

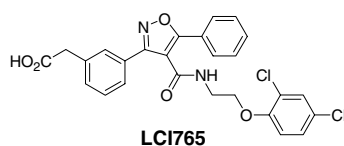
Contents

ARTICLES

3,4,5-Trisubstituted isoxazoles as novel PPAR δ agonists. Part 2

pp 5488–5492

Robert Epple,* Mihai Azimioara, Ross Russo, Yongping Xie, Xing Wang, Christopher Cow, John Wityak, Don Karanewsky, Badry Bursulaya, Andreas Kreusch, Tove Tuntland, Andrea Gerken, Maya Iskandar, Enrique Saez, H. Martin Seidel and Shin-Shay Tian



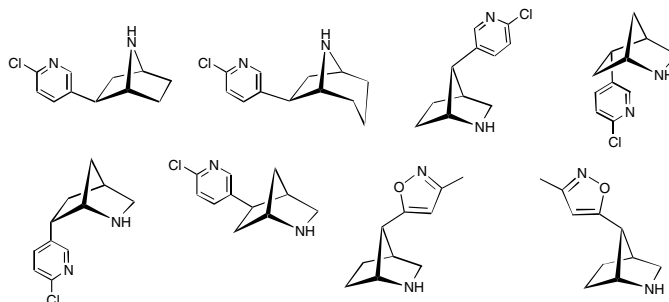
The optimization of an isoxazole series to the potent, selective, and bioavailable PPAR δ agonist LCI765 is reported. A co-crystal structure and in vivo properties of LCI765 are discussed.



Epibatidine isomers and analogues: Structure–activity relationships

pp 5493–5497

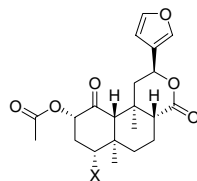
Richard White, John R. Malpass,* Sandeep Handa, S. Richard Baker, Lisa M. Broad, Liz Folly and Adrian Mogg



Synthesis and in vitro pharmacological studies of new C(4)-modified salvinorin A analogues

pp 5498–5502

David Y. W. Lee, Minsheng He, Lee-Yuan Liu-Chen, Yulin Wang, Jian-Guo Li, Wei Xu, Zhongze Ma, William A. Carlezon, Jr., and Bruce Cohen*



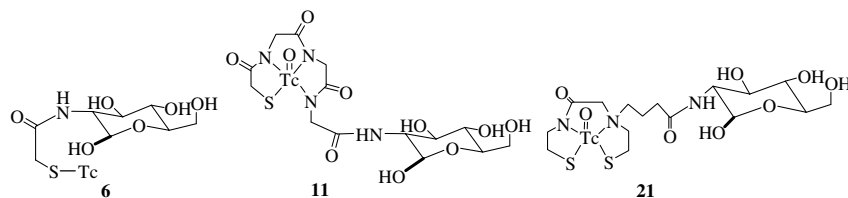
X = OR, OC(O)R, amino acid, etc.

A series of salvinorin A derivatives modified at the C(4) position were prepared and screened for binding and functional activities at the human κ -opioid receptor. Several selective κ -full agonists are reported.

Synthesis and biological evaluation of technetium-99m-labeled deoxyglucose derivatives as imaging agents for tumor

pp 5503–5506

Xiangji Chen, Liang Li, Fei Liu and Boli Liu*



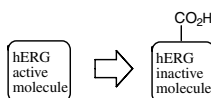
The synthesis and evaluation of three ^{99m}Tc -labeled-deoxyglucose derivatives, ^{99m}Tc -S-DG, ^{99m}Tc -MAG₃-DG, and ^{99m}Tc -MAMA-BA-DG were reported here.



Inhibitory effect of carboxylic acid group on hERG binding

pp 5507–5512

Bing-Yan Zhu,* Zhaozhong J. Jia, Penglie Zhang, Ting Su, Wenrong Huang, Erick Goldman, Daniel Tumas, Vic Kadambi, Priya Eddy, Uma Sinha, Robert M. Scarborough and Yonghong Song*

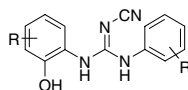


Incorporation of a carboxylic acid group into our hERG active molecules generally leads to hERG inactive compounds regardless where the carboxyl group is tethered within the molecules. The inhibitory effect of a carboxylic acid group on hERG binding has also been observed in many series of diverse structural scaffolds. These findings suggest that the negatively charged carboxylate group causes unfavorable interaction within hERG channel binding cavity by electrostatic interaction.

N,N'-Diarylcyanoquinolines as antagonists of the CXCR2 and CXCR1 chemokine receptors

pp 5513–5516

Hong Nie,* Katherine L. Widdowson, Michael R. Palovich, Wei Fu, John D. Elliott, Deborah L. Bryan, Miriam Burman, Dulcie B. Schmidt, James J. Foley, Henry M. Sarau and Jakob Busch-Petersen*

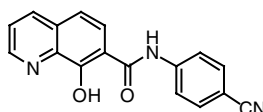


A series of *N*-(2-hydroxy-3-sulfonamidobenzene)-*N'*-arylcyanoquinolines was prepared. In general, these compounds proved to be potent antagonists of CXCR2 while the selectivity versus CXCR1 ranged from non-selective to >200-fold.

