellervik\*

**Synthesis and antitumor properties of 2,5-bis(3'-indolyl)thiophenes:**

pp 2342–2346

**Analogues of marine alkaloid nortopsentin**

Patrizia Diana,\* Anna Carbone, Paola Barraja, Alessandra Montalbano, Annamaria Martorana, Gaetano Dattolo, Ornella Gia, Lisa Dalla Via and Girolamo Cirrincione

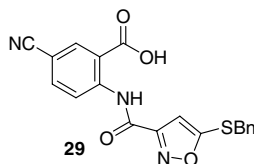


The synthesis and antitumor activity of novel 2,5-bis(3'-indolyl)thiophene derivatives are reported.

**Preparation of novel antibacterial agents. Replacement of the central aromatic ring with heterocycles**

pp 2347–2350

Jianke Li, Brian D. Wakefield, J. Craig Ruble, Cory M. Stiff, Donna L. Romero, Keith R. Marotti, Michael T. Sweeney, Gary E. Zurenko, Douglas C. Rohrer and Atli Thorarensen\*

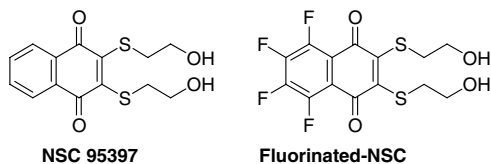


This paper describes the discovery of anthranilic acid derivatives as potent antibacterial agents against Gram-positive organisms.

**Fluorinated NSC as a Cdc25 inhibitor**

pp 2351–2354

Hwangseo Park, Brian I. Carr, Minghua Li and Seung Wook Ham\*

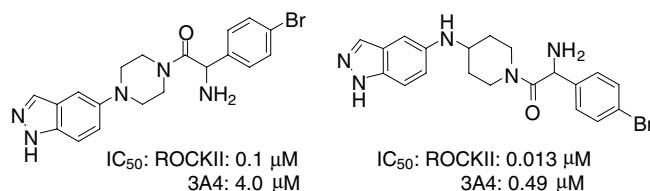


We report on the fluorinated form of NSC 95397 as a Cdc25B inhibitor.

**Structure–activity relationships, and drug metabolism and pharmacokinetic properties for indazole piperazine and indazole piperidine inhibitors of ROCK-II**

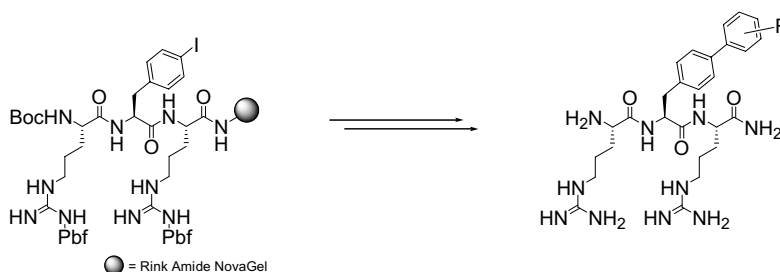
pp 2355–2360

Yangbo Feng, Michael D. Cameron, Bozena Frackowiak, Evelyn Griffin, Li Lin, Claudia Ruiz, Thomas Schröter and Philip LoGrasso\*

**Application of the Suzuki–Miyaura cross-coupling to increase antimicrobial potency generates promising novel antibacterials**

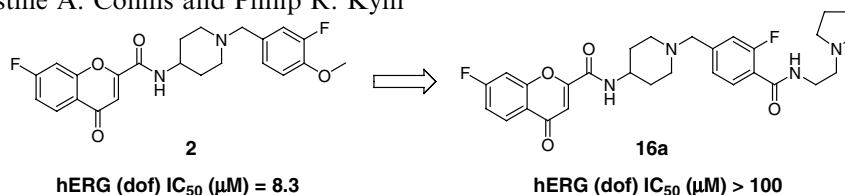
pp 2361–2364

Bengt Erik Haug,\* Wenche Stensen and John S. Svendsen

**Identification of diamino chromone-2-carboxamides as MCHR1 antagonists with minimal hERG channel activity**

pp 2365–2371

Andrew S. Judd,\* Andrew J. Souers, Dariusz Wodka, Gang Zhao, Mathew M. Mulhern, Rajesh R. Iyengar, Ju Gao, John K. Lynch, Jennifer C. Freeman, H. Douglas Falls, Sevan Brodjian, Brian D. Dayton, Regina M. Reilly, Gary Gintant, James T. Limberis, Ann Mikhail, Sandra T. Leitz, Kathryn A. Houseman, Gilbert Diaz, Eugene N. Bush, Robin Shapiro, Victoria Knourek-Segel, Lisa E. Hernandez, Kennan C. Marsh, Hing L. Sham, Christine A. Collins and Philip R. Kym

