

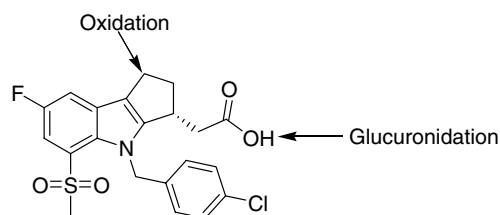
Contents

ARTICLES

In vitro biotransformations of the prostaglandin D₂ (DP) antagonist MK-0524 and synthesis of metabolites pp 301–304

Deborah A. Nicoll-Griffith,* Carmai Seto, Yves Aubin, Jean François Lévesque, Nathalie Chauret, Stephen Day, José M. Silva, Laird A. Trimble, Jean-François Truchon, Carl Berthelette, Nicolas Lachance, Zhaoyin Wang, Claudio Sturino, Matt Braun, Robert Zamboni and Robert N. Young

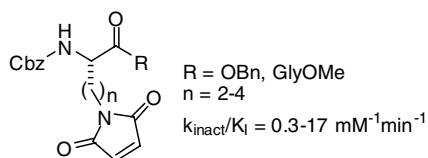
Metabolites of the potent DP antagonist, **MK-0524**, were generated using in vitro systems including hepatic microsomes and hepatocytes. Four metabolites (two hydroxylated diastereomers, a ketone, and an acyl glucuronide) were characterized by LC-MS/MS and ¹H NMR. Larger quantities of these metabolites were prepared by either organic synthesis or biosynthetically to be used as standards in other studies. The propensity for covalent protein modification was assessed and was found to be acceptable (<50 pmol-equiv/mg protein).



Synthesis and evaluation of peptidic maleimides as transglutaminase inhibitors

pp 305–308

Dany Halim, Karine Caron and Jeffrey W. Keillor*



A series of novel peptidic maleimide inhibitors of transglutaminase was prepared and evaluated as irreversible inhibitors of transglutaminase.

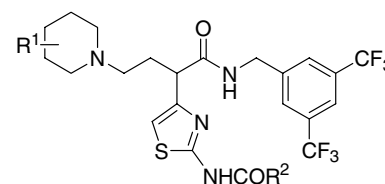


α-Aminothiazole-γ-aminobutanoic amides as potent, small molecule CCR2 receptor antagonists

pp 309–314

Changyou Zhou,* Liangqin Guo, William H. Parsons, Sander G. Mills, Malcolm MacCoss, Pasquale P. Vicario, Hans Zweerink, Margaret A. Cascieri, Martin S. Springer and Lihu Yang

A series of racemic and homochiral α-aminothiazole-γ-aminobutyroamides that display high affinities for human and murine CCR2 and functional antagonism by inhibition of monocyte recruitment are described. A representative example is (2*S*)-2-[2-(acetylamino)-1,3-thiazol-4-yl]-*N*-[3-methyl-5-(trifluoromethyl)benzyl]-4-(4-phenylpiperidin-1-yl)-butanamide, which shows 5 nM affinity for human monocytes and CHO cells expressing the human CCR2b receptor. It also inhibited MCP-1 initiated chemotaxis of human monocytes with an IC₅₀ of 0.69 nM.

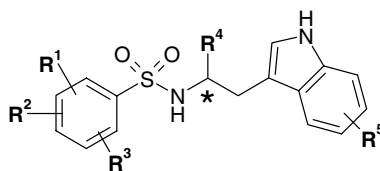


Compounds 3, 11-25

α -Methyltryptamine sulfonamide derivatives as novel glucocorticoid receptor ligands

pp 315–319

Daniel R. Marshall,* Gus Rodriguez, David S. Thomson, Richard Nelson and Allison Capolina



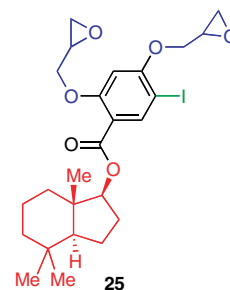
α -Methyltryptamine sulfonamides were identified as human glucocorticoid receptor (hGR) ligands. The SAR and selectivity will be discussed.

Trifunctional norrisolide probes for the study of Golgi vesiculation

pp 320–325

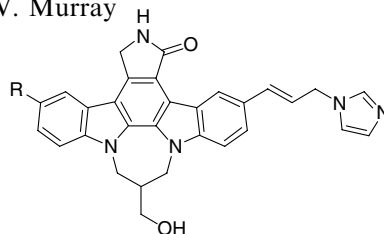
Gianni Guizzunti, Thomas P. Brady, Vivek Malhotra and Emmanuel A. Theodorakis*

The synthesis of norrisolide probes and their effect on the Golgi complex is presented. The studies led to the identification of probe **25**, that contains a Golgi localization motif attached to a bisepoxide crosslinking unit and an iodine tag. This probe induced efficient and irreversible vesiculation of the Golgi membranes and could be used for the isolation of the cellular target of norrisolide.

**Simplified staurosporine analogs as potent JAK3 inhibitors**

pp 326–331

Shyh-Ming Yang,* Ravi Malaviya, Lawrence J. Wilson, Rochelle Argentieri, Xin Chen, Cangming Yang, Bingbing Wang, Druie Cavender and William V. Murray

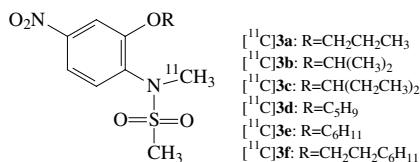
**22n**, R= H, JAK3 IC₅₀ = 11 nM**22r**, R= -CH₂OH, JAK3 IC₅₀ = 3 nM

The modification of staurosporine led to a new series of potent JAK3 inhibitors is described.