Structure-based design, synthesis, and SAR evaluation of a new series of 8-hydroxyquinolines as HIF-1 α prolyl hydroxylase inhibitors

pp 5517–5522

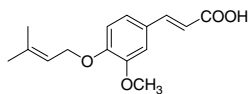
Namal C. Warshakoon,* Shengde Wu, Angelique Boyer, Richard Kawamoto, Justin Sheville, Sean Renock, Kevin Xu, Matthew Pokross, Songtao Zhou, Carol Winter, Richard Walter, Marlene Mekel and Artem G. Evdokimov

VEGF EC₅₀ = 140 nM

In vitro inhibitory activity of boropinic acid against *Helicobacter pylori*

pp 5523–5525

Francesco Epifano,* Luigi Menghini, Rita Pagiotti, Paola Angelini, Salvatore Genovese and Massimo Curini



3 MIC = 1.62 µg/mL

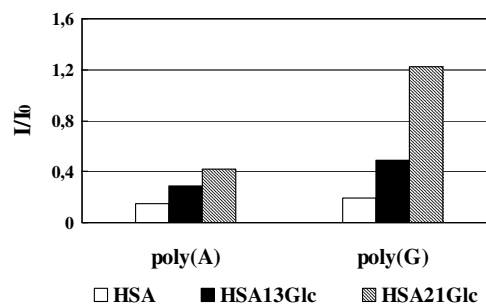
The synthesis and the in vitro inhibition of growth of *Helicobacter pylori* of boropinic acid **3**, active principle of *Boronia pinnata*, (MIC = 1.62 µg/mL) and other prenyloxy cinnamic acids and auraptene is reported.

**Affinity separation of polyribonucleotide-binding human blood proteins**

pp 5526–5529

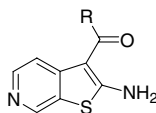
Yuliya V. Gerasimova, Irina V. Alekseyeva, Tatyana G. Bogdanova, Irina A. Erchenko, Natalya V. Kudryashova, Boris P. Chelobanov, Pavel P. Laktionov, Pavel V. Alekseyev and Tatyana S. Godovikova*

Albumin and keratins K1 and K2e are polypurine-binding blood plasma proteins. The in vitro glycated albumin binds poly(A) and poly(G) more efficiently than the unmodified protein. The 28 kDa polypyrimidine-binding blood plasma protein can catalyze the hydrolysis of poly(U).

**Microwave-assisted synthesis of thieno[2,3-*c*]pyridine derivatives as a new series of allosteric enhancers at the adenosine A₁ receptor**

pp 5530–5533

Romeo Romagnoli,* Pier Giovanni Baraldi,* Allan R. Moorman, Maria Antonietta Iaconinoto, Maria Dora Carrion, Carlota Lopez Cara, Mojgan Aghazadeh Tabrizi, Delia Preti, Francesca Fruttarolo, Stephen P. Baker, Katia Varani and Pier Andrea Borea

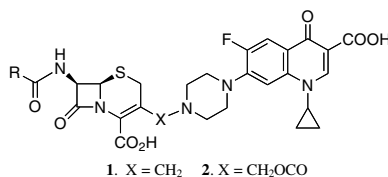


R = substituted phenyl, 1-naphthyl, 2-thienyl

Syntheses and studies of quinolone-cephalosporins as potential anti-tuberculosis agents

pp 5534–5537

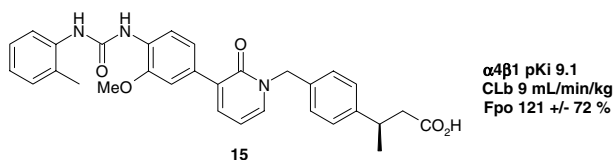
Gaiying Zhao, Marvin J. Miller,* Scott Franzblau, Baojie Wan and Ute Möllmann



Pyridone derivatives as potent, orally bioavailable VLA-4 integrin antagonists

pp 5538–5541

Jason Witherington,* Emma L. Blaney, Vincent Bordas, Richard L. Elliott, Alessandra Gaiba, Neil Garton, Philip M. Green, Antoinette Naylor, David G. Smith, David J. Spalding, Andrew K. Takle and Robert W. Ward

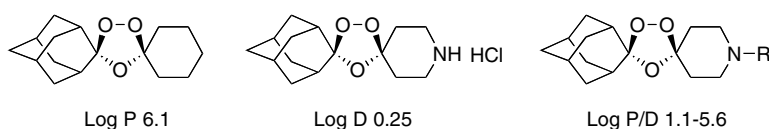


Systematic optimisation of a previously described series of novel VLA-4 antagonists has identified a potent orally bioavailable VLA-4 integrin antagonist.