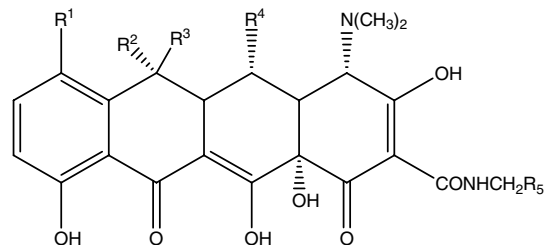


### Newer tetracycline derivatives: Synthesis, anti-HIV, antimycobacterial activities and inhibition of HIV-1 integrase

pp 2372–2375

Dharmarajan Sriram,\* Perumal Yogeewari, Geetha Senchani and Debjani Banerjee

A series of tetracycline derivatives has been synthesized by reacting appropriate tetracyclines, formaldehyde and secondary amino (piperazino) function of fluoroquinolones using microwave irradiation. Compound **10** was found to be the most promising compound active against HIV-1 replication with  $EC_{50}$  of 5.2  $\mu$ M and was nontoxic to the CEM cells until 200  $\mu$ M, and MIC of 0.2  $\mu$ g/mL against *Mycobacterium tuberculosis*, with moderate inhibition of both 3'-processing and strand transfer steps of HIV-1 IN.

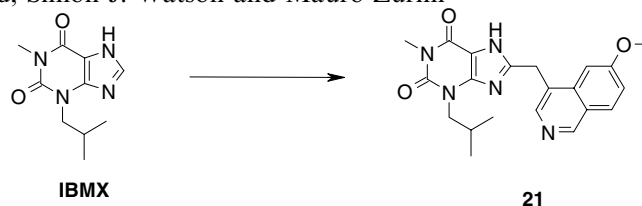


### Potent and selective xanthine-based inhibitors of phosphodiesterase 5

pp 2376–2379

Nichola J. Arnold, Ruth Arnold, David Beer, Gurdip Bhalay, Stephen P. Collingwood, Sarah Craig, Nicholas Devereux, Mark Dodds, Andrew R. Dunstan, Robin A. Fairhurst, David Farr, Joseph D. Fullerton, Angela Glen, Sylvie Gomez, Sandra Haberthuer, Julia D. I. Hatto, Colin Howes, Darryl Jones, Thomas H. Keller, Beate Leuenberger, Heinz E. Moser, Irene Muller, Reto Naef, Paul A. Nicklin, David A. Sandham,\* Katharine L. Turner, Morris F. Tweed, Simon J. Watson and Mauro Zurini

Inhibitors of PDE5 are useful therapeutic agents for treatment of erectile dysfunction. A series of novel xanthine derivatives has been identified as potent inhibitors of PDE5, with good levels of selectivity against other PDE isoforms, including PDE6. Studies in the dog indicate excellent oral bioavailability for compound **21**.



### Synthesis and biological activity of 5-aza-ellipticine derivatives

pp 2380–2384

Deborah L. Moody, Marcin Dyba, Teresa Kosakowska-Cholody, Nadya I. Tarasova\* and Christopher J. Michejda

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\*Corresponding author

+ Supplementary data available via ScienceDirect

**COVER**

Typical snapshot of **7b** bound to HIV-RT from an MC simulation. Carbon atoms of **7b** are gold; from the left, Tyr181, Tyr188, Phe227, Leu100, Lys101; Trp229 at the top, Val106 at the bottom. H-bond with Lys101 O on right. Some residues in front including Glu138 have been removed for clarity. The water on N5 is also H-bonded to a carboxylate O of Glu138. [Thakur, V. T.; Kim, J. T.; Hamilton, A. D.; Bailey, C. M.; Domaoal, R. A.; Wang, L.; Anderson, K. S.; Jorgensen, W. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5664.]

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