

## Contents

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**Publisher's Announcement — Supplementary Data**

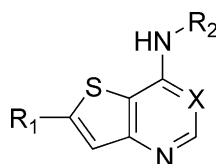
p 17  
p 19

### COMMUNICATIONS

**Design and SAR of thienopyrimidine and thienopyridine inhibitors of VEGFR-2 kinase activity**

pp 21–24

Michael J. Munchhof,\* Jean S. Beebe, Jeffery M. Casavant, Beth A. Cooper, Jonathan L. Doty, R. Carla Higdon, Stephen M. Hillerman, Catherine I. Soderstrom, Elisabeth A. Knauth, Matthew A. Marx, Ann Marie K. Rossi, Susan B. Sobolov and Jianmin Sun



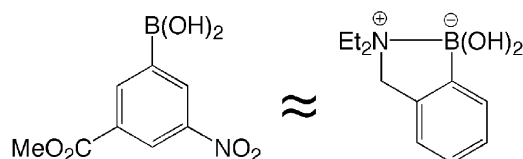
X = CH or N

Novel thienopyrimidines and thienopyridines have been identified as potent inhibitors of VEGFR-2 kinase activity. The synthesis and SAR of these compounds is presented, highlighting our successful effort to diminish the EGFR kinase activity in the lead series.

**3-Methoxycarbonyl-5-nitrophenyl boronic acid: high affinity diol recognition at neutral pH**

pp 25–27

Hormuzd R. Mulla, Nicholas J. Agard and Amit Basu\*

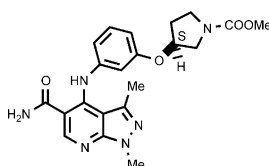


The nitro-boronic acid can be a substitute for the *ortho*-aminomethyl aryl-boronic acid motif for carbohydrate recognition.

**New orally active PDE4 inhibitors with therapeutic potential**

pp 29–32

Hiroshi Ochiai, Akiharu Ishida, Tazumi Ohtani, Kensuke Kusumi, Katuya Kishikawa, Takaaki Obata, Hisao Nakai\* and Masaaki Toda

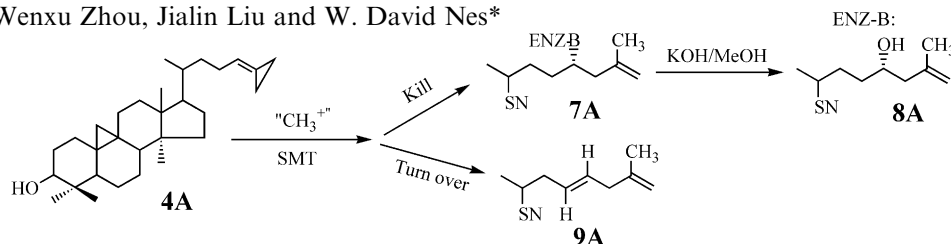


The discovery of an orally active pyrazolopyridine derivative as a structurally new PDE4 inhibitor is reported.

### Mechanism-based active site modification of the soybean sterol methyltransferase by 26,27-dehydrocycloartenol

pp 33–36

Zhihong Song, Wenxu Zhou, Jialin Liu and W. David Nes\*

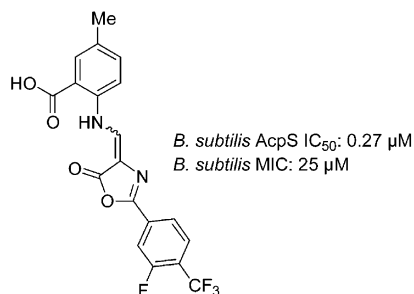


26,27-Dehydrocycloartenol was assayed with the sterol methyltransferase from soybean and found to be catalyzed to monol (turnover product **9A**) and diol (hydrolysis product assumed to be covalently attached to SMT **8A**) structures yielding a partition ratio of 0.06.

### Anthranilate 4*H*-oxazol-5-ones: novel small molecule antibacterial acyl carrier protein synthase (AcpS) inhibitors

pp 37–41

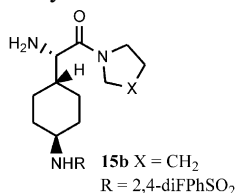
Adam M. Gilbert,\* Matthew Kirisits, Patrick Toy, David S. Nunn, Amadeo Failli, Elizabeth G. Dushin, Elena Novikova, Peter J. Petersen, Diane Joseph-McCarthy, Iain McFadyen and Christian C. Fritz



### 4-Amino cyclohexylglycine analogues as potent dipeptidyl peptidase IV inhibitors

pp 43–46

Emma R. Parmee,\* Jiafang He, Anthony Mastracchio, Scott D. Edmondson, Larry Colwell, George Eiermann, William P. Feeney, Bahanu Habulihaz, Huaibing He, Ruth Kilburn, Barbara Leiting, Kathryn Lyons, Frank Marsilio, Reshma A. Patel, Aleksandr Petrov, Jerry Di Salvo, Joseph K. Wu, Nancy A. Thornberry and Ann E. Weber

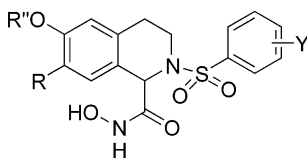


Aryl capped 4-amino cyclohexylglycine analogues were potent DP-IV inhibitors (IC<sub>50</sub> 3–200 nM). Sulfonamide **15b** was orally efficacious at 3 mpk in an OGTT in lean mice.

