

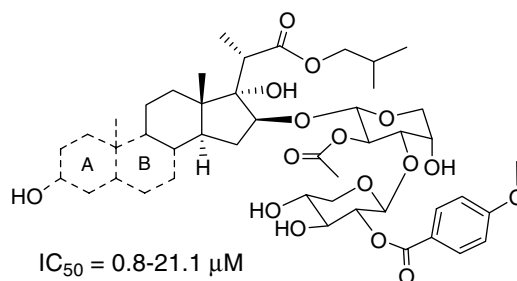
Contents

ARTICLES

Synthesis of the A,B-ring-truncated OSW saponin analogs and their antitumor activities

pp 5506–5509

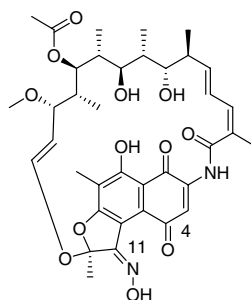
Wenjie Peng, Pingping Tang, Xiaoyi Hu, Jun O. Liu and Biao Yu*



Preparation and in vitro anti-staphylococcal activity of novel 11-deoxy-11-hydroxyiminorifamycins

pp 5510–5513

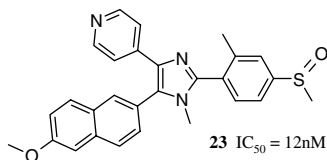
Jing Li, Zhenkun Ma, Katrina Chapo, Dalai Yan, A. Simon Lynch and Charles Z. Ding*



Optimization of triarylimidazoles for Tie2: Influence of conformation on potency

pp 5514–5517

Neil W. Johnson,* Marcus Semones, Jerry L. Adams, Michael Hansbury and Jim Winkler

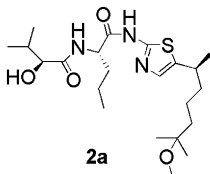


Optimization of triarylimidazoles for Tie2 potency resulted in the identification of the potent and selective tetrasubstituted imidazole **23** that was efficacious in an animal model of angiogenesis.

Thiazole-diamides as potent γ -secretase inhibitors

pp 5518–5522

Yuhpyng L. Chen,* Kevin Cherry, Michael L. Corman, Charles F. Ebbinghaus, Chandra B. Gamlath, Dane Liston, Barbara-Anne Martin, Christine E. Oborski and Barbara G. Sahagan

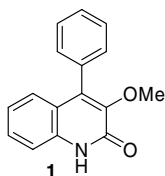


The thiazole-diamide series has been identified as highly potent γ -secretase inhibitors. Several representative compounds showed IC_{50} values of <0.3 nM. The synthesis and SAR, as well as [3H]-**2a**, are described.

Synthesis of 3-*O*-methylviridicatin analogues with improved anti-TNF- α properties

pp 5523–5524

Nigel Ribeiro, Helena Tabaka, Jean Peluso, Ludivine Fetzter, Can Nebigil, Serge Dumont, Christian D. Muller and Laurent Désaubry*

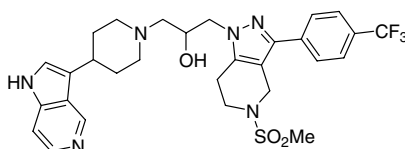


Replacement of the methoxy moiety of 3-*O*-methylviridicatin **1** by a thiomethyl dramatically enhances its ability to inhibit TNF- α secretion.

Pyrazole-based cathepsin S inhibitors with improved cellular potency

pp 5525–5528

Jianmei Wei, Barbara A. Pio, Hui Cai, Steven P. Meduna, Siquan Sun, Yin Gu, Wen Jiang, Robin L. Thurmond, Lars Karlsson and James P. Edwards*

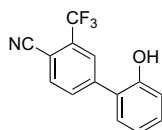


Noncovalent, pyrazole-based cathepsin S inhibitors are reported. Significant improvements in cellular potency were achieved through modification of a 4-(indol-3-yl)piperidine head group.

Preparation of 4-aryl-2-trifluoromethylbenzonitrile derivatives as androgen receptor antagonists for topical suppression of sebum production

pp 5529–5532

Jennifer A. Van Camp,* Lain-Yen Hu, Catherine Kostlan, Bruce Lefker, Jie Li, Lorna Mitchell, Zhi Wang, Wen-Song Yue, Matthew Carroll, Danielle Dettling, Daniel Du, David Pocalyko and Kimberly Wade



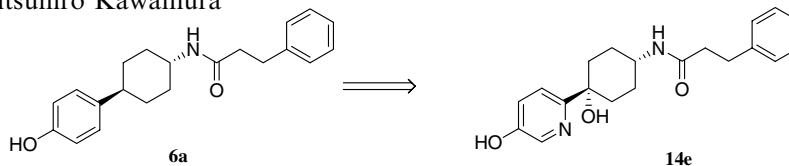
4e Cellular IC_{50} = 0.02 nM

The synthesis and SAR of a series of androgen receptor antagonists is described. The in vivo efficacy of compound **4e** is highlighted.