Antimalarial activity of *N*-alkyl amine, carboxamide, sulfonamide, and urea derivatives of a spiro-1,2,4-trioxolane piperidine

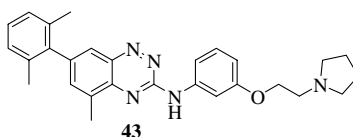
pp 5542–5545

Maniyan Padmanilayam, Bernard Scoreaux, Yuxiang Dong, Jacques Chollet, Hugues Matile, Susan A. Charman, Darren J. Creek, William N. Charman, Josefina Santo Tomas, Christian Scheurer, Sergio Wittlin, Reto Brun and Jonathan L. Vennerstrom*

**Discovery and preliminary structure–activity relationship studies of novel benzotriazine based compounds as Src inhibitors**

pp 5546–5550

Glenn Noronha,* Kathy Barrett, Jianguo Cao, Elena Dneprovskaya, Richard Fine, Xianchang Gong, Colleen Gritzen, John Hood, Xinshan Kang, Boris Klebansky, G. Li, W. Liao, Dan Lohse, Chi Ching Mak, Andrew McPherson, Moorthy S. S. Palanki, Ved P. Pathak, Joel Renick, Richard Soll, Ute Splittgerber, Wolfgang Wrasidlo, Binqi Zeng, Ningning Zhao and Y. Zhou

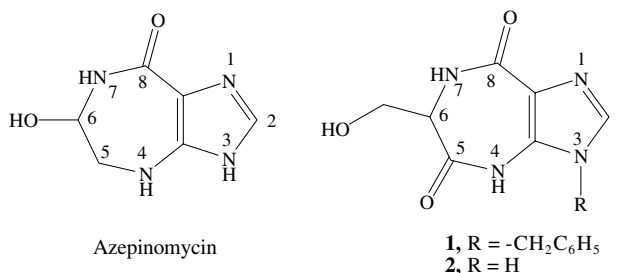


We report the SAR studies of a series of structurally novel benzotriazine analogs as inhibitors of Src. The 3-(2-(1-pyrrolidinyl)ethoxy)phenyl analog (43) was identified as one of the most potent inhibitors.

Design of inhibitors against guanase: Synthesis and biochemical evaluation of analogues of azepinomycin

pp 5551–5554

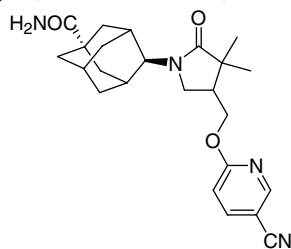
Ravi K. Ujjinamatada, Anila Bhan and Ramachandra S. Hosmane*



Discovery of orally active butyrolactam 11 β -HSD1 inhibitors

pp 5555–5560

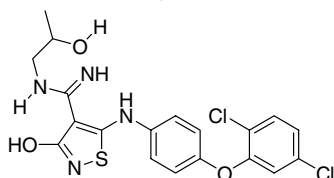
Vince S. C. Yeh,* Ravi Kurukulasuriya, Steven Fung, Katina Monzon, William Chiou, Jiahong Wang, Deanne Stolarik, Hovis Imade, Robin Shapiro, Victoria Knourek-Segel, Eugene Bush, Denise Wilcox, Phong T. Nguyen, Michael Brune, Peer Jacobson and J. T. Link



A series of metabolically stable butyrolactam 11 β -HSD1 inhibitors have been synthesized and biologically evaluated.

Identification of isothiazole-4-carboxamides derivatives as a novel class of allosteric MEK1 inhibitors pp 5561–5566

Hassan El Abdellaoui,* Chamakura V. N. S. Varaprasad, Dinesh Barawkar, Subrata Chakravarty, Andreas Maderna, Robert Tam, Huanming Chen, Matt Allan, Jim Z. Wu, Todd Appleby, Shunqi Yan, Weijian Zhang, Stanley Lang, Nanhua Yao, Robert Hamatake and Zhi Hong



IC50: 28 nM

EC50: 75nM;

Oral AUC: 23908 ng-h/ml

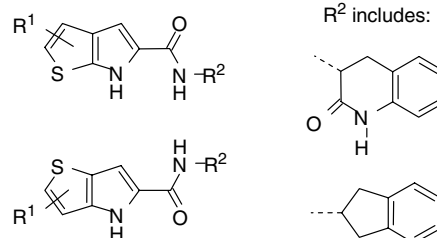
**Novel thienopyrrole glycogen phosphorylase inhibitors: Synthesis, in vitro**

pp 5567–5571

SAR and crystallographic studies

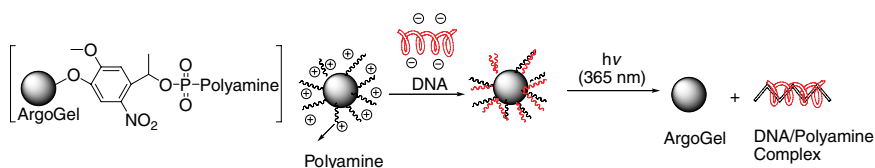
Paul R. O. Whittamore,* Matthew S. Addie, Stuart N. L. Bennett, Alan M. Birch, Michael Butters, Linda Godfrey, Peter W. Kenny, Andrew D. Morley, Paul M. Murray, Nikos G. Oikonomakos, Ludovic R. Otterbein, Andrew D. Pannifer, Jeremy S. Parker, Kristy Readman, Pawel S. Siedlecki, Paul Schofield, Andy Stocker, Melvyn J. Taylor, Linda A. Townsend, David P. Whalley and Jennifer Whitehouse

Novel thienopyrrole inhibitors of recombinant human liver glycogen phosphorylase are described, in particular: SAR, hepatocyte activity and binding at the dimer interface site of the rabbit muscle enzyme (X-ray crystallography).