### Tetrahydroisoquinoline based sulfonamide hydroxamates as potent matrix metalloproteinase inhibitors

pp 47–50

Dawei Ma,\* Wengen Wu, Guoxin Yang, Jingya Li, Jia Li and Qizhuang Ye\*



**In vitro gene delivery by a novel human calcitonin (hCT)-derived carrier peptide**

pp 51–54

Ulrike Krauss, Martin Müller, Michael Stahl and Annette G. Beck-Sickinger\*

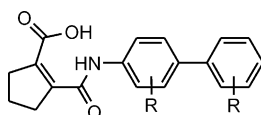


A novel hCT-derived carrier peptide was investigated for the cellular delivery of genes. This was demonstrated in in vitro-transfection assays with neuroblastoma cells SK-N-MC and a plasmid encoding for GFP.

**Discovery of a novel series of DHODH inhibitors by a docking procedure and QSAR refinement**

pp 55–58

Johann Leban,\* Wael Saeb, Gabriel Garcia, Roland Baumgartner and Bernd Kramer

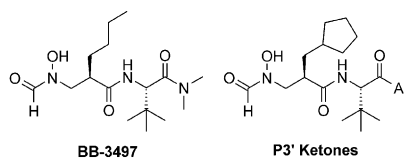


A novel series of DHODH inhibitors was developed, based on docking hits and medicinal chemistry exploration. The activity of the initial lead was improved by a QSAR method to yield low nanomolar inhibitors.

**Peptide deformylase inhibitors with activity against respiratory tract pathogens**

pp 59–62

Stephen P. East,\* R. Paul Beckett, Daniel C. Brookings, John M. Clements, Sheila Doel, Kenneth Keavey, Gilles Pain, Helen K. Smith, Wayne Thomas, Alison J. Thompson, Richard S. Todd and Mark Whittaker

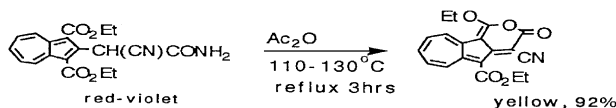


A series of analogues of the peptide deformylase (PDF) inhibitor BB-3497 where the P3' amide bond was replaced with a ketone functionality is described. The in vitro antibacterial profiling of these compounds revealed that they demonstrate activity against pathogens associated with respiratory tract infections.

**A facile synthesis of 1-ethoxy-4-cyano-5-ethoxycarbonyl-3H-azuleno[1,2-c]pyran-3-one, a selective 15-lipoxygenase inhibitor**

pp 63–65

Bing Bing Lin,\* Tadayoshi Morita, Yun-Shan Lin and Hui-Ling Chen\*

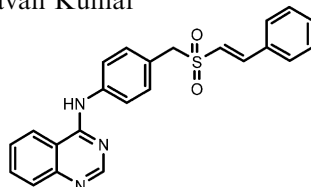


A facile method to synthesize 1-ethoxy-4-cyano-5-ethoxycarbonyl-3H-azuleno[1,2-c]pyran-3-one (in yield of 92%) which showed selective inhibition effect on 15-lipoxygenase(soybean source) at  $\text{IC}_{50} = 24.2 \pm 2.7 \mu\text{M}$  while no inhibition effect was observed at greater than 300  $\mu\text{M}$  on 5-lipoxygenase, lipid peroxidase, phospholipase  $\text{A}_2$ , protein kinase C, and cyclooxygenase.

**Synthesis and biological evaluation of [4-(2-phenylethanesulfonylmethyl)phenyl]-quinazolin-4-yl-amines as orally active anti-cancer agents**

pp 67–71

Vedula M. Sharma,\* K. V. Adi Seshu, V. Chandra Sekhar, Sachin Madan, B. Vishnu, P. Aravind Babu, C. Vamsee Krishna, J. Sreenu, V. Ravi Krishna, A. Venkateswarlu, Sriram Rajagopal, R. Ajaykumar and T. Sravan Kumar

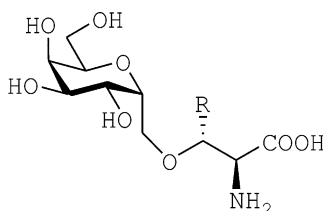


A new series of [4-(2-phenylethanesulfonylmethyl)phenyl]-quinazolin-4-yl-amines was prepared and tested for its in vitro cytotoxic activity against a panel of 12 human cancer cell lines. Active compounds were further tested for their in vivo efficacy in the HT-29 human colon adeno carcinoma xenograft model.

**Novel *O*-glycosyl amino acid mimetics as building blocks for *O*-glycopeptides act as inhibitors of galactosidases**

pp 73–75

Lars Kröger, Dirk Henkensmeier, Andreas Schäfer and Joachim Thiem\*

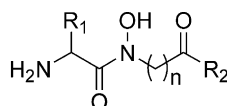


Two novel *O*-glycosyl amino acid mimetics were synthesized. They proved to be stable with glycosidases and showed competitive inhibition of an  $\alpha$ -galactosidase.

**Peptidyl hydroxamic acids as methionine aminopeptidase inhibitors**

pp 77–79

Xubo Hu, Jingge Zhu, Sumant Srivathsan and Dehua Pei\*

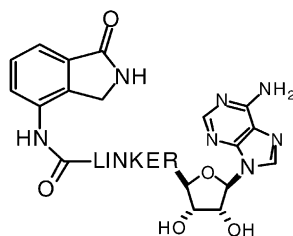


Peptidyl hydroxamic acids are found as competitive inhibitors of *Escherichia coli* and human methionine aminopeptidases, with the most potent compound having a  $K_i$  value of 2.5  $\mu$ M against the *E. coli* enzyme.

