

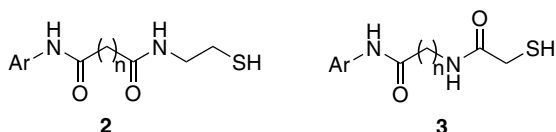
Contents

COMMUNICATIONS

Mercaptoamide-based non-hydroxamic acid type histone deacetylase inhibitors

pp 1969–1972

Sampath-Kumar Anandan,* John S. Ward, Richard D. Brokx, Mark R. Bray,
Dinesh V. Patel and Xiao-Xi Xiao

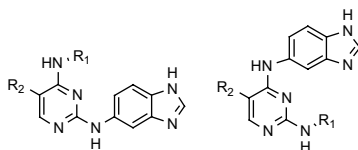


The synthesis and histone deacetylase (HDAC) inhibitory activity of mercaptoamides **2** and **3** is described.

Substituted aminobenzimidazole pyrimidines as cyclin-dependent kinase inhibitors

pp 1973–1977

Sharad Verma,* Dhanapalan Nagarathnam, Jianxing Shao, Lei Zhang, Jin Zhao, Yamin Wang,
Tindy Li, Eric Mull, Istvan Enyedy, Chunguang Wang, Qingming Zhu, Martha Altieri, Jerold Jordan,
Thu-Thi-Anh Dang and Sanjeeva Reddy



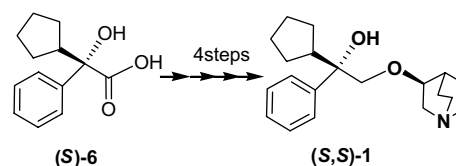
Substituted aminobenzimidazole pyrimidines were synthesized and are shown to display potent biochemical activity against CDK1. Docking studies carried out with a CDK1 homology model provides a rationale for the observed activities.

Synthesis of the optical isomers of a new anticholinergic drug, penheyclidine hydrochloride (**8018**)

pp 1979–1982

Xiang-Yu Han,* He Liu, Chun-He Liu, Bo Wu, Lan-Fu Chen, Bo-Hua Zhong
and Ke-Liang Liu

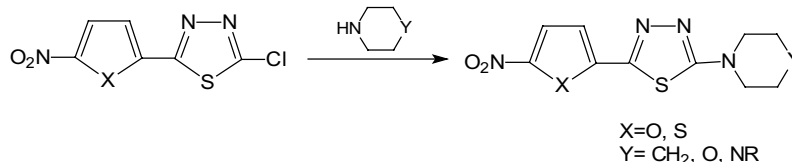
A practical diastereoselective synthesis of enantiopure isomers of **8018** is described. The intramolecular asymmetric epoxidation of mono-sulfonate **4** was applied for the execution of the synthesis of the key chiral building block for the first time. The isomers were obtained with 70–76% yields in 99–100% ee.



Synthesis and in vitro leishmanicidal activity of 2-(5-nitro-2-furyl) and 2-(5-nitro-2-thienyl)-5-substituted-1,3,4-thiadiazoles

pp 1983–1985

Alireza Foroumadi, Shirin Pournourmohammadi, Fatemeh Soltani, Mitra Asgharian-Rezaee, Shahriar Dabiri, Arsalan Kharazmi and Abbas Shafiee*



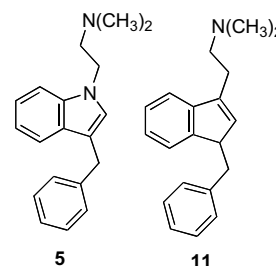
A series of 2-(5-nitro-2-furyl) and 2-(5-nitro-2-thienyl)-5-substituted-1,3,4-thiadiazoles were synthesized and tested against *Leishmania major* promastigotes. Most compounds were more active than the reference drug Pentostam.

Binding of isotryptamines and indenes at h5-HT₆ serotonin receptors

pp 1987–1991

Renata Kolanos, Uma Siripurapu, Manik Pullagurla, Mohamed Riaz, Vince Setola, Bryan L. Roth, Małgorzata Dukat and Richard A. Glennon*

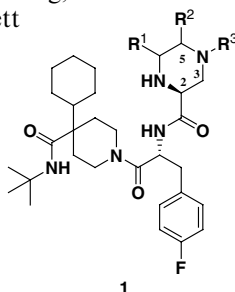
The binding of isotryptamines (e.g., **5**, $K_i = 32$ nM) and indenes (e.g., **11**, $K_i = 3$ nM) to h5-HT₆ serotonin receptors indicates that the presence of an indolic nitrogen atom is not a requirement for the binding of *N*₁-benzyltryptamines.



