

## Contents

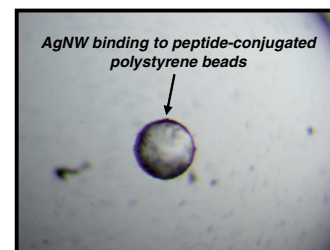
### ARTICLES

#### Generating short peptidic ligands for silver nanowires from phage display random libraries

pp 5261–5264

Priscilla Chan, Tiffany Phan, Michael C. Kao, Cheryl Dolan and Jeffrey B.-H. Tok\*

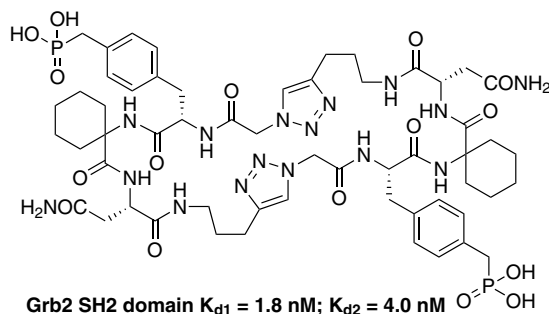
We report the generation of peptide ligands for silver nanowires using a linear 12-mer peptide phage display random library technique. A selected binding peptide, together with two mutant peptide sequences, were subsequently synthesized on Tentagel resins to examine the importance of both the identities and positions of the conserved amino acid residues.



#### Application of azide–alkyne cycloaddition ‘click chemistry’ for the synthesis of Grb2 SH2 domain-binding macrocycles

pp 5265–5269

Won Jun Choi, Zhen-Dan Shi, Karen M. Worthy, Lakshman Bindu, Rajeshri G. Karki, Marc C. Nicklaus, Robert J. Fisher and Terrence R. Burke, Jr.\*



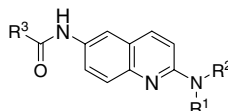
Grb2 SH2 domain  $K_{d1} = 1.8 \text{ nM}$ ;  $K_{d2} = 4.0 \text{ nM}$



#### 2-Aminoquinoline melanin-concentrating hormone (MCH)1R antagonists

pp 5270–5274

Jinlong Jiang, Myle Hoang, Jonathan R. Young, Danny Chaung, Ronsar Eid, Cherilyn Turner, Peter Lin, Xinchun Tong, Junying Wang, Carina Tan, Scott Feighner, Oksana Palyha, Donna L. Hreniuk, Jie Pan, Andreas W. Sailer, Douglas J. MacNeil, Andrew Howard, Lauren Shearman, Sloan Stribling, Ramon Camacho, Alison Strack, Lex H. T. Van der Ploeg, Mark T. Goulet and Robert J. DeVita\*

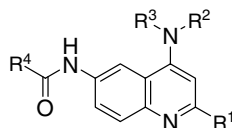


Structure–activity relationships and in vivo activity of 2-aminoquinoline MCH1R antagonists are reported.

**4-Aminoquinoline melanin-concentrating hormone 1-receptor (MCH1R) antagonists**

pp 5275–5279

Jinlong Jiang, Peter Lin, Myle Hoang, Lehua Chang, Carina Tan, Scott Feighner, Oksana C. Palyha, Donna L. Hreniuk, Jie Pan, Andreas W. Sailer, Nancy R. Morin, Douglas J. MacNeil, Andrew D. Howard, Lex H. T. Van der Ploeg, Mark T. Goulet and Robert J. DeVita\*

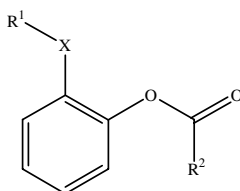


Structure–activity relationships of 4-aminoquinoline MCH1R antagonists are reported.

**Inhibitory mode of 2-acetoxyphenyl alkyl sulfides against COX-1 and COX-2: QSAR analyses**

pp 5280–5284

Hemant Kumar Jain,\* V. K. Mourya and R. K. Agrawal



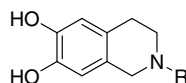
01–29

These studies suggest that indicator variables like presence of aromatic ring and triple bond play an important role in COX-2 selectivity and lesser degree of unsaturation in the molecule is conducive for COX-1 inhibition.