Synthesis of carbon-11 labeled sulfonanilide analogues as new potential PET agents for imaging of aromatase in breast cancer

pp 332–336

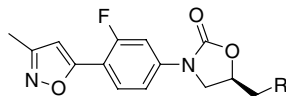
Min Wang, Gabrielle Lacy, Mingzhang Gao, Kathy D. Miller, George W. Sledge and Qi-Huang Zheng*



New carbon-linked azole oxazolidinones with improved potency and pharmacokinetics

pp 337–340

Sheila I. Hauck,* Christer Cederberg, Amanda Doucette, Lena Grosser, Neil J. Hales, Grace Poon and Michael B. Gravestock



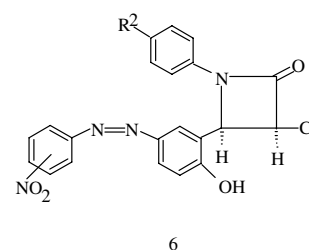
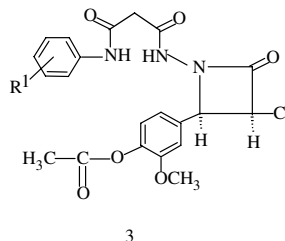
The synthesis, and the in vitro and in vivo evaluation of a new series of potent oxazolidinones are reported.

N/C-4 substituted azetidin-2-ones: Synthesis and preliminary evaluation as new class of antimicrobial agents

pp 341–345

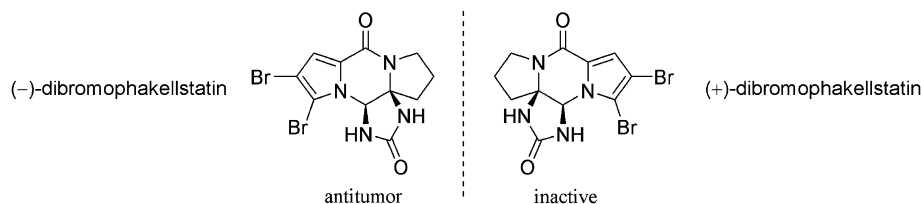
Anand K. Halve,* Deepti Bhadauria and Rakesh dubey

A new series of 3-chloro-4-(3-methoxy-4-acetoxyphenyl)-1-[3-oxo-3-(phenylamino)propanamido] azetidin-2-ones **3** and 3-chloro-4-[2-hydroxy-5-(nitro substituted phenylazo)phenyl]-1-phenylazetidin-2-ones **6** have been synthesized. The synthesized compounds were screened to antimicrobial activity against several microbes, in vitro. Significant antimicrobial activity and structure–activity relationship (SAR) trends are obtained for the tested compounds.

**Antitumor activity of the marine natural product dibromophakellstatin in vitro**

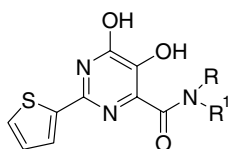
pp 346–349

Michael Zöllinger, Gerhard Kelter, Heinz-Herbert Fiebig and Thomas Lindel*

**From dihydroxypyrimidine carboxylic acids to carboxamide HIV-1 integrase inhibitors: SAR around the amide moiety**

pp 350–353

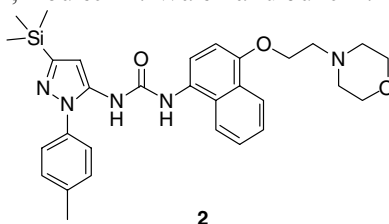
Alessia Petrocchi,* Uwe Koch, Victor G. Matassa, Barbara Pacini, Kara A. Stillmock and Vincenzo Summa



Trimethylsilylpyrazoles as novel inhibitors of p38 MAP kinase: A new use of silicon bioisosteres in medicinal chemistry

pp 354–357

Matthew J. Barnes, Richard Conroy, David J. Miller,* John S. Mills, John G. Montana, Parminder K. Pooni, Graham A. Showell, Louise M. Walsh and Julie B. H. Warneck

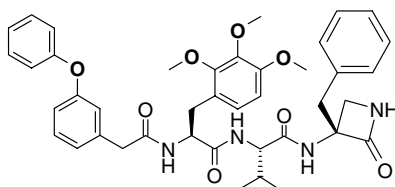


The synthesis, physicochemical properties and pharmacological profiles of two novel silicon-containing p38 MAP kinase inhibitors are described.


Novel β -lactam derivatives: Potent and selective inhibitors of the chymotrypsin-like activity of the human 20S proteasome

pp 358–362

Patricia Imbach,* Marc Lang, Carlos García-Echeverría, Vito Guagnano, Maria Noorani, Johannes Roesel, Francis Bitsch, Greta Rihs and Pascal Furet*



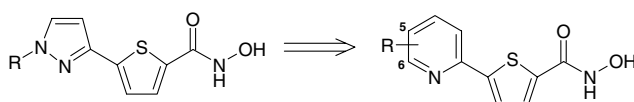
Chymotrypsin-like activity: 14 nM

Proliferation of MDA-MB-435 cells: 32nM

Identification and optimisation of a series of substituted 5-pyridin-2-yl-thiophene-2-hydroxamic acids as potent histone deacetylase (HDAC) inhibitors

pp 363–369

Steve Price,* Walter Bordogna, Ruth Braganza, Richard J. Bull, Hazel J. Dyke, Sophie Gardan, Matthew Gill, Neil V. Harris, Robert A. Heald, Marco van den Heuvel, Peter M. Lockey, Julia Lloyd, Aranzazu G. Molina, Alan G. Roach, Fabien Roussel, Jonathan M. Sutton and Anne B. White