2-Piperazinecarboxamides as potent and selective melanocortin subtype-4 receptor agonists

pp 1993–1996

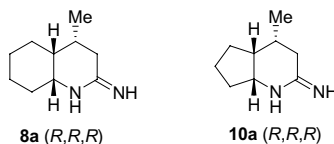
Brenda L. Palucki,* Min K. Park,* Ravi P. Nargund, Rui Tang, Tanya MacNeil, David H. Weinberg, Aurawan Vongs, Charles I. Rosenblum, George A. Doss, Randall R. Miller, Ralph A. Stearns, Qianping Peng, Constantin Tamvakopoulos, Lex H. T. Van der Ploeg and Arthur A. Patchett



Bicyclic amidine inhibitors of nitric oxide synthase: discovery of perhydro-iminopyrindine and perhydro-iminoquinoline as potent, orally active inhibitors of inducible nitric oxide synthase

pp 1997–2001

Ravindra N. Guthikonda, Shrenik K. Shah,* Stephen G. Pacholok, John L. Humes, Richard A. Mumford, Stephan K. Grant, Renee M. Chabin, Barbara G. Green, Nancy Tsou, Richard Ball, Daniel S. Fletcher, Silvi Luell, D. Euan MacIntyre and Malcolm MacCoss

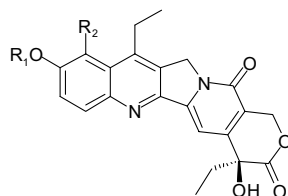


The synthesis and nitric oxide synthase inhibitory activity of bicyclic amidines are described. The 6,6 and 5,6 fused amidines **8a** and **10a** are potent, selective, and orally active iNOS inhibitors.

Synthesis and antitumor activity of 7-ethyl-9-alkyl derivatives of camptothecin

pp 2003–2006

Heyong Gao, Xiongwen Zhang, Yi Chen, Hongwu Shen, Jing Sun, Min Huang, Jian Ding,* Chuan Li and Wei Lu*

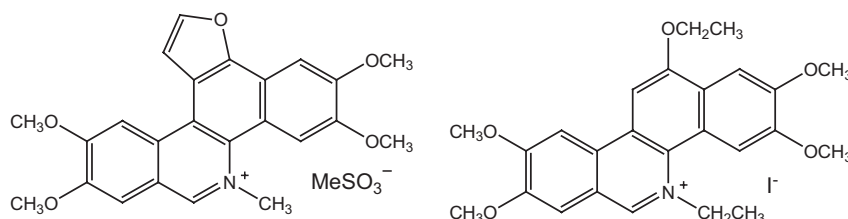


7-Ethyl-9-alkyl derivatives of camptothecin were synthesized and tested for antitumor activity in vitro and in vivo, and evaluated for the stability of lactone ring.

Antimalarial benzo[c]phenanthridines

pp 2007–2010

James M. Nyangulu, Samantha L. Hargreaves, Susan L. Sharples, Simon P. Mackay, Roger D. Waigh,* Olivier Duval, Eddie K. Mberu and William M. Watkins

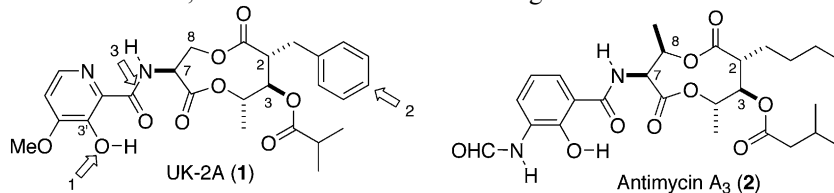


Analogues of the antimalarial alkaloid nitidine have been prepared with IC₅₀ in vitro in the low nanomolar range against chloroquine-resistant *Plasmodium falciparum*.

Semi-synthesis and biological evaluation of analogues of UK-2A, a novel antifungal antibiotic from *Streptomyces* sp. 517-02

pp 2011–2014

Yoshinosuke Usuki,* Koichi Mitomo, Noriko Adachi, Xu Ping, Ken-Ichi Fujita, Osamu Sakanaka, Katsuharu Inuma, Hideo Iio and Makoto Taniguchi*

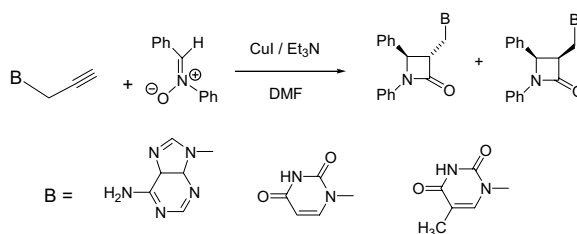


In vitro antifungal activities of several semi-synthesized analogues of UK-2A, a novel antifungal antibiotic isolated from *Streptomyces* sp. 517-02, against *Saccharomyces cerevisiae* IFO 0203 were evaluated by the conventional paper disk method. Several derivatives exhibited growth inhibitory activity similar to UK-2A.