**The discovery and synthesis of novel adenosine substituted 2,3-dihydro-1*H*-isoindol-1-ones: potent inhibitors of poly(ADP-ribose) polymerase-1 (PARP-1)**

pp 81–85

Prakash G. Jagtap,\* Garry J. Southan, Erkan Baloglu, Siya Ram, Jon G. Mabley, Anita Marton, Andrew Salzman and Csaba Szabó\*

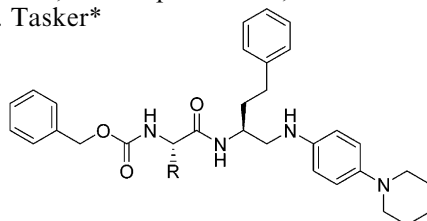


Synthesis and in vitro PARP-1 activity of adenosine-linked 2,3-dihydro-1*H*-isoindol-1-ones are reported.

**(4-Piperidinyphenyl)aminoethyl amides as a novel class of non-covalent cathepsin K inhibitors**

pp 87–90

Tae-Seong Kim,\* Andrew B. Hague, Tony I. Lee, Brian Lian, Christopher M. Tegley, Xianghong Wang, Teresa L. Burgess, Yi-Xin Qian, Sandra Ross, Philip Tagari, Chi-Hwei Lin, Carol Mayeda, Jennifer Dao, Steven Jordan, Christopher Mohr, Janet Cheetham, Vellarkad Viswanadhan and Andrew S. Tasker\*

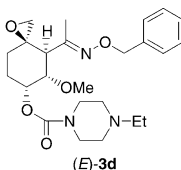


A series of (4-piperidinyphenyl)aminoethyl amides based on dipeptide anilines were synthesized and tested against cathepsin K, cathepsin L and cathepsin B. These new non-covalent inhibitors exhibited single-digit nM inhibition of the cysteine proteases. Compounds **3** and **7** demonstrated potency in both mouse and human osteoclast resorption assays.

**Investigation of novel fumagillin analogues as angiogenesis inhibitors**

pp 91–94

Hyung-Jung Pyun,\* Maria Fardis, James Tario, Cheng Y. Yang, Judy Ruckman, Dwight Henninger, Haolun Jin and Choung U. Kim

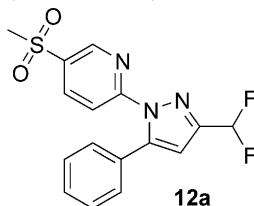


Among the fumagillin analogues prepared, (E)-**3d** showed the best activity in MetAP-2 and the HUVEC-based proliferation assays. The compound also exhibited antiangiogenic effects on matrigel plug assay and rat corneal micropocket assay.

**Discovery of a potent, selective and orally active canine COX-2 inhibitor, 2-(3-difluoromethyl-5-phenyl-pyrazol-1-yl)-5-methanesulfonyl-pyridine**

pp 95–98

Jin Li,\* Kristin M. Lundy DeMello, Henry Cheng, Subas M. Sakya, Brian S. Bronk, Robert J. Rafka, Burton H. Jaynes, Carl B. Ziegler, Carolyn Kilroy, Donald W. Mann, Eric L. Nimz, Michael P. Lynch, Michelle L. Haven, Nicole L. Kolosko, Martha L. Minich, Chao Li, Jason K. Dutra, Bryson Rast, Rhonda M. Crosson, Barry J. Morton, Glen W. Kirk, Kathleen M. Callaghan, David A. Koss, Andrei Shavnya, Lisa A. Lund, Scott B. Seibel, Carol F. Petras and Annette Silvia

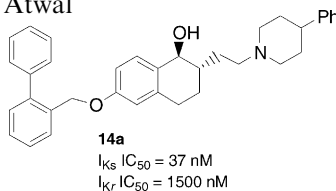


Structure–activity relationship (SAR) studies of 2-[3-di(and tri)fluoromethyl-5-arylpyrazol-1-yl]-5-methanesulfonylpyridine derivatives for canine COX enzymes are described. This led to the identification of **12a** as a lead candidate for further progression. The in vitro activity of **12a** for the canine COX-2 enzyme as well as its in vivo efficacy and pharmacokinetic properties in dog are highlighted.

**Tetrahydronaphthalene-derived amino alcohols and amino ketones as potent and selective inhibitors of the delayed rectifier potassium current  $I_{Ks}$** 

pp 99–102

Saleem Ahmad,\* Lidia Doweiko, Aaila Ashfaq, Francis N. Ferrara, Sharon N. Bisaha, Joan B. Schmidt, John DiMarco, Mary Lee Conder, Tonya Jenkins-West, Diane E. Normandin, Anita D. Russell, Mark A. Smith, Paul C. Levesque, Nicholas J. Lodge, John Lloyd, Philip D. Stein and Karnail S. Atwal

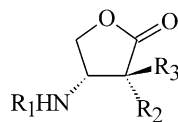


Several novel amino ketones and amino alcohols were prepared and evaluated for  $I_{Ks}$  inhibitory activity. As a representative example, compound **14a** showed good potency ( $IC_{50} = 37 \text{ nM}$ ) and up to 40-fold selectivity for  $I_{Ks}$  over  $I_{Kr}$ .

### 3-D-QSAR of *N*-substituted 4-amino-3,3-dialkyl-2(3*H*)-furanone GABA receptor modulators using molecular field analysis and receptor surface modelling study

pp 103–109

Nanda Ghoshal\* and Prasenjit K. Mukherjee

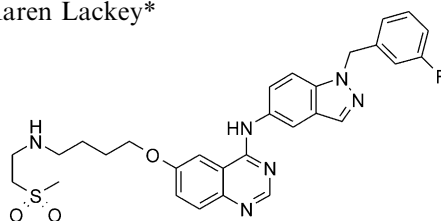


This report deals with the theoretical validation of the experimentally observed structure–activity relationships (SAR) of a set of *N*-substituted 4-amino-3,3-dialkyl-2(3*H*)-furanone GABA receptor modulators showing positive allosteric modulatory activity of the GABA<sub>A</sub> receptor similar to that shown by Loreclazole.