**Design, synthesis, and antifungal activities in vitro of novel tetrahydroisoquinoline compounds based on the structure of lanosterol 14 $\alpha$ -demethylase (CYP51) of fungi**

pp 5285–5289

Ju Zhu, Jiaguo Lu, Youjun Zhou,\* Yaowu Li, Jun Cheng and Canhui Zheng

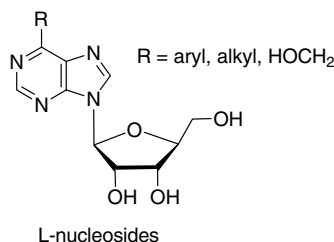


Tetrahydroisoquinoline lead molecules based on CYP51 of fungi were discovered by coupling structure-based de novo design. The chemical synthesis and the antifungal activities in vitro of them were reported. The bonding mode of the lead molecules with CYP51 is different from that of azoles.

**Cytostatic and antiviral 6-arylpurine ribonucleosides. Part 7: Synthesis and evaluation of 6-substituted purine L-ribonucleosides**

pp 5290–5293

Michal Hocek,\* Peter Šilhár, I-hung Shih, Eric Mabery and Richard Mackman

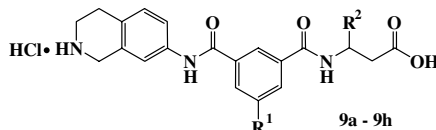


L-nucleosides

**Derivatives of 7-amino-1,2,3,4-tetrahydroisoquinoline and isophthalic acids as novel fibrinogen receptor antagonists**

pp 5294–5297

Olga L. Malovichko, Anna S. Petrus, Andrei A. Krysko,\* Tatyana A. Kabanova, Sergei A. Andronati, Tamara L. Karaseva and Anna V. Kiriya

The synthesis of the novel fibrinogen receptor antagonists **9a–9h** is reported.**Synthesis and anti-HIV-1 activity of a novel series of 1,4,2-benzodithiazine-dioxides**

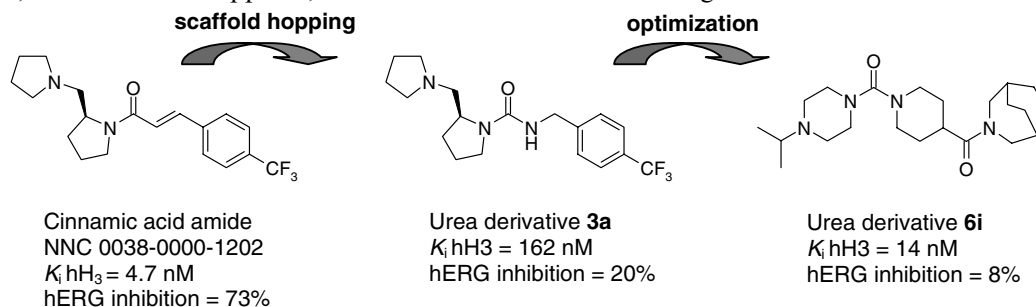
pp 5298–5302

Zdzisław Brzozowski, Franciszek Sączewski\* and Nouri Neamati

**Ureas with histamine H<sub>3</sub>-antagonist receptor activity—A new scaffold discovered by lead-hopping from cinnamic acid amides**

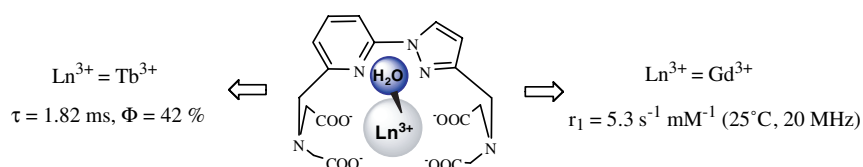
pp 5303–5308

Jesper F. Lau,\* Claus Bekker Jeppesen, Karin Rimvall and Rolf Hohlweg

**A dual lanthanide probe suitable for optical (Tb<sup>3+</sup> luminescence) and magnetic resonance imaging (Gd<sup>3+</sup> relaxometry)**

pp 5309–5312

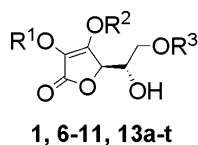
Claude Picard,\* Neri Geum, Isabelle Nasso, Béatrice Mestre, Pierre Tisnès, Sophie Laurent, Robert N. Muller and Luce Vander Elst



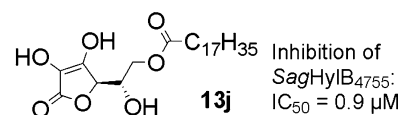
### Novel 6-*O*-acylated vitamin C derivatives as hyaluronidase inhibitors with selectivity for bacterial lyases

pp 5313–5316

Martin Spickenreither, Stephan Braun, Günther Bernhardt,  
Stefan Dove and Armin Buschauer\*