Synthesis of β -lactam nucleoside chimera via Kinugasa reaction and evaluation of their antibacterial activity

pp 2015–2018

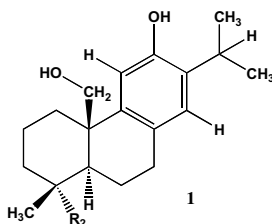
Amit Basak* and Runa Pal



Anti-tumor abietane diterpenes from the cones of *Sequoia sempervirens*

pp 2019–2021

Kwang-Hee Son, Hyun-Mi Oh, Sung-Kyu Choi, Dong Cho Han and Byoung-Mog Kwon*



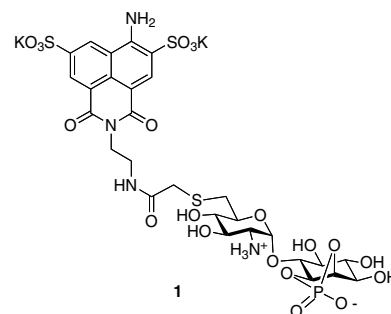
New 20-hydroxyferruginol (**1**) was isolated from the cones of *Sequoia sempervirens*. Their structures were elucidated by spectral data. Compound **1** strongly inhibited human tumor cells.

A fluorescent inositol phosphate glycan stimulates lipogenesis in rat adipocytes by extracellular activation alone

pp 2023–2025

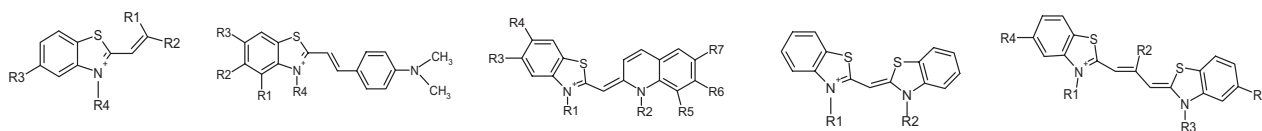
David I. Turner, Nilanjana Chakraborty and Marc d'Alarcao*

The fluorescent IPG analogue **1** was synthesized and found to stimulate lipogenesis in rat adipocytes. Since **1** does not enter the cells, this result demonstrates that stimulation of insulin-like effects by this IPG is an extracellular activity.

**Benzothiazolium compounds: novel classes of inhibitors that suppress the nitric oxide production in RAW264.7 cells stimulated by LPS/IFN γ**

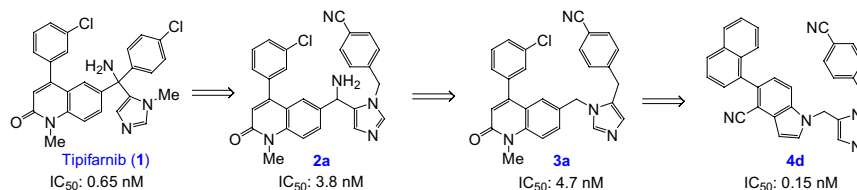
pp 2027–2032

Huan-Yi Tseng, Ssu-Hui Wu, Wen-Hsin Huang, Shao-Fang Wang, Yung-Ning Yang, Neeraj Mahindroo, Tsu Hsu, Weir-Torn Jiaang and Shiow-Ju Lee*

**Design, synthesis, and activity of achiral analogs of 2-quinolones and indoles as non-thiol farnesyltransferase inhibitors**

pp 2033–2039

Qun Li,* Keith W. Woods, Weibo Wang, Nan-Horng Lin, Akiyo Claiborne, Wen-zhen Gu, Jerry Cohen, Vincent S. Stoll, Charles Hutchins, David Frost, Saul H. Rosenberg and Hing L. Sham

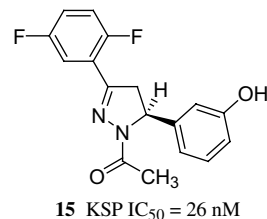


Kinesin spindle protein (KSP) inhibitors. Part 1: The discovery of 3,5-diaryl-4,5-dihydropyrazoles as potent and selective inhibitors of the mitotic kinesin KSP

pp 2041–2045

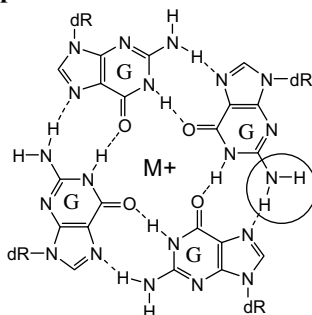
Christopher D. Cox,* Michael J. Breslin, Brenda J. Mariano, Paul J. Coleman, Carolyn A. Buser, Eileen S. Walsh, Kelly Hamilton, Hans E. Huber, Nancy E. Kohl, Maricel Torrent, Youwei Yan, Laurence C. Kuo and George D. Hartman

Optimization of high-throughput screening (HTS) hits resulted in the discovery of 3,5-diaryl-4,5-dihydropyrazoles as potent and selective inhibitors of KSP. Dihydropyrazole **15** is a potent, cell-active KSP inhibitor that induces apoptosis and generates aberrant mitotic spindles in human ovarian carcinoma cells at low nanomolar concentrations.