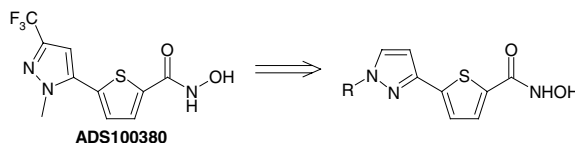


Further investigation of a series of thienyl-based hydroxamic acids identified a series of 5- and 6-substituted 5-pyridin-2-yl-thiophene-2-hydroxamic acids.

Identification and optimisation of a series of substituted 5-(1H-pyrazol-3-yl)-thiophene-2-hydroxamic acids as potent histone deacetylase (HDAC) inhibitors

pp 370–375

Steve Price,* Walter Bordogna, Richard J. Bull, David E. Clark, Peter H. Crackett, Hazel J. Dyke, Matthew Gill, Neil V. Harris, Julia Gorski, Julia Lloyd, Peter M. Lockey, Julia Mullett, Alan G. Roach, Fabien Roussel and Anne B. White



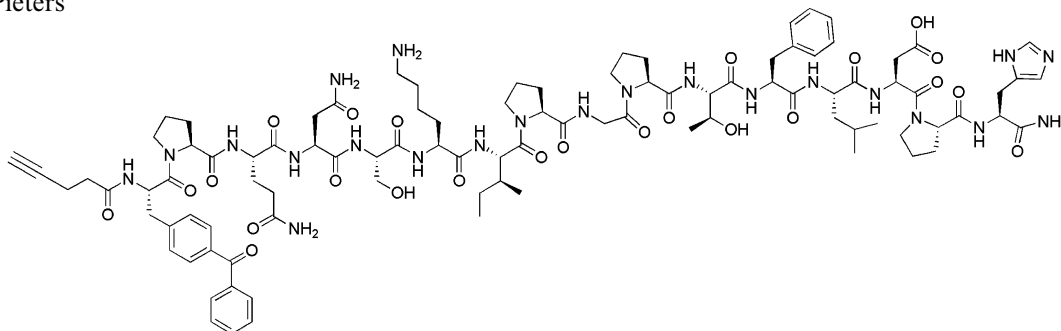
Optimisation of ADS100380, a sub-micromolar HDAC inhibitor identified using a virtual screening approach, led to a series of substituted 5-(1H-pyrazol-3-yl)-thiophene-2-hydroxamic acids, that possessed significant HDAC inhibitory activity.



Detection of galectin-3 by novel peptidic photoprobes

pp 376–378

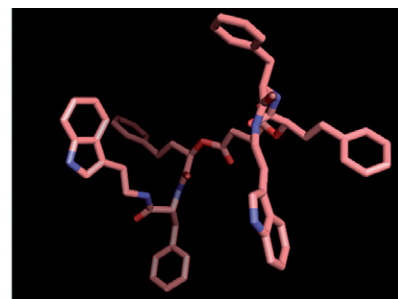
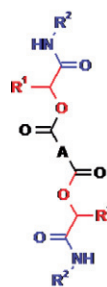
Monique van Scherpenzeel, Martin van der Pot, Christopher J. Arnusch, Rob M. J. Liskamp and Roland J. Pieters*

**Towards erythropoietin mimicking small molecules**

pp 379–384

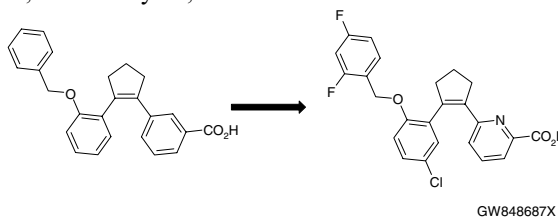
Alexander Dömling,* Barbara Beck, William Baumbach and Gregor Larbig

Design, synthesis and preliminary biological activity of small molecular weight EPO agonists is reported.

**The discovery of 6-[5-(2-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid, GW848687X, a potent and selective prostaglandin EP₁ receptor antagonist for the treatment of inflammatory pain**

pp 385–389

Gerard M. P. Giblin,* Rino A. Bit, Susan H. Brown, Hélène M. Chaignot, Anita Chowdhury, Iain P. Chessell, Nicholas M. Clayton, Tanya Coleman, Adrian Hall, Beverley Hammond, David N. Hurst, Anton D. Michel, Alan Naylor, Riccardo Novelli, Tiziana Scoccitti, David Spalding, Sac P. Tang, Alex W. Wilson and Rich Wilson

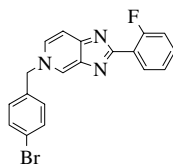
Identification of a novel cyclopentenyl series of EP₁ antagonists is described. Optimisation for in vivo DMPK and efficacy by introducing heteroaromatic rings resulted in the identification of GW848687X, a candidate for the treatment of inflammatory pain.