Discovery of novel and orally active NR2B-selective *N*-methyl-D-aspartate (NMDA) antagonists, pyridinol derivatives with reduced HERG binding affinity

pp 5533–5536

Makoto Kawai,* Hiroshi Nakamura, Isao Sakurada, Hirohisa Shimokawa, Hirotaka Tanaka, Miyako Matsumizu, Kazuo Ando, Kazunari Hattori, Atsuko Ohta, Seiji Nukui, Atsushi Omura and Mitsuhiro Kawamura

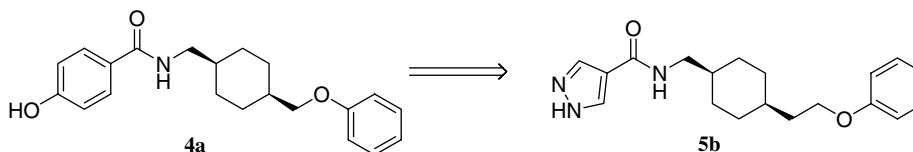


Structure–activity relationship investigation led to *N*-[*cis*-4-hydroxy-4-(5-hydroxypyridin-2-yl)cyclohexyl]-3-phenylpropanamide **14e** as an orally active NR2B-subtype selective *N*-methyl-D-aspartate (NMDA) receptor antagonist with very weak HERG binding ($IC_{50} > 30 \mu M$).

Structure–activity relationship study of novel NR2B-selective antagonists with arylamides to avoid reactive metabolites formation

pp 5537–5542

Makoto Kawai,* Isao Sakurada, Asato Morita, Yuko Iwamuro, Kazuo Ando, Hirofumi Omura, Sachiko Sakakibara, Tsutomu Masuda, Hiroki Koike, Teruki Honma, Kazunari Hattori, Tadayuki Takashima, Kunihiro Mizuno, Mayumi Mizutani and Mitsuhiro Kawamura



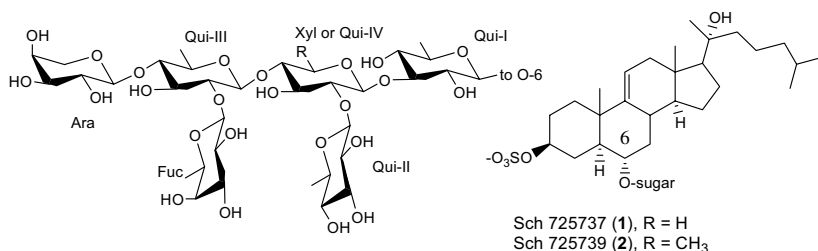
Replacement of the phenol moiety with pyrazole led to a novel potent NMDA-NR2B selective antagonist (**5b**) with an improved metabolic profile. Through this study, a close correlation between reactive metabolites formation and calculated HOMO energies of parent compounds was found.

Novel steroidal saponins, Sch 725737 and Sch 725739, from a marine starfish, *Novodinia antillensis*

pp 5543–5547

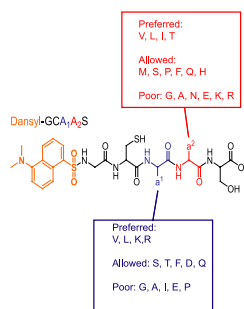
Shu-Wei Yang,* Tze-Ming Chan, Alexei Buevich, Tony Priestley, James Crona, John Reed, Amy E. Wright, Mahesh Patel, Vincent Gullo, Guodong Chen, Birendra Pramanik and Min Chu

Bioassay-guided fractionation of an active fraction from an extract of a marine starfish, *Novodinia antillensis*, led to the identification of two new saponins, Sch 725737 (**1**) and Sch 725739 (**2**). Compound **1** was identified as the NaV1.8 inhibitor with IC_{50} of $\sim 9 \mu M$.

**Evaluation of protein farnesyltransferase substrate specificity using synthetic peptide libraries**

pp 5548–5551

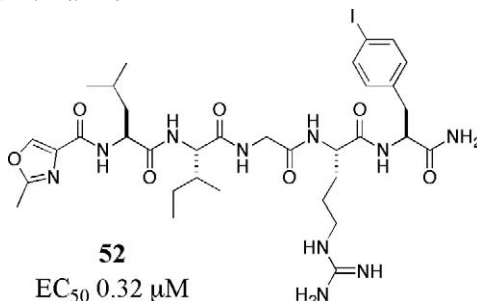
Amanda J. Krzysiak, Sarah A. Scott, Katherine A. Hicks, Carol A. Fierke and Richard A. Gibbs*



A refined agonist pharmacophore for protease activated receptor 2

pp 5552–5557

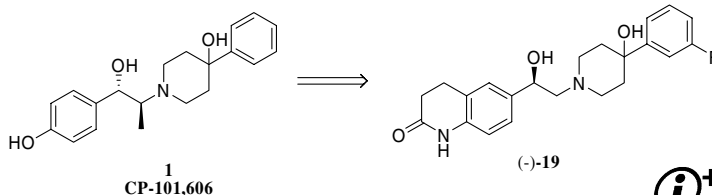
Grant D. Barry, Jacky Y. Suen, Heng Boon Low, Bernhard Pfeiffer, Bernadine Flanagan, Maria Halili, Giang T. Le and David P. Fairlie*