**Inosine substitutions demonstrate that intramolecular DNA quadruplexes adopt different conformations in the presence of sodium and potassium**

pp 2047–2050

Antonina Risitano and Keith R. Fox*

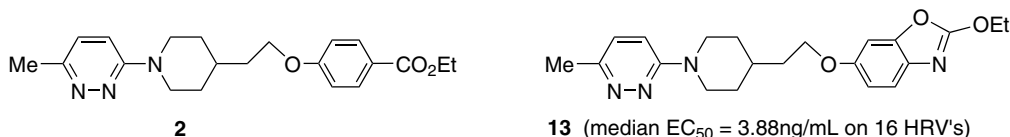


The relative stability of intramolecular quadruplexes containing inosine substitutions is different in sodium and potassium.

2-Ethoxybenzoxazole as a bioisosteric replacement of an ethyl benzoate group in a human rhinovirus (HRV) capsid binder

pp 2051–2055

Renee N. Brown, Rachel Cameron, David K. Chalmers, Stephanie Hamilton, Angela Luttick, Guy Y. Krippner, Darryl B. McConnell, Roland Nearn, Pauline C. Stanislawski, Simon P. Tucker and Keith G. Watson*

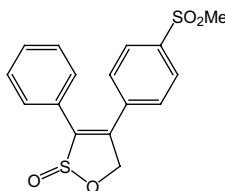


Synthesis and SAR studies of analogues of Pirodavir **2** involving replacement of the benzoate group with various benzo-azole rings led to the discovery of the 2-ethoxybenzoxazole capsid binder **13** as a highly active HRV inhibitor.

A general carbometalation, three component coupling strategy for the synthesis of α,β -unsaturated γ -sultines including thio-rofecoxib, a selective COX-2 inhibitor

pp 2057–2060

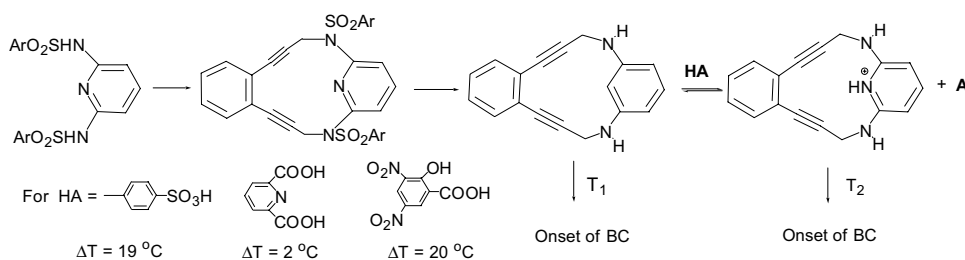
David V. Smil, Fabio E. S. Souza and Alex G. Fallis*



Dependence of reactivity of a novel 2,6-diamino pyridine-based enediyne on the extent of salt formation with external acids: a possible implication in pH based drug design

pp 2061–2064

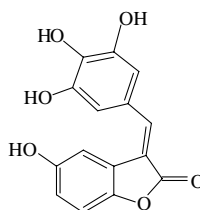
Amit Basak,* Moumita Kar and Subrata Mandal



Inhibitory activities against topoisomerase I and II by isoaurostatin derivatives and their structure–activity relationships

pp 2065–2068

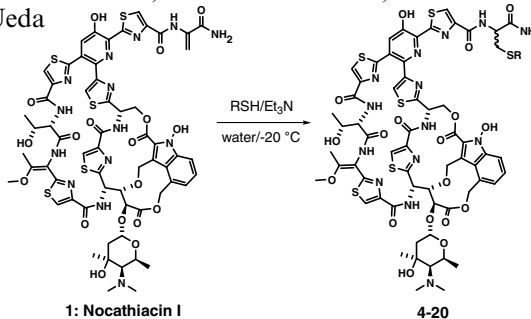
Keitarou Suzuki,* Tadashi Okawara, Tatuya Higashijima, Kazumi Yokomizo, Tohru Mizushima and Masami Otsuka



Synthesis, in vitro, and in vivo antibacterial activity of nocathiacin I thiol-Michael adducts

pp 2069–2072

B. Narasimhulu Naidu,* Margaret E. Sorenson, Joanne J. Bronson, Michael J. Pucci, Junius M. Clark and Yasutsugu Ueda

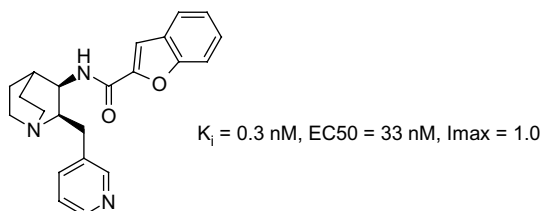


The synthesis and antibacterial activity of nocathiacin I analogues is described.