**Controlled release of DNA/polyamine complex by photoirradiation of a solid phase presenting o-nitrobenzyl ether tethered spermine or polyethyleneimine**

pp 5572–5575

Moon Suk Kim and Scott L. Diamond*

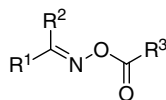


This work describes the synthesis of solid phase with polyamines and DNA binding and controlled release followed by photoirradiation.

Potent inhibitors of lipoprotein-associated phospholipase A₂: Benzaldehyde O-heterocycle-4-carbonyloxime

pp 5576–5579

Hyung Jae Jeong, Yong-Dae Park, Ho-Yong Park, Il Yun Jeong, Tae-Sook Jeong* and Woo Song Lee*

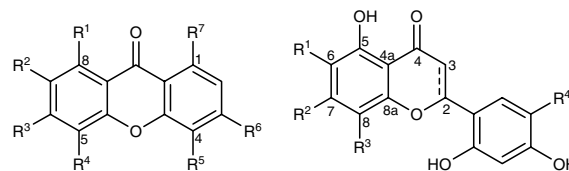


Among the tested oxime derivatives, cyano- and morpholino-substituted analogue **4f** at R² and R³ had the highest potency with an IC₅₀ value of 0.05 μM in whole human plasma.

Anti-atherosclerotic and anti-inflammatory activities of catecholic xanthenes and flavonoids isolated from *Cudrania tricuspidata*

pp 5580–5583

Ki Hun Park, Yong-Dae Park, Jong-Min Han, Kyung-Ran Im, Byong Won Lee, Il Yun Jeong, Tae-Sook Jeong* and Woo Song Lee*



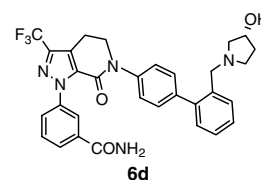
The catecholic xanthenes and flavonoids **1–13** were isolated from the chloroform extracts of the root bark of *Cudrania tricuspidata*. Compounds **1** and **3–8** exhibited significant antioxidant activity against LDL oxidation in TBARS assay. Among them, **10–12** showed an inhibitory effect on the NO production and iNOS expression in RAW264.7 cells. Also, compounds **1**, **2**, **5**, **7**, **9**, and **11** preferentially inhibited hACAT-2 than hACAT-1, whereas compounds **3**, **4**, **6**, and **8** showed a similar specificity against hACAT-1 and -2. However, flavonoids **10**, **12**, and **13** dominantly inhibited hACAT-2, not hACAT-1.

Discovery of potent, efficacious, and orally bioavailable inhibitors of blood coagulation factor Xa with neutral P1 moieties

pp 5584–5589

Donald J. P. Pinto,* Robert A. Galembo, Jr., Mimi L. Quan, Michael J. Orwat, Charles Clark, Renhua Li, Brian Wells, Francis Woerner, Richard S. Alexander, Karen A. Rossi, Angela Smallwood, Pancras C. Wong, Joseph M. Luetzgen, Alan R. Rendina, Robert M. Knabb, Kan He, Ruth R. Wexler and Patrick Y. S. Lam

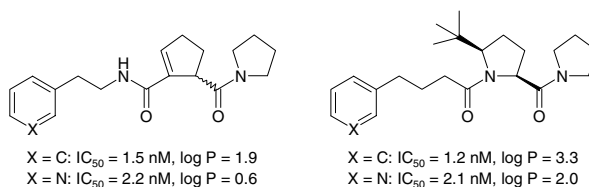
The bicyclic tetrahydropyrazolopiperidinone scaffold allowed for the incorporation of multiple neutral P1 moieties with subnanomolar binding affinities for blood coagulation factor Xa. The compound 3-[6-(2'-dimethylaminomethyl-biphenyl-4-yl)-7-oxo-3-trifluoro-methyl-4,5,6,7-tetrahydro-pyrazolo[3,4-*c*]pyridine-1-yl]-benzamide **6d** shows good Xa potency, selectivity, in vivo efficacy, and oral bioavailability. Compound **6d** was selected for further pre-clinical evaluations.