GW848687X

**Antiviral 2,5-disubstituted imidazo[4,5-c]pyridines:
From anti-pestivirus to anti-hepatitis C virus activity**

pp 390–393

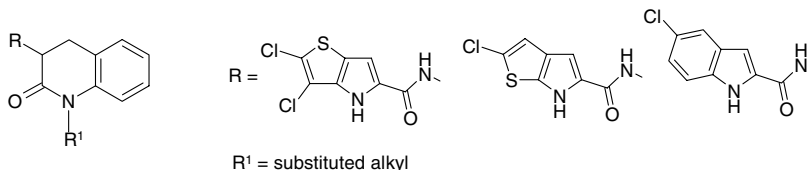
Gerhard Puerstinger,* Jan Paeshuyse, Erik De Clercq and Johan Neyts



Development of potent, orally active 1-substituted-3,4-dihydro-2-quinolone glycogen phosphorylase inhibitors

pp 394–399

Alan M. Birch,* Peter W. Kenny, Nikos G. Oikonomakos, Ludovic Otterbein, Paul Schofield, Paul R. O. Whittamore and Dave P. Whalley



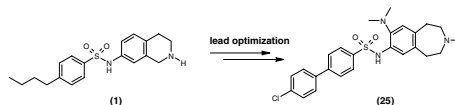
Optimisation of R¹ led to 2,3-dihydroxypropyl compounds which showed good in vitro potency and improved physical properties, together with good DMPK profiles and acute in vivo efficacy.



Studies towards the identification of a new generation of atypical antipsychotic agents

pp 400–405

Vincenzo Garzya,* Ian T. Forbes, Andrew D. Gribble, Mike S. Hadley, Andrew P. Lightfoot, Andrew H. Payne, Alexander B. Smith, Sara E. Douglas, David G. Cooper, Ian G. Stansfield, Malcom Meeson, Emma E. Dodds, Declan N. C. Jones, Martyn Wood, Charlie Reavill, Carol A. Scorer, Angela Worby, Graham Riley, Peter Eddershaw, Chris Ioannou, Daniele Donati, Jim J. Hagan and Emiliangelo A. Ratti

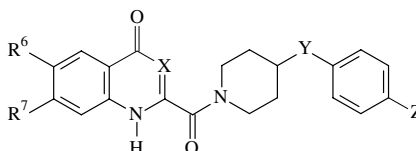


The SAR study around compound (1), led to the identification of sulfonamide (25), a molecule combining dopamine D₂/D₃ receptor antagonism with serotonin 5-HT_{2A}, 5-HT_{2C}, 5-HT₆ receptor antagonism to treat schizophrenia.

Kynurenic acid amides as novel NR2B selective NMDA receptor antagonists

pp 406–409

István Borza,* Sándor Kolok, Kornél Galgóczy, Anikó Gere, Csilla Horváth, Sándor Farkas, István Greiner and György Domány

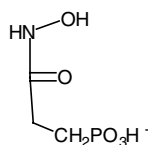


Starting from indole- and benzimidazole-2-carboxamides as lead compounds, a novel series of kynurenic acid amide derivatives was prepared and identified as NR2B selective NMDA receptor antagonists. The synthesis and SAR studies are discussed.

New competitive inhibitors of cytosolic (NADH-dependent) rabbit muscle glycerophosphate dehydrogenase

pp 410–413

Matthieu Fonvielle, Helene Therisod, Marion Hemery and Michel Therisod*



We report the synthesis and biochemical evaluation of new competitive inhibitors of the cytosolic (NADH-dependent) glycerophosphate dehydrogenase. One compound, phosphono-propionohydroxamic acid, with a K_i of 6 μM, might be of interest as an anti-obesity drug.

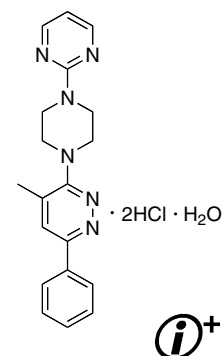


Development of a novel therapeutic suppressor of brain proinflammatory cytokine up-regulation that attenuates synaptic dysfunction and behavioral deficits

pp 414–418

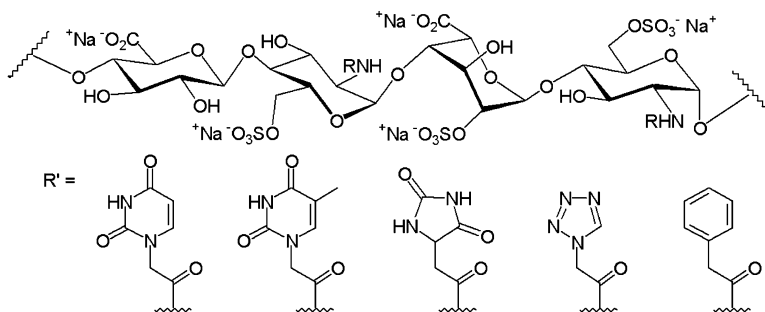
Wenhui Hu, Hantamalala Ralay Ranaivo, Saktimayee M. Roy, Heather A. Behanna, Laura K. Wing, Lenka Munoz, Ling Guo, Linda J. Van Eldik and D. Martin Watterson*

Development of an orally bioavailable, water-soluble, stable, safe, anti-neuroinflammatory compound with in vivo efficacy in altering disease progression in a neurodegenerative disease animal model is reported.