### Synthesis and SAR of potent EGFR/erbB2 dual inhibitors

pp 111–114

Yue-Mei Zhang, Stuart Cockerill, Stephen B. Guntrip, David Rusnak, Kathryn Smith, Dana Vanderwall, Edgar Wood and Karen Lackey\*



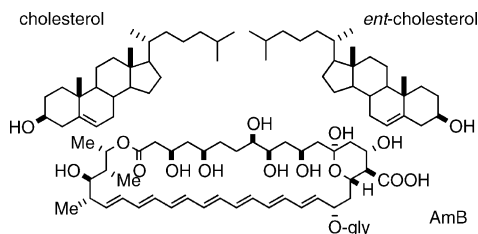
8f

A series of 6-alkoxy-4-anilinoquinazoline compounds was prepared and evaluated for in vitro inhibition of the erbB2 and EGFR kinase activity. The IC<sub>50</sub> values of the best compounds were below 100 nM. Further, several of these compounds inhibit the growth of erbB2 and EGFR over-expressing tumor cell lines at concentrations below 1 μM.

### Differential modulation of the antifungal activity of amphotericin B by natural and *ent*-cholesterol

pp 115–118

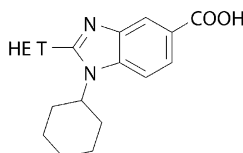
Rowena K. Richter, Daniel E. Mickus, Scott D. Rychnovsky and Tadeusz F. Molinski\*



### Non-nucleoside inhibitors of the hepatitis C virus NS5B polymerase: discovery and preliminary SAR of benzimidazole derivatives

pp 119–124

Pierre L. Beaulieu,\* Michael Bös, Yves Bousquet, Gulrez Fazal, Jean Gauthier, James Gillard, Sylvie Goulet, Steven LaPlante, Marc-André Poupert, Sylvain Lefebvre, Ginette McKercher, Charles Pellerin, Volkhard Austel and George Kukolj

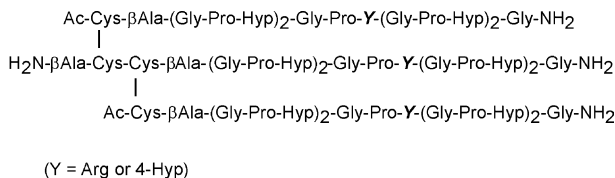


HCV NS5B polymerase:  
IC<sub>50</sub> = 1.6 μM (HET = 3-furyl)

## Synthesis of heterotrimeric collagen models containing Arg residues in Y-positions and analysis of their conformational stability

pp 125–128

Takaki Koide,\* Yoshimi Nishikawa and Yoshifumi Takahara

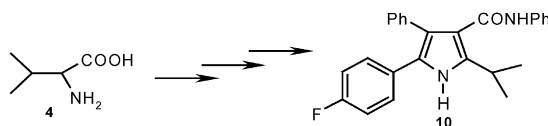


Heterotrimeric collagen-model peptides were synthesized. Effect of Arg residues on triple helical stability was examined.

## An efficient synthesis of N3,4-diphenyl-5-(4-fluorophenyl)-2-isopropyl-1H-3-pyrrolecarboxamide, a key intermediate for atorvastatin synthesis

pp 129–131

Pramod. S. Pandey\* and T. Srinivasa Rao

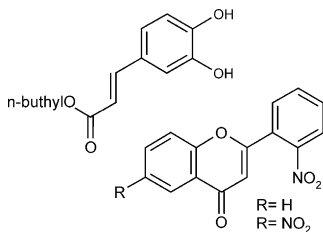


Atorvastatin intermediate **10** was synthesized from L-valine **4** via 1,3-dipolar cycloaddition reaction of mesoionic nuchnone and *N*-debenzylation as key steps.

## Antiproliferative activity of various flavonoids and related compounds: additive effect of interferon- $\alpha$ 2b

pp 133–136

Viviana C. Blank, Cecilia Poli, Mariel Marder and Leonor P. Roguin\*

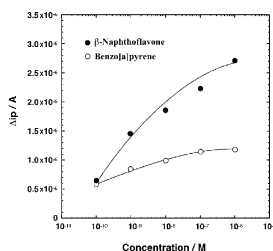


The effect of a series of natural and synthetic flavonoids and some related compounds on the proliferation of WISH cells is shown. 2'-Nitroflavone, 2',6-dinitroflavone, and caffeic acid *n*-butyl ester were the most active cytotoxic agents. When these derivatives were assayed in the presence of a suboptimal concentration of interferon- $\alpha$ 2b, an additive effect on cell growth inhibition was observed.

## An electrochemical device for the assay of the interaction between a dioxin receptor and its various ligands

pp 137–141

Masaharu Murata,\* Hatsumi Gonda, Kentaro Yano, Shinichiro Kuroki, Tatsuo Suzutani and Yoshiki Katayama

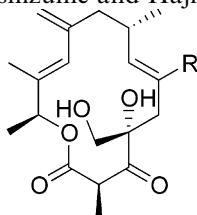


A bioaffinity sensor which carries the hAhR was developed aiming at the detection of PAHs.