R<sup>1</sup>, R<sup>2</sup> = H; alkyl; benzyl  
R<sup>3</sup> = H; alkanoyl; benzoyl; aryloxyalkanoyl; benzyloxyaryl-  
alkanoyl; biphenylylacetyl; biphenylyloxyalkanoyl;  
biphenylylmethyloxyalkanoyl



Based on an X-ray structure of a bacterial hyaluronate lyase in complex with ascorbic acid 6-*O*-palmitate the title compounds bearing lipophilic substituents were synthesized and investigated for inhibition of bacterial (HylB<sub>4755</sub> from *Streptococcus agalactiae*) and bovine testicular hyaluronidase. Compounds such as **13j** are among the most potent hyaluronidase inhibitors known to date.

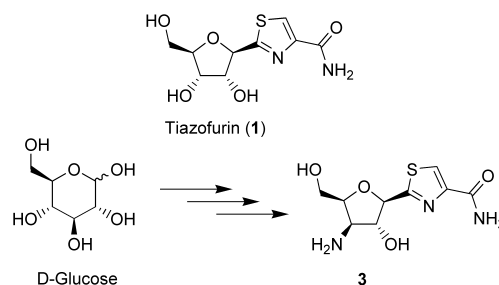
### 2-(3-Amino-3-deoxy-β-D-xylofuranosyl)thiazole-4-carboxamide:

pp 5317–5320

#### A new tiazofurin analogue with potent antitumour activity

Mirjana Popsavin,\* Saša Spaić, Miloš Svirčev, Vesna Kojić,  
Gordana Bogdanović and Velimir Popsavin

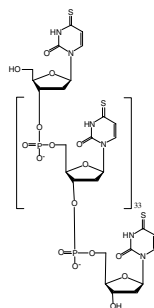
A new tiazofurin analogue **3** was synthesized starting from D-glucose and evaluated for its in vitro antiproliferative activity against a panel of human tumour cell lines.



### Effect of the extent of thiolation and introduction of phosphorothioate internucleotide linkages on the anti-HIV activity of Suligovir [(s<sup>4</sup>dU)<sub>35</sub>]

pp 5321–5323

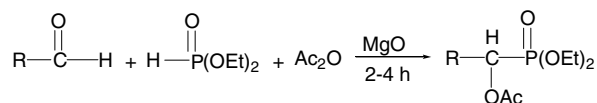
András Horváth, Zoltán Beck, Thomas J. Bardos, Joseph A. Dunn and Janos Aradi\*



### A new, efficient, and simple method for the one-pot synthesis of α-acetoxyposphonates from aldehydes under solvent-free conditions

pp 5324–5327

Babak Kaboudin\* and Masoumeh Karimi

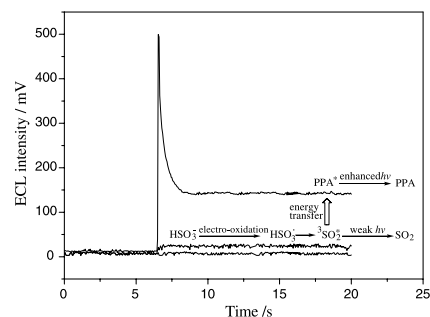


**Electrochemiluminescence determination of pipemidic acid using sulfite as energy transfer mediator**

pp 5328–5333

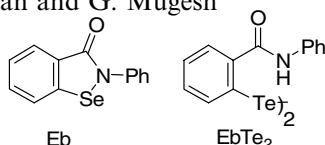
Yao-Dong Liang, Wei Gao and Jun-Feng Song\*

An electrochemiluminescence (ECL) based on energy transfer from electro-generated triplet sulfur dioxide to pipemidic acid (PPA) was studied.

**Horseradish peroxidase inhibition and antioxidant activity of ebselen and related organoselenium compounds**

pp 5334–5338

Beena Mishra, K.I. Priyadarsini, Hari Mohan and G. Mugesh\*

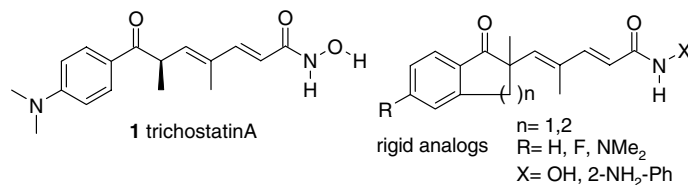


Horseradish peroxidase (HRP) inhibition and glutathione peroxidase (GPx) activities of ebselen and some related derivatives are described. These studies show that ebselen and ebselen ditelluride (EbTe<sub>2</sub>) with significant antioxidant activity, inhibit the HRP-catalyzed oxidation reactions. In addition, inhibition of lipid peroxidation and singlet oxygen quenching studies were carried out. Although the inhibition of HRP by ebselen is comparable with that of EbTe<sub>2</sub>, the inhibitory effect on  $\gamma$ -radiation induced lipid peroxidation and the GPx activity of ebselen is found to be much higher than that of EbTe<sub>2</sub>.