**Different protein-binding selectivities for *N*-acyl heparin derivatives having *N*-phenylacetyl and heterocycle analogs of *N*-phenylacetyl substituted in place of *N*-sulfo groups**

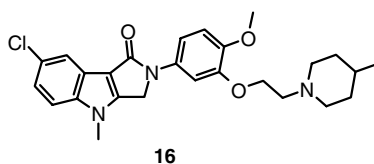
pp 419–423

Liusheng Huang, Cristina Fernández and Robert J. Kerns*

**5-HT_{2C} antagonists based on fused heterotricyclic templates: Design, synthesis and biological evaluation**

pp 424–427

Dieter Hamprecht,* Fabrizio Micheli, Giovanna Tedesco, Daniele Donati, Marcella Petrone, Silvia Terreni and Martyn Wood



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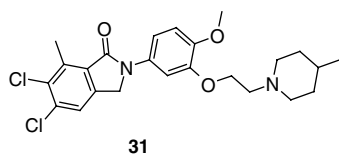
pKi 5-HT_{2C} = 8.5, F_{p.o.} = 44%

Design, synthesis and properties of a new tricyclic series of selective 5-HT_{2C} receptor antagonists are reported.

Isoindolone derivatives, a new class of 5-HT_{2C} antagonists: Synthesis and biological evaluation

pp 428–433

Dieter Hamprecht,* Fabrizio Micheli,* Giovanna Tedesco, Anna Checchia, Daniele Donati, Marcella Petrone, Silvia Terreni and Martyn Wood



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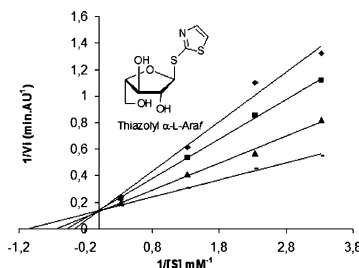
pKi 5-HT_{2C} = 8.6, F_{p.o.} = 43%

A series of isoindolone 5-HT_{2C} antagonists allows combining high potency with good selectivity and oral bioavailability.

Thioimidoyl furanosides as first inhibitors of the α -L-arabinofuranosidase AbfD3

pp 434–438

Gérald Lopez, Richard Daniellou, Michael O'Donohue, Vincent Ferrières and Caroline Nugier-Chauvin*

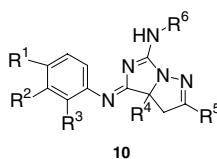


The synthesis and in vitro activity of the powerful furanosidic inhibitors of the arabinofuranosidase AbfD3 are reported.

Serendipitous discovery of novel imidazolopyrazole scaffold as selective androgen receptor modulators

pp 439–443

Xuqing Zhang,* Xiaojie Li, George F. Allan, Tifanie Sbriscia, Olivia Linton, Scott G. Lundeen and Zhihua Sui

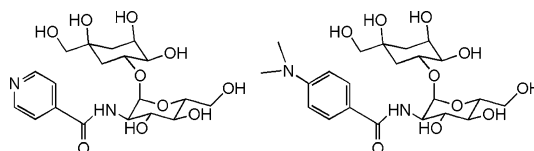


A novel imidazolopyrazole derivative has been fortuitously discovered as potent selective androgen receptor modulator with in vivo efficacy.

**Design and synthesis of substrate-mimic inhibitors of mycothiol-S-conjugate amidase from *Mycobacterium tuberculosis***

pp 444–447

Belhu B. Metaferia, Satyajit Ray, Jeremy A. Smith and Carole A. Bewley*

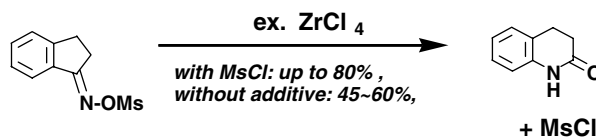


Examples of MCA inhibitors (IC_{50} values $\sim 50 \mu M$)

**Continuing efforts on the improvement of Beckmann rearrangement of indanone oxime**

pp 448–452

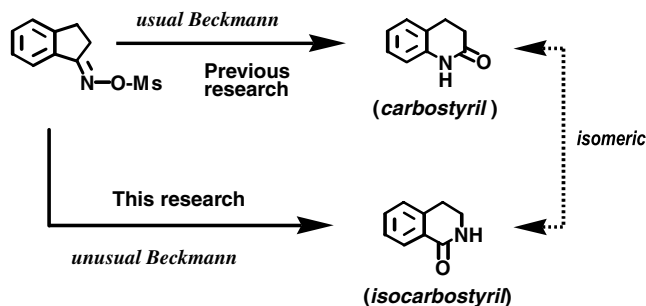
Yasuhiro Torisawa,* Takao Nishi and Jun-ichi Minamikawa



Conversion of indanone oximes into isocarbostyrils

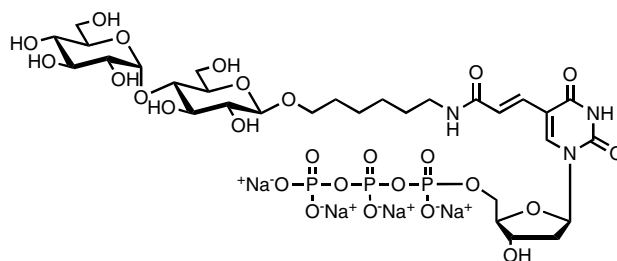
pp 453–455

Yasuhiro Torisawa,* Shinji Aki and Jun-ichi Minamikawa

**Construction of saccharide-modified DNAs by DNA polymerase**

pp 456–460

Masayuki Matsui, Yoshitaka Nishiyama, Shin-ichi Ueji and Yasuhito Ebara*

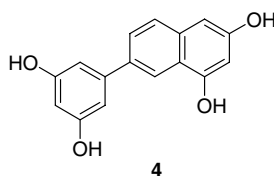


The construction of saccharide-modified DNAs using saccharide-modified dUTPs and DNA polymerase and the characterization of their biophysical properties are reported.