Discovery of (–)-6-[2-[4-(3-fluorophenyl)-4-hydroxy-1-piperidinyl]-1-hydroxyethyl]-3,4-dihydro-2(1H)-quinolinone—A potent NR2B-selective N-methyl D-aspartate (NMDA) antagonist for the treatment of pain

pp 5558–5562

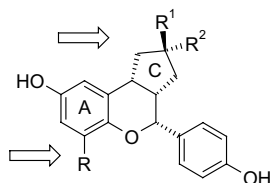
Makoto Kawai,* Kazuo Ando, Yukari Matsumoto, Isao Sakurada, Masako Hirota, Hiroshi Nakamura, Atsuko Ohta, Masaki Sudo, Kazunari Hattori, Tadashi Takashima, Masanori Hizue, Shuzo Watanabe, Isami Fujita, Mayumi Mizutani and Mitsuhiro Kawamura

Compound (–)-**19** was identified by structure–activity relationship around CP-101,606 (**1**) in order to alleviate its significant PK variability and QT prolongation issues.


Benzopyrans as selective estrogen receptor β agonists (SERBAs). Part 5: Combined A- and C-ring structure–activity relationship studies

pp 5563–5566

Timothy I. Richardson,* Jeffrey A. Dodge, Yong Wang, Jim D. Durbin, Venkatesh Krishnan and Bryan H. Norman

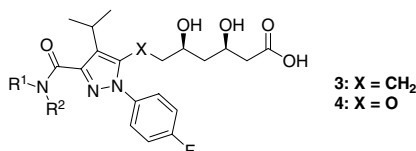


Combined A/C-ring structure–activity relationship studies on the benzopyran scaffold.

Pyrazole inhibitors of HMG-CoA reductase: An attempt to dramatically reduce synthetic complexity through minimal analog re-design

pp 5567–5572

Scott D. Larsen,* Toni-Jo Poel, Kevin J. Filipinski, Jeffrey T. Kohrt, Jeffrey A. Pfeifferkorn, Roderick J. Sorenson, Bradley D. Tait, Valerie Askew, Lisa Dillon, Jeffrey C. Hanselman, Gina H. Lu, Andrew Robertson, Catherine Sekerke, Mark C. Kowala and Bruce J. Auerbach

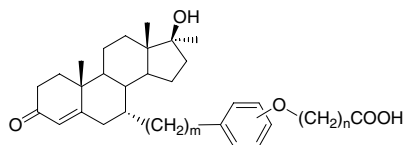


A highly effective new series of pyrazole statins **3** was transformed by a single atom change to the oxypyrazoles **4**, reducing a complex synthetic route from 14 to 7 steps. Although the new analogs retained most of the in vitro activity of the pyrazoles, they had inferior in vivo activity.

Discovery and structure–activity relationships of new steroidal compounds bearing a carboxy-terminal side chain as androgen receptor pure antagonists

pp 5573–5576

Kazutaka Tachibana,* Ikuhiro Imaoka, Hitoshi Yoshino, Nobuaki Kato, Mitsuaki Nakamura, Masateru Ohta, Hiromitsu Kawata, Kenji Taniguchi, Nobuyuki Ishikura, Masahiro Nagamuta, Etsuro Onuma and Haruhiko Sato

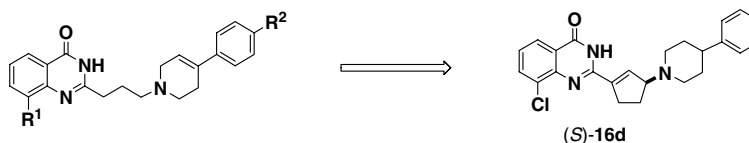


New steroidal compounds were synthesized and showed AR antagonistic activities without agonistic activities in reporter gene assay. SARs of the compounds are also presented in this report.

Rational design of conformationally restricted quinazolinone inhibitors of poly(ADP-ribose)polymerase

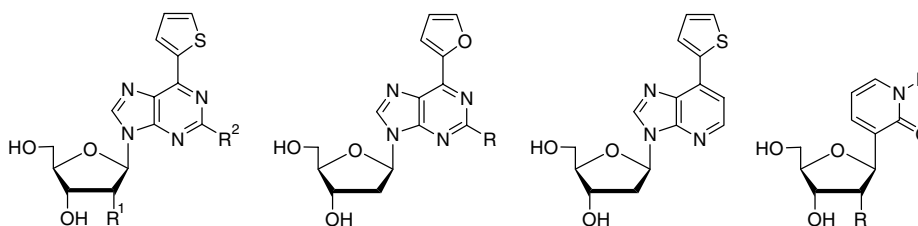
pp 5577–5581

Kouji Hattori,* Yoshiyuki Kido, Hirofumi Yamamoto, Junya Ishida, Akinori Iwashita and Kayoko Mihara


Cytostatic evaluations of nucleoside analogs related to unnatural base pairs for a genetic expansion system