**Synthesis of rigid trichostatin A analogs as HDAC inhibitors**

pp 5339–5344

Cédric Charrier, Philippe Bertrand,\* Jean-Pierre Gesson and Joëlle Roche

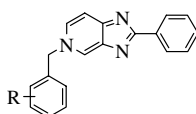


New inhibitors of histone deacetylase (HDAC) with limited conformational mobility based on rigid analogs of trichostatin A (TSA) were synthesized, by alkylation of appropriate indanones (or tetralones). Hydroxamic acid and aminobenzamide derivatives were obtained and evaluated for their activity toward non small lung cancer cell line H661.

**Substituted 5-benzyl-2-phenyl-5H-imidazo[4,5-c]pyridines: A new class of pestivirus inhibitors**

pp 5345–5349

Gerhard Puerstinger,\* Jan Paeshuyse, Piet Herdewijn, Jef Rozenski, Erik De Clercq and Johan Neyts

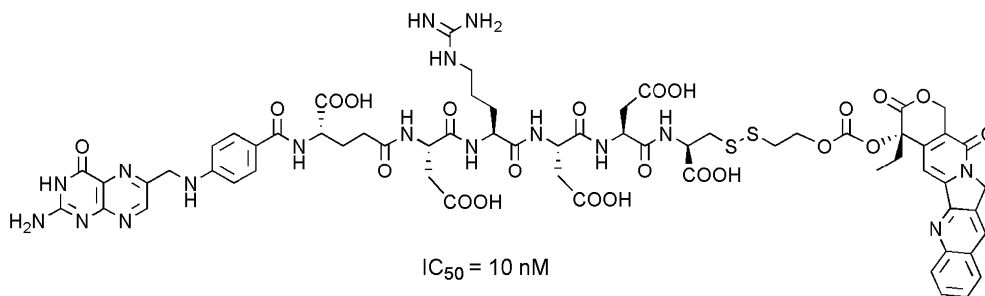


**Synthesis and activity of a folate peptide camptothecin prodrug**

pp 5350–5355

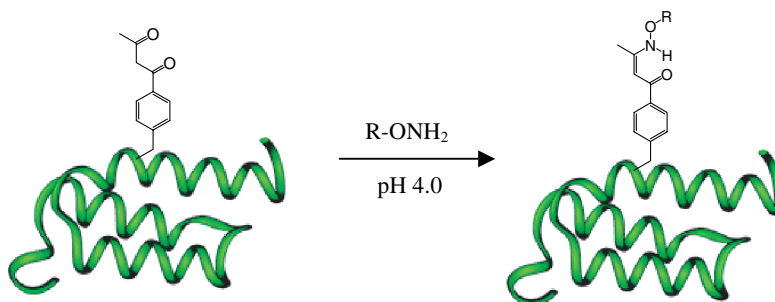
Walter A. Henne, Derek D. Doorneweerd, Andrew R. Hilgenbrink, Sumith A. Kularatne and Philip S. Low\*

The synthesis and activity ( $IC_{50} = 10$  nM) of a folate peptide camptothecin prodrug with a disulfide carbonate releasable linker is reported.

**Genetic introduction of a diketone-containing amino acid into proteins**

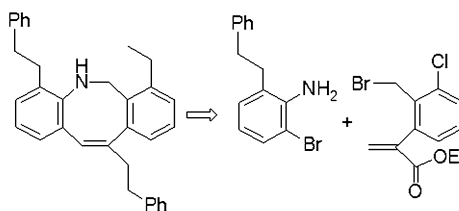
pp 5356–5359

Huaqiang Zeng, Jianming Xie and Peter G. Schultz\*

**Synthesis of highly substituted dibenzo[b,f]azocines and their evaluation as protein kinase inhibitors**

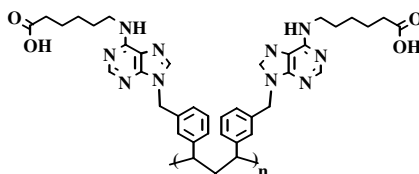
pp 5360–5363

Leggy A. Arnold and R. Kiplin Guy\*

**Phosphodiester modification by zinc metalated adenine polymer with carboxyl pendants**

pp 5364–5367

Yogita Gupta, G.N. Mathur,\* Masood Parvez and Sandeep Verma\*



Phosphate ester hydrolysis and plasmid relaxation by metalated modified adenine polymer containing carboxyl group appendages is reported.