### Novel galbonolide derivatives as IPC synthase inhibitors: design, synthesis and in vitro antifungal activities

pp 143–145

Hiroki Sakoh, Yuichi Sugimoto,\* Hideaki Imamura, Shunji Sakuraba, Hideki Jona, Rie Bamba-Nagano, Koji Yamada, Terutaka Hashizume and Hajime Morishima



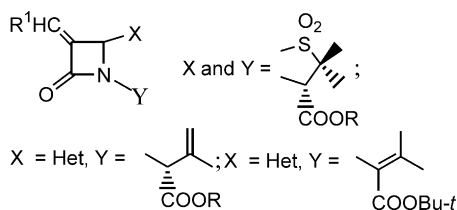
R = H, Cl, OCH<sub>2</sub>CF<sub>3</sub>, SMe

A series of novel galbonolide (rustmicin) derivatives having modified methyl enol ether moiety were prepared in total synthetic procedures and evaluated for their in vitro antifungal activities. Introduction of methylthio group at the C-6 position retained significant antifungal potency.

### Synthesis of antitumor 6-alkylidenepenicillanate sulfones and related 3-alkylidene-2-azetidinones

pp 147–150

Grigory Veinberg,\* Irina Shestakova, Maxim Vorona, Iveta Kanepe and Edmunds Lukevics

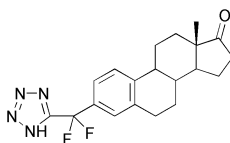


The synthesis of antitumor 6-alkylidenepenicillanate sulfones and 3-alkylidene-2-azetidinones is described.

### The difluoromethylene group as a replacement for the labile oxygen in steroid sulfates: a new approach to steroid sulfatase inhibitors

pp 151–155

Jennifer Lapierre, Vanessa Ahmed, Mei-Jin Chen, Mehdi Ispahany, J. Guy Guillemette and Scott D. Taylor\*

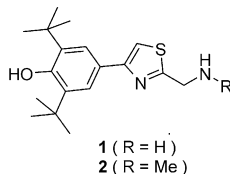


Several estrone sulfate and estrone sulfate analogues, in which sulfate group was replaced with an  $\alpha,\alpha$ -difluoromethylenesulfonate group or an  $\alpha,\alpha$ -difluoromethylenetetrazole group, were examined as inhibitors of steroid sulfatase (STS). The inhibitor bearing the  $\alpha,\alpha$ -difluoromethylenetetrazole group exhibited an affinity for STS approaching that of estrone sulfate.

### Phenolic thiazoles as novel orally-active neuroprotective agents

pp 157–160

Jeremiah J. Harnett,\* Veronique Roubert, Christine Dolo, Christelle Charnet, Brigitte Spinnewyn, Sylvie Cornet, Alain Rolland, Jean-Gregoire Marin, Dennis Bigg and Pierre-E. Chabrier



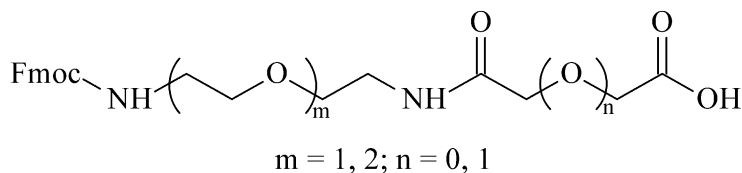
Novel phenolic thiazole compounds **1** and **2** were prepared which demonstrated potent antioxidant activity and potent in vivo neuroprotection in mitochondrial toxin models and also possess good oral bioavailability.



**Synthesis of hydrophilic and flexible linkers for peptide derivatization in solid phase**

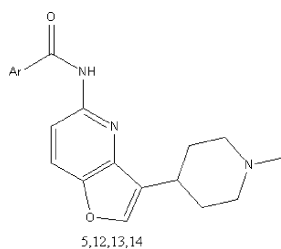
pp 161–165

Aimin Song, Xiaobing Wang, Jinhua Zhang, Jan Mařík, Carlito B. Lebrilla and Kit S. Lam\*

**Substituted furo[3,2-*b*]pyridines: novel bioisosteres of 5-HT<sub>1F</sub> receptor agonists**

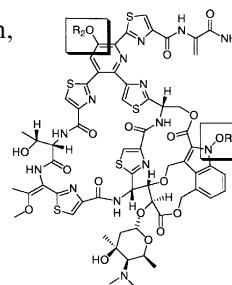
pp 167–170

Brian M. Mathes,\* Kevin J. Hudziak, John M. Schaus, Yao-Chang Xu, David L. Nelson, David B. Wainscott, Suzanne E. Nutter, Wendy H. Gough, Theresa A. Brancheck, John M. Zgombick and Sandra A. Filla

**Novel semi-synthetic nocathiacin antibiotics: synthesis and antibacterial activity of bis- and mono-*O*-alkylated derivatives**

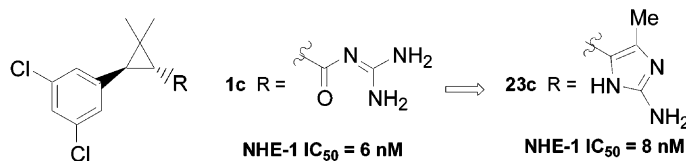
pp 171–175

Alicia Regueiro-Ren,\* B. Narasimhulu Naidu,\* Xiaofan Zheng, Thomas W. Hudyma, Timothy P. Connolly, John D. Matiskella, Yunhui Zhang, Oak K. Kim, Margaret E. Sorenson, Michael Pucci, Junius Clark, Joanne J. Bronson and Yasutsugu Ueda

The semi-synthesis and antibacterial activity of *O*-alkyl nocathiacins derivatives are reported.**Aminoimidazoles as bioisosteres of acylguanidines: novel, potent, selective and orally bioavailable inhibitors of the sodium hydrogen exchanger isoform-1**

pp 177–180

Saleem Ahmad,\* Khehyong Ngu, Donald W. Combs, Shung C. Wu, David S. Weinstein, Wen Liu, Bang-Chi Chen, Gamini Chandrasena, Charles R. Dorso, Mark Kirby and Karnail S. Atwal

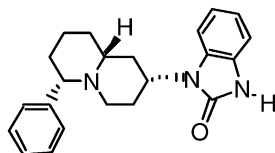


NHE-1 inhibitory activity of a series of heterocyclic cyclopropanes is described.