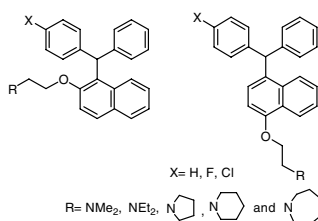
pp 5582–5585

Michiko Kimoto, Kei Moriyama, Shigeyuki Yokoyama* and Ichiro Hirao*


Design, synthesis and antitubercular activity of diarylmethylnaphthol derivatives

pp 5586–5589

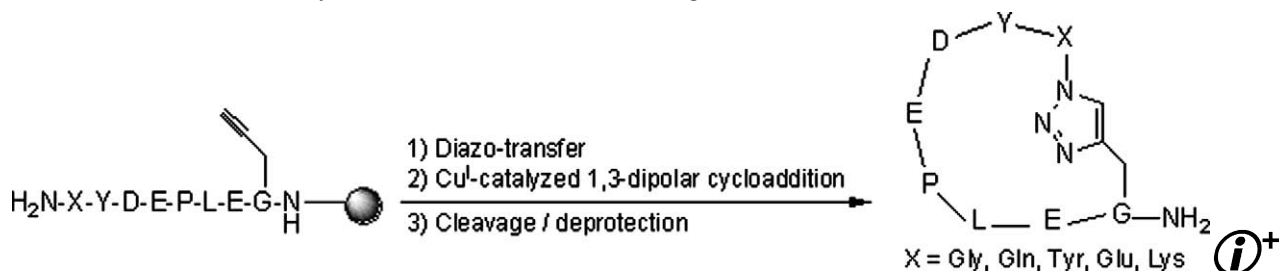
Sajal Kumar Das, Gautam Panda,* Vinita Chaturvedi, Y. S. Manju, Anil K. Gaikwad and Sudhir Sinha



On-resin cyclization of peptide ligands of the Vascular Endothelial Growth Factor Receptor 1 by copper(I)-catalyzed 1,3-dipolar azide–alkyne cycloaddition

pp 5590–5594

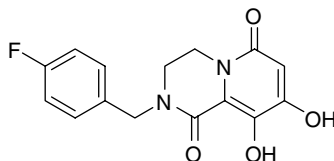
Victor Goncalves, Benoit Gautier, Anne Regazzetti, Pascale Coric, Serge Bouaziz, Christiane Garbay, Michel Vidal* and Nicolas Inguimbert*



Dihydropyridopyrazine-1,6-dione HIV-1 integrase inhibitors

pp 5595–5599

John S. Wai,* Boyoung Kim, Thorsten E. Fisher, Linghang Zhuang, Mark W. Embrey, Peter D. Williams, Donnette D. Staas, Chris Culberson, Terry A. Lyle, Joseph P. Vacca, Daria J. Hazuda, Peter J. Felock, William A. Schleif, Lori J. Gabryelski, Lixia Jin, I-Wu Chen, Joan D. Ellis, Rama Mallai and Steven D. Young

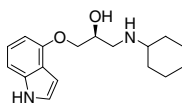


A series of potent novel dihydropyridopyrazine-1,6-dione HIV-1 integrase inhibitors was identified. These compounds inhibited the strand transfer process of HIV-1 integrase and viral replication in cells.

Indoloxypropanolamine analogues as 5-HT_{1A} receptor antagonists

pp 5600–5604

Joseph H. Krushinski, Jr.,* John M. Schaus, Dennis C. Thompson, David O. Calligaro, David L. Nelson, Susan H. Luecke, David B. Wainscott and David T. Wong



13a $K_i = 1.33$ nM @ 5-HT_{1A} receptor

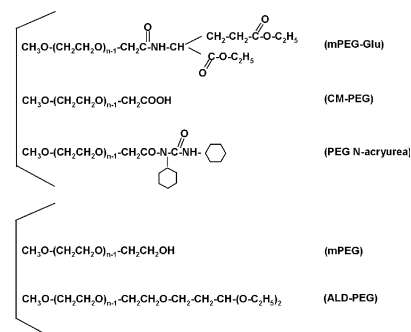
The discovery and synthesis of the 5-HT_{1A} receptor antagonist **13a** is reported.

Preparative purification of polyethylene glycol derivatives with polystyrene-divinylbenzene beads as chromatographic packing

pp 5605–5609

Pengzhan Yu, Xingqi Li, Xiunan Li, Xiuling Lu, Guanghui Ma and Zhiguo Su*

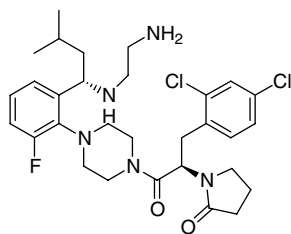
A clear and powerful purification approach of PEG derivatives was developed on polystyrene-divinylbenzene beads with ethanol/water as eluants and gave the highly pure target products. The novel methods shared the advantages of clearness, reliability and high-performance. The studies suggested that polystyrene-divinylbenzene beads were potent to serve as medium for the purification of PEG derivatives on a preparative scale.