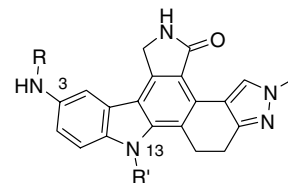


**Novel C-3 *N*-urea, amide, and carbamate dihydroindazolo[5,4-*a*]pyrrolo[3,4-*c*]carbazole analogs as potent TIE-2 and VEGF-R2 dual inhibitors**

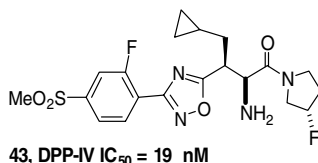
pp 5368–5372

Nadine C. Becknell,\* Allison L. Zulli, Thelma S. Angeles, Shi Yang, Mark S. Albom, Lisa D. Aimone, Candy Robinson, Hong Chang and Robert L. Hudkins

A novel series of C-3 urea, amide, and carbamate fused dihydroindazolocarbazole (DHI) analogs are reported as highly potent dual inhibitors of TIE-2 and VEGF-R2 receptor tyrosine kinases with excellent cellular potency. Structure–activity relationship (SAR) studies indicate the optimal N-13 alkyl substitutions are *n*-propyl and *i*-butyl. The isopropyl carbamate **39** displayed good dual enzyme, cell potency, and rat pharmacokinetic properties for advancement to in vivo evaluation.

**Discovery of potent, selective, and orally bioavailable oxadiazole-based dipeptidyl peptidase IV inhibitors** pp 5373–5377

Jinyou Xu,\* Lan Wei, Robert J. Mathvink, Scott D. Edmondson, George J. Eiermann, Huaibing He, Joseph F. Leone, Barbara Leiting, Kathryn A. Lyons, Frank Marsilio, Reshma A. Patel, Sangita B. Patel, Aleksandr Petrov, Giovanna Scapin, Joseph K. Wu, Nancy A. Thornberry and Ann E. Weber

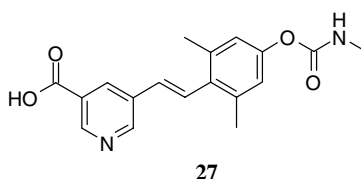


A novel series of oxadiazole-based amides have been shown to be potent DPP-4 inhibitors. The optimized compound **43** exhibited excellent selectivity over a variety of DPP-4 homologs.

**Aza-stilbenes as potent and selective c-RAF inhibitors**

pp 5378–5383

Octerloney McDonald, Karen Lackey, Ronda Davis-Ward, Edgar Wood, Vicente Samano, Patrick Maloney, Felix Deanda and Robert Hunter\*

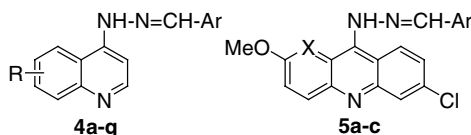


Compound **27** possesses significant potency against c-RAF and demonstrates selectivity over other protein kinases. A hypothesis for the binding mode, activity, and selectivity is proposed.

**Synthesis of *N*1-arylidene-*N*2-quinolyl- and *N*2-acrydinyldiazones as potent antimalarial agents active against CQ-resistant *P. falciparum* strains**

pp 5384–5388

Sandra Gemma, Gagan Kukreja, Caterina Fattorusso, Marco Persico, Maria P. Romano, Maria Altarelli, Luisa Savini, Giuseppe Campiani,\* Ernesto Fattorusso, Nicoletta Basilico, Donatella Taramelli, Vanessa Yardley and Stefania Butini

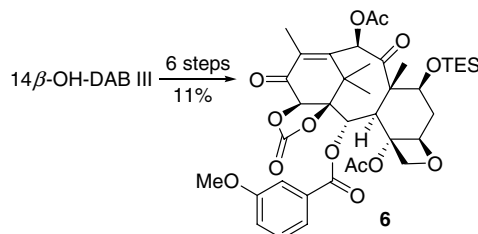


A series of *N*1-arylidene-*N*2-quinolyl- and *N*2-acrydinyldiazones were synthesized and tested for their antimalarial activity. These compounds showed remarkable anti-plasmodial activity in vitro especially against chloroquine-resistant strains.