2-(Arylmethyl)-3-substituted quinuclidines as selective $\alpha 7$ nicotinic receptor ligands

pp 2073–2077

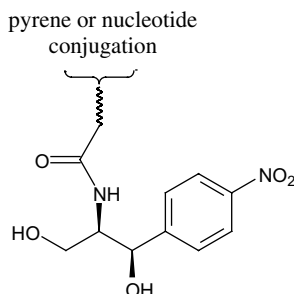
Anatoly Mazurov,* Jozef Klucik, Lan Miao, Teresa Y. Phillips, Angela Seamans, Jeffrey D. Schmitt, Terry A. Hauser, Raymond T. Johnson, Jr. and Craig Miller

A series of 2-(arylmethyl)-3-substituted quinuclidines was developed as $\alpha 7$ neuronal nicotinic acetylcholine receptor (nAChR) agonists based on a putative pharmacophore model.

Design, synthesis and ribosome binding of chloramphenicol nucleotide and intercalator conjugates

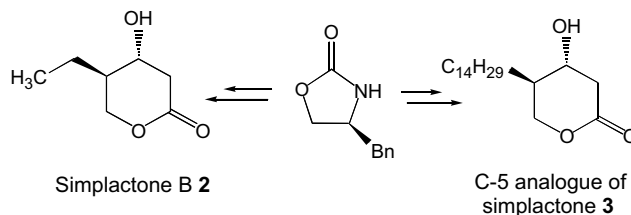
pp 2079–2083

Dorte Johansson, Carsten H. Jessen, Jacob Pøhlsgaard, Kenneth B. Jensen, Birte Vester, Erik B. Pedersen and Poul Nielsen*

**A short, stereoselective, and common approach for the synthesis of 4,5-disubstituted δ -lactones simplactone B and its C-5 analogue**

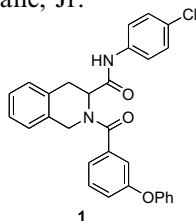
pp 2085–2086

A. Ravi Kumar, N. Sudhakar, B. Venkateswara Rao,* N. Raghunandan, A. Venkatesh and M. Sarangapani

**Discovery of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid diamides that increase CFTR mediated chloride transport**

pp 2087–2091

Bradford H. Hirth,* Shuang Qiao, Lisa M. Cuff, Brian M. Cochran, Marko J. Pregel, Jill S. Gregory, Scott F. Sneddon and John L. Kane, Jr.

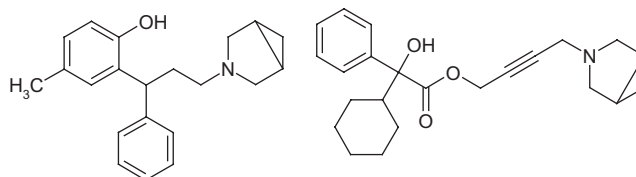


A series of compounds based on the 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid diamide core structure are reported as potent enhancers of CFTR mediated chloride transport.

Design, synthesis and activity of novel derivatives of Oxybutynin and Tolterodine

pp 2093–2096

Kirandeep Kaur,* Shelly Aeron, Miriyala Bruhaspathy, Shankar J. Shetty, Suman Gupta, Laxminarayan H. Hegde, Arun D. V. Silamkoti, Anita Mehta, Anita Chugh, Jang B. Gupta, P. K. S. Sarma and Naresh Kumar*



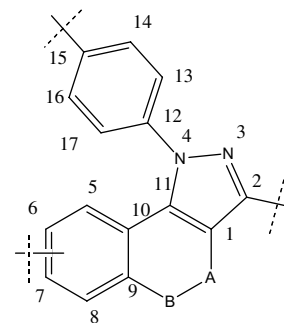
Novel analogues of Tolterodine and Oxybutynin are reported using 3-azabicyclo[3.1.0]hexane. The synthesis and SAR highlights our efforts to synthesize a bladder selective muscarinic receptor antagonist.