Syntheses of hydroxy substituted 2-phenyl-naphthalenes as inhibitors of tyrosinase

pp 461–464

Suhee Song, Hyojin Lee, Youngeup Jin, Young Mi Ha, Sungjin Bae, Hae Young Chung and Hongsuk Suh*



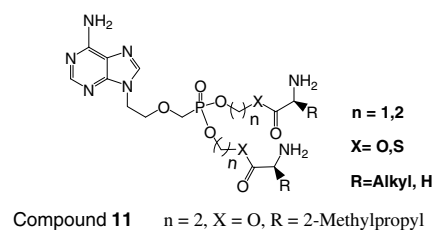
Isosteres of oxyresveratrol and resveratrol and their derivatives with 2-phenyl-naphthalene template were synthesized and evaluated as tyrosinase inhibitors.

**Design and synthesis of novel bis(L-amino acid) ester prodrugs of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA) with improved anti-HBV activity**

pp 465–470

Xiaozhong Fu, Saihong Jiang, Chuan Li, Jian Xin, Yushe Yang* and Ruyun Ji

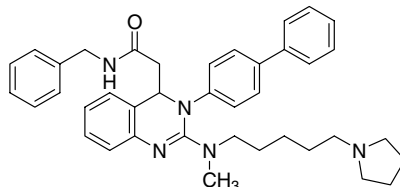
A series of novel bis(L-amino acid)ester prodrugs of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA) was synthesized and their anti-HBV activity was evaluated in HepG2 2.2.15 cells. Compound **11** exhibited five times more potent anti-HBV activity, 60 times higher selective index (SI) than adefovir dipivoxil. Moreover, compound **11** was more stable than adefovir dipivoxil with $t_{1/2}$ of 270 min.



EC₅₀ 0.0952 μM , CC₅₀ 6636 μM , SI 69532

Synthesis and biological evaluation of novel T-type calcium channel blockers

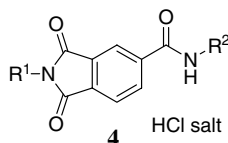
pp 471–475

Ja Youn Choi, Han Na Seo, Min Joo Lee, Seong Jun Park, Sung Jun Park,
Ji Young Jeon, Joo Hi Kang, Ae Nim Pae, Hyewhon Rhim and Jae Yeol Lee*

11b (KYS05080)
(IC₅₀ = 0.26 ± 0.01 μM against T-type)
(Selectivity = 7.5 for T/N-type channel)

**Design, synthesis, and biological evaluation of 1,3-dioxoisindoline-5-carboxamide derivatives as T-type calcium channel blockers**

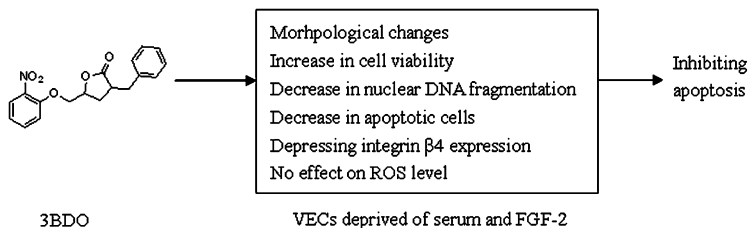
pp 476–481

Hwa Sil Kim, Yoonjee Kim, Munikumar Reddy Doddareddy, Seon Hee Seo,
Hyewhon Rhim, Jinsung Tae, Ae Nim Pae, Hyunah Choo* and Yong Seo Cho*

A small molecule library of 1,3-dioxoisindoline-5-carboxamides **4** was designed, synthesized, and biologically evaluated as potential T-type calcium channel blockers. The most active compound shows blocking activity with IC₅₀ value of 0.93 μM.

A novel butyrolactone derivative inhibited apoptosis and depressed integrin β4 expression in vascular endothelial cells

pp 482–485

Weiwei Wang, Xia Liu, Jing Zhao, Baoxiang Zhao,* Shangli Zhang
and Junying Miao*

3-Benzyl-5-((2-nitrophenoxy) methyl)-dihydrofuran-2(3H)-one (3BDO) inhibited VEC apoptosis induced by deprivation of serum and FGF-2 and depressed the expression of integrin β4. ROS were not involved in this process.

Structure–activity relationships of novel non-competitive mGluR1 antagonists: A potential treatment for chronic pain

pp 486–490

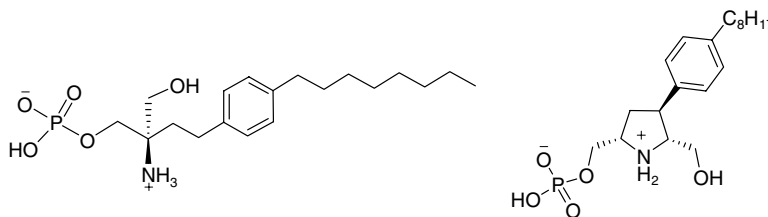
Dafydd R. Owen,* Peter G. Dodd, Simon Gayton, Ben S. Greener, Gareth W. Harbottle,
Simon J. Mantell, Graham N. Maw, Simon A. Osborne, Huw Rees, Tracy J. Ringer,
Margarita Rodriguez-Lens and Graham F. Smith

Weakly active (**4**) was converted into low molecular weight, high activity (**29**) using library chemistry.