**14 $\beta$ -Hydroxy-10-deacetylbaccatin III as a convenient, alternative substrate for the improved synthesis of methoxylated second-generation taxanes**

pp 5389–5391

Luciano Barboni,\* Guido Giarlo, Roberto Ballini and Gabriele Fontana

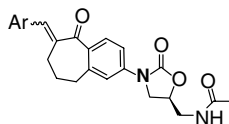


A new, improved synthesis of the 2-debenzoyl-2-*m*-methoxybenzoyl-7-triethylsilyl-13-oxo-14 $\beta$ -hydroxybaccatin III 1,14-carbonate (**6**), the key intermediate in the synthesis of two new second-generation antitumor taxanes, is described.

**Synthesis and structure–activity studies of novel benzocycloheptanone oxazolidinone antibacterial agents**

pp 5392–5397

J. V. N. Vara Prasad,\* Frederick E. Boyer, Lou Chupak, Michael Dermeyer, Qizhu Ding, K. Gavardinas, Susan E. Hagen, Michael D. Huband, Wenhua Jiao, Takushi Kaneko, Samarendra N. Maiti, Michael Melnick, Karina Romero, M. Patterson and Xiujuan Wu

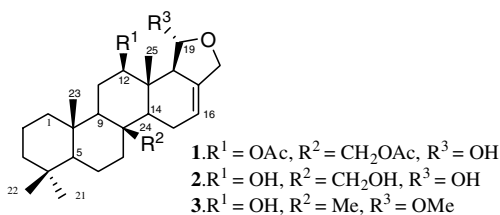


We describe a novel class of benzoheptanone derived oxazolidinone antibacterial agents. The synthesis and antibacterial activities with structure variation are described.

**Farnesoid X-activated receptor antagonists from a marine sponge *Spongia* sp.**

pp 5398–5402

Sang-Jip Nam, Hyunsil Ko, Mihee Shin, Jungyeob Ham, Jungwook Chin, Youngshin Kim, Heeyoung Kim, Kyoungjin Shin, Hyukjae Choi and Heonjoong Kang\*

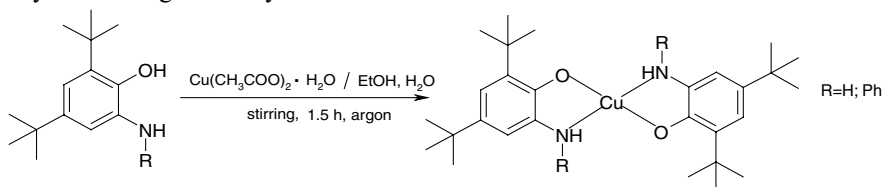


The isolation and structures of three novel scalarane sesterterpenes **1–3** and their inhibition of FXR transactivation are reported.

**Synthesis and biological evaluation of copper (II) complexes of sterically hindered *o*-aminophenol derivatives as antimicrobial agents**

pp 5403–5407

Natalia V. Loginova,\* Tat'yana V. Koval'chuk, Rimma A. Zheldakova, Nikolai P. Osipovich, Victor L. Sorokin, Genrikh I. Polozov, Galina A. Ksendzova, Gennady K. Glushonok, Anna A. Chernyavskaya and Oleg I. Shadyro



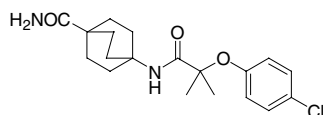
Cu(II) complexes with two sterically hindered *o*-aminophenol derivatives have been synthesized and characterized by means of elemental analysis and various physico-chemical techniques. The antimicrobial activities of compounds were tested.



### Synthesis and structural activity relationship of 11 $\beta$ -HSD1 inhibitors with novel adamantane replacements

pp 5408–5413

Vince S. C. Yeh,\* Ravi Kurukulasuriya, David Madar, Jyoti R. Patel, Steven Fung, Katina Monzon, William Chiou, Jiahong Wang, Peer Jacobson, Hing L. Sham and J. T. Link

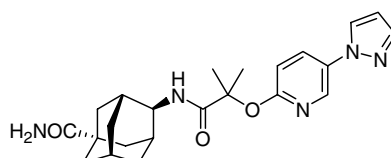


A series of structurally novel and metabolically stable bridged bicyclic carbocycle and heterocycle adamantane replacements have been synthesized and biologically evaluated. Several of these compounds exhibit excellent human and mouse 11 $\beta$ -HSD1 potency and 11 $\beta$ -HSD2 selectivity.