### The design and synthesis of a novel quinolizidine template for potent opioid and opioid receptor-like (ORL1, NOP) receptor ligands

pp 181–185

Ling Jong, Nurulain Zaveri\* and Lawrence Toll

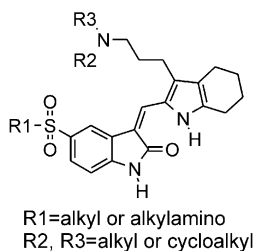


The design and synthesis of a novel scaffold for potent ORL1 and opioid ligands is described.

### Design and synthesis of aminopropyl tetrahydroindole-based indolin-2-ones as selective and potent inhibitors of Src and Yes tyrosine kinase

pp 187–190

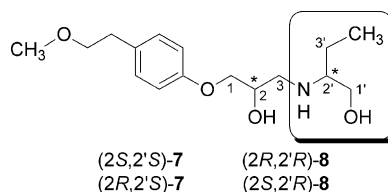
Huiping Guan, A. Douglas Laird, Robert A. Blake, Cho Tang and Chris Liang\*



### Synthesis and cardiovascular activity of metoprolol analogues

pp 191–194

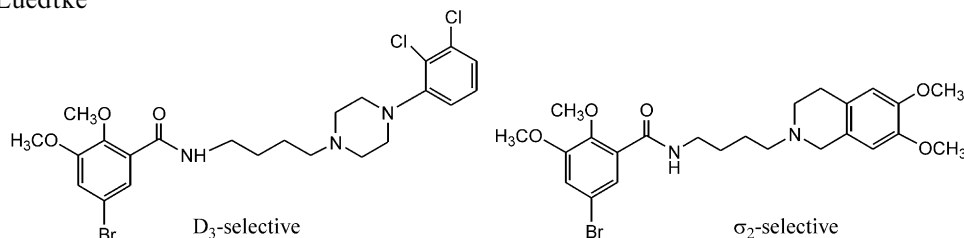
Roberto Melgar-Fernández, Patricia Demare, Enrique Hong, Miguel Angel Rosas, Jaime Escalante, Omar Muñoz-Muñiz, Eusebio Juaristi and Ignacio Regla\*



### Conformationally-flexible benzamide analogues as dopamine D<sub>3</sub> and σ<sub>2</sub> receptor ligands

pp 195–202

Robert H. Mach,\* Yunsheng Huang, Rebekah A. Freeman, Li Wu, Suwanna Vangveravong and Robert R. Luedtke

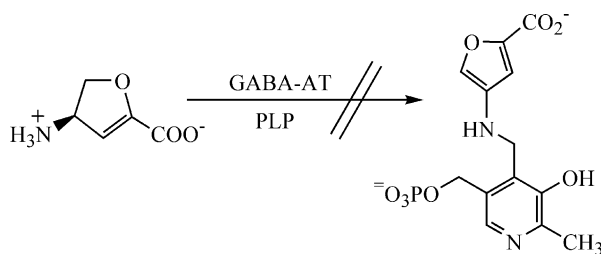


The synthesis of a series of conformationally-flexible benzamide analogues and their in vitro binding affinities for dopamine D<sub>2</sub>, D<sub>3</sub>, D<sub>4</sub> and sigma receptors are presented.

### Inactivation of $\gamma$ -aminobutyric acid aminotransferase by (*S*)-4-amino-4,5-dihydro-2-furancarboxylic acid does not proceed by the expected aromatization mechanism

pp 203–206

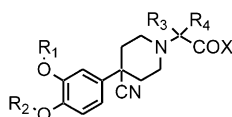
Mengmeng Fu and Richard B. Silverman\*



### Highly potent PDE4 inhibitors with therapeutic potential

pp 207–210

Hiroshi Ochiai, Tazumi Ohtani, Akiharu Ishida, Kensuke Kusumi, Masashi Kato, Hiroshi Kohno, Katuya Kishikawa, Takaaki Obata, Hisao Nakai\* and Masaaki Toda

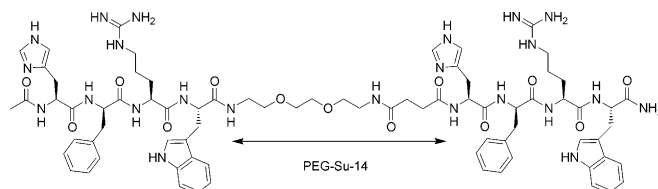


Synthesis and biological evaluation of piperidine derivatives is reported.

### Novel targeting strategy based on multimeric ligands for drug delivery and molecular imaging: homooligomers of $\alpha$ -MSH

pp 211–215

Josef Vagner,\* Heather L. Handl,\* Robert J. Gillies and Victor J. Hruby

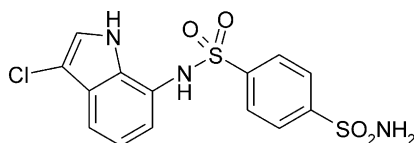


Homooligomers constructed with peptide fragments of melanocortin ( $\alpha$ -MSH) bind with higher affinity and with apparent cooperativity to melanocortin receptor hMC4R, compared to their constituent monomers.