An introduction of a pyridine group into the structure of prolyl oligopeptidase inhibitors

pp 5590–5593

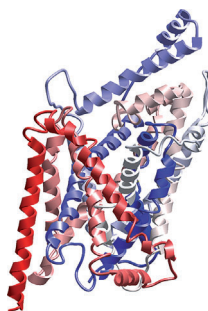
Elina M. Jarho,* Jarkko I. Venäläinen, Juha Juntunen, A. Leena Yli-Kokko, Jouko Vepsäläinen, Johannes A. M. Christiaans, Markus M. Forsberg, Tomi Järvinen, Pekka T. Männistö and Erik A. A. Wallén



A homology model of SERT based on the LeuT_{Aa} template

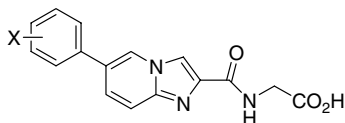
pp 5594–5597

Aina Westrheim Ravna, Malgorzata Jaronczyk and Ingebrigt Sylte*

**A novel series of imidazo[1,2-*a*]pyridine derivatives as HIF-1 α prolyl hydroxylase inhibitors**

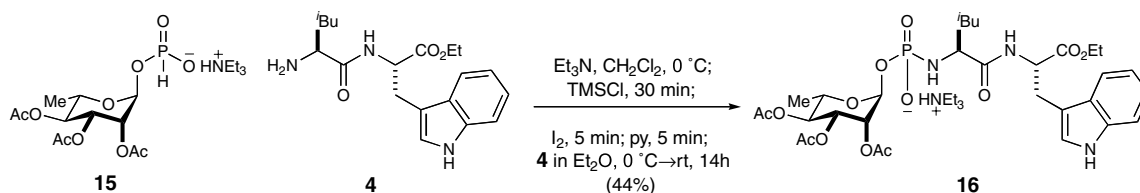
pp 5598–5601

Namal C. Warshakoon,* Shengde Wu, Angelique Boyer, Richard Kawamoto,
Justin Sheville, Sean Renock, Kevin Xu, Matthew Pokross, Artem G. Evdokimov,
Richard Walter and Marlene Mekel

**Preparation of a protected phosphoramidon precursor via an *H*-Phosphonate coupling strategy**

pp 5602–5604

Matthew G. Donahue and Jeffrey N. Johnston*

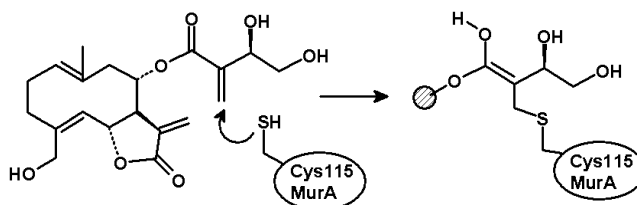


We report the preparation of a phosphoramidon precursor **16** in 44% yield from *H*-phosphonate **15** and H₂N-Leu-Trp-OEt **4**.

**Sesquiterpene lactones are potent and irreversible inhibitors of the antibacterial target enzyme MurA**

pp 5605–5609

Anke Bachelier, Ralf Mayer and Christian D. Klein*



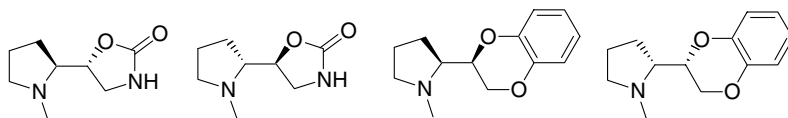
Certain sesquiterpene lactones are potent inhibitors of the antibacterial target enzyme MurA. We present structure–activity relationships and discuss biological implications.



Synthesis and $\alpha\beta 2$ nicotinic affinity of unichiral 5-(2-pyrrolidinyl)oxazolidinones and 2-(2-pyrrolidinyl)benzodioxanes

pp 5610–5615

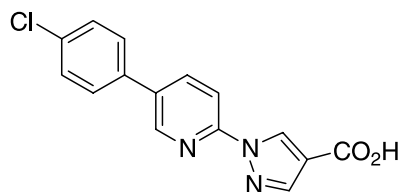
Marco Pallavicini,* Barbara Moroni, Cristiano Bolchi, Antonio Cilia, Francesco Clementi, Laura Fumagalli, Cecilia Gotti, Fiorella Meneghetti, Loredana Riganti, Giulio Vistoli and Ermanno Valoti



Design and synthesis of substituted pyridine derivatives as HIF-1 α prolyl hydroxylase inhibitors

pp 5616–5620

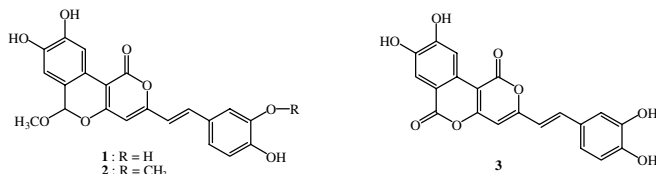
Namal C. Warshakoon,* Shengde Wu, Angelique Boyer, Richard Kawamoto, Justin Sheville, Ritu Tiku Bhatt, Sean Renock, Kevin Xu, Matthew Pokross, Songtao Zhou, Richard Walter, Marlene Mekel, Artem G. Evdokimov and Stephen East