Pyrrolidinones as potent functional antagonists of the human melanocortin-4 receptor

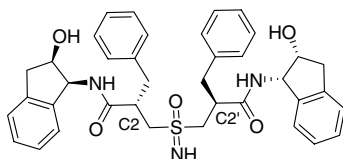
pp 5610–5613

Wanlong Jiang, Fabio C. Tucci,* Joe A. Tran, Beth A. Fleck, Jenny Wen, Stacy Markison, Dragan Marinkovic, Caroline W. Chen, Melissa Arellano, Sam R. Hoare, Michael Johns, Alan C. Foster, John Saunders and Chen Chen*

**12a:** $K_i = 0.94$ nM, $IC_{50} = 21$ nM**Discovery of potent HIV-1 protease inhibitors incorporating sulfoximine functionality**

pp 5614–5619

Ding Lu and Robert Vince*

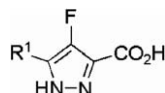


A novel class of sulfoximine-based pseudosymmetric HIV-1 protease inhibitors were designed and synthesized. The most active isomer (2*S*,2'*S*) displays potent activity against HIV-1 protease as well as virus.

Fluorinated pyrazole acids are agonists of the high affinity niacin receptor GPR109a

pp 5620–5623

Philip J. Skinner,* Martin C. Cherrier, Peter J. Webb, Young-Jun Shin, Tawfik Gharbaoui, Andrew Lindstrom, Vu Hong, Susan Y. Tamura, Huong T. Dang, Cameron C. Pride, Ruoping Chen, Jeremy G. Richman, Daniel T. Connolly and Graeme Semple

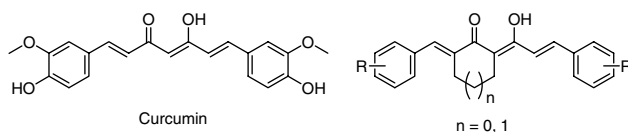


A series of 4-fluoro-5-functionalized pyrazole-3 carboxylic acids were shown to be potent, selective agonists of GPR109a. Improved free fatty acid reduction was observed when compared to niacin.

**Design, synthesis, and cytostatic activity of novel cyclic curcumin analogues**

pp 5624–5629

Dani Youssef, Christie E. Nichols, T. Stanley Cameron, Jan Balzarini, Erik De Clercq and Amitabh Jha*

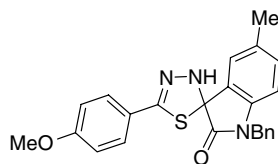


A number of curcumin analogues were prepared and evaluated for their cytostatic activity. Some of these analogues were found to have significant activity against three representative cancer cell lines.

5'-Phenyl-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazol]-2-one inhibitors of ADAMTS-5 (Aggrecanase-2)

pp 5630–5633

Matthew G. Bursavich,* Adam M. Gilbert, Sabrina Lombardi, Katy E. Georgiadis,
Erica Reifenberg, Carl R. Flannery and Elisabeth A. Morris

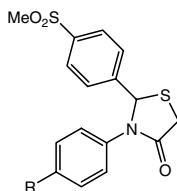


ADAMTS-5 IC₅₀: 0.64 μ M
 ADAMTS-4 IC₅₀ > 22 μ M
 MMP12 IC₅₀ > 100 μ M
 MMP13 IC₅₀ > 22 μ M

Synthesis of 2,3-diaryl-1,3-thiazolidine-4-one derivatives as selective cyclooxygenase (COX-2) inhibitors

pp 5634–5637

Afshin Zarghi,* Leila Najafnia, Bahram Daraee, Orkideh G. Dadrass and Mehdi Hedayati



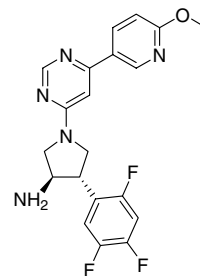
The design, synthesis, and evaluation of a series of 2,3-diaryl-1,3-thiazolidine-4-ones, possessing a methylsulfonyl pharmacophore, as potent and selective COX-2 inhibitors are described.

(3R,4S)-4-(2,4,5-Trifluorophenyl)-pyrrolidin-3-ylamine inhibitors of dipeptidyl peptidase IV: Synthesis, in vitro, in vivo, and X-ray crystallographic characterization

pp 5638–5642

Stephen W. Wright,* Mark J. Ammirati, Kim M. Andrews, Anne M. Brodeur,
Dennis E. Danley, Shawn D. Doran, Jay S. Lillquist, Shenping Liu, Lester D. McClure,
R. Kirk McPherson, Thanh V. Olson, Stephen J. Orena, Janice C. Parker,
Benjamin N. Rocke, Walter C. Soeller, Carolyn B. Soglia, Judith L. Treadway,
Maria A. VanVolkenburg, Zhengrong Zhao and Eric D. Cox

Potency, selectivity, and pharmacokinetic properties of DPP-IV inhibitors developed from a HTS hit were optimized resulting in the identification of a pre-clinical candidate for further profiling.