### Carbonic anhydrase inhibitors: E7070, a sulfonamide anticancer agent, potently inhibits cytosolic isozymes I and II, and transmembrane, tumor-associated isozyme IX

pp 217–223

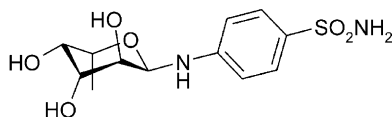
Francesco Abbate, Angela Casini, Takashi Owa,\* Andrea Scozzafava and Claudiu T. Supuran\*



**Carbonic anhydrase inhibitors: *N*-(*p*-sulfamoylphenyl)- $\alpha$ -D-glycopyranosylamines as topically acting antiglaucoma agents in hypertensive rabbits**

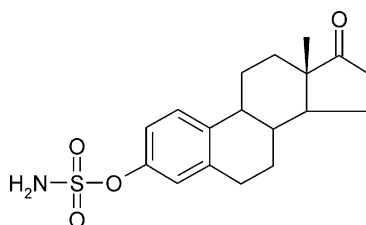
pp 225–229

Jean-Yves Winum, Angela Casini, Francesco Mincione, Michele Starnotti,  
Jean-Louis Montero, Andrea Scozzafava and Claudiu T. Supuran\*


**Carbonic anhydrase inhibitors: X-ray crystallographic structure of the adduct of human isozyme II with EMATE, a dual inhibitor of carbonic anhydrases and steroid sulfatase**

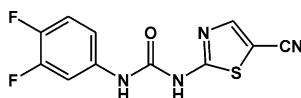
pp 231–234

Francesco Abbate, Jean-Yves Winum, Barry V.L. Potter, Angela Casini, Jean-Louis Montero,  
Andrea Scozzafava and Claudiu T. Supuran\*


**Phenyl thiazolyl urea and carbamate derivatives as new inhibitors of bacterial cell-wall biosynthesis**

pp 235–238

Gerardo D. Francisco, Zhong Li, J. Donald Albright, Nancy H. Eudy, Alan H. Katz,  
Peter J. Petersen, Pornpen Labthavikul, Guy Singh, Youjun Yang, Beth A. Rasmussen,  
Yang-I Lin\* and Tarek S. Mansour



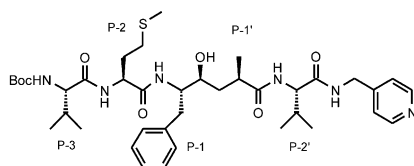
3p

Over 50 phenyl thiazolyl urea and carbamate derivatives were synthesized for evaluation as new inhibitors of bacterial cell-wall biosynthesis. Many of them demonstrated good activity against MurA and MurB and gram-positive bacteria including MRSA, VRE and PRSP. 3,4-Difluorophenyl 5-cyanothiazolylurea (**3p**) with clog P of 2.64 demonstrated antibacterial activity against both gram-positive and gram-negative bacteria.

**Phe\*-Ala-based pentapeptide mimetics are BACE inhibitors: P2 and P3 SAR**

pp 239–243

Jason Lamar, Jingdan Hu, Ana Belen Bueno, Hsiu-Chiung Yang, Deqi Guo, James D. Copp,  
James McGee, Bruce Gitter, David Timm, Patrick May, James McCarthy and Shu-Hui Chen\*

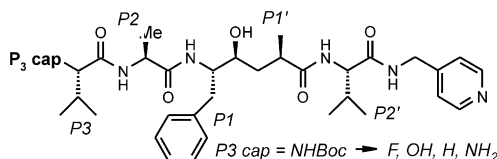


We describe herein the syntheses and evaluation of a series of Phe\*-Ala-based BACE inhibitors. The most promising inhibitors demonstrated very good enzyme and cellular activity.

**P3 cap modified Phe\*-Ala series BACE inhibitors**

pp 245–250

Shu-Hui Chen,\* Jason Lamar, Deqi Guo, Todd Kohn, Hsiu-Chiung Yang, James McGee, David Timm, Jon Erickson, Yvonne Yip, Patrick May and James McCarthy

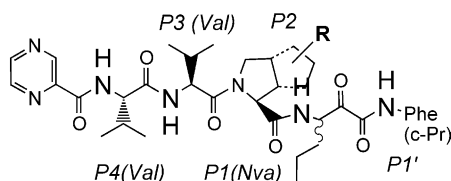


Several series of P3 cap modified BACE inhibitors were prepared in order to reduce  $M_r$  and adjust log D values of inhibitors for better BBB penetration. A number of P3 cap hydroxylated inhibitors showed good enzyme inhibitory and whole cell activities.

**Discovery of a novel bicycloproline P2 bearing peptidyl  $\alpha$ -ketoamide LY514962 as HCV protease inhibitor**

pp 251–256

Yvonne Yip, Frantz Victor, Jason Lamar, Robert Johnson, Q. May Wang, Donna Barket, John Glass, Ling Jin, Lifei Liu, Daryl Venable, Mark Wakulchik, Congping Xie, Beverly Heinz, Elcira Villarreal, Joe Colacino, Nathan Yumibe, Mark Tebbe, John Munroe and Shu-Hui Chen\*

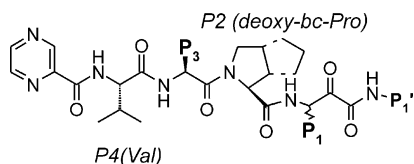


We describe herein the design, synthesis, and evaluation of a series of bicycloproline P2 bearing tetrapeptidyl  $\alpha$ -ketoamides as HCV protease inhibitors.

**P1 and P3 optimization of novel bicycloproline P2 bearing tetrapeptidyl  $\alpha$ -ketoamide based HCV protease inhibitors**

pp 257–261

Frantz Victor, Jason Lamar, Nancy Snyder, Yvonne Yip, Deqi Guo, Nathan Yumibe, Robert B. Johnson, Q. May Wang, John I. Glass and Shu-Hui Chen\*

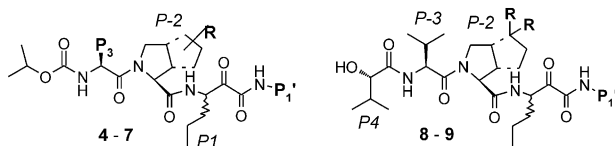


We describe herein the discovery of **LY526181**, a P2 bicycloproline tetrapeptidyl  $\alpha$ -ketoamide HCV protease inhibitor with desirable antiviral activity, ADME and toxicological profile.