### Synthesis and biological evaluation of heterocycle containing adamantane 11 $\beta$ -HSD1 inhibitors

pp 5414–5419

Vince S. C. Yeh,\* Jyoti R. Patel,\* Hong Yong, Ravi Kurukulasuriya, Steven Fung, Katina Monzon, William Chiou, Jiahong Wang, Deanne Stolarik, Hovis Imade, David Beno, Michael Brune, Peer Jacobson, Hing Sham and J. T. Link

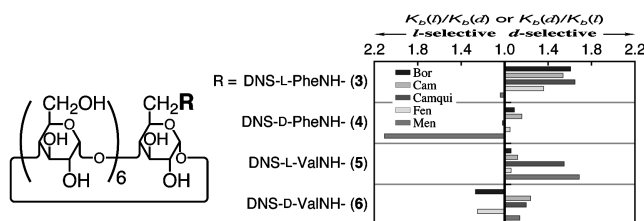


A series of metabolically stable adamantane amide 11 $\beta$ -HSD1 inhibitors have been synthesized and biologically evaluated. These compounds exhibit excellent HSD1 potency and HSD2 selectivity and good pharmacokinetic and pharmacodynamic profiles.

### Chiral recognition by fluorescent chemosensors based on *N*-dansyl-amino acid-modified cyclodextrins

pp 5420–5423

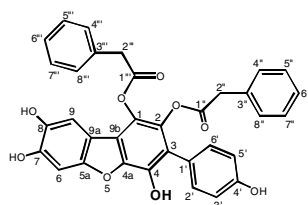
Hiroshi Ikeda,\* Qun Li and Akihiko Ueno



### Vialinin B, a novel potent inhibitor of TNF- $\alpha$ production, isolated from an edible mushroom, *Thelephora vialis*

pp 5424–5426

Chun Xie, Hiroyuki Koshino, Yasuaki Esumi, Jun-ichi Onose, Kunie Yoshikawa and Naoki Abe\*



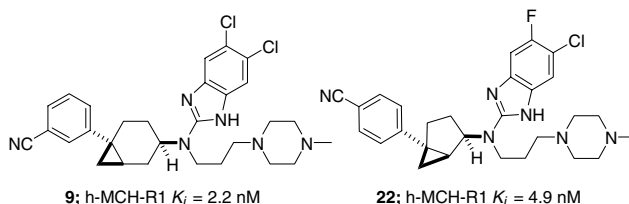
Inhibition of TNF- release	
Sample	IC <sub>50</sub> ( nM )
ganbajunin B	5000
vialinin B	0.02
cycloleucomelone	3500

Vialinin B had an IC<sub>50</sub> value of 0.02 nM, indicating that vialinin B was approximately  $2 \times 10^5$ -fold more effective than the related compounds, ganbajunin B and cycloleucomelone.

**Novel aminobenzimidazoles as selective MCH-R1 antagonists for the treatment of metabolic diseases**

pp 5427–5431

T. K. Sasikumar,\* Li Qiang, Duane A. Burnett, William J. Greenlee, Brian E. Hawes, Timothy J. Kowalski, Kim O'Neill, Brian D. Spar and Blair Weig

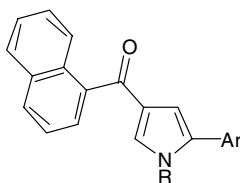


A series of potent and highly selective melanin-concentrating hormone (MCH) inhibitors is described.

**1-Alkyl-2-aryl-4-(1-naphthoyl)pyrroles: New high affinity ligands for the cannabinoid CB<sub>1</sub> and CB<sub>2</sub> receptors**

pp 5432–5435

John W. Huffman,\* Lea W. Padgett, Matthew L. Isherwood, Jenny L. Wiley and Billy R. Martin

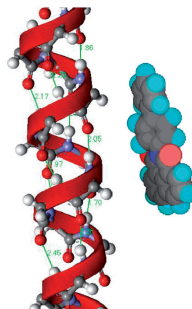


The synthesis and pharmacology of 28 1-alkyl-2-aryl-4-(1-naphthoyl)pyrroles are described. Several of these compounds have high affinity for both the CB<sub>1</sub> and CB<sub>2</sub> receptors.