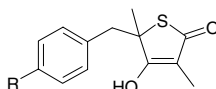


(+)-15b IC₅₀ = 7 nM

**Synthesis and biological evaluation of a C5-biphenyl thiolactomycin library**

pp 5643–5646

Veemal Bhowruth, Alistair K. Brown, Suzanne J. Senior, John S. Snaith and Gurdial S. Besra*

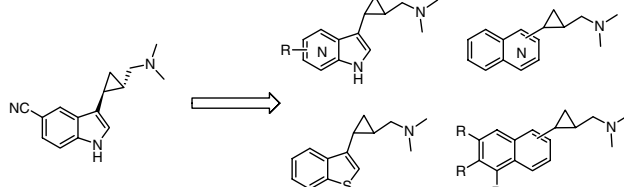


Fifteen novel C5 analogues of thiolactomycin have been synthesised and assessed for their in vitro *mtFabH* and in vivo *Mycobacterium bovis* BCG activity, respectively. The biological analysis of this library reaffirms the requirement for a linear π -rich system containing hydrogen bond accepting substituents attached to the *para*-position of the C5 biphenyl analogue to generate compounds with enhanced activity.

Conformationally restricted homotryptamines. Part 4: Heterocyclic and naphthyl analogs of a potent selective serotonin reuptake inhibitor

pp 5647–5651

H. Dalton King,* Derek J. Denhart, Jeffrey A. Deskus, Jonathan L. Ditta, James R. Epperson, Mendi A. Higgins, Joyce E. Kung, Lawrence R. Marcin, Charles P. Sloan, Gail K. Mattson, Thaddeus F. Molski, Rudolph G. Krause, Robert L. Bertekap, Jr., Nicholas J. Lodge, Ronald J. Mattson and John E. Macor

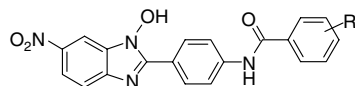


Hybrid molecules containing the cyclopropylmethylamino side chain found in the parent homotryptamine system and an isosteric heteroaryl or naphthyl core were prepared and their binding affinities for the human serotonin transporter determined.

Novel anti-infection agents: Small-molecule inhibitors of bacterial transcription factors

pp 5652–5655

Todd E. Bowser,* Victoria J. Bartlett, Mark C. Grier, Atul K. Verma, Taduesz Warchol, Stuart B. Levy and Michael N. Alekshun



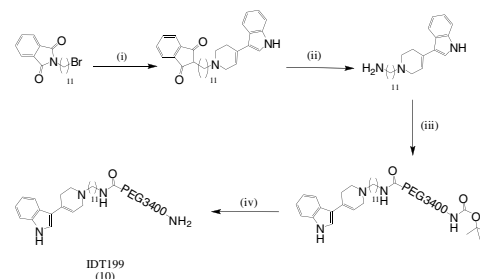
Inhibitors of AraC bacterial transcription factors are shown to limit infections by reducing virulence rather than halting growth of the organisms. This therapeutic approach is intended to prevent infection and minimize the development of bacterial resistance.

Synthesis and characterization of a pegylated derivative of 3-(1,2,3,6-tetrahydro-pyridin-4yl)-1H-indole (IDT199): A high affinity SERT ligand for conjugation to quantum dots

pp 5656–5660

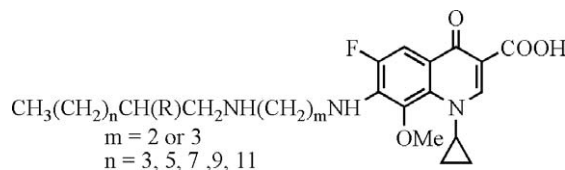
Ian D. Tomlinson, Michael R. Warnerment, John N. Mason, Matthew J. Vergne, David M. Hercules, Randy D. Blakely and Sandra J. Rosenthal*

(i) 3-(1,2,3,6-Tetrahydro-pyridin-4yl)-1H-indole, cesium carbonate, 37.5%; (ii) hydrazine monohydrate, 34.6%; (iii) Boc-NH-PEG-NHS-3400, 100%; (iv) TFA, 100%.

**Synthesis and antitubercular activity of lipophilic moxifloxacin and gatifloxacin derivatives**

pp 5661–5664

Mauro V. de Almeida,* Maurício F. Saraiva, Marcus V. N. de Souza, Cristiane F. da Costa, Felipe R. C. Vicente and Maria C. S. Lourenço



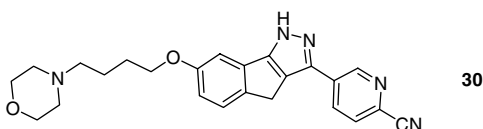
Twelve lipophilic moxifloxacin or gatifloxacin new derivatives were synthesized, seven of them having MIC < 1.25 µg/mL.



Cyanopyridyl containing 1,4-dihydroindeno[1,2-c]pyrazoles as potent checkpoint kinase 1 inhibitors: Improving oral bioavailability

pp 5665–5670

Yunsong Tong,* Magdalena Przytulinska, Zhi-Fu Tao, Jennifer Bouska, Kent D. Stewart, Chang Park, Gaoquan Li, Akiyo Claiborne, Peter Kovar, Zehan Chen, Philip J. Merta, Mai-Ha Bui, Amanda Olson, Donald Osterling, Haiying Zhang, Hing L. Sham, Saul H. Rosenberg, Thomas J. Sowin and Nan-horng Lin

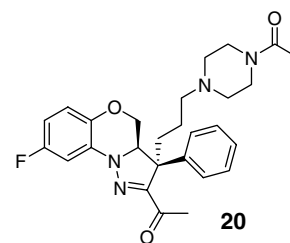


SAR studies leading to potent CHK-1 inhibitors with much improved oral bioavailability are reported.