QSAR analyses of conformationally restricted 1,5-diaryl pyrazoles as selective COX-2 inhibitors: application of connection table representation of ligands

S. Prasanna,* E. Manivannan and S. C. Chaturvedi

pp 2097–2102

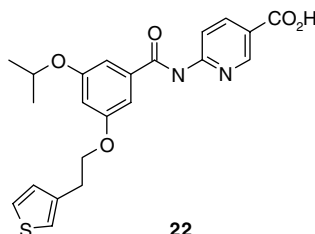
QSAR investigations using 2D, 3D molecular descriptors and Wang–Ford charges on conformationally restricted 1,5-diaryl pyrazoles as selective COX-2 inhibitors have been reported.



Discovery, synthesis and biological evaluation of novel glucokinase activators

pp 2103–2106

Darren McKerrecher,* Joanne V. Allen, Suzanne S. Bowker, Scott Boyd, Peter W. R. Caulkett, Gordon S. Currie, Christopher D. Davies, Mark L. Fenwick, Harold Gaskin, Emma Grange, Rod B. Hargreaves, Barry R. Hayter, Roger James, Keith M. Johnson, Craig Johnstone, Clifford D. Jones, Sarah Lackie, John W. Rayner and Rolf P. Walker

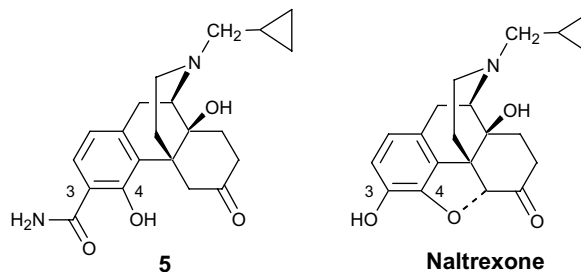


Synthesis and opioid receptor binding properties of a highly potent 4-hydroxy analogue of naltrexone

pp 2107–2110

Mark P. Wentland,* Qun Lu, Rongliang Lou, Yigong Bu, Brian I. Knapp and Jean M. Bidlack

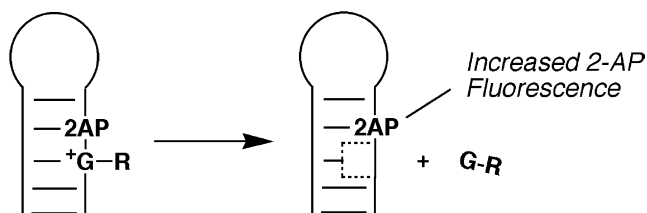
Novel analogue **5** of naltrexone displays very high affinity for opioid receptors with K_i values of 0.052 nM, 2.6 nM and 0.23 nM for μ , δ and κ , respectively.



A fluorimetric assay for the spontaneous release of an N7-alkylguanine residue from duplex DNA

pp 2111–2113

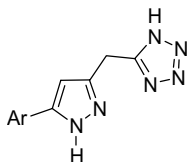
Ekaterina Shipova and Kent S. Gates*



A fluorimetric assay for monitoring depurination of the N7-alkylguanine adduct derived from the anticancer natural product leinamycin is described. This general approach could provide the foundation for a high throughput assay that detects DNA-alkylating agents or a convenient continuous fluorimetric assay for base excision repair enzymes.

Synthesis and in vivo antihyperglycemic activity of 5-(1*H*-pyrazol-3-yl)methyl-1*H*-tetrazoles pp 2115–2117

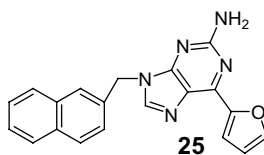
Ashoke Sharon, Ramendra Pratap, Priti Tiwari, Arvind Srivastava, P. R. Maulik and Vishnu Ji Ram*



Synthesis and in vivo antihyperglycemic activity of 5(1*H*-pyrazol-3-yl)methyl-1*H*-tetrazoles are reported.

6-(2-Furanyl)-9*H*-purin-2-amine derivatives as A_{2A} adenosine antagonists pp 2119–2122

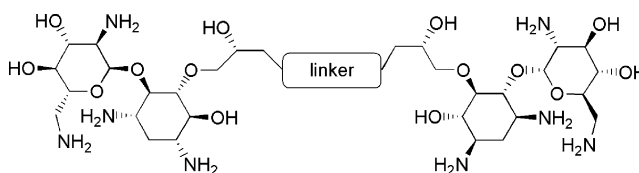
Eugenia Kiselgof, Deen B. Tulshian,* Leyla Arik, Hongtao Zhang and Ahmad Fawzi



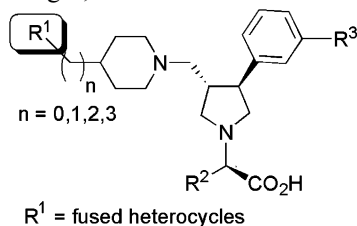
Structure–activity relationships has been investigated through substitutions at the 9-position of the 2-amino-6-(2-furanyl) purine (**5**) to identify novel and selective A_{2A} adenosine receptor antagonists. Several potent and selective antagonists were identified. In particular, compounds **20**, **25**, and **26** show very high affinity with excellent selectivity.