Constrained azacyclic analogues of the immunomodulatory agent FTY720 as molecular probes for sphingosine 1-phosphate receptors

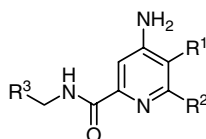
pp 491–494

Stephen Hanessian,* Guillaume Charron, Andreas Billich and Danilo Guerini*

**Hemodynamic effects of potent and selective JNK inhibitors in anesthetized rats: Implication for targeting protein kinases in metabolic diseases**

pp 495–500

Gang Liu,* Hongyu Zhao, Bo Liu, Zhili Xin, Mei Liu, Michael D. Serby, Nathan L. Lubbers, Deborah L. Widomski, James S. Polakowski, David W. A. Beno, James M. Trevillyan and Hing L. Sham



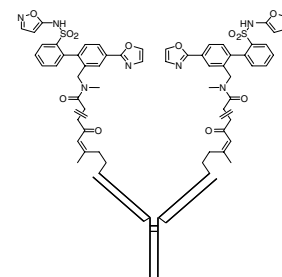
The hemodynamic effects of a series of potent and selective 4-aminopyridine carboxamide-based pan-JNK inhibitors were assessed in an anesthetized rat model. The effects of these agents on mean arterial pressure, heart rate, cardiac contractility, and peripheral vascular resistance are described, and the implication for targeting protein kinases in metabolic diseases is discussed.

**Chemically programmed antibodies: Endothelin receptor targeting CovX-Bodies™**

pp 501–506

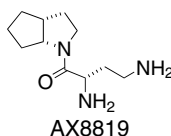
Venkata R. Doppalapudi,* Nancy Tryder, Lingna Li, Teresa Aja, David Griffith, Francesca-Fang Liao, Giovanni Roxas, Mysore P. Ramprasada, Curt Bradshaw and Carlos F. Barbas, III

β -Diketone containing aryl sulfonamide endothelin antagonists were synthesized and covalently linked to the reactive lysine of the antibody m38C2 to create a series of chemically programmed antibodies. These antibodies, named as CovX-Bodies, behaved as potent endothelin receptor antagonists in vitro and showed anti-tumor effect in vivo.

**Synthesis and activity of a potent, specific azabicyclo[3.3.0]octane-based DPP II inhibitor**

pp 507–510

Olga Danilova, Bei Li, A. Katrin Szardenings, Brigitte T. Huber* and Jonathan S. Rosenblum*

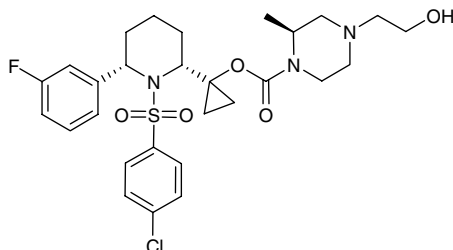


A cell permeable, selective DPP II (also known as DPP2, DPP7, and QPP) inhibitor is reported.

Discovery of γ -secretase inhibitors efficacious in a transgenic animal model of Alzheimer's disease

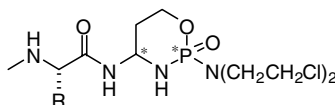
pp 511–516

Theodros Asberom, Zhiqiang Zhao, Thomas A. Bara, John W. Clader, William J. Greenlee, Lynn A. Hyde, Hubert B. Josien, Wei Li, Andrew T. McPhail, Amin A. Nomeir, Eric M. Parker, Murali Rajagopalan, Lixin Song, Gwendolyn T. Wong, Lili Zhang, Qi Zhang and Dmitri A. Pissarnitski*

**Phenylalanyl-aminocyclophosphamides as model prodrugs for proteolytic activation: Synthesis, stability, and stereochemical requirements for enzymatic cleavage**

pp 517–521

Yongying Jiang and Longqin Hu*

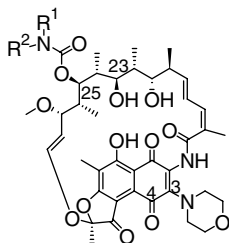


A series of novel phenylalanine-conjugated 4-aminocyclophosphamide isomers were synthesized and evaluated as potential prodrugs for proteolytic activation.

New C25 carbamate rifamycin derivatives are resistant to inactivation by ADP-ribosyl transferases

pp 522–526

Keith D. Combrink,* Daniel A. Denton, Susan Harran, Zhenkun Ma, Katrina Chapo, Dalai Yan, Eric Bonventre, Eric D. Roche, Timothy B. Doyle, Gregory T. Robertson and Anthony S. Lynch

**C25- rifamycin carbamate**

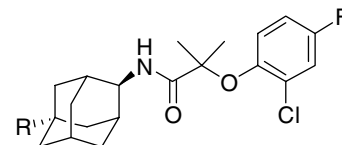
The synthesis of C25 carbamate derivatives of rifamycins and biological data are reported.

**Adamantane sulfone and sulfonamide 11- β -HSD1 Inhibitors**

pp 527–532

Bryan Sorensen, Martin Winn, Jeff Rohde, Qi Shuai, Jiahong Wang, Steven Fung, Katina Monzon, William Chiou, DeAnne Stolarik, Hovis Imade, Liping Pan, Xiaoqing Deng, Linda Chovan, Kenton Longenecker, Russell Judge, Wenying Qin, Michael Brune, Heidi Camp, Ernst U. Frevert, Peer Jacobson and J. T. Link*

The synthesis of potent and selective adamantane sulfone and sulfonamide 11- β -HSD-1 inhibitors represented by **10** and **40** is reported.