Kinesin spindle protein (KSP) inhibitors. Part 7: Design and synthesis of 3,3-disubstituted dihydropyrazolobenzoxazines as potent inhibitors of the mitotic kinesin KSP

pp 5671–5676

Robert M. Garbaccio,* Edward S. Tasber, Lou Anne Neilson, Paul J. Coleman, Mark E. Fraley, Christy Olson, Jeff Bergman, Maricel Torrent, Carolyn A. Buser, Keith Rickert, Eileen S. Walsh, Kelly Hamilton, Robert B. Lobell, Weikang Tao, Vicki J. South, Ronald E. Diehl, Joseph P. Davide, Youwei Yan, Lawrence C. Kuo, Chunze Li, Thomayant Prueksaritanont, Carmen Fernandez-Metzler, Elizabeth A. Mahan, Donald E. Slaughter, Joseph J. Salata, Nancy E. Kohl, Hans E. Huber and George D. Hartman



Dihydropyrazolobenzoxazines (i.e., **20**) are reported as potent inhibitors of the mitotic kinesin KSP.

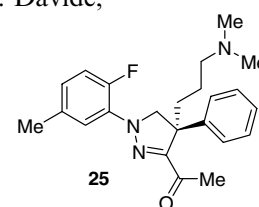
KSP IC₅₀ = 1.6 nM
Cell EC₅₀ = 5.0 nM


Kinesin spindle protein (KSP) inhibitors. Part 8: Design and synthesis of 1,4-diaryl-4,5-dihydropyrazoles as potent inhibitors of the mitotic kinesin KSP

pp 5677–5682

Anthony J. Roecker,* Paul J. Coleman, Swati P. Mercer, John D. Schreier, Carolyn A. Buser, Eileen S. Walsh, Kelly Hamilton, Robert B. Lobell, Weikang Tao, Ronald E. Diehl, Vicki J. South, Joseph P. Davide, Nancy E. Kohl, Youwei Yan, Lawrence C. Kuo, Chunze Li, Carmen Fernandez-Metzler, Elizabeth A. Mahan, Thomayant Prueksaritanont and George D. Hartman

1,4-Diaryl-4,5-dihydropyrazoles (i.e., **25**) are reported as potent inhibitors of the mitotic kinesin KSP.

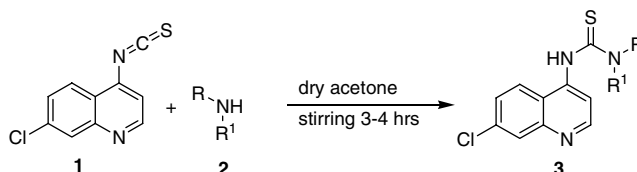


KSP IC₅₀ (nM) = 0.2 nM
Cell EC₅₀ (nM) = 3.2 nM

Synthesis of new 7-chloroquinolinyl thioureas and their biological investigation as potential antimalarial and anticancer agents

pp 5683–5685

Aman Mahajan, Susan Yeh, Margo Nell, Constance E. J. van Rensburg and Kelly Chibale*

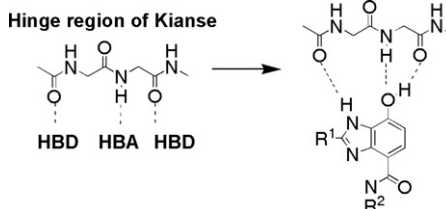


Novel 7-chloroquinolinyl thiourea derivatives derived from the corresponding 4,7-dichloroquinoline isothiocyanate were synthesized and evaluated for in vitro antimalarial and anticancer activity. The most active compound from the series displayed an inhibitory IC₅₀ value of 1.2 μM against the D10 strain of *Plasmodium falciparum*.

Design and synthesis of 7-hydroxy-1*H*-benzimidazole derivatives as novel inhibitors of glycogen synthase kinase-3 β

pp 5686–5689

Dongkyu Shin, Seung-Chul Lee, Yong-Seok Heo, Woon-Young Lee, Yong-Soon Cho, Yong Eun Kim, Young-Lan Hyun, Joong Myung Cho, Yoon Sup Lee and Seonggu Ro*

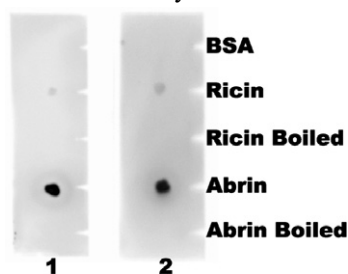


We have designed new kinase inhibitors by considering the hydrogen bond network in the hinge region and confirmed through the enzymatic assay and X-ray crystallography.