Free radical scavengers from the medicinal mushroom *Inonotus xeranticus* and their proposed biogenesis

pp 5621–5624

In-Kyoung Lee, Jin-Young Jung, Soon-Ja Seok, Wan-Gyu Kim and Bong-Sik Yun*

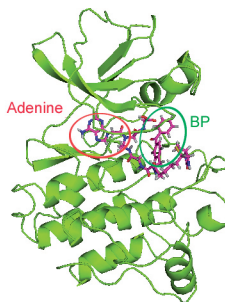


New free radical scavengers **1** and **2** were isolated from the methanolic extract of the fruiting body of the medicinal mushroom *Inonotus xeranticus*, along with the known compounds phelligrudin D, 3,4-dihydroxybenzaldehyde, and 3,4-dihydroxybenzoic acid. Their structures were established by extensive spectroscopic data. Compounds **1** and **3** were proposed to be biosynthesized from the oxidative coupling of the precursor hispidin with 3,4-dihydroxybenzaldehyde and 3,4-dihydroxybenzoic acid, respectively. These compounds exhibited significant free radical scavenging activity.

Selective photolabeling of Lck kinase in complex proteome

pp 5625–5628

Sagit Hindi, Haiteng Deng, Laurence James and Akira Kawamura*



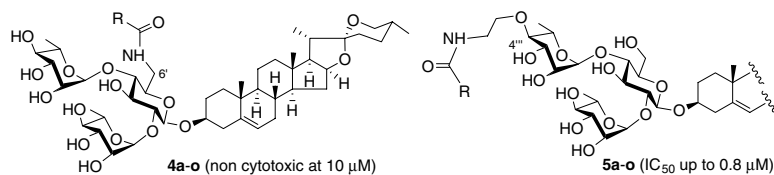
A simple molecular probe containing adenine and benzophenone was found to tag Lck in a highly selective manner.



Synthesis and cytotoxicities of dioscin derivatives with decorated chactriosyl residues

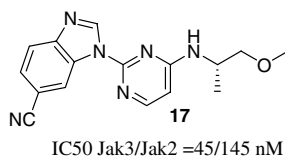
pp 5629–5632

Shilei Zhu, Yichun Zhang, Ming Li, Jia Yu, Lihong Zhang, Yingxia Li and Biao Yu*

**Development of pyrimidine-based inhibitors of Janus tyrosine kinase 3**

pp 5633–5638

Jack J. Chen,* Kumar D. Thakur, Michael P. Clark, Steven K. Laughlin, Kelly M. George, Roger G. Bookland, Jan R. Davis, Edward J. Cabrera, Vijay Easwaran, Biswanath De and Y. George Zhang

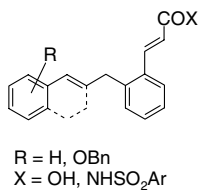


A new class of pyrimidine-based Janus tyrosine kinase 3 (JAK3) inhibitors are described. Many of these inhibitors showed low nanomolar activity against JAK3.

Comparison between two classes of selective EP₃ antagonists and their biological activities

pp 5639–5642

Michel Belley,* Chi Chung Chan, Yves Gareau, Michel Gallant, Hélène Juteau, Karine Houde, Nicolas Lachance, Marc Labelle, Nicole Sawyer, Nathalie Tremblay, Sonia Lamontagne, Marie-Claude Carrière, Danielle Denis, Gillian M. Greig, Deborah Slipetz, Robert Gordon, Nathalie Charet, Chun Li, Robert J. Zamboni and Kathleen M. Metters

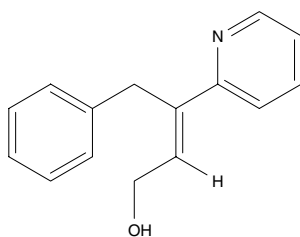


The structural differences and their effects on the biological activity in vivo, in vitro and metabolism have been analyzed.

A novel antiproliferative agent, phenylpyridineylbutenol, isolated from *Streptomyces* sp.

pp 5643–5645

Choonshik Shin, Haeyoung Lim, Sangik Moon, Seunghyun Kim, Yeonjoong Yong, Bum-Joon Kim, Chul-Hoon Lee and Yoongho Lim*



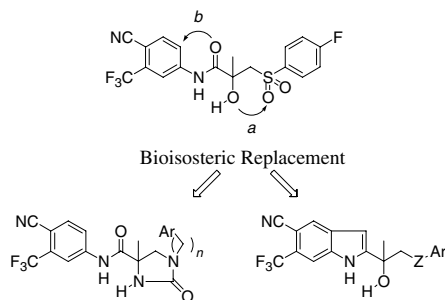
A novel compound, (*E*)-4-phenyl-3-(pyridine-2-yl)but-2-en-1-ol, showing antiproliferative effect is reported.