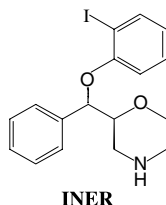
10 R = SO₂Me, h-HSD-1 K_i = 7 nM

40 R = SO₂NH₂, h-HSD-1 K_i = 6 nM

Development of SPECT imaging agents for the norepinephrine transporters: [¹²³I]INER

pp 533–537

Gilles D. Tamagnan,* Eric Brenner, David Alagille, Julie K. Staley, Colin Haile, Andrei Koren, Michelle Early, Ronald M. Baldwin, Frank I. Tarazi, Ross J. Baldessarini, Nachwa Jarkas, Mark M. Goodman and John P. Seibyl



The synthesis and in vivo evaluation of a novel iodo reboxetine analog with subnanomolar affinity for the norepinephrine transporter are described.

Identification of selective neuropeptide Y2 peptide agonists

pp 538–541

Lynn B. DeCarr, Thomas M. Buckholz, Philip D. G. Coish, Zahra Fathi, Stephen E. Fisk, Michelle R. Mays, Stephen J. O'Connor and Kevin J. Lumb*

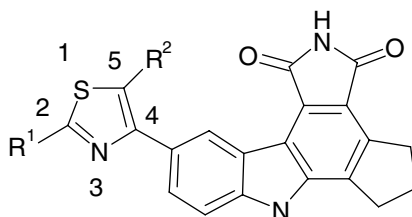


A series of potent and selective NPY2 receptor agonist peptides are described.

Novel poly(ADP-ribose) polymerase-1 inhibitors

pp 542–545

Derek Dunn, Jean Husten, Mark A. Ator and Sankar Chatterjee*

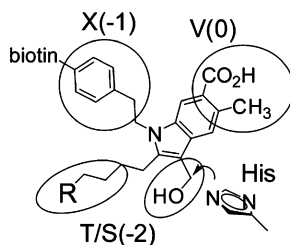


Synthesis and activity of a series of 4-thiazol-yl substituted analogs of a novel pyrrolocarbazole as poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors have been disclosed.

Design of a selective chemical probe for class I PDZ domains

pp 546–548

Naoaki Fujii,* Anang Shelat, Randy A. Hall and R. Kiplin Guy



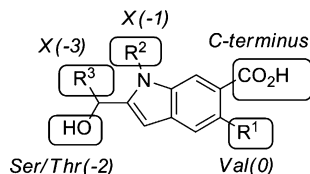
A chemical probe that contained a chemical scaffold mimicking the E/D-T/S-XV peptide differentially visualized the cellular proteome.



Rational design of a nonpeptide general chemical scaffold for reversible inhibition of PDZ domain interactions

pp 549–552

Naoaki Fujii, Jose J. Haresco, Kathleen A. P. Novak, Robert M. Gage, Nicoletta Pedemonte, David Stokoe, Irwin D. Kuntz and R. Kiplin Guy*

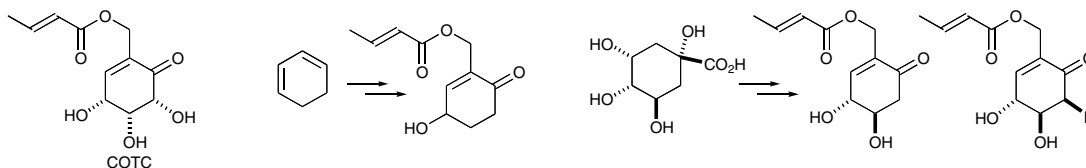


Novel small molecules were designed to specifically target the ligand-binding pocket of a PDZ domain.


Analogues of 2-crotonyloxymethyl-(4R,5R,6R)-4,5,6-trihydroxycyclohex-2-enone (COTC) with anti-tumor properties

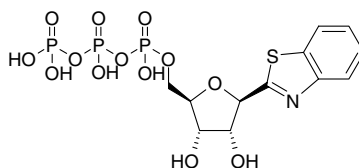
pp 553–557

Claire L. Arthurs, Natasha S. Wind, Roger C. Whitehead* and Ian J. Stratford


Novel nucleotide triphosphates as potent P2Y₂ agonists with enhanced stability over UTP

pp 558–561

Richard J. Davenport,* Paloma Diaz, Frances C. A. Galvin, Steve Lloyd, Stephen R. Mack, Ray Owens, Verity Sabin and Joanne Wynn



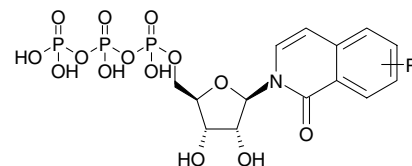
The synthesis and P2Y₂ activities of some novel C-linked nucleotide triphosphates are reported. These exhibit excellent agonist potency and selectivity for the P2Y₂ receptor. Stability studies were carried out on representative compounds from the N-linked and C-linked series; these showed enhanced metabolic stability compared with that of UTP.

Novel nucleotide triphosphates as potent P2Y₂ agonists

pp 562–565


Daniel Brookings, Richard J. Davenport, Jeremy Davis, Frances C. A. Galvin, Steve Lloyd, Stephen R. Mack, Ray Owens, Verity Sabin* and Joanne Wynn

The synthesis and P2Y₂ activities of a novel series of UTP analogs bearing 'unnatural' bicyclic bases in place of the uracil are described. Many of these compounds were potent and selective agonists of the P2Y₂ receptor.



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

*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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ISSN 0960-894X