Structure–activity relationships of bivalent aminoglycosides and evaluation of their microbiological activities pp 2123–2128

Chang-Hsing Liang, Alex Romero, David Rabuka, Paulo W. M. Sgarbi, Kenneth A. Marby, Jonathan Duffield, Sulan Yao, Mayling L. Cheng, Yoshi Ichikawa, Pamela Sears, Changyong Hu, San-Bao Hwang, Youe-Kong Shue and Steven J. Sucheck*

**Potent 1,3,4-trisubstituted pyrrolidine CCR5 receptor antagonists: effects of fused heterocycles on antiviral activity and pharmacokinetic properties** pp 2129–2134

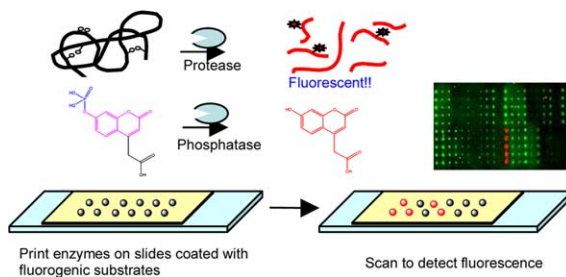
Dooseop Kim,* Liping Wang, Jeffrey J. Hale, Christopher L. Lynch, Richard J. Budhu, Malcolm MacCoss, Sander G. Mills, Lorraine Malkowitz, Sandra L. Gould, Julie A. DeMartino, Martin S. Springer, Daria Hazuda, Michael Miller, Joseph Kessler, Renee C. Hrin, Gwen Carver, Anthony Carella, Karen Henry, Janet Lineberger, William A. Schleif and Emilio A. Emini



Nanodroplet profiling of enzymatic activities in a microarray

pp 2135–2139

Mahesh Uttamchandani, Xuan Huang, Grace Y. J. Chen and Shao Q. Yao*

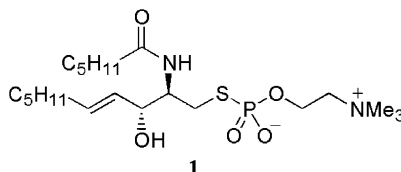


A generic method for applying microarrays in the large-scale functional characterization of enzymes is reported.

Synthesis of sphingomyelin sulfur analogue and its behavior toward sphingomyelinase

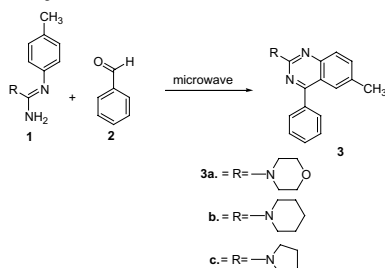
pp 2141–2144

Toshikazu Hakogi, Shinobu Fujii, Michio Morita, Kiyoshi Ikeda and Shigeo Katsumura*

**Quinazolines revisited: search for novel anxiolytic and GABAergic agents**

pp 2145–2148

R. K. Goel,* Vipin Kumar and M. P. Mahajan*

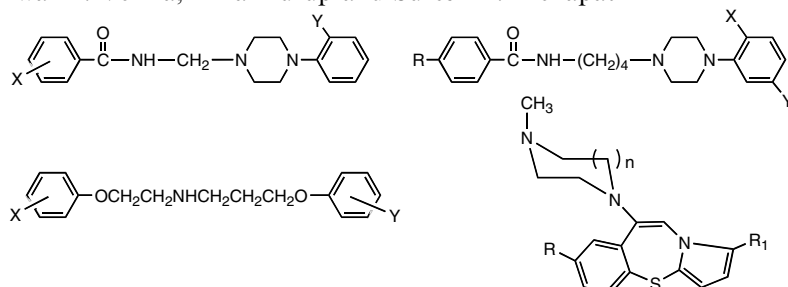


A systematic approach through computer assisted design to identify, synthesize and evaluate novel quinazolines having anxiolytic and GABAergic activities is reported.

The role of QSAR in dopamine interactions

pp 2149–2157

Corwin Hansch,* Rajeshwar P. Verma, Alka Kurup and Suresh B. Mekapati

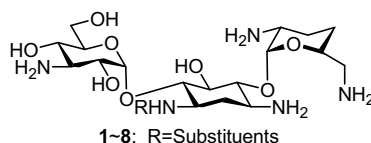


Quantitative structure–activity relationships have been performed for different sets of compounds with respect to their activities toward dopamine receptors.