A bioisosteric approach to the discovery of indole carbinol androgen receptor ligands

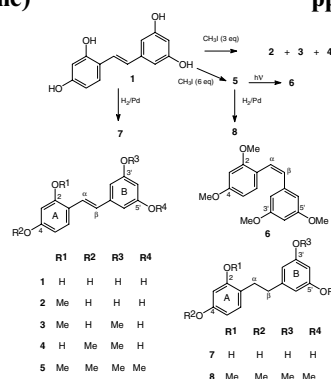
pp 5646–5649

James C. Lanter,* James J. Fiordeliso, George F. Allan, Amy Musto, Do Won Hahn and Zhihua Sui

**Chemical transformations of oxyresveratrol (*trans*-2,4,3',5'-tetrahydroxystilbene) into a potent tyrosinase inhibitor and a strong cytotoxic agent**

pp 5650–5653

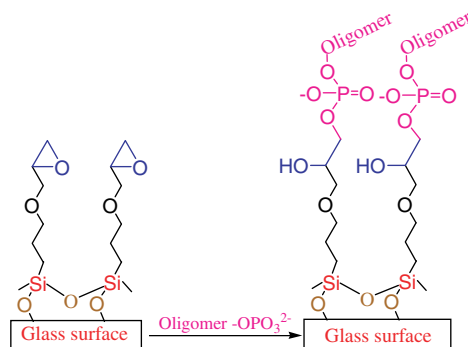
Kittisak Likhitwitayawuid,* Acom Sornsute, Boonchoo Sritularak and Poonsakdi Ploypradith

**An efficient and versatile approach for the construction of oligonucleotide microarrays**

pp 5654–5658

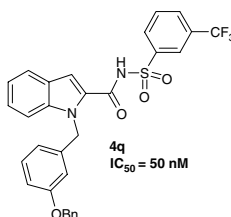
S. Mahajan, P. Kumar and K. C. Gupta*

An efficient and facile method for covalent attachment of phosphorylated oligonucleotides on epoxy-activated glass surface is described.

**Design and synthesis of novel *N*-sulfonyl-2-indole carboxamides as potent PPAR- γ binding agents with potential application to the treatment of osteoporosis**

pp 5659–5663

Corey R. Hopkins,* Steven V. O'Neil, Michael C. Lauferweiler, Yili Wang, Matthew Pokross, Marlene Mekel, Artem Evdokimov, Richard Walter, Maria Kontoyianni, Maria E. Petrey, Georgios Sabatakos, Jeff T. Roesgen, Eloise Richardson and Thomas P. Demuth

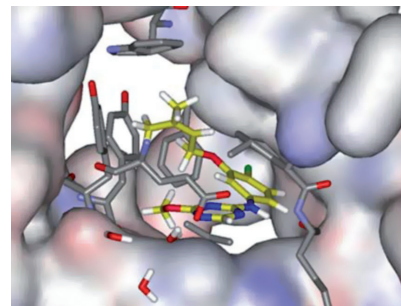


Optimization of pyrimidinyl- and triazinyl-amines as non-nucleoside inhibitors of HIV-1 reverse transcriptase

pp 5664–5667

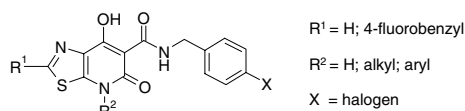
Vinay V. Thakur, Joseph T. Kim, Andrew D. Hamilton, Christopher M. Bailey, Robert A. Domaol, Ligong Wang, Karen S. Anderson* and William L. Jorgensen*

Synthesis, assaying, and computational results are reported for new anti-HIV agents that exhibit high potency, low cytotoxicity, and promising pharmacological properties.

**Synthesis and HIV-integrase strand transfer inhibition activity of 7-hydroxy[1,3]thiazolo[5,4-*b*]pyridin-5(4*H*)-ones**

pp 5668–5672

Eric E. Boros,* Brian A. Johns, Edward P. Garvey, Cecilia S. Koble and Wayne H. Miller

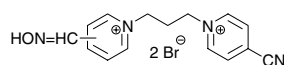


HIV integrase strand transfer IC₅₀ range = 151–0.03 μM.

Synthesis of asymmetrical bispyridinium compounds bearing cyano-moiety and evaluation of their reactivation activity against tabun and paraoxon-inhibited acetylcholinesterase

pp 5673–5676

Kamil Musilek, Ondrej Holas, Kamil Kuca,* Daniel Jun, Vlastimil Dohnal and Martin Dolezal

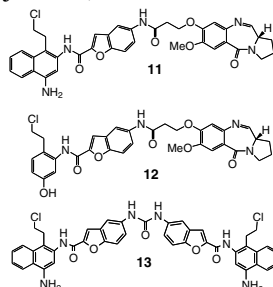


A series of asymmetrical bisquaternary reactivators of acetylcholinesterase (AChE) bearing cyano-moiety with propane connecting chain was synthesized and evaluated on tabun and paraoxon-inhibited AChE with promising results.