Selection and characterization of human monoclonal antibodies against Abrin by phage display

pp 5690–5692

Heyue Zhou, Bin Zhou, Hongzheng Ma, Charlotte Carney and Kim D. Janda*

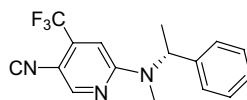


Human antibodies were selected from a phage display library that bind the potential biological warfare agent Abrin. The utility of these antibodies is envisaged as detection devices or therapeutics.

Synthesis and biological evaluation of amino-pyridines as androgen receptor antagonists for stimulating hair growth and reducing sebum production

pp 5693–5697

Lain-Yen Hu,* Huangshu John Lei, Daniel Du, Theodore R. Johnson, Victor Fedij, Catherine Kostlan, Wen Song Yue, Mark Lovdahl, Jie Jack Li, Mathew Carroll, Danielle Dettling, Jeffrey Asbill, Conglin Fan, Kimberly Wade, David Pocalyko, Kimberly Lapham, Radhika Yalamanchili, Brian Samas, Derek Vrieze, Susan Ciotti, Teresa Krieger-Burke, Drago Sliskovic and Howard Welgus

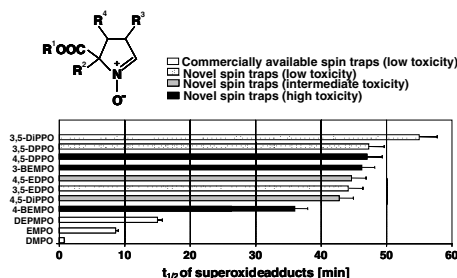


A series of amino-pyridines were synthesized and evaluated for androgen antagonist activities. Among these compounds, (*R*)-(+)-6-[methyl-(1-phenyl-ethyl)-amino]-4-trifluoromethyl-nicotinonitrile was the most active example of this class.

Cytotoxicity of the novel spin trapping compound 5-ethoxycarbonyl-3,5-dimethyl-pyrroline *N*-oxide (3,5-EDPO) and its derivatives

pp 5698–5703

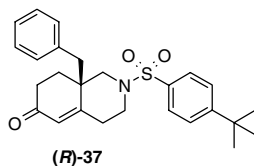
Nataliya Rohr-Udilova,* Klaus Stolze, Sandra Sagmeister, Wolfram Parzefall, Brigitte Marian, Hans Nohl, Rolf Schulte-Hermann and Bettina Grasl-Kraupp



2-Benzenesulfonyl-8a-benzyl-hexahydro-2H-isoquinolin-6-ones as selective glucocorticoid receptor antagonists

pp 5704–5708

Robin D. Clark,* Nicholas C. Ray, Paul Blaney, Peter H. Crackett, Christopher Hurley, Karen Williams, Hazel J. Dyke, David E. Clark, Peter M. Lockey, Rene Devos, Melanie Wong, Anne White and Joseph K. Belanoff

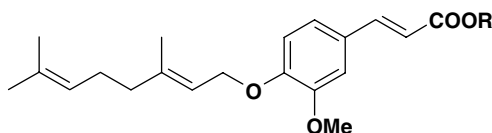


The synthesis and glucocorticoid receptor (GR) binding and functional antagonist activity of a series of substituted 2-azadecalins is reported. (*R*)-**37** was found to be a selective high GR affinity ligand (4 nM) with moderate functional activity (200 nM) in a GR reporter gene assay.

Synthesis and anti-inflammatory activity of 3-(4'-geranyloxy-3'-methoxyphenyl)-2-trans propenoic acid and its ester derivatives

pp 5709–5714

Francesco Epifano,* Salvatore Genovese, Silvio Sosa, Aurelia Tubaro and Massimo Curini

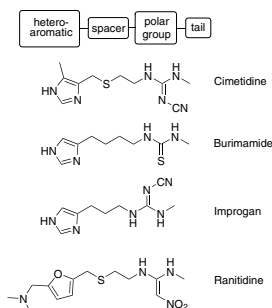


The synthesis of ester derivatives of the title acid and their anti-inflammatory activity are reported.

**Antinociceptive activity of furan-containing congeners of improgan and ranitidine**

pp 5715–5719

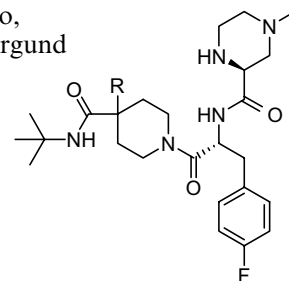
L. B. Hough,* W. M. P. B. Menge, A. C. van de Stolpe, J. W. Nalwalk, R. Leurs and I. J. P. de Esch

**Melanocortin subtype 4 receptor agonists: Structure–activity relationships about the 4-alkyl piperidine core**

pp 5720–5723


Iyassu K. Sebat,* Yingjie Lai, Khaled Barakat, Zhixiong Ye, Rui Tang, Rubana N. Kalyani, Aurawan Vongs, Tanya MacNeil, David H. Weinberg, M. Angeles Cabello, Marta Maroto, Ana Teran, Tung M. Fong, Lex H. T. Van der Ploeg, Arthur A. Patchett and Ravi P. Nargund

SAR about the piperidine core in a series of MC4R agonists is described. A number of alkyl substituents that furnish compounds with good affinity and functional potency are reported.



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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