A proof of the specificity of kanamycin-ribosomal RNA interaction with designed synthetic analogs and the antibacterial activity

pp 2159–2162

Yoshio Nishimura,* Hayamitsu Adachi, Motoki Kyo, Shoichi Murakami, Seiko Hattori and Keiichi Ajito

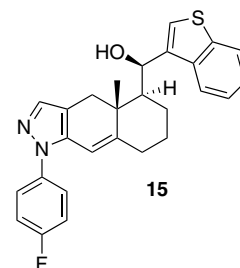


Surface plasmon resonance spectra show the nonspecific and multiple interactions of antimicrobial active analogs of kanamycin (1–8) with A-site of 16S rRNA.

Novel heterocyclic glucocorticoids: in vitro profile and in vivo efficacy

pp 2163–2167

Christopher F. Thompson,* Nazia Quraishi, Amjad Ali, James R. Tata, Milton L. Hammond, James M. Balkovec, Monica Einstein, Lan Ge, Georgianna Harris, Theresa M. Kelly, Paul Mazur, Shilpa Pandit, Joseph Santoro, Ayesha Sitlani, Chuanlin Wang, Joanne Williamson, Douglas K. Miller, Ting-ting D. Yamin, Chris M. Thompson, Edward A. O'Neill, Dennis Zaller, Michael J. Forrest, Ester Carballo-Jane and Silvi Luell

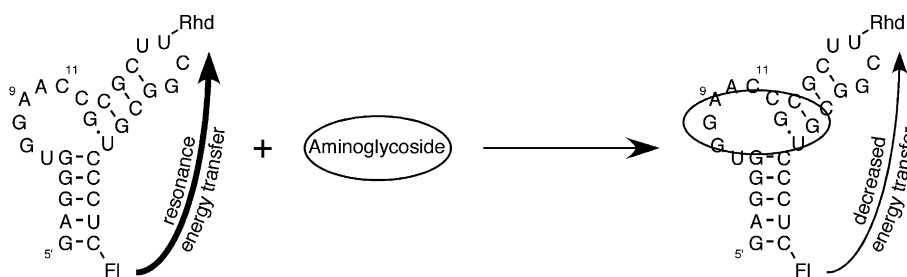


Compound **15** displayed the profile of a dissociated glucocorticoid in vitro and reduced inflammation in a mouse.

Fluorescence resonance energy transfer studies of aminoglycoside binding to a T box antiterminator RNA

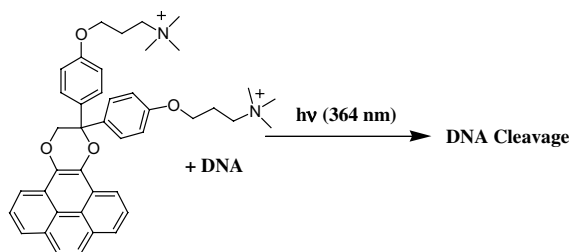
pp 2169–2172

John A. Means and Jennifer V. Hines*

**DNA photocleavage and biological activity of a pyrene dihydrodioxin**

pp 2173–2176

Eric T. Mack, Dagne Birzniece, Darren R. Veatch, William Coyle and R. Marshall Wilson*



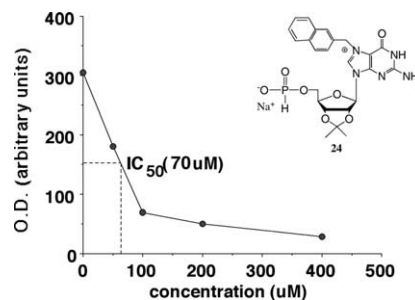
The title compound has been shown to cleave the ϕ X 174 supercoiled plasmid upon photochemical irradiation. It also exhibits cytotoxic activity at the micromolar range in a number of human cancer cell lines.

Synthesis and evaluation of potential inhibitors of eIF4E cap binding to 7-methyl GTP

pp 2177–2180

Phalguni Ghosh, Chunkyung Park, Mark S. Peterson, Peter B. Bitterman,
Vitaly A. Polunovsky and Carston R. Wagner*

A new assay for direct binding to cap-binding protein eIF4E was developed and used to screen a small library of 7-methyl guanosine nucleoside and nucleotide analogs. 5'-*H*-Phosphonate derivatives in which the 2'- and 3'-ribose hydroxyls were tethered together were shown to be a new class of inhibitors of eIF4E.

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*Corresponding author

①⁺ Supplementary data available via ScienceDirect**COVER**

Overlay of the X-ray crystal structures of a 10 mM inhibitor (pink) and a 450 nM inhibitor (yellow) bound to an allosteric site of kinesin spindle protein (KSP). The more efficient use of a hydrophobic pocket helps explain the increased potency of the latter. [Cox, C. D.; Breslin, M. J.; Mariano, B. J.; Coleman, P. J.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Huber, H. E.; Kohl, N. E.; Torrent, M.; Yan, Y.; Kuo, L. C.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2005**, 15, 2041.]



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