**Toward intrinsically fluorescent proteomimetics: Fluorescent probe response to alpha helix structure of poly-γ-benzyl-L-glutamate**

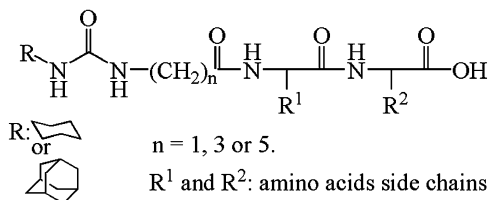
pp 5436–5438

Kenji Hutt, Randy Hernandez and Michael D. Heagy\*


**Peptidyl-urea based inhibitors of soluble epoxide hydrolases**

pp 5439–5444

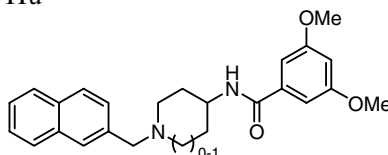
Christophe Morisseau, John W. Newman, Hsing-Ju Tsai, Preston A. Baecker and Bruce D. Hammock\*



**Identification of substituted 4-aminopiperidines and 3-aminopyrrolidines as potent MCH-R1 antagonists for the treatment of obesity**

pp 5445–5450

Nick Kim, Kenneth M. Meyers, Jose L. Mendez-Andino, Namal C. Warshakoon, Wei Ji, John A. Wos, Annyodile Colson, M. Chrissy Mitchell, Jan R. Davis, Beth B. Pinney, Ofer Reizes and X. Eric Hu\*



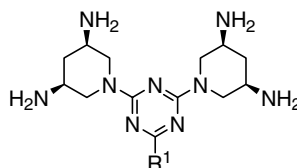
Structure modification of 4-aminopiperidine, an HTS hit, led to the identification of 4-piperidinylbenzamide (**5c**) as a potent MCH antagonist ( $K_i = 27$  nM). Further optimization via piperidine ring contraction resulted in enhanced activity in a 3-aminopyrrolidine series, where 3-pyrrolidinylbenzamide (**10i**) was found to be an excellent MCH antagonist ( $K_i = 7$  nM).

**Structure–activity relationships of novel antibacterial translation inhibitors:**

pp 5451–5456

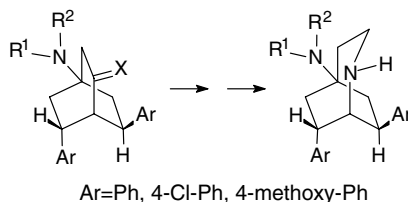
**3,5-Diamino-piperidinyl triazines**

Yuefen Zhou, Zhongxiang Sun, Jamie M. Froelich, Thomas Hermann and Daniel Wall\*

**Antiprotozoal activities of new bis-chlorophenyl derivatives of bicyclic octanes and aza-nonanes**

pp 5457–5461

Heinrich Berger, Werner Seebacher,\* Robert Saf, Marcel Kaiser, Reto Brun and Robert Weis

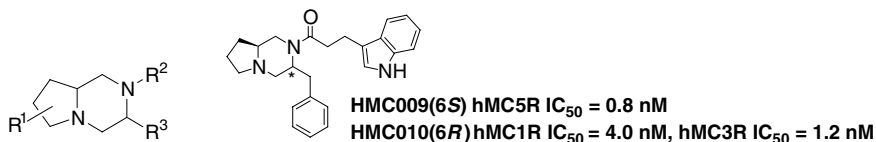


The in vitro activity of newly synthesized bis-(chlorophenyl)-azabicyclo[3.2.2]nonanes and bis-(chlorophenyl)-bicyclo[2.2.2]octanes against *Plasmodium falciparum*  $K_1$  (resistant to chloroquine and pyrimethamine) and *Trypanosoma brucei rhodesiense* was investigated.

**Design, synthesis, and biological evaluation of a new class of small molecule peptide mimetics targeting the melanocortin receptors**

pp 5462–5467

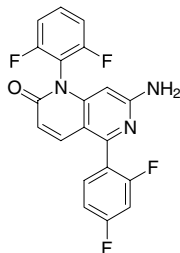
James P. Cain, Alexander V. Mayorov, Mingying Cai, Hui Wang, Bahar Tan, Kevin Chandler, YeonSun Lee, Ravil R. Petrov, Dev Trivedi and Victor J. Hruby\*



The design, synthesis, and evaluation of new high-affinity antagonists of the human melanocortin receptors (hMCRs) is reported.


**p38 MAP kinase inhibitors. Part 5: Discovery of an orally bio-available and highly efficacious compound based on the 7-amino-naphthyridone scaffold****pp 5468–5471**

Swaminathan R. Natarajan,\* Luping Liu, Mark Levorse, James E. Thompson, Edward A. O'Neill, Stephen J. O'Keefe, Kalpit A. Vora, Raymond Cvetovich, John Y. Chung, Ester Carballo-Jane and Denise M. Visco

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\*Corresponding author

\* Supplementary data available via ScienceDirect

**COVER**

View of the crystal structure of the DB819-d(CGCGAATTCGCG)<sub>2</sub> 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.]

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