**DNA interstrand crosslinking agents: Synthesis, DNA interactions, and cytotoxicity of dimeric achiral seco-amino-CBI and conjugates of achiral seco-amino-CBI with pyrrolobenzodiazepine (PBD)**

pp 5677–5681

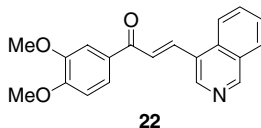
Bethany Purnell, Atsushi Sato, Amanda O'Kelley, Carly Price, Kaitlin Summerville, Stephen Hudson, Caroline O'Hare, Konstantinos Kiakos, Tetsuji Asao, Moses Lee* and John A. Hartley



In vitro and in vivo efficacy and in vitro metabolism of 1-phenyl-3-aryl-2-propen-1-ones against *Plasmodium falciparum*

pp 5682–5686

Clare E. Gutteridge,* Daniel A. Nichols, Sean M. Curtis, Darshan S. Thota, Joseph V. Vo, Lucia Gerena, Gettayacamin Montip, Constance O. Asher, Damaris S. Diaz, Charles A. DiTusa, Kirsten S. Smith and Apurba K. Bhattacharjee

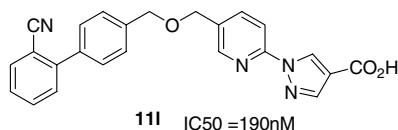


Nine in vitro submicromolar inhibitors of *Plasmodium falciparum* were identified, including compound **22**. They were inactive when administered orally to *Plasmodium berghei* infected mice, possibly due to metabolic instability.

Design and synthesis of a series of novel pyrazolopyridines as HIF 1- α prolyl hydroxylase inhibitors

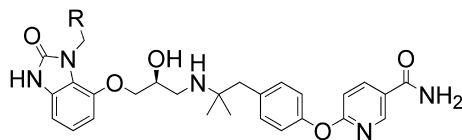
pp 5687–5690

Namal C. Warshakoon,* Shengde Wu, Angelique Boyer, Richard Kawamoto, Sean Renock, Kevin Xu, Matthew Pokross, Artem G. Evdokimov, Songtao Zhou, Carol Winter, Richard Walter and Marlene Mekel

**Potent benzimidazolone based human β_3 -adrenergic receptor agonists**

pp 5691–5694

Don R. Finley, Michael G. Bell, Anthony G. Borel, William E. Bloomquist, Marlene L. Cohen, Mark L. Heiman, Aidas Kriauciunas, Donald P. Matthews, Tania Miles, David A. Neel, Christopher J. Rito, Daniel J. Sall, Anthony J. Shuker, Thomas W. Stephens, Frank C. Tinsley, Mark A. Winter and Cynthia D. Jesudason*



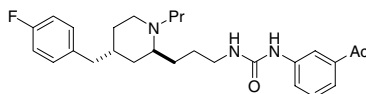
The synthesis and biological evaluation of a series of benzimidazolone β_3 adrenergic receptor agonists are described. A trend toward the reduction of rat atrial tachycardia upon increasing steric bulk at the 3-position of the benzimidazolone moiety was observed.

2,4-Disubstituted piperidines as selective CC chemokine receptor 3 (CCR3) antagonists:

pp 5695–5699

Synthesis and selectivity

Paul S. Watson,* Bin Jiang, Kim Harrison, Nao Asakawa, Patricia K. Welch, Maryanne Covington, Nicole C. Stowell, Eric A. Wadman, Paul Davies, Kimberly A. Solomon, Robert C. Newton, George L. Trainor, Steven M. Friedman, Carl P. Decicco and Soo S. Ko

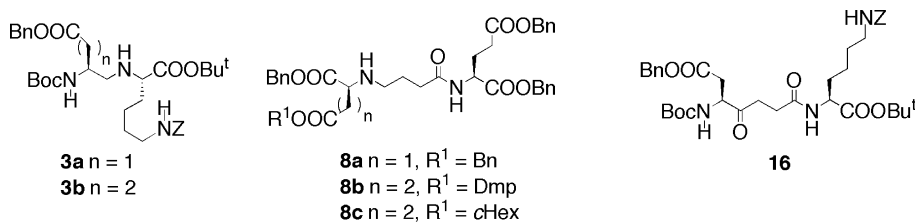


Linear unselective CCR3 antagonist leads with IC₅₀ values in the 200 nM range were converted into low nM binding compounds selective at CCR3 by moving the piperidine nitrogen substituent to the carbon at the 2-position of the ring. Substitution of the piperidine nitrogen with simple alkyl and acyl groups was found to improve the selectivity of this new compound class. In particular, *N*-{3-[(2*S*,4*R*)-1-(propyl)-4-(4-fluorobenzyl)piperidinyl]propyl}-*N'*-(3-acetylphenyl)urea exhibited single digit nanomolar IC₅₀ values for CCR3 with >100-fold selectivity against an extensive counter screen panel.

Inhibition of P-glycoprotein-mediated multidrug efflux by aminomethylene and ketomethylene analogs of reversins

pp 5700–5703

Ali Koubeissi, Imad Raad, Laurent Ettouati,* David Guilet, Charles Dumontet and Joelle Paris*



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Summary of instructions to authors

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*Corresponding author

Supplementary data available via ScienceDirect

COVER

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

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