**Novel P4 truncated tripeptidyl  $\alpha$ -ketoamides as HCV protease inhibitors**

pp 263–266

Jason Lamar, Frantz Victor, Nancy Snyder, Robert B. Johnson, Q. May Wang, John I. Glass and Shu-Hui Chen\*



We describe herein the design, synthesis, antiviral activity and cytotoxicity of two series of tripeptidyl  $\alpha$ -ketoamides based HCV protease inhibitors.

**Structure–activity relationships of novel potent MurF inhibitors**

pp 267–270

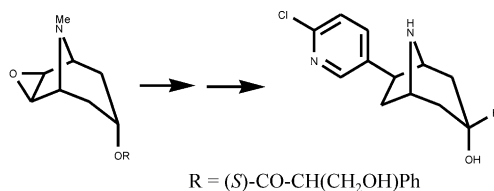
Yu Gui Gu,\* Alan S. Florjancic, Richard F. Clark, Tianyuan Zhang, Curt S. Cooper, David D. Anderson, Claude G. Lerner, J. Owen McCall, Yingna Cai, Candace L. Black-Schaefer, Geoffrey F. Stamper, Philip J. Hajduk and Bruce A. Beutel

A novel class of MurF inhibitors was discovered and structure–activity relationship studies have led to several potent compounds with  $IC_{50} = 22 \sim 70$  nM. Unfortunately, none of these potent MurF inhibitors exhibited significant antibacterial activity even in the presence of bacterial cell permeabilizers.

**Synthesis and nicotinic receptor activity of a hydroxylated tropane**

pp 271–273

John B. Bremner,\* Colette A. Godfrey, Anders A. Jensen and Reginald J. Smith

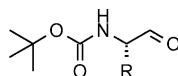


The synthesis and nicotinic receptor binding of 3 $\alpha$ -hydroxy homoepipibatidine from scopolamine is reported.

**Exploration of the P<sup>1</sup> SAR of aldehyde cathepsin K inhibitors**

pp 275–278

John G. Catalano, David N. Deaton, Eric S. Furfine, Annie M. Hassell, Robert B. McFadyen,\* Aaron B. Miller, Larry R. Miller, Lisa M. Shewchuk, Derril H. Willard, Jr. and Lois L. Wright

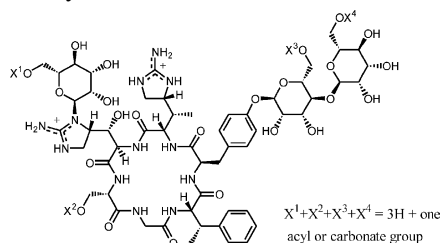


The synthesis and biological activity of a series of aldehyde inhibitors of cathepsin K are reported. Explorations of the properties of the S<sup>1</sup> subsite with a series of  $\alpha$ -amino aldehyde derivatives substituted at the P<sup>1</sup> position afforded compounds with cathepsin K  $IC_{50}$ s between 52  $\mu$ M and 15 nM.

**Mannopectimycin esters and carbonates, potent antibiotic agents against drug-resistant bacteria**

pp 279–282

Haiyin He,\* Bo Shen, Peter J. Petersen, William J. Weiss, Hui Y. Yang, Ting-Zhong Wang, Russell G. Dushin, Frank E. Koehn and Guy T. Carter

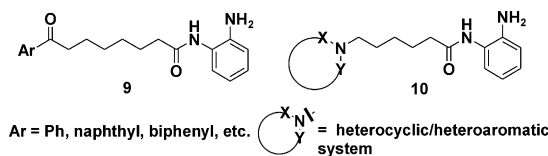


A series of ester and carbonate derivatives of the glycopeptide mannopectimycin  $\alpha$  with potent activity against drug-resistant G(+) bacteria was synthesized.

**(2-Amino-phenyl)-amides of  $\omega$ -substituted alkanolic acids as new histone deacetylase inhibitors**

pp 283–287

Arkadii Vaisburg,\* Naomy Bernstein, Sylvie Frechette, Martin Allan, Elie Abou-Khalil, Silvana Leit, Oscar Moradei, Giliane Bouchain, James Wang, Soon Hyung Woo, Marielle Fournel, Pu T. Yan, Marie-Claude Trachy-Bourget, Ann Kalita, Carole Beaulieu, Zuomei Li, A. Robert MacLeod, Jeffrey M. Besterman and Daniel Delorme

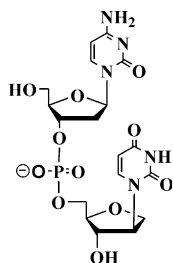


A series of benzamides (**9** and **10**) was synthesized and their biological evaluation as HDAC inhibitor is reported.

**Resistance towards exonucleases of dinucleotides with stereochemically altered internucleotide phosphate bonds**

pp 289–291

Vasu Nair\* and Suresh Pal



Remarkable resistance of synthetic dinucleotides towards exonucleases.

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**OTHER CONTENTS****Contributors to this issue****I–II****Instructions to contributors****III–VI**

\*Corresponding author

①\* Supplementary data available via ScienceDirect

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**COVER**

Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona. The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htB1 (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htB1 (center) allows for functional selection against thrombin (right). © 2003 Indraneel Ghosh. Published by Elsevier Ltd.

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ISSN 0960-894X